Neurophysiology of Prospective Memory in Typical and Atypical Ageing

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A thesis submitted to the faculty of Nottingham Trent University in partial fulfilment for the degree of Doctor of Philosophy

This research programme was carried out in collaboration with the Knowledge Engineering Discovery Research Institute, Auckland University of Technology

June 2020

Copyright Statement

Abstract

The ability to delay an intention is known as 'prospective memory' (PM) and underpins many day-to-day activities. The ubiquity of PM makes it essential for independent living in older adults. Research suggests that PM function declines as we age and may be further exacerbated with the development of mild cognitive impairment (MCI). To date, there has been no research examining the neurophysiology of PM in older adults with MCI. This thesis addresses a series of questions to help understand the neurophysiology of PM and how it may be affected by ageing and MCI: 1) Are there neurophysiological differences between highly salient PM cues and less salient PM cues? 2) Can the neurophysiological reorientation of attention be identified in PM tasks? 3) Are there behavioural and neurophysiological differences between young adults, older adults and older adults with MCI during PM tasks? 4) Are there behavioural and neurophysiological differences when maintaining a PM intention between young adults, older adults and older adults with MCI? 5) Can machine learning be used to understand spatiotemporal patterns of brain activity in response to PM between young adults, older adults and older adults with MCI? To answer these questions behavioural and time-locked electroencephalographic (EEG) responses were examined during PM tasks and were modelled with a machine learning method known as Spiking Neural Networks (SNN). Results suggest that: there are behavioural and neurophysiological differences between the PM cues and the neurophysiological reorientation of attention can be detected in PM tasks; older adults are not impaired in PM tasks possibly due to compensatory neural mechanisms; older adults with MCI may be impaired in some PM tasks, which may be due to deficits in attention and feelings of knowing; modelling PM with SNNs may offer useful ways of understanding spatiotemporal connectivity in PM and MCI.

Declaration

This thesis comprises the candidate's own work and has not been submitted to this or any other University for a degree. All aspects of the thesis were completed by the candidate.

Publications/conference proceedings

Crook-Rumsey, M., Howard, C. J., Hadjiefthyvoulou, F. & Sumich, A. (2020). *Neurophysiology markers of prospective- and working-memory in typical ageing and MCI.* Submitted for publication to the Journal of Clinical Neurophysiology, under 3rd review.

Crook-Rumsey, M. (2020). *Spatiotemporal dynamics of prospective memory in typical and atypical ageing.* Symposium at the Affect, Personality and Embodied Brain Conference, Universidade Catlica Portuguesa and Nottingham Trent University, Internationally online.

Crook-Rumsey, M., Howard, C. J., Sumich, A. (2018). *Neural Correlates of Prospective Memory in Older Adults with Mild Cognitive Impairment.* 34th Annual PsyPag Conference, Huddersfield.

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List of Abbreviations

ACC	-	Anterior cingulate cortex
AD	-	Alzheimer's disease
AI	-	Artificial intelligence
AN	-	Artificial neuron
ANN	-	Artificial neural network
aPFC	-	Anterior prefrontal cortex
ApoE4	-	Apolipoprotein E allele 4
AtoDI	-	Attention to delayed intentions theory
AtoM	-	Attention to Memory model
BA	-	Brodmann area
CRUNCH	-	Compensation-related utilisation of neural circuits hypothesis
DMN	-	Default mode network
DSI	-	Diffusion spectrum imaging
DTI	-	Diffusion tensor imaging
EEG	-	Electroencephalograph
ERP	-	Event-related potential
eSTDM	-	Evolving spatiotemporal data machine
EW	-	Edge weight
fMRI	-	Functional Magnetic Resonance Imaging
fNIRS	-	Functional near-infrared spectroscopy
HAROLD	-	Hemispheric Asymmetry Reduction in Older Adults hypothesis
HVLT-R	-	Hopkins verbal learning test-revised
ICA	-	Independent components analysis
IRR	-	Intention retrieval response (formerly the "old-new effect")
iTBS	-	Intermittent theta burst stimulation
LIFM	-	Leaky integrated-and-fire model
MEG	-	Magnetoencephalography
ML	-	Machine learning

MLP	-	Multilayer perceptron
MLR	-	Multiple linear regression
MMSE	-	Mini-mental state examination
MTL	-	Medial Temporal Lobe
NN	-	Neural network
PASA	-	Posterior-to-anterior shift in ageing
PCA	-	Principle components analysis
PCC	-	Posterior cingulate cortex
PET	-	Positron emission tomography
PFC	-	Prefrontal Cortex
PLS	-	Partial least squares
PM	-	Prospective Memory
PSP	-	Postsynaptic potential
RHAM	-	Right hemi-ageing model hypothesis
RON	-	Reorientation negativity
SCD	-	Scalp Density Analysis
SNN	-	Spiking neural network
STBD	-	Spatiotemporal brain data
STDP	-	Spike-time-dependent-plasticity
SVM	-	Support vector machine
SW	-	Small-world
tDCS	-	Transcranial direct stimulation
TMS	-	Transcranial magnetic stimulation
VBM	-	Voxel-based morphometry

Acknowledgements

To my Director of Studies, Dr Alex Sumich – Thank you for the years of support and guidance you have given me. I am sincerely grateful for all your encouragement, patience and the opportunities you have given me. Without you, this work would not have been possible.

To my supervisor, Dr Christina Howard – Thank you for your insightful thoughts, your keen eye for detail and for always grounding me when I was stressed.

To my supervisor, Professor Nikola Kasabov and my colleagues at KEDRI, in particular, Maryam and Zohreh Doborojeh and Josafath Israel Espinosa Ramos – Thank you for always finding the time to answer my technical questions and making my time at KEDRI truly enjoyable.

To my partner Danielle Liptrot – Thank you for always being by my side, making me laugh and waking me up with coffee. Words cannot express how grateful I am for the love and support you have given me over the past few years.

To my parents, Anthony and Kathleen Crook-Rumsey – Thank you for your lifelong support and always encouraging me to "try my best". Thank you for the sacrifices you have made that have afforded me the opportunities I have had.

To my friends and colleagues at Nottingham Trent University, in particular, Mark Andrews, Jammy Stacey, Sarah Gardner and Joshua Baker – Thank you for your always answering my questions and taking the time to teach me the skills I needed.

To the Bluck and Sumich families in New Zealand – Thank you for opening your homes to strangers from the other side of the world and making us feel a part of your family.

To all my older adult participants – Thank you for volunteering your time, persevering through my experiments and for making data collection truly enjoyable.

Chapter One: Introduction

1.1 What is prospective memory?

Prospective memory (PM) is the ability to remember to perform an intention at the appropriate time in the future (Einstein & McDaniel, 1990; Meacham & Leiman, 1982), or "remembering to remember" (Harris, 1984). For example, imagine you are preparing to leave work and return home. You are finalising an email and saying goodbye to a colleague before catching a train home. Just as you are about to board the train, you remember that you ran out of dog food this morning and need to buy more. You quickly purchase some dog food from a nearby store before catching the train home.

In this example, an action was required but was unable to be completed when the intention was formed. Before carrying out the intention, other activities had to first be completed which prevented performance of the intention. Then, at the right moment, the intention had to be recalled and performed. In this example, you remembered to buy dog food. However, if you did not remember to buy the dog food, you might have only remembered the intention once you returned home and saw your dog.

Our day-to-day lives and those of others are often dependent on our ability to successfully perform PM tasks. Remembering to give your colleague an important document before you leave work; remember to feed the dog; calling your mother; and remembering to wish your friend a happy birthday. The ubiquity of these actions provides a small example of the importance of PM capacity for normal functioning (McDaniel & Einstein, 2007), which remains true throughout a person's lifetime (Hering, Kliegel, Rendell, et al., 2018; Kliegel, 2008). These examples are relatively simple actions, but failures to perform these intentions are common and may have social consequences (Dismukes, 2008). Indeed, some estimates suggest that 50–80% of all memory failures are, in part, failures of PM (Kliegel & Martin, 2003).

In professions where individuals are responsible for the well-being and safety of others, even minor failures of PM can have a significant or life-altering impact on someone's life. Pilots, for example, must remember to perform a multitude of actions

before take-off and landing and a single missed step may result in fatal outcomes. Self-reported evidence from pilot errors found that, of the 75 errors reported, 74 involved failures that were prospective in nature (Nowinski et al., 2003). Moreover, a reported one-fifth of all major flight accidents were due to failures of PM (Dismukes, 2006). The now infamous example of the 1991 Los Angeles air traffic controller provides a very vivid example of a catastrophic failure of PM. Whilst performing her regular duties of directing multiple aeroplanes for take-off, clearance, and landing, the controller becomes distracted by poor visibility, inadvertent delays and problems with radio transmissions. In the commotion, the controller had forgotten to clear a waiting aeroplane on the runway. The controller then cleared an arriving aeroplane for the same runway. This small lapse in memory caused the arriving plane to crash into the holding plane, resulting in the death of 35 people (National Transportation Safety Board, 1991).

Failures of PM are pervasive and unavoidable, but there are a host of reasons that may increase and exacerbate such failures. In a study evaluating factors enhancing or inhibiting anaesthesiologists' PM performance in a patient simulator, the anaesthesiologists were distracted while completing their routine tasks. Only 3 of the 12 participants that were distracted remembered to perform the 'critical task' to cross-check the patient's blood (Grundgeiger et al., 2008) during the blood transfusion simulation. It is for this reason that the understanding of PM and factors affecting it are important for the safety of individuals and others.

Impairments in PM may be exacerbated by lifestyle choices. Studies explore the long-term effects of ecstasy/polydrug use (Hadjiefthyvoulou et al., 2011) and cannabis use (Platt et al., 2019) demonstrate significant impairment in PM tasks, which they were unaware of at a metacognitive level as evidenced through their subjective ratings of PM.

Some failures may be more prevalent due to psychiatric conditions. Studies employing measures that more closely represent the types of real-life situations of PM found that even when controlling for cognitive, executive function and retrospective memory, participants with schizophrenia were found to be significantly impaired in aspects of PM (Henry et al., 2007). This also seems to be similarly affected in individuals experiencing mood disorders such as depression (Altgassen et al., 2009; Zhou et al., 2017).

Finally, PM failures and impaired PM performance will eventually affect us all. That is, several authors report an age-related decline of PM performance in older adults (Cherry et al., 2001; Haynes et al., 2018; Maylor, 1996; Maylor & Logie, 2010; West & Covell, 2001; Zimmermann & Meier, 2006; Zöllig et al., 2007). Moreover, these age-related declines appear to accelerate when older adults experience mild cognitive impairment (MCI; Kinsella et al., 2018) and early dementia (Thompson et al., 2010). However, other studies have found no age-related PM performance declines (e.g., Aberle et al., 2010; Einstein et al., 1995; Einstein & McDaniel, 1990), with some older adults performing as well as, if not better than, their younger counterparts (Brom et al., 2014; Liu & Park, 2004; Rendell & Thomson, 1993, 1999).

The current thesis aims to provide further understanding of the effects of ageing and early cognitive decline on PM performance. In doing so, the current chapter will provide an initial overview of cognitive theories of PM relative to other domains such as executive function, episodic memory and attention. The chapter will then discuss PM and the other cognitive domains in relation to typical ageing and MCI.

1.2 Cognitive Theories of PM: Competing models

The term PM does not represent a unitary, discrete memory system (Cruz San Martin, 2014; McDaniel & Einstein, 2007), rather it is umbrella term which incorporates several cognitive processes involved in retrieval and execution of an intention at a specific time in the future (Ellis & Freeman, 2008; Kvavilashvili & Ellis, 1996). There are two main competing models of PM that attempt to explain the relative importance of these processes and will be further described throughout the current chapter. These are: the Multiprocess Framework and The Preparatory Attention and Memory Process (PAM) theory.

On a crude level, successful PM performance requires two main — retrospective and prospective — cognitive processes. The retrospective component is concerned with "what" to do, that is, the ability to recall the intended previously encoded action. The prospective component represents the detection of "when" to perform the action (Einstein et al., 2005; R. E. Smith & Bayen, 2004). This rather reductive model fails

to account for the complex interaction of several cognitive mechanisms required for successful PM execution, which will be presently discussed.

Working memory, executive functions and attention are all to a greater or lesser degree recruited depending on the type of PM task being performed (McDaniel & Einstein, 2000). The involvement of these complex, (non-unitary) cognitive domains will be elucidated in subsequent sections of the current thesis. In brief, working memory refers to the cognitive systems important for maintaining information temporally accessible for processing (Miyaki & Shah, 1999). Executive function conceptualises the broad range of cognitive processes, including abstract reasoning, decision making, inhibitory control and planning (R. C. K. Chan et al., 2008; Diamond, 2013). Attention refers to the cognitive processes responsible for the applied focus of concentration on specific aspects of information (Eckert et al., 2009) and the support of other executive functions, such as problem solving or goal-directed behaviour (Diamond, 2013). The recruitment of processes underpinning these various cognitive domains often determines prospective remembering (J. Ellis, 1996).

The general consensus proposes that PM is conceptualised to consist of four distinct stages: intention formation, retention interval, intention retrieval and execution of the intention (Brandimonte et al., 1996; Ellis & Milne, 1996; Kliegel et al., 2008), as illustrated in Figure 1.1.

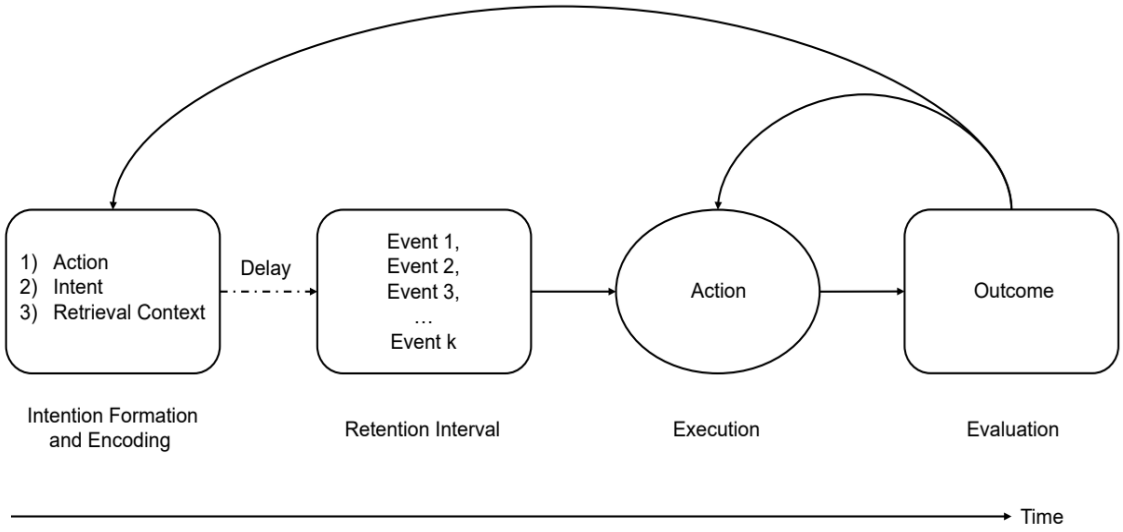

Figure 1.1. Overview of the different phase of the realisation of delayed intentions. Adapted with permission from Brandimonte et al., 1996.

1.2.1 Intention formation and encoding

The intention formation and encoding stage are related to the planning of future intentions (e.g., ”I will remember to buy dog food when I leave work”), planning skills (Kliegel, 2008) and memory encoding abilities (Addis et al., 2008; Poppenk et al., 2010). Various factors may influence the encoding of a PM intention such as the difficulty in achieving the intention (i.e., it requires the rescheduling of other intentions), self- or other-generation of the intention (i.e., intrinsic needs versus extrinsic needs), importance and pleasantness of the intention (Brandimonte et al., 2014).

1.2.2 Retention interval

The retention interval refers to the period between an encoded intention and the realisation that the intention must be retrieved (at the predefined moment in time). Typically, an individual is engaged in other activities which preclude the ability to actively maintain this intention in working memory (e.g., you must remember to buy dog food, but you are also navigating your environment to get to the train station). In experimental laboratory-based paradigms, this context is approximated by engaging the participant in an “ongoing task” (Ellis & Kvavilashvili, 2000).

According to Ellis and Kvavilashvili (2000), the PM intention is encoded in retrospective memory networks, and ‘not’ actively stored in working memory (Kliegel, Jäger, et al., 2008). In comparison, however, the PAM theory (Smith, Hunt, McVay & McConnell, 2007) and the Multiprocess Framework (McDaniel & Einstein, 2000) propose that attentional and working memory processes are required in the active maintenance of the intention (Smith & Bayen, 2004), and refer to this as “strategic monitoring” (McDaniel & Einstein, 2000). The Multiprocess Framework does also propose a solution between the encoding of intentions in retrospective memory and the maintenance of intentions in working memory (*see Section 1.4.1*).

1.2.3 Intention retrieval

The intention retrieval stage is crucial to successful PM. It is at this stage that an encoded intention is either recalled or forgotten (Brandimonte et al., 2014). The intention must be retrieved from memory and performed within a defined context. The context is dependent on the initial encoding of the intention but can vary depending on the PM intention. It is the different characteristics of these intentions that have given rise to three main types of PM tasks: event-based PM, activity-based PM and time-based PM (Brandimonte et al., 2014).

Event-based PM refers to remembering to perform an encoded action when a specific event occurs (e.g., remembering to call your mother when you arrive home). Activity-based PM refers to remembering to perform an encoded action after the completion of a preceding activity (e.g., cleaning the dishes after you have finished eating; McDaniel & Einstein, 2007). Time-based PM refers to remembering to perform an encoded action at a specific period during the day (e.g., remembering to take prescribed medication at 6pm).

As previously mentioned, the features of the PM task can make intention retrieval more or less cognitively demanding. Time-based PM is thought to require the greatest amount of cognitive processes due to the increased amount of self-initiation needed to perform the intended action. In the example of taking medication at a prescribed time, there is no explicit cue to trigger the action to be remembered. An individual could check a clock, however, the action is still dependent on self-initiated thoughts (Vanneste et al., 2016) and requires the ability to monitor time to discern the appropriateness of performing an intention (Harris & Wilkins, 1982). Therefore, if one relies entirely on remembering to perform the action without an external cue, a greater amount of cognitive processes would be required for the individual to remember to take their medication (Guynn, 2003). On the other hand, in event-based PM, an encoded PM cue will enable the retrieval of the intention relatively easily rather than via a self-generated process (Gilbert et al., 2009).

It is argued that both event- and time-based PM requires interruption to some ongoing activity and, therefore, must tax attention processes (Brandimonte et al., 2014). However, debates are ongoing within the literature as to whether event-based PM can truly occur spontaneously (Einstein et al., 2018; McDaniel & Einstein,

2007; Scullin, McDaniel, & Einstein, 2010) or whether attentional systems must still be involved to monitor for PM cues (Pereira et al., 2018; Smith, 2003; Smith et al., 2007, 2010; discussed further in *Section 1.4*).

1.2.4 Intention execution

The intention execution stage refers to the actual execution of the intended action according to the previously encoded plan and intention (Kliegel et al., 2002; Kliegel, Mackinlay, et al., 2008). The intention execution, particularly in experimental designs, requires the interruption of any ongoing task being performed. It is therefore likely that inhibition and executive function play an important role during this phase (Kliegel et al., 2002; Kliegel, Jäger, et al., 2008). Likely, the appearance of a PM cue triggers voluntary (top-down) and involuntary (bottom-up) attentional processes, that interact to execute the intention, and are followed by "reorientation" of attention back towards the ongoing task following the interruption (Escera et al., 2000; D. Friedman et al., 2001; Horváth et al., 2008).

1.2.5 Outcome evaluation

The outcome evaluation stage is concerned with the secondary phase of monitoring the output of the intention execution (Ellis, 1996). This outcome evaluation forms a record of a performed response to assist in the unnecessary repetition of an already successfully completed delayed intention or to ensure the future success of a postponed (or failed) PM intention (Ellis, 1996).

Outcome evaluation relies on executive processes, such as behavioural monitoring (Bettcher et al., 2011). Following the execution of a PM intention, the result of any executed action is compared with the internal representation of the planned action (Shallice & Burgess, 1996). If an execution is performed incorrectly, this evaluation process will then prompt a change in behaviour to redirect cognitive effort to complete the intention. Incorrect encoding of the intention will lead to a failure in prompting behavioural change (Bettcher & Giovannetti, 2009). The evaluation stage is directly related to the initial memory and planning capacity at encoding. Poor

encoding, for example, may underpin persistent errors in PM performance in some populations, such as people with schizophrenia (Henry et al., 2007).

1.3 Theories of Prospective Memory

At least two competing schools of thought exist in conceptualising PM functions. The PAM theory supposes that once an intention is encoded, it must be purposefully maintained and retrieved. The Multiprocess Framework, on the other hand, proposes that intention realisation can be spontaneously prompted by purely bottom-up processes facilitated by external cues within the environment. The question of whether PM relies on spontaneous retrieval or purposeful maintenance strategies remains unclear, as does whether these competing theories are mutually exclusive.

1.3.1 Multiprocess Framework

The Multiprocess Framework (Einstein et al., 2005, 2018; McDaniel & Einstein, 2000) is primarily derived from research using event-based PM (e.g., McDaniel et al., 2004; Scullin et al., 2013; Zuber et al., 2016). The theory proposes that intention retrieval can occur with or without preparatory attentional processes (Einstein et al., 2005). The Multiprocess Framework contends that due to the delays between intention formation and intention execution, the continued monitoring for PM stimuli would be too costly and cognitively consumptive. McDaniel and colleagues argue that such a cognitive strategy would not allow for effective day-to-day functioning as a result of the preoccupation of continued monitoring. Instead, this theory states that two different forms of PM can be engaged depending on the task at hand and the features of the PM task (i.e., stimulus saliency, intention association), demands of the underlying ongoing task, individual differences and planning. In one form, an individual could recall a PM intention strategically according to the attention-demand process of the PAM theory (discussed in the following section), but may also recall a PM intention when attention is deployed under certain stimulus-driven (bottom-up) circumstances.

Indeed, evidence showing an absence of 'cost' to the ongoing task would suggest PM can occur without monitoring for the PM target (Einstein et al., 2005; Marsh et al., 2003). However, this has only found to be the case for PM cues considered to be *focal*, perceptually distinct, or have strong cue-target association, alongside good planning. Within the PM literature, a *focal* cue refers to PM cues that possess certain characteristics that are shared with the ongoing task (e.g., responding to a particular word such as "butterfly", while performing a lexical decision task). A real-world example of this would be remembering to pass on information to your colleague when you encounter them at work (Harrison & Einstein, 2010). In this example, the ongoing activity would be you noticing your colleague and greeting them, then as these features are focal to your ongoing activity it prompts the PM intention.

Non-focal PM cues do not possess features central to the ongoing task (e.g., responding to an "animal category" while completing a lexical decision task; McDaniel & Einstein, 2007). A real-world example of this would be remembering to pay for membership at the front desk, whilst leaving a group exercise class. Navigating the environment and interacting with friends while leaving would be considered an ongoing task, which shares very few features with remembering to pay for the membership (i.e., whilst passing the front desk, non-focal cue). The Multiprocess Framework suggests that in conditions where the PM task is focal or distinct (e.g., responding to a PM word-cue presented in the colour red while performing a lexical decision task) then PM retrieval will be completed spontaneously.

1.3.2 Preparatory Attention and Memory Process Theory

The PAM theory suggests that PM retrieval can never be spontaneous and always requires a level of preparatory attention (Smith et al., 2007; Smith, 2008; Smith et al., 2010). As with the Multiprocess Framework, this theory is primarily founded on event-based PM studies (Smith et al., 2007; Smith & Bayen, 2005; West et al., 2005; West, 2007). The PAM theory proposes two processing types are required for successful PM performance (Smith, 2003; Smith & Bayen, 2004). First, cognitive processes are used for the maintenance of intention, whilst monitoring allows us to search the environment for the appropriate time to execute a PM intention. Second,

retrospective memory evaluates whether certain cues within the environment are likely to trigger a PM intention. For example, if one had the intention of taking medication with breakfast, then attention processes must first evaluate whether breakfast is being eaten or not. If the condition of eating breakfast is met, then one would evaluate whether eating breakfast was the cue for the intention to be executed. Once the intention is realised then these two processes will prepare and enable the execution of the intention of taking the medication.

Studies exploring the effect of PM intentions on the ongoing task have provided evidence in support of the PAM theory (Ellis & Milne, 1996; Smith, 2003; Smith et al., 2007; Smith & Bayen, 2004; Smith & Loft, 2014). Typically, researchers evaluate the performance and reaction time costs incurred in the ongoing task when monitoring for PM cues compared to when the ongoing task is performed alone. If ongoing task performance and reaction time are unaffected while maintaining a PM intention, then attentional processes are not required. However, if ongoing task performance and reaction time are affected, then some cognitive resources must be allocated for attending for possible PM cues (Smith & Bayen, 2004). Moreover, evidence indicates that altering the attentional demands of the ongoing task can also impact the performance of the PM task (Einstein et al., 1997), supporting the idea there are shared cognitive resources required for completing a PM task. However, PM monitoring costs are only consistently reported in experiments employing *nonfocal* PM designs (Loft & Remington, 2010; McDaniel & Einstein, 2011), suggesting that additional attentional resources are only recruited to monitor for cues that do not contain features central to the ongoing task.

Smith et al. (2007) set out to validate the Multiprocess theory of PM using two experiments of automatic retrieval of delayed intentions using a different stimuli conditions (i.e., salient cues, strong cue-target associated, focal cues). However, their results instead supported the PAM theory showing a significant cost to the ongoing task performance, even in response to PM cues thought to rely on automatic intention retrieval processes.

In recent years, the PAM model has since been extended to include a temporal proximity explanation. This account considers the relevance of task features to explain that preparatory processes may be used by individuals at flexible periods of time (Smith & Loft, 2014). Moreover, the Multiprocess theory has also received some

revisions to create the Dynamic Multiprocess Framework, which proposes that spontaneous retrieval and strategic monitoring can be employed within the same task, but may be used at different times (Scullin et al., 2013; Shelton & Scullin, 2017). Evidence has shown that in conditions where a PM cue was expected, monitoring was engaged, but in conditions where PM cues were not expected monitoring was disengaged.

In conclusion, the prominent theories of PM seem to be coming towards a convergence of ideas that PM may well use several different cognitive strategies for successful PM performance. It has been suggested that in instances where the delay between intention encoding and intention retrieval is long, then spontaneous retrieval is more likely to occur than if the retrieval is required more immediately (Scullin et al., 2013). It is for this reason that researchers are beginning to argue that PM may rely on an interplay between the top-down and bottom-up processes which are interconnected and dynamically interact to support PM functions (Shelton & Scullin, 2017).

Given the role of multiple cognitive domains required to successfully perform an PM intention, it is important to understand how ageing affects these cognitive domains before understanding age-related impairments in PM.

1.4 Ageing and Cognition

Cognitive decline as a function of age is well documented (Cabeza et al., 2002). Domains such as working and episodic memory may be particularly impaired (D. Friedman, 2000; Luo & Craik, 2008), whilst others remain spared (e.g., procedural, semantic and perceptual memory). As this thesis is primarily concerned with PM, this section will briefly describe the effect of ageing on key cognitive domains implicated in PM – memory, working memory, attention, executive function – before discussing age-related impairment in PM *per se.*

1.4.1 Memory

Episodic memory comprises two distinct components: retrospective memory and PM (Meacham & Singer, 1977), although the term episodic memory is generally used in reference to retrospective memory. Episodic memory is reportedly one of the cognitive domains most sensitive to the effects of ageing (Nilsson, 2003; Tulving, 2002). Even in relation to healthy ageing, the ability to retain episodic information declines in the elderly, relative to middle and young adulthood (Nilsson, 2003).

It is of little surprise then, that age-related impairments are well established within the retrospective memory literature (Balota et al., 2000). In particular, deficits are pronounced at the encoding and retrieval stages, whilst actual storage of the memory appears to be spared (Balota et al., 2000). While memory performance declines early in the course of ageing (Cansino, 2009), the capacity for cognitive compensation is spared through to an advanced age. For example, during intention retrieval, older adults can improve performance through item organisation (Bäckman & Wahlin, 1995), increased study time during encoding (Wahlin et al., 1995) and the use of cues during retrieval (Bäckman & Wahlin, 1995; Wahlin et al., 1995).

1.4.2 Working Memory

Working memory is a core neurocognitive ability that is required in most routine mental tasks (e.g., reading and arithmetic). Specifically, working memory refers to the ability to maintain and manipulate information over short periods of time (Baddeley, 2003). Working memory has been shown to support a wide range of complex cognitive functions, such as problem solving, reasoning, spatial thinking, language comprehension and fluid intelligence (Baddeley & Andrade, 2000; Conway et al., 2002; Engle et al., 1999). Ageing research has noted that working memory is a cognitive process that is particularly vulnerable to age-related declines (Bopp & Verhaeghen, 2005; Borella et al., 2008; Hale et al., 2011). Evidence suggests that age-related declines in working memory abilities occur linearly, such that performance decreases are found in young-old adults (i.e., 60–75 years old) but becomes further impaired in old-old adults (i.e., 75 years old and above; Gajewski et al., 2018; Hale et al., 2011).

Given that some theories of PM posit that working memory is an important feature of PM (PAM theory; Smith & Bayen, 2004) and others suggest that the ongoing working memory affects PM performance (Einstein et al., 1997), working memory may explain age-related PM performance differences.

1.4.3 Attention

Attention has been proposed as a vital component of memory processing (Cowan, 1988, 1993), and is dependent on a finite amount of cognitive resource that is exhausted with age, leading to cognitive decline (Craik & Byrd, 1982). Accordingly, deficits in attention can exacerbate memory impairments, and may increase as a function of task demands (Craik & Byrd, 1982). Even healthy older adults demonstrate decline in top-down mechanisms involved in guiding attention during working memory encoding, whilst suppressing irrelevant information (Gazzaley et al., 2005, 2008; Zanto et al., 2010; Zanto & Gazzaley, 2013). Nevertheless, even under conditions of low cognitive load, several studies demonstrate age-related decline in selective attention (Sommers & Danielson, 1999; Sommers & Huff, 2003), sustained attention (Zhuravleva et al., 2014), divided attention (Fraser & Bherer, 2013) and task-switching (Clapp et al., 2011). An explanation for this may be due to reduced neural specialisation reported to decline as a result of ageing (J. Park et al., 2012). However, drawing a general conclusion is not simple. Numerous other studies report retention of these attention abilities performing on a par with younger adults (review: Zanto & Gazzaley, 2014). Differences in the age-related attention literature may be due to heterogeneity of ageing populations in addition to the many different forms of attentional processes and tasks. It remains unclear whether attention is truly impaired and whether it might be responsible for contributing to the reported age-related declines of PM.

1.4.4 Executive Function

Executive function can be thought of as a set of cognitive processes involved in planning, organisation, coordination, implementation and evaluation of non-routine activities (Glisky, 2007). Based on considerable neurobiological and

neuropsychological evidence, an executive decline hypothesis of ageing has been developed (Crawford et al., 2000). It suggests memory-related declines are due to impairments in executive functions controlled within the frontal lobes. Researchers often detail the sensitivity of the frontal lobes to the effects of ageing (Naftali Raz, 2000; West, 1996). Support for an executive decline hypothesis comes from a series of studies comparing younger and older adults in mechanisms such as temporal order (Parkin et al., 1995), control of interference (Dempster, 1995), metamemory (Souchay et al., 2000) and conscious awareness (Parkin & Walter, 1992). These studies alongside studies of ageing and older adults with frontal lobe impairments in the encoding of spatial and temporal contexts (Craik et al., 1990) have led to the suggestion that executive functions may explain the performance effects of ageing on a variety of tasks.

1.5 Ageing and Prospective Memory

Prospective memory deficits are among the first and most common complaints to be reported by older adults due to the substantial effect that PM failures have on daily living (Hering, Kliegel, Rendell, et al., 2018). For example, an individual who is frequently forgetting appointments may be concerned and report this to their general practitioner. As outlined in the previous section, cognitive functions associated with the underlying aspects of PM are found to be sensitive to the effects of ageing. It was therefore assumed that these deficits would be responsible for PM decline reported by older adults. Early ageing studies by Einstein & McDaniel (1990), failed to find these expected deficits in PM tasks as a result of ageing. In Einstein and McDaniel's (1990) seminal study of PM and ageing, young adults (17–24 years old) and older adults (60–78 years old) completed a dual-task PM paradigm. Rehearsal prevention of the PM task was achieved through the administration of an ongoing short-term memory task. The PM task was embedded within this ongoing task, requiring participants to press a button for the encoded intention. Their results failed to demonstrate the hypothesised age-related decline in PM performance, leading the researchers to believe that these types of tasks are not sensitive to age-related effects.

A series of extensive reviews have revealed that the subsequent studies following Einstein and McDaniel's (1990) work demonstrate inconsistent effects of ageing on PM (Henry et al., 2004; Kliegel et al., 2016; Kliegel, Jäger, et al., 2008; McDaniel et al., 2008). It has been proposed that an absence of initial age-related declines might have in fact been due to an inaccurate understanding of PM as a concept, instead of a lack of age-related effects of cognitive functions of PM (Einstein et al., 1995). Considering the inconsistencies and the different methodologies for investigating PM, it became apparent that different characteristics needed to be explored to explain the age-related decline in PM.

Three key characteristics, all of which can be defined by self-initiation or spontaneous processes, have been distinguished in explaining the inconsistencies within the PM literature (Eusop-Roussel & Ergis, 2008). These are: 1) cue salience, where salient cues rely on spontaneous processes and non-salient cues rely on self-initiated retrieval; 2) the relationship between intention of the PM cue to be retrieved, where strong associations will recruit automatic retrieval strategies and weaker associations will require effortful, self-initiated retrieval strategies; and 3) PM task type, being either event- or time-based.

With regards to cue salience, research has demonstrated that when the cue is particularly salient, older adults perform as well as younger adults due to spontaneous retrieval processes facilitated by a strong link of the cue and the retrieval intention (Cherry et al., 2001). However, with less salient cues, older adults perform less well than younger participants, such as when a highly typical word served as the PM cue (i.e., the PM was less distinct and more semantically familiar, therefore less perceptually salient; Cherry et al., 2001). In a study of PM performance in young participants, McDaniel et al. (2004) demonstrated that retrieval type is dependent on the strength of the relationship of the retrieval cue and cue intention. Ageing studies have also demonstrated that PM cue type is particularly sensitive to the effects of ageing as evidenced by several studies showing a slight but noticeable decrease in PM performance when the PM task is time-based (d'Ydewalle et al., 2001; Einstein et al., 1995). It is likely, this difference is also a result of the level of self-initiation required to complete the PM task, which is consistent with research indicating that these age-related declines are linked to the engagement of self-initiated retrieval processes (Mäntylä & Nilsson, 1997).

Despite this, even within task designs which incorporate event-based PM cues, the evidence is not clear for ageing. Indeed, some studies do report a significant effect of age (Cherry & LeCompte, 1999; Dobbs & Reeves, 1996; Maylor, 1996; Uttl, 2008; West & Covell, 2001), whilst others do not (Einstein & McDaniel, 1996; McDaniel et al., 2008). The differences between these studies may be due to the variability in the task design and the required level of effortful monitoring, PM strategies and the recruitment degree of executive processes required to complete them (Henry et al., 2004). In fact, following the assumption that executive functions are somewhat diminished in older adults (Cepeda et al., 2001; De Luca et al., 2003; Zelazo et al., 2004), Kliegel, Mackinlay, et al. (2008) manipulated the inhibitory control aspect of executive function across different stages of PM. Their study altered the degree to which active task interruption was required during intention execution. They concluded that age-related PM declines were a result of a reduced ability to inhibit attention to the ongoing task and enable switching to another intended task.

One particularly interesting finding that has resulted from studies of ageing and PM is the age-prospective memory-paradox (Maylor, 2008). The age-related deficits reported in laboratory-based studies of PM (Henry et al., 2004; Uttl, 2008) are in stark opposition to the conclusions made from naturalistic studies (Rendell & Craik, 2000; Rendell & Thomson, 1999). In naturalistic study designs, participants complete PM tasks more closely aligned to a real-world setting (e.g., making a phone call to the researcher at a certain time of day). During such tasks, older adults perform on a par with, and in some instances better than, younger adults (Henry et al., 2004; Niedźwieńska & Barzykowski, 2012; Schnitzspahn et al., 2016). Despite the age-prospective memory paradox being supported in meta-analytical studies exploring the differences between laboratory and naturalistic experiments (Henry et al., 2004; Uttl, 2008), there are only a handful which repeat the laboratory study and naturalistic study in the same cohort (Kvavilashvili et al., 2013; Niedźwieńska & Barzykowski, 2012; Rendell & Thomson, 1999; Schnitzspahn et al., 2011, 2018). In Schnitzspahn et al.'s (2011) study, the researchers investigated control over the PM task, ongoing task absorption, motivation and metacognitive awareness in both the laboratory and in the naturalistic style experiments. Consistent with Henry et al.'s (2004) meta-analysis, younger adults performed better in the laboratory, but poorer in the naturalistic study, than older adults. Schnitzspahn and colleagues (2011) suggested that older adults benefit from higher levels of metacognitive awareness

and motivation in the naturalistic setting. It seems that 'normal life' offers older adults the ability to the employ their experience, knowledge and perhaps alternate PM strategies, which may be of less use in the highly controlled setting of a laboratory experiment.

There are many unresolved questions in the PM ageing literature. As it currently stands, there is no definitive answer as to which cognitive mechanisms may account for the problems that older adults experience as PM declines. Moreover, even less appears to be understood in older adult populations who are experiencing accelerated rates of cognitive decline, such as those with MCI.

1.6 Mild Cognitive Impairment

In the past, individuals exhibiting signs of cognitive dysfunction in the absence of any diagnostic impairment were first termed as having benign senescent forgetfulness (Kral, 1962). With improved understanding and more detailed accounts of individuals' experiencing cognitive decline, more sophisticated theories were developed, such as the Age-Associated Memory Impairment (AAMI; Crook et al., 1986) and the Age-Associated Cognitive Decline (AACD; Levy, 1994) theories. These theories were not created to define prodromal stages of dementia-related diseases but originally attempted to characterise the more benign forms of cognitive decline that fall within the limits of normal ageing. However, researchers began to note that a significant proportion of these individuals suffering from these cognitive declines, would also go on to develop dementia (Celsis et al., 1997; Ritchie et al., 2001). However, some authors reported older adults who were considered healthy were also going onto develop dementia at a similar rate (Hänninen et al., 1996).

More recently, the term MCI has been used to define those individuals who are thought to be on the continuum of cognitive function between normal ageing and dementia (conceptualised in Figure 1.2; Petersen et al., 1999). Originally, MCI was described as those individuals scoring a 3 on the Global Deterioration Scale (Reisberg et al., 1982). More recently, a refined and detailed criterion have been established and are currently employed for the diagnosis of MCI (Winblad et al., 2004). These current criteria specify a change in cognitive function that is greater

than what might be expected given their age and level of education, but do not meet the threshold for a diagnosis of dementia. Individuals with MCI must also have consistent memory complaints, typically confirmed by a close informant and verified using validated objective cognitive and neurophysiological assessments. Finally, they must retain functional independence and the ability to complete activities of daily living (Petersen, 2004; Petersen et al., 1999, 2001; Winblad et al., 2004).

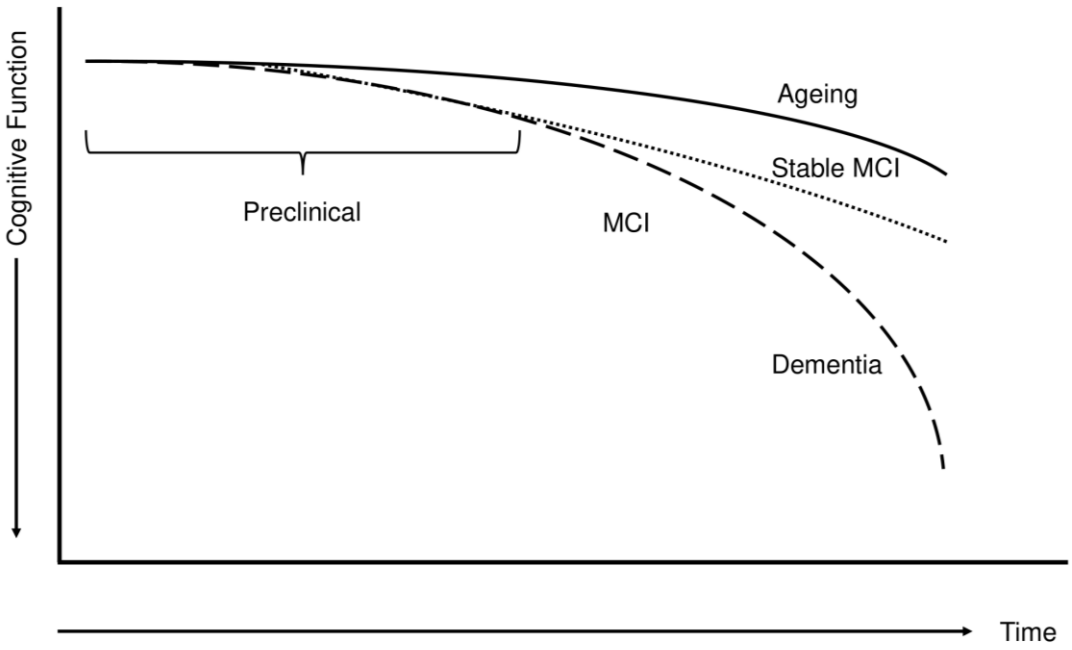

Figure 1.2. Hypothetical stages of cognitive decline from normal ageing towards dementia.

Due to the relative recency of the classification of this term, there are differences in the diagnostic assessments (Petersen et al., 1999), conflicts in the categorisation of MCI subtypes (Ward et al., 2012), and inconsistencies between population and clinical-referred participant studies (Feldman & Jacova, 2005). According to a recent systematic review of the prevalence of MCI in older populations (Ward et al., 2012), estimates place the number of adults over the age of 65 as having MCI at 20–26% and increases to 29% in adults at ages 85 years and older (Lopez et al., 2003). From those who are classified as having MCI, approximately 10–15% will go on to develop dementia annually (DeCarli, 2003; Petersen, 2004; Petersen et al., 1999) in comparison to older adults without an MCI classification developing dementia at a rate of 1–2% annually (Petersen et al., 1999).

In earlier studies of continued cognitive decline in those individuals with MCI, it was thought that the deterioration in memory domains was solely responsible for cognitive decline and other cognitive processes are, for the most part, spared (Petersen et al., 1999). However, in those studies, the diagnosis for MCI was given based solely on memory impairments. Additionally, individuals in that study had reportedly progressed to dementia at a significantly increased rate compared to the general population (Geslani et al., 2005; Morris et al., 2001; Petersen et al., 2001). Nonetheless, it is generally accepted that those individuals with MCI that are at risk of developing dementia-related diseases usually display impairment to several cognitive domains, such as attention (e.g., Saunders & Summers, 2010), language (e.g., Taler & Phillips, 2008), executive function (Kirova et al., 2015) and processing speed (e.g., Fabrigoule et al., 1998). Interestingly, it has also be noted that the deterioration in episodic memory is the most common cognitive impairment in MCI who eventually develop Alzheimer's Disease (AD; e.g., El Haj et al., 2016; Tromp et al., 2015).

To encompass the heterogeneity of individuals with MCI and to better reflect the reported differential deficits in these cognitive domains, different subtypes have been created. The two main subtypes are: amnestic and non-amnestic MCI (Petersen, 2004). Amnestic MCI (aMCI) is often typified by subjective memory complaints (mainly episodic in nature) and is thought to reflect a common precursor for the development of AD (Ghosh et al., 2014; Petersen, 2004). On the other hand, individuals with non-amnestic MCI (naMCI), primarily exhibit impairments non-memory related cognitive domains, such as attention, language and executive functioning (Ghosh et al., 2014; Petersen, 2004). However, it is debated whether there truly exists a true MCI subtype and it is likely that the majority of studies include a combination of aMCI and naMCI (Alladi et al., 2006).

1.6.1 Memory and mild cognitive impairment

Given that MCI is the prodromal form of dementia, it is perhaps unsurprising that memory is the most explored topic within the MCI literature. Many commonalities are shared between MCI and dementia, particularly in those brain regions responsible for the processing of episodic memory (Braak & Braak, 1995; discussed

further in Chapter 2). In AD and MCI, impaired episodic memory is believed to be a core feature of cognitive impairment (Baudic et al., 2006).

Alongside being a core feature, episodic memory is also one of the earliest domains to exhibit impairments (Gold & Budson, 2008; Petersen et al., 1999). Impairment of episodic memory may exist up to 10 years before dementia in individuals with a diagnosis of aMCI (Dannhauser et al., 2008). Given that episodic memory relies primarily on the knowledge of prior episodes, including free recall, recognition tests or cued recall (Yonelinas, 2001), it likely that impairment to this domain may arise from a deficiency in information encoding and/or retrieving the stored information.

Nevertheless, other recent research suggests that early impairments of semantic language-memory, working memory and attention are also strong predictors of cognitive decline of MCI to AD (Brandt et al., 2009; Klekociuk et al., 2014; Saunders & Summers, 2010). It is for these reasons that it would seem that PM may be particularly sensitive to cognitive decline and may provide a useful method to further our understanding and prediction of cognitive, yet it has received relatively little attention.

1.7 Prospective Memory and Mild Cognitive Impairment

Past studies comparing older adults with those experiencing MCI have demonstrated that PM is indeed impaired in MCI groups (van den Berg et al., 2012). A recent meta-analysis found no differences in the effect size for impairments in PM between MCI and dementia (van den Berg et al., 2012). This proposes the potential usefulness of PM as being an early indicator of cognitive decline towards dementia.

Given the relationship between retrospective memory and PM as previously discussed, and the known deficits of episodic memory in individuals with MCI (Dannhauser et al., 2008), it could be assumed that the reported deficits in PM are a result of the retrospective component of intention retrieval. Indeed, studies have set out to test this assumption by manipulating the retrospective memory component of PM through the interruption of target cue or retrieval of the intended action (Costa et al., 2010; Costa, Caltagirone, et al., 2011; Karantzoulis et al., 2009; Thompson et al., 2010). These researchers demonstrate that in individuals with MCI, deficits to the retrospective component affects PM performance.

Evidence appears to also suggest that the cognitive impairments demonstrated in MCI populations cannot be fully attributed to retrospective memory alone. Blanco-Campal et al. (2009) had older adults and MCI participants perform two retrospective memory tasks and an event-based PM task. Participants completed two different conditions while completing a lexical decision task (i.e., the ongoing task). In the first condition, participants were required to say the word animal when they observed a predefined specific target word (e.g., lion) or a predefined non-specific condition when there was any animal word observed (e.g., "cat", "rabbit", "tiger"). Additionally, the researchers manipulated the salience of the PM targets. In the salient condition, the target word was presented in italics and in the non-salient condition, the word was presented in the same style as the ongoing task. The results demonstrated greater discriminative ability of the PM task compared to the retrospective memory tasks for detecting MCI of suspected AD (MCI-AD). The non-salient condition was particularly sensitive in discriminating MCI-AD from healthy older adults. This was thought to be due to the increased need of self-initiation required to retrieve the PM intention for the non-salient condition. It was suggested, therefore, that individuals experiencing MCI are particularly impaired in cognitive functions related to PM tasks that require greater levels of self-initiation. Moreover, Blanco-Campal et al.'s (2009) study highlights the potential for better diagnosis and the detection of individuals with MCI likely to convert to AD through a range of different PM task types.

In another comparison study (Costa et al., 2010) of retrospective memory and PM, participants were required to remember to perform three distinct actions in either an event-based or time-based conditions which were: tell the researcher to turn off the computer; replace the handset of the telephone and to write their name on a piece of paper. The three conditions were selected as similar in the way the participants performed them and to demonstrate the effectiveness of their PM. The researchers then assessed the participants recall of the instructed actions that they failed to perform to examine the impact of retrospective memory failure on PM performance. Participants experiencing MCI were less accurate in both the retrospective and PM parts of the task but were disproportionally less accurate at completing the PM part of the task. Furthermore, individuals with MCI identified as possessing a dysexecutive impairment were particularly impaired in the time-based PM task. This suggests that executive functions are of particular importance for self-initiated PM.

Studies have reported that although MCI participants can recall with a fair degree of accuracy the encoded intention, they were also likely to fail to execute on the intention when required to within the study (Schmitter-Edgecombe et al., 2009). Moreover, even in studies that statistically controlled for the retrospective aspect of the PM task, MCI participants were still found to perform worse relative to controls (Thompson et al., 2010).

Much of the PM literature on MCI has compared the more effortful strategic monitoring of time-based PM with that of the less cognitively demanding event-based PM tasks (Costa, Caltagirone, et al., 2011; Troyer & Murphy, 2007; van den Berg et al., 2012). Costa et al. (2015) found that the inclusion of a time-based PM task improved the discrimination between healthy controls and MCI participants. This led to the suggestion that time-based PM is more reliable in discriminating those with cognitive impairment due to the greater amount of effortful monitoring required to complete the task. However, only a time-based study of PM was included in the study and was not compared to an event-based PM task. Van den Berg et al.'s (2012) meta-analysis reports that MCI impairments are comparable in event-based and time-based PM, suggesting that the common cognitive systems of spontaneous-retrieval and strategic monitoring processes are affected in MCI.

Alternative avenues investigating PM have been explored in the event-based PM cues, to further elucidate cue-type on PM performance in older adults with MCI. Blanco-Campal et al.'s (2009) study varied the perceptual salience of the PM cue. Their results demonstrated that the non-specific non-salient condition, which was intended to increase the recruitment of strategic monitoring processes, showed the greatest differences in PM performance between healthy older adults and MCI. However, in a recent novel study of PM salience in MCI (Thompson et al., 2017), it was found that although MCI participants did perform poorer compared to the healthy older adult controls, the less salient cue did not cause disproportionally poorer performance for the MCI participants. In other words, it was expected that MCI participants would perform less well than the healthy older adults in both PM tasks, but performance would decrease with the PM target saliency. This hypothesis was not supported. However, the researchers did acknowledge that the cognitive resources may already have been sufficiently depleted to the point where subtle task manipulations made little impact on the overall performance.

Another common task manipulation that is present within the MCI PM literature is the focality of the PM cue. In older adult studies, it is suggest that non-focal PM tasks elicit the greatest amount of age-related impairments as a result of the increased amount of processes applied to strategic monitoring (Kliegel, Jäger, et al., 2008). However, the evidence on MCI studies remains less clear. In a study of PM in participants with MCI, Tam and Schmitter-Edgecombe (2013) demonstrated that participants with MCI performed worse for non-focal PM cues relative to their age-matched controls.

Other studies have demonstrated that individuals with MCI are more impaired in the focal PM tasks relative to healthy older adults (Chi et al., 2014; Niedźwieńska et al., 2017). Interestingly, evidence has reported similar discriminatory abilities for focal PM tasks in older adults with very mild AD, thought to be similar to aMCI, and both groups were found to perform close to the lower limits of task performance (McDaniel et al., 2011). It remains difficult to determine the source of inconsistency between these studies, but one possible explanation may be due to variations in cognitive impairment (Libon et al., 2010). For example, Chi et al. (2014) demonstrated that both aMCI and naMCI had poorer PM abilities. However, they also found that the patients with aMCI were more impaired than those with naMCI and healthy controls in focal PM but also found that the patients with naMCI were more impaired in non-focal PM relative to the healthy controls and patients with aMCI. While manipulation of the PM cue can improve our understanding of PM deficits in individuals with MCI, understanding the aetiology of these deficits remains subjective. By using neuroimaging methods to examine older adults with MCI while completing different PM tasks, our understanding of cognitive impairments will be greatly improved.

1.8 Chapter Summary

This chapter has examined the cognitive mechanisms and the theories that underpin PM. The evidence suggests that PM is not a unitary memory domain but is comprised of different cognitive mechanisms which help support the memory of future intentions. Attentional, executive and retrospective memory functions were identified as comprising core features of PM. There is some disagreement between theories of PM although it seems there are also some overlaps. Namely, that some instances will require strategic monitoring using attentional processes, particularly in less salient or

non-focal stimuli. This chapter outlined the sensitivities of the above cognitive domains to ageing and their relationship to the reported deficits of PM in healthy older adults. There are inconsistencies within the literature, where some studies report that older adults are impaired in PM, while others do not. These variabilities are likely due to the task designs used to measure PM. Interestingly, in task designs that are more naturalistic in design, results often fail to find PM performance deficits in older adults compared to laboratory-based studies. Finally, this chapter highlights the PM deficits in older adults experiencing MCI and how, due to PM failures being among the first reported problems by older adults, may provide an early sensitive indicator for dementia-related diseases.

Chapter Two: Neurobiology of prospective memory, ageing and mild cognitive impairment

2.1 Introduction

In Chapter 1, the basic memory processes employed for future-orientated tasks (PM) were described along with the current understanding of PM. Reasons for PM failures were also discussed along with how ageing and cognitive decline affects PM functioning. Chapter 2 builds on the cognitive perspectives of PM and how it is affected by ageing and cognitive decline through the delineation of key neurobiological networks thought to be responsible for PM. Firstly, the frontal lobes and other neurobiological systems crucial to PM are outlined. Next an integrated model of PM throughout the cortex, known as the attention to delayed intention (AtoDI) model is described. The neurobiological systems affected by ageing are then described along with the current understanding of the neurobiological effects of ageing on PM. Finally, the neurobiology of MCI is detailed and, by using the AtoDI model of PM as a framework, inferences are made as to the expected deficits of PM in older adults with MCI.

2.2 Neurobiology of Prospective Memory

As discussed in Chapter 1, PM is a multistep process and, therefore, requires the recruitment of various cognitive systems throughout the different stages. It is generally believed that there are certain brain areas that play a more significant role in PM. Namely, the prefrontal cortex (PFC) and medial temporal (e.g., hippocampal) regions (West & Krompinger, 2005). The following section discusses these regions in relation to a proposed PM network.

2.2.1 Frontal lobes

The frontal lobes are one of the largest regions of the human brain, comprised of many subregions related to a variety of cognitive functions (Gilbert & Burgess, 2008). Initial studies of individuals with frontal lobe dysfunction described impairments in short-term goals and everyday tasks (Eslinger & Damasio, 1985; Penfield & Evans, 1935). Studies found that patients with unilateral frontal lesions were impaired in recall of spatial positions (Smith & Milner, 1984), free-recall (Jetter et al., 1986) and delayed alternation performance (Chorover & Cole, 1966). However, other early frontal lesion studies failed to find the same functional deficits (Schacter, 1987). Instead, Schacter (1987) proposed the lesions to the frontal lobes caused specific deficits to episodic remembering.

More recently, studies have shown the role of the frontal lobes across a variety of cognitive domains underpinning PM, such as executive function and working memory (reviews: Carpenter et al., 2000; Lara & Wallis, 2015; Yuan & Raz, 2014). Primarily, executive functions are mediated by the dorsolateral prefrontal cortex (Otero & Barker, 2014), comprised of Brodmann area (BA): 9, 10, 11, 12; area 45 and 46; and the superior area of 47 (Damasio, 1996). The dorsolateral PFC has multiple cortical and subcortical connections that help to organise and control input from specific regions, including the hippocampus, associative areas of the neocortex (posterior temporal, occipital and parietal), basal ganglia (dorsal caudate nucleus) and the thalamus (Fuster, 2001). Evidence has demonstrated the close relationship that the PFC has with performing executive functions such as attention shifting, planning and decision making (Siddiqui et al., 2008). In a review, Van Snellenberg and Wager (2009) suggest that the separate subregions of the PFC work together to successfully perform executive tasks. Specifically, they propose that coordinated activity of the prefrontal cortex controls representations of a stimulus in the orbital frontal and medial anterior PFC (aPFC). Whereas the processing of internal goals is handled by the anterior insular, and top-down processing of stimulus representations are performed in posterior cortices.

Working memory similarly relies on frontal lobe structures (Courtney et al., 1998). Researchers have discussed the implications that deficits of working memory have on other complex cognitive tasks that require attention, such as the manipulation of information or goal-directed behaviours (Boisgueheneuc et al., 2006; Koziol &

Budding, 2009). Prabhakaran and colleagues' (2000) fMRI study of working memory shows that the right frontal lobe plays a particularly important role in working memory function and the retention of integrated information. However, the prefrontal cortex is not solely responsible for working memory, but rather relies on a complex interaction of the frontal cortex and the basal ganglia (Eriksson et al., 2015). Koziol and Budding (2009) suggest that working memory is characterised by active maintenance of information with the frontal cortex but the information is updated within the basal ganglia and controlled through frontal-basal ganglia connections. Moreover, complex interactions between the PFC and subcortical regions, such as the medial temporal lobe (MTL), have explained encoding and retrieval of long-term memories (Campo et al., 2005; Sakai & Passingham, 2004), declarative memory (Fernández, 2017) and episodic memory (Barker et al., 2017). Given PM's reliance on a multitude of these cognitive components it would be expected that the PFC would be critical in PM.

Indeed, the aPFC is often found to be activated during PM tasks. For example, using Positron emission tomography (PET), Okuda et al. (1998) identified involvement of ventrolateral and right dorsolateral prefrontal cortices, the left frontal pole, as well as the midline medial frontal lobe, left parahippocampal gyrus and the anterior cingulate to be active during PM. These findings were later supported by other PET studies (Burgess et al., 2001, 2007, 2011) that particularly implicated BA10 (Figure 2.1; also known as the aPFC) in PM, relative to an ongoing task.

The aPFC may be critical for the maintenance of a PM intention. Burgess et al. (2001) used PET to measure cerebral blood flow changes to evaluate the role of the aPFC in PM intention maintenance across three experiments. In the first experiment, participants just completed an ongoing task; in another experiment, participants anticipated that PM cues would appear during the ongoing task; and in the other experiment, participants anticipated that PM cues would appear, but they did not. Burgess et al. found that in both experiments where participants expected a PM cue, there was considerable increases of cerebral blood flow to regions of the aPFC relative to the ongoing task. The authors proposed that aPFC was indeed involved with maintaining a PM intention. Further evidence has coupled activation of the lateral aPFC with decreased activity of the medial aPFC (Burgess et al., 2003, 2008). Burgess and colleagues propose this reflects the lateral aPFC mediating attention to internal

representations, such as future intentions, whilst the medial aPFC is responsible for attending to external perceptual information, to mediate stimulus-orientated processes. Burgess and colleagues concluded that the frontal lobes (particularly the aPFC) is more responsible for PM cue maintenance than cue retrieval (Burgess et al., 2003).

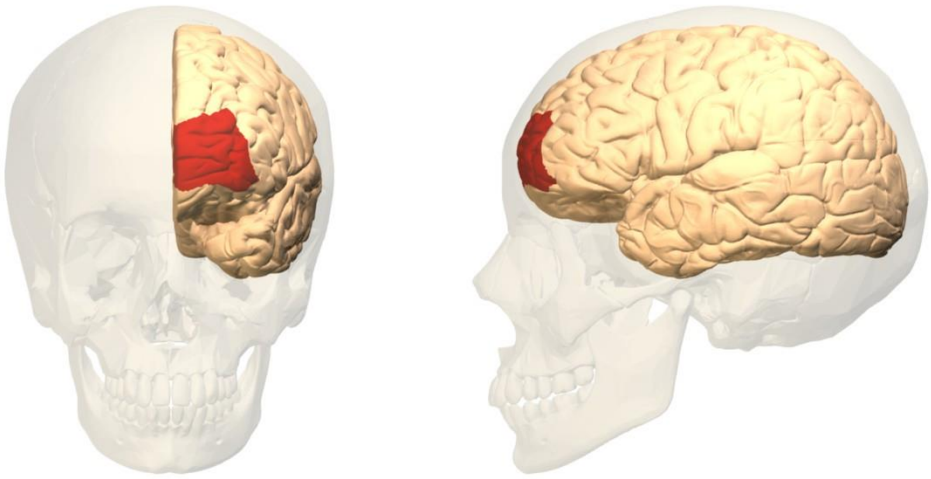

Figure 2.1. Illustration of the Brodmann area 10 (anterior prefrontal cortex; aPFC). Adapted with permission from BodyParts3d, Copyright C 2008 Life Sciences Integrated Database Center licensed by CC Attribution-Inheritance 2.1 Japan.

Since the initial neuroimaging studies of PM, a plethora of other imaging methods have been used to further understand PM functioning, including functional magnetic resonance imaging (fMRI; Barban et al., 2014; Burgess et al., 2011; Cona et al., 2015; Gilbert, 2011; Gilbert et al., 2009, 2012; Lamichhane et al., 2018; Reynolds et al., 2009), PET (Burgess et al., 2003), transcranial magnetic stimulation (TMS; Bisiacchi et al., 2011; Costa et al., 2013; Costa, Oliveri, et al., 2011; Debarnot et al., 2015; D. M. Ellis et al., 2019), event-related potentials (ERPs; Knight et al., 2010; West et al., 2006) and neuropsychology (Burgess et al., 2011; McDaniel & Einstein, 2011; Uretzky & Gilboa, 2010). Evidence from these studies strongly implicate the aPFC playing an important role in PM, particularly the maintenance of intentions. Differential activation of the medial and lateral aPFC has led to interest in the framework of 'the Gateway Hypothesis' of PM (Burgess et al., 2005; Brugess et al., 2007; 2011).

2.2.2 The Gateway Hypothesis of Prospective Memory

The Gateway hypothesis (Burgess et al., 2007; 2011) asserts that a principle purpose of the aPFC is to control differences in attending between "stimulus-independent thought" (i.e., our inner mental life) and that involved in preferential attending to the external world ("stimulus-oriented attending"; Burgess et al., 2011; p2255). According to this theory, the increased activity at the lateral aPFC in conjunction with decreased activation in the medial aPFC during PM tasks comprises an underlying attentional balance between external ongoing stimuli and the internally represented PM intention. Specifically, the lateral aPFC mediates attending to a PM intention (Burgess et al., 2005; 2007) and the medial aPFC is responsible for attending to external perceptual information (Gilbert et al., 2006; Simons et al., 2005).

Evidence of the aPFC activity in PM is reliably found in studies of cerebral blood flow (review: Burgess et al., 2011). Most studies of cognitively healthy individuals have demonstrated that while increases are found in the lateral aPFC during PM tasks, decreases are found in medial regions. The different regions seem to function in an interactive manner (Burgess et al., 2003), where the increased activity in lateral areas maintain a PM intention and the decreased activity in medial areas inhibit internal thoughts. Consider the example given at the start of this thesis about buying dog food on the way home: as your attention shifts from directing yourself to the train station the activity in the medial aPFC will decrease and as your attention shifts to remembering to buy dog food the activity in the lateral aPFC increases.

Past research suggests that the medial–lateral aPFC dissociation is not PM specific. Gilbert et al. (2005) compared attention directed towards environmental stimuli (stimulus-orientated attending) and attention toward internal representations, which are not related to information in the immediate sensory environment (stimulus-independent attending). They demonstrated that when switching between attending to environmental stimuli and internal presentations, the lateral aPFC was activated for a short time. However, they also found that the medial aPFC was consistently activated for stimulus orientated attending. This suggests the importance of the aPFC in tasks requiring selection between environmental stimuli and internal thought. Moreover, it highlights dissociative role between lateral and medial roles of the aPFC (Burgess et

al., 2005; Simons et al., 2005), which is apparent in PM but may not be an exclusive pattern of activity.

Okuda et al. (2011) found engagement of the medial aPFC in tasks requiring the automatic coordination of attentional processes. A study (Barban et al., 2014) manipulating the saliency of the PM cue and the memory load of the ongoing task, found an associative interaction of the left lateral aPFC between high memory load and the PM task. Barban and colleagues also found that the medial aPFC was related to the low memory load condition and the high saliency PM task. These studies suggest the medial aPFC plays an important function in spontaneous PM retrieval for highly salient external stimuli, while the lateral aPFC is important for internal representations of the PM cue when the working memory load is high.

There is considerable evidence for the role of the aPFC in PM but there are also several unanswered questions regarding PM functioning, particularly regarding the other stages of PM. The Gateway Hypothesis has largely neglected the encoding and intention retrieval phases of PM. Moreover, the question remains about whether the aPFC plays a general role in PM functioning or whether it is specific to certain features of PM tasks. Furthermore, it does not account for processes occurring throughout the rest of the brain, although some areas such as the precuneus, parietal lobe and anterior cingulate cortex (ACC) are also found to be activated (Barban et al., 2019; Beck et al., 2014; Burgess et al., 2011; Den Ouden et al., 2005; Eschen et al., 2007; Gilbert et al., 2009; Hashimoto et al., 2011; Okuda et al., 1998, 2007, 2011; Poppenk et al., 2010; Reynolds et al., 2009; Simons et al., 2006) but their functional relationship to PM is yet to be confirmed. Given that PM is a multistep process involving many different cognitive functions, one would expect activation in other regions particularly during the intention realisation and retrieval stage, for example, the ventrolateral parietal cortex (review: Vilberg & Rugg, 2009). Other studies have attempted to address these issues by exploring other brain areas during PM.

2.2.3 Prospective Memory in the Global Brain

In addition to aPFC regions, other frontoparietal networks have also been implicated in PM (Beck et al., 2014; Bisiacchi et al., 2011; Burgess et al., 2011; Kalpouzos et al., 2010; McDaniel et al., 2013). Notably, strategic monitoring appears to be mediated by

the dorsolateral PFC and precuneus, whilst attentional and retrieval aspects are driven primarily by ventral frontoparietal and temporoparietal networks (Beck et al., 2014; Kalpouzos et al., 2010; McDaniel et al., 2013).

The detection of PM cues and intention retrieval has primarily been attributed to the ACC, posterior cingulate cortex (PCC), temporal cortex and insula (Beck et al., 2014; Gilbert et al., 2012; Gonneaud et al., 2014; Hashimoto et al., 2011; Oksanen et al., 2014; Rusted et al., 2011; Simons et al., 2006). For example, Gonneaud et al. (2014) used fMRI to record the brain activity of healthy adults while they completed a time-based PM and an event-based PM task. They demonstrated common neural substrates across both tasks in the inferior and middle frontal gyri, the insula and the cerebellum along with deactivations in the right medial aPFC and the left middle temporal gyrus. Differences were also noted between the tasks. In the event-based task, there was greater activation of the occipital lobe. Whereas the time-based task elicited greater activation in the right hemisphere, notably the middle superior frontal gyri, the cuneus and precuneus. Activation differences were reportedly due to the different mechanisms applied to perform the PM tasks. However, the increased level of perceptual information available in the event-based task may have required different cortical areas compared to the time-based task (Rosenthal & Soto, 2016). Across both PM tasks, however, Gonneaud and colleagues' (2014) results confirmed the deactivation of the medial aPFC during intention maintenance, providing further support for the Gateway hypothesis of frontal PM functioning.

Additionally, Gonneaud and colleagues (2014) found that the ventral frontoparietal network (i.e., ventrolateral prefrontal regions, supramarginal gyrus and inferior parietal lobule) was more activated during the retrieval stages of the PM tasks. The PCC and temporal cortex regions have also been found to be activated during intention retrieval (Poppenk et al., 2010; Gilbert et al., 2012). Together, research suggests that multiple brain regions are required to successfully perform a PM task, necessitating the development of novel theories that incorporate these findings across different stages of PM.

2.2.4 The Attention to Delayed Intention Model

In a recent meta-analysis by Cona et al. (2015), the brain areas which are consistently activated across the different phases of PM were reviewed (i.e., encoding, intention maintenance and intention retrieval). The authors corroborate the gateway hypothesis of PM, showing that across multiple studies, the aPFC is indeed consistently activated. Their findings support the increase in lateral aPFC and decrease in medial aPFC during PM. Moreover, they highlight the importance of the aPFC in retrieval and encoding of intentions. However, it was found that some studies do not support the lateral aPFC involvement in PM encoding (Gilbert, 2011). Furthermore, Cona and colleagues (2015) report a dissociation between dorsal and ventral networks of parietal regions. The dorsal parietal cortex, including the superior parietal lobule and precuneus (BA7 & BA19, respectively), were more activated during the maintenance of intentions. Whereas the ventral parietal cortex, including the inferior parietal lobule and supramarginal gyrus (BA40), were particularly activated for the retrieval of intentions. The authors explain this dissociation by linking two previous cognitive models of attention and episodic memory together — the dual-attention (Corbetta & Shulman, 2002) and the Attention to Memory (AtoM) model (Cabeza et al., 2002; Ciaramelli et al., 2010) — to form the AtoDI model (Figure 2.2).

The 'dual-attention' model within the attention domain (Corbetta & Shulman, 2002) suggests that dorsal and ventral parietal regions are components of two separate yet interacting frontoparietal attentional systems. The dorsal frontoparietal networks mediate top-down goal-directed attention towards stimuli. Whereas, the ventral frontoparietal networks are reportedly responsible for the bottom-up direction of attention to salient events (Corbetta & Shulman, 2002). The Attention to Memory (AtoM) model (Cabeza et al., 2008; Ciaramelli et al., 2010) of episodic memory, posits that the maintenance of goal retrieval is governed by the dorsal parietal cortex and directs attention to memory contents. Cona and colleagues (2015) explain that prospective remembering represents a bridge between the attentional and the episodic memory domains, incorporating these two models into one.

The meta-analysis by Cona and colleagues (2015) also supports reliable activation of the ACC, the PCC and insular cortices during PM. The ACC (BA24/23) was predominately activated during the retrieval phase, which supports previous research proposing it as central to a "Cognitive Control Network" (Burgess et al., 2001; Cabeza

et al., 2003; Coull et al., 1996; Duncan & Owen, 2000; Gilbert et al., 2010; Miller & Cohen, 2001). In contrast, the PCC (BA23/31) was found to be predominately activated during encoding and retrieval and had the strongest relationship with retrospective memory (Beck et al., 2014; Gilbert et al., 2012; Simons et al., 2006). Cona and colleagues suggest that the PCC works with the parietal regions to shift attention from external PM cues to the internal to be encoded or retrieved. This is in line with previous research suggesting that the PCC has a strong role in processing intentions (Beck et al., 2014; Den Ouden et al., 2005).

The AtoDI model (Cona et al., 2015) of PM is an attempt to extend and further both the dual-attention model and the AtoM models of memory and attention. It can be thought of as a neural comparative to the Multiprocess Framework (outlined in Chapter 1). The AtoDI model proposes that strategic monitoring would be mediated by the ventral parietal network in conjunction with the PCC, underpinning the neurophysiological changes between bottom-up attention and the stored memory. Spontaneous retrieval is initially coordinated by the insula due to the reliance on an *alert process* occurring with relevant or distinct PM cues. Following the occurrence of the *alert process*, spontaneous retrieval of the PM intention is then further processed through a reflexive associative process leading to the retrieval of the linked intention (Moscovitch, 1994). Cona and colleagues (2015) explain that through cooperative activity between regions of the ventral parietal cortex and lateral aPFC. The theory also posits that the MTL regions may contribute to the reflexive retrieval of an intention, although evidence for this remains scarce.

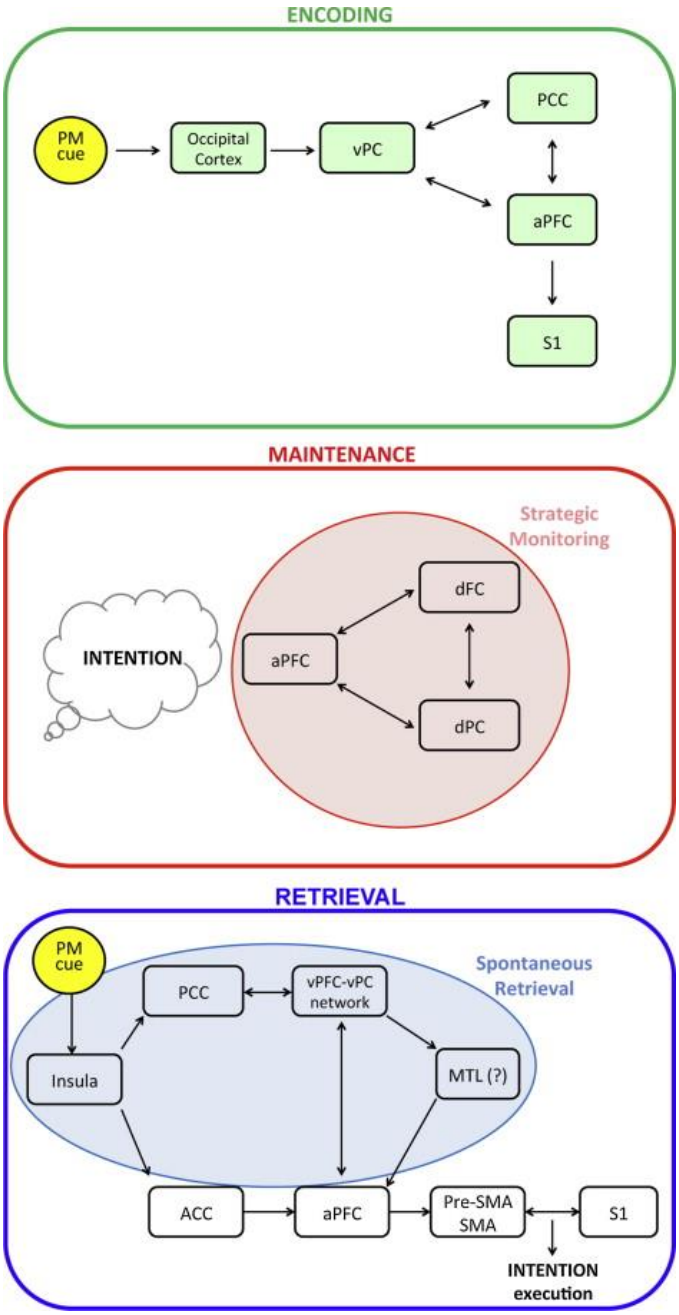

Figure 2.2. Graphic illustration of the AtoDI model for the three phases of Prospective Memory: Encoding, Maintenance and Retrieval. *N.B.* ventral parietal cortex = vPC; posterior cingulate cortex = PCC; anterior prefrontal cortex = aPFC; primary somatosensory area = S1; dorsal frontal cortex = dFC; dorsal parietal cortex = dPC; posterior cingulate cortex; vPFC = ventral prefrontal cortex; ventral parietal cortex = vPC; medial temporal lobe = MTL; anterior cingulate cortex = ACC; sensory motor area = SMA. Reprinted with permission from Cona et al., 2015.

It should be noted that the majority of these studies used to form these theories of PM have been performed on cognitively healthy young adults. Little evidence has explored how these theories hold up against those from different populations such as ageing,

cognitive decline and other cognitive disorders. Given the reported decline of PM in ageing samples and in those experiencing cognitive problems, it is imperative that more research is conducted with these populations. The AtoDI model presents itself as a useful model for evaluating neurophysiological age-related declines in PM.

2.3 Neurobiology of Ageing

The majority of older adults will experience some form of cognitive decline, which appears to be a key feature of the human life cycle. There are many explanations for mild and marked age-related cognitive decline, including depletion of neurotransmitters and enzymes (Bahous et al., 2019), global neuronal loss (Bishop et al., 2010), amyloid deposition (Rodrigue et al., 2009), oxidative stress (Hajjar et al., 2018), and the development of neurotic plaques (Malek-Ahmadi et al., 2016). The recent advances of neuroimaging and analysis methods have driven an exceptional increase in knowledge, insight and the development of novel theories into the ageing brain.

Neurophysiological differences between the older and younger brains are readily found (reviews: Bennett & Rypma, 2013; Brehmer et al., 2014; Lugtmeijer et al., 2019). A common general pattern reported in the ageing literature is that of brain tissue reduction throughout the lifespan (Gunning-Dixon et al., 2009; Naftali Raz et al., 2005), with the rate of shrinkage accelerating precipitously after 50 years of age (Naftali Raz & Rodrigue, 2006). Several neuroimaging studies have reported a greater age-associated decline in white matter volume (Bartzokis et al., 2003; Farokhian et al., 2017; Guttmann et al., 1998; Jernigan et al., 2001; Resnick et al., 2003), but others report a greater decrease to grey-matter volumes (Blatter et al., 1995; Naftali Raz et al., 2005; Sowell et al., 2003; Sullivan et al., 2004). A reason for these reported differences may be that macro level decreases in white matter is a feature of more advanced age (Liu et al., 2003), while grey matter decline is slow and gradual decline throughout an adult's lifespan (Gunning-Dixon et al., 2009; Naftali Raz et al., 2005).

Several studies report that specific regions are vulnerable to age-related decline. The PFC appears to be particularly sensitive to age-related decline relative to other cortical structures, including the hippocampus (Fjell et al., 2009; Resnick et al., 2003). The lateral PFC and the dorsomedial PFC may undergo the greatest structural decline as a

function of age (Fjell et al., 2009; Good et al., 2001; Resnick et al., 2003). For example, Raz et al. (1997) showed that the grey matter volume in the dorsolateral PFC decreases with age at a rate of 4.9% per decade in healthy older adults. Nevertheless, some inconsistent findings exist, with cross-sectional studies showing no differences in ventromedial PFC grey matter volume as a function of age (Chee et al., 2009; Fjell et al., 2009; Salat et al., 2004), while other studies using both longitudinal (Frings et al., 2014) and cross-sectional designs (Fotenos et al., 2005; Tisserand & Jolles, 2003) do report evidence of structural decrease to the ventromedial PFC.

The 'Frontal Hypothesis of Ageing' (Greenwood, 2000; West, 2000) proposes that selective frontal lobe pathology underlies the neurophysiological decline apparent in ageing. Indeed, several authors claim the PFC precedes most, if not all, other areas in the ageing process (Dempster, 1992; Rajah & D'Esposito, 2005; West, 2000). Others suggest that age-related changes in frontal (Nyberg et al., 2014) and hippocampal systems underpin memory problems (Maguire & Frith, 2003), primarily due to age-related depletion of frontal lobe resources (Moscovitch & Winocur, 1992). Jennings and Jacoby (1993) suggest that controlled processing orchestrated in the frontal lobe is particularly affected by ageing, leading to poorer explicit memory, whilst automatic processes are spared. Magnetic resonance diffusion tensor imaging (DTI) offers further support for the frontal hypothesis of ageing showing that degradation of white matter circuits is restricted to frontal regions, leaving posterior and inferior brain regions intact (Pfefferbaum et al., 2005). However, other DTI studies of ageing fail to find the same frontal lobe declines (Barrick et al., 2010). Critiques of the frontal lobe hypothesis of ageing have stated that the theory may be too reductionist and oversimplified to explain age-related neurological changes (Kievit et al., 2014).

Several other brain areas are also reported to be affected by ageing (Greenwood, 2000), albeit not as consistently as frontal regions. A significant moderate neurophysiological decline is seen in occipital, parietal and temporal cortices (Raz & Rodrigue, 2006). Generally, there is only weak evidence suggesting smaller hippocampal volumes and poorer memory performance in older adults (Van Petten, 2004), which contrasts the results observed in pathological populations (Raz, 2000). In recent years, research has provided growing support for the "neural dedifferentiation hypothesis" of ageing (review: Koen & Rugg, 2019).

The neural dedifferentiation hypothesis proposes that dedifferentiation and cognitive decline arise from a reduction of neural efficiency due to reduced integrity of neuronal systems (review: Li & Rieckmann, 2014). The hypothesis suggests that a reduction in the neuromodulatory abilities of cortical areas reduces the signal-to-noise ratio of neurons and subsequently leads to a blurring of precision of neural representations. Therefore, while young adults form specific representations of information, older adults exhibit distributed activity across overlapping neuronal sources which are less distinct (Koen & Rugg, 2019).

The majority of studies of neural dedifferentiation in older adults has been performed using fMRI (review: Koen et al., 2020). Researchers through a variety of different study designs have demonstrated evidence for age-related dedifferentiation in the fusiform face area (Goh et al., 2010), parahippocampal place area (Koen & Rugg, 2019; Park et al., 2004; Voss et al., 2008) and the visual word form area during the passive viewing of scenes, objects, pseudowords and faces (Park et al., 2004). Evidence suggests that neural dedifferentiation follows a linear decrease in neural selectivity throughout an individual's lifetime (Park et al., 2012). Moreover, the results of neural dedifferentiation are reliably replicated in the ventral occipitotemporal cortex across a variety of methodological study designs (Berron et al., 2018; Burianová et al., 2013; Koen & Rugg, 2019; Voss et al., 2008). However, neural age-related dedifferentiation is not observed across all stimulus types. For example, Voss et al., (2008) reported no age-related neural dedifferentiation in extrastriate regions for colour patches or familiar words in colour. Others have found no neural dedifferentiation in neural responses for visual words and objects (Thakral et al., 2019; T. H. Wang et al., 2016). This suggests that the processing of perceptual features may be spared from dedifferentiation and further research is required to determine if neural dedifferentiation extends beyond perceptual stimuli (Abdulrahman & Henson, 2016; Dennis & Cabeza, 2011; Martins et al., 2015; St-Laurent et al., 2011).

The neural dedifferentiation hypothesis may be particularly important for explaining declines in PM due to the importance of high-fidelity neural representations required for encoding and retrieval processes (Bowman et al., 2019; St-Laurent et al., 2014; St-Laurent & Buchsbaum, 2019). This is yet to be explored in PM, but evidence has demonstrated that a reduction in whole brain resting-state functional specificity is predictive of episodic memory performance, event after controlling for age (Chan et

al., 2014). One study of neural dedifferentiation reported greater neural distinctiveness correlated positively with working memory performance following training in older adults (Iordan et al., 2018). It is worth noting, however, that whilst some studies control for age (Chan et al., 2014), the majority have not made direct comparisons between young and older adults. Research so far suggests strong relationships between neural dedifferentiation and cognitive performance, including episodic memory (Koen et al., 2020). However, no studies have examined age-related neural dedifferentiation in PM. Moreover, it is unclear whether dedifferentiation is related to neurodegeneration and dementia related diseases (Maass et al., 2019). Given that the majority of work in this area has come from fMRI, other methods that offer higher temporal resolution (e.g., EEG/MEG) may offer further insight into the functional significance of age-related neural dedifferentiation (Koen et al., 2020).

2.4 Neurobiology of Ageing and Prospective Memory

Drawing on PM neuroimaging studies of younger adults and the known cognitive disruptions in older adults, McDaniel and Einstein (2011) have proposed that degeneration of frontal function would underpin age-related disruption in PM. This idea was based on findings that older adults rely more on frontal brain systems (Braver et al., 2001; Raz et al., 1997; West, 1996), which are implicated in PM tasks (i.e., those tasks which require a heavy planning component or strategic monitoring for PM intentions). Furthermore, McDaniel & Einstein (2011) suggest that those tasks which rely on more involuntary or reflexive retrieval, are thought to be associated with medial temporal structures (J. D. Cohen & O'Reilly, 1996; Moscovitch, 1994) and are likely spared by the effects of typical ageing. McDaniel & Einstein (2011) did not directly evaluate neurocognitive functioning in older adults during PM performance, although their study provided a direction for future research in this area.

Investigation of fMRI in older adults during PM tasks is relatively novel. Recently, Peira et al. (2016) compared healthy older adults to younger counterparts on a dual-task fMRI paradigm in which demands of PM and working memory components were manipulated. Older adults showed poorer performance during the 'high-load' working memory and PM conditions, but no differences were seen when cognitive demands in working memory and PM were low. Increased activation of the frontostriatal and MTL

regions was shown for younger adults compared to older adults during the PM tasks. The authors concluded that PM impairments resulted from failure to recruit these PM-related brain networks, in line with behavioural studies that indicate poorer age-related performance in tasks reliant on frontal functions (Cabeza & Dennis, 2013; McDaniel & Einstein, 2011). Furthermore, Peira et al. (2016) reported a negative relationship between PM response time and activation of the left inferior frontal gyrus for younger adults, which was not apparent in older adults. Peira and colleagues (2016) also implicate the importance of other regions, such as the hippocampus and basal ganglia.

Despite being hypothesised by Cona et al.'s (2015) AtoDI model of PM, evidence of MTL neural recruitment had not been found prior to Peira and colleagues' (2016) study. MTL impairment has been reported in ageing studies of episodic memory (Nyberg et al., 2010; Persson et al., 2006). Thus, it has been proposed that the MTL plays an important role in the retrospective component of PM retrieval. The results from Peira et al. (2016) highlight the importance of the MTL in age-related declines in PM. Considering the importance of the MTL and the demonstrated frontal lobe deficits (McDaniel & Einstein, 2011), it is hypothesised that older adults would be impaired in PM tasks that required extended monitoring of cues and would have difficulty retrieving the intention once it was realised. However, the current evidence remains scarce and Peira et al.'s (2016) sample consisted of two relatively small groups (younger adults n = 15; older adults n = 16). Therefore, further work with larger sample sizes is necessary to understand neural areas affected by ageing in PM.

Furthering Peira's work, Gonneaud et al. (2017) investigated differences between younger and older adults using fMRI in event-based and time-based PM. In contrast to Peira et al.'s (2016) results, Gonneaud et al.'s (2017) found higher activity in the older adults relative to the younger adults in both the event-based and time-based PM tasks. Additionally, they found no deactivation of the medial aPFC in older adults during the PM tasks, which was apparent in the younger adults. Their analysis revealed older adults were also recruiting additional areas (particularly in the frontal, parietal, supplementary motor area and the precuneus), which were not displayed in the younger adults and, therefore, more likely to reflect supportive roles than being specific to areas required for PM functioning. Other regions recruited by older adults included the left inferior and right middle frontal, superior parietal, left superior

temporal, the bilateral supplementary motor area as well as the occipital cortices and the precuneus, which were also found by Gao et al. (2014). However, Gonneaud and colleagues' study failed to find correlations between PM performance and activation of these additional areas and were, therefore, deemed unlikely to be performing a compensatory role for successful PM functioning. The difficulties for older adults to recruit the networks specific and selective for strategic monitoring are in line with the dedifferentiation hypothesis (Baltes & Lindenberger, 1997; Reuter-Lorenz & Lustig, 2005), suggesting that older adults were able to recruit the necessary areas for successful PM but were not able to do so exclusively. Firm conclusions with regards to neuronal dedifferentiation are difficult to draw given the number of studies reporting evidence of compensatory networks described in a variety of different tasks (review: Cabeza et al., 2018).

Gonneaud and colleagues (2016) analysed the medial aPFC with the expectation of finding deactivation during PM maintenance in young and older adults. Their results failed to show this pattern of deactivation for event-based or time-based PM in the older adults, but the younger adults did show the deactivation. It is possible then that the PM differences seen in behavioural studies are a result of an inability of older adults to disengage their attention from external stimuli and reorient towards internal representations of the PM cue. Potentially, the Gateway Hypothesis (Burgess et al., 2003; 2007) is only applicable to younger and not older adults.

Other methodologies have also been employed to explore brain areas involved in PM in older adults. Debarnot et al. (2015) used intermittent theta-burst stimulation (iTBS) via TMS and found that single iTBS administration over the left aPFC results in a performance boost for older individuals. This further affirms the importance of the aPFC in PM functioning. That being said, a similar study using transcranial direct stimulation (tDCS) by Rose et al. (2019), did not find any performance increase to PM for younger or older adults. However, methodological differences are apparent, particularly as the former used a virtual-reality-based design and the latter used a more naturalistic design. The mixed results using this methodology does not help to clarify the role of the prefrontal cortices in PM functioning.

The currently available literature demonstrates mixed results and inconsistent patterns of activity. However, it could be speculated that age-related declines of PM performance are in part due to an inability to properly regulate frontal lobe activity

and therefore may account for the poorer performance found in those tasks requiring active maintenance of an intention (McDaniel & Einstein, 2011). Older adults may also be employing additional cognitive systems to supplement declines in the MTL and in frontostriatal connections. Further work is required to address the neurocognitive discrepancies within the PM literature and to further the understanding of age-related PM performance declines.

Despite the discrepancies within typical ageing literature for PM, to date there is no neuroscientific work into PM and atypical ageing, such as MCI or dementia. Nevertheless, findings from the typical ageing literature provide a useful reference to draw hypotheses about PM and MCI.

2.5 Neurobiology of Mild Cognitive Impairment

The neuropathological features identified in older adults with MCI typically fall within an intermediary stage of severity from normal ageing and early AD (Stephan et al., 2012). The various features that are present in MCI include diffuse cortical amyloid deposition, degeneration of the cholinergic system, synaptic loss and neurofibrillary tangles in the MTL (Mufson et al., 2012; Petersen et al., 2006; Stephan et al., 2012). Additionally, atrophy is consistently found in the MTL, particularly the hippocampus, entorhinal cortex, and in the PCC (Kim et al., 2010). It is often the case that these areas are the first to experience atrophy, but as the cognitive decline continues, the atrophy will spread to parietal association areas and then onto the frontal and primary cortices (Braak & Braak, 1991). Nevertheless, there is a great deal of heterogeneity within these neuropathological features; some individuals with MCI do not exhibit the neuropathological changes expressed in those that go on to develop AD (Stephan et al., 2012; Mufson et al., 2012). Yet, evidence suggests that neuronal loss in the hippocampus, entorhinal cortex and subiculum are commonly found and are predictive of conversion to AD (Su et al., 2018).

Following the continuation of white matter decline found in ageing, individuals with MCI also exhibit further significant reductions in multiple white matter regions (Medina et al., 2006) and reduced cortical thickness in the precuneus and temporal cortex (Román & Pascual, 2012). Longitudinal evidence from MRI data has shown that cortical thinning in the temporal poles and left MTL is detectable before the

development of cognitive decline symptoms in those who go on to develop AD (Pacheco et al., 2015). Moreover, individuals with MCI who develop AD also show greater cortical thinning at baseline measurements relative to those who remain stable after seven years in the superior and middle frontal, inferior temporal gyri, fusiform gyrus and the parahippocampal regions (Julkunen et al., 2009).

A definitive diagnosis of AD relies on the detection of amyloid-beta plaques in autopsy (Mirra et al., 1991). Despite poor understanding of the cause of amyloid-beta plaques, the Apolipoprotein E allele 4 (ApoE4) is a reported risk factor for increased amyloid deposition (Villemagne et al., 2008) and the development of AD (Nagele et al., 2004). Neuroimaging studies have demonstrated that ApoE4 genotypes have a remarkable influence on reducing both grey matter (Pievani et al., 2009) and white matter volume (Wang et al., 2017) in subjects with aMCI. Additionally, cortical atrophy of the hippocampus, anterior cingulate and amygdala have been found in stable MCI patients with ApoE4 (Hämäläinen et al., 2008; Tang et al., 2015) and extending to frontal, parietal and temporal lobes with the development of AD (Hämäläinen et al., 2008). It remains unclear how ApoE4 alters the brain's neuroarchitecture, although evidence does appear to indicate poorer memory function is related to higher beta-amyloid (Mormino et al., 2009; Rodrigue et al., 2012) and having the ApoE4 allele (Li et al., 2014; Striepens et al., 2011), albeit not consistently (Aizenstein et al., 2008).

Structural neuroimaging studies provide strong evidence of the progressive decline from healthy ageing towards AD. The MTL, including the hippocampus and the entorhinal cortex are among the most prominent indicators of cognitive decline (Du et al., 2004; Pennanen et al., 2004). Individuals with AD show hippocampal and entorhinal cortex volume reductions of 26–27% and 38–40%, respectively, relative to healthy controls (Du et al., 2004). Individuals with MCI show intermediate levels of atrophy in these areas (Pennanen et al., 2004). Moreover, atrophy of the MTL within AD has been linked to poorer memory and executive functioning in AD (Oosterman et al., 2012) and is a strong indicator of progression for MCI to AD (Nesteruk et al., 2015). Other studies correlating executive function and grey matter loss have found noticeable impairments in the basal forebrain (Kilimann et al., 2017) and in the frontal and temporal cortices in MCI (Duarte et al., 2006), although frontal impairments are not consistently found. In a review on white matter integrity (Madden et al., 2012),

differences in the frontal cortices were absent in MCI but were apparent in AD suggesting frontal lobe decline may only become evident with disease progression.

Diffusion tensor imaging studies of MCI and AD have provided further support of abnormalities in the basal forebrain (Brüggen et al., 2015), and have found that these abnormalities are associated with executive function (Sjöbeck et al., 2010) and episodic performance (Hirni et al., 2013) in AD. Marked hypoperfusion, shown by cerebral blood flow, has also been shown in the posterior cingulate, occipital, temporal, precuneus and parietal cortices in MCI and AD (Alexopoulos et al., 2012; Dai et al., 2009; Gao et al., 2014; Sexton et al., 2011), although this is notably greater in AD than in MCI. Moreover, MCI patients demonstrate limited compensatory mechanisms within the basal ganglia, amygdala and hippocampus as shown by increased cerebral blood flow relative to healthy controls (Dai et al., 2009).

Compensatory mechanisms in older adults with MCI have also been demonstrated in fMRI studies, showing hyperactivation of hippocampal regions during encoding in memory tasks relative to healthy controls (Trivedi et al., 2008; Parra et al., 2013). Despite this, other studies have shown those with MCI do exhibit comparable levels of hippocampal deactivation to older adults with AD during memory recall (Petrella et al., 2007). Functional MRI studies of attention (C. Li et al., 2009; Van Dam et al., 2013) and working memory (Clément et al., 2013) similarly have reported overactivation of bilateral and middle temporal, middle frontal, anterior cingulate, fusiform gyrus posterior parietal regions in those with MCI.

Studies examining the complex interactions of resting-state functional connectivity have found impaired PCC–MTL functional connectivity in individuals with aMCI (Sorg et al., 2007) and with AD (Zhou et al., 2008). Some results demonstrate decreased connectivity between the PCC and the temporal cortex and increased functional connectivity of the PCC and the frontal cortex in aMCI patients relative to healthy controls (Bai et al., 2009). Functional connectivity within the default mode network (DMN) has been of interest in dementia-related diseases.

The DMN is comprised of the medial and dorsal PFC, inferior parietal cortex, ventral anterior cingulate, inferior lateral temporal cortex, orbitofrontal cortex, PCC and parahippocampal gyrus (Greicius et al., 2003). Research shows patterns of dysfunctional connectivity in individuals with MCI between the MTL and other regions

of the DMN (Das et al., 2013) and from the areas outside of the DMN to the PCC (E. Yu et al., 2017). However, limited increases in connectivity were also show in these studies within the anterior and ventral DMN, which is similarly found in those with early AD before exhibiting a decline in these connectivity patterns in line with disease progression (Damoiseaux et al., 2012). The evidence suggests that during stages of connectivity decline, some areas of connectivity diminish but are compensated through the increased reliance on other cortical networks (Damoiseaux et al., 2012).

The different neuroimaging studies of MCI have highlighted that the MTL (hippocampal and entorhinal regions), PCC, temporal cortex, and the basal forebrain as being particularly sensitive to cognitive decline and to a lesser extent the occipital and parietal cortices. The literature suggests that as networks become impaired through cognitive decline, compensatory mechanisms through alternative routes may become active to support cognitive functioning.

2.6 Neurobiology of Prospective Memory in Mild Cognitive Impairment

To date no neuroimaging studies of PM have been conducted either on MCI or AD. However, given the behavioural and psychological evidence of MCI performance and PM (outlined in Chapter 1), and the current understanding of the underlying neuromechanisms of PM, hypotheses can be drawn on how PM might be neurophysiologically impaired in those with MCI relative to healthy older adults.

Older adults carrying a copy of the ApoE4 allele demonstrate poorer cognition in comparison to those who are not carriers (Marioni et al., 2016; Small et al., 2004; Wisdom et al., 2011) and even poorer cognition in those who are homozygotic carriers (Caselli et al., 2008; Small et al., 2004). ApoE4 carriers with mild AD were more impaired on focal PM retrieval accuracy compared to non-ApoE4 matched controls (Duchek et al., 2006). An ApoE4 disadvantage has also been found in focal and non-focal PM retrieval performance in healthy older adults (Driscoll et al., 2005), but was not supported in a later study for both the focal and non-focal tasks (McDaniel et al., 2011). The relationship between the ApoE4 gene and cortical atrophy may account for PM deficits in MCI, although this has not yet been conducted directly on individuals

with MCI. This notion is partially supported by evidence suggesting a genotype-specific variation in neural activity during PM, as evidenced by cognitive enhancements to the right hippocampal formation in ApoE4 carriers after receiving nicotine (S. Evans et al., 2013). It is important to note, however, that studies of ApoE4 and cognition are not consistently reported (Bunce et al., 2004, 2014; Salo et al., 2001). This is likely due to sensitivity of the domain under study, creating variability in the reported results.

A more promising means of determining the affected neurobiological areas of PM in those with MCI is by using the AtoDI model as a framework. By using the AtoDI model, each of the neurobiological structures believed to be involved with PM functioning at different stages can be compared with research on MCI within that neurobiological area. Inferences about which stage of PM and which neurobiological structures are the most likely to be impaired in those with MCI can then be drawn.

Considering the encoding stage of PM, it might be speculated that the poor ability to encode an PM intention underlies poorer PM performance in MCI (Costa et al., 2011), which may be because of degeneration in the PCC (*see Section 2.5*). Indeed, Papma et al. (2017) demonstrated a significant relationship between the PCC and hippocampus during episodic memory encoding and the correct recognition of items in MCI patients. They suggest that during episodic memory encoding network deterioration is the most important predictor of PCC functioning in MCI. However, given the absence of a control group, the effect of typical and atypical ageing on episodic memory based on their study remains unclear. Nevertheless, other studies of episodic memory encoding support deterioration in a network centred around PCC and the MTL (Chetelat et al., 2003; Gomar et al., 2017; Hampstead et al., 2016). For example, Hampstead et al. (2016) used fMRI to assess functional connectivity during memory encoding. They suggest that episodic memory encoding in healthy older adults is principally driven by the inferior frontal junction, anterior intraparietal sulcus and the PCC. However, individuals with MCI had reduced PCC connectivity and instead relied more on the retrosplenial cortex (BA29/30) and the frontal eye fields (BA8). It would be expected, therefore, that the functional impairments of the PCC may account for the poor PM performance of individuals with MCI.

Regarding maintenance of the PM intention, generally little evidence demonstrates impaired structural integrity of the aPFC, dorsal PFC and dorsal parietal cortex in individuals with MCI relative to healthy older adults. Thus, following correct encoding,

the maintenance of the intention should remain relatively intact compared to healthy older adults. However, functional studies of attention show attenuated prefrontal activation on a divided attention task in MCI (Dannhauser et al., 2005). This would suggest that the attentional network responsible for PM intention maintenance of may be impaired. This seems fitting given the previously discussed studies showing that PM performance was poorer for the MCI patients despite them successfully remembering the encoded PM intention (Costa et al., 2010). However, the frontal systems are more impaired in individuals with MCI that go on to develop AD than those who do not (Ogama et al., 2016). Therefore, the frontal systems and intention maintenance may decline later in dementia-related diseases and may serve as a sensitive indicator of progression towards AD.

The evidence suggests that the retrieval stage of PM will be significantly impaired in older adults with MCI. In combination with the behavioural evidence suggesting poorer PM retrieval because of MCI, memory studies have also implicated those neurological systems important for the retrieval of memories in MCI. According to the AtoDI model of PM, the insula is the first neurological system in intention retrieval. Insula grey matter atrophy has frequently been reported in MCI (Caroli et al., 2010; Davatzikos et al., 2011; Fan et al., 2008; Spulber et al., 2012). Additionally, Xie et al. (2012) have linked the intrinsic connectivity of the insula in those with MCI to poorer episodic memory scores. Other areas involved in retrieval that are consistently found to be affected in MCI are the MTL and the PCC (Das et al., 2013; L. Zhang et al., 2019). Both of these systems are known to be critical in the role of memory (Maddock et al., 2001; Suzuki & Amaral, 2004) and have specifically been implicated in the role of memory retrieval (Rugg & Vilberg, 2013; Schacter & Wagner, 1999). Taken together, PM in older adults with MCI may be affected by atypical functioning in the insula, PCC and MTL and it would, therefore, impact the ability to successfully retrieve a PM intention.

As illustrated in Figure 2.3, the neurobiological evidence suggests that the most likely stage to be impaired in PM is the retrieval stage. This is based on the reported impairments in the insula, PCC and MTL in MCI. Given the role of the PCC in the encoding stage of PM, it may be expected that those with MCI will have poor PM intention encoding abilities, which may affect the ability to later recall an intention. It is unclear whether intention maintenance will be affected in MCI. However, given the

reduced activation found in those with MCI during divided attention tasks, the attentional demands of a PM task may also affect the prefrontal cortices and, therefore, the ability to maintain an intention. The neurobiological impairments in MCI cross-referenced with AtoDI, provides a useful reference to begin exploring the potential neurophysiological impairments of PM in MCI.

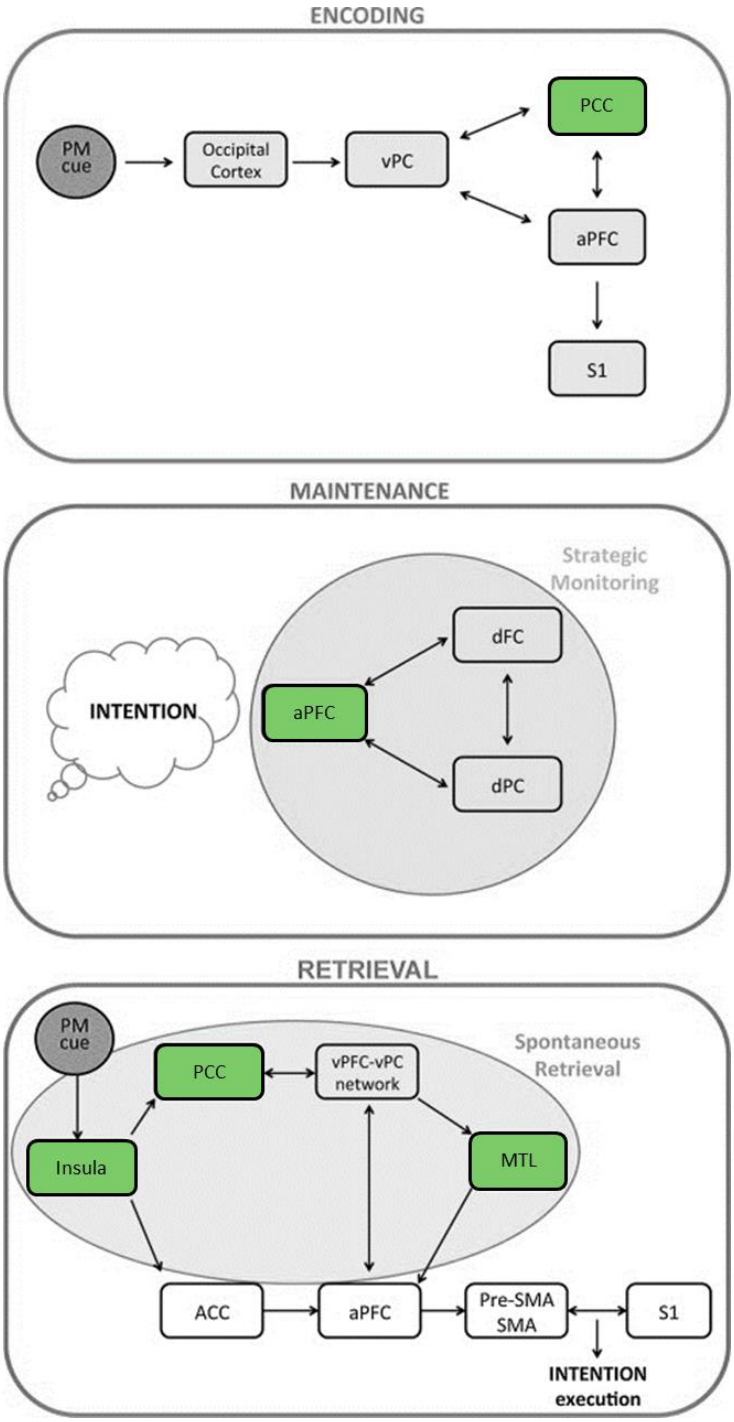

Figure 2.3. Graphic illustration of the impaired stages and brain areas of prospective memory in older adults MCI proposed in S*ection 2.6*. Areas highlighted in green are reported to have impairments due to MCI. *N.B.* ventral parietal cortex = vPC; posterior cingulate cortex = PCC; anterior prefrontal cortex = aPFC; primary somatosensory area = S1; dorsal frontal cortex = dFC; dorsal parietal cortex = dPC; posterior cingulate cortex; vPFC = ventral prefrontal cortex; ventral parietal cortex = vPC; medial temporal lobe = MTL; anterior cingulate cortex = ACC; sensory motor area = SMA.

2.7 Chapter Summary

Chapter 2 has outlined the two predominant neurobiological theories of PM, namely the 'Gateway Hypothesis' (Burgess et al., 2005) based on the reliably found mediolateral dissociation of the aPFC and the AtoDI model (Cona et al., 2015), which attempts to combine the AtoM model of episodic memory (Cabeza et al., 2008; Ciaramelli, 2010) with the dual-attention model (Corbetta & Shulman, 2002). Additionally, this chapter has outlined the brain areas commonly affected by ageing, particularly implicating deficits found in the PFC and an emerging line of research suggesting cognitive decline may be, in part, due to dedifferentiation of neuronal sources. Furthermore, the scant research surrounding the neurobiological effects of ageing on PM is highlighted showing that current understanding is both limited and mixed. The neurobiology of MCI is detailed, highlighting areas such as the PCC as a predominate area indicative of cognitive decline. Finally, using the AtoDI model of PM and the predominant areas thought to be implicated in cognitive decline, hypotheses are formed regarding the neurobiological structures most likely to account for impairments of PM in older adults with MCI. Chapter 3 describes how these neurobiological networks may be reflected in electrophysiological neuroimaging methods and how they may vary between typical and atypical ageing.

Chapter Three: Electrophysiology of prospective memory, ageing and mild cognitive impairment

3.1 Introduction

Chapter 3 builds upon the neurobiological theories and networks outlined in Chapter 2. Specifically, this chapter describes the current understanding of the electrophysiological findings of PM in young and healthy older adults. The current chapter also describes the effect of cognitive decline on electrophysiology and hypothesises are made regarding how cognitive decline will impact PM related electrophysiology. The established findings of electrophysiology related to PM are discussed along with the findings that are less clear. Finally, this chapter discusses the use of an innovative artificial intelligence (AI) technique known as Spiking Neural Networks, which has the potential to improve our understanding of PM, ageing and cognitive decline.

3.2 Electroencephalography and Event-Related Potentials

Electroencephalography (EEG) was first recorded in humans by Hans Berger (1924). It was described as amplified extracellular activity surrounding postsynaptic neurons, which can be recorded at the scalp (Berger, 1929). It is, therefore, a relatively direct measure of underlying electrocortical activity. These electrocortical signals are the summation of many thousands of synchronous firings of excitatory and inhibitory postsynaptic potentials (Cohen, 2014). Estimates place 10,000–50,000 pyramidal cells to be synchronously discharging for EEG and MEG sensors to register a detection (Murakami & Okada, 2006). This detection is possible due to the parallel alignment of the pyramidal neurons and the size of the cell bodies being large enough to create a detectable electric field.

Electroencephalographic signals that are time-locked to the presentation of a behaviour or response to stimulus are known as event-related potentials (ERPs). An ERP can be broken down into several subcomponents reflecting stimulus-related processes (Luck, 2014; Luck, 2006). They are visualised as positive and negative deflections relative to a baseline known as a reference, which can be altered for optimal voltage contrast. Both the relative amplitudes (measured in microvolts) and latencies (measured in milliseconds) can be analysed and compared between conditions and across groups to determine how experimental changes might influence specific cognitive processes. Usually, component amplitudes are measured from the peak of a component with reference to a baseline[1] and latencies are calculated from the component peak following stimulus onset.

Components recorded at the scalp consist of a series of temporally overlapping subcomponents and therefore changes exhibited at one component will affect components later in time (Luck, 2014). This effect is most robust across earlier occurring components and often results in enhancement or attenuation of the amplitude along with delays to the component's latency. Through the comparison of ERP amplitudes and latencies, one can determine how neurocognitive processes are altered in neurological disease. ERPs, therefore, present a particularly useful way to understand neurophysiological dysfunction (Donchin, 1979; Luck, 2014; Rugg & Coles, 1995).

A single time locked ERP response may be relatively small compared to the ongoing background noise of the brain and it is often difficult to discriminate task related ERP components from a single trial (Luck, 2006). As noise is assumed to be constant during EEG, averaging ERPs across multiple events reduces the background noise and helps to enhance the signal-to-noise ratio of the ERP (Luck, 2005). Averaging across multiple trials removes unwanted modulations in the data and boosts the statistical power. The resulting averaged waveform represents a single task-specific response (Luck, 2006). The positive and negative deflections of the averaged waveform can be then used to examine the subcomponents related to cognitive processes. Typically, the voltage deflections are named after the polarity in which they are detected and the approximate time that they occur. For example, a positive deflection at 300ms after

[1] The area under an ERP component can also be measured but is not used within the current thesis.

stimulus onset is known as the P3 (or P300; Coles & Rugg, 1996; Otten & Rugg, 2005). A negative deflection occurring approximately 200ms post-stimulus onset is known as the N2 (or N200; Folstein & Van Petten, 2008). It should be noted however, that due to the complex folds of the gyri and sulci within the cortex, it is difficult to determine the real physical direction of the ERP deflection without an MR image of the subject's head. Therefore, the naming convention used for an ERP subcomponent does not necessarily pertain to its underlying neurophysiology (Otten & Rugg, 2005).

Nevertheless, ERP methods offer a considerable advantage over MR imaging methods due to their high temporal resolution. Hemodynamic measures (e.g., fMRI and PET) of functional activity have a temporal resolution of several seconds (Luck, 2005). ERPs, however, have a temporal resolution in the order of milliseconds (Otten & Rugg, 2005) making it well suited to measure rapid neuronal changes reflective of underlying cognitive processes. For example, ERP components occurring between 80–120ms post stimulus reflect sensory processing and selective attention (Gallinat et al., 2002). ERPs occurring between 160–350ms, such as the posterior N2, are related to visual attention (Folstein & Van Petten, 2008) and stimulus discrimination (Hoffman, 1990). The later components occurring after 300ms are associated with top-down processes and higher cognitive functions (Coles & Rugg, 1996).

Compared to other neuroimaging methods, the spatial resolution of EEG methods is relatively low. The poor spatial resolution is due to the summation of distal and proximal sources affecting scalp-recorded activity, and diffusion of current through biological tissue (Makeig et al., 1996). Spatial resolution for EEG is estimated to be between 5–9cm (Babiloni et al., 2001; Nunez et al., 1994). Moreover, because ERPs are generated by multiple neural sources, it is often difficult to delineate specific subcomponents from the ERP waveform. However, reliable source localisation is achievable and improved through high-density EEGs and novel analysis methods (J. Song et al., 2015).

Studies of PM using ERPs have identified three primary components related to PM functioning. These include the N300, the frontal positivity and parietal positivity (West, 2011). The N300 and frontal positivity are related to PM cue detection, while the parietal positivity is related to the retrieval of PM intentions. The following section details the ERPs related to PM along with the current understanding of how they affected by ageing and MCI. Additionally, the following section proposes the relevance

of an additional ERP component to PM and ageing, which reflects the reorientation of attention following response to a PM stimulus known as the reorientation negativity (Berti, 2008).

3.3 Prospective Memory Event-related Potentials

3.3.1 N300 / Frontal positivity

The N300 (illustrated in Figure 3.1) has previously been identified as being related to PM cue detection (Einstein & McDaniel, 1996; West et al., 2006b). It is characteristically identified as a negative potential over occipitotemporal scalp regions. It usually begins between 200–300ms following stimulus presentation and reaches a peak around 300–500ms (West, 2007, 2008; West et al., 2001, 2011). N300 amplitudes are typically greater (i.e., more negative) for successful PM behavioural responses, than for PM performance failures and for ongoing activity (West, 2011). The larger N300 amplitudes to successful PM cue responses suggest that the N300 is an essential component of event-based PM. N300 amplitude increases have been observed when embedded in various ongoing cognitive tasks (e.g., *n*-back, lexical decision and continuous recognition tasks) and in varied PM stimulus types (e.g., word identity, letter case, colour; Cruz et al., 2016; West et al., 2003; West & Krompinger, 2005; West & Wymbs, 2004). This suggests that the N300 is a reliably occurring ERP component of PM.

Nevertheless, some research has demonstrated that N300 ERPs are not found in response to PM stimuli that are non-perceptual in nature (J. Wilson et al., 2013). Wilson and colleagues (2013) reported that non-perceptual PM cues did not produce an N300 response due to the semantic nature of the PM task (e.g., an animal word). Similarly, Cousens et al. (2015) also did not detect an N300 response to non-perceptual (semantic) PM stimuli despite finding an N300 response to perceptual PM stimuli. Taken together these results suggest that the N300 may not be a general marker of underlying PM cue detection. However, in another study evaluating conceptual and perceptual PM stimuli, Cruz et al. (2016) did find a PM cue detection response for both stimulus types, but the non-perceptual N300 was delayed by 100ms. Thus, it is unclear whether conceptual, semantic-based PM will elicit an N300 response in comparison to

the ongoing working memory tasks. A possible explanation for the discordant results between Cruz and colleagues' study (2016) and Cousens and colleagues' study may be due to how the PM stimuli comparisons were made. In Cousens and colleagues' (2015) study, ERP amplitudes in response to PM stimuli were compared to the averaged waveforms of two different ongoing task responses (related and unrelated lexical decisions). However, in Cruz and colleagues' (2016) study, the PM-related ERPs were compared against ERPs to related and unrelated ongoing stimuli. Averaging ERPs in response to two ongoing stimulus types may have inappropriately changed the ERP waveforms and therefore affected the ability to detect the ERPs related to PM cue detection.

The frontal positivity component (illustrated in Figure 3.1) is also associated with PM cue detection and is found to correspond to the onset of the N300, but occurs over midline frontal sites (West, 2011). In addition to cue detection, the frontal positivity is reportedly related to task switching (West, Bowry & Krompinger, 2006; West, 2007; Bisiacchi, Schiff, Ciccola & Kleigel, 2009; West, 2011) and target checking (West, 2007). Given the dual-task nature of most PM experiments, it could be argued that the frontal positivity reflects executive control processes recruited when moving from the ongoing task to the PM aspects of the task (Bisiacchi et al., 2009). Indeed, research has made a strong case for executive functions being an essential predictor of PM performance (Schnitzspahn et al., 2013) and the frontal positivity may reflect the engagement of such functions (Nyhus & Barceló, 2009).

Studies have confirmed the relationship of the N300 and frontal positivity to PM cue detection through experiments using PM lures, which share some, but not all the features of the PM cue. West and Covell (2001) found sustained negativity over aPFC scalp regions and an N300 response in young adults in response to PM cues and PM lures. West and Covell suggest that the frontal positivity and N300 were elicited for PM cues and lures because the features elicited cue detection responses, which were not found in response to the ongoing task stimuli. Like the N300, the frontal positivity has been reliably distinguished from the ongoing activity across a range of PM stimulus types (West et al., 2007; West & Ross-Munroe, 2002). The results suggest that both the N300 and frontal positivity are central features to the detection of PM cues.

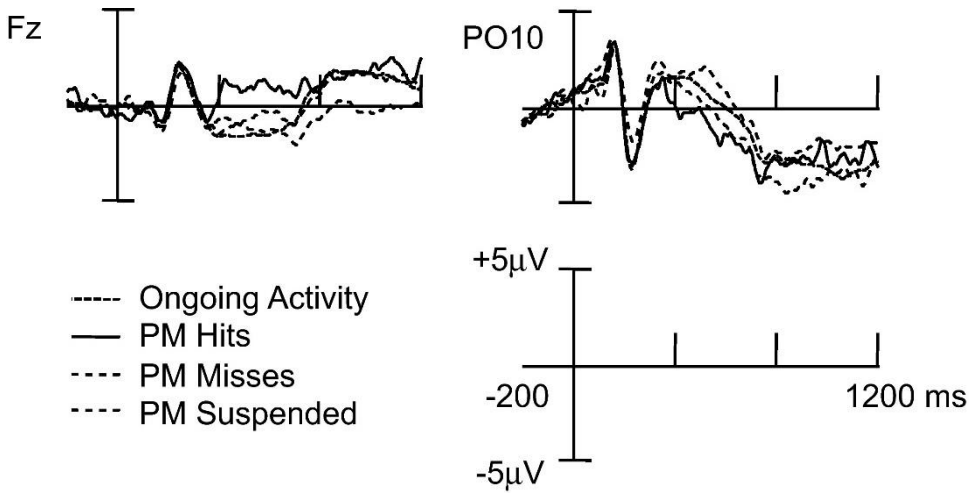

Figure 3.1. Grand-averaged ERPs of the N300 (right) and the frontal positivity (left) differentiating PM hits from ongoing activity trials, PM misses and PM cues. The tall bar represents stimulus onset and the short bars represent 400ms intervals. From "Temporal dynamics of prospective memory: A review of the ERP and prospective memory literature" by West 2011, *Neuropsychologia*. Copyright Elsevier 2011. Adapted with permission.

3.3.2 Parietal positivity

The parietal positivity is a late positivity complex generated over the parietal region of the scalp between 400–1200ms after stimuli presentation (West, 2011). Whereas the N300 and frontal positivity can be thought of as reflecting the *prospective* component of PM, the parietal positive reflects the *retrospective* component and the realisation of delayed intentions (West, 2011). The parietal positivity is a robust component of PM research and is reported throughout a variety of PM paradigms (e.g., Cona et al., 2014; Cruz et al., 2016; Hering et al., 2016, 2018; West, Herndon, et al., 2003; West & Krompinger, 2005). It is suggested that the parietal positivity incorporates three ERP subcomponents. These are the P3b, the parietal old-new effect and the prospective positivity (West, 2011). The parietal positivity has a strong relationship with ERPs related to the detection of low-frequency events. This relationship makes disentangling neurocognitive correlates of the parietal positivity difficult in determining the precise processes related to PM.

3.3.2.1 P3b

The P3b (illustrated in Figure 3.2) is a well-observed ERP component associated with the allocation of attentional processes towards low probability events (Kok, 2001; Polich, 2007). Onset typically occurs between 300–400ms over centroparietal and parietal regions and is commonly observed in studies using oddball designs (Luck, 2014), which shares commonalities with PM task designs. Numerous studies have been successful in distinguishing the parietal positivity components from that of the P3b (West et al., 2006b; West & Krompinger, 2005; West & Wymbs, 2004). West & Krompinger (2005) were able to effectively differentiate the prospective positivity from the P3b through manipulation of the ongoing task design. The results found that while the P3b was sensitive to changes in the design, the prospective positivity was not. West & Krompinger suggested that the sustained positivity may represent a general function of PM.

Support for this differentiation between the parietal positivity and the P3b was further demonstrated through manipulation of the ongoing task working memory load (West et al., 2006b). The results from West and colleagues' (2006) experiments found that the P3b could be reduced depending on the cognitive load that was placed on the participant's working memory. However, the amplitude of the prospective positivity would remain unaffected. The prospective positivity being unaffected by working memory load provides an important distinction because although the P3b might be necessary for the detection of rare stimuli (Polich. 2007) it is functionally distinct from the prospective positivity. The P3b, therefore, is a vital feature to the parietal positivity as cue detection is required but does not reflect retrieval processes of PM cues.

3.3.2.2 Prospective Positivity

The later part of the prospective positivity complex (illustrated in Figure 3.2) is comprised of the so-called parietal "old-new effect"[2] and the prospective positivity (West, 2011). The old-new effect occurs between 400–600ms after stimulus onset, and the prospective positivity occurs between 600–1000ms, predominately over parietal regions. The old-new effect ERP reportedly reflects the retrospective processes

[2] The author believes that this nomenclature is not appropriate for PM, as it implies that the encoded PM intention has been seen before, which is often not the case in PM experiment designs.

involved with PM (West, 2011) and is thought to engage similar neural mechanisms to episodic memory, such as recognition and cued-recall (Einstein & McDaniel, 1996; McDaniel & Einstein, 2000). In a study by West and Krompinger (2005), the ERP activity in response to a PM and a recognition memory task were compared. The results show that the recognition old-new effect was produced in response to correct responses in the recognition task and in the PM task relative to ongoing activity. Given the similarities of the prospective positivity to the old-new effect, such that it is often a sustained amplitude continuation of the old-new effect, it is uncertain if these are distinct neural correlates.

Nevertheless, a series of studies have provided evidence to suggest that the old-new effect and prospective positivity may be cognitively independent (West, 2007; West et al., 2007; West & Krompinger, 2005). In West and Krompinger's (2005) study comparing ERPs in response to recognition hits and PM hits, the authors used a multivariate, partial least squares (PLS), analysis to determine whether the old-new effect and prospective memory could be differentiated. A PLS analysis is designed to extract distributed signal changes related to the designs of a cognitive task. It is similar to principles components analysis (PCA), which is able to uncover and reduce ERP activity to latent variables that are responsible for patterns of covariation (Dien et al., 2007). However, PLS is different from PCA as it can use a reduced covariance matrix that includes only variance related to the task, such as ERP modulations that differentiate the task conditions. Through this technique, West and Krompinger found that the prospective positivity could be differentiated from the old-new effect in response to PM hits and found that it occurred later in time relative to the old-new effect.

It remains unclear precisely what the prospective positivity reflects, although one theory suggests its relationship to task configuration and task switching (West, 2011). Bisiacchi et al. (2009) explored the hypothesis that the prospective positivity is associated with task switching by examining the prospective positivity in a dual-task and task-switch condition. Their results demonstrated that ERPs in response to PM cues could be distinguished from ongoing activity in both conditions, but the task-switch condition caused greater sustained prospective positivity amplitudes. The authors therefore concluded that the prospective positivity was related to the task configuration and task-switching. However, little evidence has provided further

support for this conclusion. Moreover, many studies differ on their definition of the prospective positivity and time of onset. Some researchers group the prospective positivity with the old-new effect (e.g., Cousens et al., 2015; Wilson et al., 2013; Zöllig et al., 2007), while others will treat the components as separate (Cona et al., 2012; West, 2007; West et al., 2006a; West, Herndon, et al., 2003). Combing the two components causes difficulties when drawing conclusions from different researchers. Research into the prospective positivity remains limited and warrants further study (West, 2011). It is important for research to determine the cognitive function of the prospective positivity and whether it is appropriate to combine these components under the umbrella term of 'parietal positivity' for specific tasks.

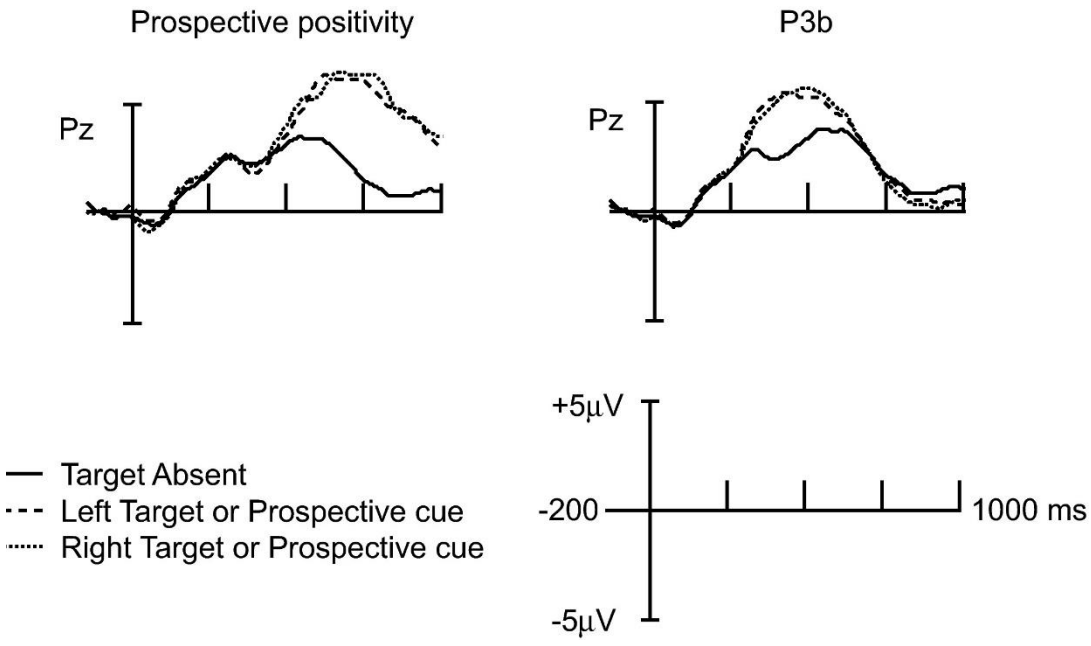

Figure 3.2. Grand-averaged ERPs illustrating the P3b (right) and the parietal positivity (left) for PM hits. The tall bar represents stimulus onset and the short bars represent 250ms intervals. From "Temporal dynamics of prospective memory: A review of the ERP and prospective memory literature" by West 2011, *Neuropsychologia*. Copyright Elsevier 2011. Reprinted with permission.

3.3.3 ERPs of prospective memory monitoring

The PAM theory of PM (Smith, 2008; Smith et al., 2007, 2010) states that allocation of attentional processes must be employed to perceive PM cues successfully. However, the Multiprocess framework suggests that attentional processes are only allocated when reliance on spontaneous processes are insufficient (Einstein et al., 2005; Knight et al., 2011; Scullin, McDaniel, & Einstein, 2010). Behavioural evidence has often reported that response times to the ongoing task are slower when participants are required to remember a PM intention compared to when performing just the ongoing task (Einstein et al., 2005; Heathcote et al., 2015; Smith, 2003). Neuroimaging studies have noted specific activity in the dorsal aPFC and precuneus while monitoring ongoing stimuli for PM cues (e.g., Beck et al., 2014; Kalpouzos et al., 2010; Oksanen et al., 2014). Similarly, electrophysiological studies have explored the effects of monitoring on ERPs and the "PM interference effect" (e.g., Czernochowski et al., 2012; Hering et al., 2020; West, 2007; West et al., 2006a).

Initial studies by West (2006; 2007) reported an ERP monitoring effect when examining perceptually salient PM cues. The researchers found increased posterior negativity for the N2 when ongoing tasks were performed concurrently with PM tasks relative to performing the ongoing task independently. ERP studies have since replicated these results across different variations within the PM and ongoing tasks (Cona, Arcara, et al., 2015; Czernochowski et al., 2012; Knight et al., 2010). The prevalence of the N2 modulations during PM monitoring suggests a robust effect of top-down attentional networks in perceptual event-based PM tasks (Knight et al., 2010). Furthermore, enhanced N2 modulations have also been shown for less perceptually salient conceptually based PM cues (Cruz et al., 2016). Using an independent component analysis (ICA), Cruz and colleagues (2016) demonstrated that this earlier monitoring effect is predominately found in parietooccipital regions.

Monitoring effects are found to also modulate frontal amplitudes between 400–900ms (Cona et al., 2012b, 2014; Czernochowski et al., 2012) and between 800–1600ms (Hering et al., 2020). For instance, Czernochowski and colleagues (2012) contrasted sustained frontal ERP modulations in responses to ongoing task stimuli when monitoring for PM cues relative to ongoing-only task stimuli. They found that when monitoring for a PM cue, there was sustained frontocentral activity thought to reflect

monitoring behaviour and the application of attentional processes, which has been associated a PM 'retrieval mode' (West et al., 2011).

3.3.4 The reorientation negativity; a missing piece of the prospective memory puzzle?

A few studies have explored the ERPs related to the role of task switching and PM (Bisiacchi et al., 2009; West et al., 2011) primarily to test the strategic monitoring aspect of the PAM theory (Smith, 2005). As previously mentioned, Bisiacchi and colleagues (2009) were able to discern ERP response to PM cues from ongoing trials within a dual-task and task-switching conditions but found that the prospective positivity amplitudes in the task-switch condition were increased. West et al. (2011) demonstrated that PM-related ERP components were also modulated during conditions requiring task-switching. The authors conclude that these amplitude changes relative to ongoing activity and non-switch conditions represent the switching of attention from the ongoing task to the PM task. However, to date, no studies have examined ERP components that might reflect the switching of attention from the PM task back to the ongoing task. Research into distraction and the reorientation of attention may help to clarify this issue.

In the last few years, there has been a dramatic increase in the number of studies exploring the reassignment of attentional processes to a primary task following a distracting stimulus (review: Justo-Guillen et al., 2019). Typically, distraction and subsequent reorientation have been studied through oddball and dual-task paradigms (e.g., Allard & Isaacowitz, 2008; Parmentier & Hebrero, 2013; Rämä et al., 2018; Scheer et al., 2016; Wester et al., 2008). Recently, modified versions of these paradigms have been used to further tease out the neurophysiological impact of reorienting of attention (e.g., Berti & Schröger, 2003; Yago et al., 2001). The results from one such study (Schröger & Wolff, 1998) revealed that along with the expected mismatch negativity (MMN) and P3a response (two prominent distraction related ERP components), a distinct negative component occurring between 400–600ms following distraction stimuli was also found. This negative component was subsequently termed the reorienting negativity (RON).

Many experiments since Schröger & Wolff's (1998) study have manipulated experimental features to gain better insight into the associated cognitive mechanisms of the RON. For example, Yago et al. (2001) tested participants on a visual discrimination task with deviant pitch changes in a preceding auditory stimulus. The pitch changes varied in its frequency as a percentage difference from the ongoing standard tone. Despite behavioural changes only being found for one distractor condition, the RON amplitude increased in line with the rise in stimulus deviance from the ongoing stimuli. The finding was replicated in a purely auditory version of this task, but it was also found that distractors increased reaction times (Berti et al., 2004). These findings indicate that the features of the distractor tasks influence the strength of the RON. This led Berti and colleagues to the belief that non-auditory forms of distractor stimuli may also elicit such a response in other dual-task designs. A study by Berti (2012) compared the efficacy of rare versus novel stimuli as deviants in a multimodal oddball. Across three conditions, the deviant stimuli varied in their novelty and rarity. The RON was found to be more pronounced in the novel and rare conditions compared to the ongoing task. Additionally, the novel and rare RON responses did not differ from one another, suggesting a common neural response for reorienting from the target back to the ongoing task.

Studies have investigated the role of working memory in the RON ERP. Berti and Schröger (2003) administered a standard oddball paradigm but required participants to withhold their response until the subsequent trial. Delaying the response increased the required working memory processes to complete the task and consequently resulted in slowed reaction times and decreased RON amplitudes. The connection between reaction times and the RON amplitude suggests that as working memory difficulty increases, the RON amplitude decreases. It would be expected then, that if an individual had poor working memory, then the RON response would be subsequently reduced relative to an individual with good working memory.

SanMiguel et al. (2008) also varied the use of working memory during an auditory/visual oddball task using a memory and a no-memory condition. The memory condition resulted in poorer reaction time and accuracy compared to the no-memory condition. However, the RON amplitude increased within the memory condition, contrasting with Berti and Schröger's (2003) results. Possibly, the variations may reflect different features of the RON. According to Munka and Berti,

(2006), the differences between these two studies may be due to the refocusing on task-relevant information in working memory or a general reorientation of attention mechanisms (Escera et al., 2001) as evidenced in their study which varied the demands of the visual task. Therefore, Berti and Schröger's (2003) results may reflect reorientation of attention and SanMiguel et al.'s (2008) results may reflect the greater engagement of working memory as task-relevant information is reactivated in working memory for the ongoing task.

It is well established that task-switching is required for experimentally based PM tasks (Fronda et al., 2020; Meier & Rey-Mermet, 2018). Given the similarity of the described experimental designs used in the distraction literature and in the PM literature (i.e., both use a dual-task or task-switch design), it is surprising that a RON response has not been described before in PM studies. PM tasks require a momentary interruption from the ongoing task to complete the PM task. Following completion of the PM task one must reallocate attention towards to the ongoing task once again. Cognitive resources may, therefore, be used to shift attention and to prepare for reengagement with the ongoing task, similar to studies of distraction. The latency of the RON would therefore indicate the timing termination of the PM task and redirection of resources.

Over various studies, the RON has been found to occur over frontal brain regions (Correa-Jaraba et al., 2016; Escera et al., 2001), occurring anywhere between 300–750ms post stimulus onset (Getzmann et al., 2015; Munka & Berti, 2006). However, a study employing scalp density analysis (SCD; an analysis method for calculating current densities that are tangential to the currents produced by neuronal dipoles) revealed that the RON is produced by multiple neural generators (Schröger et al., 2000). It is likely then, that RON may be prominent in different scalp regions depending on the task being performed. Due to the variability in RON onset reported across these studies and the different reported locations of the RON, identification of the largest peak across the whole RON time window and all scalp regions would allow for a better understanding of the RON in PM.

In summary, research has yet to describe a RON response for experimental PM tasks. It would be expected that given the similarities between the dual-task designs that are incorporated for both distraction studies and PM studies that there exists a RON response. By exploring ERPs across the scalp in response to different PM cues, a vital part of understanding experimental PM tasks might be uncovered. Moreover, if a RON

response exists within a PM task, it may help to understand differences in PM performance between typical and atypical ageing given the reported deficits of executive function and attention in older adults (Crawford et al., 2000; Gazzaley et al., 2005) and in those experiencing MCI (Ghosh et al., 2014; Petersen, 2004).

3.4 Event-Related Potentials and Ageing

Over recent years ERP based studies have become increasingly important for understanding the neurophysiological changes which affect our cognition as we age. Chapter 2 detailed the changes experienced by the ageing brain and how these neuroarchitectural differences affect cognition. However, the temporal resolution of EEG provides a considerable advantage in understanding the speed of processing following the occurrence of an event.

The ageing literature suggests that in many circumstances, recollection-based processing diminishes in older adults (D. Friedman, 2013). Episodic memory studies have found that early medial-frontal old-new effects (300–500ms; related to familiarity processes) are relatively well preserved (D. Friedman, 2013). Research also suggests that the left parietal old-new effect (500–800ms; recollection-based processes) and the late right frontal old-new effect (800–1600ms) are reduced or, in some instances, abolished (Czernochowski et al., 2008; Nessler et al., 2008; Rousselet et al., 2010; Swick et al., 2006; Trott et al., 1999). However, these results are not reported consistently (Gutchess et al., 2007; Li et al., 2004; Mark & Rugg, 1998; Trott et al., 1997).

ERP studies employing an *n*-back working memory task have demonstrated age-related neural modulations (Basak & Verhaeghen, 2011; Missonnier et al., 2004). Older adults have exhibited slower responses and reduced target detection, reflected in reduced P3a during 2-back conditions (Gajewski & Falkenstein, 2014) and increased P3 latencies (Saliasi et al., 2013). These P3a modulations indicate a reduction in processing processes and a slowing of stimulus evaluation (review: Friedman, 2012). Other studies have demonstrated that frontocentral P2 and N2 components are also sensitive to age-related effects during *n*-back working memory paradigms (McEvoy et al., 2001; Missonnier et al., 2004). However, while reports suggest higher early frontal

positive amplitudes at approximately 200ms (P2) for older adults (McEvoy et al., 2001), other researchers report attenuation of the N2 and P2 amplitudes in older adults compared to younger adults (Missonnier et al., 2004; Missonnier et al., 2011). Evidence appears to suggest age-related differences in the neurophysiology of working memory; however, it is unclear how the ERP modulations manifest.

Other executive functions such as inhibition and task-switching are also found to be affected by age-related declines (Herman et al., 2010). The P2 ERP component has been associated with executive functions and stimulus feature detection (Luck & Hillyard, 1994; Potts, 2004). Some research suggests age-related P2 amplitude increases in some tasks involving stimuli processing and cognitive control processes (Daffner et al., 2015; West & Alain, 2000; Zurrón et al., 2014), suggesting that the P2 is sensitive to the effects of ageing in executive functions. However, in a recent review by Gajewski, Ferdinand, et al. (2018), evidence suggests that these amplitude increases are only apparent in those tasks requiring task-switching and do not occur in single task processing. Additionally, research on the N2 component, related to inhibition tasks (Falkenstein et al., 1999) has also found ERP amplitude reductions and latency delays associated with ageing (reviews: Hämmerer et al., 2014; Pires et al., 2014). It is expected that cognitive tasks relying on executive functions will exhibit age-related modulations in early ERP components, although it is not clear how these changes will manifest.

While this section has outlined some of the age-related differences in ERPs associated with cognitive functions related to PM, the following section will explore the literature directly examining age-related differences in ERPs for PM tasks.

3.5 Ageing and Prospective Memory Event-Related Potentials

Following the frontal lobe hypothesis of age-related decline (Moscovitch & Winocur, 1995; West, 2000; *see Chapter 2, Section 3*), West and Covell (2001) were the first to explore the related ERPs in PM for older adults. Using an ongoing word pair decision task, participants responded to PM cues or were instructed to ignore PM lures. The PM cues were a pair of words both presented in uppercase, while the PM lure only

contained one uppercase word from the word pair. Older adults made fewer correct PM responses and were also more likely to make false PM responses to the PM lures than younger adults. There were amplitude reductions of the N300 and the parietal positivity in the older adult group. Accordingly, the decline was likely a result of diminished attentional mechanisms used to support PM cue detection reflected in the earlier N300 component (Petersen et al., 2001). However, the researchers also highlight that it is unclear which of the later positivity components were contributing to the observed attenuation in the parietal positivity. Given the high sensitivity of the P3b to ageing (Friedman et al., 1997; West, Herndon, et al., 2003), it is possible that this component may have had a considerable influence on the attenuation of this later component (West, Herndon, et al., 2003).

West, Herndon, and colleagues (2003) continued this work to disentangle the contributions of the P3b to the parietal positivity in response to PM cues. Employing a similar task design to West and Covell (2001), the researchers reduced the distinctiveness of the PM cue to reduce the influence of the P3b component on the parietal positivity. Older adults showed slower reaction times and reduced accuracy compared to the young adults. Additionally, N300 amplitudes were attenuated for the older adults over the right hemisphere, which was not apparent in the left hemisphere. Contrary to their previous study (West & Covell, 2001), there were no differences between the older and younger adults in the prospective positivity complex. The N300 amplitude attenuations and lack of difference of the parietal positivity between younger and older adults led the researchers to conclude that deficits were likely due to declines in attentional mechanisms related to PM cue detection and not the recall of the intention. This was suggested because West (2001) had proposed that attentional mechanisms serve to modulate the activity of the neural systems responsible for discerning features of the PM cue. Subsequent research provided further support for this claim, finding relationships between attention mechanisms and the N300 and the right hemisphere (West & Wymbs, 2004). This evidence suggests that while there may be some cognitive decline in attentional networks related to cue detection, the neural mechanisms for the retrieval of delayed intentions may be spared by age-related decline.

Zöllig et al. (2007) further explored the later components of PM and whether the failures were a result of the inefficiencies of the prospective components or

retrospective components in older adults. Using a similar paradigm to West et al. (2003), participants encoded the PM intention related to a letter and its colour. The participants were required to recall this intention while completing a semantic-relatedness ongoing task. Older adults performed more false responses during PM inhibit conditions, had more PM misses, and had slowed reaction times compared to the younger adults. Increases in the N300 were observed for the older adults relative to the younger adults during the PM inhibit but not the PM execute trials. The parietal positivity complex, however, was reduced in the older adults compared to the younger adults. An age-related reduction in the parietal positivity conflicts with prior studies (West, Herndon et al., 2003; West & Wymbs, 2004) and instead suggests age-related PM deficiencies are a result of declining memory systems rather than reduced attentional mechanisms. Considering the number of false positive PM responses produced by the older adults relative to the younger adults, West and colleagues (2003) concluded that the reductions in the parietal positivity implied age-related declines in the retrospective component of PM. Indeed, prior studies of episodic memory have linked reduced parietal old-new effect amplitudes in older adults relative to young adults with deficient retrieval mechanisms (Ally et al., 2008), which is likely due to regional brain volume reductions in the MTL (Head et al., 2008).

Using a modified encoding-retrieval paradigm, Mattli et al. (2011) explored neural correlates of PM across the lifespan (illustrated in Figure 3.3). They failed to find N300 and frontal positivity amplitude differences between younger and older adults. However, components did distinguish PM hits from misses and supported the claim that the frontal positivity and the N300 are related to PM cue detection (West, Herndon, et al., 2003; Zöllig et al., 2007). The parietal positivity also differentiated PM hits from misses but was found to be reduced with age, consistent with previous research (West, Herndon, et al., 2003; Zöllig et al., 2007). Additionally, Mattli and colleagues (2011) found significant modulations of posterior N2 and anterior P2 components in the adolescent group, which was associated with successful PM responses. It was suggested that this was indicative of differences in support systems for cue detection. However, these early ERP modulations may be related to the developmental differences in executive functions, which stabilise later in an individual's life (Friedman et al., 2016). Research into the N2 and P2 has suggested a strong relationship between these components and executive function (Brydges et al., 2014), although they are rarely examined in PM studies. Further exploration of these

earlier components may provide important insight into age-related differences in PM abilities.

Mattli et al.'s (2011) study also examined age-related differences in the neural correlates of strategic monitoring. Their results demonstrated sustained frontal activity when monitoring ongoing stimuli for PM cues compared to when PM monitoring was not required. Importantly, there were no neurophysiological differences between younger and older adults. The authors concluded that the cognitive systems involved with strategic monitoring for PM cues were robust across the lifespan.

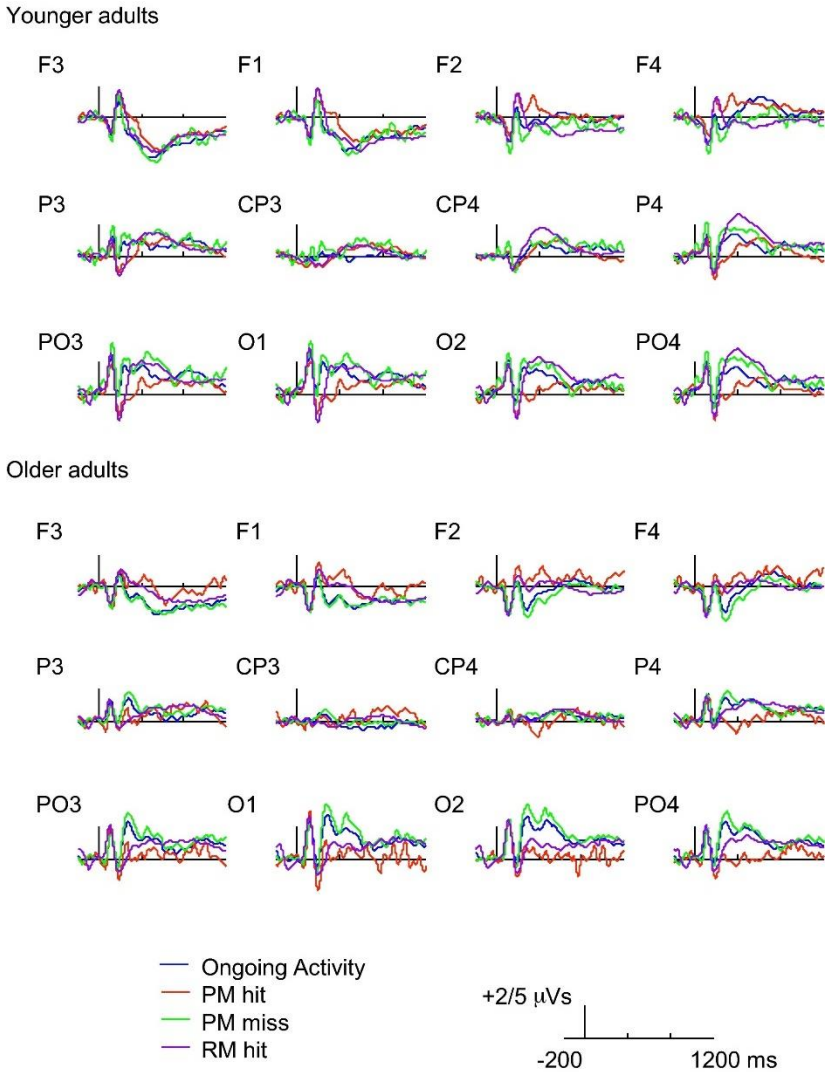

Figure 3.3. Grand-averaged event-related brain potentials across 12 electrode sites for younger and older adults for ongoing activity stimuli, PM hits, PM misses, and retrospective memory hits. The tall bar represents stimulus onset and 2μV; each of the short vertical bars represent 400ms increments. Reprinted with permission from Mattli, Zöllig & West, 2011.

More recently, researchers have explored the early PM monitoring (Hering et al., 2016) and late slow-wave components of PM (Hering et al., 2020). With regards to monitoring, Hering and colleagues (2016) found no significant differences in the N300, despite poorer PM performance by the older adults relative to the younger adults. The younger adults did, however, show N1 amplitude modulations that differentiated PM from the ongoing task activity, which was not evident in the older adults. The older adults did, however, show amplitude modulations of the P3b in response to the PM cues relative to ongoing activity. These results led the authors to conclude that there might be multiple subcomponents related to PM stimulus identification. They also concluded that PM detection may have been completed at the earlier stage of stimulus identification (i.e., the N1) but the older adults performed this detection at a later stage (i.e., the P3b).

With regards to the later slow-wave components, Hering et al. (2020) examined differences between younger and older adults while maintaining either one or two PM intentions. Consistent with previous research (Kliegel et al., 2016; West, Herndon, et al., 2003; West & Covell, 2001; Zöllig et al., 2007), younger adults outperformed older adults. In line with Zöllig et al. (2007), older adults displayed attenuated parietal positivity amplitudes during the PM retrieval stage. Both adult groups demonstrated increased frontocentral sustained activity when maintaining a PM intention compared to no intention. Generally, these results suggest no age-related declines in PM intention maintenance, but PM performance may be affected by decreased intention retrieval ability in older adults.

In summary, the limited research into the neurophysiological changes due to ageing in PM shows some inconsistencies. Some studies find that the cue detection components (N300 & frontal positivity) are reduced in older populations, while others report no differences. In general, however, research suggests parietal positivity amplitude reductions for older adults, although some earlier studies failed to find these differences. Earlier mechanisms in PM related to attention and executive function have begun to be explored, but it is unclear to what degree these components are affected by age. Some studies conclude that age-related differences are due to attention and working memory networks. However, other researchers suggest age-related declines are likely due to a weaker ability in older adults to recall the PM intention. The

differences between studies are possibly due to the variability in the experimental paradigms. Given that most experimental designs use a perceptual event-based PM stimulus (e.g., colour), it would be useful to expand the types of PM cues used to assess age-related PM differences. Through the use of non-perceptual cues, a deeper understanding of age-related differences may be uncovered.

3.6 Event-related potentials and mild cognitive impairment

The structural differences between older adults with MCI and healthy older adults are readily found (*see Chapter 2, Section 2.5)*. The effective spatial resolution of imaging methods such as fMRI have provided knowledge of areas in the brain that are affected by cognitive decline at rest and during memory processes. However, ERPs offer the ability to more precisely decipher temporal changes in cognitive processes, such as memory. Given the temporal immediacy at which cognitive functions take place, modelling cognitive decline at high temporal resolution offers insights that might go unnoticed in other neuroimaging methodologies.

Oddball ERP paradigms have often been used to understand neurocognitive function in MCI (e.g., Bennys et al., 2007; Missonnier et al., 2007; Papaliagkas et al., 2011). During an oddball task, participants are presented with a repetitive stimulus that is frequently interrupted by a deviant, target stimulus, which reliably evokes a centroparietal P3 response. Jiang et al. (2015) recently conducted a meta-analysis of the oddball P3 response in older adults with MCI. They report consistent reduction in amplitudes and delayed latencies of the P3 in participants with MCI, relative to healthy older adults.

ERP components with latencies earlier than the P3 have also been studied. The N2b component, for example, is thought to reflect stimulus detection change, and has been found with reduced amplitudes (Bennys et al., 2007; Papaliagkas et al., 2011; Ritter et al., 1979) and delayed latencies (Bennys et al., 2007; Missonnier et al., 2007; Papaliagkas et al., 2008; Papaliagkas et al., 2011) in older adults with MCI, compared to healthy controls. However, some studies find no differences in the N2b component between typical ageing adults and those with MCI (Golob et al., 2002; Lai et al., 2010;

Van Deursen et al., 2009), and others report greater amplitudes for those experiencing cognitive decline (Papaliagkas et al., 2008; Papaliagkas et al., 2011). The evidence suggests that early ERP components may be important for understanding cognitive decline, but further research is needed to understand the neurocognitive processes they reflect and how these are impaired in cognitive decline.

Whilst the oddball paradigm is the most frequently used ERP paradigm in MCI studies, other paradigms have been used to further explore neurocognitive domains, such as executive function. For example, Cid-Fernández et al. (2014) compared the N2 and P3 components of individuals with MCI and healthy older adults during a Go/NoGo task. In both the Go and NoGo conditions, participants with MCI produced significantly smaller N2 amplitudes relative to controls. However, the P3 amplitudes and N2 and P3 latencies did not differ between healthy older adults and those with MCI. The authors concluded that MCI-related impairment in executive functions is marked by N2 amplitude reductions. In a similar study, Mudar et al. (2016) found lower N2 amplitudes in older adults with MCI during a Go/NoGo experiment, but also found prolonged N2 latencies in the participants with MCI relative to controls unlike the results from Cid-Fernández et al. (2014). Differences across studies reflect variation in the task design. In comparison to Mudar et al. (2016), Cid-Fernández et al. (2014) required participants to ignore an auditory distraction stimulus while they responded to a visual Go/NoGo stimuli. The auditory stimulus would likely have recruited additional cognitive processes involved in integrating across modalities, and this may have led to the reported differences. In any case, these studies indicate that ERP features related to executive functions are impaired in older adults with MCI and likely affect N2 components. Other experimental paradigms which rely on executive functions should also be investigated.

Studies evaluating working memory consistently report delays in early ERP components during *n*-back tasks in older adults with MCI relative to healthy older adults. Missionnier et al. (2005; 2007) found delayed ERP latencies for both the P2 and N2 in participants with MCI relative to healthy controls. This effect has been replicated by Zunini et al. (2016), where delayed and attenuated P2/N2 ERP responses were reported along with attenuated P3 amplitudes across all *n*-back conditions. Similarly, Gozke et al. (2016) report delayed N2 and P3 responses alongside P3 amplitude reductions. As it currently stands, the precise function of the P2 is yet to be

determined. However, some evidence links the P2 to attention (Näätänen, 1992) and attention allocation (Lijffijt et al., 2009; Näätänen, 1992). Therefore, differences in the P2 component may reflect compromised attentional functions due to cognitive decline. Past research has demonstrated P2 latency delays among familial AD mutation carriers (Golob et al., 2009), indicating that early cognitive processes such as the P2 may be compromised in pre-AD stages. However, this evidence is scarce and is generally not accepted as being a stable feature of AD (Chang et al., 2014).

The N2 is argued to reflect different functions dependent on the location of the scalp in which it is recorded (Folstein & Van Petten, 2008). The posterior N2 is thought to reflect stimulus identification, classification and visual attention (Folstein & Van Petten, 2008; Patel & Azzam, 2005). Similar to older adults with MCI, N2 latency delays are demonstrated in low performing young and healthy older adults during *n*-back tasks compared to their high performing counterparts (Daffner et al., 2011). The N2 latency delays were reportedly due to an inability to allocate attentional processes effectively in these low performing samples. Given the poorer working memory abilities of individuals experiencing MCI (Saunders & Summers, 2011) it would be expected that posterior N2 latency delays would also be found in older adults with MCI. It is possible the neural correlates associated with executive functioning and working memory reflect a slowing down of these processes related to early stimulus evaluation and may reflect initial signs of neural degradation.

Researchers have also explored the neural correlates of episodic memory in older adults experiencing MCI. Ally et al. (2009) used ERPs to examine verbal and visual recognition memory in healthy and older adults and older adults with MCI. Poorer performance was found for the older adults with MCI relative to the healthy older adults in both the verbal and visual tasks. Moreover, older adults with MCI did not exhibit a frontal or parietal old-new effect response in the verbal recognition task but did display a frontal old-new effect for the visual task. Their results suggest that word recognition may be a particularly sensitive biomarker of cognitive decline.

In a study using both ERPs and voxel-based morphometry (VBM), Hoppstädter et al. (2013) furthered Ally and colleagues' (2009) research into verbal recall and familiarity in older adults with MCI. Alongside poorer abilities to discriminate between old and new items, participants with MCI also show prolonged reaction times compared to healthy older adults. The VBM revealed grey matter loss in the medial and inferior

temporal lobes in the MCI group compared to the healthy controls (Hoppstädter et al., 2013). Similar to Ally et al.'s (2009) results, a frontal old-new effect was not found in the lexical tasks for older adults with MCI but they also found that neither the healthy older adults or the MCI participants demonstrated a parietal old-new effect. This may suggest that recall is affected by ageing, and that it undergoes further decline in frontal areas in MCI. Additionally, Hoppstädter and colleagues (2013) found a correlation between the frontal old-new effect and grey matter volume in the MTL. Given that memory recollection depends on the hippocampus (Baddeley, 2001; Eichenbaum et al., 2007; Eldridge et al., 2000) and the hippocampus is sensitive to the effects of ageing (Raz et al., 2005) and MCI (Eckerström et al., 2010), the absence of a frontal old-new effect may reflect degradation of the MTL.

3.7 Mild cognitive impairment and prospective memory related event-related potentials

As it currently stands, no research has assessed differences in the neurophysiology of older adults with MCI during a PM task. However, considering behavioural evidence from PM tasks, biological differences in older adults with MCI alongside ERP studies of ageing and PM, hypotheses can be drawn about electrophysiological responses in older adults with MCI during PM tasks.

It would be expected that the earlier ERP components will be affected during PM tasks in older adults with MCI. Considering that many of the ongoing tasks used within PM studies are working memory tasks, one would expect similar ERP amplitude reductions and delayed latencies in working memory features in older adults with MCI relative to heathy older adults (e.g., Gozke et al., 2016; Missonnier et al., 2005, 2007). Therefore, the N2 and P2 would be expected to have smaller amplitudes and be delayed relative to healthy older adults during an ongoing working memory task. Moreover, given the reported executive function deficits within MCI and the associated N2 latency delays (Papaliagkas et al., 2008; Papaliagkas et al., 2011), it is possible that latency and amplitude differences between healthy older adults and participants with MCI will also be apparent in response to PM stimuli. Furthermore, it would be expected that the additional cognitive efforts required during PM monitoring would further

affect the amplitudes and latencies of the working memory stimuli in older adults with MCI relative to healthy older adults.

Behavioural evidence suggests deficits in the retrospective component of PM functioning in older adults with MCI (Costa et al., 2010; Costa, Caltagirone, et al., 2011; Karantzoulis et al., 2009; Thompson et al., 2010). The inability to successfully recall an event in the past shares similar cognitive functions to the recollection of a PM intention (i.e., the parietal positivity; West et al., 2011). Research has demonstrated attenuations of the prospective positivity for older adults (Hering et al., 2020; Kliegel et al., 2016; Mattli et al., 2011; Zöllig et al., 2007). It is likely that amplitudes will be further attenuated in older adults with MCI reflecting the deterioration of neural structures related to intention recall (*see Chapter 2, Section 2.6*).

3.8 Limitations of event-related potentials

Electroencephalographic studies have been paramount in understanding the underlying neural mechanisms of PM and the neurophysiological changes experienced through ageing and cognitive decline. It is well known that EEG provides temporally rich neurocognitive data; however, it is important to highlight the limitations of this method and possible techniques that can be employed to improve understanding from ERP data.

Often studies will only analyse ERP data from a few select channels (e.g., Fz, Cz & Pz; Cid-Fernández et al., 2014; Czernochowski et al., 2012). The selection of only a few channels is often made for statistical simplicity and to minimise interference from noise artifacts (Alotaiby et al., 2015). However, it is difficult to draw any inferences about the neuronal sources of information. Some analysis methods such as source localisation and independent components analysis (ICA; Stone, 2004) can capture this information, but the results sacrifice the temporal data. It remains challenging to analyse temporal and spatial data together. However, recent advances in machine learning and AI have enabled the ability to analyse EEG data in both temporal and spatial domains simultaneously (Kasabov, 2019).

3.9 New Approaches to Understanding Spatiotemporal Brain Data: Spiking Neural Networks

To understand the application of these AI techniques to EEG data, the foundation of these principles must be clear. This section will provide an overview of some of the conventional methods applied in AI research, particularly concerning EEG data and how they operate with large amounts of spatiotemporal brain data (STBD).

3.9.1 Machine learning

Machine learning (ML) is a branch of AI that can model and learn from large amounts of data to make predictions or classifications based on the data. It can discover previously unknown patterns in data (Mannila, 1996) or make inferences that the system was not explicitly programmed to do (Ghahramani, 2015). Pattern discovery, and inference can be made by using a subset of the data which is used to "train" a model. There currently exist many different types of learning methods for ML; however, this section will only cover the most relevant and most popular: supervised and unsupervised learning (Caruana & Niculescu-Mizil, 2006).

Supervised learning creates a predictive statistical model, where both the input and desired output is known. Each data sample is provided in an iterative process to reduce a loss function, which seeks to minimise the squared differences between existing and estimated target values. The loss function enables the learning of the model to be trained to correctly predict the output of new, unknown input data (Kotsiantis et al., 2007). In unsupervised learning, data without labelling information is provided to the ML algorithm. The unsupervised learning model creates groups or clusters based on similarities in the data in the hopes of discovering previously unknown but useful clusters of items (Jain et al., 1999). For example, EEG data from individuals could be provided to a ML algorithm without a labelling information and the model would create groups or clusters based on similarities in the EEG activity. The algorithms chosen for any specific method make different assumptions and will ultimately affect the clustering that takes place. ML algorithms can be employed to solve many different problems such as classification, prediction and clustering.

The classification of EEG data has previously been performed using conventional ML methods such as decision trees (Aydemir & Kayikcioglu, 2014), multiple linear regression (MLR; X. J. Yao et al., 2004) and support vector machines (SVM; Guler & Ubeyli, 2007; Panda et al., 2010). SVM, for instance, is a supervised learning model with associated algorithms capable of classifying data through output in the form of an optimal hyperplane (a subspace of the problem vector space). If an EEG dataset contained labelled data belonging to two different groups (the term 'classes' is used within the ML literature and will henceforth be referred to as such when discussing labelled data in ML contexts), for example older adults with and without MCI, a SVM could be trained on this data. The SVM will then, in theory, be capable of assigning new unmodelled data to one of these defined groups. This method has been applied to EEG data with some success (S. Li et al., 2013; Panda et al., 2010). These conventional ML methods are usually effective when EEG data is easy to linearly separate, such as EEG seizure data (Li et al., 2013) or the detection of EEG sleep spindles (Acır & Güzeliş, 2004). However, in classification problems where data cannot be discriminated via a straight line through the data, known as a non-linear classification problem, other methods need to be employed.

3.9.2 Artificial neural networks

Neural Networks (NN), as the name suggests, are based on the biological neural networks within the brain. In the case of a biological neuron, information is received as an electrochemical signal, which alters the internal voltage of the cell. Once this internal voltage reaches a certain voltage threshold over a short period, the neuron will release its electrochemical pulse, known as an action potential. In much the same way, an artificial neuron (AN) receives information from one or multiple sources, but instead of a cell body, this neuron is a mathematical function. Information is fed into these ANs, which then combine with their internal activation state and produce an output if a defined threshold is reached. Figure 3.4 illustrates a diagram of an AN (a) and a simple NN (b) with two input neurons and two hidden layers with one output neuron.

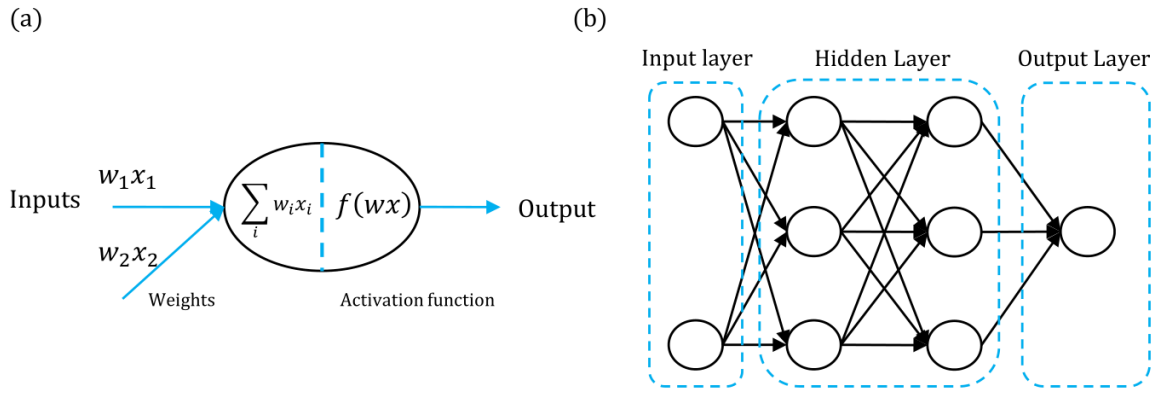

Figure 3.4. A block diagram showing components of an artificial neuron. (a) A single artificial neuron unit. (b) A simple neural network with a single input layer containing two neurons, two hidden layers containing three neurons each and an output layer containing a singly output neuron.

Groups of ANs are known as artificial neural networks (ANN). In general, an ANN acts as an adaptive system that alters its structure based on the internal or external information passed into the network. These models are designed to demonstrate the dynamics of neuronal circuitry and their interactions between other individual neurons. On a local level, interactions between neurons can cause the synchronisation of neuron outputs and form oscillatory activity (Aleksander & Morton, 1990). Unlike methods such as MLR and SVM, NNs are capable of processing nonlinear classification problems by modelling nonlinear relationships between inputs and outputs in parallel. ANNs have demonstrated robust efficacy for a variety of applications such as speech recognition (Lippmann, 1989), object detection and image classification (Egmont-Petersen et al., 2002). Similarly, ANNs have demonstrated their potential for helping to further EEG research in brain-controlled interfaces (BCI; Lotte et al., 2007) and in disease detection such as epilepsy (Acharya et al., 2018).

Despite the improvements of this methodology over the classic ML methods and the successful applications of distinguishing between more complex EEG data, the process remains somewhat of a 'black box'. In other words, researchers are still not sure what the neural network is doing in between the input layer and the output layer and how the classification problem is solved (hidden layer of Figure 3.4(b)). The changes to network can be understood but how these changes produce accurate classifications is still largely unknown.

Therefore, while it is possible to classify EEG activity with these methods, it is difficult to extract meaningful knowledge in biologically plausible terms about the modelled processes. Moreover, despite ANNs possessing some biologically plausible properties of brain function (Hall et al., 2015; Hodgkin et al., 1952), the AN's state depends on the current time of the inputs provided. Therefore, any temporal information of the data is lost. To compensate for this, the third generation of ANNs, known as Spiking Neural Networks (SNNs), was developed to explicitly include time as an inherent part of the model and, therefore, models and encodes the AN's firing-time information.

3.9.3 Spiking neural networks

Spiking neural networks enable us to explore how the training data not only affects the network but the modelled data can also be interpreted spatially and temporally. SNNs are inspired by and incorporate biologically plausible principles at each stage of its design, such that it: constructs a 3D model that maps the location of brain structures to a brain template, preserving the spatial information of the EEG data; encodes EEG signals into 'spike-trains' (a series of binary events dependent on when the EEG signal reaches a threshold value) at a millisecond time scale; initialises a SNN model using a brain inspired small-world (SW) connectivity rule and uses biologically plausible learning rules to evolve the SNN functional connectivity through unsupervised and supervised learning (Indiveri et al., 2015; W. Maass, 1997). Each of these stages are explained in the following sections.

At the basic component level, an artificial spiking neuron is an information processing unit, which can learn from temporal data simulating the presumed processes of the brain. These spiking neurons are linked via their synapses, which encode these patterns into memory. These neurons are able to integrate time into their computational operations and are, therefore, deemed superior in biological plausibility compared to previous ANN models (Agatonovic-Kustrin & Beresford, 2000; Schmidhuber, 2015). This integration of the temporal characteristics of the AN's behaviour are modelled in an integrated way with other ANs allowing the ability to capture the spatial and temporal dynamics of EEG data (Kasabov, 2019). Several different implementations of SNN have been developed so far, however only the 'Leaky Integrated-and-Fire model' (LIFM) will be covered in the scope of this thesis.

The LIFM, also known as the 'forgetful' model (Knight, 1972), increases the 'membrane potential' of a AN with each incoming spike at a time *t*, multiplied by synaptic efficacy (strength) until it reaches the defined threshold θ. Once the threshold is reached, an output spike is emitted, and the membrane potential returns to its initial state. Like a biological neuron, after a spike is emitted, the AN enters a refractory period where it is unable to produce any new spikes as its membrane potential 'leaks'. The membrane potential leakage between spikes can be defined by a parameter τ. The LIFM is defined via:

$$\tau_m \frac{dv}{dt} = v_{rest} - v(t) + RI(t)$$

Where τ_m represents the membrane time constant, v_{rest} reflects the resting potential, *R* is the resistance and *I* is the input current.

The SNN architecture is based on a framework of evolving spiking neural networks called NeuCube (Kasabov 2019). The architecture contains various functional models (as illustrated in Figure 3.5): (a) an input encoding module; (b) a 3D SNN module for unsupervised training; (c) an output regression/classification module for supervised learning; (d) an optimisation module; (e) a visualisation module for visualisation and knowledge extraction (Bullmore & Sporns, 2009; Kasabov, 2014). These modules are further detailed in the following sections.

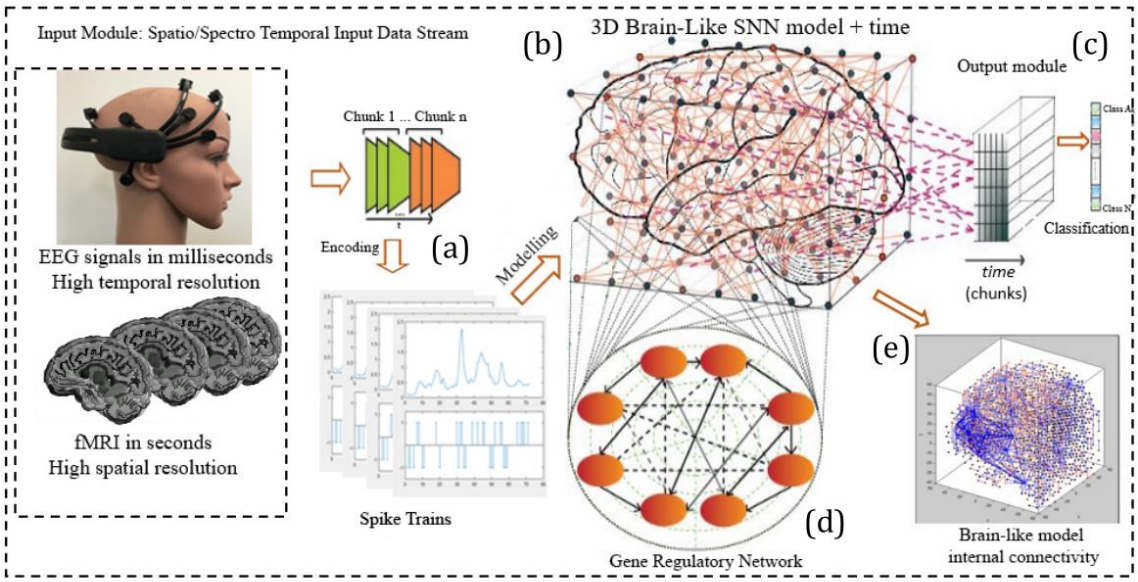

Figure 3.5. An illustration of the NeuCube SNN architecture. Modules include: (a) input spike-time data encoding; (b) a 3D SNN module for unsupervised learning; (c) a SNN classification/regression module for supervised learning; (d) a parameter optimisation model; (e) visualisation module. Figure adapted with permission from Kasabov (2014).

3.9.4 Input mapping and encoding data for a spiking neural network

Before EEG data can be modelled, it must be mapped onto a 3D spatial template structure of an appropriate size. Templates such as the Talairach (Talairach & Tournoux, 1988) and the Montreal Neurological Institute (MNI) template (Brett et al., 2001) or coordinates for an individual's brain data can be used[3].

The initial 3D structure is scalable and can evolve in size according to the data set and the study problem. Three parameters control the size of the SNN model: *nx*, *ny*, *nz* symbolising the x, y, z spatial coordinates within the 3D SNN model. These coordinates are used to preserve the spatial dimensions of the recorded EEG

[3] It is also possible to model STBD without a 3D brain structure. Without a 3D brain structure, input variables are instead grouped together within a 3D space based on their temporal correlations.

data by fixing them to a coordinate within the SNN model space, which become 'input neurons'. An input neuron is identical to a recorded EEG channel and is represented in the 3D space as an AN. This allows the EEG data to be propagated into the network while modelling its spatial location on the scalp.

For the EEG data to be modelled within a SNN, it must first be translated into a spike-train. The timing of these spikes corresponds to the changes within the EEG data. Spike-trains represent the EEG data through positive or negative binary spikes. If there is a positive increase in the EEG data above the defined threshold, then a 1 will be encoded as a positive spike. On the other hand, if there is a negative decrease in the EEG data below the defined threshold, then a -1 in the form of a negative spike will be encoded. If there is no increase or decrease (in relation to the threshold) in the data, no spike will be emitted (illustrated in Figure 3.6 showing encoded spikes for one channel of EEG activity). The formula for encoding positive and negative spikes is given as:

$$\text{spike}(t) = \begin{cases} 1 \text{ then } V(t) \leftarrow V(t-1) + \theta; & \text{if } S(t) \geq V(t-1) + \theta \\ -1 \text{ then } V(t) \leftarrow V(t-1) - \theta; & \text{if } S(t) \leq V(t-1) - \theta \\ 0 & \text{otherwise} \end{cases}$$

The variability in signal amplitude over time is denoted by *V(t)* for a signal *S(t)* over time $t = 1, 2, \ldots, n$ where at baseline, $V(1) = S(1)$. If the upcoming signal amplitude *S(t)* is greater than $V(t-1) + \theta$ (where θ is a defined threshold) at the next point *t,* then a positive spike is produced, whilst a negative spike is created for a decreased signal. These spike-trains are then propagated through into the SNN model via the previously defined input neurons in the brain template.

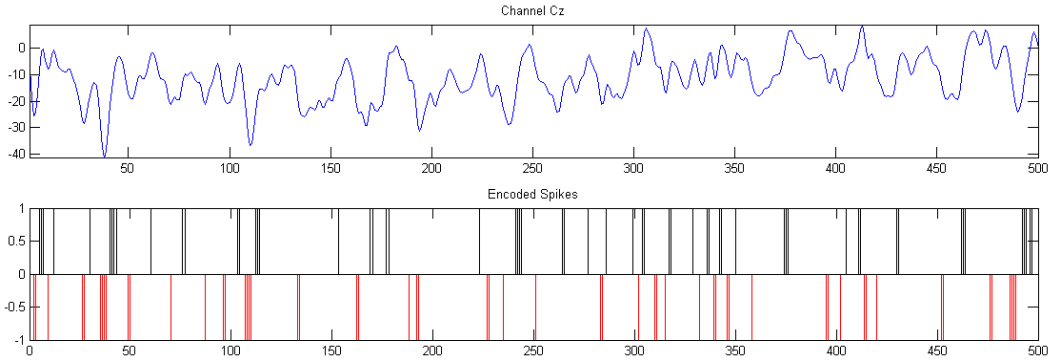

Figure 3.6. An example of EEG data encoded into a spike-train. Positive Spikes (+1) are shown in black and negative spikes (-1) are shown in red using a threshold-based algorithm. The image shows the first 500 data points from the Cz channel from Cappeci et al., 2016 © 2016 IEEE.

Once the 3D SNN model has been defined and the EEG data encoded into spike-trains, the data has to be initialised with a SW connectivity rule (Liao et al., 2017). SW connectivity is a phenomenon observed in biological systems, including physiological brain networks (Bullmore & Sporns, 2009) and synchronisation of cortical neurons (Yu et al., 2008). In the SW connectivity rule, neurons are probabilistically connected according to a preselected radius so that anatomically adjacent neurons are highly likely to be connected and those anatomically distant from each other are highly unlikely to be connected. In other words, the initial connection weight between AN *i* and AN *j* within the SNN depends on the distance between to the two ANs, such that larger distances will results in smaller connections weights. Therefore, it can be determined if two ANs are connected or not and if they are connected, then their connection weight will depend on their distance from one another.

The inclusion of a SW connectivity rule furthers the biological plausibility by constraining the possible connections throughout the model in a way that reflects global and local networks within the brain to some extent (Masuda & Aihara, 2004). For example, anatomical connectivity studies have found SW topology at the macroscopic level (Hilgetag et al., 2000) and microscopic scale in the simple neuronal network of *Caenorhabditis Elegans* (Watts & Strogatz, 1998). Additionally, evidence also demonstrates SW properties evident in human fMRI and EEG data (review: Yao et al., 2015). The initialisation of the SNN model will randomly assign weights and

connections to ANs based on the SW connectivity rule. These connections are then modified based on the learnt information of the new incoming spikes from the EEG data during unsupervised learning.

3.9.5 Unsupervised learning in a spiking neural network model

A Spike-Time-Dependent Plasticity (STDP; formula given in Appendix A) rule is applied to the incoming spikes being propagated into the network. This rule modifies the initialised connection weight $W_{i,j}$ between two ANs based on the timing of the output spikes. In STDP, each AN's postsynaptic potential (PSP) will increase with every input spike at time t until it reaches the firing threshold. When the PSP exceeds the firing threshold, a spike is emitted to all other ANs which share a connection. If AN i fires before j then the connection weight $W_{i,j}$ will increase. Otherwise, the connection weight will decrease. Additionally, each AN will also accumulate spiking activity from its neighbouring ANs. As a result, the STDP rule can model the 'hidden' spatiotemporal associations between EEG variables in the form of 'neuronal connections'. The STDP adds to the biological plausibility of the model by reflecting long-term potentiation between ANs during learning in the brain. Once the unsupervised learning process has altered the initial connections weights within the SNN, the learnt patterns of spatiotemporal activity can then be evaluated through supervised learning in their ability to classify or predict previously unmodelled data.

3.9.6 Supervised learning in a spiking neural network model

Upon completion of the supervised learning, a dynamic evolving SNN (deSNN; Kasabov et al., 2013) is used to classify the data based on its associated data labels, which define its class. For each training sample (i.e., participant's EEG activity), an output AN is generated (evolved) in the output layer and is connected to all other ANs in the trained SNN model. This corresponds to the classification/regression module in Figure 3.5(c). Similar to the connections between ANs within the 3D SNN space, the connections between the ANs in the SNN and the ANs in the output layer must first be initialised.

The initial connection weight *W* between an individual AN *i* of the SNN and an output AN *j* is determined by using a Rank Order (RO) learning rule (Soltic & Kasabov, 2010).

Once the initial connections weights between the SNN and the output ANs are established, the STBD used for unsupervised learning will again be repropagated through the trained SNN one sample (corresponding to recorded activity of one participant) at a time. The spatiotemporal patterns of each sample will be used to train an output AN capable of recognising the neural pattern of each class. At time *t* the PSP of AN *j* is calculated as follows:

$$PSP(j,t) = \sum mod^{order(i)} W_{ij}$$

Where *mod* is a modulation factor (a parameter between 0 and 1) and *order(i)* represents the order of the spikes in time between ANs *i* and *j.* The first spike that reaches the output AN is given the greatest value and the largest subsequent increase in connection weight. Following the initial spike, all subsequent incoming spikes to the post-synaptic AN will be further modified based on a synaptic plasticity learning rule incorporating a drift parameter. This drift parameter modifies connection weight $W_{i,j}$ by accounting for the following spikes at AN *j* at time *t,* denoted as $spike_j(t)$. In other words, if at moment *t* there is no spike, the weight between *i* and *j* will decrease by a defined drift value in the following:

$$W_{ij}(t) = \begin{cases} W_{ij}(t-1) + \text{drift} & \text{if } spike_j(t) = 1 \\ W_{ij}(t-1) - \text{drift} & \text{if } spike_j(t) = 0 \end{cases}$$

Once supervised learning is complete, the classification accuracy of the model is verified through cross-validation for various sets of parameters (e.g., STDP rate, *mod, drift* and firing threshold) during an optimisation stage.

3.9.7 Parameter optimisation

The classification accuracy of the SNN model is sensitive to the values and combinations of the parameters chosen. These settings can be optimised through the application of different algorithms, which will find the best-performing model. Examples of these include exhaustive grid search, genetic algorithms and quantum-inspired evolutionary algorithm (Schliebs & Kasabov, 2013). This thesis will only cover and apply the simplest of these methods, the exhaustive grid search.

An exhaustive grid search simply searches through combinations of parameter values to identify the best combination. In an exhaustive grid search, each parameter requires a value range to search within and requires a step size for the increments of the search to be performed. This search moves from the minimum to the maximum value. For each model that is created, different parameter settings are applied before the SNN model undergoes unsupervised and supervised learning and then finally is validated. The results are then saved, and the most successful is selected for visualisation, knowledge extraction and further analyses for the better understanding of spatiotemporal relationships within the data (Kasabov et al., 2016).

3.10 Chapter Summary

This chapter has outlined current understanding of the ERPs associated with PM. The evidence suggests that there are prevailing ERPs that are reliably associated with PM functioning. The N300 and the frontal positivity likely reflect PM stimulus detection. The parietal positivity, which is comprised of the P3b, the so-called parietal old-new effect and the prospective positivity, appear to reflect the retrieval of PM intentions from memory. Other ERP components such as the N2 are also often reported in PM studies mainly due to their associations with executive functions. A methodological problem was also highlighted regarding the appropriateness of averaging ERPs in response to different ongoing stimuli before being compared to PM-related ERPs. Furthermore, this chapter outlines a possibly overlooked ERP component involved with the reorientation of attention, namely the RON. The RON is well described in the distraction literature and occurs when an individual must reorient their attention back from a distraction toward an ongoing task. This has not previously been described

within the PM ERP literature and may provide a useful marker for understanding typical and atypical ageing deficits in PM.

In addition, this chapter has described the current understanding of PM ERPs of age-related decline. In healthy older adults, most research indicates that older adults exhibit smaller amplitudes for the parietal positivity than younger adults although earlier studies failed to find this difference. Some evidence appears to indicate there are no neurophysiological differences between healthy older adults and younger adults when monitoring for PM cues. However, there currently only exists of handful of studies, which have only used a limited number of PM cue types. To date, no studies have explored PM ERP activity in older adults with MCI. It is expected that older adults with MCI will have reduced parietal positivity amplitudes and will be impaired in the early processing of stimulus features.

Finally, this chapter has described a new methodology for analysing and understanding STBD. SNNs can perform classification of EEG data and, unlike other ML methods, enables improved interpretability of the learnt patterns of activity because it explicitly incorporates time and space into the model allowing for interpretation of temporal patterns within the model.

Chapter Four: Thesis aims and hypotheses

4.1 Introduction

The preceding chapters have evaluated the different cognitive aspects of PM, the neurophysiological understanding of PM, ageing and MCI, and has detailed a novel methodology for understanding STBD. Considering the literature covered in the previous chapters, some methodological issues regarding approaches to ERP research in PM must be first be addressed. Additionally, a possibly important factor of the neurophysiology of PM has thus far been overlooked. Namely, the RON, which has been demonstrated in a variety of other dual-task paradigms and has proved a useful biomarker for cognitive disorders (Justo-Guillen et al., 2019). Moreover, a considerable amount of further research is needed to improve the neurophysiological understanding of PM in healthy older adults and older adults experiencing MCI. As it currently stands, the electrophysiological research is inconclusive in explaining the reported age-related declines in PM. The previous chapters have suggested that older adults with MCI have impaired PM functioning, however, to date no studies have sought to understand these differences neurophysiologically.

To address these issues, the current thesis proposes a series of experiments involving two different forms of PM, which vary in their cognitive demands. Three different population groups will be used: young adults, healthy older adults, and older adults with MCI. Additionally, the current thesis will be the first to apply SNNs to ERPs in response to working memory and PM in attempt to evaluate its efficacy as a tool for discerning cognitive decline.

The first experiment (Chapter 5) is designed to address the following in questions in healthy young adults: 1) Is an ERP average that combines responses to different types of ongoing stimuli appropriate as a comparison measure for PM-related ERPs? 2) Are there behavioural and ERP differences between a highly salient and less salient event-based PM task? 3) Is there an RON ERP response following a PM stimulus, similar to ERP studies of distraction?

The results from Chapter 5 will inform how subsequent analyses should be performed. The ERP components most likely to aid in understanding the neurophysiology of PM

in healthy older adults and older adults with MCI will be used. Chapter 6 aims to answer the following questions: 1) How do young adults, older adults and older adults with MCI differ behaviourally on PM tasks as a function of stimulus saliency? 2) How does typical ageing affect ERP components during PM tasks? 3) Are there neurophysiological differences between typical ageing adults and older adults with MCI in PM related ERPs?

Chapter 7 aims to further the understanding of neurophysiological and behavioural differences between young adults, older adults, and older adults with MCI in PM tasks. The experiment aims to assess whether the maintenance of a PM intention could explain differences between the group's PM performance through the following questions: 1) Are there behavioural working-memory differences between young adults, older adults and older adults with MCI when a PM intention is maintained? 2) Are there differences between young adults, older adults and older adults with MCI in intention maintenance related ERPs?

The most common method for exploring the neurophysiology of PM is through ERPs, whereby conclusions are primarily derived from changes in amplitudes. Chapter 8 addresses some limitations of ERP research by applying novel SNNs to understand the spatiotemporal relationships within the entire brain during PM and working memory in young adults, older adults and older adults MCI. The experiments of Chapter 8 aim to address the following questions: 1) can SNNs accurately classify different patterns of brain activity using working memory and PM? 2) Does PM provide better classification accuracy than working memory? 3) Can new knowledge of the spatiotemporal connectivity at a local and global level be extracted to gain new insights into ageing and cognitive decline?

4.2 Summary of Thesis Aims

1) To address the methodological problem of averaging ERPs in response to different ongoing working memory stimuli.

2) To explore the differences between salient (perceptual/feature-based) and less salient (conceptual) PM ERPs; and to explore whether a RON response following a PM stimulus can be detected.

4) To determine the effects that typical ageing and MCI have on the behavioural performance and ERPs in response to perceptual and conceptual PM tasks.

5) To determine the effects that typical ageing and cognitive decline have on the behavioural performance and ERPs in response to the ongoing working memory stimuli when maintaining a PM intention.

6) To determine whether SNNs can model neurophysiological connectivity differences between younger adults, older adults and older adults experiencing MCI. Additionally, to determine whether brain activity in response to PM is better than working memory for classification between young adults, older adults and older adults with MCI.

Chapter Five: Differences in perceptual and conceptual prospective memory and reorientation negativity ERPs in young adults

5.0 Overview

The previous chapters reviewed the PM literature from a behavioural, neurobiological, and electrophysiological perspective to formulate a series of research questions. The following chapter explores the behavioural differences between perceptual and conceptual PM stimuli. Additionally, this chapter explores the differences in ERPs related to PM. Specifically, the N300 and frontal positivity are examined as markers of cue detection, and the subcomponents of the parietal positivity (P3b, old-new effect and prospective positivity) are investigated as markers of PM intention retrieval. Additionally, a methodological issue concerning the appropriateness of averaging ERPs in response to different ongoing stimulus types is addressed. This was performed by examining amplitude differences between the ongoing stimuli in the N2, P2 and N400. Finally, the study explores whether a RON ERP is produced following successful response to perceptual and conceptual PM stimuli.

5.1 Introduction

As mentioned in Chapter 1, PM is the ability to remember to perform an encoded intention at a defined period in the future. It is a fundamental personal resource, which underpins many day-to-day tasks, such as remembering to buy dog food on the way home from work (Hering, Kliegel, Rendell, et al., 2018; Kliegel, Jäger, et al., 2008). PM cues prompted by the occurrence of an event are known as an event-based PM cue. An example of an event-based cue would be seeing your colleague and remembering to pass on a message. There are various stages that are required for the successful execution of a delayed intention. Firstly, provided a PM cue has been correctly encoded, the cue must then be recognised within the environment or, in an

experiment, within the ongoing task. Secondly, following cue detection, one must recall what the intention was, for it to be enacted upon.

Past studies have demonstrated performance differences when the PM cue type is varied, for example in their salience, focality and colour (McDaniel & Einstein, 1993; Scullin, McDaniel, Shelton, et al., 2010). PM cue type differences are particularly evident when the perceptual salience of the cue is varied compared to PM cues that are considered conceptually salient (Cohen et al., 2003; McBride & Abney, 2012). However, there is limited research into the neurophysiological effect of varied cue salience and PM cue types. For the most part, neurophysiological studies have primarily varied the perceptual features of the PM task, i.e., those features that make the PM cue distinct from the ongoing task. Therefore, it remains unclear whether the components and activities described within studies reflect common responses to PM cues or whether they are specific to perceptual task features (Cruz San Martin, 2014).

In EEG studies, each of the stages of PM can be attributed to different ERP components. The detection of a PM cue, when embedded within an ongoing task, is linked to an increase in an N300 and frontal positivity component relative to the ongoing task (West, 2011). The realisation of a PM intention is related to the relative increase of the parietal positivity complex compared to the ongoing task. The parietal positivity complex is comprised of the P3b, the old-new effect (referred to throughout this chapter as the intention-retrieval response, IRR) and the prospective positivity. Each of these ERP components is reportedly sensitive to PM cue features (West, 2011).

Perceptual PM cues have reliably demonstrated an increase in N300 amplitudes relative to ongoing stimuli in different PM cue types and ongoing task designs (e.g., Cruz et al., 2016; West, Wymbs, et al., 2003; West & Krompinger, 2005; West & Wymbs, 2004). Findings for N300 in response to non-perceptual PM cues are less consistent however, with some researchers showing no effect (Cousens et al., 2015; J. Wilson et al., 2013) and others showing a delayed onset (Cruz et al., 2016). Understanding differences between these stimulus types, would shed light on these inconsistencies, and may provide further insight on the functional significance of the N300 component in the context of PM.

As highlighted in Chapter 3, one reason for differences between the findings in PM studies may be due to how the comparisons are made between the ongoing task and

the PM stimuli. Some studies choose to average the ERP waveforms of different ongoing stimuli. For example, Cousens et al. (2015) averaged the ERPs of semantically related and semantically unrelated ongoing responses. However, Cruz et al. (2016) treated the semantically related and unrelated stimuli as separate. Even though averaging two stimulus types together will increase the number of trials and improve the stability of the ERP waveform (Luck, 2005), evidence has reliably demonstrated an N400 congruency effect between semantically related and unrelated words (Cruz San Martin, 2014; review: Kutas & Federmeier, 2011). Therefore, if ERPs produced by semantically related and unrelated stimuli are averaged to form one waveform, then comparisons between ERP responses to ongoing stimuli and PM stimuli may be affected, at least for those components occurring at approximately 400ms and beyond.

The evidence is less clear for earlier ERP components, however, Kramer and Donchin (1987) found increased amplitudes for the N2 when a presented pair of words were unrelated. Kutas and Van Petten (1994) similarly looked at P2 ERP modulations in response to word pairs but failed to find amplitude modulations when the words were unrelated. Thus, it is unclear whether averaging ERPs related to different ongoing task stimuli will affect the earlier ERP components and whether ongoing stimuli should be treated as separate when used as a neurophysiological baseline for ERP analyses. The current study seeks to address this issue prior to performing further statistical analyses with the PM ERPs.

An integral part of PM, which may explain why certain populations perform better than others has, for the most part, been overlooked. The ability to reorient attentional processes back towards the ongoing task following response to a PM cue is an important part of successfully performing an experimental PM paradigm (Bisiacchi et al., 2009; West et al., 2011). Studies by Bisiacchi et al. (2009) and West et al. (2011) have highlighted the cost of switching between the ongoing task and PM task, but have not accounted for possible neurophysiological effects that may explain switching attention from the PM task to the ongoing task. A growing body of literature has begun to point towards a RON ERP response in dual-task paradigms (review: Justo-Guillén et al., 2019), which are conceptually similar to paradigms applied in PM research.

Schröger et al. (2000) suggest that the RON represents two distinct functional processes of attention reorientation following a distraction. These two distinct processes are the re-focusing of working memory toward task-relevant information,

and preparation for the next stimulus or a general reorientation. Given the similarities of the paradigms applied in the studies of distraction literature (e.g., Wester, Böcker, Volkerts, Verster & Kenemans, 2008; Scheer, Bülthoff & Chuang, 2016; Rämä et al., 2018) and PM, it would be expected that a RON would be apparent in PM paradigms and may explain differences in PM performance between individuals and groups.

The results of the current study will help to further our methodological understanding for appropriately analysing PM related ERPs. Firstly, by evaluating possible early and late neurophysiological differences in the ongoing working memory task ERPs, the appropriateness of combing the ERPs related to ongoing stimuli can be considered before evaluating the differences between PM related ERPs. Considering the recent research detailing a RON response after a distraction stimulus, the current study will determine whether a RON exists in PM tasks and whether it is equally apparent for feature-based/perceptual and conceptual PM paradigms.

The current study used two forms of PM (perceptual and conceptual) to explore the neurophysiology of PM. Participants first completed a semantic ongoing working memory task. Then the PM cues were incorporated into the ongoing task to form the PM task conditions. The perceptual PM task was defined as words presented all in capital letters. The conceptual PM task was presented as the word of a four-footed animal. All participants completed the ongoing task and then the two PM task conditions. While the ongoing task was always completed first, the two PM conditions were randomly presented. PM cues comprised no more than 10% of the total stimuli presented. The ongoing task was used as a baseline for comparisons for PM stimuli for behavioural and neurophysiological responses. Due to the variability in the RON and scalp region, the RON was defined after inspection of the PM ERPs relative the ongoing-only response.

5.1.2 Aims and hypothesises

The current study aimed to further understand the behavioural and neurophysiological responses to perceptual and conceptual PM stimuli. Additionally, the current study sought to determine whether a RON ERP could be found following the presentation of a PM stimulus. However, prior to evaluating the neurophysiological

differences of the PM stimuli, the current study had to firstly address the appropriateness of averaging ERPs in response to ongoing working memory stimuli by comparing early and later ERP components between the ongoing stimulus types. To this end, the current study was performed as three separate analyses. Firstly, the behavioural differences between the ongoing task and the perceptual and conceptual PM tasks were analysed. Next, the electrophysiological analyses were performed as two separate experiments. The first experiment evaluated possible differences in early (P2 & N2) and later (N400) ERP components between the two types of ongoing working memory (semantically related and unrelated) stimuli. Conclusions of the first electrophysiological experiment would be used to inform the subsequent analyses of Experiment 2. Experiment 2 compared PM related ERPs with the ongoing task ERPs and evaluated whether there was a RON response.

Regarding the behavioural analysis, the current study hypothesises that: 1) There will be no differences in the reaction time and number of correct responses between the ongoing task and the perceptual PM stimuli, but the behavioural performance will be worse in response to conceptual PM stimuli. Regarding ERP Experiment 1, the current study hypothesises that: 1) There will be a congruency effect for non-repeated stimuli indicated by a higher N400 response relative to repeated stimuli in the ongoing-only task. 2) There will be differences in posterior N2 amplitudes, but not in the anterior P2 amplitudes. In Experiment 2, the current study hypothesises that: 1) both PM cue types will cause significantly larger N300 and frontal positivity amplitudes relative to the ongoing-only task. 2) Both PM stimuli will cause significantly larger P3b, IRR and prospective positivity amplitudes compared to the ongoing-only task. 3) PM stimuli will produce a RON response significantly larger than in the ongoing-only task.

5.2 Methods

5.2.1 Materials

All experiments were programmed in PsychoPy v1.82.01 (Peirce, 2009). Participants were seated 57cm away from the computer monitor. During the interstimulus intervals, there was a fixation cross in the centre of the screen with a size of 0.75

degrees for each of the vertices. Words were presented at 1.5 degrees in height in white on a grey background.

5.2.2 Participants

Thirty right-handed adults (17 males, mean age = 24.7 years, SD = 3.43) were recruited from the Nottinghamshire area, UK. Inclusion criteria required participants to have: normal or corrected to normal vision, be 18–35 years of age, no history of dyslexia, no history of drug abuse, no history or current diagnosis of psychiatric or neurological disorder or medication that may impact the EEG recordings. Additionally, participants were required to abstain from alcohol for 24 hours and from caffeine and nicotine 3 hours prior to the study. Participants received £20 in Amazon vouchers for their participation. The study approval was issued by the Health Research Authority, UK (REC reference: 17/EM/1010).

5.2.3 Procedure

Data were recorded in a quiet room with a stable temperature (~20°C). After the study procedure was explained, the participants provided informed consent. Participants were then sat approximately 57cm away from a 19" (48.26cm) – diagonal colour LCD monitor (1,600 x 900 resolution: 60Hz refresh rate). EEG equipment was then attached to the participant before offsets checks were made.

Participants were required to complete two PM tasks. These differed in their salience but maintained the same cognitive demands on working memory and intention retrieval. Stimuli were the kept the same between the ongoing-only task and PM tasks. Different instructions were given for each PM task, thereby altering the nature of the encoded PM intention. As with similar studies (Chen et al., 2009; Cona et al., 2012b), the ongoing-only working memory task was completed first to minimise potential long-lasting interference effects of the PM instructions. This has been considered due to the noted effect of strategic monitoring engagement even when PM intentions were no longer required (Marsh et al., 2006; West, 2007). The two PM tasks built upon the ongoing task with the PM cues embedded within the stream of stimuli comprising the

ongoing task (see Figure 5.1). For both PM tasks, therefore, participants completed the PM task and the ongoing task simultaneously. The PM instructions were given at the start of the PM tasks followed by a delay, where participants were presented with at least 12 stimuli of the ongoing task before the first PM cue appeared (Figure 5.1b). In line with past research (Cruz et al., 2016; West et al., 2005), only 10% of all stimuli presented were PM stimuli. This allows participants to re-engage with the ongoing task and better simulate real-life PM events (i.e., remembering to perform an action after a delay). A mandatory break of five to ten minutes was given to all participants after each condition.

5.2.4 Ongoing task

A 1-back word categorisation task was used as the ongoing task. Participants made continuous semantic judgements of whether the word presented on the computer screen is of the same semantic category as the preceding word. Participants were shown a list of 10 categories and told that within each of these categories there are 10 words. Participants were instructed to press a button on a response box with their right index finger if the word was semantically related to the previous word (i.e., the category repeated from the previous word) and to refrain from responding if the word was unrelated to the previous word (i.e., the category is not repeated from the previous word). The instructions included examples and a short practice block which provided feedback on whether the participant was correct or incorrect.

Categories were created from the updated and expanded version of the Battig and Montague (1969) Category Norms (Van Overschelde et al., 2004) using the top 10 words from each category. The ongoing task was comprised of 300 stimuli with a 25% chance of a word belonging to the same semantic category as the previous category. Each word was presented for 500ms with a 2 second stimulus onset asynchrony between words. In order to minimise fatigue, short optional break-blocks were offered after every 30 stimuli, which varied in duration from 20 seconds and up to 3 minutes. All words were presented in lowercase.

The 1-back targets (stimuli requiring a response during the ongoing task) will be referred to as a 1-back_{target}. No feedback was given to the participant during the ongoing task. The 1-back non-targets (stimuli that do not require a response during

the ongoing task) will be referred to as 1-back$_{nontargets}$. 'Ongoing' encompasses both 1-back$_{targets}$ and 1-back$_{nontargets}$.

5.2.5 Prospective memory task

Most PM studies to date use a relatively small number of trials (approximately 20) to form a grand average waveform (e.g., West & Craik, 2001; West & Krompinger, 2005). Using a small number of trials to form an ERP is problematic because of reduced signal-noise ratio, which can cause type I and type II errors (Button et al., 2013). A minimum of 60–80 events have been recommended to establish reliable waveforms for later memory related components (Luck, 2005; Thigpen, Kappenman & Keil, 2017), particularly if within-participant designs are being used to evaluate cognitive differences between task types (Boudewyn et al., 2018). Collecting data for a higher number of PM events is a difficult problem to solve in PM research, as PM events are intrinsically rare. However, it is important to include an appropriate number of PM cues, particularly when attempting to make comparisons between groups (Fischer et al., 2017). It was, therefore, imperative for the current study to ensure an appropriate number of PM stimuli were included within the PM conditions following suggestions proposed by Luck (2005) and Thigpen et al. (2017). It should be noted, however, that no direct evaluation for the number of required trials for determining statistical power for within- and between-group effects in PM stimuli has been performed.

The PM task is an adapted version of Cruz's (2016) PM paradigm incorporating two PM conditions: feature-based (referred to as *perceptual* within the literature and throughout the rest of the current study) and conceptual PM (illustrated in Figure 5.1b). Participants were first presented with a list of 10 categories. Words (10 words from each category; 100 in total) were quasi-randomly presented. To mitigate practice effects, the experiments were programmed to not repeat a previously presented set of categories. Participants were instructed to press a labelled button on the response box with their right index finger if the word on the screen was from the same semantic category as the word before it. Participants were then instructed on the secondary PM task, which was based on either 1) stimulus features (perceptual PM) or 2) semantics (conceptual PM).

For the perceptual PM condition ($PM_{percept}$), participants were told to remember to press the labelled button on the response box with their left index finger if they noticed the word appearing in capital letters, for example, the word 'SWORD'. For the conceptual PM condition ($PM_{concept}$), participants were told to remember to press the labelled button on the response box with their left index finger if they read the word of a four-footed animal, for example, the word 'lion'. The instructions included examples and a short practice block, which provided feedback informed the participants whether their response was correct or incorrect. The order of presentation of the PM tasks was counterbalanced to mitigate fatigue effects (tasks 2/3 Figure 5.1b). Each PM task contained 600 stimuli, with breaks offered every 30 stimuli. PM cues occurred no more than 10% of the time and were presented pseudo-randomly to allow participants to re-engage with the ongoing task and to remove the chance of a PM cue repeating.

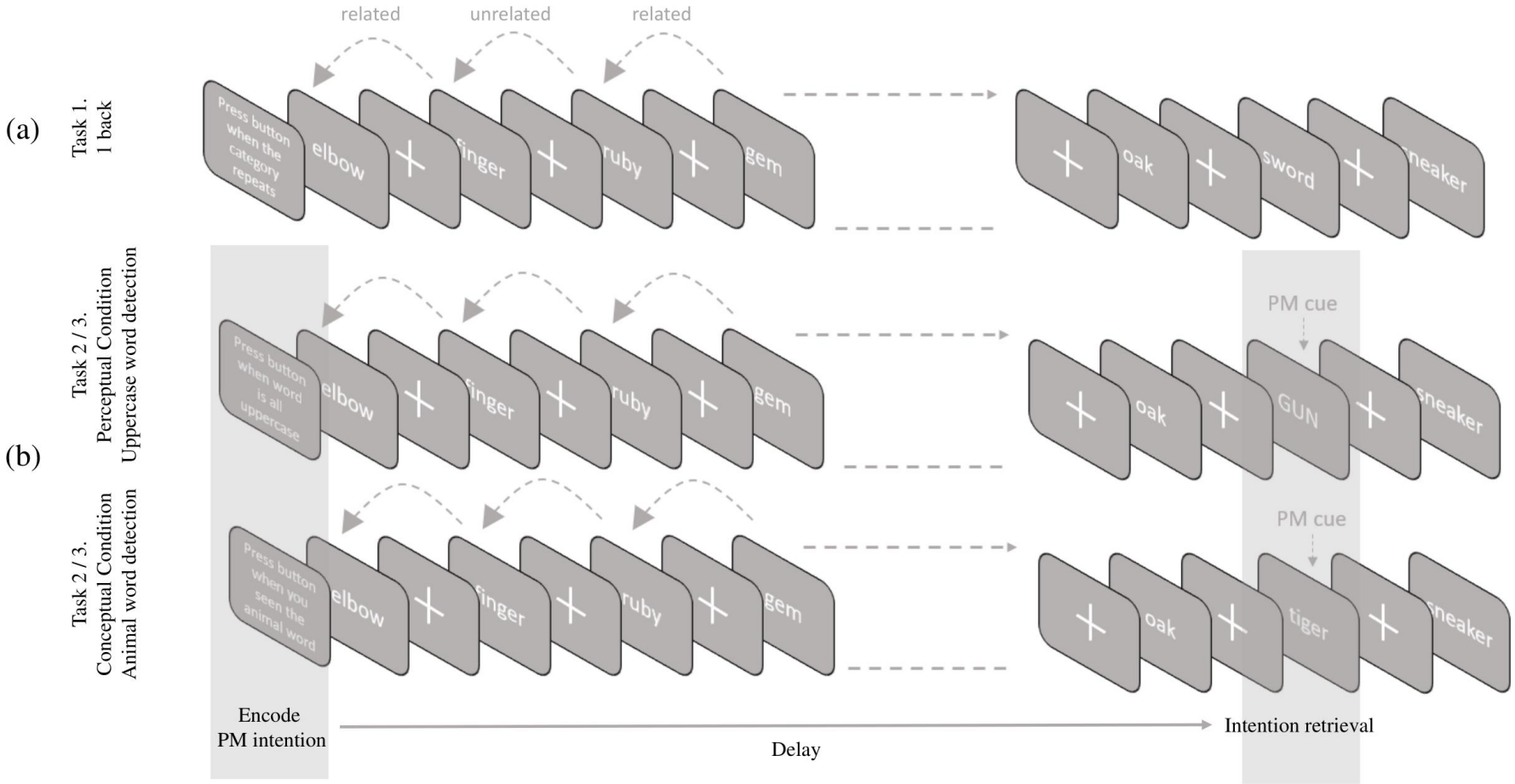

Figure 5.1. Experimental paradigm. (a) The ongoing working memory task. The dashed arrows denote the response required to be made to the previous stimulus. Related words were those stimuli that were from the same semantic category as the word previously presented word. Unrelated words are those words that are not from the same semantic category. (b) The prospective memory stimuli were embedded within the ongoing task. The light grey box indicates PM intention encoding and the retrieval after a delay. Examples of the perceptual PM cue and conceptual PM cues are marked with a small dashed arrow.

5.2.6 Electrophysiological data acquisition

Electroencephalographic activity was measured on the surface of the scalp using an active-electrode, 128 channel Active Two Acquisition system (BioSemi, Amsterdam, Netherlands) sampling at 2048Hz and digitised at 24-bits. Referencing was performed online using CMS/DRL feedback loop with a low pass filter (5th order since response with a -3dB at 1/5th sampling rate). During the electrode application, offsets were examined to ensure they were <20μV. Seven additional Ag/AgCl electrodes were placed around the face to help with artifact detection. Data were collected using ActiView V6.05 (National Instruments, TX, USA) on a Windows PC. A response box was used to record the participant's responses. Digital response and event markers were inserted into the recording data via a parallel port.

5.2.7 Behavioural data analysis

To evaluate the differences between perceptual and conceptual PM performance, the accuracy and reaction times of the PM tasks were compared using the ongoing working memory task performance as a baseline. Two three-way ANOVAs (*Stimuli*: 1-back$_{target}$, PM$_{percept}$, PM$_{concept}$) were conducted for reaction time and percentage of correct responses. Only data from successful responses to stimuli were analysed for reaction time.

5.2.8 Electrophysiological data analysis

EEG data analysis and preprocessing were performed in MATLAB R2015a (The Mathwords, Inc) using custom-written scripts and the EEGlab plugin (Delorme & Makeig, 2004). Data was imported referenced to linked mastoids and downsampled to 256Hz. Following recommendations by Tanner et al. (2015) a high-pass finite impulse (FIR) filter was applied at 0.01Hz and a low pass FIR filter at 35Hz. Line noise was removed using the CleanLine plug-in before a visual inspection was performed to reject bad channels. Following an ICA (runica) decomposition, independent components were visually inspected, and ocular and muscular artifacts were rejected from the data based on their scalp topographies and activity spectra. Next, the stimulus

triggers were recoded to incorrect and correct responses before epochs were extracted with 200ms pre-stimulus baseline.

A virtual electrode method (Baker et al., 2018; Gilmore et al., 2005; Krusemark et al., 2008; Rousselet et al., 2010) was employed to generate maximal value ERPs from a defined cluster of electrodes. This method enables individual differences to be considered and minimises multiple comparisons from an area of interest. Clusters were informed through the consideration of previous EEG research (Scolaro et al., 2014; West, 2011; Zöllig et al., 2012) for the 1-back$_{target}$, PM$_{percept}$ and PM$_{concept}$ task conditions. The 128 channels were clustered into 18 clusters (Figure 5.2; Appendix B for a table of the clusters). 1-back$_{nontarget}$ stimuli ERP amplitudes from the ongoing task were also extracted and analysed to evaluate differences between the two ongoing stimuli and to explore passive working memory processes.

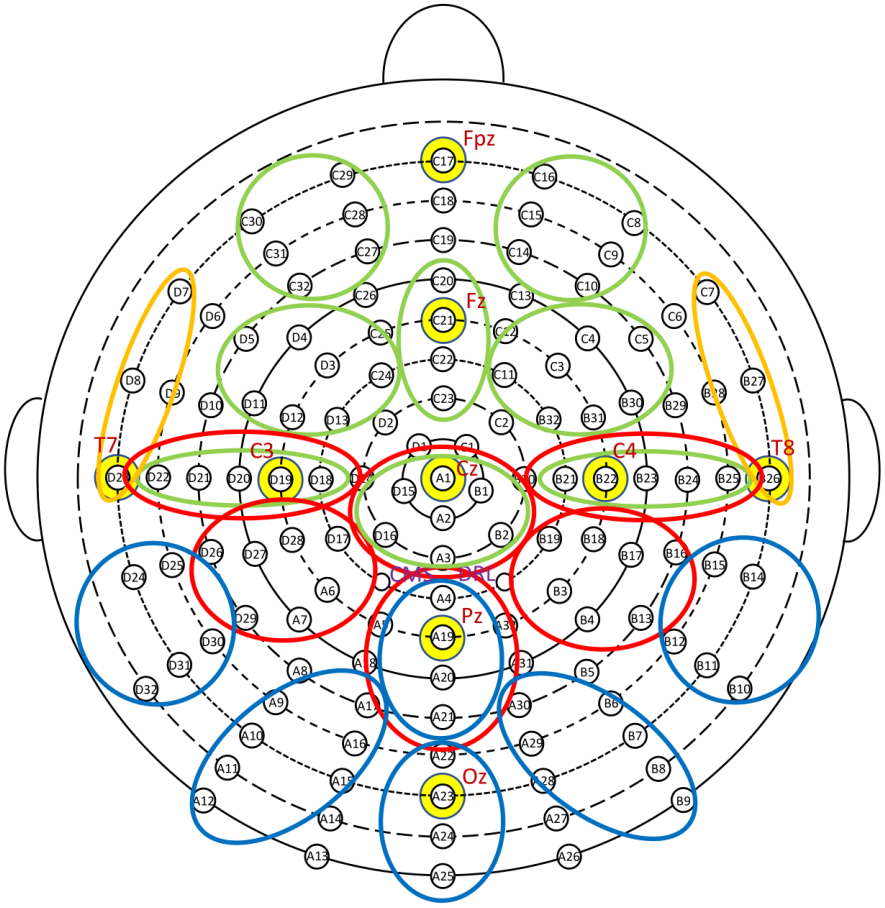

Figure 5.2. Illustration of the PM related ERP cluster definitions for the virtual electrode method. Green = P2 and Frontal Positivity. Red = P3b, Old-New Effect and Prospective Positivity. Blue = N300. Orange = RON.

Peak detection was performed using custom-written scripts in Matlab 2015a using the EEGLAB toolbox on each waveform (Delormne & Makeig, 2004). P2 was defined as the maximum positive peak at midline frontal and central clusters and bilateral frontocentral and central clusters between 160–220ms. N2 was defined as the most negative peak at midline parietal and occipital, and at bilateral parietal, inferior parietal and occipital clusters between 160–220ms. The N300 was defined as the most negative peak at midline parietal and occipital clusters, and bilateral inferior parietal and occipital clusters between 300–500ms. Frontal positivity was defined as the most positive peak at midline frontal and central, and bilateral frontal, central and frontocentral clusters between 300–500ms. The N400 was defined as the most negative peak between 350–550ms over its maximal distribution at midline and bilateral central and parietal clusters (Kutas & Federmeier, 2011; 1-back$_{target}$ and 1-back$_{nontarget}$ stimuli only). The P3b and the IRR were defined as the most positive peaks at midline and bilateral central and parietal clusters occurring between 300–400ms and 400–600ms, respectively. The prospective positivity was defined as being the largest sustained amplitude at midline and bilateral central and parietal clusters between 600–1000ms. The spatial location of the RON ERP was identified by visual inspection of the ERP waveforms across clusters and were defined as the most negative peak amplitude between 400–750ms. Amplitudes were measured as baseline to peak. All statistical analyses were performed using JASP (0.10.2).

The following analyses were used for ERP Experiment 1 to address possible differences between the 1-back$_{target}$ and 1-back$_{nontarget}$ stimuli in N2, P2 and N400 components. Each ERP component was independently analysed and was further subdivided between midline and bilateral analyses in a series of mixed measures ANOVAs. The ANOVA variables were S*timuli* (1-back$_{target}$, 1-back$_{nontarget}$), *Cluster* for midline and the bilateral clusters included *Hemisphere* (left, right). The level in *Cluster* varied depending on the component: P2 (frontal, frontocentral, central), N2 (parietal, inferior parietal, occipital) and N400 (central, parietal).

To analyse differences in PM-related components in Experiment 2, the following components were analysed: N300, frontal positivity, P3b, IRR, prospective positivity, and RON. Each component was analysed independently and was further divided between midline and bilateral analyses in the following within measures ANOVAs. The ANOVAs included *Stimuli* (1-back$_{target}$, 1-back$_{nontarget}$, PM$_{percept,}$ PM$_{concept}$) x *Cluster* at

midline clusters with the addition of *Hemisphere* (left, right) variable for bilateral clusters. Level in the *Cluster* variable varied depending on the component: P2 and frontal positivity (frontal, frontocentral, central), N2 (parietal, inferior parietal, occipital), N300 (parietal, occipital), P3b, IRR and prospective positivity (central, parietal), RON (frontotemporal). Lower-order ANOVAs were used to explore significant interactions and post-hoc analyses were used to determine differences. Bonferroni corrections were applied to account for multiple comparisons (Cabin & Mitchell, 2000). Greenhouse-Geisser was used to correct for violations of sphericity and are reported. Partial eta squared (η_p^2), which was selected based on its generalisability to different experiment designs (Richardson, 2011), was reported for each main and interaction effect as an indicator of effect size (Bakeman, 2005).

5.3 Results

5.3.1 Behavioural results

Behavioural results are illustrated in Figure 5.3.

5.3.1.1 Reaction time

There was a significant effect of *Stimuli* ($F_{2,29} = 63.63$, $p < 0.001$, $\eta_p^2 = 0.69$), such that it took a significantly greater amount of time to correctly respond to $PM_{concept}$ stimuli (938ms, SD = 0.13) relative to both 1-$back_{target}$ stimuli (763ms, SD = 0.12) and $PM_{percept}$ stimuli (711ms, SD = 0.09). In addition, reaction times to $PM_{percept}$ stimuli were significantly faster than 1-$back_{target}$ stimuli ($p = 0.017$).

5.3.1.2 Correct responses

There was a significant effect of *Stimuli* ($F_{2,29} = 25.75$, $p < 0.001$, $\eta_p^2 = 0.47$), which was due to a significantly greater number of correct responses for $PM_{percept}$ stimuli (97.26%, SD = 6.29) relative to 1-$back_{target}$ stimuli (80.67%, SD = 10.63, $p < 0.001$) and $PM_{concept}$ stimuli (86.39%, $p < 0.001$). Whilst the number of correct responses for

$PM_{concept}$ stimuli was higher than 1-$back_{target}$ stimuli, this effect fell short of the significance threshold (p = 0.051).

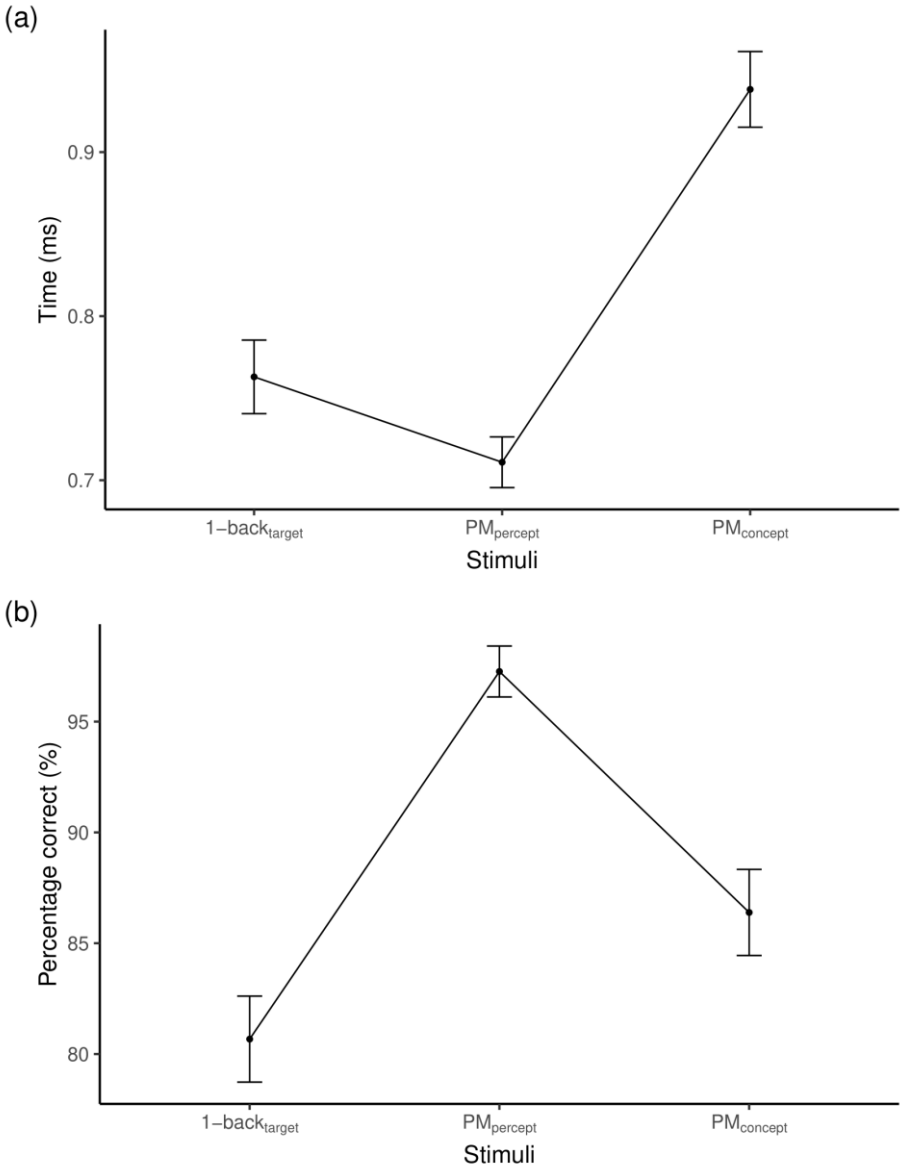

Figure 5.3. Descriptive plots for the reaction time (a) and the percentage of correct responses (b). 1-$back_{target}$ = repeated ongoing stimuli, $PM_{percept}$ = perceptual PM stimuli, $PM_{concept}$ = conceptual PM stimuli. Error bars show standard error.

5.3.2 Electrophysiological Analysis: Experiment 1, 1-back$_{target}$ versus 1-back$_{nontargets}$

One participant was removed due to poor EEG data. Thus, n = 29 participants were included in the final analysis.

5.3.2.1 ERPs to ongoing 1-back$_{target}$ versus 1-back$_{nontarget}$ stimuli.

All statistically significant main effects and post hoc-tests are presented in Table 5.1. Means and standard deviations for the N2, P2 and N400 amplitudes for 1-back$_{target}$ and 1-back$_{nontarget}$ stimuli can be found in Appendix C, Table C.1.

5.3.2.2 Midline anterior P2 amplitudes.

There was a significant main effect of *Cluster* ($F_{1,28} = 12.75$, $p < 0.001$, $\eta_p^2 = 0.32$), such that the frontal cluster had significantly greater amplitudes relative to the central cluster ($p = 0.001$). There were no other significant effects.

5.3.2.3 Lateral anterior P2 amplitudes.

There was a significant main effect of *Stimuli* ($F_{1,28} = 30.00$, $p < 0.001$, $\eta_p^2 = 0.56$), such that 1-back$_{target}$ stimuli produced significantly greater P2 amplitudes relative to the 1-back$_{nontarget}$ stimuli. Additionally, there was a significant main effect of *Cluster* ($F_{2.31,55.45} = 12.80$, $p < 0.001$, $\eta_p^2 = 0.35$), where frontocentral P2 amplitudes were significantly greater than all other clusters ($ps < 0.001$). There were no other significant effects.

5.3.2.4 Midline posterior N2 amplitudes.

There was a significant main effect of *Cluster* ($F_{1,28} = 50.28$, $p < 0.001$, $\eta_p^2 = 0.65$), such that N2 amplitudes were significantly greater at the midline occipital cluster relative to the midline parietal cluster. There were no other significant effects.

5.3.2.5 Lateral Posterior N2 Amplitudes

There was a significant main effect of *Stimuli* ($F_{1,28}$ = 4.77, p = 0.038, η_p^2 = 0.16), which was due to greater negativity of the N2 amplitude ERP in response to 1-back$_{target}$ stimuli relative to 1-back$_{nontarget}$ stimuli. There was also a significant effect of *Cluster* ($F_{1.52,39.49}$ = 37.07, p < 0.001, η_p^2 = 0.59), such that occipital N2 amplitudes were significantly greater (more negative) than parietal (p < 0.001) and inferior parietal (p = 0.008) clusters. Additionally, inferior parietal clusters evoked significantly greater N2 responses than parietal clusters (p < 0.001). There were no other significant effects.

Table 5.1

Summary of Significant Effects for the P2, N2 and N400 ERP Amplitudes (1-back$_{target}$ versus 1-back$_{nontarget}$)

Midline P2 ERP Amplitude	**Lower**	**F-Value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Cluster		12.75	1,28	< 0.001	0.32	F > C
Lateral Anterior P2 Amplitudes						
Stimuli		30.00	1,28	< 0.001	0.56	1-back$_{target}$ > 1-back$_{nontarget}$
Cluster		12.80	2.31,55.45	< 0.001	0.35	FC > F & C
Midline Posterior N2 Amplitudes						
Cluster		50.28	1,28	< 0.001	0.65	OC < P
Lateral posterior N2 amplitudes						
Stimuli		4.77	1,28	0.038	0.16	1-back$_{nontarget}$ < 1-back$_{target}$
Cluster		37.07	1.52,39.49	< 0.001	0.59	OC < IP < P
Midline N400 Amplitudes						
Stimuli		6.63	1,28	0.016	0.20	1-back$_{nontarget}$ < 1-back$_{target}$
Cluster		107.30	1,28	< 0.001	0.80	C < P
Lateral N400 Amplitudes						
Stimuli		17.20	1,28	< 0.001	0.34	
Cluster		147.28	1,28	< 0.001	0.85	
*Stimuli*Hemisphere*		10.77	1,28	0.003	0.29	
	R	29.55	1,28	<0.001	0.52	1-back$_{nontarget}$ < 1-back$_{target}$
*Stimuli*Cluster*		4.84	1,28	0.037	0.15	
	1-back$_{target}$	122.89	1,28	< 0.001	0.82	C < P
	1-back$_{nontarget}$	138.55	1,28	< 0.001	0.84	C < P
	P	19.99	1,28	< 0.001	0.43	1-back$_{nontarget}$ < 1-back$_{target}$

1-back$_{target}$ = repeated ongoing stimuli, 1-back$_{nontarget}$ = non-repeated ongoing stimuli. Clusters: FC = frontocentral, F = frontal, C = central, OC = occipital, IP = inferior parietal, P = parietal. R = right hemisphere. *N.B* '>' means amplitudes are more positive for the P2 amplitudes and '<' means that amplitudes were more negative for N2 and N400 amplitudes.

5.3.2.6 Midline N400 amplitudes.

Midline N400 amplitudes are illustrated in Figure 5.4. There was a significant main effect of *Stimuli* ($F_{1,28}$ = 6.63, p = 0.016, η_p^2 = 0.20), where 1-back$_{nontarget}$ stimuli produced greater N400 amplitude response relative to 1-back$_{target}$ stimuli. There was also a significant main effect of *Cluster* ($F_{1,28}$ = 107.30, p < 0.001, η_p^2 = 0.80), where central clusters exhibited a greater N400 response than at parietal clusters. There were no other significant effects.

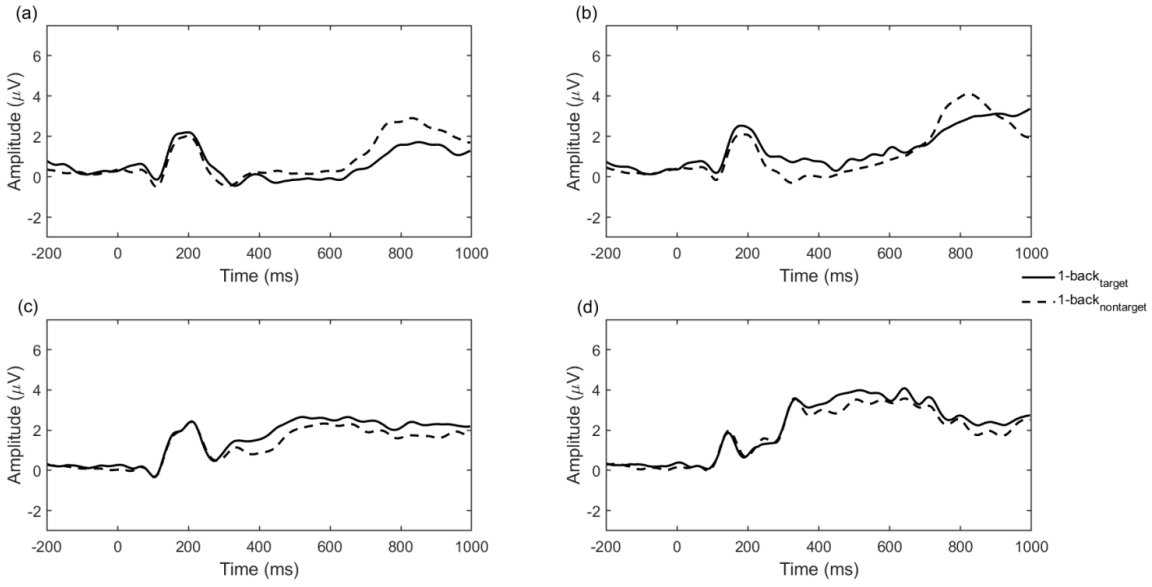

Figure 5.4. ERP waveforms for repeated ongoing stimuli (1-back$_{target}$) and non-repeat ongoing stimuli (1-back$_{nontarget}$). (a) Left frontal cluster and (b) right frontal cluster showing a P2 amplitude increase for 1-back$_{target}$ stimuli. (c) Midline central cluster (d) midline parietal cluster illustrates the increased N400 for 1-back$_{nontarget}$ stimuli.

5.3.2.7 Lateral N400 amplitudes.

There was a significant main effect of *Stimuli* ($F_{1,28}$ = 17.20, p < 0.001, η_p^2 = 0.34) and a significant main effect of *Cluster* ($F_{1,28}$ = 147.28, p < 0.001, η_p^2 = 0.85). There was also a significant interaction effect of *Stimuli* x *Hemisphere* ($F_{1,28}$ = 10.77, p = 0.003,

$\eta_p^2 = 0.29$), which was due to a significant effect of *Stimuli* in the right hemisphere, where 1-back$_{nontarget}$ stimuli produced a significantly greater N400 ERP (incongruence effect) than 1-back$_{target}$ stimuli ($F_{1,28} = 29.55$, $p < 0.001$, $\eta_p^2 = 0.52$), but was not found over the left hemisphere.

There was also a significant *Stimuli* x *Cluster* interaction effect ($F_{1,28} = 4.84$, $p = 0.037$, $\eta_p^2 = 0.15$). This interaction was in part due to a significant effect of *Cluster* for 1-back$_{target}$ ($F_{1,28} = 122.89$, $p < 0.001$, $\eta_p^2 = 0.82$) and 1-back$_{nontarget}$ stimuli ($F_{1,28} = 138.55$, $p < 0.001$, $\eta_p^2 = 0.84$), where central clusters evoked the greater N400 amplitude responses relative to the parietal clusters and also due to a significant effect of *Stimuli* at parietal clusters ($F_{1,28} = 19.99$, $p < 0.001$, $\eta_p^2 = 0.43$), where 1-back$_{nontarget}$ evoked a greater N400 ERP than 1-back$_{target}$ stimuli.

5.3.3 Summary and interim discussion for Experiment 1: repeated versus non-repeated ongoing stimuli

Experiment 1 was performed with 1-back$_{target}$ and 1-back$_{nontarget}$ stimuli in the ongoing-only task condition to determine whether there are neurophysiological response differences between the two stimuli. These comparisons were made to assess whether ongoing stimuli can be averaged together before being compared against PM stimuli. The P2 and N2 were used as earlier cognitive measures of attention and executive function in the semantic working memory task (Folstein & Van Petten, 2008; Schmitt et al., 2000). The N400 ERP was measured to assess the possible differences in semantic processing and differences at the later stage of the ERP. The results revealed there is indeed a semantic congruency effect, as indicated by the N400, and amplitude differences at the earlier N2 and P2 components.

As expected, the ongoing stimuli exhibited a clear congruency effect where 1-back$_{nontarget}$ stimuli produced a greater N400 response at midline and bilateral centroparietal clusters (Kutas & Federmeier, 2011). This finding is in line with past research demonstrating that 1-back$_{target}$ stimuli produce significantly smaller (less negative) N400 amplitudes relative to unrelated stimuli (Cruz San Martin, 2014; Kutas & Federmeier, 2011). Interestingly, a greater N400 was found in the right hemisphere for 1-back$_{nontarget}$ relative to 1-back$_{target}$ stimuli, but this was not found in the left

hemisphere. It is possible that this hemispheric asymmetry reflects word-meaning comprehension as demonstrated in numerous other studies (reviews: Federmeier, 2007; Federmeier et al., 2008). For example, an ERP study conducted by Coulson et al. (2005), compared N400 congruency effects in sentence and world level comprehension. Both hemispheres demonstrated a greater N400 ERP in response to incongruent stimuli, but analyses of word level comprehension revealed that the right hemisphere is more sensitive to word-word relationships than the left hemisphere, which was primarily associated with sentence meaning.

It was expected that there would be ERP amplitude differences in the N2 but not the P2 in response two ongoing task stimuli. However, the results here demonstrated greater N2 and P2 ERP amplitudes in response to related words relative to unrelated words. It could be argued that experimental design follows a go/no-go format, however, it would be expected that there would be increases in the N2 amplitudes in response to the unrelated stimuli relative to the related stimuli (Heil et al., 2000; Pfefferbaum et al., 1985). Given that the opposite amplitude effect is found here, and the related words are rarer relative to the unrelated words (i.e., related words had a 25% chance of occurring), it is more likely that the current study follows a design more similar to an oddball or *n*-back task. As such, given that the processing of semantic information can be processed as early as 160ms (Amsel et al., 2013; Hauk et al., 2012) the increase in the N2 might reflect visual awareness for the related stimuli (Koivisto et al., 2018) while the increase in the P2 likely reflects processes associated with stimulus classification, evaluation (Z. G. Doborjeh, Kasabov, et al., 2018; Potts, 2004) and the shifting of attention (Wongupparaj et al., 2018).

From these results, it can be concluded that for comparisons of ERPs between ongoing working memory and PM, careful consideration should be taken with respect to averaging ERPs in response to ongoing task stimuli. The differences between the amplitudes of the two different stimuli here show that incorrect conclusions may have been made by Cousens et al. (2015), where ERPs related to related and unrelated words were treated as the same and were averaged together. The current results support Cruz et al.'s (2016) assertion to treat related and unrelated ongoing task stimuli as separate and compare PM with each of the ongoing task stimuli. Throughout the rest of this thesis, the 1-back$_{target}$ and 1-back$_{nontarget}$ stimuli will be treated separately.

5.3.4 Electrophysiological Analysis: Experiment 2, prospective memory ERPs

Experiment Two aimed to explore the differences in the ERP components related to perceptual and conceptual PM stimuli and whether a RON response is produced following a PM stimulus. All grand-averaged waveforms across all clusters for the 1-back$_{target}$, 1-back$_{nontarget}$, PM$_{percept}$ and PM$_{concept}$ can be found in Figure 5.4.

5.3.4.1 Prospective Memory Cue Detection

Descriptions of the N300 and frontal positivity amplitudes are presented in Appendix D, Table D.1 and Table D.2, respectively.

5.3.4.2 N300 ERP amplitudes

A summary of all significant effects is presented in Table 5.2.

5.3.4.3 Midline N300 ERP amplitudes

There was a significant main effect of *Stimuli* ($F_{1.89,51.12} = 4.62$, $p = 0.016$, $\eta_p^2 = 0.15$) and a significant main effect of *Cluster* ($F_{1,28} = 32.40$, $p < 0.001$, $\eta_p^2 = 0.55$).

There was a significant *Stimuli* x *Cluster* interaction ($F_{1.83,49.52} = 12.85$, $p < 0.001$, $\eta_p^2 = 0.32$). The interaction was due to an effect of *Stimuli* in the parietal cluster ($F_{1.89,51.06} = 6.97$, $p = 0.002$, $\eta_p^2 = 0.21$), where N300 amplitudes in response to PM$_{concept}$ were greater than PM$_{percept}$ ($p < 0.001$). The interaction was also due to a significant effect of *Stimuli* in the occipital cluster ($F_{1.80,48.67} = 7.97$, $p = 0.001$, $\eta_p^2 = 0.23$), where both PM$_{percept}$ and PM$_{concept}$ stimuli caused significantly greater N300 amplitudes than 1-back$_{nontarget}$ stimuli ($p = 0.016$ and $p = 0.004$, respectively). However, only the N300 in response to PM$_{concept}$ was greater than 1-back$_{target}$ stimuli, as the PM$_{percept}$ was only considered trending towards significance ($p = 0.05$). Furthermore, the interaction is explained by a significant effect of *Cluster* across all stimuli, where the occipital cluster

had greater N300 amplitudes than the parietal cluster (1-back$_{nontarget}$, p = 0.003, all other ps < 0.001).

5.3.4.4 Lateral N300 ERP amplitudes

Similar to midline clusters, there was a significant main effect of *Stimuli* ($F_{1.99,51.72}$ = 15.56, p < 0.001, η_p^2 = 0.37) and a significant main effect of *Cluster* ($F_{1,28}$ = 14.66, p < 0.001, η_p^2 = 0.36).

Additionally, there was a significant interaction effect of *Stimuli* x *Cluster* ($F_{2.24,58.35}$ = 7.06, p = 0.001, η_p^2 = 0.21). This can be explained by a significant effect of *Stimuli* in the inferior parietal clusters ($F_{2.23,60.09}$ = 20.03, p < 0.001, η_p^2 = 0.43), where PM$_{percept}$ stimuli caused significantly greater N300 responses than 1-back$_{target}$ (p < 0.001), 1-back$_{nontarget}$ (p = 0.001) and PM$_{concept}$ stimuli (p = 0.002). Moreover, amplitudes in response to 1-back$_{target}$ was found to be more negative than in response to 1-back$_{nontarget}$ stimuli (p = 0.001). The *Stimuli* x *Cluster* interaction was also due to a significant effect of *Stimuli* in the occipital cluster ($F_{1.89,49.23}$ = 6.91, p = 0.003, η_p^2 = 0.21), where PM$_{concept}$ stimuli produced significantly greater N300 responses than 1-back$_{nontarget}$ (p < 0.001) and 1-back$_{target}$ (p = 0.035), but was not found for PM$_{percept}$ (ps > 0.05).

The *Stimuli* x *Cluster* interaction was also explained by a significant effect of *Cluster,* such that inferior parietal clusters generated significantly greater N300 amplitude responses than occipital clusters for 1-back$_{target}$ (p < 0.001), 1-back$_{nontarget}$ (p = 0.004) and PM$_{percept}$ (p < 0.001) stimuli. However, the effect of *Cluster* for PM$_{concept}$ stimuli fell just short of significance (p = 0.053).

Table 5.2

Summary of Significant Effects for the N300 ERP Amplitudes

Midline N300 ERP Amplitude	**Lower**	**F-Value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Stimuli		4.62	1.89,51.12	0.016	0.15	
Cluster		32.40	1,27	< 0.001	0.55	
*Stimuli*Cluster*		12.85	1.83,49.52	< 0.001	0.32	
	P	6.97	1.89,51.06	0.002	0.21	$PM_{concept}$ > $PM_{percept}$
	OC	7.97	1.80,48.67	0.001	0.23	PM > $1\text{-back}_{nontarget}$ | $PM_{concept}$ > 1-back_{target} | $PM_{percept}$ > 1-back_{target}†
	1-back_{target}	19.72	1,28	< 0.001	0.42	P > OC
	$1\text{-back}_{nontarget}$	11.04	1,28	0.003	0.29	P > OC
	$PM_{percept}$	32.74	1,28	< 0.001	0.54	P > OC
	$PM_{concept}$	22.78	1,28	< 0.001	0.45	P > OC
Lateral N300 ERP Amplitudes	**Lower**	**F-Value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Stimuli		15.56	1.99,51.72	< 0.001	0.37	
Cluster		14.66	1,28	< 0.001	0.36	
*Stimuli*Cluster*		7.06	2.24,58.35	0.001	0.21	
	IP	20.03	2.23,60.09	< 0.001	0.43	$PM_{percept}$ > $PM_{concept}$ & 1-back_{target} > $1\text{-back}_{nontarget}$
	OC	6.91	1.89,49.23	0.003	0.21	$PM_{concept}$ > $1\text{-back}_{nontarget}$ & 1-back_{taget}

Lateral N300 ERP Amplitudes	**Lower**	**F-Value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
	1-back_{target}	20.87	1,28	< 0.001	0.45	IP > OC
	$1\text{-back}_{nontarget}$	9.91	1,28	0.004	0.28	IP > OC
	$PM_{percept}$	15.12	1,28	< 0.001	0.36	IP > OC
	$PM_{concept}$	4.08	1,28	0.053†	0.28	

Stimuli: 1-back_{target} = repeated ongoing stimuli, $1\text{-back}_{nontarget}$ = non-repeated ongoing stimuli, $PM_{percept}$ = perceptual prospective memory stimuli, $PM_{concept}$ = conceptual prospective memory stimuli. Clusters: P = parietal, OC = occipital, IP = inferior parietal. † = trending effect. PM = both $PM_{percept}$ & $PM_{concept}$. *N.B.* '>' indicates amplitudes being more negative in this table.

5.3.4.5 Frontal positivity ERPs

A summary of all significant effects is presented in Table 5.3.

5.3.4.6 Midline frontal positivity ERP amplitudes

There was a significant main effect of *Stimuli* ($F_{2.39,64.56} = 66.65$, $p < 0.001$, $\eta_p^2 = 0.71$) and a significant main effect of *Cluster* ($F_{1,28} = 24.73$, $p < 0.001$, $\eta_p^2 = 0.48$).

There was a significant interaction of *Stimuli* x *Cluster* ($F_{1.85,62.98} = 8.92$, $p < 0.001$, $\eta_p^2 = 0.25$). This, in part, was due to a significant effect of *Stimuli* at the frontal cluster where $PM_{percept}$ produced a significantly greater ERP response than all other stimuli ($ps < 0.001$) and $PM_{concept}$ was greater than $1\text{-back}_{nontarget}$ stimuli ($p < 0.001$). At the frontal cluster, 1-back_{target} stimuli was significantly greater than $1\text{-back}_{nontarget}$ stimuli ($p = 0.002$). Similarly, a significant effect of *Stimuli* was found at the central cluster ($F_{2.39,64.56} = 66.65$, $p < 0.001$, $\eta_p^2 = 0.71$), where $PM_{percept}$ amplitudes were more positive than 1-back_{target}, $1\text{-back}_{nontarget}$ and $PM_{concept}$ ($ps < 0.001$), but no differences were found between any other stimuli ($ps > 0.05$). The *Stimuli* x *Cluster* interaction is also explained by significantly more positive amplitudes for all stimuli at the central relative to the frontal cluster ($ps < 0.05$).

5.3.4.7 Lateral frontal positivity ERP amplitudes

There was a significant main effect of *Stimuli* ($F_{3,84} = 22.02$, $p < 0.001$, $\eta_p^2 = 0.46$). There was also a significant interaction of *Stimuli* x *Hemisphere* ($F_{3,84} = 5.00$, $p = 0.003$, $\eta_p^2 = 0.16$) and *Stimuli* x *Cluster* ($F_{3.52,91.59} = 7.18$, $p < 0.001$, $\eta_p^2 = 0.22$).

The *Stimuli x Hemisphere* interaction is explained by a significant effect of *Stimuli* in the left hemisphere ($F_{3,84} = 11.35$, $p < 0.001$, $\eta_p^2 = 0.30$), where $PM_{percept}$ and $PM_{concept}$ had significantly more positive amplitudes than $1\text{-back}_{nontarget}$ stimuli ($p < 0.001$ & $p = 0.018$, respectively) and $PM_{percept}$ was larger than 1-back_{target} stimuli ($p = 0.001$). In the right hemisphere ($F_{3,84} = 24.46$, $p < 0.001$, $\eta_p^2 = 0.48$), $PM_{percept}$ stimuli amplitudes were significantly more positive than $1\text{-back}_{nontarget}$ ($p < 0.001$), 1-back_{target} ($p = 0.001$) and $PM_{concept}$ stimuli ($p = 0.006$); $PM_{concept}$ stimuli was significantly more positive than 1-

back$_{nontarget}$ stimuli (p < 0.001) but not 1-back$_{target}$ stimuli (p > 0.05); 1-back$_{target}$ was significantly greater than 1-back$_{nontarget}$ (p < 0.001). Additionally, the interaction is also due to an effect of H*emisphere,* where the right had greater amplitudes than the left for 1-back$_{target}$ stimuli ($F_{3.52,91.59}$ = 7.18, p < 0.001, η_p^2 = 0.22).

The *Stimuli* x *Cluster* interaction is explained by a significant effect of *Stimuli* at frontal clusters ($F_{3,84}$ = 2.91, p = 0.040, η_p^2 = 0.10), where PM$_{concept}$ stimuli was significantly larger than 1-back$_{nontarget}$ stimuli (p = 0.035); at frontocentral clusters ($F_{2.28,61.46}$ = 35.09, p < 0.001, η_p^2 = 0.57), where PM$_{percept}$ was significantly larger than 1-back$_{target}$, 1-back$_{nontarget}$ and PM$_{concept}$ (ps < 0.001) and PM$_{concept}$ was larger than 1-back$_{nontarget}$ (p < 0.001) but not 1-back$_{target}$ (p > 0.05) and 1-back$_{nontarget}$ was larger than 1-back$_{target}$ (p = 0.004); at central clusters ($F_{2.14,61.77}$ = 33.16, p < 0.001, η_p^2 = 0.55), where PM$_{percept}$ stimuli was significantly larger than all other stimuli (ps < 0.001) and PM$_{concept}$ was significantly larger than 1-back$_{nontarget}$ (p = 0.015) but not 1-back$_{target}$ (p > 0.05). Additionally, this interaction can be explained by a significant effect of *Cluster* for PM$_{percept}$ stimuli ($F_{1.56,43.54}$ = 9.22, p = 0.002, η_p^2 = 0.26), such that frontocentral and central clusters evoked significantly larger amplitudes compared to frontal clusters (ps = 0.001). There were no other significant effects.

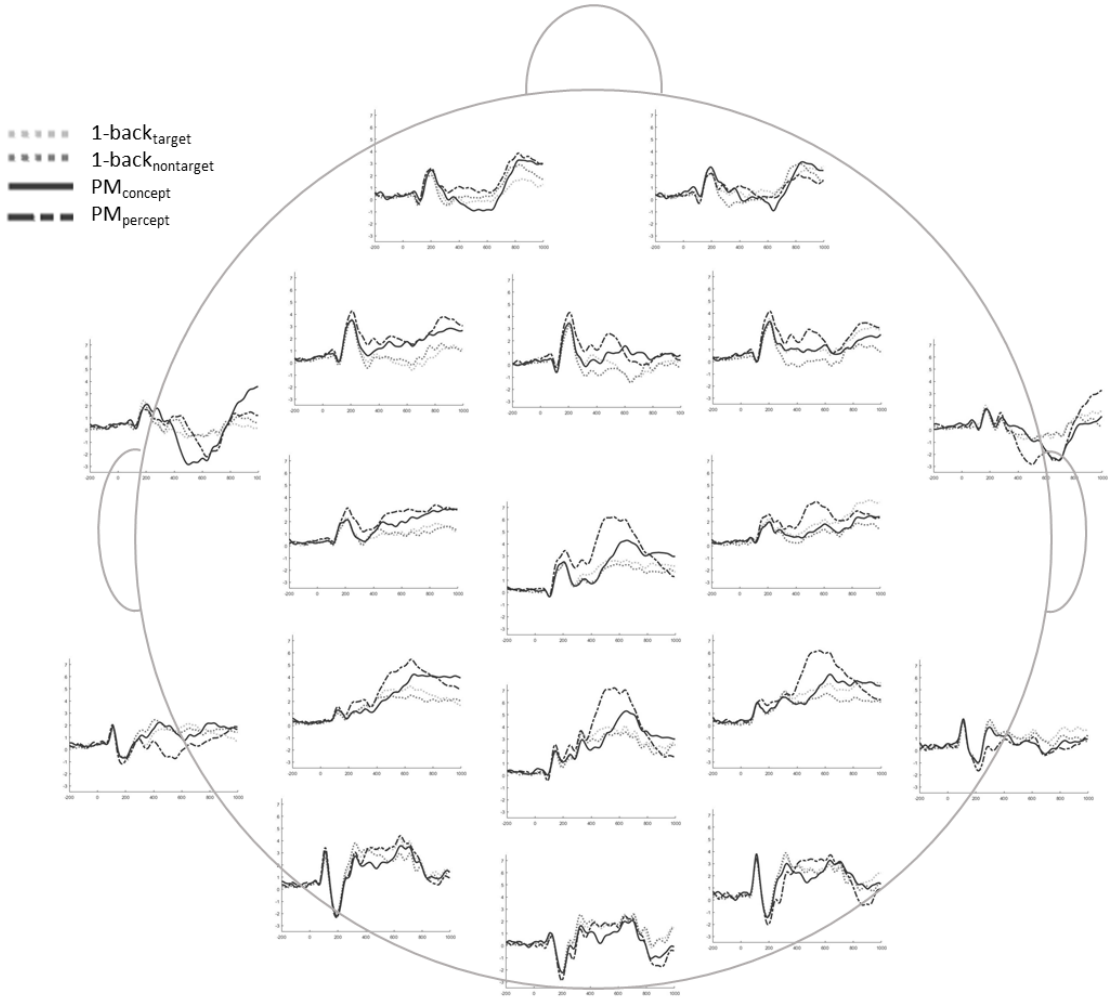

Figure 5.4. Grand-averaged ERP waveforms across the 18 clusters for repeated ongoing-only stimuli (1-back$_{target}$), non-repeated ongoing-only stimuli (1-back$_{nontarget}$), conceptual prospective memory stimuli (PM$_{concept}$) and perceptual prospective memory stimuli (PM$_{percept}$). The y-axis of for each of the ERP waveforms is from -3μV to 7μV. The x-axis for each ERP waveform is from -200 to 1000ms.

Table 5.3

Summary of Significant Effects for Frontal Positivity ERP Amplitudes

Midline Frontal Positivity	**Lower**	**F-Value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Stimuli		66.65	2.39,64.56	< 0.001	0.25	
Cluster		24.73	1,28	< 0.001	0.48	
*Stimuli*Cluster*		8.92	1.85,62.98	< 0.001	0.25	
	F	31.78	2.39,64.56	< 0.001	0.54	$PM_{percept}$ > $PM_{concept}$ & 1-$back_{target}$ > 1-$back_{nontarget}$
	C	58.95	2.21,59.65	< 0.001	0.69	$PM_{percept}$ > $PM_{concept}$ & 1-$back_{target}$ & 1-$back_{nontarget}$
	1-$back_{target}$	11.80	1,28	0.002	0.30	C > F
	1-$back_{nontarget}$	29.68	1,28	< 0.001	0.52	C > F
	$PM_{percept}$	28.11	1,28	< 0.001	0.50	C > F
	$PM_{concept}$	4.24	1,28	0.049	0.13	C > F
Lateral Frontal Positivity						
Stimuli		22.02	2,84	< 0.001	0.46	
*Stimuli*Hemisphere*		5.00	3,84	0.003	0.16	
	L	11.35	3,84	< 0.001	0.30	PM > 1-$back_{nontarget}$ | $PM_{percept}$ > 1-$back_{target}$
	R	24.46	3,84	< 0.001	0.48	$PM_{percept}$ > $PM_{concept}$ > 1-$back_{nontarget}$ |$PM_{percept}$ > 1-$back_{target}$
	1-$back_{target}$	7.18	3.52,91.59	< 0.001	0.22	R > L
*Stimuli*Cluster*						
	F	2.91	3,84	0.040	0.10	$PM_{concept}$ > 1-$back_{nontarget}$
	FC	35.09	2.28,61.46	< 0.001	0.57	$PM_{percept}$ > $PM_{concept}$ > 1-$back_{nontarget}$ | $PM_{percept}$ > 1-$back_{target}$

Lateral Frontal Positivity	Lower	F-Value	DF	*p*-value	η_p^2	Post-Hoc Tests
	C	33.16	2.14,61.77	< 0.001	0.55	$PM_{percept}$ > $PM_{concept}$ > 1-$back_{target}$ | $PM_{percept}$ > 1-$back_{target}$
	$PM_{percept}$	9.22	1.56,43.54	0.002	0.26	FC & C > F

Stimuli: 1-$back_{target}$ = repeated ongoing stimuli, 1-$back_{nontarget}$ = non-repeated ongoing stimuli, $PM_{percept}$ = perceptual prospective memory stimuli, $PM_{concept}$ = conceptual prospective memory stimuli. Clusters: F = frontal, FC = frontocentral, C = central. L = left hemisphere, R = right hemisphere. PM = both $PM_{percept}$ & $PM_{concept}$. *N.B.* '>' indicates amplitudes are more positive in this table. | = separator between post-hoc tests.

5.3.5 Realisation of Intentions: Parietal Positivity

5.3.5.1 P3b ERPs

A summary of significant effects is presented in Table 5.4. Means and standard deviations for the P3b amplitudes can be found in Appendix D, Table D.3

5.3.5.2 Midline P3b ERP amplitudes

There was a significant main effect of *Stimuli* ($F_{3,84} = 11.46$, $p < 0.001$, $\eta_p^2 = 0.23$), which was due to a significantly greater P3b response for $PM_{percept}$ stimuli relative to 1-$back_{taget}$ stimuli ($p = 0.001$) and $PM_{concept}$ stimuli ($p < 0.001$). There was also a significant main effect of *Cluster* ($F_{1,28} = 22.27$, $p < 0.001$, $\eta_p^2 = 0.45$) whereby across all stimuli, P3b responses were significantly greater at parietal clusters.

5.3.5.2 Lateral P3b ERP amplitudes

There was a significant main effect of *Stimuli* ($F_{2.29,61.78} = 9.85$, $p < 0.001$, $\eta_p^2 = 0.27$) and *Cluster* ($F_{1,28} = 21.12$, $p < 0.001$, $\eta_p^2 = 0.44$), which was due to significantly greater amplitudes across all stimuli in the parietal cluster.

Furthermore, there was a significant interaction of *Stimuli* x *Hemisphere* ($F_{3,84}$ = 4.02, p = 0.010, η_p^2 = 0.13). This was due to a significant effect of *Hemisphere* ($F_{1,28}$ = 4.88, p = 0.036, η_p^2 = 0.15) for 1-back$_{target}$ stimuli, where the right hemisphere had greater amplitudes than the left. This hemispheric asymmetry was not found for other stimuli (ps > 0.05). Additionally, the *Stimuli* x *Hemisphere* interaction is explained by a significant effect of *Stimuli* in the left hemisphere ($F_{3,84}$ = 8.38, p < 0.001, η_p^2 = 0.24), such that PM$_{percept}$ stimuli produced significantly greater P3b ERP amplitudes than 1-back$_{target}$ (p = 0.042) and PM$_{concept}$ stimuli (p = 0.011); 1-back$_{nontarget}$ stimuli produced significantly greater P3b amplitudes than 1-back$_{target}$ (p = 0.003) and PM$_{concept}$ Stimuli (p = 0.002). In the right hemisphere, there was also a significant effect of *Stimuli* ($F_{3,84}$ = 6.06, p < 0.001, η_p^2 = 0.18) due to significantly greater amplitudes in response to PM$_{percept}$ stimuli relative to 1-back$_{nontarget}$ (p = 0.043) and PM$_{concept}$ stimuli (p = 0.004). There were no other significant effects.

Table 5.4

Summary of Significant Effects for the P3b ERP Amplitudes

Midline P3b Amplitudes	**Lower**	**F-Value**	**DF**	***p*-value**	**η^2p**	**Post-Hoc Tests**
Stimuli		11.46	3,84	< 0.001	0.23	$PM_{percept}$ > 1-$back_{target}$ & $PM_{concept}$
Cluster		22.27	1,28	< 0.001	0.45	P > C
Lateral P3b ERP Amplitudes						
Stimuli		9.85	2.29,61.78	< 0.001	0.27	
Cluster		21.12	1,28	< 0.001	0.44	P > C
*Stimuli*Hemisphere*		4.02	3,84	0.010	0.13	
	1-$back_{target}$	4.88	1,28	0.036	0.15	R > L
	L	8.38	3,84	< 0.001	0.24	$PM_{percept}$ > 1-$back_{target}$ & $PM_{concept}$ | 1-$back_{nontarget}$ > 1-$back_{target}$ & $PM_{concept}$
	R	6.06	3,84	< 0.001	0.18	$PM_{percept}$ > 1-$back_{nontarget}$ & $PM_{concept}$

Stimuli: 1-$back_{target}$ = repeated ongoing stimuli, 1-$back_{nontarget}$ = non-repeated ongoing stimuli, $PM_{percept}$ = perceptual prospective memory stimuli, $PM_{concept}$ = conceptual prospective memory stimuli. Clusters: P = parietal, C = Central. L = left hemisphere, R = right hemisphere. | = separator between post-hoc tests. *N.B.* '>' indicates amplitudes being more positive in this table.

5.3.5.3 Intention retrieval ERPs

A summary of all significant effects is presented in Table 5.5. Means and standard deviations for the IRR ERP can be found in Appendix D, Table D.4

5.3.5.4 Midline intention retrieval ERP amplitudes

There was a significant main effect of *Stimuli* ($F_{2.18,58.81}$ = 45.54, p < 0.001, η_p^2 = 0.63), such that $PM_{percept}$ stimuli caused significantly greater amplitudes than all other stimuli (ps < 0.001) and $PM_{concept}$ stimuli evoked significantly greater positive amplitudes

relative to 1-back$_{nontarget}$ stimuli (p = 0.026). There was also a significant main effect of *Cluster* ($F_{1,28}$ = 13.54, p = 0.001, η_p^2 = 0.33), such that parietal clusters produced greater positive amplitudes relative to the central cluster.

5.3.5.5 Lateral intention retrieval ERP amplitudes

There was a significant main effect of *Stimuli* ($F_{2.33,62.78}$ = 61.78, p < 0.001, η_p^2 = 0.70) and a significant effect of *Cluster* ($F_{1,28}$ = 33.84, p < 0.001, η_p^2 = 0.56). Additionally, there was a significant interaction of *Stimuli* x *Hemisphere* ($F_{1,28}$ = 5.44, p = 0.005, η_p^2 = 0.17) and *Stimuli* x *Cluster* ($F_{2.27,28}$ = 4.40, p = 0.013, η_p^2 = 0.14).

Furthermore, there was a three-way interaction of *Condition* x *Hemisphere* x *Cluster* ($F_{2.32,62.63}$ = 6.59, p = 0.002, η_p^2 = 0.20). Further analysis revealed that this interaction effect was due to a significant a *Stimuli* x *Hemisphere* interaction over central clusters ($F_{2.39,64.34}$ = 5.82, p = 0.003, η_p^2 = 0.12), where the right hemisphere evoked significantly larger amplitudes relative to the left for 1-back$_{target}$ stimuli ($F_{1,28}$ = 4.77, p = 0.038, η_p^2 = 0.15). Over the left central cluster PM$_{percept}$ produced greater positive amplitudes compared to PM$_{concept}$ stimuli (p = 0.013) but both PM$_{percept}$ and PM$_{concept}$ stimuli produced significantly greater amplitudes relative to 1-back$_{target}$ stimuli (p < 0.001 & p = 0.037, respectively) and 1-back$_{nontarget}$ stimuli (p < 0.001 & p = 0.045, respectively).

A significant *Stimuli* x *Hemisphere* interaction was also found at parietal clusters ($F_{2.22,65.52}$ = 5.73, p = 0.004, η_p^2 = 0.18). This can be explained by a significant *Hemisphere* effect for PM$_{percept}$ stimuli ($F_{1,28}$ = 8.52, p = 0.007, η_p^2 = 0.23), where the right hemisphere had significantly more positive amplitudes than the left hemisphere. Additionally, this can be explained by a significant effect of *Stimuli* over the left hemisphere ($F_{2.14,57.81}$ = 22.40, p < 0.001, η_p^2 = 0.45), such that PM$_{percept}$ amplitudes were significantly greater than all other stimuli (ps < 0.001). The significant *Stimuli* x *Hemisphere* interaction was also due to a significant effect of *Stimuli* in the right *Hemisphere* ($F_{2.22,59.95}$ = 53.62, p < 0.001, η_p^2 = 0.67), which was due to significantly larger amplitudes for the PM$_{percept}$ stimuli relative to all other stimuli (ps < 0.001) and due to significantly larger PM$_{concept}$ amplitudes relative to 1-back$_{target}$ stimuli (p = 0.027); 1-back$_{target}$ was significantly larger relative to 1-back$_{nontarget}$ (p = 0.001).

The three-way interaction was also explained by a significant *Stimuli* x *Cluster* interaction in the left hemisphere ($F_{2.43,65.66}$ = 3.28, p = 0.035, η_p^2 = 0.11), such that parietal clusters had significantly greater amplitudes than central clusters (1-back$_{target}$, 1-back$_{nontarget}$ & PM$_{percept}$, ps < 0.001; PM$_{concept}$ p = 0.040); significantly greater amplitudes for PM$_{percept}$ relative to 1-back$_{target}$ and 1-back$_{nontarget}$ (ps < 0.001) and PM$_{concept}$ (p = 0.031), while PM$_{concept}$ had significantly larger amplitudes than 1-back$_{target}$ and 1-back$_{nontarget}$ (ps < 0.05).

Moreover, a significant *Stimuli* x *Cluster* interaction was found in the right hemisphere ($F_{2.47,66.72}$ = 7.93, p < 0.001, η_p^2 = 0.23), such that for all stimuli the parietal clusters evoked larger amplitudes relative to the central cluster (ps < 0.001); PM$_{percept}$ evoked significantly larger amplitudes than all other stimuli (ps < 0.001); PM$_{concept}$ evoked significantly greater amplitudes than 1-back$_{nontarget}$ (p = 0.027) and 1-back$_{target}$ amplitudes were significantly greater than 1-back$_{nontarget}$ amplitudes (p = 0.001).

Table 5.5

Summary of Significant Effects for the Intention Retrieval Response (IRR) ERP Amplitudes

Midline IRR amplitudes	**Lower**	**F-Value**	**DF**	***p*-value**	***η²p***	**Post-Hoc Tests**
Stimuli		45.54	2.18,58.81	< 0.001	0.63	$PM_{percept}$ > $PM_{concept}$ > 1-$back_{nontarget}$ | $PM_{percept}$ > 1-$back_{target}$
Cluster		1.54	1,28	0.001	0.33	P > C
Lateral IRR amplitudes						
Stimuli		61.78	2.33,62.78	< 0.001	0.70	
Cluster		33.84	1,28	< 0.001	0.56	
*Stimuli*Hemisphere*Cluster*		6.59	2.32,62.63	0.002	0.20	
*Stimuli*Hemisphere*	C	5.82	2.39,64.34	0.003	0.12	1-$back_{target}$: R > L | L: PM > ongoing
	P	5.73	2.22,65.52	0.004	0.18	$PM_{percept}$: R > L | L: $PM_{percept}$ > $PM_{concept}$ & ongoing | R: $PM_{percept}$ > $PM_{concept}$ > 1-$back_{target}$ > 1-$back_{nontarget}$
*Stimuli*Cluster*	L	3.28	2.43,65.66	0.035	0.11	All stimuli: P > C | $PM_{percept}$ > $PM_{concept}$ > ongoing
	R	7.93	2.47,66.72	< 0.001	0.23	All stimuli: P > C | $PM_{percept}$ > $PM_{concept}$ > 1-$back_{nontarget}$ < 1-$back_{target}$

Stimuli: 1-$back_{target}$ = repeated ongoing stimuli, 1-$back_{nontarget}$ = non-repeated ongoing stimuli, $PM_{percept}$ = perceptual prospective memory stimuli, $PM_{concept}$ = conceptual prospective memory stimuli. Clusters: P = parietal, C = central. L = left hemisphere, R = right hemisphere. PM = both $PM_{percept}$ & $PM_{concept}$, ongoing = 1-$back_{target}$ & 1-$back_{nontarget}$. | = separator between post-hoc tests. *N.B.* '>' indicates amplitudes being more positive in this table.

5.3.5.6 Prospective positivity ERPs

A summary of all significant effects is presented in Table 5.6. Means and standard deviations of the Prospective Positivity amplitudes can be found in Appendix D, Table D.5.

5.3.5.7 Midline prospective positivity ERP amplitudes

There was a significant main effect of *Stimuli* ($F_{2.11,62.07} = 25.45$, $p < 0.001$, $\eta_p^2 = 0.49$) due to $PM_{percept}$ generating a larger positive amplitude than 1-$back_{taret}$ ($p < 0.001$), 1-$back_{nontarget}$ ($p = 0.001$) and $PM_{concept}$ stimuli ($p = 0.005$). $PM_{concept}$ stimuli caused larger positive amplitude than 1-$back_{target}$ ($p = 0.037$) and 1-$back_{nontarget}$ stimuli ($p = 0.001$). There was also a significant main effect of *Cluster* ($F_{1,28} = 8.81$, $p = 0.006$, $\eta_p^2 = 0.25$), whereby amplitudes were more positive over parietal clusters than central clusters.

5.3.5.8 Lateral Prospective Positivity ERP Amplitudes

There was a significant main effect of *Stimuli* ($F_{2.30,68.23} = 27.77$, $p < 0.001$, $\eta_p^2 = 0.51$) and *Cluster* ($F_{1,28} = 21.95$, $p < 0.001$, $\eta_p^2 = 0.45$). Additionally, there was a significant interaction of *Stimuli* x *Hemisphere* ($F_{2.26,61.03} = 6.11$, $p = 0.003$, $\eta_p^2 = 0.19$) and *Stimuli* x *Cluster* ($F_{3,84} = 3.82$, $p = 0.013$, $\eta_p^2 = 0.12$).

Moreover, there was a significant three-way *Stimuli* x *Hemisphere* x *Cluster* interaction ($F_{3,84} = 5.48$, $p = 0.002$, $\eta_p^2 = 0.17$). This three-way interaction is due to a significant *Stimuli* x *Hemisphere* interaction at central clusters ($F_{3,84} = 9.13$, $p < 0.001$, $\eta_p^2 = 0.25$). At the left central cluster, the prospective positivity was significantly greater for $PM_{percept}$ stimuli relative to 1-$back_{target}$ ($p = 0.001$) and 1-$back_{nontarget}$ ($p < 0.001$), along with greater amplitudes for $PM_{concept}$ stimuli relative to 1-$back_{nontarget}$ stimuli ($p = 0.003$). For right central clusters, the prospective positivity was significantly greater for $PM_{percept}$ relative to 1-$back_{nontarget}$ ($p = 0.002$), but not 1-$back_{target}$ ($p > 0.05$). $PM_{concept}$, however, was significantly greater than 1-$back_{target}$ ($p = 0.044$) and 1-$back_{target}$ was significantly greater than 1-$back_{nontarget}$ stimuli ($p < 0.001$). At central

clusters, 1-back$_{target}$ stimuli produced a significantly larger amplitude over the right hemisphere relative to the left ($p < 0.001$).

The *Stimuli* x *Hemisphere* x *Cluster* interaction was also explained by a significant *Stimuli* x *Cluster* interaction in the right hemisphere ($F_{2.16,61.23} = 18.23$, $p < 0.001$, $\eta_p^2 = 0.40$). In right central clusters, PM$_{percept}$ and 1-back$_{target}$ stimuli were significantly greater than 1-back$_{nontarget}$ stimuli ($p = 0.002$ & $p < 0.001$, respectively) and 1-back$_{target}$ was significantly greater than PM$_{concept}$ stimuli ($p = 0.044$). In the right parietal clusters, PM$_{percept}$ and PM$_{concept}$ produced significantly greater amplitudes than 1-back$_{nontarget}$ stimuli ($ps < 0.001$); PM$_{percept}$ caused significantly larger amplitudes than 1-back$_{target}$ ($p < 0.001$) and PM$_{concept}$ ($p = 0.014$). Additionally, right parietal clusters evoked significantly more positive amplitudes than central clusters for 1-back$_{nontarget}$ ($p = 0.001$), PM$_{percept}$ and PM$_{concept}$ ($ps < 0.001$), but not for 1-back$_{target}$ ($p > 0.05$).

The *Stimuli* x *Hemisphere* x *Cluster* interaction was also due to a significant *Hemisphere* x *Cluster* interaction for 1-back$_{target}$ stimuli ($F_{1,28} = 8.25$, $p = 0.008$, $\eta_p^2 = 0.23$). In the left hemisphere, there was greater amplitudes in response to 1-back$_{target}$ for the parietal cluster relative to the central cluster ($p = 0.007$), which was not found in the right hemisphere ($p > 0.05$); in the central cluster there was larger positive amplitudes over the right hemisphere relative to the left ($p < 0.001$), which was not found in the parietal clusters ($p > 0.05$). There were no other significant effects.

Table 5.6

Summary of Significant Effects for the Prospective Positivity ERP Amplitudes

Midline prospective positivity amplitudes	**Lower**	**F-Value**	**DF**	***p*-value**	**η^2p**	**Post-Hoc Tests**
Stimuli		25.45	2.11,62.07	< 0.001	0.49	PM > ongoing
Cluster		8.81	1,28	0.006	0.25	P > C
Lateral prospective positivity amplitudes						
Stimuli		27.7	2.30,68.23	< 0.001	0.51	
Cluster		1,28	21.95	< 0.001	0.45	
*Stimuli*Hemisphere*		5.48	3,84	0.002	0.17	
**Cluster*						
*Stimuli*Hemisphere*	C	9.13	3,84	< 0.001	0.25	L: PM > 1-back$_{nontarget}$ | PM$_{percept}$ > 1-back$_{target}$ | R: PM$_{percept}$ > 1-back$_{target}$| PM$_{concept}$ > 1-back$_{target}$ > 1-back$_{nontarget}$
*Stimuli*Cluster*	R	18.23	2.16,61.23	< 0.001	0.40	C: PM$_{percept}$ > ongoing | 1-back$_{target}$ > PM$_{concept}$ | P: PM > 1-back$_{nontarget}$ | PM$_{percept}$ > 1-back$_{target}$ & PM$_{concept}$
*Hemisphere*Cluster*	1-back$_{target}$	8.25	1,28	0.008	0.23	L: P > C | C: R > L

Stimuli: 1-back$_{target}$ = repeated ongoing stimuli, 1-back$_{nontarget}$ = non-repeated ongoing stimuli, PM$_{percept}$ = perceptual prospective memory stimuli, PM$_{concept}$ = conceptual prospective memory stimuli. Clusters: P = parietal, C = central. L = left hemisphere, R = right hemisphere. PM = both PM$_{percept}$ & PM$_{concept}$, ongoing = 1-back$_{target}$ & 1-back$_{nontarget}$. | = separator between post-hoc tests. *N.B.* '>' indicates amplitudes being more positive in this table.

5.3.6 Task reorientation

From visual inspection of ERP waveforms across all clusters, the RON component was identified as occurring bilaterally in the frontotemporal clusters between 400–750ms,

with a mean peak RON response = 611.02ms. Means and standard deviations for the RON can be found in Appendix D, Table D.6.

5.3.6.1 Lateral Reorientation Negativity ERP amplitudes

There was a significant main effect of *Stimuli* ($F_{3,84} = 16.77$, $p < 0.001$, $\eta_p^2 = 0.41$), which was due to significantly more negative amplitudes for $PM_{percept}$ stimuli relative to 1-$back_{target}$ and 1-$back_{nontarget}$ stimuli ($ps < 0.001$) and significantly more negative amplitudes for $PM_{concept}$ relative 1-$back_{target}$ and 1-$back_{nontarget}$ stimuli ($p = 0.026$ & $p = 0.024$, respectively). The greater negative amplitudes in response to PM stimuli were taken to reflect the RON. $PM_{percept}$ stimuli generated a significantly more negative RON ERP than $PM_{concept}$ ($p = 0.036$). No differences were found between 1-$back_{target}$ and 1-$back_{nontarget}$ ($p > 0.05$).

5.4 Discussion

The current study had three primary aims: 1) to evaluate performance differences between perceptual and conceptual PM cues; 2) to examine the neurophysiological differences in response to perceptual and conceptual PM; 3) to determine whether a RON ERP response was detectable in a PM paradigm.

Behavioural performance was better (indicated by reaction times and percentage of correct responses) for perceptual PM stimuli relative to ongoing and conceptual PM stimuli. The results show poorer performance for the conceptual PM stimuli relative to the ongoing task, as hypothesised. Comparisons between the ERPs produced by the different ongoing stimuli (1-$back_{target}$ & 1-$back_{nontarget}$) revealed differences at the N400 and the earlier N2 and P2 components. All subsequent analyses are, therefore, compared against both activate and passive forms of ongoing stimuli (i.e., 1-$back_{target}$ & 1-$back_{nontarget}$).

In general, both PM stimuli exhibited ERPs reflecting cue detection, indicated by greater N300 and frontal positivity responses relative to the ongoing stimuli. However, perceptual PM stimuli caused a stronger response over frontal clusters compared to the conceptual stimuli. Both PM stimuli evoked IRRs relative to the ongoing stimuli.

The prospective positivity was prevalent at midline parietal clusters in response to PM stimuli. The prospective positivity response was diminished over bilateral clusters, only being retained over the left central cluster and right parietal cluster. Interestingly, across almost all ERPs, repeated ongoing stimuli demonstrated a right-hemispheric bias, which was not seen in the other stimuli. Both IRR and prospective positivity ERPs were stronger for perceptual PM stimuli relative to the conceptual stimuli. A RON was identified at frontotemporal clusters with a peak amplitude occurring between 400–800ms (mean at approximately 610ms).

5.4.1 Behavioural performance

The current results partially support the hypothesis that conceptual PM stimuli performance will be significantly worse compared to perceptual PM stimuli. This is evidenced by fewer correct PM responses and a reaction time increase relative to perceptual PM stimuli. It was also expected that there would be no performance differences between the ongoing-only task and perceptual PM stimuli. However, results failed to support this hypothesis. Indeed, perceptual PM stimuli were responded to more quickly and with more correct responses than the ongoing-only stimuli. From this, two conclusions can be drawn: 1) ongoing stimuli were sufficiently engaging working memory processes as the results were not close to ceiling and were similar to other performance results for lexical working memory (Cappell et al., 2010) and 2) the perceptual PM stimuli were extremely salient for participants.

The results here are comparable to other studies evaluating perceptual and conceptual PM. For example, Cousens et al. (2015) similarly found faster reaction times for perceptual PM stimuli relative to the conceptual PM stimuli. However, they did not find a performance difference between the ongoing and perceptual PM stimuli. The lack of performance difference in their study is potentially due to the difference in the task design. While both use a similar lexical decision task, Cousens and colleagues' task required a decision between two stimuli presented simultaneously, which almost always resulted in correct responses. The current study, on the other hand, required participants to remember the category of the previously presented stimulus. Therefore, the additional processes required to remember the previous category will

have likely taxed working memory and executive functions to a greater extent than the task used by Cousens et al. (2015).

The current study's results contrast Cousens et al.'s (2015) regarding the number of correct responses to conceptual relative to perceptual PM stimuli. In Cousens et al.'s study, a greater percentage of correct responses were made to the conceptual relative to perceptual PM stimuli. These differences are possibly explained by the differences in the focality and saliency of the PM cues used. In Cousens' study the conceptual cue (two animal words) is considered focal because its features are processed as part of the ongoing task. Their perceptual stimuli (two words in red) can be considered non-focal as they were not processed as part of the ongoing lexical decision task. Cousens and colleagues' (2015) results are similar to other studies of focality (Altgassen et al., 2009; Brewer et al., 2010), where better performance is found for focal relative to non-focal cues due to the fewer attentional processes required for stimulus detection (Scullin, McDaniel, Shelton, et al., 2010). The conceptual PM stimuli in the current study can also be considered focal, given that they are processed as part of the ongoing task, however, the results here demonstrate a greater percentage of correct responses for perceptual relative to conceptual stimuli. The results here more closely align with studies demonstrating better performance for highly salient cues (Brandimonte & Passolunghi, 1994; Kliegel et al., 2013; Thompsons et al., 2017). Better perceptual PM cue performance, therefore, suggests that saliency is a better contributor to the successful completion of PM tasks than focality.

5.4.2 Right hemispheric bias for repeated ongoing working memory

Within the frontal positivity, P3b, IRR and prospective positivity (central only) the repeated ongoing stimuli (1-back$_{target}$) ERPs produced greater amplitudes over the right hemisphere relative to the left. This was not found for the non-repeated ongoing stimuli (1-back$_{nontarget}$) or either PM stimuli. Possibly, the right hemisphere bias reflects increased activation of the right hemisphere during ortholinguistic evaluation of the ongoing stimulus. Previous research has highlighted the role of the right hemisphere in paralinguistic processes, including contextual integration of meaning, intent and emotion processing (Eldridge et al., 2000; Lindell, 2006). Lindell's (2006)

review concluded that the right hemisphere had an important function in word recognition, but also plays a vital role in syntax extraction and mediating prosodic and paralinguistic aspects of language. On the other hand, a meta-analysis examining the contribution of the right hemisphere during ortholinguistic tasks has provided evidence to suggest that the right hemisphere is not specific to language components but reflects the recruitment of additional executive processes, such as the manipulation of working memory and selective attention of verbal information (Vigneau et al., 2011). This suggestion is compatible with other research reporting the inhibition of the left hemisphere during the processing of meaning as evidenced in studies of aphasia recovery (Price & Crinion, 2005). Therefore, the increase of the right hemisphere during repeated ongoing stimuli may suggest recruitment of cognitive networks responsible for supporting the manipulation of the semantic features for repeated ongoing stimuli.

5.4.3 Prospective memory cue detection ERPs

The results here confirm the findings of previous research demonstrating cue detection related ERP responses for PM stimuli relative to an ongoing task (Cona et al., 2014; Cruz et al., 2016; West, 2011; West & Covell, 2001). In general, the current study shows that perceptual PM stimuli caused the largest cue detection ERP responses (i.e., more negative N300 and more positive frontal positivity amplitudes) compared to the conceptual PM task. This may suggest that highly perceptually salient stimuli easily stimulate PM cue detection responses compared to conceptual PM stimuli.

Previous research on PM cue detection has demonstrated that when the PM cue is defined by some perceptually salient feature an N300 response is clear relative to the ERPs from ongoing stimuli (Cousens et al., 2015; Cruz et al., 2016; West, 2011; Wilson et al., 2013). The results here and from previous studies (Cousens et al., 2015; Cruz et al., 2016; West, 2011; Wilson et al., 2013) suggest that regardless of whether the ongoing stimuli ERPs are treated as separate or averaged, perceptual PM stimuli will likely cause a strong enough response for a cue detection response to be detected. Therefore, it is suggested that perceptually salient PM stimuli will reliably elicit cue detection ERPs.

Cue detection response for conceptual PM stimuli did produce greater amplitude responses compared to the ongoing stimuli although the results were less clear than responses to perceptual PM stimuli. At the parietal cluster, the N300 in response to conceptual PM stimuli was only greater than the repeated ongoing stimuli, similar to Cruz et al.'s (2016) results. At bilateral occipital clusters, however, the conceptual PM N300 was greater than both ongoing stimuli. Over the anterior clusters, the conceptual PM frontal positivity response was only greater than the non-repeated stimuli. As the frontal positivity was only apparent when contrasted with the non-repeated ongoing stimuli, it may explain why other studies that averaged ongoing stimuli ERPs may not have found an effect for cue detection responses (e.g., Cousens et al. 2015). It may also suggest that similar levels of frontal neural processes are being recruited for the repeated ongoing and the conceptual stimuli, therefore, masking possible differences between the two stimuli. Alternatively, different neuronal sources may be responsible for successful conceptual PM cue detection. The results from the current study may suggest that conceptual PM cue detection may rely less on anterior neural sources than cue detection for perceptual PM cues.

In sum, the N300 and frontal positivity are reliably generated for perceptual PM stimuli. However, differences between studies (i.e., Cousens et al., 2015 & Cruz et al., 2016) may be due to how comparisons were made between PM and the ongoing stimuli ERPs. If the ongoing stimuli ERPs are treated as separate, it seems conceptual stimuli does cause cue detection responses, but may be lost if the ERPs are averaged across the stimulus types. The current study's results support the conclusions of Cruz et al. (2016) finding differences in the cue detection responses for different PM cue types.

5.4.4 Intention retrieval ERPs

In concordance with the previous literature (Cousens et al., 2015; Cruz et al., 2016; J. Wilson et al., 2013), both perceptual and conceptual PM stimuli generated a parietal positivity response over central and parietal clusters. Similar to the PM cue detection ERPs, perceptual PM stimuli caused a greater parietal positivity response compared to the conceptual PM stimuli. The perceptual PM stimuli generated greater P3b responses compared to the ongoing stimuli. However, greater P3b amplitudes for perceptual

stimuli were mainly found in relation to the repeated ongoing stimuli. It was hypothesised that both PM stimuli would generate larger P3b amplitudes compared to the ongoing stimuli due to rarity of the PM events relative to the ongoing-only task (Polich et al., 1996). However, no P3b amplitude increase was found for the conceptual PM stimuli compared to the ongoing stimuli. It is possible that the semantic features that constitute the conceptual PM stimuli may have been processed at a later point in time or over a different region of the brain. Indeed, Cruz et al. (2016) noted neural sources were detected at centroparietal and frontocentral scalp sites and the detection response was at 400ms instead of 300ms. Additionally, it is worth noting that amplitudes of the P3b are affected through the choice of EEG reference (Luck, 2005). Researchers have demonstrated greater peak P3b amplitudes when linked mastoids or a nose reference is used compared to an averaged reference (Schröder et al., 2016). Thus, the P3b amplitude is likely to have been less prominent due to the use of average referencing. However, it was important to use an average reference to enable comparisons between other studies and mitigate biasing towards any specific scalp location (Luck, 2014). Furthermore, averaging is deemed appropriate when a high density of electrodes (i.e., 128 channels) are used (Nunez & Srinivasan, 2006).

Both PM stimuli were found to generate significant IRR and prospective positivity responses relative to the ongoing stimuli, similar to the other ERP studies exploring perceptual and conceptual PM (Cousens et al., 2015; Cruz et al., 2016; J. Wilson et al., 2013). However, perceptual stimuli had a significantly greater IRR amplitude response compared to the conceptual stimuli, which contradicts Cousens et al. (2015) who did not find any differences between the two stimulus types. While most other studies only looked at the parietal positivity as one component, the current study explored all three subcomponents. Through the examination of the individual components, the results show that the sustained amplitudes of the prospective positivity were not retained to the same degree for conceptual PM as was found in the perceptual PM stimuli. Sustained prospective positivity amplitudes relative to ongoing stimuli, were only found at mid parietal, left central and right parietal clusters in response to conceptual PM stimuli. The current results suggest that compared to conceptual PM, perceptually salient PM stimuli enables more efficient recall of the PM intention and engagement of neural systems that support intention retrieval (West & Ross-Munroe, 2002). Moreover, these results suggest that the prospective positivity is indeed affected by PM saliency, contrasting previous research (West, Wymbs, et al., 2003).

One could argue that the more pronounced P3b of the perceptually salient PM cue may have affected the increased amplitude of the IRR. However, previous research has demonstrated that the P3b can be dissociated from the prospective positivity (West et al., 2006b; West & Wymbs, 2004). Thus, it is more likely that the increased amplitude of the IRR and the sustained prospective positivity for perceptual PM stimuli are related to the better recall performance of the perceptual PM stimuli. Perhaps this is mainly driven by the increased saliency of the perceptual PM cue. However, further research would be required to confirm this conclusion.

5.4.5 Reorientation negativity in PM

This study is the first to explore the possibility of a RON response during PM tasks. Indeed, the results here find evidence that following a PM response, a RON component is demonstrated over bilateral frontotemporal scalp clusters at approximately 600ms. The timing of the RON here is similar to previous studies (Getzmann et al., 2015; Munka & Berti, 2006). The similarity between past literature and the current results support the current study's hypothesis that there will be a RON response following PM stimuli. This finding further contributes to the neurophysiological understanding of PM and adds further evidence to the RON during dual-task designs (Allard & Isaacowitz, 2008; Parmentier & Hebrero, 2013; Rämä et al., 2018; Scheer et al., 2016; Wester et al., 2008).

The RON response following stimuli presentation was found for both perceptual and conceptual stimuli relative to both ongoing stimuli. The detection of a RON within a PM task suggests that attentional processes must be refocused from the PM stimulus back towards the ongoing task in PM task designs (Munka & Berti, 2006). Considering the previous research into the RON (Berti, 2008; Escera et al., 2001), it is unlikely that this response is unique to PM, but rather reflects the reorientation of attention towards the primary task (SanMiguel et al., 2008). Therefore, it would be expected that data from most other PM studies employing a dual-task design will contain such a component. It is possible that the RON has been overlooked in the past because of electrode location choice. The majority of studies have examined more centrally located electrodes (e.g., Chen et al., 2007, 2009; Scolaro et al., 2014; West & Bowry, 2005; Zöllig et al., 2012).

The current study's results also demonstrated a greater RON amplitude for perceptual PM compared to conceptual PM stimuli. A possible explanation for this difference may be due to focality of the PM task. As the conceptual PM stimuli is processed as part of the ongoing task it may take less cognitive processes to reorient attention back to the ongoing task, which manifests as a smaller RON response. Previous research has shown that the strength of the RON amplitude is influenced by the features of the distracting stimulus, where greater deviance from the main task caused a greater RON response (Berti et al., 2004; Yago et al., 2001). It should be noted however, that most RON studies have only documented the RON primarily at frontal clusters (Correa-Jaraba et al., 2016; Escera et al., 2001). The current study instead found the RON over frontotemporal scalp regions. In their scalp density analysis, Schröger et al. (2000) found evidence that the RON has multiple neuronal sources. It is possible then that the topographical location of the RON will be different for each PM task configuration. It is important, therefore, for future PM studies to further explore RON components across the scalp and across a range of times to define its scalp and neuronal source and whether differences exist between PM experimental designs.

5.4.6 Limitations

Due to the conductivity of the skull and the relatively low spatial resolution of the EEG, it is possible that frontal positivity amplitudes overlapped with the start of the parietal positivity. The start of the parietal positivity often occurs before the end of the frontal positivity. Given that both were measured at central scalp regions, the increased amplitudes of the parietal positivity may have influenced the detected amplitudes at frontal scalp regions and contributed to the frontal positivity. There is a possibility that the increased amplitudes in response to the perceptual PM stimuli also contributed to the increased frontal cue detection responses. However, it is difficult to determine whether the spread of activation will have contributed within the current study.

Given that all participants completed all conditions (i.e., ongoing-only, perceptual PM and conceptual PM) of the study, participants may have experienced a decline in their PM performance due to the sustained attention required from the ongoing task. Evidence has demonstrated that the longer attention is applied to a task, the poorer the performance becomes (Warm et al., 2008). Moreover, research has shown

performance decrements can occur after five minutes if task demands are high (Helton et al., 1999). Therefore, there is the potential that participants became mentally fatigued throughout the duration of the study. Research has demonstrated that mental fatigue can decrease ERP amplitudes and increase ERP latencies (Guo et al., 2016). However, it was deemed necessary for longer durations for each of the experiments to allow sufficient re-engagement to the ongoing task and to better simulate a real-world PM event. Moreover, break blocks were offered to participants within the study and mandatory breaks were given in between each of the experimental conditions helping to offset mental fatigue.

5.4.7 Future research

An increasing amount of evidence is demonstrating the RON component as a reliable feature of task-switching and working memory performance (Berti & Schröger, 2003; SanMiguel et al., 2008). The current study demonstrates that following the presentation of a PM stimulus, there is a clear RON response. This presumably reflects an attentional shift back toward the ongoing stimuli. However, further work is required to confirm if this response can explain working memory and PM task performance during experimental PM tasks. Further research should examine this effect across a range of different PM stimuli to determine whether a RON is found across all PM stimuli or whether it is only found in those PM tasks requiring semantic evaluation. Moreover, research should explore whether the RON is expressed to a greater degree for those PM stimuli that are more non-focal and more dissimilar to the ongoing task. For example, an ongoing lexical decision task and a time-based PM stimuli task. Additionally, this component should be evaluated in older adult populations and in older adults with MCI. The RON component may explain the reported differences between younger and older adults and between those older adults with and without cognitive decline.

As highlighted in the limitations, gaining an accurate understanding of ERP components of prospective memory is challenging. Future research should seek to gain greater insights into the cognitive domains associated with PM using computational approaches. Recent work into functional connectivity in working memory has begun to reveal dynamic changes of cortical network activity during working memory tasks

providing unique insights to understanding memory processes (review: Dagenbach, 2019). It is possible that novel insights may also be gained through applying connectivity methodologies to the study of PM.

5.4.8 Summary

In conclusion, the results from the current study were able to improve ERP methodology by confirming that it is inappropriate to average ERPs of different ongoing task stimuli. The results show that at early and later ERP components, averaging ongoing stimuli has the potential to modulate the ERP waveform and these modulations may lead to the masking of ERP effects when comparisons are made between the ongoing task ERPs and PM ERPs. Therefore, the current study proposes that all future ERP studies should not average the ongoing task stimuli but compare all stimulus types separately.

The current study confirms the presence of previously reported ERPs for both perceptual and conceptual PM cue types. In general, however, the perceptual PM stimuli caused greater ERP amplitudes than the conceptual PM stimuli. In conjunction with the high behavioural performance of the perceptual PM stimuli, one may conclude that easier PM tasks result in greater ERP responses.

Finally, the current study is the first to document a RON response following PM stimuli presentation. Future studies should further explore whether these can explain performance differences between groups and whether this effect can be replicated in other PM cue types e.g., time-based PM.

Chapter Six: Neurophysiological markers of prospective- and working-memory in typical ageing and mild cognitive impairment

6.0 Overview

In Chapter 5, behavioural and neurophysiological differences between an ongoing memory task, perceptual PM task and conceptual PM task were evaluated. The Chapter provided evidence of a RON in response to PM stimuli. The following chapter extends the previous chapter by exploring the differences between young adults, older adults and older adults with MCI during a perceptual and conceptual PM task. Specifically, this chapter will explore amplitude and latency group differences in PM cue detection ERPs (N300 and frontal positivity) along with the IRR. The RON was examined to determine whether ageing and cognitive decline affects the RON following PM stimuli. Additionally, the early N2 and P2 ERP components, often linked to cognitive decline, is examined to determine whether ageing and cognitive decline affect these components while completing PM tasks.

6.1 Introduction

Mild cognitive impairment is an intermediary state between that of typical ageing and dementia (Petersen et al., 1999). Older adults who meet diagnostic criteria for MCI are ten times more likely to develop dementia-related diseases (approximately 10–15% risk), such as AD, than those without MCI (approximately 1–2% risk; Petersen et al., 2009). Given that the individual, family, societal and economic costs ($817bn/year globally) of dementia are immense and expected to double within 25 years, it is critical to understand underpinning neurocognitive mechanisms, to work towards solutions for the anticipated epidemic. Cognitive domains such as episodic memory, executive function, attention, language and working memory have been intensively investigated (Brandt et al., 2009; Dubois et al., 2009; Klekociuk et al., 2014; Saunders & Summers,

2011). Blanco-Campal et al. (2009) suggest PM as a sensitive early indicator of memory failure in MCI of suspected AD aetiology, and subsequent work has begun to identify associated cognitive mechanisms (Costa et al., 2010).

Prospective memory refers to the self-initiated execution of a planned action, contingent on contextual recognition of a retrieval cue at an appropriate period in time (McDaniel & Einstein, 2007). PM constitutes a large part of everyday memory (Kliegel et al., 2008; Boelen et al., 2011; e.g., remembering to take prescribed medications at the correct time) and everyday memory failures (Kliegel & Martin, 2003; e.g., forgetting to turn off the stove). The ubiquity of these actions underlies basic personal day-to-day functioning and is, therefore, an essential precursor for independent living. Impairment in PM can therefore be more distressing than that of retrospective memory (Smith et al., 2000), and is often the first patient-reported complaint to family members and health professionals (Brandimonte et al., 2014). Thus, PM has clinical relevance, particularly regarding atypical ageing (Kliegel et al., 2011).

Experimentally assessed PM has good ecological validity, predicting everyday function and independence (Woods et al., 2012). A meta-analysis supports significant PM deficits across a variety of tasks in older adults with MCI (van den Berg et al., 2012). This may be due to deficits in 1) the intention encoding, 2) the strategic and/or effortful monitoring for PM cues or 3) retrieval of PM intentions (McDaniel & Einstein, 2000, 2007). Typically, dual-task designs have been used to test PM. These usually involve a commonly occurring ongoing working memory task designed to keep the participant engaged and prevent rehearsal of a secondary part of the experiment (the PM task), which could be time-based PM or event-based PM. Time-based PM almost exclusively relies on self-initiation to successfully perform the PM task, and consequently appears more difficult to perform.

In event-based PM tasks, performance is usually facilitated by the visual appearance of the retrieval cue, prompting the intended response (McDaniel & Einstein, 2000; 2007). For example, while completing a revised version of the virtual-week task, alongside PM and retrospective tasks, significantly poorer performance was found for the PM tasks in the MCI group compared to healthy controls (Thompson et al., 2010). In another study (Blanco-Campal et al., 2009), participants said aloud the word ‘animal’ whenever they saw the word of a predefined animal word (e.g., ‘lion’, or, specific condition) or responded when they saw any animal word (non-specific

condition) while completing an ongoing task. Moreover, the researchers manipulated the saliency of the event-based PM cue by presenting the cue in either italic (salient condition) or the same font as the ongoing task (non-salient condition). PM assessed this way had greater sensitivity and specificity in discriminating between typically ageing adults and those with MCI compared to 'traditional' declarative memory tests (84% and 95%, respectively). The literature consistently demonstrates poorer PM performance in MCI participants compared to healthy older adults, but performance varies depending on the type of PM cue used. Blanco-Campal et al. (2009) found greater differences between healthy older adults and those with MCI in non-salient cues, but Thompson et al. (2017) failed to find this disproportional impairment and instead found similar impairments regardless of the saliency of the cue.

The neurocognitive mechanisms of PM impairment in atypical cognitive ageing remain largely unknown. Nevertheless, emerging structural and functional neuroimaging studies in healthy adults implicate the aPFC (BA10; Beck et al., 2014; Burgess et al., 2007; Gilbert et al., 2010) and to a lesser degree the ACC and PCC, temporal cortex and insula in PM processing (review: Burgess et al., 2011; Cona, Scarpazza, et al., 2015). To date, only one study using TMS has tested these areas in PM (Debarnot et al., 2015). Debarnot et al.'s (2015) results demonstrated that theta-burst stimulation of the left PFC can improve PM performance in older adults.

Compared to other neuroimaging methods, EEG techniques, such as ERPs offer superior temporal resolution and have identified several components associated with PM performance (West, 2011). The N300, a negative deflection with a maximum amplitude parietooccipitally between 300–500ms post-onset, is thought to reflect cue identification (West, 2011). It is coupled with a midline frontal positive component, implicated in task switching (i.e., from the ongoing to the PM task; West et al., 2006; West, 2011). The recognition of a delayed intention is reflected in a late positivity complex, with a centroparietal maxima extending across 400–1200ms post-stimulus-onset (West et al., 2001; West & Krompinger, 2005). The parietal positivity is comprised of three subcomponents; the P3b (300–400ms, related to subjective expectancy of stimuli), the IRR (400–600ms, reflecting intention retrieval) and the prospective positivity (600–1000ms, associated with task switching and support of intention retrieval; Bisiacchi et al., 2009; West, 2011; West & Krompinger, 2005; West & Wymbs, 2004).

The majority of ERP studies in PM have manipulated the visual features of event-based PM cues (e.g., target salience, word/non-word, colour, emotional valence; Cona, Kliegel, et al., 2015; Knight et al., 2010b; Scolaro et al., 2014). However, some studies have begun to explore conceptually-relevant PM cues, such as different semantic categories of words (Cousens et al., 2015; J. Wilson et al., 2013), and a few studies compare semantically-based and feature-based PM cues (Cousens et al., 2015; Cruz et al., 2016). Cousens et al. (2015) found that perceptual features strongly elicited the N300 and prospective positivity responses in young adults. However, for semantic PM stimuli, the N300 was absent but the prospective positivity was still distinct relative to ongoing stimuli. Using EEG source estimate methods, Cruz et al. (2016) investigated this further. Their results identified occipital and parietal sources for the N300 in response to feature-based PM stimuli. For conceptual PM stimuli, a cue detection response was found but it was delayed to approximately 400ms and originated from the ACC. Cruz et al. (2016) found similar prospective positivity ERP responses for feature-based and conceptual-based PM to the Cousens et al. (2015) study. These studies highlight a common post-retrieval response for the realisation and recall of a PM intention but the N300 may depend on the nature of the PM task.

Two other components that are of theoretical relevance to PM and MCI, but remain under investigated, are the P2 and RON. Currently the P2 component (150–275ms) is not fully understood. Some researchers suggest that the P2 reflects processes involved in selective attention (Hackley et al., 1990; Lijffijt et al., 2009; Wongupparaj et al., 2018). Others propose the P2 to be an index of feature detection processes (Dunn et al., 1998; Luck & Hillyard, 1994; Potts, 2004), working memory (Lefebvre et al., 2005) or the retrieval of semantic information from long term memory (Preston et al., 1977; Raney, 1993; Stelmack et al., 1988). However, studies also suggest that the P2 is related to familiarity (Doyle, Rugg, & Wells, 1996; Rugg & Nieto-Vegas, 1999) and the feeling of knowing in episodic memory tasks (Irak et al., 2014; Irak, Soylu, & Turan, 2019; Irak, Soylu, Turan, et al., 2019b), where larger amplitudes are related to increased familiarity (K. M. Evans & Federmeier, 2007). While it is not clear precisely what the P2 reflects, the research does allude toward representing top-down mechanisms for rapid semantic stimulus evaluation (Irak et al., 2019; Paynter et al., 2009) and a peri-perceptual sense of familiarity (Z. G. Doborjeh, Kasabov, et al., 2018). Recent evidence demonstrates that P2 amplitudes may be preserved in older adults during semantic working memory (Kuo et al., 2014) but amplitude reductions and latency delays are

found in older adults with MCI (Fix et al., 2015; Li et al., 2016; Li et al., 2010; Yamasaki & Tobimatsu, 2012; Zunini et al., 2016). Given the documented early impairments of semantic memory in older adults with MCI (Pineault et al., 2018) and semantic encoding (Olichney et al., 2011), one would expect that a conceptual event-based PM paradigm would be particularly sensitive to functional changes in P2 due to MCI.

The RON reflects two distinct functional processes of attentional reorientation after distraction: the re-focusing toward task-relevant information within working memory, and a general attentional reorientation/preparation for the next stimulus (Schröger et al., 2000). The RON remains uninvestigated in MCI, but has been found to be impaired in schizophrenia, Parkinson's disease and traumatic brain injury (review: Justo-Guillén et al., 2019). Moreover, reduced amplitude and prolonged latency have also been observed in older adults during an inhibitory control task, which was interpreted as a general slowing of cognitive processes (Cona et al., 2013). This indicates that reorientation capabilities may be susceptible to age-related cognitive decline. Given that behavioural studies demonstrate impaired task-switching in MCI (Belleville et al., 2008; Schmitter-Edgecombe & Sanders, 2009), RON should be investigated as an underpinning mechanism. The requirement to switch between the PM task and the ongoing working memory task in experimental PM studies, would be expected to elicit an RON ERP. Indeed, the results in Chapter 5 have demonstrated a RON after a successful PM response in response to perceptual and conceptual PM cues. The importance of examining this component in the current study is to determine the effect of typical and atypical ageing on the RON.

Very few ERP studies have investigated PM as a function of typical ageing (Hering et al., 2016, 2018, 2020; Mattli et al., 2014; West, Herndon, et al., 2003; West & Covell, 2001; Zöllig et al., 2007, 2010, 2012) and no research has explored PM ERPs in atypical ageing. West & Covell (2001) report reduced N300 amplitudes in older adults relative to younger adults when a perceptually based PM cue, in the form of capital letters, was used. Additionally, when the perceptually PM cue was a colour, similar N300 amplitude reductions for older adults compared to the younger adults were found but only over the right hemisphere (West et al., 2003). This would suggest that age-related PM differences may be due to the affected ability to detect PM cues. However, this effect is not consistently found throughout the literature. A study employing a similar task design failed to replicate the same N300 differences between younger and older

adults (Zöllig et al., 2007). This discrepancy creates difficulties in concluding whether the neural underpinnings of cue detection contribute to the reported age-related PM differences and, therefore, warrants further study.

The majority of studies examining age-related differences in PM ERPs find attenuated parietal positivity amplitudes in older adults compared to younger adults (Mattli et al., 2011; West & Covell, 2001; Zöllig et al., 2007). Parietal positivity attenuation may imply a decrease in the ability to recruit the neural mechanisms required to successfully recall the encoded PM intention. However, these results are not consistently reported. West, Herndon, et al. (2003), failed to find age-related differences of the parietal positivity, suggesting that intention retrieval may be spared by age-related declines. The inconsistency between these studies may be in part be due to differences in the PM cues used, or differences in the neural mechanisms used by the different groups to complete the task (Kliegel et al., 2011). Further clarity would be gained from investigating the parietal positivity components of PM in older adults through variations in PM task type. By using similar task designs that have varied the characteristics of the PM cue, different facets of PM can be tested (Cousens et al., 2015; Cruz et al., 2016; Wang et al., 2013; Wilson et al., 2013). It is likely that not all real-world PM cues will be predominately perceptual in nature and may vary in their salience and relation to the encoded intention (Cousens et al., 2015). Therefore, by examining both perceptual and conceptual based PM cues, PM differences can be better understood between ageing populations and their younger counterparts as well as those experiencing cognitive impairments.

6.1.2 Aims and hypothesises

The current study aims to investigate behavioural and neurophysiological differences in PM in healthy older adults (OA) and in older adults with MCI (MCI). A semantic working memory task (the *n*-back task) acted as the ongoing task, with two types of embedded PM cue: perceptual and conceptual. The perceptual PM task was to remember to press a certain button if a word was presented in uppercase. This condition was intended to involve perceptually salient PM cues (i.e., words in very visible uppercase lettering). The conceptual PM task was to remember to press a certain button if a word referred to a four-legged animal, thus measuring semantic PM.

Given the known behavioural impairments across PM cue types in OA and participants with MCI, examining performance in, and neurophysiological correlates of different PM tasks will further our understanding of PM in typical ageing and MCI.

To this end we hypothesise that: 1) Both older adult groups will perform significantly worse on both PM tasks relative to younger adults. 2) MCI participants will perform significantly worse on both PM tasks and will have disproportional deficits in the conceptually based PM task. 3) Both older adult groups will show attenuated PM-related ERPs along with delayed latencies, which will be further pronounced in MCI participants. 4) There will be an anterior P2 amplitude reduction in MCI participants. 5) RON amplitudes will be significantly attenuated and delayed in MCI participants relative to older and younger adults.

6.2 Methods

6.2.1 Participants

The thirty young adults used in the previous chapter were included as a baseline to evaluate age-related PM differences (*see Chapter 5, Section 5.2.2*). In addition to the young adults, thirty-nine right-handed typically ageing older adults (OA; 24 females, mean age = 72.87, SD = 4.18) were recruited through the Trent Ageing Panel, an internal database of older adult study volunteers. Inclusion criteria for participation: fluent in English; ≥ 65 years of age; no paranoid of paraphrenic illness; no expression of memory impairments. Seventy-three individuals with MCI were referred to the study through Memory Assessment Clinics in the Nottinghamshire area or through the study matching service: Join Dementia Research (JDR). Of the 73 referred, 27 individuals with a confirmed diagnosis of MCI (MCI; 12 females, mean age = 77.54, SD = 6.49) were eligible to take part in the study. Participants referred by JDR or the memory assessment clinics had been diagnosed with MCI based on scores between 15–25 on the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005), 60–94 on the Addenbrookes Cognitive Examination III (ACEIII; Hsieh et al., 2013) or the 18–26 on the Mini Mental State Examination (MMSE; Vertesi et al., 2001), depending on which measures each clinic used. Figure 7.1 illustrates a flow diagram showing the

recruitment process of older adults with and without MCI. Participants' exclusion for both older adult groups included: definite or probably AD; definite or probable dementia/dementia-related disease; previous history of epilepsy/stroke; any evidence of clouding of consciousness; history of drug abuse or dependence (including alcohol). All participants were required to abstain from alcohol for 24 hours, and from caffeine and nicotine for 3 hours prior to study. Participants provided written informed consent. The study approval was issued by the Health Research Authority, UK (REC reference: 17/EM/1010).

6.2.2 Dementia screening

Prior to participation in the study, all participants completed the Hopkins Verbal Learning Test-Revised (HVLT-R; Benedict et al., 1998). This was employed to ensure that older adults with MCI were not likely to have AD and to ensure the healthy older adults were not likely to be experiencing MCI. This was possible with the HVLT-R due to higher sensitivity and specificity of differentiating between MCI and healthy controls compared to other cognitive tests such as the Mini-Mental State Examination (MMSE; de Jager et al., 2003). Particularly, evidence demonstrates that the HVLT-R total recall has the highest sensitivity and specificity compared to all other cognitive screenings tests for differentiating between MCI and dementia (de Jager et al., 2009). The optimal cut-off for MCI and dementia classification were based on the Xu et al.'s (2014) HVLT literature review, where <15.5 was considered as probable dementia and <21.5 was considered as being reflective of MCI.

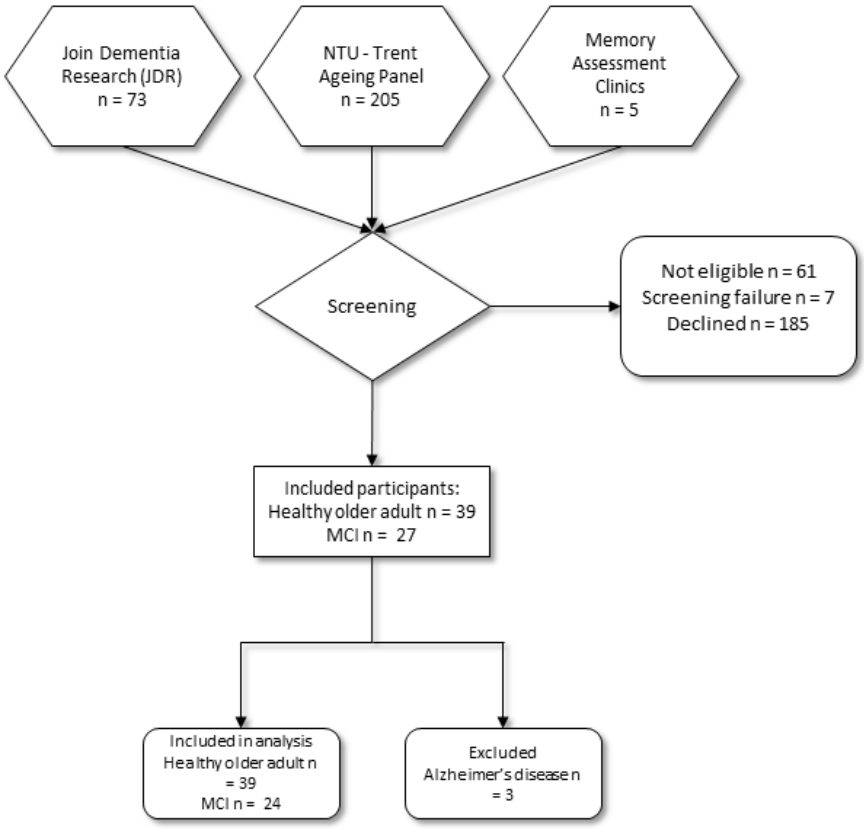

Figure 6.1. Flow diagram of participant recruitment for healthy older adults and older adults with mild cognitive impairment (MCI).

6.2.3 Procedure

Core methodology has been documented in Chapter 5, Section 5.2.3.

6.2.4 Electrophysiological data acquisition

Data acquisition has been documented in Chapter 5, Section 5.2.6

6.2.5 Behavioural performance analysis

To assess the behavioural differences between YA, OA and MCI in response to PM stimuli, two mixed measures ANOVAs were conducted. Reaction time and percentage

of correct responses were analysed using a 3 (*Stimuli*: 1-back$_{target}$, PM$_{percept}$, PM$_{concept}$) x 3 (*Group*: YA, OA, MCI) mixed measures ANOVA. Only data from successful responses to stimuli were analysed for reaction time.

6.2.6 Electrophysiological data analysis

The core methods used for data preprocessing can be found in Chapter 5, Section 5.2.8.

Peak detection was performed using custom-written scripts in Matlab 2015a on each waveform using the EEGLAB toolbox (Delorme & Makeig, 2004). P2 was defined as the maximum positive peak at midline frontal and central clusters and bilateral frontal, frontocentral and central clusters between 160–220ms. N300 was defined as the most negative peak at midline parietal and occipital clusters and bilateral inferior parietal and occipital clusters between 300–500ms. Frontal positivity was defined as the most positive peak at midline frontal and central, and bilateral frontal and frontocentral clusters between 300–500ms. The most reliably elicited component of the parietal positivity in Chapter 5 was the IRR. Therefore, the current study used the IRR to evaluate group differences in PM intention retrieval. The IRR was defined as the largest positive amplitude between 400–600ms at midline and bilateral central and parietal clusters. RON was defined as being the most negative peak between 400–750ms over bilateral frontotemporal clusters. Latencies were measured at maximum peak and amplitude was measured as baseline–peak.

Statistical analyses were performed using JASP (0.10.2). The following analyses were used to test for group differences in P2, N300, frontal positivity, IRR and RON. Each component was analysed independently and was further divided between midline and bilateral analyses in the following mixed measures ANOVAs. For all components, ANOVAs included *Stimuli* (1-back$_{target}$, 1-back$_{nontarget}$, PM$_{percept,}$ PM$_{concept}$) x *Group* (YA, OA, MCI) as variables. In addition, ANOVAs of bilateral measures included *Hemisphere* (left, right) and *Cluster*. Level in the *Cluster* variable varied depending on the component: P2 and frontal positivity (frontal, frontocentral, central), N300 (parietal, occipital), IRR (central, parietal), RON (frontotemporal). Separate ANOVAs were performed for amplitudes and latencies. Lower-order ANOVAs were used to explore significant interactions. Post-hoc analysis of *Group* and controls for multiple comparisons was performed with Bonferroni corrections (Cabin & Mitchell, 2000).

Greenhouse-Geisser was used to correct for violations of sphericity and are reported. Only ERP data from correct responses were analysed.

6.3 Results

Three MCI participants were removed due to indications of probable dementia as indicated by the HVLT-R. One YA participant was removed due to poor EEG data. One participant from the OA and one from the MCI group were removed as they did not complete all conditions. Thus, the number of participants used in the final analysis were: YA = 29; OA = 36; MCI = 23.

6.3.1 Behavioural results

Means and standard deviations of the reaction times and percentage of correct responses are presented in Table 6.1. The behavioural results are illustrated as an interaction plot in Figure 6.1.

6.3.1.1 Reaction time

There was a significant effect of *Stimuli* ($F_{2,180} = 72.97$, $p < 0.001$, $\eta_p^2 = 0.46$), such that it required a significantly greater amount of time to correctly respond to $PM_{concept}$ stimuli relative to $PM_{percept}$ stimuli ($p < 0.001$) and correct 1-back_{target} stimuli ($p < 0.001$) for all participants. There were no other significant effects.

Table 6.1

Means and Standard Deviations of Behavioural Responses for Reaction Time and Correct Response.

Group	Reaction time (ms)			Correct responses (%)		
	1-back$_{target}$	**PM$_{percept}$**	**PM$_{concept}$**	**1-back$_{target}$**	**PM$_{percept}$**	**PM$_{concept}$**
YA	0.76 (0.17)	0.71 (0.09)	0.94 (0.13)	80.67 (10.63)	97.26 (6.29)	86.39 (10.64)
OA	0.77 (0.11)	0.76 (0.17)	0.96 (0.15)	78.38 (10.11)	96.40 (7.59)	90.12 (9.91)
MCI	0.89 (0.23)	0.77 (0.14)	1.01 (0.19)	64.98 (16.42)	97.34 (6.40)	80.15 (21.55)

Standard deviations are given in parentheses.

6.3.1.2 Correct responses

There was a significant effect of *Stimuli* ($F_{1.85,166.38} = 82.76$, $p < 0.001$, $\eta_p^2 = 0.50$). For all groups, PM$_{concept}$ performance was significantly worse relative to PM$_{percept}$ (all *ps* < 0.05).

Additionally, there was a significant main effect of *Group* ($F_{2,89} = 8.90$, $p < 0.001$, $\eta_p^2 = 0.18$) and a *Stimuli* x *Group* interaction ($F_{3.70,166.38} = 4.82$, $p < 0.002$, $\eta_p^2 = 0.11$). The interaction was due to significant effects of *Group* for ongoing ($F_{2,89} = 12.172$, $p < 0.001$, $\eta_p^2 = 0.22$) and PM$_{concept}$ ($F_{2,89} = 3.522$, $p = 0.034$, $\eta_p^2 = 0.08$), but not PM$_{percept}$ stimuli. MCI performed worse for ongoing (MCI < OA & YA, *p*s < 0.001) and for PM$_{concept}$ (MCI < OA, $p = 0.026$).

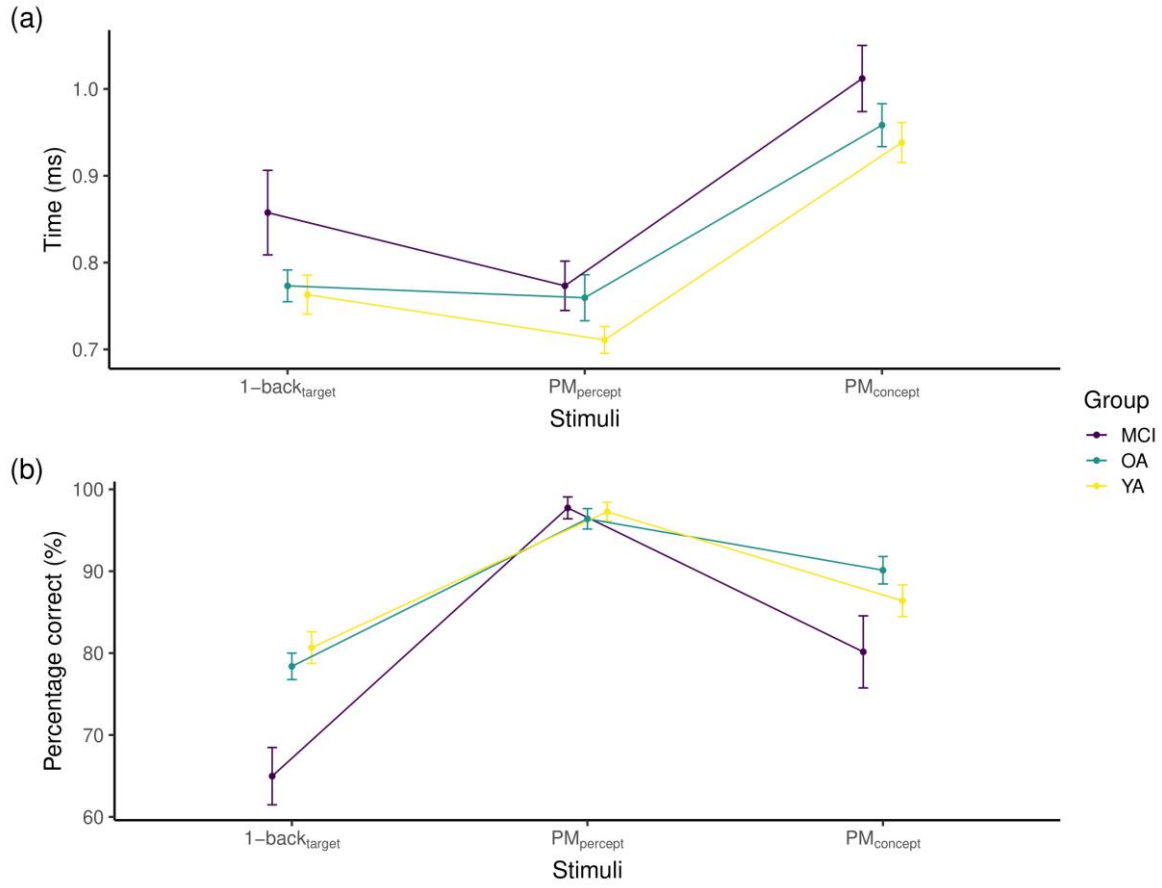

Figure 6.2. The interaction plots of reaction time and percentage of correct responses. (a) Reaction times for correct response to the ongoing-only (1-back$_{target}$), perceptual prospective memory task (PM$_{percept}$) and the conceptual prospective memory task (PM$_{concept}$) for young adults (YA), healthy older adults (OA) and older adults with mild cognitive impairment (MCI). (b) Percentage of correct responses to the ongoing-only task, perceptual prospective memory task and conceptual prospective memory task for each group. Error bars represent standard error.

6.3.2 Electrophysiology results

Descriptions of amplitudes and latencies can be found in Appendix E.

6.3.2.1 Effects of atypical ageing: MCI-specific deficits

6.3.2.1.1 Frontocentral P2

A summary of all significant P2 *Group* effects and interactions can be found in Table 6.2.

There was a significant *Cluster* x *Group* interaction over bilateral P2 amplitudes ($F_{2,87}$ = 3.28, p = 0.033, η_p^2 = 0.09; visualised in Figure 6.3). The MCI groups showed significantly lower amplitudes at frontocentral clusters, relative to the OA and YA across all conditions (all ps < 0.05).

There was a significant *Stimuli* x *Group* interaction at the midline frontocentral clusters for P2 amplitudes ($F_{5.14,221.04}$ = 5.37, p < 0.001, η_p^2 = 0.14). This was due to a *Stimuli* effect for YA ($F_{3,54}$ = 5.34, p = 0.003, η_p^2 = 0.23; 1-back$_{target}$ > 1-back$_{nontarget}$ | PM$_{percept}$ > 1-back$_{nontarget}$, ps < 0.05) and for OA ($F_{3,75}$ = 4.27, p = 0.008, η_p^2 = 0.15; 1-back$_{target}$ > 1-back$_{nontarget}$ & PM$_{percept}$, ps < 0.05), which was not found for MCI (p > 0.05).

There was a significant *Hemisphere* x *Group* interaction for lateral P2 latencies ($F_{2,87}$ = 3.55, p = 0.034, η_p^2 = 0.10). The MCI group showed significantly delayed right hemisphere responses relative to the left hemisphere ($F_{1,22}$ = 7.39, p = 0.019, η_p^2 = 0.38).

Table 6.2

Summary of Significant Group Effects for P2 ERP Amplitudes and P2 ERP Latencies

Midline P2 ERP amplitude	**Lower**	**F-value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Stimuli*Group		5.37	5.14,221.04	<0.001	0.14	
	YA	5.34	3,54	0.003	0.23	1-back$_{target}$ > 1-back$_{nontarget}$ | PM$_{percept}$ > 1-back$_{nontarget}$ & PM$_{concept}$
	OA	4.27	3,75	0.008	0.15	1-back$_{target}$ > 1-back$_{nontarget}$ & PM$_{percept}$
Lateral P2 ERP amplitude						
Cluster*Group		4.79	2.83,113.26	0.005	0.14	
	FC	3.28	2,87	0.033	0.09	OA & YA > MCI
Lateral P2 latencies						
Hemisphere*Group		3.55	2,87	0.034	0.10	
	MCI	7.39	1,22	0.019	0.38	R > L

YA = young adults. OA = healthy older adults. MCI = older adults with MCI. x = did not survive Bonferroni corrections. 1-back$_{target}$ = repeated ongoing stimuli. 1-back$_{nontarget}$ = non-repeat ongoing stimuli. FC = Frontocentral. F = Frontal. C = Central. R = Right hemisphere. L = Left hemisphere. *N.B.* '>' indicates amplitudes being more positive in this table. For latencies, '>' indicates the component occurring later in time.

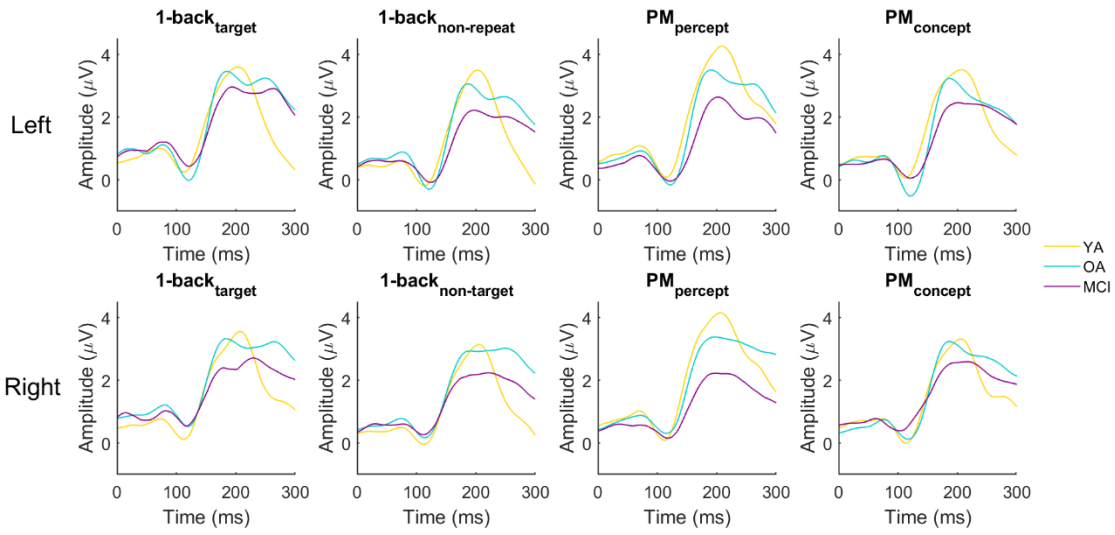

Figure 6.3. Grand-averaged ERP amplitudes for the P2 at bilateral frontocentral cluster for 1-back$_{target}$, 1-back$_{nontarget}$, PM$_{percept}$ and PM$_{concept}$. (a) Left hemisphere; (b) right hemisphere for young adults (YA), healthy older adults (OA) and older adults with MCI (MCI).

6.3.2.1.2 RON latency

Results of the significant *Group* analyses for the lateral reorientation negativity can be found in Table 6.3 and are visualised in Figure 6.4. Descriptions of the means and amplitudes of the RON latencies can be found in Appendix E, Table E.3.

A *Stimuli* x *Group* interaction was due to a significant effect of *Group* in response to PM$_{percept}$ stimuli ($F_{2,87}$ = 12.78, p < 0.001, η_p^2 = 0.24; YA < OA, p = 0.008; YA < MCI, p < 0.001; OA < MCI, p = 0.019). Furthermore, there was a significant effect of *Stimuli* in YA ($F_{3,84}$ = 16.77, p < 0.001, η_p^2 = 0.41; PM$_{concept}$ > PM$_{percept}$, p < 0.001; PM$_{concept}$ > 1-back$_{nontarget}$ stimuli, p = 0.022) and in OA ($F_{3,111}$ = 3.31, p = 0.024, η_p^2 = 0.11; PM$_{concept}$ < 1-back$_{nontarget}$, p = 0.022), which was not found in the MCI group.

Table 6.3

Summary of Significant Group Effects for Reorientation Negativity (RON) ERP Amplitudes and RON ERP Latencies

Lateral RON ERP amplitude	**Lower**	**F-value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Group		4.06	2,87	0.022	0.12	
Stimuli*Group		6.93	4.72,205.20	0.001	0.17	
	$PM_{percept}$	12.78	2,87	<0.001	0.24	YA > OA & MCI
	$PM_{concept}$	10.49	2,87	<0.001	0.21	YA > OA & MCI
	YA	16.77	3,84	<0.001	0.41	$PM_{percept}$ & $PM_{concept}$ > 1-$back_{target}$ & 1-$back_{nontarget}$
	OA	3.31	3,111	0.024	0.11	$PM_{concept}$ > 1-$back_{target}$
Hemisphere*Group		6.72	2,87	0.002	0.17	
	R	9.70	2,87	<0.001	0.22	YA > OA & MCI
	OA	22.51	1,37	<0.001	0.45	L > R
	MCI	13.85	1,22	0.002	0.50	L > R
Lateral RON latencies						
Group		9.89	2,87	<0.001	0.23	
Stimuli*Group		3.90	6,261	0.001	0.11	
	1-$back_{nontarget}$	9.13	1,87	<0.001	0.18	YA < OA & MCI
	$PM_{percept}$	14.75	2,87	<0.001	0.27	YA < OA < MCI
	YA	7.07	3,84	<0.001	0.23	$PM_{percept}$ & 1-$back_{nontarget}$ < $PM_{concept}$
	OA	3.87	3,111	0.012	0.12	$PM_{concept}$ < 1-$back_{nontarget}$

YA = young adults. OA = healthy older adults. MCI = Older adults with MCI. 1-$back_{target}$ = repeated ongoing stimuli. 1-$back_{nontarget}$ = non-repeat ongoing stimuli. L = left hemisphere. R = right hemisphere. *N.B.* '>' indicates amplitudes being more negative in this table and '<' indicates component latencies occurring earlier in time.

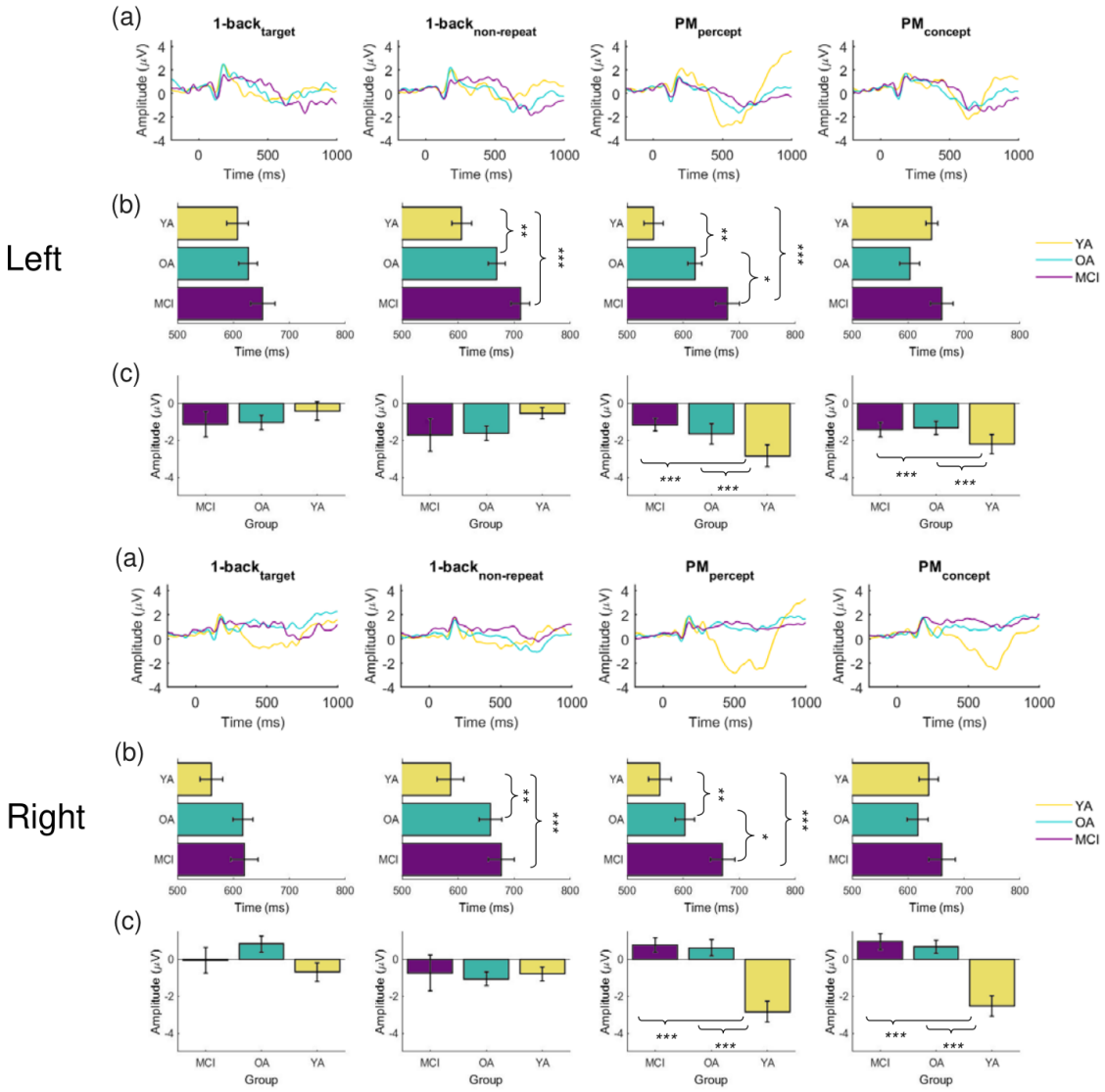

Figure 6.4. ERP amplitudes and latencies for the reorientation negativity (RON) at bilateral frontotemporal clusters. Left and right denote the hemisphere of the frontotemporal clusters. (a) Grand-averaged ERP waveforms for repeated ongoing (1-back$_{target}$), non-repeated ongoing (1-back$_{nontarget}$), perceptual PM (PM$_{percept}$) and conceptual PM (PM$_{concept}$) stimuli for young adults (YA), healthy older adults (OA) and older adults with mild cognitive impairment (MCI). (b) A bar chart of the latency of the RON across the YA, OA and MCI groups. (c) Bar charts of amplitudes of the RON across the YA, OA and MCI groups. Significant effects are highlighted with curly braces. * = $p < 0.05$; ** $p < 0.01$; *** = $p < 0.001$. Error bars represent standard error.

6.3.2.1.3 Intention retrieval amplitude

There was a significant *Stimuli* x *Hemisphere* x *Group* interaction ($F_{5.15,224.18} = 4.12$, $p = 0.001$, $\eta_p^2 = 0.10$), due to a significant *Stimuli* x *Group* interaction in the right hemisphere ($F_{4.83,209.89} = 3.68$, $p = 0.004$, $\eta_p^2 = 0.09$) for PM$_{percept}$ stimuli (YA > MCI, $p = 0.005$), which was not seen in the left. Additionally, there was a *Stimuli* x *Hemisphere*

interaction for $PM_{percept}$ in YA (right > left) and 1-$back_{target}$ in OA (right > left), which was not found in the MCI group.

6.3.2.2 Effects of typical ageing: how do MCI and OA differ from YA?

All significant ANOVA *Group* effects for amplitude and latencies of the IRR can be found in Table 6.4. Figure 6.5 shows averaged ERPs at the midline parietal cluster for each *Stimulus* as a function of *Group*.

6.3.2.2.1 Intention retrieval amplitude

At midline clusters there was a significant *Stimuli* x *Group* interaction ($F_{4.87,211.97} = 4.87$, $p < 0.001$, $\eta_p^2 = 0.12$). Further analysis showed that YA showed significantly greater IRR amplitudes for $PM_{percept}$ relative to both OA and MCI groups (*p*s < 0.001). Additionally, YA displayed significantly greater amplitudes for 1-$back_{target}$ and 1-$back_{nontarget}$ stimuli relative to individuals with MCI (*p*s < 0.05). There was also a significant *Cluster* x *Group* interaction ($F_{2,87} = 4.21$, $p = 0.019$, $\eta_p^2 = 0.11$), that was due to a significant effect of *Group* at the parietal cluster (YA > OA and MCI groups, *p*s < 0.001) and at central clusters (YA > MCI, $p = 0.041$).

6.3.2.2.2 Intention retrieval latency

There was a significant effect of *Stimuli* at midline clusters ($F_{2.70,218.63} = 16.74$, $p < 0.001$, $\eta_p^2 = 0.19$), where $PM_{concept}$ was significantly delayed relative to $PM_{percept}$ ($p < 0.001$) and both ongoing stimuli (*p*s < 0.01). $PM_{percept}$, however occurred significantly earlier than both ongoing stimuli (*p*s < 0.01). Similarly, an effect of *Stimuli* at bilateral clusters ($F_{2.78,227.87} = 12.70$, $p < 0.001$, $\eta_p^2 = 0.15$) was due an earlier $PM_{percept}$ response relative to $PM_{concept}$ and 1-$back_{target}$ stimuli (*p*s < 0.001).

There was a significant *Cluster* x *Group* interaction at midline clusters ($F_{2,87} = 4.81$, $p = 0.011$, $\eta_p^2 = 0.12$), which was due to a significant effect of *Group* at the parietal cluster (YA < OA, $p = 0.035$; YA < MCI, $p < 0.001$; OA < MCI, $p = 0.064$ (trend)). There was also a *Stimuli* x *Group* interaction ($F_{2.68,181.98} = 3.31$, $p = 0.006$, $\eta_p^2 = 0.09$), due to an effect of

Stimuli for 1-back$_{target}$ (YA < OA, p = 0.039) and 1-back$_{nontarget}$ (YA < OA, p = 0.036). This was not found for the PM stimuli (ps > 0.05).

The significant *Stimuli* x *Group* interaction at bilateral clusters ($F_{5.40,186.26}$ = 2.66, p = 0.07, η_p^2 = 0.07), was due to an effect of *Group* for PM$_{percept}$ stimuli ($F_{2,87}$ = 10.01, p < 0.001, η_p^2 = 0.20; YA < OA, p = 0.025). A significant effect of *Group* was found for PM$_{concept}$ stimuli ($F_{2,87}$ = 3.24, p = 0.044, η_p^2 = 0.14) but did not remain significant after Bonferroni corrections were applied.

Table 6.4

Summary of Significant Group Effects for IRR ERP Amplitudes and IRR ERP Latencies

Midline IRR ERP amplitude	**lower**	**F-value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Group		8.82	2,87	<0.001	0.20	
Stimuli*Group		4.87	4.87,211.97	<0.001	0.12	
	1-back_{target}	3.44	2,87	0.037	0.08	YA > MCI
	$1\text{-back}_{nontarget}$	4.82	2,87	0.011	0.11	YA > MCI
	$PM_{percept}$	12.46	2,87	<0.001	0.23	YA > OA & MCI
Cluster*Group		4.21	2,87	0.019	0.11	
	C	3.27	2,87	0.044	0.43	YA > MCI
	P	10.42	2,87	<0.001	0.22	YA > OA & MCI
Lateral IRR ERP amplitude						
Stimuli*Hemisphere *Group		4.12	5.15,224.18	0.001	0.10	
Stimuli*Group	R	3.68	4.83,209.89	0.004	0.09	$PM_{percept}$: YA > MCI
Stimuli*Hemisphere	YA	5.49	3,84	0.005	0.17	$PM_{percept}$: R > L
	OA	15.75	2.54,93.73	<0.001	0.33	1-back_{target}: R > L
Midline IRR latencies						
Group		3.56	2,87	0.034	0.10	
Stimuli*Group		3.31	2.68,181.98	0.006	0.09	
	1-back_{target}	3.75	2,87	0.028	0.09	YA < OA
	$1\text{-back}_{nontarget}$	3.48	2,87	0.036	0.08	YA < OA
Cluster*Group		4.81	2,87	0.011	0.12	
	P	7.59	2,87	0.001	0.09	YA < OA & MCI†
Lateral parietal positivity latencies						
Stimuli*Group		2.66	5.40,186.26	0.021	0.07	
	$PM_{percept}$	10.01	2,87	<0.001	0.20	YA < OA & MCI
	$PM_{concept}$	3.24	2,87	0.044	0.07	x

† = Trending (p = 0.064) after corrections. x = no significant effects after DF corrections. YA = young adults. OA = healthy older adults. MCI = Older adults with MCI. 1-back$_{target}$ = repeated ongoing stimuli. 1-back$_{nontarget}$ = non-repeated ongoing stimuli. P = parietal. C = central. R = right hemisphere. L = left hemisphere. *N.B.* '>' indicates amplitudes being more positive in this table. For latencies '<' indicates the component occurring earlier in time.

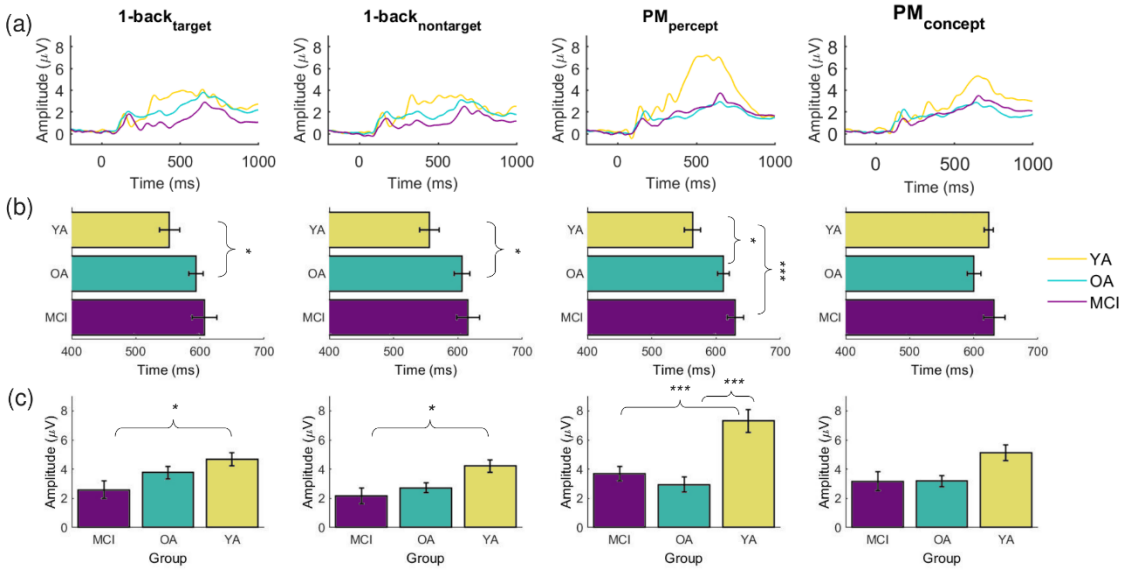

Figure 6.5. ERP amplitudes and latencies for the parietal positivity (IRR) at the midline parietal cluster. (a) Grand-averaged ERP waveforms for repeated ongoing (1-back$_{target}$), non-repeated ongoing (1-back$_{nontarget}$), perceptual PM (PM$_{percept}$) and conceptual PM (PM$_{concept}$) stimuli for young adults (YA), healthy older adults (OA) and older adults with mild cognitive impairment (MCI). (b) Bar charts of the latency of the IRR across the YA, OA and MCI groups. (c) Bar charts of amplitudes of the IRR across the YA, OA and MCI groups. Significant effects are highlighted with curly braces. * = p < 0.05; *** = p < 0.001. Error bars represent standard error.

6.3.2.3 Compensatory effects of ageing: how do OA differ from MCI and YA?

A summary of all N300 significant *Group* effects for ERPs and latencies can be found in Table 6.5.

6.3.2.3.1 N300 amplitude

At midline clusters the N300 amplitudes demonstrated a significant main effect of *Group* ($F_{2,87}$ = 4.95, p = 0.010, η_p^2 = 0.12; YA < OA, p = 0.010).

There was a significant three-way interaction of *Stimuli* x *Cluster* x *Group* at lateral posterior clusters ($F_{5.01,215.24}$ = 3.05, p = 0.011, η_p^2 = 0.08). Further analysis revealed that over bilateral inferior parietal clusters ($F_{4.86,211.37}$ = 4.28, p = 0.001, η_p^2 = 0.11), the OA evoked significantly greater amplitudes compared to the YA for 1-back$_{nontarget}$ (p < 0.001) and PM$_{concept}$ stimuli (p = 0.017). Descriptively, MCI evoked more negative amplitudes for both the 1-back$_{nontarget}$ and PM$_{concept}$ stimuli relative to YA but were not significantly different to YA or OA (ps > 0.05).

6.3.2.3.2 N300 latency

The midline analysis of N300 latencies demonstrated a significant *Stimuli* x *Group* interaction ($F_{6,261}$ = 3.58, p = 0.002, η_p^2 = 0.09), which was due to a significant *Group* effect for 1-back$_{nontarget}$ stimuli ($F_{2,87}$ = 6.17, p = 0.003, η_p^2 = 0.13), where YA evoked an N300 response earlier than OA (p = 0.002). Additionally, a *Group* effect for PM$_{percept}$ stimuli was found ($F_{2,87}$ = 10.01, p < 0.001, η_p^2 = 0.20), where YA evoked an N300 responses earlier than OA (p < 0.001) and MCI (p = 0.004). There was also a significant effect of *Stimuli* ($F_{2.12,57.09}$ = 6.75, p = 0.002, η_p^2= 0.20) for YA, where PM$_{concept}$ was significantly delayed relative to 1-back$_{target}$ (p = 0.013) and PM$_{percept}$ (p = 0.019).

Over bilateral clusters a significant *Cluster* x *Group* interaction ($F_{2,87}$ = 7.05, p = 0.002, η_p^2 = 0.16) was due to a significant effect of *Group* at occipital clusters ($F_{2,87}$ = 3.87, p = 0.025, η_p^2 = 0.10; YA < OA, p = 0.026).

Moreover, there was a significant three-way Stimuli x Hemisphere x *Group* interaction ($F_{6,261}$ = 9.21, p = 0.012, η_p^2 = 0.07). This interaction effect was due to a significant *Stimuli* x *Hemisphere* interaction for YA ($F_{3,84}$ = 6.41, p < 0.001, η_p^2 = 0.32). For YA, left N300 latency was significantly earlier for 1-back$_{target}$ than 1-back$_{nontarget}$ (p = 0.032) and PM$_{percept}$ (p = 0.009); right N300 latency was earlier for PM$_{percept}$ than 1-back$_{target}$ (p < 0.001), 1-back$_{nontarget}$ (p = 0.025) and PM$_{concept}$ (p = 0.002). Additionally, there was a significant *Stimuli* x *Hemisphere* interaction in OA ($F_{3,99}$ = 3.20, p = 0.027, η_p^2 = 0.09), such that left N300 latency in response to 1-back$_{nontarget}$ was later than 1-back$_{target}$ (p = 0.006), whilst right N300 latency in response to 1-back$_{nontarget}$ was delayed, relative to both 1-back$_{target}$ (p < 0.001) and PM$_{percept}$ (p = 0.010). Furthermore, there was a significant *Hemisphere* x *Group* interaction ($F_{2,87}$ = 7.05, p = 0.002, η_p^2 = 0.15), which

was due to an earlier left relative to the right hemisphere N300 latency for 1-back$_{target}$ in YA ($F_{1,28} = 20.57$, $p < 0.001$, $\eta_p^2 = 0.15$).

Table 6.5

Summary of Significant Group Effects for N300 ERP Amplitudes and N300 ERP Latencies

Midline N300 ERP amplitude	**Lower**	**F-value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Group		4.95	2,87	0.010	0.12	YA < OA
Lateral N300 ERP amplitude						
Stimuli*Group		2.94	4.70,202.25	0.015	0.08	
	1-back$_{target}$	5.16	2,87	0.008	0.11	YA < OA & MCI
	1-back$_{nontarget}$	11.79	2,87	<0.001	0.23	YA < OA & MCI
	PM$_{concept}$	4.99	2,87	0.009	0.11	YA < OA
Stimuli*Cluster* Group		3.05	5.01,215.24	0.011	0.08	
Stimuli*Group	IP	4.28	4.86,211.37	0.001	0.11	1-back$_{nontarget}$: YA < OA | PM$_{concept}$: YA < OA
Stimuli*Cluster	Young	7.06	2.23,60.96	<0.001	0.21	IP < OC & P | IP: PM$_{percept}$ > 1-back$_{nontarget}$ & 1-back$_{target}$ & PM$_{concept}$ | OC: PM$_{concept}$ > 1-back$_{target}$ & 1-back$_{nontarget}$
Cluster*Group	PM$_{percept}$	3.64	2,87	0.031	0.08	x
Midline N300 latencies						
Group		7.59	2,87	0.001	0.17	
Stimuli*Group		3.58	6,261	0.002	0.09	1-back$_{nontarget}$: YA < OA | PM$_{percept}$: YA < OA & MCI
Lateral N300 latencies						
Cluster*Group		7.05	2,87	0.002	0.16	
	OC	3.87	2,87	0.025	0.10	YA < OA
Stimuli*Hemisphere* Group		9.21	6,261	0.012	0.07	

Lateral latencies	N300 Lower	F-value	DF	*p*-value	η_p^2	Post-Hoc Tests
Stimuli*Hemisphere	YA	6.41	3,84	<0.001	0.32	L: 1-back$_{target}$ < 1-back$_{nontarget}$ & PM$_{percept}$ | R: PM$_{percept}$ < 1-back$_{target}$ & 1-back$_{nontarget}$ & PM$_{concept}$
	OA	3.20	3,99	0.027	0.09	L: 1-back$_{nontarget}$ > 1-back$_{target}$ | R: 1-back$_{nontarget}$ > 1-back$_{target}$ & PM$_{percept}$ |PM$_{concept}$ > PM$_{percept}$
Hemisphere*Group	1-back$_{target}$ 7.05		2,87	0.002	0.15	YA: L < R

YA = young adults. OA = healthy older adults. MCI = Older adults with MCI. 1-back$_{target}$ = repeated ongoing stimuli. 1-back$_{nontarget}$ = non-repeat ongoing stimuli. OC = occipital. IP = inferior parietal. P = parietal. R = right hemisphere. L = Left hemisphere. | = separator between post-hoc tests. *N.B.* '<' indicates amplitudes being less negative in this table. For latencies '<' indicates the component occurred earlier in time.

6.3.2.3.3 Frontal positivity amplitude

All significant *Group* effects for the frontal positivity can be found in Table 6.6.

Midline frontal positivity showed a significant *Stimuli* x *Group* interaction ($F_{5.07,217.04}$ = 2.59, p = 0.027, η_p^2 = 0.07), due to significantly greater amplitudes in OA and MCI, compared to YA, for 1-back$_{target}$ ($F_{2,87}$ = 7.20, p = 0.001, η_p^2 = 0.15), 1-back$_{nontarget}$ ($F_{2,87}$ = 16.22, p < 0.001, η_p^2 = 0.29) and PM$_{concept}$ ($F_{2,87}$ = 9.12, p < 0.002, η_p^2 = 0.18) stimuli (all ps < 0.001 for OA and ps < 0.02 for MCI), but not for PM$_{percept}$ (p > 0.05). Similarly, for bilateral frontal positivity, a significant *Group* effect was found ($F_{2,87}$ = 10.76, p < 0.001, η_p^2 = 0.23; OA > YA, p < 0.001; MCI > YA, p = 0.025).

Table 6.6

Summary of Significant Group Effects for Frontal Positivity ERP Amplitudes and Frontal Positivity ERP Latencies

Midline frontal positivity amplitude	**Lower**	**F-value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Group		10.76	2,87	<0.001	0.23	
Stimuli*Group		2.59	5.07,217.04	0.027	0.07	
	1-back$_{target}$	7.20	2,87	0.001	0.15	OA & MCI > YA
	1-back$_{nontarget}$	16.22	2,87	<0.001	0.29	OA & MCI > YA
	PM$_{concept}$	9.12	2,87	<0.001	0.18	OA & MCI > YA
Lateral frontal positivity amplitude						
Group		12.48	2,87	<0.001	0.27	OA & MCI > YA

YA = young adults. OA = healthy older adults. MCI = older adults with MCI. F = frontal. FC = frontocentral. L = left hemisphere. R = right hemisphere. 1-back$_{nontarget}$ = non-repeat ongoing. 1-back$_{target}$ = repeated ongoing. | = separator between post-hoc tests. *N.B.* '>' indicates amplitudes being more positive in this table.

6.4 Discussion

The current study is the first, to the authors' knowledge, to use ERPs to examine neurophysiological mechanisms underpinning atypical age-associated decline in PM. A comparison is made between perceptual and conceptual event-based PM, as well as the ongoing working memory task in which these tasks were embedded. Participants, particularly the MCI group, performed worse in the conceptual PM task than other tasks. MCI participants had poorer performance (for the ongoing working memory task and conceptual PM), lower bilateral frontocentral P2 amplitudes, delayed RON than both other groups and lower IRR amplitudes (relative to young adults only). Extending the results from Chapter 5, healthy older adults also elicit greater RON amplitudes following PM stimuli relative to the ongoing task (conceptual PM only). However, this effect was absent in MCI. RON latency in older adults was earlier than for those with MCI and delayed compared to young adults for non-repeat ongoing stimuli and perceptual PM stimuli.

Regarding typical ageing, compared to young adults, both healthy older adults and MCI participants had lower amplitudes and delayed latencies for the IRR, and higher

amplitudes for the N300 and frontal positivity. Lower RON amplitudes and a left hemisphere bias (i.e., greater RON amplitudes relative to ongoing stimuli were only found over the left hemisphere) were seen in both older (compared to younger) adult groups. For perceptual PM stimuli, both older adult groups had reduced IRR amplitudes at midline clusters and a longer latency at midline and bilateral regions. However, the hypothesised reduction in N300 amplitude in older groups was not supported.

6.4.1 Mild cognitive impairment specific deficits

The current study reveals poorer performance in terms of accuracy but not reaction time in those with MCI compared to other groups for the ongoing working memory task, suggesting an impairment in semantic based working memory. This could reflect a speed-accuracy trade-off for those with MCI (Larner, 2015; Lassen-Greene et al., 2017). That is, participants with MCI were prioritising speed over accuracy in the ongoing task. However, without evaluating differences between correct and incorrect responses, a speed-accuracy trade-off remains speculative. The absence of group differences in salient perceptual-based PM, which is thought to rely more on spontaneous retrieval (Knight et al., 2011), may reflect intact spontaneous recall of PM in MCI. However, the impairment for those with MCI in the conceptual PM task suggests that active monitoring for PM stimuli may be affected in MCI. This is in line with studies showing that response to PM tasks that required strategic monitoring are affected in MCI (Blanco-Campal et al., 2009; Karantzoulis et al., 2009; Niedźwieńska et al., 2017; Troyer & Murphy, 2007).

The current results demonstrate attenuated frontocentral P2 amplitudes in older adults with MCI compared to healthy older and younger adults. This is in line with recent studies examining the P2 component in older adults with MCI (B.-Y. Li et al., 2016; Waninger et al., 2018). The precise function of the P2 remains unclear, however, considering the recent work relating the P2 to rapid semantic processing (Irak, Soylu, & Turan, 2019; Paynter et al., 2009) and a peri-perceptual sense of familiarity (Doborjeh et al., 2018), then this may suggest that older adults with MCI possess an impaired ability to process semantic information or impaired semantic working memory (Kuo et al., 2014). Alternatively, studies have linked the P2 to familiarity

(Evans & Federmeier, 2007) and the feeling of knowing in episodic memory tasks (Irak et al., 2014; Irak, Soylu, & Turan, 2019; Irak, Soylu, Turan, et al., 2019). Given the similarity between episodic and PM tasks (Brewer et al., 2010), the P2 here may also reflect cognitive processes related to familiarity and a feeling of knowing. With this interpretation, one might assume that a P2 amplitude reduction is indicative of a decrease in familiarity and a feeling of knowing of the presented stimulus. Indeed, evidence implicates deficits of familiarity as a marker of early cognitive impairment (Embree et al., 2012; Pitarque et al., 2016; Wolk et al., 2008), although this is contested. Other researchers find familiarity to be spared in cognitive decline (Koen & Yonelinas, 2014; Lombardi et al., 2018; Serra et al., 2010) and may only become apparent with the development of AD (Koen & Yonelinas, 2014). It would seem then, that the P2 is an important marker of cognitive decline in relation to early semantic memory processing, but further research is needed to understand its functionality. Future research should explore different aspects of the P2 in working and PM through task manipulation, analysis methods (e.g., ICA; source localisation) and over the different stages of PM (i.e., encoding, retention and intention retrieval; Brandimonte et al., 1996).

The current findings implicate altered task reorientation in PM and suggest that typical age-associated changes in RON amplitudes are accelerated in MCI. Age-related differences in lateralisation are in line with the right-hemi-ageing model (RHAM) that predicts greater age-related decline over the right hemisphere (Albert & Moss, 1988; Brown & Jaffe, 1975). Prior evidence for this theory has been predominately based on behavioural performance (Dolcos et al., 2002), and has recently been superseded by a neuroimaging-based hypothesis of ageing known as the Hemispheric Asymmetry Reduction in Older Adults (HAROLD; Cabeza, 2002). HAROLD proposes that prefrontal activity during cognitive performance tends to be less lateralised in older relative to younger adults (Cabeza, 2002; Hommet et al., 2008). The results here do not support the HAROLD hypothesis and provides neurophysiological evidence in support of the RHAM. However, the results here may suggest that hemispheric asymmetry may be function-specific (i.e., affect mechanisms underpinning reorientation of attention) as the HAROLD model is based on other cognitive features but not specifically attention.

The lateralisation of RON with age, seen in the current study, concurs with findings from a visual inhibitory control task (Cona et al., 2013), showing greater RON

amplitudes for younger adults compared to older adults over the right (but not left) frontotemporal scalp regions during detect trials. Together, the results from Cona et al. (2013) and the current study suggest lateralisation of reorienting networks. Source localisation of high-density electrode data implicate frontotemporal scalp regions in RON (Schröger et al., 2000). Thus, whilst symmetry may decline anteriorly with age, exaggerated lateralisation in frontotemporal networks underpinning orientation of attention may occur.

6.4.2 Neurophysiological age-related deficits

Cona et al. (2013) attribute an age-related latency delay in the RON to a specific deficit in attentional shifting and not to a general slowing of processes with advancing age. This is in line with the only other study of RON in older adults during an auditory distraction task (Horváth et al., 2009). The current results further support and extend these findings, suggesting age-related RON delays exist in older adults following responses to PM cues. In MCI, this decline was particularly exaggerated for perceptual PM cues. Thus, reorienting back to an ongoing task following a perceptual PM cue may be particularly sensitive to atypical ageing. Such results are the first to highlight the potential of the RON during PM as an early biomarker of cognitive decline. Moreover, the results here support fMRI evidence implicating attention networks and the right inferior frontal cortex during task-switching as a preclinical marker of AD (Gordon et al., 2015; Oh et al., 2016). Further research should draw a comparison between MCI and dementia-related diseases on RON in response to PM cues.

As hypothesised, both healthy older adult groups and MCI participants evoked an attenuated IRR ERP relative to the younger adults, providing further support for reduced PM intention recall in older adults (West & Bowry, 2005; West & Covell, 2001). However, it should be noted that the aforementioned studies also reported behavioural impairments of PM response, which was not found in the current study. However, IRR attenuation with absent behavioural differences relative to younger adults have been found before. Sebastián et al. (2011) found that that older adults did not exhibit poorer behavioural performance but did show parietal positivity attenuation during a recognition memory task. One explanation may be the fine-tuning of networks responsible for memory retrieval (Filippini et al., 2012) or may reflect the

dedifferentiation of neuronal source distinctiveness, where the specialisation and tight localisation of activity may become more dispersed through the cortex (Goh, 2011). Importantly, we did not find any further attenuation of the IRR for the MCI group, suggesting that intention retrieval may remain unaffected in older adults experiencing cognitive decline.

Furthermore, the present study reveals temporal differences for IRR onset. The results indicate an earlier response for the younger adults compared to the healthy older adults and MCI groups. The results show a trending effect for a slower IRR response in those with MCI relative to older adults. This may not have reached statistical significance due to the heterogeneity of the MCI group and the possible inclusion of different MCI subtypes. The earlier IRR response by younger adults may reflect an ability to rapidly recall the PM intention. Yet, this ability does not seem to improve behavioural performance. Earlier IRR latency without an increase in reaction time in younger adults may suggest differences in the neural strategies recruited between younger and older adults. Evidence has previously demonstrated in other ERP studies requiring task-switching that latency delays can occur without behavioural deficits (Gaál & Czigler, 2015).

6.4.3 Neurophysiological age-related compensation

Consistent with some previous studies (Hering et al., 2016), the N300 and frontal positivity did not show age-related amplitude attenuation. While these studies found no group differences, the current results in fact show the opposite. Greater negativity was evoked for N300 and greater positive amplitudes were evoked for the frontal positivity for both older adult groups relative to younger adults. Past studies have found increased N300 amplitudes in childhood (Sumich, Sarkar, Hermens, Kelesidi, et al., 2012) and in some development disorders such as subclinical depression and schizophrenia (Sumich et al., 2006, 2013; Sumich, Sarkar, Hermens, Ibrahimovic, et al., 2012). No differences were seen between the healthy older adults and participants with MCI, implying that cue detection aspects of PM are retained with MCI and are likely not contributing to the reported PM deficits in MCI.

Previous evidence indicates that N300 amplitude attenuations are due to an inability to recruit preparatory attentional processes, which was supported by reported

behavioural deficits (R. E. Smith & Bayen, 2006). However, as behavioural deficits were not found in the current study, the N300 may not be reflecting an inability to recruit preparatory attentional processes. This may suggest differences in the recruitment of neural strategies and approaches to completing the task between younger and older adults (West & Bowry, 2005). This suggestion is supported by the increased frontal positivity amplitudes in the aged populations in the current study. Similar increase of the frontal positivity has been demonstrated before in older adults relative to younger adults during a simple working memory task (Tays et al., 2011). In Tays et al.'s (2011) study, younger participants reportedly relied on an earlier attentional mechanism (i.e., N100 for target discrimination). Additionally, lower frontal positivity amplitudes have been found previously in younger adults during PM tasks (West & Covell, 2001). It is possible that older adults are recruiting frontal networks to a greater extent to support the maintenance of intentions as proposed in a recent fMRI study (Peira et al., 2016) and should be further explored using ERPs.

Furthermore, we found an earlier N300 response for younger adults compared to both older adult groups. However, this earlier cue detection response does not manifest in earlier response times, it further supports the notion that older adults are relying on a different neural mechanism for successful cue detection or that the N300 is not the only component which reflects PM cue detection (Hering et al., 2016; West & Bowry, 2005).

6.4.4 Limitations and future studies

Despite motivation not being measured quantitatively, based on experimenter observation, older adults may have had greater motivation to perform well compared to younger adults. This is in line with previous work on attention and motivation as a function of age (Tomporowski & Tinsley, 1996) showing a more rapid reduction in attention and motivation in young (relative to older) adults over the course of an experiment. Future research should, therefore, monitor motivation during task performance. As this study is the first to document the RON in MCI, future research should further explore this effect in different PM task designs and replicate this effect in MCI and early AD. In addition, RON differences between conceptual and perceptual stimuli may be due to focality of the PM task. Despite being salient, the perceptual PM

stimuli may be considered non-focal. This is because the semantic features are not processed as part of the ongoing task, whereas the conceptual PM stimuli can be considered focal due to being evaluated with the semantic features of the ongoing task. Thus, reorienting attention might have been more efficient for participants for conceptual PM cues. Future research should vary the focality of PM cues when evaluating the RON in PM. Finally, it is to be noted that subtypes of MCI were not recorded, which due the heterogeneity of MCI (Panza et al., 2007) may have masked other potential neurophysiological differences between groups.

6.4.5 Summary

To conclude, participants with MCI were associated with poorer behavioural performance in the ongoing working memory and conceptual PM task. Neurophysiological evidence demonstrated reduced frontocentral P2 amplitudes for older adults with MCI, possibly reflecting deficits in networks associated with familiarity or semantic memory processing. Behavioural differences between young and healthy older adults were not found. Nevertheless, their neurophysiological responses suggest different neural mechanisms related to PM cue detection and intention retrieval. Finally, neurophysiological evidence indicates the presence of a RON in young and older adults but was markedly decreased in older adults over the right hemisphere. Furthermore, latency delays of the RON indicate attention shifting deficits in older adults and an increased delay may serve as an early biomarker of cognitive decline.

Chapter Seven: Prospective memory interference effect in typical and atypical ageing

7.0 Overview

The previous chapter explored the behavioural and neurophysiological differences between younger adults, older adults and older adults with MCI when responding to perceptual and conceptual PM stimuli. The following chapter explores the effect that maintaining a PM intention has on the ongoing task. Specifically, anterior scalp regions at 300–500ms and 600–1000ms are investigated to understand the neurophysiological differences in PM intention maintenance as a result of ageing and cognitive decline. Additionally, the amplitude and latencies of the P2 and N2 are investigated to explore early feature-based attention processes of PM monitoring.

7.1 Introduction

The ability to successfully remember to perform a future intention is a fundamental personal resource. Performance declines in ageing are well documented (Henry et al., 2004; Kliegel, Jäger, et al., 2008; McDaniel et al., 2008; Phillips et al., 2008) and are reportedly one of the first complaints of older adults experiencing MCI (Brandimonte et al., 2014). Despite this, relatively little is known about the neurophysiological effects of typical and atypical ageing on PM performance. In Chapter 6, increased cue-related ERP responses (N300 and frontal positivity) and decreased intention retrieval related ERPs (parietal positivity) were found relative to young adults. Additionally, in older adults with MCI, ERPs related to semantic working memory (P2) were attenuated and the reorienting of attention (RON) was delayed. The Multiprocess framework of PM (Einstein et al., 2000; 2005; *see Chapter 1, Section 1.3.1*) suggests that under certain circumstances (i.e., non-focal or low salience cues) PM intention retrieval may only occur when attentional processes are applied to monitoring the environment for PM

cues. The PAM theory (Smith et al., 2007; Smith 2008; 2010; *see Chapter 1, Section 1.3.2*) suggests that attentional processes are always required to monitor for PM cues within the environment. Once a cue is encountered the executive attentional system interrupts the ongoing activity for the intention to be performed. It is assumed that the application of attention processes to monitor for PM cues will interfere with any ongoing activities. The aim of the current chapter, therefore, is to examine the possible behavioural and neurophysiological impact on the ongoing working memory task when PM intentions are maintained in typical and atypical ageing.

The dual-task nature of PM experiments requires an individual to stop performing the ongoing activity to complete the PM intention (Graf & Uttl, 2001). The PM task may interfere with the ongoing task incurring greater errors or slower reaction times (Smith, 2003). The performance cost to the ongoing task is known as the PM interference effect (Scullin, McDaniel, & Einstein, 2010). Investigations into the interference effect remain limited (Boywitt & Rummel, 2012; Hefer et al., 2017; Loft & Remington, 2010; Marsh et al., 2005) and have been predominately conducted on young adults (Chen et al., 2009; Hefer et al., 2017; Loft et al., 2008, 2014; Loft & Remington, 2010; Shelton & Christopher, 2016). Studies have generally found a PM interference effect for stimuli that require a greater amount of PM monitoring (e.g., low salience or non-focal PM cues; Loft et al., 2014; Loft & Remington, 2010; Scullin, McDaniel, Shelton, et al., 2010). The greater effort required for monitoring requires increased cognitive processes as proposed in the Multiprocess Framework (Einstein et al., 2000; Einstein et al., 2005) and PAM theory of PM (Smith et al., 2007; Smith 2008; 2010).

Only a few studies have explored the PM interference effect in healthy older adults (A. Cohen et al., 2005; Enrique et al., 2013; Kominsky & Reese-Melancon, 2017; Scullin et al., 2013; W. Wang et al., 2010). Generally, older adults show similar PM monitoring abilities relative to younger adults (Ball & Bugg, 2018; Enrique et al., 2013; Kliegel, 2008; Kominsky & Reese-Melancon, 2017). However, some studies also show that with the addition of PM cues that require more attentional processes (e.g., low salience or non-focal), older adults often perform worse on the ongoing task (Ball et al., 2019; Kliegel, Jäger, et al., 2008; Scullin et al., 2013; Uttl, 2008, 2011). Studies of older adults with MCI show performance impairments in all types of PM but show particular impairment for those tasks requiring more effortful monitoring (Blanco-Campal et al.,

2009; Karantzoulis et al., 2009; Tam & Schmitter-Edgecombe, 2013; Troyer & Murphy, 2007). Some researchers propose that this is due to impairments in the PFC and the MTL (McFarland & Glisky, 2009), however, this is yet to be investigated directly. In contrast, other researchers report that older adults with MCI and very mild AD are more impaired in tasks relying on spontaneous retrieval (Chi et al., 2014; McDaniel et al., 2011; Niedźwieńska et al., 2017). Niedzwieńska et al. (2017) suggest that individuals with MCI and early AD may not be impaired in the non-focal tasks as the participants may recruit compensatory mechanisms of the prefrontal cortex, which are generally not compromised at the early stages of cognitive decline (Braak & Braak, 1991). Neurophysiological experiments are yet to determine whether prefrontal cortices provide compensatory mechanisms for PM monitoring in older adults with MCI. Considering the mixed behavioural evidence, further work is needed to delineate whether older adults with MCI have impaired PM monitoring abilities and under what conditions these potential impairments manifest.

The neurophysiological evidence of PM monitoring, for the most part, has focused on response differences between ongoing stimuli when monitoring for a perceptual PM cue and the ongoing working memory task stimuli (Brewer et al., 2010; Burgess et al., 2001, 2003; Cona et al., 2012b; Cona, Scarpazza, et al., 2015; Gilbert et al., 2009; Reynolds et al., 2009). Some evidence implicates the anterior prefrontal cortex in PM intention maintenance during the ongoing task (Cona et al., 2015). Neurophysiological studies evaluating ERPs in response to the ongoing stimuli, find significant amplitude modulations when monitoring for a PM intention compared to the ongoing task when the PM cue is absent (West, 2007; West & Bowry, 2005). The research suggests that during intention maintenance, frontal slow waves ranging from 400–900ms emerge (Cona et al., 2012b, 2014; Czernochowski et al., 2012). For example, Czernochowski et al. (2012), compared the ongoing task when no PM cues were present with stimuli from the ongoing task when PM cues were present. Their results demonstrated sustained frontocentral activity, which has been linked to PM monitoring (Czernochowski et al., 2012b; Hering et al., 2018). Moreover, this anterior activity is thought to reflect an active continued awareness for possible PM cues (Guynn, 2003) and being in a readiness state known as the PM 'retrieval mode' (West et al., 2011). Specifically, monitoring for a PM cue has been shown to increase positive amplitudes between 300–500ms (Bailey et al., 2016; Chen et al., 2007; Cona et al., 2012b; West et al., 2006b; West & Bowry, 2005) and also between 600–900ms compared to an

ongoing-only condition at anterior scalp regions (Czernochowski et al., 2012). This corroborates evidence from fMRI studies indicating sustained activity within the PFC when monitoring for PM cues relative to no-cue conditions (Burgess et al., 2007; Peira et al., 2016; Reynolds et al., 2009).

Early ERP component differences in the posterior scalp and frontal regions have also been documented during PM monitoring tasks. The N2 and the P2 have been shown to demonstrate an amplitude increase when individuals were monitoring for PM cues as opposed to completing the ongoing tasks without PM cues (Chen et al., 2009; Czernochowski et al., 2012; J. B. Knight et al., 2010). This has been hypothesised to reflect feature-based attention (Knight et al., 2010), similar to attention task results finding a "selection negativity" and "selection positivity" ERP response over parietooccipital and frontocentral scalp regions (Harter & Aine, 1984; Hillyard & Anllo-Vento, 1998; Kopp et al., 2007; Schoenfeld et al., 2007). Preparatory attentional processes are likely required during PM monitoring to rapidly process the features of the incoming stimuli to determine if a stimulus is a PM cue or an ongoing stimulus.

The ERP evidence regarding the effects of ageing during monitoring for PM cues is limited and mixed. On the one hand, research has shown sustained ERP modulations over frontal and parietal scalp sites to differ between younger and older adults (West & Bowry, 2005). In particular, younger adults appear to recruit more frontopolar and frontocentral sources compared to older adults who demonstrate greater activity over central scalp sites while monitoring for perceptual PM cues (Hering, Kliegel, Bisiacchi, et al., 2018; West & Bowry, 2005). Similar differences are also apparent between younger and older adults during time-based PM and emotion-based PM cues (Cona et al., 2012b; Hering, Kliegel, Bisiacchi, et al., 2018) suggesting that age-related monitoring differences are similar across PM cue types. Cona and colleagues (2012) report sustained slow-wave activity over frontal scalp sites in younger adults, which was not found in the older adult group. This was thought to reflect an age-related decrease in the efficiency of executive and frontal functions and a decrease in overall cognitive processes, although this was not directly tested. On the other hand, some research has indicated no age-related anterior activity differences during monitoring for PM cues (Mattli et al., 2011; Rose et al., 2015). Mattli et al. (2011) found sustained neural activity over frontal and posterior scalp regions but contrary to their

hypothesis, activity did not differ across the lifespan. Further work is required to address these age-related neural discrepancies in PM monitoring.

To date, no studies have examined the neurophysiology of PM monitoring in older adults with MCI. However, evidence does demonstrate ERP differences during working memory tasks. In *n*-back tasks, older adults with MCI have been found to have smaller positive amplitudes between 400–500ms and delayed P2 and N2 responses relative to healthy older adults (Fraga et al., 2018; Mamani et al., 2017; Zunini et al., 2016). Additionally, tasks designed to evaluate sustained attention have shown global decreases in ERP amplitudes for individuals with MCI relative to healthy older adults (Waninger et al., 2018) suggesting difficulties with attention in MCI. It would be expected then that the ERPs of the older adults with MCI would have smaller amplitudes relative to healthy older adults. Further ERP attenuations would also be expected when monitoring for PM cues due the additional cognitive processes required to monitor for the PM cues.

By examining working memory with the addition of a highly salient PM task (perceptual) and a less salient PM (conceptual) task, differences in the amount of attentional processes can be assessed. These differences can be evaluated because highly salient PM is thought to rely more on spontaneous intention recall whereas less salient cues require more cognitive processes to monitor for the PM cue (Einstein et al., 2005). Through the assessment of working memory when monitoring for different PM cues, the current chapter aims to better understand the neurophysiology of in individuals with MCI during PM intention maintenance.

7.1.2 Aims and hypothesises

The current study aims to investigate the behavioural and neurophysiological PM interference effect in older adults with and without MCI. The ongoing task, in the absence of PM cues, is compared against the ongoing task when monitoring for perceptual and conceptual PM stimuli. Considering the mixed evidence for older adults and the lack of neurophysiological evidence regarding PM maintenance in older adults with MCI, examining ongoing working memory performance during PM monitoring will further our understanding of the PM interference effect in typical and atypical ageing.

The current study hypothesises that: 1) Older adults (OA) will perform significantly worse relative to younger adults (YA) during the ongoing task when monitoring for conceptual PM cues but not perceptual PM cues. 2) Older adults with MCI (MCI) will perform significantly worse across all ongoing tasks and will have disproportional impairments when monitoring for conceptual PM cues relative to perceptual cues. 3) Both older adult groups will have attenuated ERP amplitudes at anterior scalp clusters between 300–500ms and 600–1000ms when monitoring for PM cues, which will be further pronounced in participants with MCI. 4) Older adults with MCI will have reduced N2 and P2 ERP amplitudes, which will also be delayed relative to young and older adults.

7.2 Methods

7.2.1 Participants

Participants descriptions are detailed in Chapter 6, Section 6.2.1.

7.2.2 Procedure

Core methodology has been documented in Chapter 5, Section 5.2.3.

7.2.3 Electrophysiological data acquisition

Data acquisition has been documented in Chapter 5, Section 5.2.6

7.2.4 Behavioural data analysis

To examine the PM interference effect, differences in ongoing task performance were compared between YA, OA and MCI when monitoring for a perceptual PM cue (ongoing + $PM_{percept}$), a conceptual PM cue (ongoing + $PM_{concept}$) and just the ongoing-only task (ongoing-only). Two mixed measures, 3 (*Stimuli*: ongoing-only, ongoing + $PM_{percept}$, ongoing + $PM_{concept}$) x 3 (*Group*: YA, OA, MCI) ANOVAs were used for the two dependent

variables: reaction time and percentage of correct ongoing task responses. Only reaction times from correct responses were included in the analysis.

7.2.5 Electrophysiological data analysis

The core methods used for data preprocessing can be found in Chapter 5, Section 5.2.8.

Peak amplitude detection was performed using custom-written scripts in Matlab 2015a using the EEGLAB toolbox for each waveform. The P2 was defined as the maximum positive peak at midline frontal and central clusters. The P2 amplitudes were also defined at bilateral frontal, frontocentral and central clusters. The N2 was defined as the most negative peak at midline parietal and occipital clusters. Additionally, the N2 was also defined as the most negative peak at bilateral inferior parietal, parietal and occipital clusters. Both the P2 and N2 were identified between 160–220ms.

Sustained PM monitoring amplitudes were defined as the maximum amplitudes at frontal and central clusters and bilateral frontal, frontocentral, central and frontotemporal clusters between 300–500ms, referred to throughout as the early frontal positivity (EFP) and between 600–1000ms referred to as the late frontal positivity (LFP). P2 and N2 ERP latencies were also extracted to assess group differences. Averaged ERP amplitudes for each condition were also used to create topographic brain maps to examine the distribution of activity between the groups.

All statistical analyses were performed using JASP (0.10.2). The following analyses were used to test for stimulus and group differences in the P2, N2, EFP and LFP. Each component was analysed independently and was further divided between midline and bilateral analyses in the following mixed measures ANOVAs. For all ERP components, ANOVAs included *Stimuli* (ongoing-only, ongoing + $PM_{percept}$, ongoing + $PM_{concept}$) x *Group* (YA, OA, MCI) x *Cluster* as variables. Level in the *Cluster* variable varied depending on the component at midline clusters: P2 (frontal, central), N2 (parietal, occipital), EFP and LFP (frontal, central). At bilateral clusters the *Cluster* variable varied depending on the component: P2 (frontal, frontocentral, central), N2 (parietal, inferior parietal, occipital), EFP and LFP (frontal, frontocentral, central, frontotemporal). Separate ANOVAs were performed for the latencies and amplitudes

of the P2 and N2. Lower order ANOVAs were used to explore significant interactions. Post-hoc tests were used to determine significant differences and Bonferroni corrections were used to control for multiple comparisons (Cabin & Mitchel, 2000). Greenhouse-Geisser was used to correct for violations of sphericity.

7.3 Results

7.3.1 Behavioural results

The behavioural results are illustrated as an interaction plot in Figure 7.1. Mean reaction times and mean percentage of correct responses for each group and stimulus type are presented in Table 7.1.

7.3.1.1 Reaction time

There was a significant main effect of *Stimuli* ($F_{1.81,153.64} = 17.25$, $p < 0.001$, $\eta_p^2 = 0.17$), such that response to ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ were significantly slower relative to the ongoing-only responses ($p = 0.033$ & $p < 0.001$, respectively). The results also show that ongoing + $PM_{concept}$ responses were significantly slower than the ongoing + $PM_{percept}$ stimuli ($p < 0.001$). This suggests that participants experienced a reaction time PM interference effect, particularly for conceptual PM cues. There were no other significant effects for reaction time.

Table 7.1

Means and Standard Deviations for Reaction Time and Correct Response

Group	Reaction time (ms)			Correct responses (%)		
	Ongoing-only	**Ongoing+ $PM_{percept}$**	**Ongoing+ $PM_{concept}$**	**Ongoing-only**	**Ongoing+ $PM_{percept}$**	**Ongoing+ $PM_{concept}$**
YA	0.76 (0.12)	0.81 (0.11)	0.84 (0.12)	80.67 (10.63)	80.74 (13.68)	66.51 (10.36)
OA	0.77 (0.11)	0.78 (0.10)	0.80 (0.09)	78.38 (10.11)	76.34 (14.19)	67.85 (9.64)
MCI	0.86 (0.23)	0.86 (0.13)	0.88 (0.11)	64.98 (16.42)	64.19 (17.69)	60.23 (11.79)

Standard deviations are given in parentheses.

7.3.1.2 Correct responses

There was a significant effect of *Stimuli* ($F_{1.83,155.63} = 36.41$, $p < 0.001$, $\eta_p^2 = 0.30$), where participants correctly responded to fewer correct ongoing + $PM_{concept}$ stimuli relative to ongoing-only ($p < 0.001$) and ongoing + $PM_{percept}$ ($p < 0.001$). No significant differences were found between ongoing-only and ongoing + $PM_{percept}$ stimuli ($p > 0.05$). This suggests that for correct responses there was a PM interference effect only for conceptual PM stimuli. There was also a significant effect of *Group* ($F_{2,87} = 9.36$, $p < 0.001$, $\eta_p^2 = 0.18$), which was due to MCI making significantly fewer correct responses across all ongoing stimuli relative to OA ($p = 0.001$) and YA ($p < 0.001$). There was no interaction effect of *Stimuli* x *Group* ($p > 0.05$).

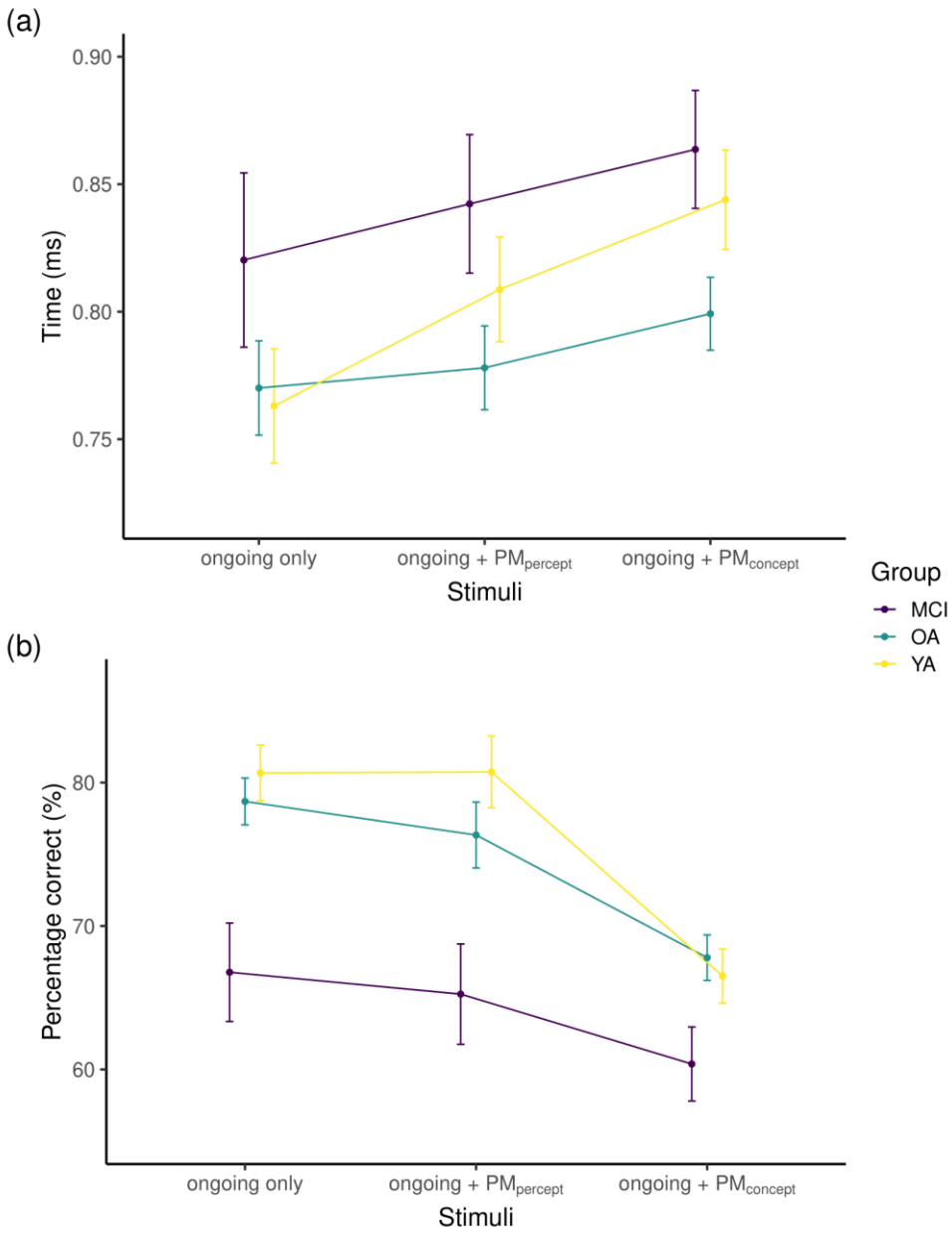

Figure 7.1. Interaction plots of reaction time and percentage of correct responses. (a) Reaction times for correct responses to the ongoing-only, ongoing + $PM_{percept}$ and the ongoing + $PM_{concept}$ stimuli for young adults (YA), healthy older adults (OA) and older adults with mild cognitive impairment (MCI). (b) Percentage of correct responses to the ongoing-only task, ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ stimuli for each group. Error bars represent standard error.

7.3.2 Electrophysiological results

7.3.2.1 P2

Grand average bilateral frontocentral ERPs are illustrated in Figure 7.2 and topographic maps of activity at 200ms are illustrated in Figure 7.3. Means and standard deviations for the P2 amplitudes and latencies for ongoing-only, ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ can be found in Appendix F, Table F.1 and Table F.2, respectively. A summary of all statistically significant effects are presented in Table 7.2.

7.3.2.1.1 Midline P2 amplitudes

There was a significant effect of *Stimuli* ($F_{2,174}$ = 6.66, p = 0.002, η_p^2 = 0.09), such that relative to ongoing-only stimuli, ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ had significantly lower amplitudes (p = 0.013 & p = 0.003, respectively). There was also a significant effect of *Cluster* ($F_{1,87}$ = 8.14, p = 0.006, η_p^2 = 0.10), where larger P2 amplitudes were found at frontal clusters relative to the central clusters. There were no other significant effects.

7.3.2.1.2 Lateral P2 amplitudes

Similar to midline clusters, there was a significant effect of *Stimuli* ($F_{2,174}$ = 8.66, p = 0.010, η_p^2 = 0.07), where P2 amplitudes were significantly larger for ongoing-only stimuli relative to ongoing + $PM_{percept}$ (p = 0.034) and ongoing + $PM_{concept}$ (p = 0.020).

There was a significant effect of *Cluster* ($F_{2.33,194.62}$ = 20.84, p < 0.001, η_p^2 = 0.25), where frontocentral clusters had greater amplitudes relative to frontal (p = 0.010) and central (p < 0.001) clusters and frontal had greater amplitudes relative to central (p < 0.001).

Additionally, there was a significant interaction effect of *Cluster* x *Group* ($F_{4.58,194.62}$ = 3.44, p = 0.003, η_p^2 = 0.10). The *Cluster* x *Group* interaction can be explained by a significant effect of *Group* at bilateral frontocentral clusters ($F_{2,87}$ = 4.03, p = 0.022, η_p^2 = 0.11), such that MCI had significantly smaller amplitudes relative to OA (p = 0.019)

and were trending towards smaller amplitudes relative to YA (p = 0.069). This can also be explained by a significant effect of *Cluster* for YA ($F_{2,52}$ = 30.44, p < 0.001, η_p^2 = 0.55), such that frontocentral clusters had significantly larger P2 amplitudes relative to frontal and central clusters (ps < 0.001). A *Cluster* effect was also found in OA ($F_{2,74}$ = 5.34, p = 0.021, η_p^2 = 0.17) and MCI ($F_{2,44}$ = 4.03, p = 0.022, η_p^2 = 0.11) where frontal clusters had significantly greater amplitudes than central clusters for OA (p = 0.006) and MCI participants (p = 0.002).

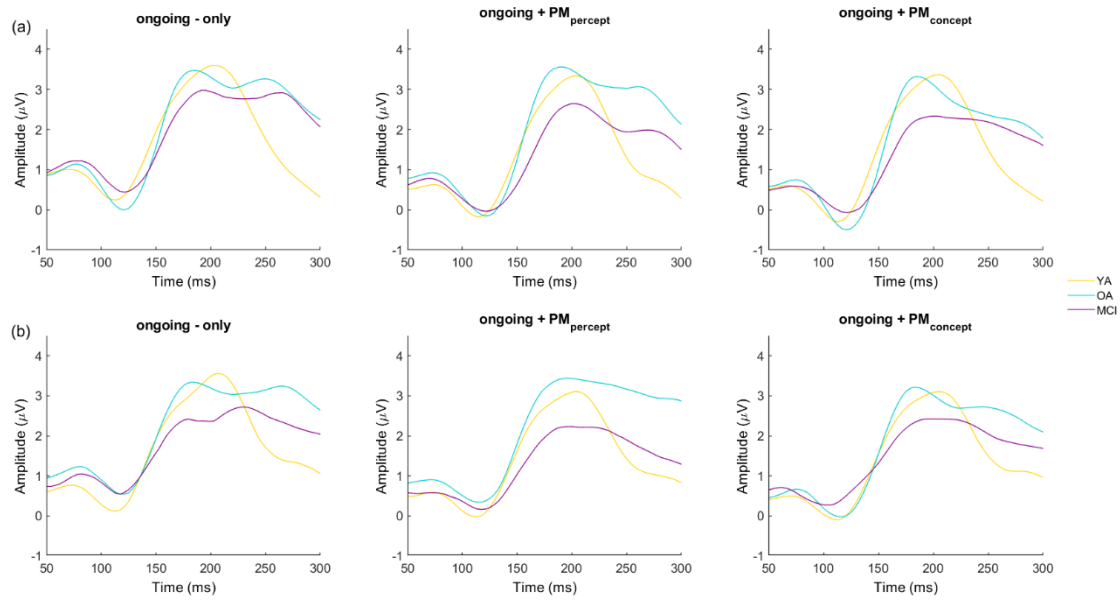

Figure 7.2. Grand-averaged ERP amplitudes for the P2 at frontocentral cluster for ongoing-only, ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$. (a) Left hemisphere; (b) right hemisphere for young adults (YA), healthy older adults (OA) and older adults with MCI (MCI).

7.3.2.1.3 Midline P2 Latencies

There were no significant effects of P2 latency at midline frontal and central clusters.

7.3.2.1.4 Lateral P2 Latencies

There was a significant effect of *Stimuli* ($F_{2,174}$ = 6.23, p = 0.030, η_p^2 = 0.08), which was due to a significant P2 delay for ongoing + $PM_{concept}$ relative to ongoing-only (p = 0.002).

There was also a significant effect of *Hemisphere,* where the right hemisphere was significantly delayed relative to the left ($F_{1,87} = 4.24$, $p = 0.043$, $\eta_p^2 = 0.06$).

Table 7.2

Summary of Significant Group Effects for P2 ERP Amplitudes and P2 ERP Latencies

Midline P2 ERP amplitude	**Lower**	**F-value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Stimuli		6.66	2,174	0.002	0.09	Ongoing-only > ongoing + $PM_{percept}$ & ongoing + $PM_{concept}$
Cluster		8.14	1,87	0.006	0.10	F > C
Lateral P2 ERP amplitude						
Stimuli		8.66	2,174	0.010	0.07	Ongoing-only > ongoing + $PM_{percept}$ & ongoing + $PM_{concept}$
Cluster		20.84	2.33,194.62	<0.001	0.25	FC > F > C
Cluster*Group		3.44	4.58,194.62	0.003	0.010	
	FC	4.03	2,87	0.022	0.11	OA > MCI | YA > MCI†
	YA	30.44	2,52	<0.001	0.55	FC > F & C
	OA	5.34	2,74	<0.001	0.17	F > C
	MCI	4.03	2,44	0.022	0.11	F > C
Lateral P2 latencies						
Stimuli		6.23	2,174	0.03	0.08	Ongoing-only < ongoing + $PM_{concept}$
Hemisphere		4.24	1,87	0.043	0.06	L < R

YA = young adults. OA = healthy older adults. MCI = Older adults with MCI. F = frontal, FC = frontocentral, C = central, R = right hemisphere. L = Left hemisphere. | = separator between post-hoc tests. *N.B.* '>' indicates amplitudes being more positive in this table. For latencies '<' indicates the component occurred earlier in time. † indicates a trending effect.

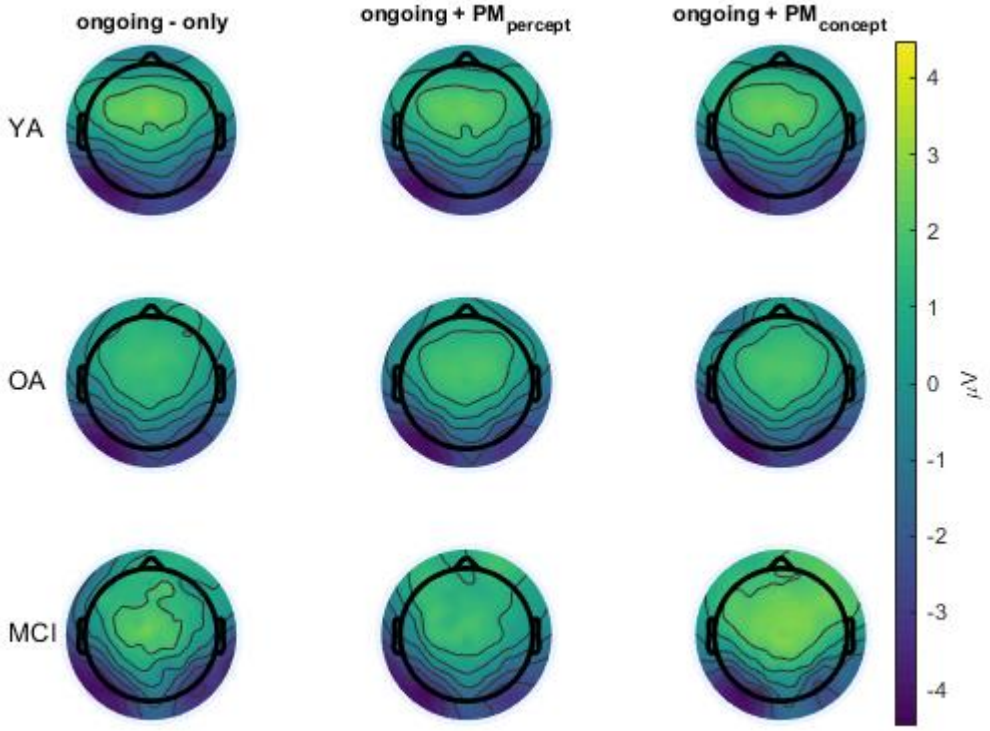

Figure 7.3. Topographic heatmaps of ERP activity at 200ms generated by ongoing-only, ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ in young adults (YA), older adults (OA) and older adults with mild cognitive impairment (MCI).

7.3.2.2 N2

All means and standard deviations for the N2 amplitudes for the ongoing-only, ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ stimuli can be found in Appendix F, Table F.3 and the latencies are presented in Table F.4. A summary of all statistically significant effects are presented in Table 7.3.

7.3.2.2.1 Midline N2 amplitudes

There was a significant effect of *Cluster* ($F_{1,87} = 122.86$, $p < 0.001$, $\eta_p^2 = 0.63$), such that there were more negative N2 amplitudes at occipital clusters relative to parietal ($p < 0.001$). There were no other significant effects.

7.3.2.2.2 Lateral N2 amplitudes

There was a significant effect of *Cluster* ($F_{1.70,115.41} = 109.82$, $p < 0.001$, $\eta_p^2 = 0.62$), which was due to significantly more negative N2 amplitudes for occipital compared to both inferior parietal and parietal clusters (*p*s < 0.001) and parietal clusters were significantly more negative than inferior parietal clusters ($p < 0.001$).

7.3.2.2.3 Midline N2 latencies

There were no significant effects at midline parietal and occipital clusters.

7.3.2.2.4 Lateral N2 latencies

There was a significant effect of *Stimuli* ($F_{2,174} = 18.32$, $p < 0.001$, $\eta_p^2 = 0.21$), where both $PM_{percept}$ and $PM_{concept}$ were significantly delayed relative to ongoing-only (both *p*s < 0.001). Additionally, there was a significant effect of *Cluster* ($F_{1.82,158.28} = 9.93$, $p < 0.001$, $\eta_p^2 = 0.13$), where bilateral inferior parietal and parietal clusters were delayed relative to occipital clusters (both *p*s < 0.001).

There was also a significant interaction of *Stimuli* x *Group* ($F_{4,174} = 3.59$, $p = 0.008$, $\eta_p^2 = 0.10$). This interaction is in part explained by a significant effect of *Group* in ongoing + $PM_{percept}$ stimuli ($F_{2,87} = 7.37$, $p = 0.001$, $\eta_p^2 = 0.15$), where YA generated an earlier N2 response relative to OA ($p < 0.001$). The MCI group, however, did not significantly differ from OA or YA for the ongoing + $PM_{percept}$ stimuli (*p*s > 0.05). The *Stimuli* x *Group* interaction can also be explained by a significant effect of *Stimuli* for OA ($F_{2,74} = 15.47$, $p < 0.001$, $\eta_p^2 = 0.35$), where ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ stimuli were significantly delayed relative to ongoing-only ($p < 0.001$ & $p < 0.009$, respectively) and can be explained by a significant effect of *Stimuli* for MCI ($F_{2,44} = 7.44$, $p = 0.003$, $\eta_p^2 = 0.36$), where ongoing + $PM_{concept}$ was significantly delayed relative to ongoing-only stimuli ($p = 0.018$).

There was a and a significant interaction effect of *Stimuli* x *Cluster* ($F_{3.21,279.43} = 4.51$, $p = 0.004$, $\eta_p^2 = 0.06$). This interaction was due to an effect of *Stimuli* at parietal ($F_{2,178} = 16.43$, $p < 0.001$, $\eta_p^2 = 0.19$) and inferior parietal clusters ($F_{2,174} = 6.85$, $p = 0.001$, $\eta_p^2 = 0.09$) where ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ stimuli were significantly

delayed relative to ongoing-only stimuli (parietal: *p*s < 0.001; inferior parietal: *p*s < 0.05).

Table 7.3

Summary of Significant Group Effects for N2 ERP Amplitudes and N2 ERP Latencies

Midline N2 ERP amplitude	**Lower**	**F-value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Cluster		112.86	1,87	<0.001	0.63	OC < P
Lateral N2 ERP amplitude						
Cluster		109.82	1.70,115.41	<0.001	0.62	OC < P < IP
Lateral N2 latencies						
Stimuli		18.32	2,174	<0.001	0.21	Ongoing-only < ongoing + $PM_{percept}$ & $PM_{concept}$
Cluster		9.93	1.82,158.28	<0.001	0.13	OC < IP & P
Stimuli*Group		3.59	4,174	0.008	0.10	
	ongoing + $PM_{percept}$	7.37	2,87	0.001	0.15	YA < OA
	OA	15.47	2,74	<0.001	0.35	Ongoing-only < ongoing + $PM_{percept}$ & ongoing + $PM_{concept}$
	MCI	7.44	2,44	0.003	0.36	Ongoing-only < ongoing + $PM_{concept}$
Stimuli*Cluster		4.51	3.21,279.43	0.004	0.06	
	P	16.43	2,174	<0.001	0.19	Ongoing-only < ongoing + $PM_{percept}$ & ongoing + $PM_{concept}$
	IP	6.85	2,174	0.001	0.09	Ongoing-only < ongoing + $PM_{percept}$ & ongoing + $PM_{concept}$

YA = young adults. OA = healthy older adults. MCI = Older adults with MCI. OC = occipital. IP = inferior parietal. P = parietal. | = separator between post-hoc tests. *N.B.* '<' indicates amplitudes being more negative in this table. For latencies '<' indicates the component occurred earlier in time.

7.3.2.3 Early frontal positivity (300–500ms)

All means and standard deviations for the amplitudes of the EFP in response to ongoing-only, ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ stimuli can be found in

Appendix F Table F.5. Grand average ERPs at bilateral frontal clusters for the EFP and LFP are illustrated in Figure 7.4. The topographic distribution of the ERP activity across the scalp at 300ms is illustrated in Figure 7.5. A summary of all statistically significant effects can be found in Table 7.4.

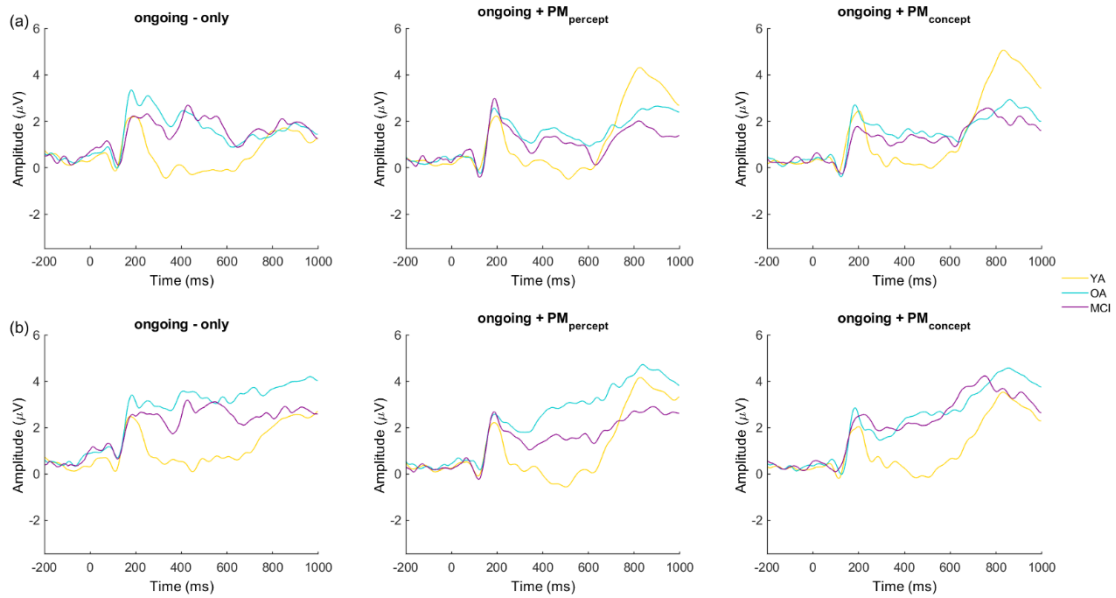

Figure 7.4. Grand average ERPs for the early frontal positivity (EFP) and late frontal positivity (LFP) for ongoing-only, ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$. (a) Left hemisphere; (b) right hemisphere for young adults (YA), healthy older adults (OA) and older adults with mild cognitive impairment (MCI).

7.3.2.3.1 Midline EFP amplitudes

There was a significant effect of *Stimuli* ($F_{2,174}$ = 7.66, p < 0.001, η_p^2 = 0.11) such that ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ had significantly lower amplitudes relative to the ongoing-only stimuli (p = 0.012 & p = 0.005, respectively). There was a significant effect of *Cluster* whereby amplitudes were larger at frontal compared to central clusters ($F_{1,87}$ = 9.66, p = 0.003, η_p^2 = 0.13). There were no other significant effects.

7.3.2.3.2 Lateral EFP amplitudes

There was a significant effect of *Stimuli* ($F_{2,174}$ = 7.11, p = 0.001, η_p^2 = 0.11) where relative to ongoing-only stimuli, lower amplitudes were found for ongoing + $PM_{percept}$ (p = 0.002) and ongoing + $PM_{concept}$ (p = 0.018). A significant effect of *Group* ($F_{2,87}$ = 5.22, p = 0.008, η_p^2 = 0.15) was explained by significantly greater amplitudes in OA relative to YA (p = 0.008). A significant effect of *Cluster* ($F_{2.18,191.82}$ = 16.27, p < 0.001, η_p^2 = 0.21), was due to significantly greater amplitudes at frontocentral clusters relative to all other clusters (ps < 0.001).

There was also a significant interaction of *Cluster* x *Group* ($F_{4.36,191.82}$ = 16.28, p < 0.001, η_p^2 = 0.35). This interaction can in part be explained by a significant effect of *Group* at the frontal clusters ($F_{2,87}$ = 22.05, p < 0.001, η_p^2 = 0.42) where both OA and MCI had significantly larger amplitudes than YA (ps < 0.001). The interaction is also due to a significant effect of *Cluster* for YA ($F_{1.84,54.12}$ = 52.88, p < 0.001, η_p^2 = 0.68) where frontocentral clusters had the greatest amplitude relative to all other clusters (ps < 0.001). There was no difference between central and frontotemporal clusters (p > 0.05) but both were significantly larger than frontal clusters (ps < 0.001). A significant effect of *Cluster* was also found for OA ($F_{2.31,87.77}$ = 8.67, p < 0.001, η_p^2 = 0.27), such that frontocentral clusters were significantly larger than central (p = 0.030) and frontotemporal (p < 0.001) clusters and frontal clusters were significantly larger than frontotemporal clusters (p = 0.023). A significant effect of *Cluster* for MCI ($F_{1.88,41.38}$ = 6.01, p = 0.021, η_p^2 = 0.33) was due to frontal clusters having larger amplitudes relative to central and frontotemporal clusters (ps = 0.005). There were no other significant effects.

Table 7.4

Summary of Significant Group Effects for EFP ERP Amplitudes

Midline EFP ERP amplitude	**Lower**	**F-value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Stimuli		7.66	2,174	<0.001	0.11	Ongoing-only > ongoing + $PM_{percept}$ & ongoing + $PM_{concept}$
Cluster		9.66	1,87	0.003	0.13	F > C
Lateral EFP ERP amplitude						
Stimuli		7.11	2,174	0.001	0.11	ongoing > ongoing + $PM_{percept}$ & $PM_{concept}$
Group		5.22	2,87	0.008	0.15	OA > YA
Cluster		16.27	2.18,191.82	<0.001	0.21	FC > F, FC, C & FT
Cluster*Group		16.28	4.36,191.82	<0.001	0.35	
	F	22.05	2,87	<0.001	0.42	OA & MCI > YA
	YA	52.88	1.84,54.12	<0.001	0.68	FT > C = FT > F
	OA	8.67	2.31,87.77	<0.001	0.27	FC > C & FT | F > FT
	MCI	6.01	1.88,41.38	0.021	0.33	F > C & FT

YA = young adults. OA = healthy older adults. MCI = Older adults with MCI. F = frontal, FC = frontocentral, C = central, FT = frontotemporal. | = separator between post-hoc tests. *N.B.* '>' indicates amplitudes being more positive in this table.

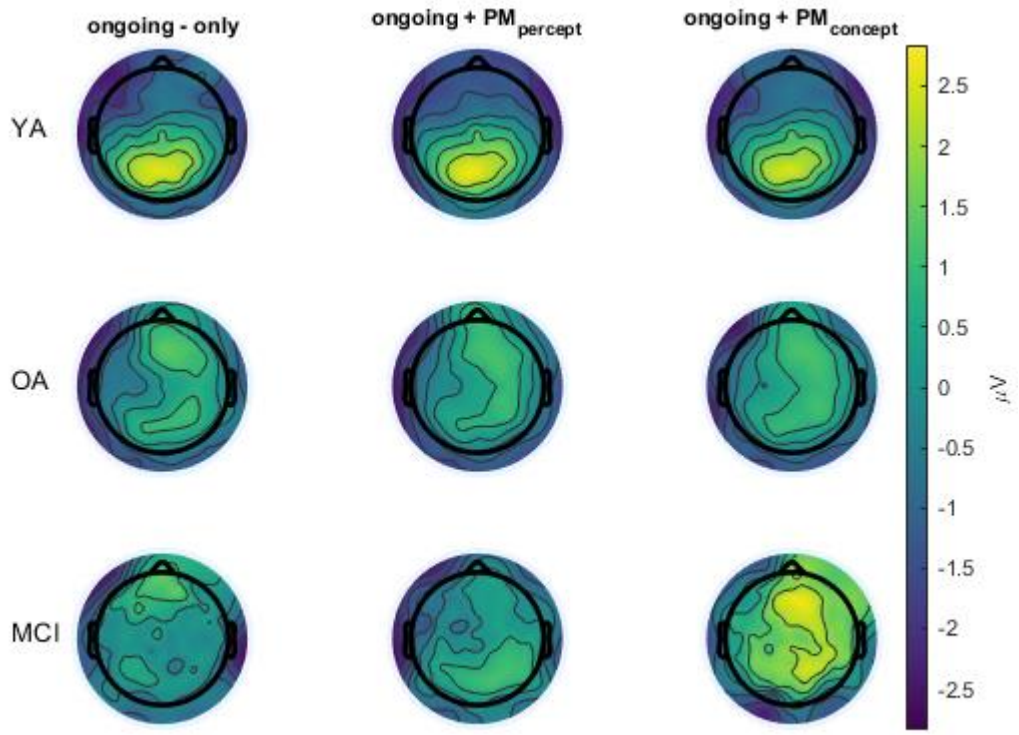

Figure 7.5. Topographic heatmaps of the early frontal positivity (EFP) ERP component generated by ongoing-only, ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ in young adults (YA), older adults (OA) and older adults with mild cognitive impairment (MCI).

7.3.2.4 Late frontal positivity (600–1000ms)

All means and standard deviations for LFP amplitudes and latencies can be found in Appendix F, Table F.6 for responses to ongoing-only, ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ stimuli. The topographic distribution of ERP activity at 900ms is displayed in Figure 7.6. A summary of all statistically significant effects are presented in Table 7.5.

7.3.2.4.1 Midline late frontal positivity amplitude

There was a significant effect of *Group* ($F_{1,87} = 4.25$, $p = 0.018$, $\eta_p^2 = 0.10$), such that OA had significantly greater amplitudes relative to YA. There was also significant effect of *Cluster* ($F_{1,87} = 10.05$, $p = 0.002$, $\eta_p^2 = 0.09$) where central clusters had greater amplitudes than frontal clusters.

There was also a significant interaction of *Cluster* x *Group* ($F_{2,87}$ = 3.43, p = 0.038, η_p^2 = 0.09). This interaction was due to a significant effect of *Group* at the frontal cluster ($F_{2,87}$ = 6.66, p = 0.002, η_p^2 = 0.15) where OA demonstrated more positive amplitudes than YA (p = 0.001). Activity of MCI participants was intermediate of OA and YA, but amplitudes did not statistically differ from either group (ps > 0.05). Additionally, YA demonstrated larger amplitudes at central relative to frontal clusters ($F_{1,27}$ = 23.32, p < 0.001, η_p^2 = 0.46).

7.3.2.3.2 Lateral late frontal positivity amplitude

There was a significant effect of *Hemisphere* where the right was greater than the left in all groups ($F_{1,87}$ = 25.16, p < 0.001, η_p^2 = 0.26). There was a significant three-way *Stimuli* x *Cluster* x *Group* interaction ($F_{12,522}$ = 2.05, p = 0.019, η_p^2 = 0.06). The three-way interaction in part can be explained a *Stimuli* x *Cluster* interaction for YA ($F_{3.56,99.79}$ = 3.78, p = 0.010, η_p^2 = 0.12), such that in central clusters ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ had significantly lower amplitudes than the ongoing-only stimuli (p = 0.024 & p = 0.015, respectively). Additionally, the significant *Stimuli* x *Cluster* for YA can be explained by significantly larger positive amplitudes in frontal clusters for ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ relative to all other clusters (ps < 0.014).

The three-way interaction can also be explained by a significant *Cluster* x *Group* interaction for ongoing + $PM_{percept}$ stimuli ($F_{4.33,188.37}$ = 2.72, p = 0.030, η_p^2 = 0.06), where frontal clusters were significantly more positive than all other clusters in YA (ps < 0.01); In OA, frontal clusters were larger than central (p = 0.029) and frontotemporal clusters (p < 0.001), and frontocentral were larger than frontotemporal (p < 0.001). No amplitude differences were found in MCI (ps > 0.05).

Table 7.5

Summary of Significant Group Effects for LFP ERP Amplitudes

Midline LFP ERP amplitude	**Lower**	**F-value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Group		4.25	1,87	0.018	0.10	OA > YA
Cluster		10.05	1,87	0.002	0.09	C > F
Cluster*Group		3.43	2,87	0.038	0.09	
	F	6.66	2,87	0.002	0.15	OA > YA
	YA	23.32	1,27	<0.001	0.46	C > F
Lateral LFP ERP amplitude						
Hemisphere		25.16	1,87	<0.001	0.26	R > L
Stimuli*Cluster* Group		2.05	12,522	0.019	0.06	
Stimuli*Cluster	YA	3.78	56,99.79	0.010	0.12	C: ongoing-only > ongoing + $PM_{percept}$ & ongoing + $PM_{concept}$ | ongoing + $PM_{percept}$: F > all other clusters | ongoing + $PM_{concept}$: F > all other clusters
Cluster*Group	Ongoing + $PM_{percept}$	2.72	4.33,188.37	0.030	0.06	YA: F > all other clusters | OA: F > C & FT, FC > FT

YA = young adults. OA = healthy older adults. MCI = Older adults with MCI. F = frontal, FC = frontocentral, C = central, FT = frontotemporal. | = separator between post-hoc tests. *N.B.* '>' indicates amplitudes being more positive in this table.

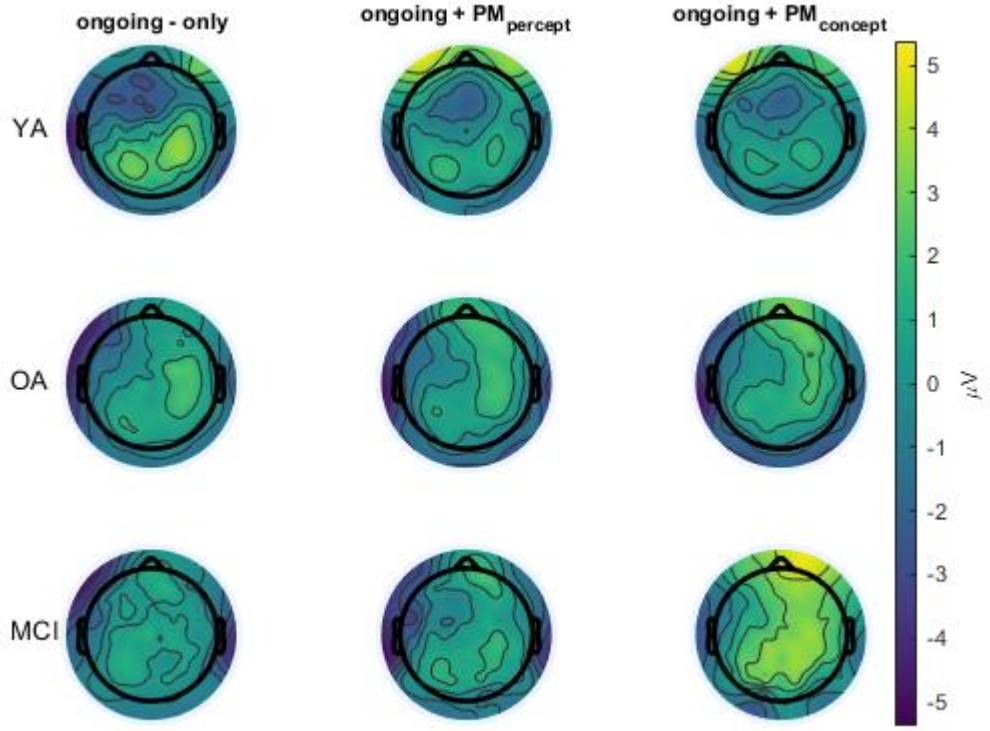

Figure 7.6. Topographic heatmaps of the late frontal positivity (LFP) ERP component generated by ongoing-only, ongoing + $PM_{percept}$ and ongoing + $PM_{concept}$ in young adults (YA), older adults (OA) and older adults with mild cognitive impairment (MCI).

7.4 Discussion

The current study investigated the effect of PM monitoring on an ongoing working memory task in younger adults, older adults and older adults with MCI. The PM interference effect was evaluated through behavioural and electrophysiological data using two forms of PM, which varied in their salience and were embedded within an *n*-back lexical decision task. A comparison between performance in the ongoing tasks when monitoring for the perceptual and conceptual PM cues was also made. In sum, the results demonstrate that across all ongoing working memory stimuli, participants with MCI made fewer correct responses. Additionally, reaction times to ongoing stimuli increased for all groups with the addition of a PM task and was even further increased when the cue was conceptual. Moreover, monitoring for conceptual PM cues resulted in fewer correct responses but perceptual cues did not reduce the number of correct ongoing responses. Frontocentral P2 amplitudes were reduced in older adults

with MCI relative to healthy older adults across all ongoing stimuli. Larger sustained frontal amplitudes were found for older adults with and without MCI compared to younger adults in the early frontal positivity (300–500ms) but the later frontal positivity (600–1000ms) was only greater for healthy older adults relative to younger adults. Healthy older adults demonstrated delayed N2 ERPs to ongoing stimuli when monitoring for both perceptual and conceptual PM cues relative to the ongoing-only stimuli. Older adults with MCI also demonstrated a delayed N2 ERP but only when monitoring for conceptual PM cues relative to ongoing-only stimuli.

7.4.1 Behavioural performance

The behavioural results of the current study confirm a PM interference effect on the ongoing task when monitoring for PM cues. Both perceptual and conceptual PM cues affected the reaction times of the ongoing task. Presumably, this is due to participants taking additional time to process the features of the target through the allocation of added attention processes towards the PM component (Marsh & Hicks, 1998). Moreover, across all participant groups, the monitoring for conceptual PM stimuli caused a significant decrease in the number of correct ongoing responses. The results here add further support to the preparatory attentional processes and memory processes theory (PAM) and the Multiprocess Framework, such that responses to PM cues indeed require preparatory attentional processes to successfully perform a PM intention (Guynn, 2003; McDaniel & Einstein, 2000). While ongoing task reaction times were affected when monitoring for both types of PM cues, the conceptual PM cue had a disproportional effect. The increased ongoing task reaction times when monitoring for conceptual PM cues partially supports the previous results of Cruz et al. (2016), who found that conceptual PM cues increased the reaction times to unrelated ongoing task responses. However, the reaction times to related items in Cruz and colleagues' study, which are similar to the ongoing task stimuli in the current study, were unaffected. It is possible that a reaction time increase was only found for the unrelated stimuli in Cruz et al. (2016) because unrelated stimuli required slightly more processing than if the words were related, as evidenced through increased reaction times for unrelated stimuli across all conditions. Thus, unrelated items may have made the effect more apparent through the additional involvement of cognitive processes.

The results here are in contrast with those reported by Cousens et al. (2015), who found increased reaction times when participants were monitoring for perceptual relative to non-perceptual PM cues. The differences between Cousens and colleagues' results and the current results might be explained by differences in the perceptual PM cue. Within the Cousens et al. study, the perceptual PM intention was to press a button if the two simultaneously presented words were the same colour. However, as their PM cue was not processed as part of the ongoing task (a lexical decision task between the two words), it is considered non-focal (i.e., the perceptual features of the PM cue are not processed as part of the lexical decision task). Scullin et al. (2010) investigated the impact of perceptual non-focal and conceptual semantic focal PM cues within an ongoing lexical decision task. Their results found the non-focal PM cues had a greater interference effect on the ongoing task reaction times. Within the current study, however, although the perceptual PM cue may be considered non-focal, the PM cue is highly salient. Thus, it is likely that the focality is less important than the saliency of the cue as indicated by the faster ongoing task reaction times when monitoring for the highly salient non-focal perceptual PM cues compared to the monitoring for the less salient focal PM cues.

The behavioural results from the current study support the hypothesis that older adults with MCI will have poorer performance across all ongoing tasks. Despite all groups demonstrating a reduction in accuracy when monitoring for conceptual PM cues, older adults with MCI were not disproportionally impaired as expected. The lack of increased impairment when monitoring for conceptual PM cues contrasts with previous conclusions made by Costa et al. (2015) who reported that individuals with MCI were disproportionally more impaired in those tasks requiring a higher degree of effortful monitoring. However, Costa et al. (2015) assessed effortful monitoring with time-based PM, which may require a greater amount of monitoring compared to a conceptual PM cue that contains a large amount of perceptual information (Khan et al., 2008). The results here suggest that monitoring for a conceptual event-based cue did not tax the cognitive processes sufficiently to further impact the ongoing working memory performance in older adults with MCI. Alternatively, the cognitive processes in participants with MCI may have already been considerably affected with the addition of PM cues and struggled with any PM task, which therefore did not further affect their performance. The reduction in the number of correct responses in older adults with MCI may reflect lexico-semantic processing deficits (Duong et al., 2006).

Semantic impairments are one of the earliest features of cognitive decline in neurodegenerative diseases such as AD (Joubert et al., 2010; Libon et al., 2013; R. S. Wilson et al., 2011). Although episodic memory impairments are the prevailing characteristic of MCI (Moscoso et al., 2019), deficits are also readily found in semantic memory (Adlam et al., 2006; Ally, 2012; Kirchberg et al., 2012; Verma & Howard, 2012). Possibly the results here suggest a general reduction in the ability to rapidly access semantic information stored in memory when performing a lexical decision task in those with MCI.

7.4.2 P2 modulations in MCI and ageing

The electrophysiological results of the current study demonstrate significant differences between younger adults, healthy older adults and older adults experiencing MCI. Most notably, across all ongoing stimuli, older adults with MCI had lower P2 amplitudes at frontocentral clusters relative to older adults. A frontocentral P2 amplitude reduction is in line with previous research MCI (B.-Y. Li et al., 2016; Waninger et al., 2018). However, the precise function of the P2 is yet to be understood, one line of reasoning proposes a relationship to rapid semantic processing (Irak, Soylu, & Turan, 2019; Paynter et al., 2009) and a peri-perceptual sense of familiarity and knowing (Z. G. Doborjeh, Kasabov, et al., 2018; Irak, Soylu, & Turan, 2019; Irak, Soylu, Turan, et al., 2019). The previous chapter similarly found reduced frontocentral P2 amplitudes in older adults MCI when responding to PM stimuli. The current study further supports a feature recognition processing deficit conclusion as the amplitude reduction was consistent across stimuli and not impacted by the inclusion of PM monitoring. Evidence of recognition memory of faces in MCI (Schefter et al., 2013) similarly found P2 amplitude attenuations in older adults with MCI. Schefter and colleagues concluded that the P2 is reflective of impairments in early facial recognition systems, similar to other studies of the P2 amplitudes (Caharel et al., 2002; Halit et al., 2000). However, the P2 may be more reflective of a general early recognition system which would conflate the findings of feelings of knowing, familiarity, early semantic processing, and recognition. This neurophysiological conclusion could potentially explain the psychometric evidence finding impaired recognition abilities in those with

MCI (Bennett et al., 2006), although further research is necessary to determine this relationship of the P2 as a general marker of early recognition.

The differences in neural activity in the P2 provides some insights into the distribution of activity between the different groups. The topographic maps for younger adults appear to show very localised activity in frontocentral scalp regions. The older adults demonstrate more dispersed activity, which appears to be further distributed in older adults with MCI. Greater activation in older adults compared to younger adults is frequently attributed to compensatory processes (Grady, 2012), although cross-section study designs do not usually enable an ability to answer whether the increased activation is compensatory (Grady, 2008). Following a compensatory mechanism line of reasoning, the dispersed topographic distribution at 200ms for the healthy older adults and older adults with MCI may be representative of neuronal dedifferentiation and the distributed activity of overlapping neuronal sources (Koen & Rugg, 2019). The greater distributed activity in older adults with MCI may also reflect compensatory mechanisms which are an attempt to compensate their working memory performance with the recruitment of additional areas. Previous studies have demonstrated that older adults who show dedifferentiation will outperform older adults who do not demonstrate this distribution of activity (Dennis & Cabeza, 2011; Rieckmann et al., 2010). Indeed, the current study shows that young adults had maximal amplitudes at frontocentral clusters, yet the healthy older adults show similar levels of activation across frontal and frontocentral clusters coupled with the absence of behavioural performance declines. This perhaps offers support for neural dedifferentiation as the spatial localisation has blurred and incorporated frontal sources in the older adult groups. However, it may also be argued that the frontal processes are being recruited to facilitate supporting functions of early processes. Cabeza and Dennis (2012) explain that in the absence of decreased behavioural performance, additional recruitment of brain areas reflects the reorganisations of brain networks to facilitate compensatory processes as a result of age-related declines. It might be assumed then that without the over recruitment of brain sources as a compensatory mechanism the older adults would exhibit poorer performance in the ongoing working memory tasks (Zarahn et al., 2007).

7.4.3 Anterior PM monitoring modulations

The current study supports the previous literature showing sustained modulations at anterior scalp clusters when monitoring for PM cues between 300–500ms (Cona et al., 2012b; Czernochowski et al., 2012; Mattli et al., 2011). However, these past studies have shown increased positive modulations when monitoring for PM cues, yet the current study identifies more negative amplitudes at the anterior scalp clusters when monitoring for PM cues as opposed to no monitoring. A recent study by Hering and colleagues (2020) explored age-related differences in PM and also found negative anteriorly sustained amplitudes in the ongoing stimuli when monitoring for PM cues in the younger adults. The authors concluded that similar to previous studies, the amplitude modulation represented memory-specific sustained activity indicative of the PM readiness mode proposed by Guynn (2003). In contrast to other studies (Cona et al., 2014; Hering et al., 2020), the current results here did not find further amplitude modulations when monitoring for a PM intention that theoretically required a greater degree of monitoring (i.e., the conceptual PM cue). The lack of further amplitude modulation, therefore, suggests that high and low salient PM stimuli require comparable frontal resources to maintain the PM intention in mind. The comparable level of modulatory activity between the PM cues subsequently does not support theories of spontaneous PM retrieval (Scullin, Einstein & McDaniel, 2009), such that the high saliency PM cue required the same attentional maintenance processes to maintain the PM intention.

The sustained activity at anterior scalp clusters differed between younger and older adults, such that older adults had more positive sustained amplitudes than the younger adults. Amplitude modulations during prospective monitoring have previously been reported within the literature (Hering et al., 2020; Schnitzspahn et al., 2016; Zöllig et al., 2007). Hering and colleagues (2020) found that older adults had more positive amplitudes between 400–900ms relative to younger adults. Here, the current study further differentiates this effect, showing that both healthy older and older adults with MCI had more positive amplitudes at bilateral frontal clusters relative to younger adults between 300–500ms and at the midline frontal cluster between 600–1000ms. This suggests possible neurophysiological dysregulation in the underlying cortical regions during intention maintenance. The Gateway Hypothesis of PM (Burgess et al., 2007; 2011) proposes that the deactivation of the medial aPFC reflects the

disengagement from stimulus-orientated attending to the maintenance of an intention. Therefore, the results here suggest that older adults may have difficulty in modulating the attentional balance between external ongoing stimuli and the internal PM intention. Evidence from a recent fMRI study of PM in ageing (Gonneaud et al., 2017) has demonstrated that older adults are impaired in their ability to deactivate the aPFC during PM monitoring. However, caution should always be taken when concluding underlying cortical activity in EEG. The current study does however offer further temporal acuity to the neurophysiological differences of PM monitoring in ageing.

Alternatively, the neurophysiological differences in the anterior scalp clusters between the younger and older adults may reflect age-related changes in memory processes. A prevailing idea within the fMRI literature is the posterior-to-anterior shift in ageing (PASA; Davis et al., 2008; D. C. Park & Reuter-Lorenz, 2009). This theory states that the additional recruitment often shown in the PFC during cognitive performance contributes to the retention of the cognitive function due to deterioration of posterior brain regions. Within the framework of the PASA theory, the greater positive amplitudes found here in the older adult groups, shows general compensatory mechanisms to perform the ongoing working memory task. Studies using ERP analyses have similarly shown that the P3 also exhibits a shift towards anterior brain regions as individuals age, reportedly helping cognitive function (Kopp et al., 2014; Reuter et al., 2016; van Dinteren et al., 2014). However, fMRI and ERP studies have provided contrary evidence to the PASA theory (Morcom & Henson, 2018; Tays et al., 2011). Morcom and Henson (2018) performed two large fMRI experiments on long-term memory encoding and short-term memory maintenance in younger and older adults to test the PASA theory. Their results show that while older adults do indeed increase prefrontal activation, the results do not find that the increased PFC activity is related to better performance. The authors conclude that increased PFC activation reflects less specific or less efficient activity in older adults. Considering the mixed evidence for increased prefrontal activity in older adults, interpretation of the current study's results remains open. Future neurophysiological studies should seek to address whether the increased activity reflects better performance in PM monitoring and the ongoing working memory tasks.

7.4.4 Age-related differences in N2 PM monitoring

Age-related differences were found for N2 latencies when monitoring for PM cues. When monitoring for perceptual PM cues older adults generated an N2 response later than the younger adults. Additionally, when monitoring for both PM cue types older adults' N2 responses were significantly delayed relative to the ongoing task. A similar effect was also found for older adults with MCI but only when monitoring for conceptual PM cues. A previous study of PM monitoring suggests that the N2 is related to the activity of feature-based attention (Czernochowski et al., 2012). Under this assumption, the current study's results suggest that feature-based attention is slowed in the aged population. Furthermore previous research has linked the N2 to classification and stimulus identification (Patel & Azzam, 2005). Therefore, within the current study, the N2 may represent feature-based attention to match/mismatch processes between the stimulus and the PM intention currently held in memory (Folstein & Van Petten, 2008). The results here then, suggest that the evaluation of whether a stimulus is a PM cue or not may be affected in older adults and takes the brain a longer amount of time to complete, possibly due to slowed cognitive processing speeds (Gajewski et al., 2008; Polich & Criado, 2006). While older adults had delayed N2 responses when monitoring for PM stimuli, the older adults were only delayed relative to the young adults when monitoring for perceptual PM stimuli. Potentially, the semantic nature of the conceptual PM stimuli enabled faster access to memory. Müller and Hagoort (2006) demonstrated that words of living things (e.g., animal words) were responded to faster than non-living words. Moreover, Amsel et al. (2013) show that the N2 responses are produced earlier for living compared to non-living words. Therefore, the lack of an N2 delay in older adults may show that the ability to rapidly access information about animal words is unaffected and therefore enables the differentiation of the ongoing stimuli from PM stimuli at a similar speed found in the younger adult group.

7.4.5 PM monitoring and P2 uncertainty

The latency and amplitude of the P2 ERP offer important insights into the neurophysiological impact of monitoring for PM cues on working memory. The current study shows that across all participants the ongoing-only stimuli produce a larger P2 amplitude than ongoing stimuli when monitoring for PM cues. Considering the evidence linking P2 amplitude increases with a feeling of knowing (Irak, Soylu, & Turan, 2019; Irak, Soylu, Turan, et al., 2019b), a reduction in the P2 may reflect a feeling of not knowing or uncertainty. Indeed, evidence has shown that in conditions of uncertainty P2 amplitudes are reduced (Lin et al., 2017; Tanovic et al., 2018). Therefore, the results here may indicate an increased feeling of uncertainty during the early evaluation of the ongoing task when participants are monitoring for PM cues. The increased reaction time in response to ongoing stimuli when monitoring for conceptual PM cues along with the delayed latency of the P2 response compared to the ongoing-only stimuli may represent decreased certainty in the evaluation of the stimulus. However, this remains to be confirmed. Future studies could explore this by evaluating participant reports of certainty and feelings of knowing within an experimental PM framework.

7.4.6 Limitations

The behavioural and neurophysiological evidence of the current study suggests that perceptual and conceptual PM cues both rely on continued monitoring of PM stimuli within the ongoing task. However, the current study's design may have limited the participant's ability to disengage from maintaining the PM cue within working memory networks due to the frequency of which the PM cue was presented. Potentially, the PM cues may have been spontaneously recalled if there was a longer duration between cues or by greater engagement of the working task demands. The ERP modulations related to monitoring may not have been found. However, increased duration between PM cues would have increased the length of the study, which may have affected the ERP amplitudes due to participant fatigue (Boksem et al., 2005). Decreasing the number of PM ERP events would have negatively affected the signal-to-noise ratio of ERPs (Luck, 2005; Thigpen et al., 2017). Potentially, the ongoing task difficulty could have been modified, although the study was designed to not cognitively

overload individuals with MCI, which would have reduced their performance in the PM task (Costa et al., 2011) and reduced the number of chances to record PM related brain activity. The balance between intention maintenance and engagement of working memory was not explored within this chapter, but future research should explore neurophysiological differences in older adults and those with MCI with different durations between PM cues.

7.4.7 Future Research

Research has shown that both healthy older adults and older adults with MCI demonstrate greater PM performance decrements in time-based memory compared to event-based memory (Costa et al., 2015; Einstein et al., 1995; D. C. Park et al., 1997). Jäger & Kliegel (2008) have shown that compared to younger adults, older adults have more pronounced ongoing task impairments in time-based than event-based PM. Cona and colleagues (2012) found that when monitoring for PM cues, prefrontal activity in older adults was reduced relative to the younger adults. To date, no other studies have explored the neurophysiology of PM monitoring in older adults with MCI. It would be expected, given the greater performance declines found in time-based PM in older adults with MCI, that greater modulations over anterior regions would be found compared to when monitoring for event-based PM cues. Therefore, future research should explore time-based PM interference within the ongoing stimuli in older adults with MCI.

While the current study has provided initial steps towards understanding PM monitoring differences in older adults with MCI in the frontal cortices, a deeper understanding is still required. In tasks requiring effortful monitoring, it is speculated that the MTL plays an important role in understanding the behavioural deficits in MCI (McFarland & Glisky, 2009). Therefore, neuroimaging methods such as fMRI stand to uncover considerable amounts of knowledge about the neurophysiology of PM monitoring in older adults with MCI. Moreover, the author encourages the use of functional connectivity analyses to discover the relationships of patterns of activity across the cortex to understanding typical and atypical ageing in PM.

7.4.8 Summary

The current chapter is the first to examine the neurophysiological effects of monitoring for PM cues on the ongoing working memory task in older adults with MCI. The results support the presence of a PM interference effect in the ongoing task when monitoring for a highly salient perceptual cue and a less salient conceptual cue. The results support the PAM and Multiprocess Framework theories of PM, such that both PM cues required additional attentional processes for monitoring. The study also shows that monitoring for conceptual PM cues required greater attentional processes compared to the perceptual cue as indicated by poorer ongoing task performance when monitoring for conceptual PM stimuli.

The results here show that participants with MCI made fewer correct responses and had reduced frontocentral P2 amplitudes across all stimulus types relative to younger and older adults. Taken together, the results suggest that older adults with MCI have impairments in feature recognition processing networks and in feelings of knowing and familiarity, as indicated by P2 amplitude reductions. However, this remains to be confirmed as the neurophysiological underpinning of the P2 are yet to be determined.

Finally, the current study shows significant frontal activity differences between younger and older adults in responses to the ongoing stimuli. Sustained positive amplitudes exhibited by the older adults were believed to reflect difficulties of balancing attention between internally held PM intentions and the ongoing task. However, the increased frontal amplitudes may reflect compensatory mechanisms employed by the older adults to successfully perform the ongoing task. Additionally, the older adults demonstrated delayed posterior N2 latencies, potentially indicating a slowing of feature-based attention mechanisms of stimulus identification between ongoing and PM stimuli.

Chapter Eight: Spatiotemporal ERP dynamics of prospective memory in ageing and mild cognitive impairment

8.0 Overview

The previous chapters have explored the neurophysiological differences in PM intention maintenance (Chapter 7) and intention retrieval (Chapter 6) between young adults, older adults and older adults experiencing MCI. The current chapter attempts to address some of the limitations of ERP analyses by using a SNN architecture to model the spatiotemporal dynamics across the entire scalp. Using the classification functionality of SNNs, this chapter explores whether brain activity in response to a PM task provides better classification accuracy than the ongoing working memory task. The current chapter applies a network analysis to the learnt patterns of activity from the SNN to understand connectivity differences between each of the groups.

8.1 Introduction

Little is known about the neurophysiology of PM in healthy older adults and older adults experiencing MCI. In Chapter 6, the neurophysiology of PM was explored in older adults (in typically ageing and MCI samples). In Chapter 7, the neurophysiological basis of PM monitoring was examined in typically ageing and participants with MCI. In both chapters, older adults with MCI were found to have smaller frontocentral P2 amplitudes relative to healthy older adults. Additionally, both older adult groups demonstrated reduced amplitudes of components related to PM intention retrieval (IRR) and had aberrant sustained frontal amplitudes when monitoring for PM cues. While these studies have provided important insights into the neurophysiology of PM in relation to typical and atypical ageing, much of the spatial and temporal information is not examined. The current study, therefore, aims to use a novel AI approach (outlined in *Chapter 3, section 3.8*) to model the spatiotemporal

dynamics of working memory and PM in young adults, healthy older adults and older adults with MCI.

Neurocognitive research has particularly implicated the aPFC in PM functioning. Evidence from both fMRI (McDaniel & Einstein, 2011; Peira et al., 2016) and ERP studies (Cona et al., 2012b; Mattli et al., 2011; West et al., 2005) have demonstrated the importance of the aPFC in PM encoding, maintenance and retrieval. Concerning PM intention retrieval, cortical areas such as the insula, PCC and MTL are of particular importance (Cona et al., 2015; *see Chapter 2, section 2.3.4*). Moreover, these areas, and connections between them, are found to be impaired in older adults with MCI (Mak et al., 2014; Mufson et al., 2012; Stephan et al., 2012). PM tasks, therefore, may present a potential sensitive indicator of early cognitive decline in older adults (Blanco-Campal et al., 2009).

Studies analysing ERPs have demonstrated reduced amplitudes in older adults relative to younger adults during PM tasks (Hering et al., 2020; West, Herndon, et al., 2003; Zöllig et al., 2007, 2010). The N300 ERP, related to cue detection and the allocation of attention processes and the parietal positivity, related to the retrieval and processing of PM cues, have both been shown to be reduced in older adult populations (Mattli et al., 2011; West, Herndon, et al., 2003; West & Covell, 2001; Zöllig et al., 2007). However, these amplitude reductions are not consistently demonstrated. Some studies report no amplitude differences between younger and healthy older adults (West et al., 2003). Chapter 6 shows that older adults demonstrated increased PM cue detection related ERPs. While an absence of amplitude differences may suggest that systems involved with PM remain unaffected by ageing, the increased amplitudes may reflect different neural mechanisms used by young and older adults when completing PM tasks (Zöllig et al., 2010). Chapter 6 of the current thesis revealed that poorer PM performance in older adults experiencing MCI may be due to deficits in early frontocentral processing and the ability to reorient attention processes in frontotemporal networks.

Studies of the neurophysiology of PM in ageing and MCI have provided important initial insights into the nature of cognitive decline, however, a great deal of spatial and temporal information is not explicitly captured when individual electrodes are compared between groups. It is understood that there are co-occurrences of the N300 over the posterior regions and the frontal positivity in anterior cortices (West, 2011), yet we do not understand the spatiotemporal functional connectivity across the

cortex. Furthermore, we do not understand how the functional connectivity changes as we age or alter from cognitive decline in PM. To date, no research has explored the spatiotemporal networks of neural systems underlying PM in ageing and MCI. Most extant analytical techniques create models by separately processing the spatial and temporal information. Considering this knowledge, the current study proposes a novel computational framework to build models and extract new knowledge of PM and working memory in ageing and MCI.

The computational models of the PM data proposed in this research are based on one of the most promising trends of ANN, called SNN (*see Chapter 3, Section 3.8*). SNN models have been developed as neurobiologically-inspired computational architecture that incorporates both spatial and temporal characteristics of data into the computation. They are considered a suitable tool for the analysis of the spatiotemporal data, where both space and time components are crucial to the development of the model (Kasabov et al., 2013).

The application of SNNs to dimensionally high, spatiotemporal data has proved to be an effective way of modelling and extracting knowledge from a variety of data sets which possess time and space qualities (Kasabov, 2019). Previous studies have proven the efficacy of SNN modelling in fMRI (M. G. Doborjeh et al., 2014; Kasabov, Zhou, et al., 2016), EEG resting-state (Capecci et al., 2016) and ERP data (Doborjeh, Kasabov, Doborjeh & Sumich, 2018).

8.1.2 Aims and hypotheses

This current study aims to build on the SNN methodologies for modelling the spatiotemporal dynamics of ERP data. The study proposes new approaches for modelling, learning, visualising and extracting knowledge from ERP data relating to working memory, PM and cognitive decline. The study aims to explore and further understand the spatiotemporal and functional differences between younger adults, older adults and older adults experiencing MCI. Through the ML functionality of SNNs, the current study also aims to evaluate the efficacy of using PM as an earlier indicator of cognitive decline in older adults. For the most part, classification studies of MCI have used resting-state EEG data (review: Yang et al., 2019). However, little research has evaluated the ability to classify brain activity of individuals with and without MCI

when performing those tasks most relevant to their diagnosis, namely, memory. It has been proposed that evaluating cognitive aspects of memory may be more effective than using resting-state or structural MRI data for classification of individuals with MCI (Farina et al., 2020). Therefore, by comparing the neurocognitive functioning of individuals performing working memory and PM tasks the current study will determine which of these aspects of cognition is more effective in differentiating between the groups. It would be expected that given PM is one of the first cognitive complaints of those who go on to develop MCI, one would expect to find greater classification accuracy for PM stimuli. The current study is broken down into two experiments: firstly, working memory and responses to PM stimuli will be modelled and classification accuracy will be evaluated; secondly, using statistical methods new knowledge will be extracted from the SNN models.

To this end, the current study hypothesises that: 1) there will be differences in visualised SNNs between young adults, older adults and older adults with MCI. 2) SNNs will provide better classification accuracy between the groups when modelling responses to PM stimuli relative to working memory stimuli and 3) SNNs will have superior classification accuracy compared to traditional ML methods. 4) There will be differences in local and global connectivity between young and older adults, and older adults with MCI will have decreased levels of connectivity at the local and global level.

8.2 General Methods

8.2.1 Participants

Participants descriptions are detailed in Chapter 6, Section 6.2.1 for older adults and in Chapter 5, Section 5.2.2 for younger adults.

8.2.2 Procedure

Core methodology has been documented in Chapter 5, Section 5.2.3.

8.2.3 Electrophysiological data acquisition

Data acquisition has been documented in Chapter 5, Section 5.2.6.

8.2.4 Electrophysiological data analysis

The core methods used for data preprocessing can be found in Chapter 5, Section 5.2.8.

The current study will use the ERPs related to the correct responses to the ongoing working memory stimuli (1-back$_{target}$), perceptual PM stimuli (PM$_{percept}$) and conceptual PM stimuli (PM$_{concept}$). The methods for Experiment 1 and 2 are detailed in Section 8.2.5 and 8.3.1, respectively.

8.2.5 Experiment 1 Methods: Spiking Neural Networks

8.2.5.1 SNN computational architecture for modelling and visualising working memory and prospective memory activity between groups

The proposed SNN architecture is an evolving spatiotemporal data machine (eSTDM) modelled on neuromorphic, brain-inspired SNN processing concepts (Kasabov, Scott, et al., 2016). It is designed to map brain data into a 3D brain space of spiking ANs while preserving the topological information of the recorded brain activity. Principally, this architecture draws its inspiration from the biological rules (e.g., SW connectivity and LIFM), which govern memory and learning dynamics of neurons exhibited within the brain.

Each AN within the SNN behaves as an information-processing unit. It learns from the temporal data that is propagated through it, adapting and memorising the patterns of activity by influencing the interconnected neurons within the network. Akin to the brain, SNNs incorporate time into their computation and thus are superior in biological plausibility compared to previous NNs that do not account for temporal dynamics. The architecture to be employed possesses several different modules based on the evolving SNN framework (Kasabov, 2014). As illustrated in Figure 8.1, the modules consist of: an input-encoder module (Figure 8.1d), where data is encoded into spike-trains and the spatiotemporal variables are mapped into input neurons that transfer

the spike-trains to the SNN model; a 3D SNN module (Figure 8.1e), where the characteristics of space and time are recorded and learnt in an unsupervised mode; a visualisation module (Figure 8.1f), where captured spatiotemporal connectivity of the brain can be visualised; a SNN classification module, where the spatiotemporal patterns from the 3D SNN module are classified or used to predict an output (Figure 8.1g); an optimisation module (Figure 8.1h), to fine-tune the parameters of the system; a pruner module (Figure 8.1i) where inactive ANs are removed and only functional ANs (ANs that emitted spikes during the unsupervised learning) and neural connections are retained for further analysis. The following steps detail the methods applied in this study:

1. The temporal data are encoded into sequences of spikes using the threshold-based representation algorithm (Petro et al., 2019).

2. A 3D SNN model of LIFM ANs is created, where the spatial mapping of the ANs is defined using the Talairach brain template (Talairach & Tournoux, 1988).

3. The EEG channels are mapped as input ANs to their corresponding location in the Talairach template.

4. The mapped SNN model is initialised, where ANs are connected using the SW connectivity proposed in Braitenberg and Schüz, (2013), and Bullmore and Sporns (2009), which is inspired by the neural connectivity in the brain.

5. The initialised SNN model is trained with the encoded spike sequences from ERP data, entering via the input ANs. The learning rule is the unsupervised STDP (S. Song et al., 2000) that changes the weight of the connection between every pair of connected ANs. During this process, the SNN model learns from the temporal information and forms pathways that can be interpreted, which the SNN will use to classify new information.

6. The spike sequences of the EEG data are again propagated through the SNN for supervised learning related to the classification tasks. Output ANs are created for each sample (i.e., one output AN for each participant). Each output AN is connected to all ANs of the 3D SNN model.

7. The deSNN algorithm is applied for supervised learning (Kasabov et al., 2013) and adapts the connections between the 3D SNN model and the output ANs.

8. For the classification of a new temporal data, steps 6 and 7 are repeated. Then, the data are classified by applying the K-nearest neighbours algorithm using the K nearest (similar) output ANs created during step 6 to the new output neuron.

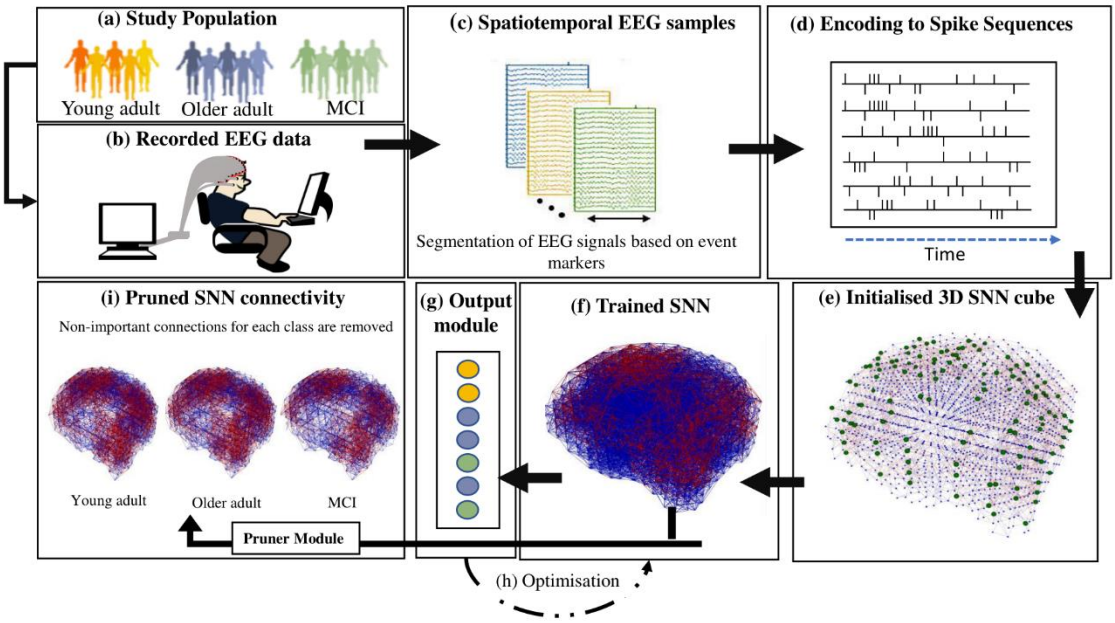

Figure 8.1. Proposed Spiking Neural Network Architecture for prospective memory ERP analysis. ERP data collection across the three participants groups: (a) younger, healthy older and older adults with mild cognitive impairment. (b) recording of the data during the experimental working and prospective memory tasks. (c) ERP data is extracted and cleaned. (d) cleaned ERP data is transformed into spike-trains. (e) spike-trains for each EEG channel are propagated into a 3D space of artificial neurons. (f) trained SNN can visualised. (g) output neurons are created and represent the final classification of the data. (h) a grid search method is used to find optimal parameter settings for classifying between the participant groups (i) pruner module removes all connections which did not change for each group to create sparse models for each participant group and are visualised.

8.2.5.2 Input ERP data encoding in the SNN model

The pre-processed and baseline corrected ERP data were firstly ordered into a temporal sequence of real-value vectors. These vectors were then encoded into a series of discrete spike-trains using a threshold-based representation method (TBR), demonstrated to be able to construct large scale networks with arbitrary, configurable synaptic connectivity (Indiveri et al., 2015). This algorithm is employed to identify relevant changes in the ERP signal thus reducing noise. If the value of change in the signal surpasses a predefined threshold value, then a spike is encoded. Upward and

downward changes in the ERP data are interpreted as positive or negative (1 or -1) spikes. Bi-directional algorithms like this are well suited to EEG data due to their sensitivity to significant changes within gradient signal changes.

8.2.5.3 SNN initialisation, mapping, learning, classification and visualisation

Following the encoding of the ERP signal to spike-trains, a 3D SNN structure was created that can map the functional and structural characteristics of the data from which it is recorded. To this end, Talairach coordinates (Talairach, 1988) were used to map the 128 EEG channels to the 3D SNN model (visualised as the green ANs in Figure 8.1(e)). These coordinates define the position of the spiking ANs in a brain-like SNN model and the position of the EEG electrodes (Giacometti et al., 2014) as the input ANs. Each neuron in the network then represents one cm^3 of the human brain and the entire network consists of 1471 neurons (Koessler et al., 2009).

A LIF architecture was used to model the ANs (Knight, 1972). The SNN was initialised according to a biologically plausible model of SW connectivity (Liao et al., 2017), where neurons that are topographically closer possess stronger interconnectedness and therefore capture patterns of interest from the model. Following completion of the unsupervised learning, a deSNN algorithm (Kasabov et al., 2013) was used to train an output classifier in a supervised learning method. A RO learning rule (Thorpe & Gautrais, 1998) was applied to initialise the connection weights and then the STDP rule (S. Song et al., 2000) was used to adjust these weights according to the spikes that follow the initial spikes to the postsynaptic AN. The STDP accounts for the timing of pre and postsynaptic action potentials causing automatic adjustments to be made to the synaptic strengths and sensitivity of the postsynaptic ANs and consequently captures the spatiotemporal dynamics of the input data. Two other important variables for the classifier module are *mod* and *drift*. Each training sample provided to the model is associated with an output AN, which is connected to all the other ANs in the 3D SNN and the connection weights are initially set to zero. The weights of these output ANs change as a function of the RO learning rule, which itself is calculated by the order of incoming spikes (*mod*) from different connections. The earlier a spike arrives in the output AN from 3D SNN, the greater its importance in increasing the

corresponding connection weights. In terms of ERP data, it is useful to think of this as where the greatest amount of emphasis is placed within the ERP (i.e., toward to start or the end of the ERP). These newly formed connection weights will then increase or decrease according to the following number of spikes (*drift*) when the next spikes arrive at the AN over time.

8.2.5.4 Experimental framework

To extract the learnt patterns of activity of the SNN models, computational experiments are performed for each of the memory tasks and their class (i.e., participant group). Each class contains *n* samples which are used to train the SNN model and is validated through a 10-fold cross-validation to assess the accuracy of the model. This procedure randomly shuffles the data before splitting into 10 groups. One of these groups is held-out while the remaining nine groups are used to train the data. The fitted model of the training data is then tested on the held-out group and the accuracy of the model is retrained. The model is then discarded and the training and testing procedure is performed on all other groups. The final accuracy of the model is then averaged to give an overall accuracy score. Once the best model was found then it is possible to extract the individual contributions of each of the network classes over different periods of time. After training, those ANs that did not emit a spike were identified and removed (pruned) along with their connections.

8.2.6 Experiment 1 Results

8.2.6.1 ERP data modelling using the SNN Architecture

To explore the differences in cognition between YA, OA and MCI, an SNN architecture used for modelling, learning, classification and visualisation of EEG data related to different memory tasks (1-back$_{target}$, PM$_{percept}$ and PM$_{concept}$). A SW connectivity radius of 2.5 units (distance between two consecutive neurons) was used for the SNN model, which has previously demonstrated its effectiveness for ERP modelling using SNN (Doborjeh, et al., 2018). The SW connectivity rule allows the network the potential to form neuronal connections two ANs away in each of the x, y, z directions of the coordinate space. Small random weights are applied to each neuron (-0.1, +0.1).

In previous studies modelling EEG data with SNNs, an 80/20 positive–negative initial connection weight ratio has been applied (Capecci et al. 2016; Doborjeh et al., 2018). This ratio of inhibitory neurons is reflective of the 20–30% of inhibitory, GABAergic neurons found in the mammalian brain and is demonstrated as an optimal percentage for maximising the learning of a NN (Capano et al., 2015; Sultan & Shi, 2018). However, initial results demonstrated that this ratio was not optimal for modelling the current data. Figure 8.1 illustrates the trained network for the 80/20 positive–negative ratio (a) and the 50/50 positive–negative ratio (b). The results show a greater amount of model learning for the 50/50 ratio as evidenced by the greater amount of connection changes from the initial connections. Therefore, a model containing 50% inhibitory connections demonstrated a better level of discrimination between the classes and was subsequently used for modelling the ERP data.

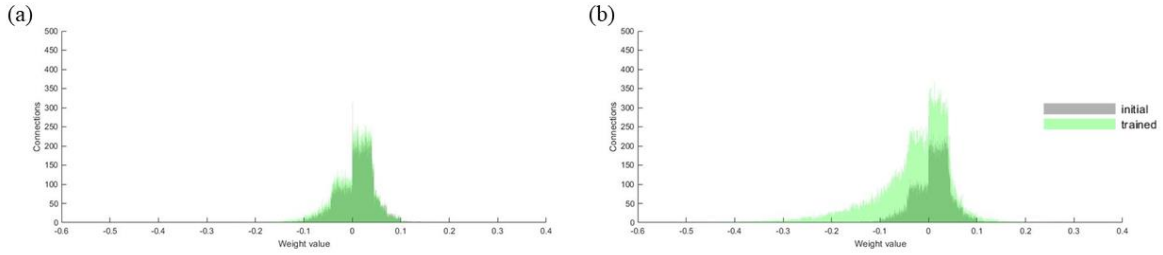

Figure 8.2. The number of connections and the connection weights in the SNN models for the 80/20 positive to negative neuron ratio model (a) and the 50/50 positive to negative neuron ratio model (b).

Similar to a biological neuron, when the simulated LIF AN receives spikes over time, its membrane potential increases until it reaches a pre-defined threshold. When the AN fires and emits an output spike, it cannot produce a new spike within a refractory period and its membrane potential is said to leak. The membrane potential can have certain leakage between spikes, which is defined by a leak parameter. The training of the SNN model requires EEG signals to be transformed into a spike-train of binary positive and negative spikes (-1 or 1; Figure 8.3). These spikes reflect the changes in amplitude of the EEG signal and are created based on an encoding algorithm. A bi-directional TBR (Petro, Kasabov & Kiss, 2019), was applied to all the EEG channel signal's gradient relative to the time series. The neural connections in the initialised

SNN model were later modified during an unsupervised learning process with the input spikes streaming to the SNN model via the input ANs.

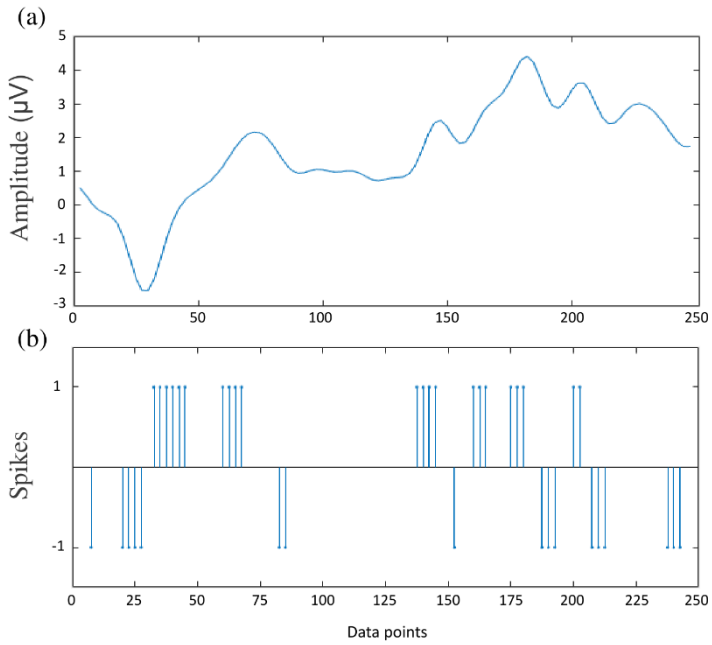

Figure 8.3. Example of how an event-related potential encoded into a spike-train. (a) Event-related potential taken from one participant (electrode Cz) in response to a conceptual prospective memory stimulus. (b) Event-related potential encoded into a binary spike-train using the TBR algorithm.

The model was then trained using these spikes-trains in an unsupervised mode employing a STDP learning rule (S. Song et al., 2000). The application of this algorithm allows spiking ANs to learn successive temporal relationships between data points from the data across and within EEG channels. These connections in the model architecture can be analysed and used to draw new understanding of the data. Figure 8.4 shows the final SNN following the creation of neuronal connections created during STDP learning, which reflect the dynamic patterns of connectivity.

When the supervised learning process is completed, the connection weights between the output ANs and the 3D SNN model are established. Then in the validation phase, the new ERP samples which were excluded from the learning phases are used to test the model. For every new testing ERP sample, an output testing AN is evolved and connected to the already trained SNN model and its connections are modified while the ERP sample is passed to the SNN model. Then for classification of this testing AN a K-nearest neighbour (KNN) algorithm was used, where the newly formed testing AN connection vector is compared with the existing output ANs' connections and the top

k similar output ANs (referring to the top similar ERP samples) identify the class label of this testing AN (ERP sample). This procedure is repeated for all the testing samples, one by one, through creating different output testing samples and classifying them.

A grid search method was used in the current study for fine-tuning a combination of parameters and reducing the classification error. Each parameter was searched within a range, specified by a minimum and maximum, through 5 iterations. A 10–fold cross-validation was used to validate the results. Therefore, for every model creation, 78,125 iterations of training (using 9 folds of samples except the holdout fold) and testing (using the holdout fold) were performed with different combinations of these parameters. The parameters that resulted in the best accuracy have been reported as the optimal parameters:

- The threshold for firing was set to 0.5, the refractory times was set to 5 and the LIF neuron model was set to 0.005.
- The STDP rate of the unsupervised learning algorithm was set to 0.002 for positive synaptic modifications and 0.003 for negative connections.
- The *mod* parameter was set to 0.4 and the positive and negative *drift* was set to 0.002, 0.004, respectively.
- The KNN was set to 13 nearest neighbours.

Table 8.1

Classification Results of the ERP Samples Across the Three Class Groups.

SNN-based methodology (1-back$_{target}$)					
ERP data classes	YA	OA	MCI	Accuracy (%)	Total Accuracy (%)
YA	**8**	0	0	**100**	
OA	2	**9**	0	**81.82**	**73.94**
MCI	0	3	**2**	**40**	
Traditional Machine Learning Methods					
Methods		MLP	SVM		MLR
Accuracy (%)		49.94	50.29		46.98
SNN-based methodology (PM$_{percept}$)					
ERP data classes	YA	OA	MCI	Accuracy (%)	Total accuracy (%)
YA	**8**	0	0	**100**	
OA	0	**9**	1	**90**	**83.33**
MCI	0	2	**3**	**60**	
Traditional Machine Learning Methods					
Methods		MLP	SVM		MLR
Accuracy (%)		62.07	47.28		50.29
SNN-based methodology (PM$_{concept}$)					
ERP data classes	YA	OA	MCI	Accuracy (%)	Total accuracy (%)
YA	**8**	0	0	100	
OA	1	**8**	1	80	**80**
MCI	0	2	**3**	60	
Traditional Machine Learning Methods					
Methods		MLP	SVM		MLR
Accuracy (%)		50.8	44.52		51.08

Younger adults (YA), healthy older adults (OA) and older adults with MCI (MCI) for each of the stimulus types: working memory (1-back$_{target}$), perceptual prospective memory (PM$_{percept}$) and conceptual prospective memory (PM$_{concept}$). The classification method was a 10–fold cross validation. The number of correctly classified samples in each class are located in the diagonal of the confusion table and highlighted in bold. The classification accuracy of the SNN-based models was compared against traditional methods: support vector machine (SVM), multilayer perceptron (MLP) and multilinear regression (MLR).

The optimisation procedure finds the best performing model for each of the SNN models. Table 8.1 presents the final test-fold of the best performing model (i.e., the held-out fold). Each of the SNN models was compared against other machine learning methods. At each memory stimulus type, the SNN model outperformed the other methods. Additionally, the results show that the PM$_{percept}$ and PM$_{concept}$ SNN models were better at classifying brain activity of the groups (83.33% and 80%, respectively) compared to the 1-back$_{target}$ models (73.94%). It is also seen that with the use of ERP data, YA are well discriminated from the other two groups, while the ERPs of OA and MCI overlap to a certain degree.

From the trained 3D SNN networks we can begin to see the patterns of connectivity emerge. All three of the models appear to share similar characteristics, where inhibitory connections (shown in red in Figure 8.4) are strongest over mid frontocentral and parietooccipital regions. However, over these areas the SNN trained using PM$_{percept}$ stimuli, appears to be generating a greater amount of these inhibitory connections.

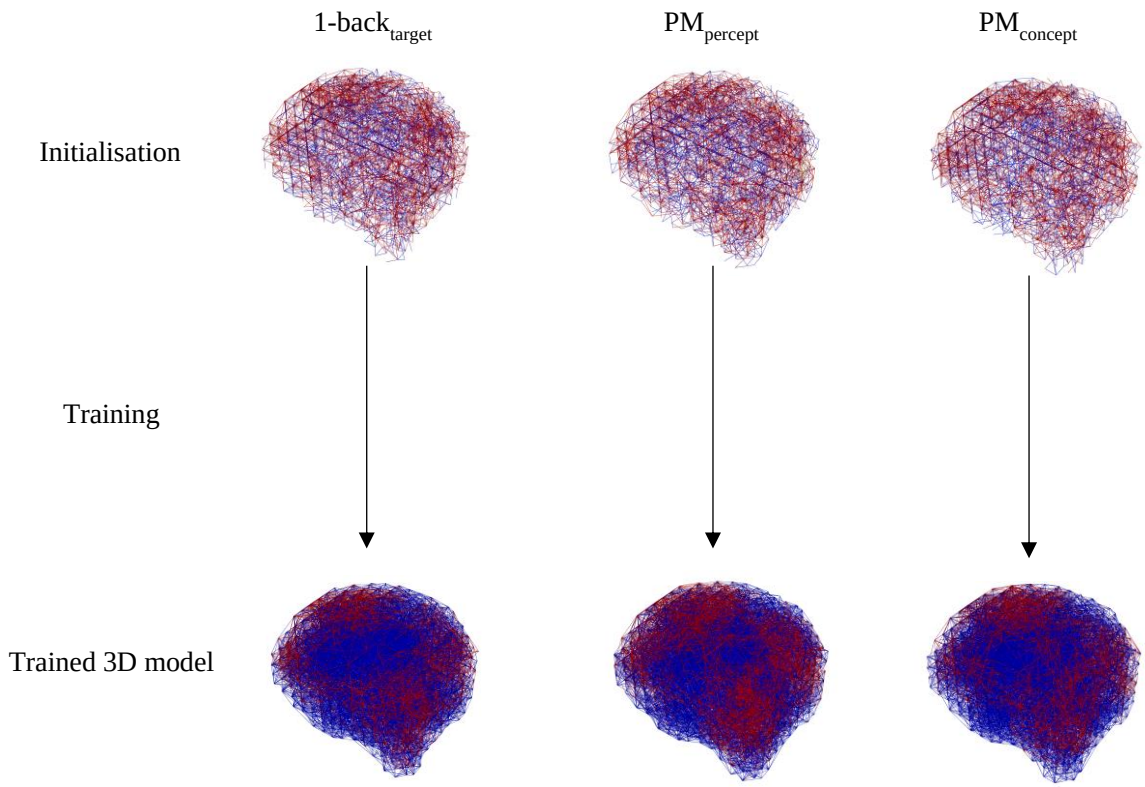

Figure 8.4. The learnt patterns of activity from the initialised SNN models. The top SNN models show the initialisation of random connections. The bottom SNN models show the learnt patterns of spatiotemporal activity for each of the different stimuli.

To understand within-group differences, the training samples were separated by propagating only the information for that class (i.e., YA, OA or MCI) through newly created networks that kept the same initialised network and parameter settings attained during the supervised learning stage. By using the same initialised connections and only allowing the EEG data from one group to make changes to the network, different patterns of connectivity for each group can be learnt. Thus, three separated SNN models were trained with each of the classes. The initialised SNN models were modified during the STDP learning that adapted the spatiotemporal connections. After the training, those neural connections that had not changed for each model were considered inactive and were pruned from the network.

The removal of inactive ANs enables the creation of a fine-tuned, sparser networks (LeCun et al., 1990) showing only the most important connections for the pre-trained class, enabling better visualisation of the differences between the groups. This step was performed across three different time periods to reveal the neural connections across time. The first time period was selected as 200–400ms to capture the early

cognitive processes associated with cue detection and monitoring (West & Wymbs, 2004). The second time epoch was 400–800ms, which encapsulates the later processing of stimuli and is related to deeper contextual and memory processes (West, 2011). Finally, the full epoch was propagated through the network for each class to understand the learnt connections across the entire data range. The pruned networks can be visualised for each stimulus type in Figure 8.5 for the 1-back$_{target}$, Figure 8.6 for PM$_{percept}$ and Figure 8.7 for PM$_{concept}$.

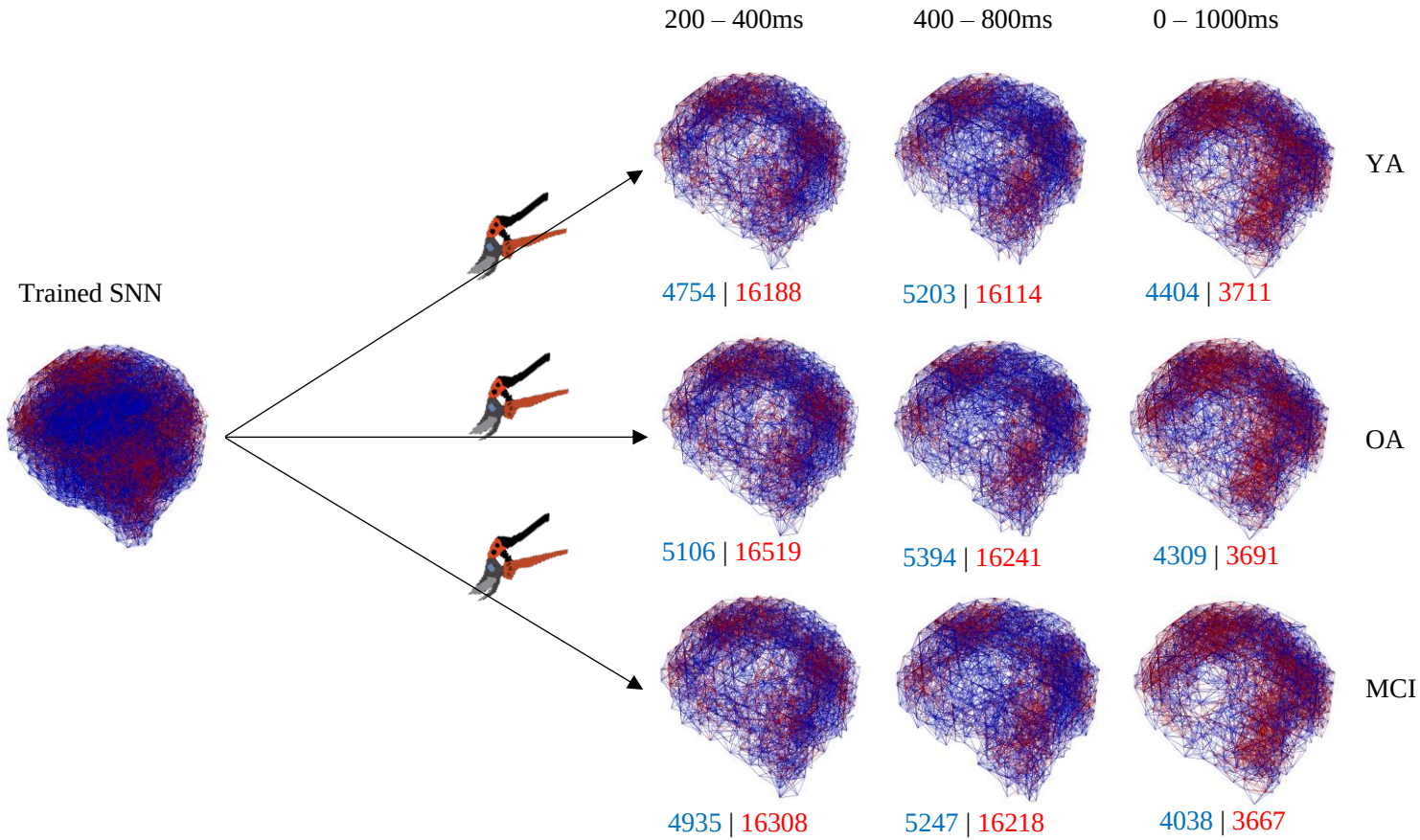

Figure 8.5. 1-back$_{target}$ SNN following pruning at 200–400ms, 400–800ms and 0–1000ms for each of the three classes: younger adults (YA), healthy older adults (OA) and older adults with MCI (MCI). Positive connections are displayed in blue, and inhibitory connections are displayed in red. The amount of positive-negative connections is shown under each pruned model.

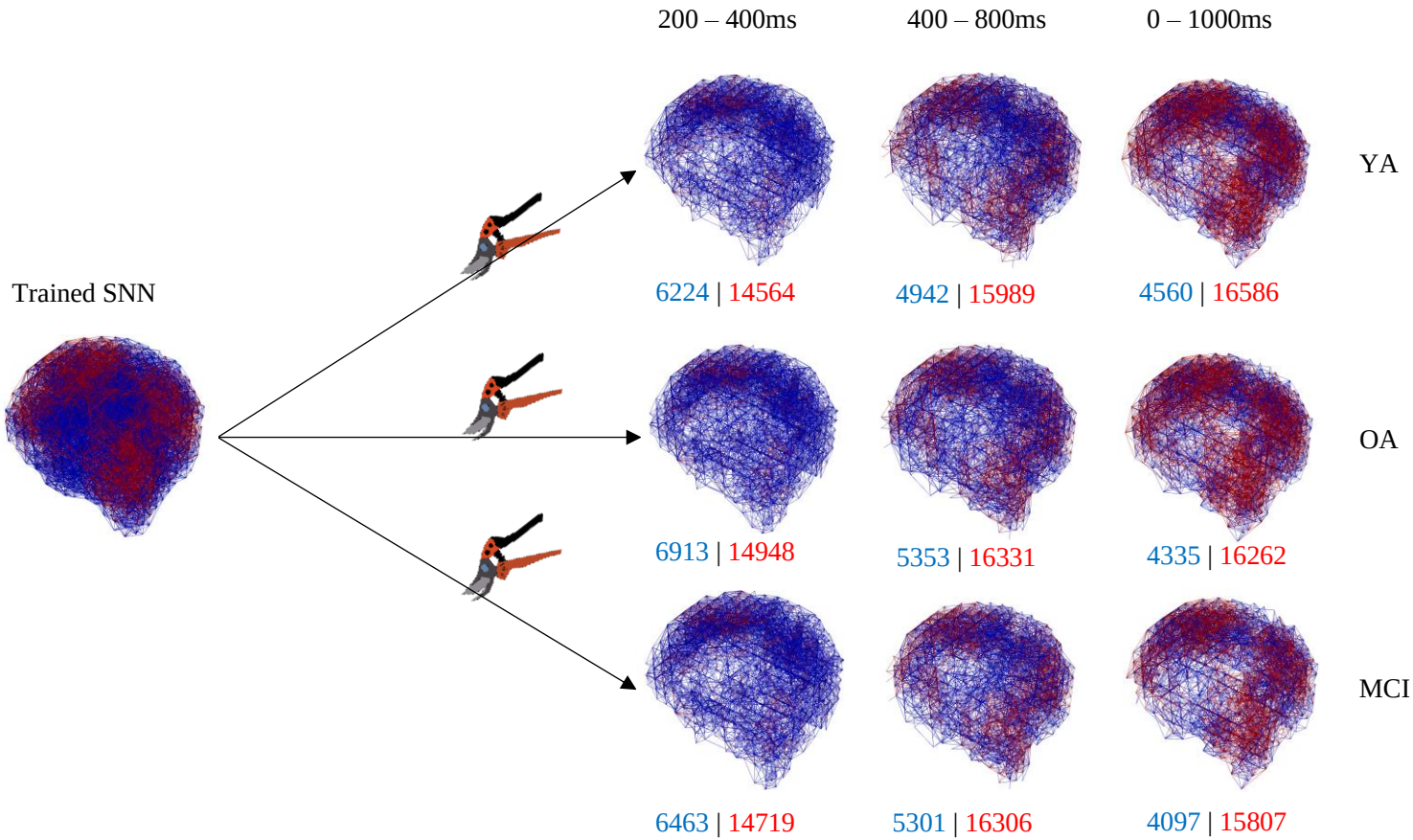

Figure 8.6. $PM_{percept}$ SNN following pruning at 200–400ms, 400–800ms and 0–1000ms for each of the three classes: younger adults (YA), healthy older adults (OA) and older adults with MCI (MCI). Positive connections are displayed in blue, and inhibitory connections are displayed in red. The amount of positive-negative connections is shown under each pruned model.

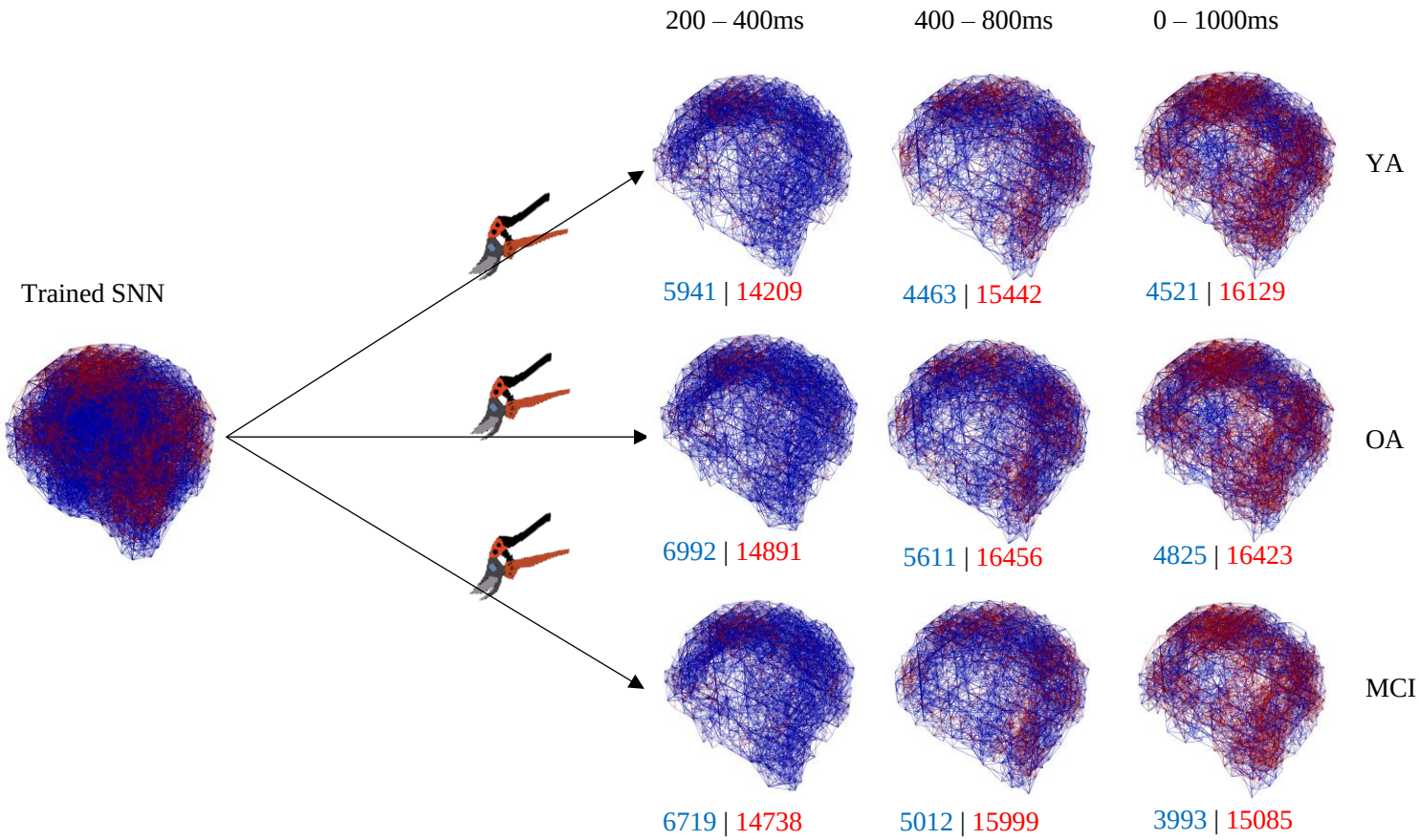

Figure 8.7. $PM_{concept}$ SNN following pruning at 200–400ms, 400–800ms and 0–1000ms for each of the three classes: younger adults (YA), healthy older adults (OA) and older adults with MCI (MCI). Positive connections are displayed in blue, and inhibitory connections are displayed in red. The amount of positive-negative connections is shown under each pruned model.

From Figure 8.5, it is apparent there are similar patterns of activity occurring for each of the defined time periods across the groups. However, it is difficult to see how the network is differentiating between the classes at both the 200–400ms and 400–800ms time range. Differences appear to be more prominent when the whole 0–1000ms epoch is pruned for each of the classes. This may suggest that information outside of the 200–800ms epoch is important in understanding ageing and cognitive decline. In particular, differences between OA and MCI appears to be substantial in the 0–1000ms $PM_{concept}$ model. There are fewer positive and negative connections for the MCI group. Interestingly, the pruning method appears to have removed many ANs in the left frontotemporal region for the 0–1000ms model in the MCI group in each of the models, implying relatively little spatiotemporal activity for the 1-back_{target} during the ongoing working memory task.

Additionally, for PM stimuli across the wider epoch (0–1000ms), MCI demonstrated fewer positive and inhibitory connections relative to OA and YA. In the $PM_{percept}$ stimuli, these inhibitory connections are spread more globally across the 3D SNN for healthy groups (YA, OA), but within the MCI group the inhibitory connections are restricted to occipitoparietal, frontocentral and frontal regions. It appears inhibitory connections are spread in a similar manner across the network, albeit fewer overall inhibitory connections for the MCI group. However, there appeared to be more positive connections for the healthy groups relative to MCI.

While the above figures provide a visual representation of the learnt patterns of activity, statistical analyses will need to be performed to understand the connection weights changes for each group. Through the application of network analyses, graphs of interactions can be derived to uncover the dynamics of information exchange within brain areas in difference subject groups.

To validate the visualised changes from the pruned SNN models, histograms were plotted showing the pruned SNN connections weights (Figure 8.8). Compared to the initialised weights of each SNN, each model placed more emphasis on negative connection weights through training. Moreover, it is apparent that the weights now follow a somewhat Laplacian distribution, characterised by the heavy tails as demonstrated in the QQ-plots (Figure 8.8b) and the high Kurtosis values (Table 8.2), with the addition of the failure to reject the distribution being from a normal distribution (Table 8.2). This distribution type has been shown to respond well to

variable selection features, such as different applied methods of the adaLASSO (Wahid et al., 2017).

Table 8.2

Skewness and Kurtosis and Normality Test P-Value from a Kolmogorov-Smirnov Test of the SNNs Following Pruning.

1-back_{target} normality test			
Group	Skewness	Kurtosis	p-value
YA	-0.70	4.80	< 0.001
OA	-0.70	4.79	< 0.001
MCI	-0.67	4.71	< 0.001
$PM_{percept}$ normality test			
Group	Skewness	Kurtosis	p-value
YA	-0.81	4.50	< 0.001
OA	-0.78	4.44	< 0.001
MCI	-0.75	4.35	< 0.001
$PM_{concept}$ normality test			
Group	Skewness	Kurtosis	p-value
YA	-0.80	5.03	< 0.001
OA	-0.84	5.10	< 0.001
MCI	-0.78	4.93	< 0.001

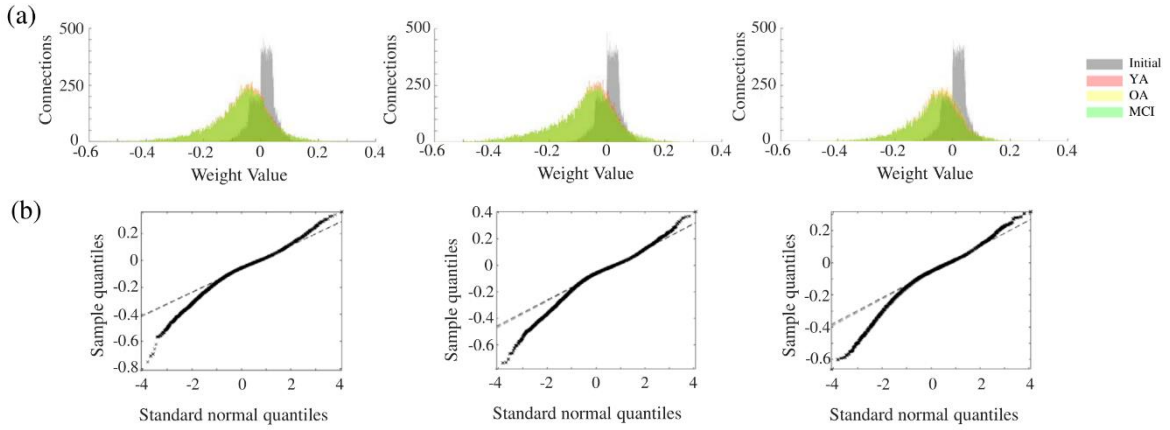

Figure 8.8. Validation of changes in SNN models. (a) Connection weights of each of the SNN models following pruning. Left to right: 1-back$_{target}$, PM$_{percept}$, PM$_{concept}$. (b) QQ-plots of distributions.

8.2.7 Experiment 1: Discussion

Experiment 1 aimed to improve the modelling and understanding of the neurocognitive dynamics that underpin PM across young adults, older adults and older adults experiencing MCI using a brain-inspired computational framework. Through the classification functionality of the SNN architecture, the current experiment sought to determine whether PM stimuli would enable better classification accuracy of brain activity between the groups compared to working memory stimuli. Two conclusions can be drawn from the results: firstly, greater accuracy was achieved by using a SNN methodology relative to the traditional ML methods (SVM, MLP, MLR); secondly, greater SNN classification accuracy was achieved with brain responses to PM stimuli compared to the ongoing working memory task at classifying brain activity between the groups. The greater accuracy for the SNN method compared to the traditional machine learning methods may be because of the following advantages: 1) it preserves the *spatial* and *temporal* information together in one model and can be interpreted in terms of neurophysiology as this model is spatially structured according to a brain template; 2) it learns spatiotemporal patterns from data through biologically plausible learning rules. The ability to retain the spatiotemporal patterns learnt from the ERP data, therefore, is advantageous as it can better model activity across cortex in a biologically plausible way. Whereas, in other ML methodologies, one of the spatial or

temporal dimensions must be collapsed, thus reducing the amount of preserved information the classification is performed with.

Regarding the differences in SNNs classification accuracy between the different types of memory, accuracy was superior for PM compared to working memory. SNNs are possibly better able to differentiate between groups due to PM requiring recruitment of multiple cognitive domains such as executive function, attention and working memory (Kliegel et al., 2002) and is, therefore, more cognitively involved than just working memory and will involve more cognitive processes. However, under this assumption it would be expected that the conceptual PM task would produce greater classification accuracy due to the increased cognitive processes needed to complete the task, yet this was not found. Future studies might be able to answer this by investigating PM versus other more cognitively demanding tasks to test whether it is PM specifically or simply cognitive demand that increases SNN classification accuracy.

It is reliably demonstrated that coping with additional cognitive demand is problematic for older adults with MCI (Missonnier et al., 2007; Vijayakumari et al., 2019; Yeung et al., 2016). The neural deficits experienced under increased cognitive load is more likely to be detected by the SNN allowing for more accurate classifications to be made. Thus, the current study proposes that earlier detection of dementia-related diseases may be achieved through the application of ML methods in cognitively demanding memory tasks as opposed to simple cognitive tasks, although this would need to be confirmed, for example, within a longitudinal design. The results here suggest that PM tasks may be suitable for discerning neurocognitive differences in those with MCI, particularly as PM is one of the first reported cognitive complaints of older adults who go on to develop MCI and dementia (Bischkopf et al., 2002).

The proposed SNN architecture of the current study offers a new method for extracting meaningful knowledge from ERPs in response to memory tasks. The current study demonstrates that once the optimal parameters are found for classification, the information can be used to further understand the spatiotemporal differences between groups from high-density EEG recordings. The learnt parameters of the SNN model can be used to create new models of each group by propagating the ERP data (as spike-trains) from a group. For example, when modelling the neurophysiological responses to the working memory stimuli in the MCI group, a 3D SNN model is created with the same initialised connection weights used during classification; the optimal

parameters are used to train the model using only the ERP data from the MCI group in response to working memory stimuli generating a network modelling the learnt neural activity of the participants with MCI.

The current study further demonstrates that interpretability of these models can be enhanced through "pruning" the network. Pruning involves the removal of all network connections that did not change when the information for an individual group was propagated to form the group model. The removal of these connections produced sparse SNN models which demonstrate only interactions that reflect patterns of learnt activity in that model. Therefore, these sparse networks offer a novel method to interpret models of task-based neurophysiological activity. Additionally, the method proposed here also offers the ability to pass through data from specific times or different cortical regions. ERP data from each group was modelled over different time periods to gain a deeper understanding of the patterns of connectivity through spatial and temporal dimensions related to the cognitive mechanisms modelled. Finally, pruning the non-important connections for each model enabled the connection weights to follow distributions that allow for statistical analyses to performed on the models.

8.3 Experiment 2: Knowledge extraction from SNN models

The current experiment aims to further extract knowledge from the SNN models from Experiment 1. Knowledge extraction was performed in two ways:

1) ANOVA was applied to test for differences in local connection weights in each of the SNN models as a function of group and topography (scalp region).
2) Network analysis was applied to uncover the global neurocognitive interactions between the different topographical areas for each of the SNN models.

8.3.1 Experiment 2: Method

The weights of the input ANs (i.e., EEG electrodes) were averaged according to the outlined topographical clusters depicted in Figure 8.9 (appendix B), which were informed through previous PM ERP research (Cruz et al., 2016; Scolaro et al., 2014;

West, 2011; Zöllig et al., 2012). Averaging the connection weights of the input neurons offers a way of understanding differences in local connection weight changes between the groups within a specific area. Average clusters were created as a means of controlling the number of comparisons (Rousselet et al., 2010; Baker, Castro, Dunn & Mitra, 2018). Analyses were performed in JASP 0.10.2. A series of mixed measures ANOVAs were performed for each of the created SNN models. Therefore, each stimulus type at each time point (i.e., 200–400, 400–800 & 0–1000) was analysed separately using a 4 (*Cluster*: frontal, central, parietal, occipital) x 3 (*Group*: YA, OA, MCI) ANOVA to analyse group differences at midline clusters. For lateral clusters, a 7 (*Cluster*: frontal, frontocentral, central, frontotemporal, parietal, inferior parietal, occipital) x 2 (*Hemisphere*: left, right) x 3 (*Group*: YA, OA, MCI) ANOVA was used to analyse group differences in the networks. Post-hoc tests were used to further explore group differences and Bonferroni corrections were applied to account for multiple comparisons. Partial eta squared was reported for each *Group* effect as an indicator of effect size (Bakeman, 2006).

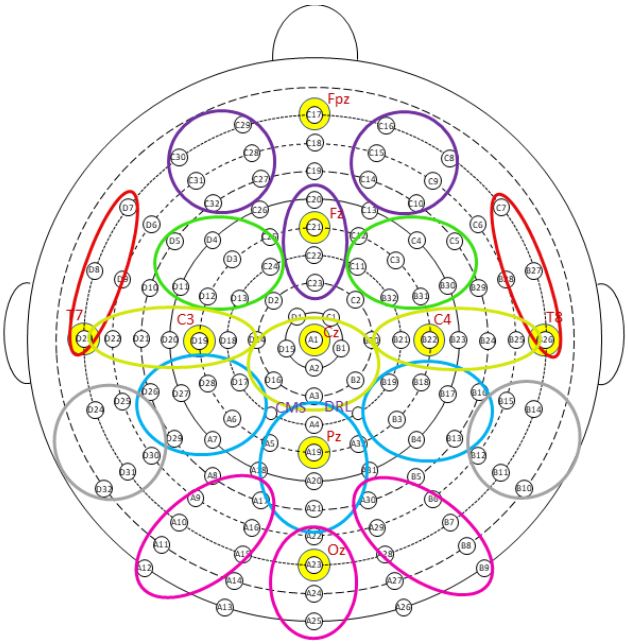

Figure 8.9. Topographical clusters used for ANOVAs and network analyses. Purple = frontal; green = frontocentral; yellow = central; red = frontotemporal; blue = parietal; pink = occipital; grey = inferior parietal.

The averaged connection weights were then used for the network analysis to understand global connectivity between areas across the cortex at each time frame (i.e., 200–400ms, 400–800ms, 0–1000ms). The network used describes a graphical representation (as seen in Figure 8.10) of the correlations between each of the clustered weights. In these networks, clusters are represented as nodes and the correlations as edges connecting nodes together. This is the same terminology used in graph theory, where the edges represent connections between two nodes. The line thickness and transparency of the network graph represents the strength of the correlation, where thicker edges represent stronger correlations. The generated network displays are fixed in line with the cluster layout of the scalp map in Figure 8.9 for ease of comparison between groups.

A network model that analyses all possible correlations within the network requires the estimation of many parameters, including n threshold parameters for the nodes and $n*(n-1)/2$ for pairwise correlations between nodes. Estimations in the current study are equal to 153 parameters. One available solution to this problem is to apply the 'least absolute shrinkage and selection operator' (LASSO) technique (Tibshirani, 1996). This method enables some edges to shrink to zero and be omitted from the model. This is achieved by LASSO through the continuous shrinking of coefficients towards 0 as λ increases. A benefit of applying LASSO is the ability to handle more variables than observations (Meinshausen & Yu, 2009; Zhao & Yu, 2006). However, given the high expected correlations between topographically close variables, i.e., averaged cortical clusters, the irrepresentable condition assumption would be violated (Zhao & Yu, 2006). This assumption requires that variables relevant to the model may not be highly correlated with irrelevant variables. An alternative method proposed by (Zou, 2006), known as 'adaptive least absolute shrinkage and selection operator' (adaLASSO), can be employed to adjust for this violation. While variables are all equally penalised with the LASSO method, variables are assigned different weights in adaLASSO and can subvert the irrepresentable condition assumption.

The adaLASSO produces a sparse, more conservative network model with only a small number of edges enabling a more interpretable model of the relationship between node weights for each participant group. Prior to analysis, a tuning parameter is required to control the level to which the omission of small correlations is applied. This tuning parameter was selected through bootstrapping and was validated using

cross-validation. The importance of each node in the network was then evaluated through betweenness and degree indices. Betweenness provides a measure of the number of shortest paths passing through a specific node. A node with higher betweenness is said to have more network control as more information is passing through that node (Barthelemy, 2004). Degree is the total amount of connections each node has, therefore indicating the strength of links to other areas (reported as 'node strength'). A node with a higher degree can be thought of as having a greater influence on connecting nodes (Borgatti, 2005).

Graphical models of brain data have proven their efficacy in a variety of imaging modalities, such as fMRI (Rosa et al., 2015), EEG (Kemmer et al., 2015; Micheloyannis et al., 2006), magnetoencephalography (MEG; Stam, 2004), DTI (Gong et al., 2009). Of these, sparse graphical models are distinctly efficient at determining connectivity between in highly interconnected brain data and at offering a robust and interpretable model of the most significant interactions between cortical areas (Dauwels et al., 2012).

8.3.2 Experiment 2: Results

Due to the non-normal distribution of the SNN weights, data connection weights were firstly transformed using a natural logarithm. The adaLASSO regularisation was performed to discover the most important connections for each pruned epoch for the early (200–400ms) and later (400–800ms) pruned SNN epochs, along with the complete (0–1000ms) epoch. A 10-fold cross-validation was performed for each of the variables. To increase the robustness of the results, each process was repeated 1000 times. Network plots were mapped to a scalp array dependent on their topographical features. For example, Figure 8.10 graphically illustrates the most important edges within the working memory (1-back$_{target}$) network as a result of non-essential connections being forced to zero. The thickness and colour intensity of the lines is proportional to the connection strength given as edge weight (EW). Positive connections are displayed in blue and negative connections are displayed in red. From these networks, the differences and similarities between groups are revealed.

8.3.2.1 Ongoing working memory (1-back$_{target}$)

A summary of all significant local connectivity *Group* effects and interactions for the 1-back$_{target}$ stimuli are presented in Table 8.3. No *Group* differences were found at midline clusters or in the 0–1000ms SNN model. Graphical networks are presented in Figure 8.10.

8.3.2.1.1 Ongoing: 200–400ms ANOVA connection weights

At bilateral clusters, there was a significant *Cluster* x *Group* interaction ($F_{10.27,446.07}$ = 2.06, p = 0.025, η_p^2 = 0.05) due to greater connection weights for YA relative to OA (frontal, p = 0.019; frontocentral, p = 0.009; central, p < 0.001; frontotemporal, p = 0.005; inferior parietal, p = 0.029) and YA relative to MCI (parietal, p = 0.011). OA had greater connection weights at bilateral central clusters relative to MCI (p = 0.008). The interaction was also explained by an effect of *Cluster* for all participants, where bilateral central clusters had larger connection weights than all other clusters (ps < 0.001). In YA, bilateral inferior parietal cluster connection weights were larger than in parietal clusters (p < 0.001).

8.3.2.1.2 Ongoing: 400–800ms ANOVA connection weights

At lateral clusters there was a significant effect of *Group* ($F_{2,87}$ = 12.67, p < 0.001, η_p^2 = 0.24), where YA had significantly greater connection weights across all bilateral clusters than OA (p < 0.001) and MCI (p < 0.001). No differences were found between the OA and MCI groups (p > 0.05). There were no other significant *Group* effects for 1-back$_{target}$ stimuli.

Table 8.3

Summary of Significant Effects 1-back$_{target}$ SNN Model

200–400ms lateral SNN weights	**Lower**	**F-Value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
Group		9.57	2,87	< 0.001	0.19	
*Cluster*Group*		2.06	10.27,446.07	0.025	0.05	
	F	5.71	2,87	0.005	0.12	YA > OA = MCI
	FC	4.79	2,87	0.011	0.11	YA > OA
	C	9.81	2,87	< 0.001	0.20	YA > OA > MCI
	FT	5.69	2,87	0.005	0.12	YA > OA = MCI
	P	3.48	2,87	0.035	0.08	YA > MCI
	IP	4.47	2,87	0.014	0.10	YA > OA = MCI
	YA	15.93	6,162	< 0.001	0.37	C > FC = F = FT = IP > P = OC
	OA	18.58	5.36,198.39	< 0.001	0.33	C > FC = F = FT = IP = OC > P
	MCI	8.31	6,75	< 0.001	0.33	C > FC = F = FT = IP = OC > P
400–800ms lateral SNN weights						
Group		12.67	2,87	< 0.001	0.24	YA > OA = MCI

YA = young adults. OA = healthy older adults. MCI = older adults with mild cognitive impairment. Clusters: F = frontal; FC = frontocentral; C = central; FT = frontotemporal; P = parietal; IP = inferior parietal. *N.B.* '>' represents greater connections weights in this table.

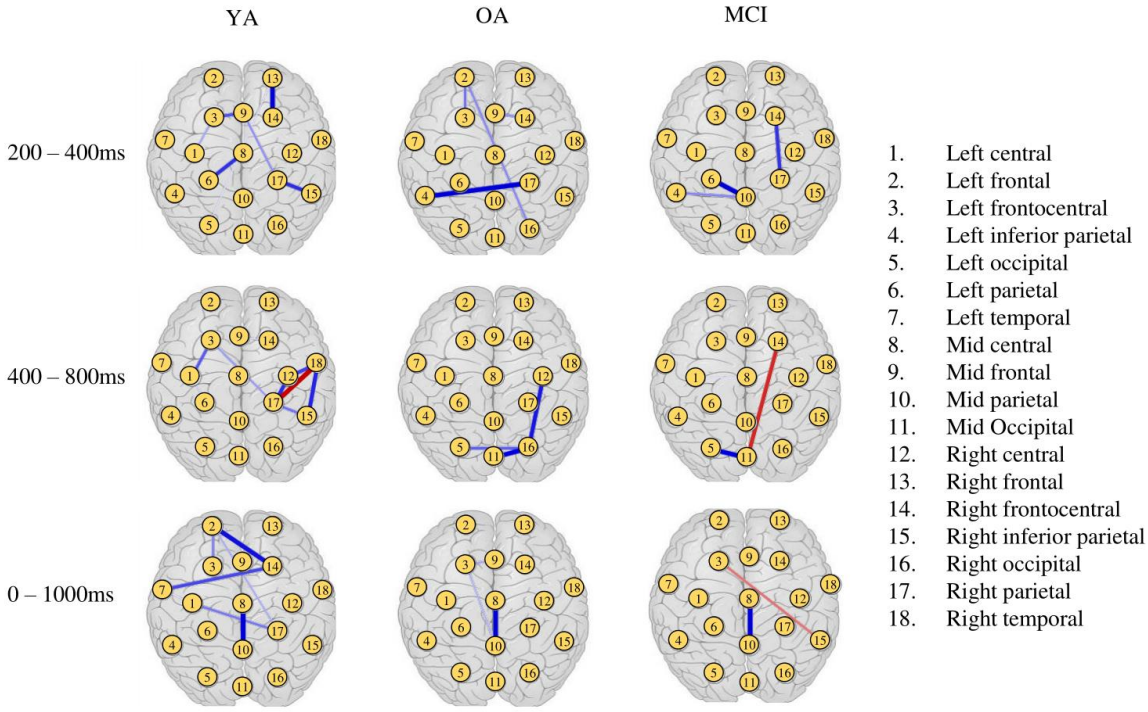

Figure 8.10. Working memory features extracted from the trained SNN using adaLASSO network analysis across the 200–400ms, 400–800ms and across the entire 0–1000ms trained epoch. YA = young adults; OA = healthy older adults; MCI = older adults with mild cognitive impairment.

8.3.2.1.3 Ongoing task: network analysis 200–400ms

For the 200–400ms network analysis of SNN models of the working memory ongoing task, the number of edges reduced to zero were approximately 95%, 97% and 98% for YA, OA, and MCI, respectively. The centrality indices reveal a common area of importance across all participants groups over the *right parietal* cluster (YA node strength = 1.49; OA node strength = 1.73; MCI node strength = 1.18). The cluster interactions that are formed with the right parietal are: the *right inferior parietal* (EW = 0.64) for the YA; the *left inferior parietal* in the OA (EW = 0.53) and the *right frontocentral* in the MCI group (EW = 0.61). For both the YA and OA networks, there are connections from the *frontal* clusters to the *frontocentral* clusters (YA EW = 0.70; OA EW = 0.32), albeit on the opposite hemispheres. The hemispheric symmetry between OA and YA is also found over *frontocentral* clusters, whereby the *mid central* cluster shares connections with *left frontocentral* clusters in the YA (EW = 0.51), but

is instead shared with the *right frontocentral* cluster for OA (EW = 0.17). The same patterns of activity are not found within the MCI group.

8.3.2.1.4 Network analysis 400–800ms

Edges were reduced by approximately 92% for young adults, 98% for OA and MCI networks over the 400–800ms epoch. In the OA and MCI networks at 400–800ms, importance is placed occipitally such that most connections are retained within the occipital clusters relative to the rest of the cortex. In the OA group, the *mid occipital* cluster was connected to *right occipital* (EW = 0.46), which in turn was connected to the *right central* (EW = 0.46) and the *left occipital* cluster (EW = 0.26). In the MCI group, the *mid occipital* cluster had a positive connection with the *left occipital* cluster (EW = 0.63) and a negative connection with the *right frontocentral* cluster (EW = -0.43). Furthermore, both the OA and MCI groups retain network relevance for the *left occipital* cluster (OA node strength = 0.46; MCI node strength = 2.64), but the *right occipital* cluster is also important in the OA group (node strength = 3.45). A different connection pattern is found for the YA group, where connectivity is localised over the *right frontotemporal* clusters with connections to: *right inferior parietal; right parietal; right temporal; right central* (average EW = 0.32) with the *right inferior parietal* cluster demonstrating the greatest network control (betweenness = 2.62).

8.3.2.1.5 Network Analysis 0–1000ms

For the entire epoch edges were reduced to approximately 95% for YA, 98% for OA and MCI groups. Across all groups the *mid central* cluster demonstrates the largest node strength (YA = 0.89; OA = 2.03; MCI = 2.40) along with connections being retained between *mid central – mid parietal* clusters (YA EW = 0.55; OA EW = 0.73; MCI EW = 0.78). Additionally, the network analysis shows significant node strength for the *left frontocentral cluster* for all groups; the YA demonstrate the lowest *left frontocentral* node strength (0.04) compared to the older adult groups who exhibit comparable strength indices (OA = 1.25; MCI = 1.03). However, connectivity differences are apparent between the older adult groups. From the *left frontocentral* cluster OA had positive connections with the *mid parietal* (EW = 0.17) and *mid frontal*

(EW = 0.15) clusters. The MCI group demonstrated a negative connection from the *left frontocentral* cluster with the *right inferior parietal* cluster (EW = -0.42). Moreover, positive connections were found in anterior scalp regions in the YA. In the YA group, the *right frontocentral* cluster had the largest node strength (2.15). The *right frontocentral* was connected to the *left frontotemporal* cluster (EW = 0.47) and the *left frontal* cluster (EW = 0.62), which in turn shared connection with the *left frontocentral* cluster (EW = 0.31).

8.3.2.2 Perceptual prospective memory statistical analysis

A summary of all statistically significant *Group* effects from the ANOVAs are presented in Table 8.4. No significant *Group* differences were found over midline clusters. Graphical networks are presented Figure 8.11.

8.3.2.2.1 Perceptual PM 200–400ms ANOVA connection weights

At lateral clusters there was a significant interaction effect of *Cluster* x *Group* ($F_{12,510}$ = 1.87, p = 0.036, η_p^2 = 0.05). This interaction effect can be explained by a significant effect of *Group* at frontal clusters ($F_{2,87}$ = 5.30, p = 0.007, η_p^2 = 0.12; OA > MCI, p = 0.030; OA > YA, p = 0.018). Additionally, the interaction can be explained by an effect of *Cluster* for YA ($F_{6,168}$ = 10.74, p < 0.001, η_p^2 = 0.29; inferior parietal < all other clusters, ps < 0.05), OA ($F_{6,198}$ = 16.40, p < 0.001, η_p^2 = 0.33; inferior parietal < all other clusters, ps < 0.001; frontal > all other clusters, ps < 0.001 but not including central, p > 0.05) and MCI ($F_{6,132}$ = 6.76, p < 0.001, η_p^2 = 0.26; inferior parietal < central, frontal, occipital, parietal, ps < 0.05; central > frontocentral, p = 0.020; frontocentral > parietal, p = 0.028).

8.3.2.2.2 Perceptual PM 400–800ms ANOVA connection weights

At lateral clusters there was a significant *Cluster* x *Hemisphere* x *Group* interaction ($F_{12,510}$ = 1.90, p = 0.046, η_p^2 = 0.05). This in part can be explained by a *Cluster* x *Group* interaction in the right hemisphere ($F_{12,510}$ = 1.90, p = 0.043, η_p^2 = 0.05; central: YA > OA, p = 0.031; YA > MCI, p = 0.032). Additionally, it can be explained by a *Hemisphere* x

Group interaction at frontal clusters ($F_{2,87}$ = 5.54, p = 0.006, η_p^2 = 0.12; all groups: right > left, ps < 0.05; right hemisphere: OA > YA, p = 0.027) and in parietal clusters ($F_{2,87}$ = 5.56, p = 0.005, η_p^2 = 0.12; YA: left > right, p = 0.032; left: YA > MCI, p = 0.034). The three-way interaction can also be explained by a *Cluster* x *Hemisphere* for YA ($F_{6,168}$ = 15.21, p < 0.001, η_p^2 = 0.36; left > right in frontal, frontocentral, frontotemporal occipital, inferior parietal, ps < 0.05; right > left in parietal, p < 0.001; left hemisphere: frontotemporal, central > frontocentral, ps < 0.05; parietal > occipital, p = 0.007; right hemisphere: central, frontotemporal, parietal > all other clusters, ps < 0.01; frontocentral, inferior parietal, occipital > frontal, ps < 0.01), OA ($F_{6,198}$= 14.41, p < 0.001, η_p^2 = 0.30; left > right in frontal, frontotemporal, occipital; left hemisphere: central, frontotemporal, parietal > frontocentral, ps < 0.05; right hemisphere: frontotemporal > central, frontal, frontocentral, occipital, ps < 0.01; parietal > frontal, frontocentral, occipital, ps < 0.05) and MCI ($F_{6,132}$= 13.31, p < 0.001, η_p^2 = 0.45; left > right in frontal, frontocentral, central, frontotemporal, occipital, inferior parietal; right > left in parietal; left hemisphere: frontotemporal > all other clusters except central, ps < 0.05; right hemisphere: frontotemporal > all other clusters, ps < 0.05).

8.3.2.2.3 Perceptual PM 0–1000ms ANOVA connection weights

At lateral clusters, there was a significant interaction of *Cluster* x *Group* ($F_{3.07,130.50}$ = 3.29, p = 0.022, η_p^2 = 0.08), due to a *Group* effect at frontotemporal clusters ($F_{2,87}$ = 4.12, p = 0.020, η_p^2 = 0.09; YA > MCI, p = 0.029; YA > OA, p = 0.062 (trend)). Additionally, the interaction is explained by a significant effect of *Cluster* for YA ($F_{.62,45.37}$ = 116.09, p < 0.001, η_p^2 = 0.81; frontotemporal < all other clusters, p < 0.001; frontal > inferior, parietal, occipital, ps < 0.05; central > frontocentral, p = 0.003) OA ($F_{1.54,91}$ = 89.17, p < 0.001, η_p^2 = 0.73; frontotemporal < all other clusters, p < 0.001; frontal > inferior, parietal, occipital, ps < 0.05; central > inferior parietal, p = 0.045; inferior parietal > occipital, p = 0.006) and MCI ($F_{1.43,31.45}$ = 33.60, p < 0.001, η_p^2 = 0.65; frontotemporal < all other clusters, ps < 0.001; inferior parietal < all clusters except frontotemporal, ps < 0.05).

Table 8.4

Summary of Significant Group Effects and Interactions for the Perceptual PM SNN Models

Lateral 200–400 SNN weights	**Lower**	**F-Value**	**DF**	***p*-value**	η_p^2	**Post-Hoc Tests**
*Cluster*Group*		1.87	12,510	0.036	0.05	
	F	5.30	1,87	0.007	0.12	OA > MCI = YA
	YA	10.74	6,168	< 0.001	0.29	F = FC = C = P = OC > FT = IP
	OA	16.40	6,198	< 0.001	0.33	F = C | F > FC = C = FT = P = OC | F, FC, C, P, OC > IP
	MCI	6.76	6,132	< 0.001	0.26	C, F, OC, P > IP | C > FC > P
Lateral 400–800ms SNN weights						
*Cluster*Hemisphere*Group*		1.90	12,510	0.046	0.05	
*Cluster*Hemisphere*	YA	15.21	6,168	< 0.001	0.36	F, FC, FT, P, IP, OC: L > R | L: FT & C > FC | P > OC | R: FT = C = IP > FC = IP = OC > F
	OA	14.41	6,198	< 0.001	0.30	F, FT, OC: L > R | L: FT = C = P = C = IP = OC > FC | R: FT > C, F, FC, OC | P > F, FC, OC
	MCI	13.31	6,132	< 0.001	0.45	F, FC, C, FT, IP, OC: L >R | P: R > L | L: FT > P = IP = OC = FC = F | R: FT > all clusters | C = IP > P = OC = FC = F | IP > F

Lateral 400–800ms SNN weights	**Lower**	**F-Value**	**DF**	***p*-value**	η_p^2	**Post-Hoc Tests**
*Cluster*Group*	R	1.90	12,510	0.033	0.05	C: YA > OA = MCI
*Hemisphere*Group*	F	5.54	2,87	0.006	0.12	R: OA > YA | YA, OA, MCI: L > R
	P	5.56	2,87	0.005	0.12	L: YA > MCI | YA: L > R
Lateral 0–1000ms SNN weights						
*Cluster*Group*		3.29	3.07,130.50	0.022	0.08	
	FT	4.12	2,87	0.020	0.09	YA > MCI | YA > OA†
	YA	116.09	1.62,45.37	< 0.001	0.81	F > FC, IP, P, OC | C > FC | all clusters > FT
	OA	89.17	1.54,56.91	< 0.001	0.73	F > IP, P, OC | C > IP | IP > OC | all clusters > FT
	MCI	33.60	1.43,31.45	< 0.001	0.65	F, FC, P, OC > IP | all clusters > FT

YA = young adults. OA = healthy older adults. MCI = older adults with mild cognitive impairment. Clusters: F = frontal; FC = frontocentral; C = central; FT = frontotemporal; P = parietal; IP = inferior parietal; OC = occipital. L = left hemisphere. R = right hemisphere. | = separator between post hoc-tests. † = trending toward significance. *N.B.* > in this table represents greater connection weights.

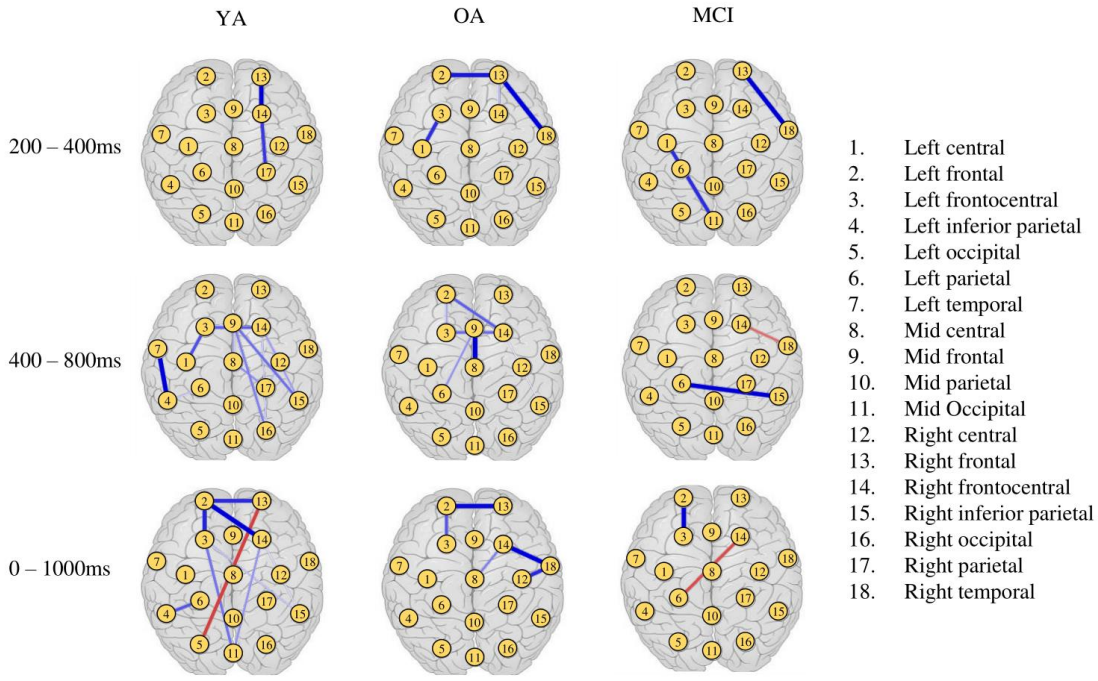

Figure 8.11. Perceptual prospective memory ($PM_{percept}$) features extracted from the trained SNN using network analysis (adaLASSO) across the 200–400ms, 400–800ms and across the entire 0–1000ms trained epoch. YA = young adults; OA = healthy older adults; MCI = older adults with mild cognitive impairment.

8.3.2.2.4 Perceptual PM network Analysis: 200–400ms

Network models for 200–400ms induced a sparsity level of 97% for OA and 98% for YA and MCI groups. As seen in Figure 8.11 the right *frontal* cluster has strong associations with neighbouring clusters across all participant groups. In the YA, the network reveals a strong positive connection between the *right frontal* and the *right frontocentral* cluster (EW = 0.33), which also exhibits significant network control (betweenness = 4.01) through a strong positive relationship with the *right parietal* cluster (EW = 0.27). A similar level of betweenness is exhibited in the OA group, however network control is instead demonstrated by the *right frontal cluster* with connections to the *left frontal* cluster (EW = 0.38) and *right frontotemporal* cluster (EW = 0.49), which is not apparent for the MCI group. Additionally, for both the OA and MCI groups, positive connections and increased strength were found in the *left central* cluster (OA node strength = 0.80; MCI node strength = 1.58). The OA group

demonstrates a positive *left central* to *left frontocentral* regions (EW = 0.43), whereas MCI shows a *left central* to *mid occipital* cluster relationship (EW = 0.35).

8.3.2.2.5 Perceptual PM network Analysis: 400–800ms

For the network models of 400–800ms, approximately 91%, 96% and 98% of all edges were set to zero for the YA, OA and MCI groups, respectively. The models demonstrate the importance of the *right frontocentral* cluster over this epoch as all participant groups show similar levels of degree strength (YA node strength = 1.55; OA node strength = 1.91; MCI node strength = 1.08), although only significant levels of betweenness for YA (2.70) and OA (3.56) were found implying a possible loss of network control in MCI. Similarly, the *mid frontal* cluster also shows strong network strength and network control but only for YA (node strength = 1.62; betweenness = 1.79) and OA (node strength = 2.10; betweenness = 1.62) but not in the MCI group. A comparable pattern is also seen in the *left frontocentral* cluster, where network strength is found for both YA (node strength = 1.50) and OA (node strength = 1.09), but not for MCI groups. The MCI groups instead show strong betweenness and network strength for the *right inferior parietal* (node strength = 2.43; betweenness = 4.01) cluster and node strength in the *left parietal cluster* (2.31).

8.3.2.2.6 Perceptual PM network Analysis: 0–1000ms

The approximate percentage of edges set to zero for the entire epoch are 94%, 97% and 99% for the YA, OA and MCI groups, respectively. The node strength indices highlight two areas of particular importance for $PM_{percept}$ stimuli for all groups: the *right frontocentral* cluster (YA = 1.24; OA = 1.63; MCI = 1.36) and the *left frontal* cluster (YA = 2.60; OA = 1.85; MCI = 2.20). These clusters exhibit the greatest strength within the network, although differences were found in the measures of betweenness. The *left frontal* cluster exhibits significant network control in the YA (2.82) and OA groups (1.08) but not in the MCI group. In the YA, there were strong positive connections from the *left frontal* cluster with the *right frontal* (EW = 0.38), *right frontocentral* (EW = 0.49) and with the *left frontocentral* cluster (EW = 0.42). A similar pattern is observed between the *left frontal* cluster in OA with the *right frontal* (EW = 0.41) and the *left*

frontocentral cluster (EW = 0.29). This connectivity pattern is not found in the MCI group. The YA group exhibits positive bilateral *frontocentral* connections with the *mid occipital* cluster (*left frontocentral* EW = 0.25; *right frontocentral* EW = 0.16) and a negative *right frontal – left occipital* connection (EW = -0.31). The OA group exhibits a local network feature over the *right frontotemporal* scalp region, characterised by the strong positive *right central – right temporal* (EW = 0.30), *right temporal – right frontocentral* (EW = 0.36) and *mid central – right frontocentral* (EW = 0.25) connections, where network control is ascribed to the *right frontocentral* cluster (betweenness = 2.57). The same local network is not found in the MCI group, but a negative connection is found for *right frontocentral – left parietal* clusters (EW = -0.38).

8.3.2.3 Conceptual prospective memory statistical analysis

All significant *Group* effects ANOVA results are presented in in Table 8.5. There were no significant *Group* effects over midline clusters. Graphical networks are presented Figure 8.12.

8.3.2.3.1 Conceptual PM 200–400ms connection weights ANOVA

At lateral clusters there was a significant *Cluster* x *Group* interaction ($F_{8.65,376.22} = 2.73$, $p = 0.005$, $\eta_p^2 = 0.06$), due to an effect of *Group* at occipital ($F_{2,87} = 4.14$, $p = 0.019$, $\eta_p^2 = 0.09$; YA > OA, $p = 0.025$), inferior parietal ($F_{2,87} = 3.53$, $p = 0.034$, $\eta_p^2 = 0.06$; YA > OA, $p = 0.056$ (trend)) and central clusters ($F_{2,87} = 9.59$, $p < 0.001$, $\eta_p^2 = 0.19$; YA > OA, $p < 0.001$; YA > MCI, $p = 0.006$). The interaction effect was also due to an effect of *Cluster* in YA ($F_{3.82,106.92} = 16.12$, $p < 0.001$, $\eta_p^2 = 0.37$; occipital > all other clusters, $ps < 0.001$; inferior parietal > frontocentral, $p < 0.001$; inferior parietal > frontotemporal, $p = 0.045$; parietal > frontocentral, $p = 0.001$), OA ($F_{3.62,133.82} = 30.17$, $p < 0.001$, $\eta_p^2 = 0.45$; occipital > all other clusters, $ps < 0.001$; central < all other clusters, $ps < 0.05$; inferior parietal > frontal, $p = 0.023$; inferior parietal > frontotemporal, $p = 0.005$) and MCI ($F_{3.72,81.88} = 25.58$, $p < 0.001$, $\eta_p^2 = 0.59$; occipital > all other clusters, $ps < 0.001$; central < frontal, $p = 0.002$; central < parietal, inferior parietal, $ps < 0.001$; frontotemporal > inferior parietal, parietal, $ps < 0.05$).

8.3.2.3.2 Conceptual PM 400–800ms connection weights ANOVA

At lateral clusters there was a significant three-way *Cluster* x *Hemisphere* x *Group* interaction ($F_{10.30,448.12}$ = 1.96, p = 0.035, η_p^2 = 0.05). This can be explained by a significant *Cluster* x *Group* in the left hemisphere ($F_{8.29,360.50}$ = 2.33, p = 0.018, η_p^2 = 0.05), such that YA had significantly larger connection weights than OA in frontal (p = 0.005), frontocentral (p = 0.004), central (p = 0.002) and parietal clusters (p = 0.021) and larger connections weight than MCI in frontocentral (p = 0.015) and central clusters (p = 0.003). The three-way interaction can also be explained by a *Hemisphere* x *Group* effect at frontotemporal clusters ($F_{2,87}$ = 3.51, p = 0.035, η_p^2 = 0.08), whereby in the right hemisphere OA had larger connection weights than in YA (p = 0.015). The three-way interaction can also be explained by a *Cluster* x *Hemisphere* for YA ($F_{4.01,112.39}$ = 16.44, p < 0.001, η_p^2 = 0.37; left > right in frontal, frontotemporal, parietal, inferior parietal, ps < 0.05; right hemisphere: frontal, central, parietal > frontotemporal, occipital, ps < 0.005; inferior parietal > occipital, p = 0.001; left hemisphere: frontotemporal < all other clusters, ps < 0.001; central > frontal, inferior parietal, ps < 0.01), OA ($F_{4.54,167.95}$ = 14.58, p < 0.001, η_p^2 = 0.28; left > right in frontal, frontotemporal, parietal, inferior parietal, ps < 0.05; right hemisphere: frontal, frontocentral, central, occipital > frontotemporal, parietal, ps < 0.005; central, occipital > inferior parietal, ps < 0.001; left hemisphere: frontal, parietal, inferior parietal > frontotemporal, ps < 0.05; parietal > frontocentral, occipital, ps < 0.01) and MCI ($F_{4.65,102.27}$ = 15.57, p < 0.001, η_p^2 = 0.46; left > right in frontal, frontotemporal, parietal, inferior parietal, ps < 0.05; right hemisphere: central, occipital > frontotemporal, parietal, ps < 0.05; central > frontal, p = 0.008; frontal > frontotemporal, p = 0.002; left hemisphere: inferior parietal > frontotemporal, p = 0.033; parietal > central, occipital, ps < 0.05). All groups demonstrated greater connection weights in the right relative to the left hemisphere in occipital clusters (ps < 0.05).

8.3.2.3.3 Conceptual PM 0–1000ms ANOVA connection weights

At lateral clusters a significant *Hemisphere* x *Group* interaction *Group* ($F_{2,87}$ = 3.89, p = 0.025, η_p^2 = 0.09) is explained by a significant effect of *Group* in the right hemisphere ($F_{2,87}$ = 4.23, p = 0.015, η_p^2 = 0.10; MCI > YA, p = 0.024) and a significant effect of

Hemisphere in OA ($F_{1,37}$ = 25.18, p < 0.001, η_p^2 = 0.41) and MCI ($F_{1,22}$ = 9.46, p = 0.007, η_p^2 = 0.35), such that the right hemisphere connection weights were significantly greater than the left hemisphere (OA: p < 0.001; MCI: p = 0.007).

Table 8.5

Summary of Significant Effects for 200–400 Conceptual PM SNN Models

Lateral 200–400 SNN weights	**Lower**	**F-Value**	**DF**	***p*-value**	**η_p^2**	**Post-Hoc Tests**
*Cluster*Groups*		2.73	8.65,376.22	0.005	0.06	
	C	9.59	2,87	< 0.001	0.19	YA > OA, MCI
	IP	3.53	2,87	0.034	0.08	YA > OA†
	OC	4.14	2,87	0.019	0.09	YA > OA
	YA	16.19	3.82,106.92	< 0.001	0.37	OC > F, FC, C, FT, P | IP > FC, FT |P > FC
	OA	30.17	3.62,133.82	< 0.001	0.45	C < all clusters | OC > all clusters | IP > F, FT
	MCI	25.58	3.72,81.88	< 0.001	0.59	OC > all clusters | F, IP, P > C | IP, P > FT
Lateral 400–800ms SNN weights						
*Cluster*Hemisphere*Group*		1.96	10.30,448.12	0.035	0.05	
*Cluster*Hemisphere*	YA	16.44	4.01,112.39	< 0.001	0.37	F, FT, P, IP, OC: L > R | R: F, C, P > FT = OC | IP > OC | L: FT < all clusters | C > F = IP | OC: R > L

Lateral weights	**400–800ms SNN**	**Lower**	**F-Value**	**DF**	***p*-value**	η_p^2	**Post-Hoc Tests**
		OA	14.58	4.54,167.95	< 0.001	0.28	F, FT, IP, P: L > R | | R: F, FC, C, OC > FT = P | OC, C > IP| L: F = P = IP > FT | P > FC = OC | OC: R > L
		MCI	15.57	4.65,102.27	< 0.001	0.46	F, FT, IP, P: L > R | OC: L > R | L: IP > FC | P > OC = C| R: C = OC > FT = P | C > F > FT
*Cluster*Group*		Left	2.33	8.29,360.50	0.018	0.05	F: YA > OA | FC: YA > OA = MCI | C: YA > MCI = OA| P: YA > OA
		Right	3.50	10.66,463.87	< 0.001	0.08	F: YA > MCI | C: YA > OA = MCI | FT: OA > YA | P: YA > MCI
*Hemisphere*Group*		FT	3.51	2,87	0.035	0.08	R: OA > YA
Lateral weights	**0–1000ms SNN**						
*Hemisphere*Group*			3.89	2,87	0.025	0.09	
		R	4.23	2,87	0.015	0.10	MCI > YA
		OA	25.18	1,37	< 0.001	0.41	R > L
		MCI	9.46	1,22	0.007	0.35	R > L

YA = young adults. OA = healthy older adults. MCI = older adults with mild cognitive impairment. Clusters: F = frontal; FC = frontocentral; C = central; FT = frontotemporal; P = parietal; IP = inferior parietal; OC = occipital. L = left hemisphere. R = right hemisphere. | = separator between post hoc-tests. † = trending toward significance. *N.B.* > represents greater connections weights in this table.

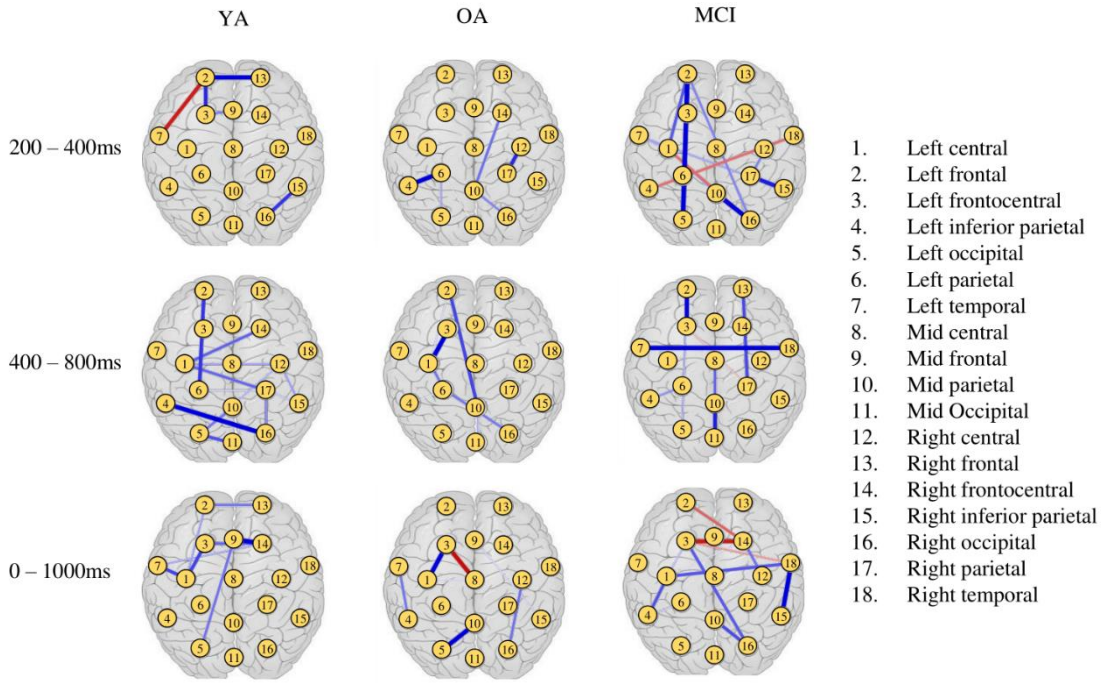

Figure 8.12. Conceptual prospective memory ($PM_{concept}$) features extracted from the trained SNN using network analyses (adaLASSO) from the 200–400ms, 400–800ms and across the entire 0–1000ms trained epoch. YA = young adults; OA = healthy older adults; MCI = older adults with mild cognitive impairment.

8.3.2.3.4 Conceptual PM network analysis: 200–400ms

Over 200–400ms, approximately 97% of edges for YA and OA and 95% of edges for the MCI group were set to zero. A common cluster across all groups for this earlier epoch is the *right occipital* cluster, where the MCI group exhibits the greatest node strength (1.66), relative to YA (0.60) and OA (0.25). From the *right occipital* cluster connections to *mid parietal* clusters were found for both the OA (EW = 0.33) and MCI groups (EW = 0.34), along with a *right parietal – right central* relationship (OA EW = 0.49; MCI EW = 0.23). Additionally, the MCI group shares similar network strength in the *left frontal* cluster (node strength = 1.78) as the YA group (node strength = 1.25). Both the MCI and YA groups demonstrate the greatest amount of network control originating from the *left frontal* cluster (YA betweenness = 3.36, MCI betweenness = 1.31). However, while the YA group demonstrates connections from the *left frontal*

cluster to the *right frontal* (EW = 0.32), *left temporal* (EW = -0.31) and *left frontocentral* (EW = 0.44), the model shows longer connections toward posterior regions for the MCI group with the *left frontal* cluster connecting to *left occipital* (EW = 0.70), *right occipital* (EW = 0.20) and the *left central* clusters (EW = 0.42).

8.3.2.3.5 Conceptual PM network analysis: 400–800ms

Model sparsity was approximately 90% for YA, 96% for OA and 94% for MCI. There are several network similarities between the groups at this period. All groups demonstrate considerable degree strength at *left frontal* clusters (YA = 0.12; OA = 0.93; MCI = 1.43). The network highlights the importance, as indicated by a measure of betweenness, of *mid parietal* and *left parietal* for YA (*mid parietal* = 0.05; *left parietal* = 0.48), OA (*mid parietal* = 1.20; *left parietal* = 1.53) and MCI (*mid parietal* = 1.76; *left parietal* = 0.27) groups. Differences are apparent in the connections between groups. In the frontal clusters the YA demonstrate a *left frontal – left parietal* connection (EW = 0.46); OA demonstrate a similar *left frontal – mid parietal* connection (EW = 0.25), but MCI exhibits a shorter *left frontal – left frontocentral* connection (EW = 0.58). The MCI group displays a strong interhemispheric connection between *left temporal – right temporal* clusters (EW = 0.56).

8.3.2.3.6 Conceptual PM network analysis: 0–1000ms

The approximate number of edges reduced to zero for the entire $PM_{concept}$ epoch was 95% for YA and OA, and 92% for MCI. The *left frontocentral* cluster contains the most amount of network control (YA betweenness = 1.66; OA betweenness = 4.01; MCI betweenness = 2.98). Additionally, YA and OA both show *left frontocentral* connections with the *left central* cluster (YA EW = 0.32; OA EW = -0.44). Conversely, where a connection for the YA is found between the *left frontocentral* cluster and *right frontocentral* cluster (EW = 0.32) a negative connection is found between the two clusters for the MCI group (EW = -0.60). Figure 8.12 shows network connections between *left frontal – right frontal* (EW = 0.19) and *left frontocentral – right frontocentral* (EW = 0.18) in YA. MCI show a negative connection from the *right frontocentral* cluster to the *left frontocentral* cluster (EW = -0.18). The YA model

favours a *left frontocentral* connectivity pattern, whereas the older adult groups incorporate more temporal-posterior regions.

8.3.4 Experiment 2: Discussion

Experiment 2 aimed to uncover insights into differences in spatiotemporal relations in terms of connectivity between young adults, older adults, and older adults with MCI. The current experiment performed a series of ANOVAs and network analyses on each of the SNN models over 200–400ms, 400–800ms and 0–1000ms. Performing ANOVAs provided insight into the local cluster connectivity differences between the groups within the SNN models created in experiment 1. The network analyses enabled further understanding of the global spatiotemporal relations between scalp clusters.

The results of the current experiment reveal that all groups had strong midline central parietal connectivity in the 0–1000ms model of working memory. However, younger adults also had strong frontal and frontocentral connectivity patterns, which were less prominent in older adults and were negatively related to one another in the MCI group. Similarly, in the 200–400ms models, all groups demonstrated strong network activity in the frontocentral and parietal clusters, but the cluster connectivity was greatest in anterior regions. Both the younger and healthy older adults had strong patterns of connectivity from the frontocentral cluster to other cortical areas. In the MCI group, frontocentral connectivity was diminished along with lower local cluster connectivity weights relative to their healthy counterparts. Previous research has linked verbal working memory to the left PFC (Jonides et al., 1997; E. E. Smith & Jonides, 1999) and the left lateral PFC to the cognitive control of memories (Badre & Wagner, 2007). Indeed, fMRI evidence demonstrates reduced left inferior PFC activation in older adults during a semantic memory task despite no behavioural impairments relative to younger adults (Lacombe et al., 2015). In individuals with AD or MCI, prefrontal activation is further reduced when performing semantic memory tasks relative to healthy controls (Joubert et al., 2010) and is related to poorer semantic working memory performance. It is possible, therefore, that connectivity in the PFC declines as a function of age and is further affected by MCI when performing semantic working memory tasks. The results support the role of the PFC in semantic working memory

and suggest that frontal network connectivity to other cortical areas declines with age but may be more rapidly deteriorating in those with MCI.

The results highlight the importance of the anterior clusters for all participant groups in responding to perceptual PM stimuli. Both younger and older adults had significantly greater levels of connectivity throughout the cortex relative to the older adults with MCI, particularly in frontal and frontocentral clusters across all time epochs. It is understood that the aPFC plays an important role in the balance of attention between performing the ongoing task and the internal presentation of the PM stimuli (Burgess et al., 2007). Recent fMRI evidence has also implicated functional deterioration in attention networks (dorsal and ventral networks) in older adults with amnestic MCI and AD (Franzmeier et al., 2017; Yamashita et al., 2019; Z. Zhang et al., 2015). The decrease of frontocortical connectivity in older adults with MCI possibly represents a deterioration in the functional networks responsible for performing the attentional balance between the working memory and PM intention maintenance. However, the mentioned studies were not recorded when performing an attention-based task but instead correlated resting-state activity with behavioural performance.

Across the models of perceptual PM, both younger and healthy older adults had strong patterns of connectivity across the hemispheres, but this connectivity was markedly reduced within the MCI group. Functional connectivity studies have similarly demonstrated abnormal patterns of interregional connectivity in those with MCI (Bai et al., 2011). Bai et al. (2011) explored whole-brain connectivity of those at risk of AD development compared to healthy controls. Their results show reduced interregional correlations primarily in the frontal cortex and subcortical structures suggesting a loss of coordinated cortical activity. While the current results support the suggestion of reduced cortical coordination in the frontal cortices of those with MCI, inferences about subcortical networks cannot be made.

Similar to perceptual PM, the analyses show that the frontal cortices are important in successfully responding to conceptual PM stimuli (Cona et al., 2015). In general, younger adults displayed greater local cluster connectivity compared to the older adults in left anterior clusters, bilateral central and occipital clusters (200–400ms only). Unlike the perceptual PM models, however, older adults with MCI showed a greater amount of cluster–to–cluster connectivity across the cortex than younger and older adults. Moreover, older adults with MCI had greater local connection weights in

the right hemisphere compared to younger adults (0–1000ms only). Potentially, the increased connectivity in the older adults with MCI reflects the recruitment of additional processes to complete the more cognitively challenging task. Compared to perceptual PM stimuli, conceptual PM cues are less salient making detection harder and subsequently requiring more cognitive processes (Cousens et al., 2015; Cruz et al., 2016; Wilson et al., 2013). In tasks that are more cognitively demanding, researchers have found enhanced cortical activity in older adults with MCI relative to controls (Bajo et al., 2010; Z. Jiang & Zheng, 2006; Y. Zhang et al., 2016). For example, Zhang et al. (2016) evaluated the functional connectivity during an episodic memory task in older adults with AD and MCI. They found greater connectivity in the cognitively impaired relative to healthy controls in the middle frontal gyrus, parahippocampus and the parietal cortex. Given the close relationship of episodic memory and PM (Martin et al., 2007), the results here may support previous studies linking hyperconnectivity to faster memory decline (Salami et al., 2014) and poorer episodic memory performance (Pasquini et al., 2015) but only in conceptually based PM tasks.

In response to all stimuli, older adults with MCI had a greater amount of inhibitory connectivity patterns. The current results suggest that these inhibitory connections are representative of functional impairments of those with MCI. This conclusion is based on the absence of such patterns of activity within the healthy older adults and young adults. The greater inhibitory connectivity was particularly pronounced in frontal clusters in the entire epoch for conceptual PM stimuli. Similar frontal patterns in MCI were found by Bai et al., (2010) and were related to episodic memory, attention, and other cognitive functions in the MCI participants. Further, researchers have demonstrated similar increased inhibitory connectivity in resting-state and task-based EEG studies in patients with AD (Bokde et al., 2006; K. Wang et al., 2007), such that increased inhibitory frontal connectivity was a predominate feature in differentiating AD relative to healthy controls. Therefore, the current study further highlights the potential utility of inhibitory frontal connectivity as a biomarker in the detection of dementia-related diseases.

8.4 General Discussion

The current chapter presents a study that is, to the author's knowledge, the first to apply a SNN architecture model to electrocortical activity during PM tasks. It is also the first study to apply adaLASSO as a measure of network connectivity within SNN models. Moreover, the study has applied these methods to typical and atypical ageing groups. The results show that 1) SNNs are more sensitive to traditional ML methods in providing classification between young adults, healthy older adults and older adults with MCI during working memory and PM tasks; 2) greater discriminatory capacity is achieved through modelling PM in SNNs compared to working memory; and 3) in general, younger adults had greater local cluster connectivity compared to healthy older adults and older adults with MCI as indicated by greater local cluster connection weights across the scalp. Furthermore, the network analyses largely show that older adults with MCI had decreased connectivity across the cortex in response to working memory and perceptual PM tasks. However, network activity in response to conceptual PM revealed greater cortical connectivity in those with MCI relative to young and healthy older adults and a greater number of inhibitory connections in response to all memory stimuli.

8.4.1 Hypo- and hyper- global connectivity in mild cognitive impairment

Within the functional EEG connectivity literature, there are differences in the reported patterns of activity in MCI and early AD. Some researchers report decreased functional connectivity in those with MCI and early AD (König et al., 2005; López-Sanz et al., 2017; Tóth et al., 2014; Vecchio et al., 2016), while others have reported increases in cortical connectivity (Bajo et al., 2010; M. D. Sullivan et al., 2019; Van Deursen et al., 2009; Zhiqun Wang et al., 2012; Y. Zhang et al., 2016). Most connectivity studies primarily examine the differences in resting-state neurophysiological activity. Resting-state activity is more susceptible to inter-individual differences and spurious activity such that there is a large amount of individual variability when a participant is at rest (Fox & Raichle, 2007; Nolte et al., 2004). However, differences in studies of connectivity during memory tasks are also found (e.g., Ahmadlou et al., 2014; Pijnenburg et al., 2004). In a comparison of resting and task-based connectivity, Jiang

& Zheng (2006) demonstrated that while functional connectivity in an MCI group decreased relative to healthy controls while at rest, in the working memory task, the MCI group exhibited greater inter- and intra-hemispheric connectivity. Jian and Zheng suggest that due to atrophy in cortical regions such as the temporal, parietal lobes and the hippocampus, the levels of cortical connectivity increase as a means of supporting cognitive functioning during memory tasks. Although the current study did not compare the results with resting-state activity, the current findings may suggest that similar compensatory mechanisms are being utilised throughout the cortex in the MCI group during the more difficult conceptual PM tasks relative to the highly salient perceptual PM task and the relatively simple working memory task. Indeed, evidence has shown greater inter-hemispheric EEG connectivity in those with MCI when the demands of the memory task increase (Zheng et al., 2007), which was not found in the healthy controls. Furthermore, increased functional connectivity between the parahippocampus and the middle frontal gyrus has also been shown with MRI to be associated with decreased episodic memory performance in those with MCI (Zhang et al., 2016). Taken together with the current findings, it is possible that decreases in connectivity are apparent in resting-state and simple memory tasks in those with MCI. Potentially, however, as the difficulty of the task increases, so might the connectivity for individuals with MCI possibly reflecting compensatory mechanisms.

8.4.2 Local cluster connectivity differences in mild cognitive impairment

The results of the current study show that in general, the SNN models of older adults with MCI form fewer positive and negative neural connections during working memory and PM tasks relative to the younger adults and older adults with MCI. Possibly this reflects the reduction of global cortical power reported in EEG frequency analyses (Roh et al., 2011). To understand these connectivity changes between groups, the local cluster connectivity within each cluster was explored. Evaluating local clustering connectivity has been suggested as a superior method for studying cognitive disease networks relative to the longer-range cortical connections (Pereira et al., 2016). The results here show that older adults with MCI had lower local connectivity relative to young and older adults in certain cortical areas and times. Most notably, over 200–400ms, older adults with MCI had decreased local connectivity in central

regions relative to healthy older adults and in parietal clusters relative to young adults during working memory. During PM tasks, older adults with MCI had decreased local cluster connection weights in the frontotemporal cluster (400–800ms) in response to perceptual PM stimuli and reduced connectivity in bilateral frontocentral and central clusters in response to conceptual PM stimuli (400–800ms) relative to young adults. Similar results have been shown before in older adults with MCI in a local cluster connectivity analysis by López-Sanz et al. (2017). López and colleagues found that in a resting-state, participants with MCI had decreased local cluster activation across the cortex relative to healthy controls in theta and beta MEG frequency bands. Previous research has demonstrated a reduction in cluster connectivity in AD (Morabito et al., 2015; Sanz-Arigita et al., 2010) and MCI (Ahmadlou et al., 2014) reflecting a loss of SW connectivity. The SW networks, modelled in the current study as clusters, represent short-range connections within the local areas with small neural cost, while long-range connections represent efficient information transfer between distant brain regions (Salvador et al., 2005). Local cluster connectivity disruptions in resting-state recordings have been demonstrated previously in AD in other neuroimaging methods such as MRI (J. B. Pereira et al., 2016) and PET (Ortiz et al., 2016). The current study highlights a loss of local cluster connectivity in central regions in working memory, frontotemporal clusters in perceptual PM and bilateral frontocentral and central clusters as potential early biomarkers of cognitive decline in older adults.

8.4.3 Spatiotemporal compensation in typical ageing

For the most part, younger adults demonstrate greater local connectivity in response to working memory stimuli. However, in response to perceptual PM stimuli older adults demonstrated increased local cluster connectivity in bilateral frontal clusters relative younger adults (200–400 & 400–800ms) and MCI (200–400ms only). Potentially, this represents neural compensatory mechanisms during the completion of PM tasks, possibly reflecting the frontal activity during intention maintenance (Hering et al., 2020). However, an increase in frontal local cluster connectivity was not found for older adults in response to conceptual PM stimuli. This may suggest that similar neural strategies are being employed by the older adults and younger adults to complete the conceptual PM task (Zöllig et al., 2007). However, analysis of the 0–1000ms SNN model in response to conceptual PM stimuli show that both older adult

groups have greater local cluster connectivity across the right hemisphere relative to the left. It is unclear why the right hemisphere had greater connectivity in the older adult groups relative to young adults, and this finding does not fit with the HAROLD theory of ageing (Cabeza, 2002). The HAROLD theory suggests that as we age, there is a reduction in hemispheric lateralisation. However, the current study suggests older adults have increased lateralisation relative to young adults, at least for some memory tasks. In older adults, language-area counterpart regions in the right hemisphere have been found to provide a supportive role in language-based tasks (Obler et al., 2010). Potentially, the right hemisphere lateralisation in the older adults may reflect a supportive role in more intensive semantic meaning search for the conceptual PM cue (Hagoort et al., 1996) although this remains speculative without further research.

8.4.4 Spiking neural networks in prospective memory

While the current study primarily aimed to determine differences in SNN models of working memory and PM, the current results offer insights into the functional spatiotemporal activity in PM. In both PM SNN models, network analyses demonstrate the importance of frontal systems during successful PM responses. In the model of the entire epoch for perceptual PM, considerable node strengths in left frontal and right frontocentral clusters were found. Similarly, across the entire epoch of the SNN modelling spatiotemporal activity in response to conceptual PM stimuli, the results show that, for all participants, the left frontocentral clusters had the largest network control. In contrast, the greatest network control in the working memory models was found in the centroparietal clusters potentially reflecting activity of the PCC during working memory (Hampson et al., 2006). However, it remains difficult to speculate on the precise underlying function of brain activity during successful PM responses, the functional connectivity of these regions reflects the importance of the network and the interconnected regions which support PM responses. In response to both PM stimulus types, the left frontocentral cluster plays an important function. Larger connection weights and network control was found for the frontocentral clusters relative to other clusters. Additionally, the results show co-occurring activity of regions of the posterior brain in PM with the frontal clusters. This adds further support to the AtoDI model (Cona et al., 2015) of PM which suggests that importance of frontal and parietal sources in attention control directed to external or internal sources.

The current study also demonstrates significant network activity at the frontotemporal clusters in response to PM stimuli. In response to perceptual PM, frontotemporal clusters had more negative local connectivity weights than all other clusters. Similarly, in response to conceptual PM stimuli over the 400–800ms model, the frontotemporal clusters had more negative connection weights than most other clusters. Potentially the negative connection weights reflect the RON reported over these time ranges in Chapter 6. Therefore, these results provide further support for the suggestion that reorientation networks become active when an individual is distracted from the ongoing task by a PM stimulus, subsequently engaging frontotemporal region.

8.4.5 Limitations

The current study used a 50/50 positive to negative connection ratio to initialise the SNN models. While this provided a better rate of learning within the current study than the more commonly used 80/20 ratio (Capecci et al. 2016; Doborjeh et al., 2018), other configurations were not tried. Potentially there may have been better positive to negative ratios for modelling ERP data that would enable better classification of brain activity between the groups. Therefore, future researchers are encouraged to incorporate the experimentation of different initial connection weight ratios during the optimisation stage in SNNs.

While the clustering method used in the current study had the advantage of reducing the number of multiple comparisons made during the statistical analyses, more information could be gained from including all input features (i.e., EEG electrode locations) during the network analysis. This would have created more connections and enabled more nuanced interpretations of connectivity, especially given the ability of adaLASSO to deal with more variables than observations (Meinshausen & Yu, 2009; Zhao & Yu, 2006). The method used here may have overrepresented differences in cortical connectivity because of the induced sparsity of adaLASSO to select the most important connections of the networks. Better interpretations may be achieved through different network analysis techniques, such as weighted and group LASSO.

8.4.6 Future studies

The current chapter proposes the utility of comparing cortical connectivity in those with MCI between simple cognitive tasks and more cognitively demanding tasks. Future research should explore other cognitive domains that can be varied in their difficulty to confirm the differences in hypo- and hyper-connectivity in MCI. It would be expected that as cognitive decline progresses, the more challenging cognitive tasks will also be associated with decreases of functional connectivity in line with the declines found in AD (Engels et al., 2015).

A previous study exploring ERPs within a SNN framework (Z. G. Doborjeh, Doborjeh, et al., 2018) has developed a novel way of understanding the differences between cognitive task conditions. By subtracting the spatiotemporal connections of one condition from the other the differences between the cognitive conditions were better visualised. This was not feasible in the current study due to the different initialised connection weights between the task conditions, but future studies of working memory and PM should employ a similar method to clearly identify spatiotemporal differences between the memory domains.

8.4.7 Summary

To conclude, the current study shows that the spatiotemporal connectivity in working memory and PM tasks can be modelled and visualised using SNNs to gain an increased understanding of the effects of ageing and cognitive decline. The SNNs demonstrated that classification accuracy of brain activity related to working memory and PM is better than conventional ML methods. Moreover, STBD in response to PM stimuli provides better classification accuracy than working memory in SNNs. Visualisation of the task-based memory activity can be improved through pruning of inactive ANs and neural connections in the SNN models. Analyses of the SNN models revealed different spatiotemporal connectivity between the groups at a local and global level. In general, local cluster connectivity was greater for younger adults but older adults had increased connectivity in frontal clusters during the perceptual PM models. The older adults with MCI had decreased global connectivity relative to healthy older adults and younger adults in the working memory and perceptual PM, but in the conceptual PM

models, MCI patients had increased cortical connectivity potentially reflecting compensatory mechanisms during a more cognitively demanding PM task.

Chapter Nine: General Discussion

9.1 Thesis Overview

The current thesis seeks to understand the neurophysiology of PM in younger adults, typical ageing older adults and those with MCI. The first two chapters presented the previous understanding of the cognitive and neurobiological aspects of PM, in particular, how PM is affected by ageing and cognitive decline. This was followed in Chapter 3 by a detailed description of the neurophysiology of ERPs related to PM, ageing and MCI. From these discussions a series of questions were formulated and addressed throughout the thesis:

1) Are there differences between behavioural and neurophysiological responses when responding to perceptual and conceptual PM stimuli?
2) Following the response to a PM stimulus, is there a RON ERP?
3) Are there behavioural and neurophysiological differences between younger and older adults when completing a perceptual and conceptual PM task?
4) Are there behavioural and neurophysiological differences between younger, healthy older adults and older adults with MCI when maintaining a PM intention?
5) Can SNNs be used to discriminate brain activity of aged individuals from those experiencing MCI and young adults?
6) Do SNNs discriminate brain activity better between groups better when using brain activity in response to PM compared to working memory? Additionally, can SNNs classify brain activity of young adults, older adults and older adults with MCI better with PM than working memory stimuli.

This thesis used ERPs to study PM because it offers a direct measure of the underlying cortical activity. Moreover, ERPs offer better temporal resolution closer to the speed of cortical processes than other neuroimaging methodologies. Prior to addressing the primary research questions, in Chapter 5, the question of whether it is appropriate to average the ERPs in response to different ongoing task stimuli was addressed in young adults. Findings from that chapter suggest that ERPs related to ongoing working memory tasks should be treated as separate. This conclusion was evidenced by

differences at the anterior P2 and posterior N2, along with a centroparietal congruency effect (N400) between the related and unrelated stimulus types. The findings suggest that in previous studies that combine ongoing task ERPs may have masked PM effects (e.g., Cousens et al., 2015) and instead supports the conclusions made in other studies (Cruz et al., 2016; Cruz San Martin, 2014). Addressing the main research aims, Chapter 5 demonstrated that behaviourally, participants performed the perceptual PM task better than the conceptual PM task. Moreover, the study demonstrated neurophysiological differences between perceptual and conceptual PM tasks. Finally, Chapter 5 provided the first evidence of a RON in PM tasks.

In Chapter 6, healthy older adults and older adults with MCI were recruited to understand the behavioural and neurophysiological differences between response to perceptual and conceptual PM stimuli. Older adults with MCI had poorer performance in the ongoing working memory task and the conceptual PM task relative to the young and older adults. Moreover, older adults with MCI had reduced frontocentral P2 amplitudes across all stimulus types and delayed RON responses relative to younger and older adults. While no behavioural differences were found between the young and older adults, the older adults did have reduced and delayed IRR ERPs. However, both older adult groups demonstrated greater cue detection responses (i.e., greater N300 and frontal positivity amplitudes) relative to young adults.

Chapter 7 explored the effects of monitoring for a PM cue on the ongoing working memory task in young adults, older adults and older adults with MCI. Relative to young and older adults, older adults with MCI had poorer ongoing task performance regardless of whether they were monitoring for a PM cue. Furthermore, the MCI participants had reduced frontocentral P2 amplitudes in response to all ongoing stimuli regardless of PM monitoring relative to older adults. Both older adult groups demonstrated larger sustained frontal amplitudes between 300–500ms and 600–1000ms relative to young adults. Moreover, older adults demonstrated delayed N2 amplitudes in response to ongoing stimuli when monitoring for perceptual PM cues relative to the young adults.

When measuring ERPs, much of the spatial and temporal information is not analysed as researchers often only examine specific electrodes and ERP subcomponents. To overcome these limitations, a brain-inspired SNN architecture was used in Chapter 8 to incorporate a full range of the spatial and temporal dimensions of the recorded ERP

activity. SNNs were able to classify brain activity from each of the three groups better than traditional machine learning techniques. Additionally, the results demonstrated that SNNs were better at classifying patterns of brain activity in response to PM stimuli relative to the ongoing working memory stimuli. Chapter 8 also explored the application of network analyses to the SNN models to gain a deeper understanding of the connectivity differences between the groups across the cortex.

The current chapter discusses these findings and how they improve our understanding of PM in typical and atypical ageing. Additionally, the application of SNNs and network analyses are discussed in relation to understanding STBD. Finally, the limitations are discussed alongside avenues for future research.

9.2 The effect of prospective memory cue type

9.2.1 Prospective memory cue detection

The current thesis does not support some of the conclusions made by other ERP studies comparing perceptual and non-perceptual PM cue types (Cousens et al., 2015; Wilson et al., 2015). Cousens et al. (2015) and Wilson et al. (2013) suggest that non-perceptual PM cues do not produce an N300 cue detection response. However, the results of Chapter 5 found that cue detection responses were indeed found for the non-perceptual (conceptual) PM cues. The results here instead support those found by Cruz et al. (2016), which suggest that an N300 response is produced in response to conceptual PM stimuli, but it might be delayed by 100ms. The results of Chapter 6 found that at midline parietal and occipital clusters the N300 in response to conceptual PM cues were indeed delayed relative to the ongoing and perceptual PM stimuli, although this was only for young adults. The current thesis, therefore, suggests that cue detection responses are a reliable feature of PM, but their temporal onset may depend on the characteristics of the PM cue. Potentially, the delayed N300 in both the current thesis and Cruz et al.'s (2016) study are delayed because of the semantic features of the conceptual PM stimuli, which occurs approximately at 400ms (review; Kutas & Federmeier, 2011). Therefore, cue detection is likely to have only taken place when the semantic features of conceptual PM stimuli have been processed.

Chapter 5 demonstrated that cue detection responses to perceptual PM stimuli were greater than those to conceptual PM stimuli (i.e., a more negative N300 and a more positive frontal positivity). It was suggested that the highly salient features of the perceptual PM cue triggered the greater response. This concurs with findings showing increased cue detection amplitudes of the P3 in response to highly salient stimuli (Honbolygó & Csépe, 2013). However, the larger amplitudes of the perceptual PM task might be due to decreased relative amplitudes to the conceptual stimuli as a result of additional attentional demands. Chapter 7 demonstrated a greater PM interference effect on the working memory task when monitoring for PM cues, suggesting that attention processes are being consumed when monitoring for conceptual PM cues. The additional attentional requirements applied when monitoring for conceptual PM stimuli may have reduced the amplitude of the cue detection responses. Indeed, West et al. (2006) demonstrated that PM-related cue detection components are sensitive to working memory demands. In their study, the amplitude of the N300 was found to be reduced when PM cues were embedded within a 3-back working memory task relative to a 1-back task. This suggests that the attentional processes of the working memory task and PM task are shared and underlie prospective remembering (Smith, 2003). The current thesis extends West et al.'s (2006) findings by suggesting that the level of attentional processes required to monitor for a PM cue may affect the amplitude of the N300 and frontal positivity cue detection responses.

9.2.2 Prospective memory intention retrieval

Previous studies have examined the neurophysiology of responses to perceptual and non-perceptual PM stimuli (Cousens et al., 2015; Cruz et al., 2016; Wilson et al., 2013). In line with the previous research, the current thesis demonstrates that both conceptual and perceptual PM stimuli reliably produce a parietal positivity response. The current thesis extends the previous research in three ways: 1) the different subcomponents of the parietal positivity were explored; 2) the latency of the IRR onset was explored; 3) the IRR ERP in response to perceptual and conceptual PM was examined in older adults.

The results of Chapter 5 revealed a distinct P3b response to the perceptual PM stimuli. However, in response to conceptual PM stimuli, the P3b was found to be absent. This

may be due to the semantic nature of the conceptual PM cue and therefore may have been more apparent at a different scalp region or later in time (Cruz et al., 2016).

Although the IRR was found in response to both PM stimuli and both young and older adult groups, there were differences between IRR responses for the different PM cue types. Both Cousens et al. (2015) and Wilson et al. (2013) suggest there are no differences in IRR responses to conceptual and perceptual PM responses. However, this thesis suggests that the IRR ERP has reduced amplitudes and a delayed onset relative to perceptual PM stimuli. This may suggest that due to the distinct features of the perceptual PM stimuli, more efficient and faster recall of an encoded intention was enabled. Considering the earlier N300 response to perceptual PM stimuli relative to the conceptual stimuli, it might be suggested that the earlier intention recall (IRR) is facilitated by the earlier cue detection response (N300). This likely explains why the perceptual PM stimuli were responded to faster and with greater accuracy. However, this was not explored directly in the current thesis and therefore the relationship between the N300, IRR and behavioural performance should be further investigated. Moreover, due to the greater reaction time variability in response to the conceptual PM stimuli relative to perceptual PM stimuli, there is the possibility that the amplitudes have been attenuated as a result of ERP blurring. When reaction times and the coupled neurophysiological responses have greater variability, then, as a result of ERP averaging, component amplitudes can be artificially reduced (Ouyang et al., 2016). Therefore, due to the higher variability in the reaction times to conceptual relative to perceptual stimuli, the ERP components in response to conceptual PM stimuli may have been attenuated.

Additionally, recent research has suggested that the neurophysiological markers of intention retrieval may extend beyond the 1000ms post-stimulus onset examined in this thesis and previous studies. Recent evidence suggests that frontal and parietal slow waves up to 1800ms may also be related to intention retrieval (Hering et al., 2020; Hering, Kliegel, Bisiacchi, et al., 2018). It would be useful, therefore, for future research to explore these later cognitive components with different PM cue types.

9.2.3 Prospective memory monitoring

Behavioural research has demonstrated an interference effect of PM on the ongoing task (Boywitt & Rummel, 2012; Hefer et al., 2017; Hicks et al., 2005; Marsh et al., 2005), often finding increased reaction times and decreased accuracies when monitoring for PM cues. Concordantly, the current behavioural results (Chapter 7) demonstrate poorer ongoing task performance in the young and both older adults during PM cue monitoring, as indicated by slowed reactions times for the ongoing task. In line with previous research (Loft & Remington, 2010; Scullin, McDaniel, Shelton, et al., 2010; R. E. Smith & Loft, 2014), this was particularly the case for the less perceptually distinct, conceptual PM cues, which also showed a decrease in successful responses. Thus, current interference effect findings support the PAM theory of PM (Smith, 2010), in that attention is indeed required to perform both a perceptual and conceptual PM tasks.

Neuroimaging evidence (presented in Chapter 2) suggests the importance of the frontal cortices in PM monitoring (review: Cona et al. 2015), the function of which was previously proposed to be reflected in the N2 and P2 components (Cona, Arcara, et al., 2015; Czernochowski et al., 2012; J. B. Knight et al., 2010; West, 2007; West et al., 2006a), and in later frontal ERP deflections (Cona et al., 2012b, 2014; Czernochowski et al., 2012; Hering et al., 2020). This thesis provides further evidence of the effects of PM monitoring on the early ERP components and suggests that attentional processes are required during PM maintenance. However, unlike previous studies (Chen et al., 2009; Czernochowski et al., 2012; J. B. Knight et al., 2010), the current findings do not support increased N2 and P2 amplitudes during PM maintenance. Nevertheless, the results do offer some support to a monitoring cost, as N2 components were found to be delayed when monitoring for PM cues compared to the ongoing-only task. To the author's knowledge, this is the first evidence of delayed ERP component latencies during PM monitoring. Given the relationship between the posterior N2 and reaction times (Bahramali et al., 1998; Bostock & Jarvis, 1970), the N2 delays found here when monitoring for PM cues may suggest that the N2 is related to the increased reaction times in the ongoing task during PM monitoring. Therefore, when monitoring for PM cues, perceptual attentional processes may be slowed.

In contrast to previous research (Czernochowski et al., 2012), P2 amplitudes were not found to increase but instead decreased when monitoring for PM cues relative to the

ongoing-only task. Additionally, when monitoring for conceptual PM cues, the P2 latencies were found to be delayed relative to the ongoing-only task. Possibly, this is explained by the relationship of the anterior P2 to feelings of knowing (Irak et al., 2014; Irak, Soylu, Turan, et al., 2019). That is, P2 amplitudes were reduced due to uncertainty in the ongoing task whilst the stimulus is evaluated as being a PM cue or not (Lin et al., 2017; Tanovic et al., 2018). The shared features of the conceptual PM stimuli to ongoing task stimuli may have increased the perceived uncertainty in evaluative processes and subsequently delayed the P2 response. Based on these findings, it is recommended that future studies should evaluate delays to the earlier ERP components during PM monitoring.

It was expected that PM intention maintenance would cause significant frontal modulations relative to the ongoing-only task (Cona et al., 2012b, 2012a; Czernochowski et al., 2012; Mattli et al., 2011). Indeed, the results from Chapter 7 demonstrate that PM cue monitoring affects sustained anterior amplitudes. The results, therefore, appear to support the Gateway hypothesis (Burgess et al., 2007; 2011) and AtoDI models of PM (Cona et al., 2015), which highlight the importance of the frontal cortices in intention maintenance. In line with previous ERP research (West et al., 2011; Hering 2020), the ERP amplitude deflections found in response to PM cue monitoring may reflect a retrieval mode, where preparatory processes induce a 'readiness-state' for the appearance of a PM cue (Guynn, 2003; West et al., 2011). During PM cue monitoring, participants will be maintaining the intention and monitoring the ongoing task for potential PM cues. Considering that cognitive resources are finite, the application of the frontal attentional resources may have contributed to the behavioural costs incurred to the ongoing task.

Based on previous research (Burgess et al., 2005; 2007), it was proposed that the perceptual PM stimuli would rely more on spontaneous retrieval processes; and the that the frontal ERP amplitudes during conceptual PM cue monitoring would be greater than when monitoring for the perceptual PM cues. However, this hypothesis was not supported by the current findings (Chapter 7). It is suggested that the activation of frontal cortices (attentional processes) during PM may be independent of cue features in line with the PAM theory (R. E. Smith, 2003; R. E. Smith & Bayen, 2004).

In sum, this thesis suggests that the additional feature-based processing that is required during PM cue monitoring may slow the reaction times in the ongoing task.

However, decreases to feelings of knowing and certainty from the shared features of the conceptual and ongoing task may cause delays to the anterior P2. Furthermore, this thesis suggests frontal processes are required to maintain a PM intention, regardless of the cue type. However, it should be noted that the current study used laboratory-based PM tasks; and the continual maintenance of PM intentions with day-to-day functioning may be context-dependent. Thus, future studies should seek to better simulate real-world PM events that better represent contextual information (e.g., virtual-reality).

9.3 The reorientation negativity in prospective memory

Studies by Bisiacchi et al. (2009) and West et al. (2011) demonstrated that attention allocation is required when switching from the ongoing task to the PM task. Bisiacchi and colleagues' study (2009) found that when switching from the ongoing task to the PM task the amplitudes of the parietal positivity were more positive than they were in a dual-task PM condition. However, no studies had previously explored the RON ERP component in a PM task to evaluate the reorientation of attention from the PM cue back to the ongoing task.

Chapter 5 provides the first evidence of a RON following the response to a highly salient perceptual PM stimulus and a less salient conceptual PM stimulus. Considering the previous evidence suggesting that the RON is related to processes of reorienting attention (Munka & Berti, 2006), the results from this thesis suggest that attentional reorientation following PM responses is measurable in the ERP. Given that both stimulus types show a RON following successful PM cue responses, this suggests that this may be a common feature in event-based PM tasks. However, as previously discussed, the RON in response to both PM stimulus types seems more likely to reflect a common neural response shared between distraction and attention reorientation rather than reflecting specific PM-related processes. Future research may confirm the presence of a RON in PM tasks by comparing successful PM ERPs with ERPs related to PM misses. This was not feasible in the current thesis due to the low number of PM misses. It would be expected that the RON would only be detectable in correct PM ERP responses and would be absent in events where participants forgot to respond to the PM cue.

It was expected the RON response would be found over the anterior regions of the scalp following a PM stimulus in line with studies of distraction (Correa-Jaraba et al., 2016; Escera et al., 2001). Chapter 5 partially supports the previous literature identifying a RON at bilateral frontotemporal clusters occurring at approximately 600ms after stimulus onset. The results suggest that the RON is also found at frontotemporal scalp regions in older adults, although predominately over the left hemisphere. However, Figure 5.4 also suggests that the RON following PM stimuli is observable at other locations. For example, in response to perceptual PM stimuli, a negative deflection between 400–600ms in the left inferior parietal cluster can also be seen. In response to conceptual PM stimuli, a negative deflection in the bilateral frontal clusters is evident between 400–800ms. The results here suggest then that there might be common neural generators of the RON following a PM stimulus, but may recruit additional cortical sources depending on the features of the cue.

While both PM stimulus types produced greater frontotemporal RON amplitudes relative to ongoing stimuli, the perceptual PM stimuli produced greater RON amplitudes and were associated with faster ERP latencies than the conceptual PM stimuli. In Chapter 5, it was suggested that the non-focal features of the perceptual PM task caused the greater RON response due to increased processes required to reorient attention back to the ongoing task. This conclusion supports some research suggesting that the RON amplitude is related to the level of deviance from the ongoing task (Berti et al., 2004; Yago et al., 2001). However, similar to the attenuation of the cue detection responses in the conceptual PM task, the RON amplitude may have also been reduced due to increased involvement of cognitive processes. Indeed, Berti and Schröger's (2003) study suggests that the RON amplitude decreases in line with increases in the working memory demands of the ongoing task. Additionally, considering the IRR latency delay in response to conceptual PM stimuli relative to perceptual stimuli, it would follow that the RON would also be delayed. This delay would be expected as the reorientation of attention from the PM task to the ongoing task cannot occur until the intention has been recalled.

Therefore, the results in the current thesis suggest that the RON is apparent in younger and older adults during event-based PM tasks. However, it remains to be confirmed whether in response to different PM cues, different cortical sources are recruited to reorient attention back towards the ongoing task and the degree to which the latencies and amplitudes are affected by involvement of cognitive processes.

9.4 The impact of ageing on prospective memory

Contrary to other laboratory-based PM studies (e.g., Henry et al., 2004; Kliegel et al., 2016; Kliegel, Jäger, et al., 2008; McDaniel et al., 2008), the older adults in the current thesis showed no behavioural impairments in reaction times or accuracy when completing the PM and ongoing tasks compared to the young adults. Based on previous research (Cherry et al., 2001; Eusop et al., 2008), it was expected that the behavioural performance would not differ between young and older adults in the perceptual PM task due the high salience of the cue, however, performance decrements were expected for the conceptual PM stimuli. It is possible that the ongoing semantic judgement task was relatively simple for the older adults. The lack of difference between young and older adults in the lexical decision task appears to support the stability of vocabulary and crystallised intelligence in older adults (D. C. Park et al., 2002). Therefore, the comparable performance of the older adults to the younger adults may be explained by relatively low involvement of the attentional processes required to complete the working memory task, which could, therefore, be directed towards the completion of the PM task (Rendell et al., 2007). However, the current thesis kept the working memory demands the same across the experiments and, thus, this conclusion remains speculative.

It might be proposed that the older adults were employing compensatory neural processes to complete the prospective memory tasks. Chapter 6 shows that both older adult groups had greater cue detection responses (more negative N300 and more positive frontal positivity) relative to young adults. This contrasts some previous PM ERP studies (R. E. Smith & Bayen, 2006; West & Covell, 2001) which suggest attenuations of the cue detection ERP components in older relative to younger adults. However, these are often accompanied by performance deficits in the working memory task, which was not found within the current thesis. Therefore, in line with the compensation-related utilisation of neural circuits hypothesis (CRUNCH) theory of ageing (Reuter-Lorenz & Cappell, 2008), cue detection related ERPs of greater amplitude likely support the completion of the tasks. That is, it is argued that the recruitment of frontal networks supports the maintenance of intentions (Peira et al., 2016). Indeed, Chapter 7 provided evidence to support this interpretation. Relative to young adults, older adults had significantly more positive amplitudes at both the 300–

500ms and 600–1000ms epochs suggesting that, in general, older adults were relying on frontal processes to a greater degree.

Despite the results suggesting a compensatory neural mechanism in cue detection, the results also show that the N300 latencies were delayed in the older adults compared to the young adults. This may have contributed to delayed latencies found in IRR in the older adults relative to the young adults. Interestingly, the relative delays of the cue detection responses were not related to the PM performance. Moreover, consistent with previous research (West & Bowry, 2005; West & Covell, 2001; Zöllig et al., 2007), the IRR amplitudes were found to be reduced in the older adults relative to young adults. Given the absence of performance deficits in the older adults relative to young adults, it is suggested that IRR amplitude reductions are indicative of neural dedifferentiation, in line with previous research (Goh, 2011). This implies that cortical activity in older adults has become less efficient and the activity has become more distributed, potentially to compensate for the reduced cortical efficiency. The topographic maps presented in Chapter 7 (e.g., Figure 7.3) provide further support for the neural dedifferentiation hypothesis in older adults, showing that relative to younger adults, cortical activity appears more distributed. The current thesis, therefore, adds further support to studies linking better performance with reduced neural distinctiveness in working memory tasks (Iordan et al., 2018) and suggests that this may be apparent in PM as similarly reported in episodic memory (M. Y. Chan et al., 2014).

The neurophysiological evidence of the current thesis appears to suggest age-related disruptions to attentional networks. Sustained frontal activity during intention maintenance was found to differ between young and older adults in line with previous research (Hering et al., 2016, 2020; Zöllig et al., 2007). The older adults were found to have increased amplitudes during the early and late frontal ERP modulations. In line with recent fMRI evidence (Gonneaud et al., 2017), it is suggested that this represents an inability to deactivate that aPFC during PM monitoring and a difficulty in the efficient allocation of attentional processes between the ongoing stimuli and the PM intention.

Moreover, the results also demonstrated delayed N2 ERP latencies in response to the perceptual cues for older adults relative to the young adults. This is thought to reflect a slowing of feature-based attention. Together, these results suggest that there may be

attentional network impairments in the older adults, but it may not be disrupted enough to affect working memory or PM performance.

The results from Chapter 6 demonstrated age-related differences in the RON. Compared to young adults, older adults had reduced RON amplitudes for both conceptual and perceptual PM stimuli and delayed latencies for the perceptual PM stimuli. Furthermore, in older adults, the RON was found to be left lateralised. The findings by Cona et al. (2013) similarly found age-related latency delays for the RON. Cona and colleagues suggest that this was a result of deficits in the ability to shift attention between stimuli. Considering 1) the sustained frontal ERP deflections during intention maintenance, 2) the delays to N2 latencies, and 3) the amplitude reductions and delays of the RON, the current thesis suggests that the neurophysiological basis of attentional networks may be affected in ageing. However, in the current PM task design, this may not have caused behavioural impairments due to the stable vocabulary and crystallised intelligence of the older adults and the recruitment of compensatory neural mechanisms.

9.5 The impact of mild cognitive impairment on prospective memory

Based on behavioural evidence (Blanco-Campal et al., 2009; Kliegel, Jäger, et al., 2008; Thompson et al., 2017; van den Berg et al., 2012), it was expected that older adults with MCI would be impaired in PM. Indeed, the results from this thesis suggest that older adults with MCI are impaired in some PM tasks. More specifically, participants with MCI had poorer accuracy relative to typically ageing adults in the conceptual PM task but not in the perceptual PM task (Chapter 6). This partially supports the conclusions made by Blanco-Campal et al. (2009), suggesting that greater performance deficits are found in less perceptually salient PM stimuli. However, findings from their study also suggests that participants with MCI had poorer performance in the perceptually distinct PM task. Furthermore, the behavioural results from Chapter 6 contrast with Thompson et al.'s (2017) study, which suggests that older adults with MCI have poorer PM performance relative to older adults regardless of the cue saliency. Instead, the current results suggest that older adults with MCI may not have impaired PM performance if the PM cue is highly salient. The high saliency of the PM

may enable older adults with MCI to easily detect the cue and recall it from memory. Indeed, the ERP results from Chapter 6 suggest that PM cue detection responses are spared in MCI to a similar level to the older adult group.

Given evidence in MCI for atrophy in regions such as the insula (Caroli et al., 2010; Davatzikos et al., 2011; Fan et al., 2008; Spulber et al., 2012), PCC and MTL (Das et al., 2016; L. Zhang et al., 2019), it was expected that participants with MCI would have reduced retrieval related ERPs (i.e., IRR). Contrary to expectation, the ERP evidence showed no differences between older adults with and without MCI in IRR. This may suggest that the ability to recall a PM intention is spared in cognitive decline. However, the results did show a trending effect for delays in the IRR ERP in the participants with MCI relative to the older adults. It is possible that there may be delays in some individuals with MCI when recalling an intention, reflecting declines in the efficiency of retrieval networks in PM. This may potentially have not reached significance because of the heterogeneity of the MCI group, such that participants were not differentiated by MCI subtypes (e.g., aMCI, naMCI). Previous studies have shown that during certain PM task designs older adults with aMCI are more impaired than those with naMCI (e.g., Chi et al., 2014). Therefore, it is recommended that future research explore whether ERPs related to intention retrieval are spared in different forms of MCI.

The results from Chapter 7 suggest that PM intention maintenance in those with MCI is comparable to typically ageing adults. The ERP evidence did not demonstrate any amplitude modulations for the older adults with MCI relative to the healthy older adults when monitoring for a PM cue. Considering the similar neurophysiological activity between the MCI participants and healthy older adults, alongside the lack of further performance declines in the ongoing task when monitoring for PM cues, it may be suggested that PM intention maintenance is spared in MCI. Potentially, this may indicate that activity of the anterior prefrontal cortex, that is responsible for PM intention maintenance (Cona et al., 2015), is unaffected in MCI. However, given the reported disruptions of connectivity between the hippocampus and the aPFC in AD (L. Wang et al., 2006), the ability to maintain a PM intention might provide a useful measure for monitoring cognitive decline. That is, as connectivity to the aPFC deteriorates, it would be expected frontal amplitudes during monitoring for PM cues would decline relative to typical ageing older adults.

Older adults with MCI had poorer ongoing task performance regardless of whether they were monitoring for a PM cue. It was expected that given the additional processes required for PM cue monitoring, ongoing task performance would be disproportionally affected in those with MCI. However, the results did not support this hypothesis. This may suggest that semantic working memory performance was already impaired to such a degree that the additional task of monitoring for a PM cue did not further disrupt working memory performance further. The poorer working memory performance may coincide with the attenuations found in the frontocentral P2 amplitudes in the participants with MCI relative to the healthy older adults. As it currently stands the functional relationship of the frontocentral P2 is yet to be fully understood. However, considering recent research suggesting that the anterior P2 is related to a peri-perceptual sense of familiarity (Doborjeh et al., 2018) and feelings of knowing (Irak et al., 2014; Irak, Soylu, & Turan, 2019; Irak, Soylu, Turan, et al., 2019), it may be suggested that older adults with MCI have reduced general familiarity during memory tasks. However, given that all the stimuli in this thesis were words, it is possible that a reduction in familiarity in those with MCI is limited to semantically-based tasks. The P2, therefore, may be a potentially useful biomarker in understanding cognitive decline and future studies are required to understand its functionality and relationship to dementia-related diseases and PM.

The current work is the first, to the author's knowledge, to examine a RON response in older adults with MCI. Findings suggest delays in RON in those with MCI relative to young and typically ageing older adults. This suggests that older adults with MCI have neurophysiologically-reflected impairments in their ability to reorient their attention back to the ongoing stimuli following a perceptual PM stimulus. The lack of behavioural impairments in the perceptual PM task, or further impairments in the ongoing working memory task when monitoring for perceptual PM cues, may suggest that attentional networks are disrupted before noticeable behavioural impairments.

Neuroimaging evidence suggests that attention networks during task-switching are a sensitive marker of AD (Gordon et al., 2015; Oh et al., 2016). Therefore, irrespective of identifiable behavioural impairments, the delayed RON might provide an effective early biomarker of cognitive decline. Future research should seek to confirm RON delays in both PM tasks and distraction tasks in older adults with MCI. Given that the delay was found following the perceptual PM stimuli and not the conceptual PM

stimuli, those stimuli which are more deviant (i.e., are less similar to the ongoing task) might elicit the clearest RON delays in the older adults with MCI.

9.6 Spiking neural networks and network analyses for understanding spatiotemporal brain data

Chapter 8 proposed using a novel SNN architecture for modelling, visualising and understanding spatiotemporal ERP activity between young adults, older adults and older adults with MCI. This chapter built on the proposed SNN architecture proposed by Doborjeh et al. (2018) for modelling ERP activity within a 3D brain-inspired space. This chapter demonstrated, for the first time, that ERPs in response to working memory and PM tasks can be modelled using SNNs from a high-density EEG recording. Additionally, the study highlighted the importance of using a 50/50 positive–to–negative connection ratio for initialisation of the network when modelling ERP data.

Using the classification functionality of SNNs, the study attempted to address whether PM-related brain activity would provide better classification accuracy than working memory-related activity. Indeed, the classification results of the perceptual PM stimuli (83.33%) and conceptual PM models (80%), provided better classification accuracy than the models of working memory (73.93%). This was suggested to be due to the additional attentional processes required to complete the PM tasks. Moreover, the classification results were compared against conventional ML methods of SVM, MLP and MLR. For the most part, the conventional ML methods achieved a classification accuracy of approximately 50%, except for the MLP for perceptual stimuli, which achieved 62.07%. This chapter demonstrates the efficacy of SNNs in discriminating brain activity between groups during ERP related to memory processes.

As seen in Figure 8.4, the amount of information propagated into the 3D network by the 128 channels caused a large amount of changes to the neural connections in the SNN models. With the pruning module proposed within the SNN architecture, the non-important connections (i.e., those connections and ANs that were not changed during learning stages) were removed. This reduced the number of connections within the model enabling easier visualisation of the spatiotemporal activity (e.g., Figure 8.7) and made the models more plausible and parsimonious. The application of this pruning method to a trained SNN model has the potential to enhance the visualisation across a

variety of neuroimaging data such as fMRI, functional near-infrared spectroscopy (fNIRS) or any other data containing spatial and temporal dimensions.

Chapter 8 is the first study to apply an adaLASSO network analysis to understand the patterns of activity in SNN models. Previous SNN studies exploring EEG activity have used feature interaction networks to understand the learnt patterns of activity of the input EEG channels (Doborjeh et al., 2018a,b). However, the analysis methods presented in Chapter 8 can induce sparsity and retain only the most important connections that explain network connectivity. This method is particularly useful for spatially rich data due to its ability to handle more variables than observations (Meinshausen & Yu, 2009; Zhao & Yu, 2006). The methods used in Chapter 8 also used a clustering method to reduce the number of cortical features that were analysed within the ANOVAs, but the network analysis holds the potential to model all input features (EEG channels in this thesis) of the SNN model. Furthermore, the network analysis could be applied to any group of ANs or all the ANs modelled within the SNN models. This could facilitate nuanced interpretations of the modelled spatiotemporal brain activity at any defined space and time.

The results from the network analyses revealed insights into MCI. The results demonstrated decreased global network connectivity in older adults with MCI in response to working memory and perceptual PM stimuli relative to young and older adults. However, global connectivity in the conceptual PM model demonstrated increased connectivity throughout the cortex for the MCI participants relative to the other groups. It is suggested that the increased global connectivity of the older adults with MCI served compensatory functions to complete the more challenging conceptual task. This supports previous research of functional connectivity demonstrating increased connectivity in MCI participants relative to controls as the demands of the memory task increase (Jiang & Zheng, 2006; Zheng et al., 2007). The current thesis, therefore, suggests that in MCI, the cortical connectivity is reduced relative to typically ageing adults during simple or resting-state tasks, but as task difficulty increases, the connectivity throughout the cortex will increase. However, it might also be further speculated that as task difficulty increases further to very high levels, the cortical connectivity of those with MCI would begin to decrease relative to controls for the most cognitively demanding tasks following an inverted-U shape of cortical connectivity. Future research should, therefore, continue to explore task-based

connectivity within MCI to understand the relationship between cognitive load and connectivity as a biomarker of cognitive decline.

The results of Chapter 8 add further support to the ERP results from the other chapters. Specifically, the results highlight the importance of the frontal cortices in the PM tasks, such that for both PM cue types the frontocentral clusters demonstrated high network control and had larger local connectivity cluster weights relative to other areas. Moreover, the older adults demonstrated increased local cluster connectivity in the frontal clusters relative to both young adults and older adults with MCI when processing the perceptual PM stimuli. This may reflect the suggested neural compensatory mechanisms demonstrated in Chapters 6 and 7.

Chapter 8 presents a novel method for understanding the spatiotemporal dynamics of memory processes. However, there are a few limitations that need to be considered. Firstly, creating SNNs with ERP data has intrinsic limitations due to the spatial resolution of the data. Due to the orientation of the cortical dipoles, it is difficult to determine whether the positive and negative changes in the SNN represent increases or decreased in connectivity. Additionally, as this is the first-time network analyses have been applied to SNNs, the accuracy of the networks compared to other methods of functional connectivity remains to be confirmed. Future research should compare the proposed methods of Chapter 8 relative to other neuroimaging methods and network analysis techniques.

9.7 Limitations

Some of the limitations of this thesis have been discussed in previous chapters relating specifically to those results. However, a few limitations that apply to each of the experimental chapters should also be acknowledged. Firstly, the conclusions of this thesis have been predominantly drawn with ANOVAs. While this conforms to methods used in much of the research conducted within the field of PM, understanding differences between variables can only provide a certain level of interpretation. As such, some of the conclusions regarding the functionality of PM and how it is impacted by ageing or cognitive decline remain speculative. Future studies could capture finer grained differences in the variables using regression analyses, which would enable the

statistical modelling of estimations of slopes or functions. For example, the influence of the N2 ERP latency on ongoing task reaction time could be examined.

Similarly, although the connections of the adaLASSO network analyses in Chapter 8 can be thought of as the most significant connections within each network, understanding the differences between networks remains largely qualitative and under the interpretation of the researcher. This is a pervasive problem in brain-network science (Khambhati et al., 2018). However, recent developments have enabled comparisons between network structures (van Borkulo et al., 2017). Van Borkulo et al. (2017) have developed a network analysis t-test, which offers the ability to quantitatively test the differences between networks via invariant network structure, invariant edge strength and invariant global strength. These test statistics provide a measure of whether networks are identical between populations, and whether there are differences in the edges and the strength of the entire network. However, given that this is a t-test, it remains to be determined how this might be applied effectively to more than two groups.

Potentially, there exist limitations here and within other PM experimental task designs that may have contributed to the differences found between the two forms of PM stimuli. Firstly, it is important to consider the potentially confounding factors of focality and salience of the PM stimuli. It is possible that the non-focal nature of the perceptual PM stimuli used here may have weakened the effects of the cue being salient. Evidence has demonstrated larger ERPs to be associated with focal PM cues relative to non-focal PM cues (Cona et al., 2014). Therefore, based on the Multiprocess framework of PM, it would be expected that the ERP amplitudes in response to the perceptual stimuli used here would have been attenuated in contrast to a perceptually salient, focal PM cue. Secondly, it is worth noting that there may be differences between the PM tasks that are not simply due to being either perceptual or conceptual. The perceptual PM task possessed one of two possible states that the stimulus could be in — uppercase or lowercase. In contrast, the conceptual PM task could be presented in 10 ways out of a possible 100 stimuli. The conceptual PM task may, therefore, have additionally taxed working memory resources and affected behavioural and neurophysiological responses. Future studies should seek to control such potential confounds. For example, equivalent non-focal perceptual stimuli might be used, which only varies in their saliency. One might include a highly salient

perceptual PM stimulus similar to what has been used in the current thesis and a less salient stimulus which only capitalises the first letter of the PM stimulus word.

Furthermore, a limitation that should be considered in the context of this thesis is that conclusions are drawn from designs of groups by membership and are, therefore, only quasi-experimental. In other words, the experimental design used here lacks the element of random assignment needed for a 'true experiment'. This lack of randomisation of participants to the different groups makes it harder to account for confounding variables and may affect the internal validity of the study (Robson et al., 2001). Therefore, we cannot know for certain to what extent the group differences found within the current thesis are caused by group membership or other uncontrolled variables. Longitudinal studies or TMS to simulate cognitive impairments might be used to improve the reliability of quasi-experimental designs of ageing and MCI.

A considerable limitation that concerns many experiments with older adults experiencing MCI is the relatively small sample size. The small sample size of the MCI group provides less statistical power to observe differences between the groups. As mentioned previously, deriving conclusions from a heterogeneous group, such as those with MCI is problematic due to the different cognitive impairments, which has led to the diagnosis and the potential for different types of MCI and their propensity to convert to AD (Vos et al., 2013). The current thesis did not further differentiate individuals with MCI into subtypes to retain as much statistical power as possible. Ideally, the differences between the different subtypes should also be examined in PM by recruiting larger samples of older adults with MCI and testing participants longitudinally.

9.8 Future studies

9.8.1 Prospective memory encoding in mild cognitive impairment

The current thesis has attempted to provide further understanding of how PM functioning is neurophysiologically affected by MCI in older adults. In Chapter 2 (*Section 2.6*) it was suggested that the individuals with MCI would most likely to be impaired in the retrieval stage of PM. However, an important task feature that was outside the scope of this thesis is the encoding stage of PM.

The ability to recall an intention is routed in the initial ability to encode said intention. Recent evidence has demonstrated that PM performance deficits may be due to poor encoding strategies used by older adults with MCI (A. Pereira et al., 2015), which can be improved by employing different intention encoding strategies (A. Pereira et al., 2018). The neurophysiological impairments that might explain this poor encoding ability in those with MCI is yet to be understood. However, a neuroimaging study evaluating connectivity during memory encoding and retrieval in older adults with MCI presents a potential explanation (Hampstead et al., 2016). In an object location association task, which required participants to remember where objects were located within a visual scene, Hampstead and colleagues found that while healthy older adults activated regions of the frontoparietal networks, the MCI patients predominately relied on the right frontal eye field. The authors concluded that the MCI patients had a loss of top-down control during encoding and instead relied more on basic visual search functions. Therefore, deficits in attentional networks during encoding of PM intentions might potentially underpin poorer PM performance. Furthermore, this may explain why the reduction in familiarity indicated by frontocentral P2 amplitude reductions in those with MCI was found in Chapters 6 and 7. Indeed, evidence has shown that if top-down attentional mechanisms are impaired during encoding then familiarity is likely to be impaired in those with MCI (Ally et al., 2009).

To further extend the results of the current thesis, future research should evaluate the neurophysiological differences in PM encoding in older adults with MCI. Recent studies have explored the effects of encoding in younger and older adults (Hering et al., 2020; Hering, Kliegel, Bisiacchi, et al., 2018; Zöllig et al., 2010). Hering and colleagues' (2020) results show increased frontal slow waves for the older adult participants during

intention encoding between 400–700ms thought to be due to increased attention allocation (Walter & Meier, 2014). Perhaps, given the decreased attention allocation in older adults with MCI (Ally et al., 2009), there may be decreased frontal slow wave activity in the participants with MCI. However, as highlighted in this thesis, the frontal P2 amplitude should also be explored during encoding in older adults with MCI.

9.8.2 Time-based prospective memory in mild cognitive impairment

The current thesis has focused exclusively on event-based PM. Event-based PM cue types were used because it is the most well understood with regards to brain function and therefore provided the best reference to interpret the neurophysiological results of the studies documented here. However, several different PM cues types could also be used to understand PM deficits in MCI.

Behavioural studies have used time-based PM cues to understand PM in MCI (Gonneaud et al., 2011; Troyer & Murphy, 2007). Some studies have reported increased capacity of time-based PM tasks to discriminate between healthy controls and participants with MCI (Costa et al., 2015). Some evidence suggests that older adults with MCI are disproportionally impaired on time-based task relative to healthy controls (Costa et al., 2010). This is likely due to the increased attentional demands required to maintain and remember to perform an action without explicit cues (Brandimonte & Passolunghi, 1994; Maylor et al., 2002; D. C. Park et al., 1997). It would be expected then that maintenance stages during time-based PM would be particularly impaired in older adults with MCI. Cona et al. (2012) explored the neural correlates of time-based PM in young and healthy older adults. Their results found that along with poorer time-based PM performance, older adults demonstrated an increased PM interference effect when monitoring for PM cues. Similar to the results of Chapters 6 and 7, the neurophysiological results from Cona and colleagues' (2012) study also found increased frontal ERPs from 300ms onwards. It would be expected that given the poorer performance reported in time-based PM tasks, further frontal amplitude modulations would be found in older adults with MCI.

Future research should, therefore, explore whether the ERP components related to time-based PM intention retrieval and monitoring are affected in older adults with

MCI. To examine this, studies should employ a time-based PM design similar to Cruz et al. (2017). In Cruz and colleagues' study, the participants were required to perform an ongoing task (similar to the one used in the current thesis) and to also reset a clock every four minutes by a button press. The participants could also press a button to check the clock. However, this method could also be extended by including a PM condition that relies entirely on participants' time-estimation to perform the PM task and therefore would be cue-independent (Cruz San Martin, 2014). This would be feasible in older adults with MCI because generally, their perception of elapsed time does not seem to be impaired as a result of cognitive decline (Coelho et al., 2016; Rueda & Schmitter-Edgecombe, 2009), therefore, it would provide an appropriate measure of a cue free time-based PM.

9.9 Thesis conclusion

In summary, this thesis demonstrates that there are behavioural and neurophysiological differences between responses to a highly salient perceptual and a less salient conceptual PM cue. Specifically, the perceptual PM task is associated with better performance and produces greater PM-related ERPs relative to those for conceptual PM cues. Additionally, the conceptual PM cues are detected later, which cause delays to the intention retrieval related ERPs. The current thesis supports the PAM theory of PM, suggesting that both PM cue types require attentional processes to be detected and are not spontaneously recalled from memory. This is evidenced by an interference effect and neurophysiological 'cost' incurred in early and late ERP components relative to the ongoing-only task. The current thesis also demonstrates, for the first time, that RON ERPs are detectable following a PM stimulus. The RON was found in both young and older adults, and future studies should seek to determine whether a RON response is reliably found in other PM task designs (i.e., tasks that are not based on semantics).

This thesis suggests that older adults may have comparable PM task performance to young adults, but that they may require the recruitment of compensatory neural mechanisms. Furthermore, this thesis provides the first evidence of neurophysiological processing in PM tasks in older adults with MCI. The results indicate that conceptual PM may be particularly challenging for older adults with MCI.

However, the neurophysiological evidence suggests that PM intentional retrieval and maintenance may be spared in MCI. Instead, the neurophysiological evidence suggests that feelings of knowing (i.e., indicated by reduced anterior P2 amplitudes) and the ability to reorient attention (indicated by RON latency delays) may underpin the performance impairments found for the working memory and PM tasks. Future studies should further explore the functionality of the P2 in relation to PM and MCI.

Finally, the current thesis demonstrates for the first time that PM processes can be spatiotemporally modelled to gain a greater understanding of the differences between groups and provide insight into the nature of typical and atypical ageing processes. Moreover, the SNN architecture utilised in this thesis offers improved interpretability of the model's learnt patterns of activity.

In conclusion, this thesis applies novel SNN methods to provide important insights into the neurophysiology of PM, and age-related changes in brain mechanisms underpinning PM. It adds to an emerging body of literature using spatiotemporal brain dynamics to understand psychological and neurological conditions, supporting a classification advantage of SNN methods over traditional ML methods. This work offers improved understanding of the effects of typical and atypical ageing in PM and provides an important foundation for future research to understand the neurophysiology of PM in dementia-related diseases and the application of SNN techniques to understand memory-related processes.

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Appendix A: Spike-time dependent plasticity rule

$$F(\Delta t) = \begin{cases} A_+ \exp\left(\Delta t/\tau_+\right) & if\ \Delta t < 0 \\ -A_- \exp\left(-\Delta t/\tau_-\right) & if\ \Delta t \geq 0 \end{cases}$$

$F(\Delta t)$ describes the adjustment of synaptic plasticity with respect to the pre-synaptic and post-synaptic spiking time in the interval of $\Delta t = t_{pre} - t_{post}$. The parameters A+ and A- are the maximum amounts for synaptic adjustment, which apply if Δt is close to zero. The parameters τ_+ and τ_- control the interval of pre- to post-synaptic spikes during which the weakening and the strengthening of the synaptic connection occur.

Appendix B: Table of the defined clusters

Cluster	Electrode locations							
Left frontal	AF7	AFF5	AFF5h	FP1	AF3	AFF3h		
Right frontal	AFF4h	AF4	FP2	AFF6h	AFF6	AF8		
Mid frontal	AFFz	Fz	FFCz	FCz				
Left frontocentral	FC5h	FC3	FC3h	FFC5h	F3	FFC3h	FC1	F1
Right frontocentral	FC4h	FC4	FC6h	FFC4h	F4	FFC6h	FC2	F2
Left central	C3h	C3	C5h	C5	T7h			
Mid central	Cz	CCPz	CPz	C2h	CCP2h	C1h	CCP1h	
Right central	C4h	C4	C6h	C6	T8h			
Left frontotemporal	T7	FT7	F7					
Right frontotemporal	F8	FT8	T8					
Left parietal	CPP3h	P3	CCP1	CP5	CP5h	CP3	CPP5h	
Mid parietal	CPPz	Pz	PPOz	POz				
Right parietal	CPP3h	P4	CPP6h	CP6	CP6h	CP4	CCP2	
Left inferior parietal	TP7	TP7h	P5	P7	P9			
Right inferior parietal	P10	P8	P6	TP8	TP8h			
Left occipital	PPO5	PO7	PO9	PO11	O1	POO5	PO3h	
Mid occipital	POOz	Oz	OIz	Iz				
Right occipital	O2	POO6	PO4h	PPO6	PO8	PO10	PO12	

Electrodes locations are given in relation to the 10-5 system.

Appendix C: Chapter Five, Experiment 1.

Table C.1

Descriptions of P2, N2 and N400 Amplitudes across Stimuli, Cluster and Hemisphere.

P2		**1-back$_{nontarget}$**		**1-back$_{target}$**	
Cluster	**Hemisphere**	M (μv)	SD	M (μv)	SD
Frontal	Left	2.53	1.69	2.83	2.15
	Midline	3.56	1.34	4.07	2.26
	Right	2.57	1.50	3.02	1.72
Frontocentral	Left	3.81	1.19	4.07	1.53
	Right	3.46	1.11	3.91	1.42
Central	Left	2.51	0.85	2.67	1.07
	Midline	2.84	1.26	2.92	1.39
	Right	2.42	1.13	2.71	1.36
N2		**1-back$_{nontarget}$**		**1-back$_{target}$**	
Cluster	**Hemisphere**	M (μv)	SD	M (μv)	SD
Parietal	Left	-2.13	1.89	0.14	1.07
	Midline	0.30	1.24	0.27	1.29
	Right	0.49	1.00	0.46	1.12
Inferior Parietal	Left	-1.09	1.13	-1.38	1.43
	Right	-1.55	1.33	-1.67	1.99
Occipital	Left	-2.56	1.76	-2.67	1.85
	Midline	-2.86	1.91	-3.06	2.11
	Right	-2.13	1.89	-2.21	1.99
N400		**1-back$_{nontarget}$**		**1-back$_{target}$**	
Cluster	**Hemisphere**	M (μv)	SD	M (μv)	SD
Central	Left	0.41	1.45	0.15	1.59
	Midline	0.58	1.31	1.19	1.25
	Right	-0.17	1.18	0.40	1.29
Parietal	Left	3.15	1.51	3.61	1.65
	Midline	4.22	2.25	4.68	2.29
	Right	3.10	1.56	3.85	1.69

Appendix D: Chapter Five, Experiment 2.

Table D.1.

Descriptions of ERP N300 Amplitudes across Stimuli, Hemisphere and Cluster

Stimuli	Cluster	Hemisphere	M (μv)	SD
1-back$_{target}$	Parietal	Midline	1.62	1.77
	Inferior parietal	Left	-0.47	1.61
		Right	0.13	2.11
	Occipital	Left	1.21	2.15
		Midline	-0.01	2.43
		Right	1.36	2.39
1-back$_{nontarget}$	Parietal	Midline	1.36	1.58
	Inferior parietal	Left	0.62	1.54
		Right	0.38	2.10
	Occipital	Left	1.61	2.22
		Midline	0.28	2.14
		Right	1.53	2.20
PM$_{percept}$	Parietal	Midline	2.20	2.73
	Inferior parietal	Left	-1.53	2.23
		Right	-1.46	2.86
	Occipital	Left	0.73	3.03
		Midline	-1.16	3.03
		Right	0.26	3.10
PM$_{concept}$	Parietal	Midline	0.87	1.74
	Inferior parietal	Left	0.11	1.84
		Right	-0.26	2.19
	Occipital	Left	0.42	2.25
		Midline	-0.99	2.11
		Right	0.57	2.42

Table D.2.

Descriptions of Frontal Positivity ERP Amplitudes across Stimuli, Hemisphere, Cluster

Stimuli	Cluster	Hemisphere	M (μv)	SD
1-back$_{target}$	Frontal	Left	1.23	2.32
		Midline	1.76	2.14
		Right	2.16	2.84
	Frontocentral	Left	1.56	2.12
		Right	2.03	1.79
	Central	Left	1.64	1.44
		Midline	2.92	1.41
		Right	2.17	1.27
1-back$_{nontarget}$	Frontal	Left	1.24	3.40
		Midline	0.55	1.67
		Right	1.17	2.21
	Frontocentral	Left	1.26	1.53
		Right	0.92	1.55
	Central	Left	1.85	1.42
		Midline	2.27	1.48
		Right	1.48	1.21
PM$_{percept}$	Frontal	Left	1.62	2.78
		Midline	3.57	2.26
		Right	2.25	2.60
	Frontocentral	Left	3.54	2.15
		Right	3.57	2.39
	Central	Left	3.25	2.00
		Midline	6.30	2.59
		Right	3.70	1.93
PM$_{concept}$	Frontal	Left	2.44	2.48
		Midline	1.79	1.66
		Right	2.31	1.99
	Frontocentral	Left	2.42	1.70
		Right	2.05	1.67

	Central	Left	2.45	1.86
		Midline	2.60	1.99
		Right	2.07	1.45

Table D.3

Descriptions of P3b ERP Amplitudes across Stimuli, Hemisphere, Cluster

Stimuli	**Cluster**	**Hemisphere**	**M (μv)**	**SD**
1-back_{target}	Parietal	Left	2.46	1.54
		Midline	4.15	2.37
		Right	3.37	1.78
	Central	Left	1.24	1.10
		Midline	1.27	1.27
		Right	1.82	1.16
$1\text{-back}_{nontarget}$	Parietal	Left	3.15	1.51
		Midline	4.22	2.25
		Right	3.10	1.56
	Central	Left	1.91	1.44
		Midline	2.73	1.42
		Right	1.65	1.24
$PM_{percept}$	Parietal	Left	2.90	2.02
		Midline	4.94	3.49
		Right	3.72	2.00
	Central	Left	2.14	1.86
		Midline	3.48	1.90
		Right	2.31	1.67
$PM_{concept}$	Parietal	Left	1.96	1.35
		Midline	3.42	2.57
		Right	2.88	1.75
	Central	Left	1.42	1.63
		Midline	1.66	1.70
		Right	1.68	1.42

Table D.4

Descriptions of Intention Retrieval ERP Amplitudes across Stimuli, Hemisphere, Cluster

Stimuli	Cluster	Hemisphere	M (μv)	SD
1-back$_{target}$	Parietal	Left	3.61	1.67
		Midline	4.68	2.29
		Right	3.85	1.69
	Central	Left	1.78	1.37
		Midline	3.28	1.54
		Right	2.58	1.41
1-back$_{nontarget}$	Parietal	Left	3.15	1.51
		Midline	4.22	2.25
		Right	3.10	1.56
	Central	Left	1.91	1.44
		Midline	2.73	1.42
		Right	1.65	1.24
PM$_{percept}$	Parietal	Left	5.47	2.60
		Midline	8.35	4.30
		Right	6.67	2.44
	Central	Left	3.68	2.11
		Midline	6.93	2.61
		Right	4.16	1.80
PM$_{concept}$	Parietal	Left	3.59	1.71
		Midline	5.14	2.95
		Right	4.02	1.95
	Central	Left	2.78	1.90
		Midline	4.09	2.22
		Right	2.28	1.43

Table D.5.

Descriptions of Prospective Positivity ERP Amplitudes across Stimuli, Hemisphere, Cluster

Stimuli	Cluster	Hemisphere	M (μv)	SD
1-back$_{target}$	Parietal	Left	4.10	2.09
		Midline	5.02	3.00
		Right	4.64	2.15
	Central	Left	2.78	2.20
		Midline	2.86	2.60
		Right	4.51	1.79
1-back$_{nontarget}$	Parietal	Left	3.28	1.78
		Midline	4.35	2.30
		Right	3.38	1.48
	Central	Left	2.28	1.68
		Midline	3.02	1.86
		Right	2.63	1.37
PM$_{percept}$	Parietal	Left	6.13	2.14
		Midline	7.99	4.28
		Right	6.44	2.37
	Central	Left	4.93	2.54
		Midline	6.44	2.47
		Right	4.52	2.41
PM$_{concept}$	Parietal	Left	5.43	2.04
		Midline	6.16	3.12
		Right	5.13	1.98
	Central	Left	4.13	2.39
		Midline	5.33	2.56
		Right	3.32	1.46

Table D.5

Descriptions of Reorientation Negativity ERP Amplitudes across Stimuli and Hemisphere at Frontotemporal Clusters

Stimuli	Hemisphere	M (μv)	SD
1-back$_{target}$	Left	-1.95	2.69
	Right	-2.15	2.67
1-back$_{nontarget}$	Left	-1.64	1.60
	Right	-1.93	1.89
PM$_{percept}$	Left	-4.02	3.14
	Right	-4.82	3.09
PM$_{concept}$	Left	-3.18	2.73
	Right	-3.51	2.95

Appendix E: Chapter Six, ERP amplitude and latencies.

Table E.1

Means and Standard Deviations of P2 Amplitudes across Stimuli, Hemisphere, Cluster and Group

			YA		OA		MCI	
Stimuli	**Cluster**	**Hemisphere**	**M (μv)**	**SD**	**M (μv)**	**SD**	**M (μv)**	**SD**
1-back$_{target}$	Frontal	Midline	4.08	2.33	4.31	1.54	3.12	1.34
		Left	3.14	2.06	4.25	2.33	2.98	2.32
		Right	3.15	1.71	4.43	2.32	3.23	2.25
	Frontocentral	Left	4.13	1.52	4.35	1.49	3.47	1.18
		Right	3.90	1.41	4.30	1.58	3.13	1.29
	Central	Midline	3.97	1.27	3.85	1.77	3.11	0.99
		Left	2.68	1.06	3.10	1.95	2.78	1.05
		Right	2.75	1.38	2.81	1.41	2.65	1.16
1-back$_{nontarget}$	Frontal	Midline	3.58	1.32	3.70	1.73	2.91	1.40
		Left	2.82	1.52	346	2.36	2.99	2.32
		Right	2.58	1.53	3.65	2.13	3.11	1.57
	Frontocentral	Left	3.85	1.17	3.74	1.63	2.46	1.07
		Right	3.54	1.67	3.87	1.80	2.80	0.93
	Central	Midline	2.55	1.21	3.04	1.36	2.68	1.29
		Left	2.54	0.84	2.80	1.56	2.15	1.05
		Right	2.55	1.21	3.04	1.36	2.68	1.29
Ongoing + PM$_{percept}$	Frontal	Midline	3.58	1.46	3.82	1.57	2.67	1.39
		Left	2.56	1.47	3.14	1.59	3.66	3.83

		Right	2.60	1.47	3.25	1.27	3.40	3.65
	Frontocentral	Left	3.70	1.19	4.16	1.45	2.83	1.29
		Right	3.52	1.31	4.06	1.45	2.83	1.08
	Central	Midline	3.07	1.26	3.88	1.81	2.71	1.08
		Left	2.65	1.11	3.50	1.87	2.31	1.03
		Right	2.54	1.25	3.50	2.01	2.58	1.09
Ongoing + $PM_{concept}$	Frontal	Midline	3.58	1.37	3.74	1.81	2.56	0.88
		Left	2.90	1.62	350	2.19	2.42	1.24
		Right	2.69	1.52	3.41	2.37	2.66	1.37
	Frontocentral	Left	3.79	1.21	3.82	1.59	2.75	0.94
		Right	3.57	1.22	3.95	1.61	2.90	0.79
	Central	Midline	2.98	1.22	3.54	1.55	3.04	1.90
		Left	2.51	0.88	3.11	1.58	2.20	0.78
		Right	2.59	1.03	3.20	1.22	2.59	0.76

Table E.2

Means and Standard Deviations of RON Amplitudes across Stimuli, Hemisphere, Cluster and Group

		YA		OA		MCI	
Stimuli	**Hemisphere**	**M (μv)**	**SD**	**M (μv)**	**SD**	**M (μv)**	**SD**
1-back_{target}	Left	607.22	106.12	626.13	104.61	652.17	104.43
	Right	560.61	111.01	616.78	110.28	619.91	117.46
$1\text{-back}_{nontarget}$	Left	606.27	97.10	668.59	92.16	710.94	81.50
	Right	586.34	128.76	657.48	125.86	676.80	112.55
$PM_{percept}$	Left	547.28	93.93	620.89	77.13	678.67	102.31
	Right	558.32	108.00	603.21	106.20	670.18	106.00
$PM_{concept}$	Left	642.24	56.58	603.00	108.92	660.33	97.10

	Right	636.99	93.53	616.98	113.87	660.33	114.16

Table E.3

Means and Standard Deviations of RON Amplitudes across Stimuli, Hemisphere, Cluster and Group

		YA		OA		MCI	
Stimuli	**Hemisphere**	**M (ms)**	**SD**	**M (ms)**	**SD**	**M (ms)**	**SD**
1-back_{target}	Left	-1.95	2.69	-2.40	2.38	-2.68	2.96
	Right	-2.15	2.67	-0.63	2.73	-0.63	3.01
$1\text{-back}_{nontarget}$	Left	-1.64	1.30	-2.66	2.33	-2.34	3.87
	Right	-1.93	1.89	-1.95	2.28	-1.12	4.26
$PM_{percept}$	Left	-4.02	3.14	-2.52	3.33	-2.51	1.49
	Right	-4.82	3.09	-0.59	2.66	-0.22	1.79
$PM_{concept}$	Left	-3.18	2.73	-2.19	2.09	-4.47	1.71
	Right	-3.51	2.95	-0.57	2.10	-0.02	1.99

Table E.4

Means and Standard Deviations of IRR Amplitudes across Stimuli, Hemisphere, Cluster and Group

			YA		OA		MCI	
Stimuli	**Cluster**	**Hemisphere**	**M (μv)**	**SD**	**M (μv)**	**SD**	**M (μv)**	**SD**
1-back_{target}	Parietal	Midline	4.68	2.29	3.77	2.63	2.59	6.64
		Left	3.61	1.67	2.89	2.05	2.60	1.74
		Right	3.85	1.69	3.99	1.90	3.54	2.13
	Central	Midline	3.28	1.54	2.85	1.96	2.48	2.22
		Left	1.78	1.37	1.25	1.90	2.45	2.41
		Right	2.58	1.41	3.22	1.66	2.92	1.57

1-back$_{nontarget}$	Parietal	Midline	4.22	2.25	2.73	2.02	216	2.35
		Left	3.15	1.51	2.81	1.91	2.10	1.04
		Right	3.10	1.56	2.77	1.64	2.07	1.70
	Central	Midline	2.73	1.42	2.95	1.91	1.83	1.83
		Left	1.91	1.44	2.33	1.56	2.41	2.72
		Right	1.65	1.24	2.01	1.47	1.41	1.01
PM$_{percept}$	Parietal	Midline	8.35	4.30	4.40	3.14	4.13	2.21
		Left	5.47	2.60	5.01	2.72	4.27	1.99
		Right	6.67	2.44	5.00	2.64	4.09	2.49
	Central	Midline	6.93	2.61	4.87	2.93	4.00	3.66
		Left	3.68	2.11	3.69	2.23	3.57	2.40
		Right	4.16	1.80	3.74	2.13	3.04	1.73
PM$_{concept}$	Parietal	Midline	5.14	2.95	3.18	2.45	3.18	2.90
		Left	3.59	1.71	3.87	2.79	3.35	1.84
		Right	4.02	1.95	3.18	2.42	3.50	2.16
	Central	Midline	4.09	2.22	3.72	2.36	3.08	3.45
		Left	2.78	1.90	3.46	2.60	2.85	1.57
		Right	2.28	1.43	2.95	2.58	2.83	2.20

Table E.5

Means and Standard Deviations of IRR Latencies across Stimuli, Hemisphere, Cluster and Group

			YA		**OA**		**MCI**	
Stimuli	**Cluster**	**Hemisphere**	**M (ms)**	**SD**	**M (ms)**	**SD**	**M (ms)**	**SD**
1-back$_{target}$	Parietal	Midline	552.46	82.38	593.75	72.32	606.99	81.70
		Left	569.75	81.49	613.49	46.37	593.01	76.92
		Right	564.04	79.34	598.07	59.91	597.87	71.80

	Central	Midline	564.87	73.74	591.80	77.61	566.84	94.14
		Left	560.97	86.18	545.74	76.08	525.61	83.33
		Right	557.62	75.81	565.07	87.91	585.73	56.67
1-back$_{nontarget}$	Parietal	Midline	555.80	78.98	606.63	73.36	615.67	75.75
		Left	558.73	90.93	598.99	68.81	571.62	86.80
		Right	565.99	79.19	604.34	69.92	594.62	61.96
	Central	Midline	718.61	124.34	740.45	100.16	777.34	103.17
		Left	849.19	199.67	795.13	116.91	814.35	122.16
		Right	808.45	117.63	790.09	115.44	797.29	128.62
PM$_{percept}$	Parietal	Midline	646.82	40.31	699.44	96.19	708.40	96.90
		Left	791.99	121.44	752.50	119.42	791.99	121.44
		Right	643.32	63.02	725.69	127.32	768.56	134.66
	Central	Midline	653.42	75.88	715.93	113.34	768.56	127.39
		Left	793.64	131.91	808.16	133.28	850.59	132.36
		Right	753.23	136.39	785.05	137.74	832.03	132.35
PM$_{concept}$	Parietal	Midline	712.28	104.32	776.32	112.14	780.66	104.57
		Left	798.36	118.42	803.42	122.79	833.79	115.47
		Right	765.89	134.62	814.76	129.10	857.42	95.61
	Central	Midline	753.64	138.93	771.22	112.34	834.38	125.25
		Left	825.97	124.22	862.12	108.21	883.01	128.69
		Right	837.15	145.70	802.94	143.84	864.45	133.24

Table E.6

Means and Standard Deviations of N300 Amplitudes across Stimuli, Hemisphere, Cluster and Group

			YA		OA		MCI	
Stimuli	**Cluster**	**Hemisphere**	**M (μv)**	**SD**	**M (μv)**	**SD**	**M (μv)**	**SD**

1-back$_{target}$	Occipital	Midline	-0.01	2.43	-1.35	2.13	-1.30	2.44
		Left	1.21	2.15	-0.14	2.02	-0.46	2.10
		Right	1.36	2.39	0.13	2.02	-0.08	2.58
	Inferior parietal	Left	-0.47	1.61	-1.39	2.41	-0.98	1.94
		Right	0.11	2.11	-0.40	2.10	-0.68	1.30
	Parietal	Midline	1.62	1.77	0.83	1.98	0.003	1.98
		Left	0.97	1.36	0.13	1.54	0.71	1.51
		Right	1.53	1.46	1.20	1.34	0.80	1.17
1-back$_{nontarget}$	Occipital	Midline	0.28	2.14	-1.85	2.80	-1.36	2.42
		Left	1.61	2.22	-0.33	1.93	0.08	1.87
		Right	1.53	2.20	-0.56	2.11	0.07	1.77
	Inferior parietal	Left	0.62	1.54	-1.31	1.47	-0.53	1.50
		Right	0.38	2.10	-0.81	2.40	-0.59	1.35
	Parietal	Midline	1.36	1.58	0.70	1.59	0.29	2.00
		Left	0.97	1.28	0.76	1.40	0.72	0.99
		Right	1.22	1.47	0.97	1.33	0.50	1.19
Ongoing PM$_{percept}$ +	Occipital	Midline	-1.16	3.03	-2.95	2.93	-2.17	3.79
		Left	0.73	3.03	-1.04	2.84	-0.33	2.95
		Right	0.26	3.10	-0.83	2.56	-0.47	2.11
	Inferior parietal	Left	-1.58	223	-1.82	2.02	-0.87	1.42
		Right	-1.46	2.86	-1.53	2.05	-0.48	1.65
	Parietal	Midline	2.20	2.73	0.36	1.91	0.62	2.01
		Left	1.10	1.90	0.88	1.79	0.76	1.73
		Right	1.80	1.60	1.26	1.74	0.68	2.12

Ongoing $PM_{concept}$ +	Occipital	Midline	-0.99	2.11	-2.76	3.21	-1.78	2.23
		Left	0.42	2.45	-0.79	2.13	-0.06	1.70
		Right	0.57	2.42	-0.70	2.52	0.05	1.75
	Inferior parietal	Left	0.11	1.84	-0.96	1.99	-1.10	1.83
		Right	-0.26	2.19	-1.21	2.12	-0.73	1.61
	Parietal	Midline	0.87	1.74	0.67	1.72	0.56	1.65
		Left	0.53	1.20	0.74	1.35	0.66	1.62
		Right	0.93	1.22	0.79	1.36	1.51	1.61

Table E.7

Means and Standard Deviations of N300 Latencies across Stimuli, Hemisphere, Cluster and Group

			YA		OA		MCI	
Stimuli	**Cluster**	**Hemisphere**	**M (ms)**	**SD**	**M (ms)**	**SD**	**M (ms)**	**SD**
1-back_{target}	Occipital	Midline	353.93	66.12	380.76	68.88	371.71	73.15
		Left	365.93	66.05	393.30	68.31	399.88	74.85
		Right	416.38	63.70	390.73	71.89	396.38	78.14
	Inferior parietal	Left	354.91	52.08	390.83	63.31	390.63	78.58
		Right	418.95	63.31	367.50	70.19	393.45	81.17
	parietal	Midline	352.40	66.02	366.37	60.44	395.56	74.76
		Left	345.29	53.89	408.10	57.32	415.50	72.41
		Right	389.79	63.12	378.08	61.92	401.52	69.95
$1\text{-back}_{nontarget}$	Occipital	Midline	365.37	77.21	428.15	69.82	400.29	83.80
		Left	394.67	77.45	434.83	62.19	431.74	72.56

			Right	417.82	70.23	445.72	70.25	432.36	68.51
		Inferior parietal	Left	376.95	79.44	402.86	64.29	380.96	75.03
			Right	429.83	69.53	411.80	74.81	412.76	78.27
		parietal	Midline	354.21	63.30	405.74	77.56	387.95	75.80
			Left	351.28	57.20	376.75	58.43	409.95	68.18
			Right	403.88	57.56	431.95	67.31	431.74	56.93
Ongoing $PM_{percept}$	+	Occipital	Midline	359.91	69.72	403.43	73.23	512.31	80.33
			Left	375.14	73.77	405.49	65.32	396.83	77.92
			Right	349.95	65.39	399.74	74.33	395.31	82.40
		Inferior parietal	Left	425.78	72.36	396.27	70.45	411.52	80.03
			Right	100.86	73.23	372.72	56.13	385.74	66.44
		parietal	Midline	335.94	46.02	409.40	72.31	392.58	77.51
			Left	350.49	44.07	376.74	56.05	384.18	68.97
			Right	344.02	33.33	382.92	59.36	362.89	54.42
Ongoing $PM_{concept}$	+	Occipital	Midline	401.23	84.72	436.47	70.05	399.02	87.60
			Left	390.63	77.38	422.08	74.02	412.11	79.75
			Right	420.80	75.10	433.80	71.80	409.77	80.53
		Inferior parietal	Left	37136	67.10	379.83	61.60	353.91	60.45
			Right	442.48	60.26	409.13	70.53	403.13	71.88
		parietal	Midline	401.27	84.72	436.47	70.05	399.02	87.60
			Left	390.63	77.83	422.08	74.02	412.11	79.45
			Right	420.80	75.10	433.80	71.80	409.77	80.53

Table E.8

Means and Standard Deviations of Frontal Positivity Amplitudes across Stimuli, Hemisphere, Cluster and Group

			YA		OA		MCI	
Stimuli	**Cluster**	**Hemisphere**	**M (μv)**	**SD**	**M (μv)**	**SD**	**M (μv)**	**SD**
1-back$_{target}$	Frontal	Midline	1.76	2.14	3.85	2.40	2.97	1.84
		Left	1.23	3.32	3.74	3.15	3.42	2.45
		Right	2.16	2.84	4.68	2.28	4.20	1.96
	Frontocentral	Left	1.56	2.12	3.49	1.81	3.18	2.03
		Right	2.03	1.79	4.37	1.81	2.98	1.51
	Central	Midline	2.92	1.41	2.45	1.38	2.01	1.60
		Left	1.64	1.44	1.80	1.45	2.81	2.07
		Right	2.17	1.27	2.78	1.63	2.85	1.65
1-back$_{nontarget}$	Frontal	Midline	0.55	1.67	3.62	2.65	2.44	1.64
		Left	1.24	2.40	3.73	3.75	3.61	2.01
		Right	1.17	2.21	3.30	2.58	3.03	1.49
	Frontocentral	Left	1.26	1.53	3.68	2.42	2.78	1.80
		Right	0.92	155	3.53	1.99	2.20	1.53
	Central	Midline	2.27	1.48	2.57	1.74	1.68	1.56
		Left	1.85	1.42	2.17	1.37	2.56	2.39
		Right	1.49	1.21	2.05	1.43	1.55	1.04
Ongoing + PM$_{percept}$	Frontal	Midline	3.57	2.26	5.21	3.06	3.86	2.86
		Left	1.62	2.78	4.33	2.27	3.91	3.05
		Right	2.25	2.60	4.73	2.35	4.19	3.79
	Frontocentral	Left	3.54	2.15	5.39	2.79	4.56	2.89

		Right	3.57	2.39	5.62	3.11	3.77	1.98
	Central	Midline	6.30	2.59	4.03	2.38	2.84	2.25
		Left	3.25	1.99	3.31	1.89	2.86	1.52
		Right	3.70	1.93	3.64	1.88	2.76	1.84
Ongoing $PM_{concept}$ +	Frontal	Midline	1.79	1.66	4.11	2.64	3.23	1.94
		Left	2.44	2.48	4.01	2.93	3.87	2.29
		Right	2.31	1.99	4.47	2.71	4.24	4.33
	Frontocentral	Left	2.42	1.70	4.52	2.23	3.47	1.61
		Right	2.05	1.67	4.65	2.84	2.96	1.92
	Central	Midline	2.60	1.90	3.16	2.02	2.92	2.78
		Left	2.45	1.87	3.12	2.26	2.61	1.21
		Right	2.07	1.45	3.01	2.26	2.90	2.05

Appendix F: Chapter Seven, Prospective Memory Monitoring ERP Descriptions

Table F.1

Means and Standard Deviations of P2 Amplitudes across Stimuli, Hemisphere, Cluster and Group

			YA		OA		MCI	
Stimuli	**Cluster**	**Hemisphere**	**M (μv)**	**SD**	**M (μv)**	**SD**	**M (μv)**	**SD**
Ongoing-only	Frontal	Midline	4.08	2.33	4.31	1.54	3.12	1.34
		Left	3.14	2.06	4.25	2.33	2.98	2.32
		Right	3.15	1.71	4.43	2.32	3.23	2.25
	Frontocentral	Left	4.13	1.52	4.35	1.49	3.45	1.21

			Right	3.90	1.41	4.30	1.58	3.07	1.31
		Central	Midline	3.97	1.27	3.85	1.77	3.11	0.99
			Left	2.68	1.06	3.10	1.95	2.78	1.05
			Right	2.75	1.38	2.81	1.41	2.65	1.16
Ongoing $PM_{percept}$	+	Frontal	Midline	3.58	1.46	3.82	1.57	2.67	1.39
			Left	2.56	1.78	3.14	1.59	6.67	3.83
			Right	2.60	1.47	3.25	1.27	3.40	3.65
		Frontocentral	Left	3.70	1.19	4.16	1.50	2.85	1.32
			Right	3.52	1.31	4.06	1.48	2.82	1.11
		Central	Midline	3.07	1.26	3.88	1.81	2.71	1.08
			Left	2.65	1.11	3.50	1.87	2.31	1.03
			Right	2.54	1.25	3.50	2.01	2.58	1.10
Ongoing $PM_{concept}$	+	Frontal	Midline	3.58	1.37	3.74	1.81	2.56	0.88
			Left	2.90	1.62	3.50	2.19	2.42	1.24
			Right	2.69	2.52	3.41	2.37	2.66	1.37
		Frontocentral	Left	3.79	1.21	3.82	1.59	2.83	0.90
			Right	3.57	1.22	3.95	1.61	2.95	0.80
		Central	Midline	2.98	1.22	3.54	1.55	3.05	1.90
			Left	2.51	0.88	3.11	1.57	2.20	0.78
			Right	2.59	1.03	3.20	1.22	2.59	0.76

Table F.2

Means and Standard Deviations of P2 ERP Latencies across Stimuli, Hemisphere, Cluster and Group

			YA		**OA**		**MCI**	
Stimuli	**Cluster**	**Hemisphere**	**M (ms)**	**SD**	**M (ms)**	**SD**	**M (ms)**	**SD**

Ongoing-only		Frontal	Midline	197.27	22.94	198.80	29.80	201.89	30.84
			Left	193.22	36.07	196.85	33.68	196.83	31.02
			Right	184.85	25.83	198.51	32.07	203.78	33.07
		Frontocentral	Left	195.87	23.36	204.67	32.74	203.56	30.23
			Right	200.20	22.89	202.49	32.78	210.53	35.30
		Central	Midline	198.94	27.70	191.73	33.75	194.44	30.33
			Left	205.50	21.22	196.24	34.02	212.79	33.23
			Right	190.43	34.58	201.28	30.80	197.99	35.18
Ongoing $PM_{percept}$	+	Frontal	Midline	199.23	17.66	199.01	25.47	202.73	27.41
			Left	20.37	24.32	204.64	30.20	203.91	27.02
			Right	196.53	24.33	203.97	30.73	204.98	29.99
		Frontocentral	Left	201.37	16.19	207.03	31.97	195.70	22.42
			Right	200.84	18.92	200.06	26.22	207.23	32.91
		Central	Midline	196.39	25.78	187.39	19.76	195.31	24.38
			Left	201.78	20.73	197.74	27.50	209.77	25.67
			Right	18.55	26.90	203.55	32.21	194.92	31.35
Ongoing $PM_{concept}$	+	Frontal	Midline	198.82	21.23	193.75	22.06	197.66	28.83
			Left	194.64	24.24	203.91	33.91	212.70	30.43
			Right	192.21	27.35	196.65	30.03	206.25	29.68
		Frontocentral	Left	199.49	21.19	202.67	31.76	197.85	27.83
			Right	199.89	22.44	202.01	31.69	205.66	36.23
		Central	Midline	191.41	25.55	194.36	28.32	201.17	34.44
			Left	204.20	25.23	202.55	30.24	197.66	36.57

		Right	195.99	31.63	203.78	33.07	204.49	37.54

Table F.3

Means and Standard Deviations of N2 ERP Amplitudes across Stimuli, Hemisphere, Cluster and Group

			YA		OA		MCI	
Stimuli	**Cluster**	**Hemisphere**	**M (μv)**	**SD**	**M (μv)**	**SD**	**M (μv)**	**SD**
Ongoing - only	Parietal	Midline	-0.02	1.22	0.36	1.43	-0.60	1.57
		Left	-0.06	0.93	0.35	1.17	0.15	0.90
		Right	0.10	1.06	0.74	1.16	0.49	1.29
	Inferior parietal	Left	-1.67	1.29	-1.81	2.00	-1.97	1.55
		Right	-1.88	1.20	-2.06	1.46	-1.65	1.83
	Occipital	Midline	-3.22	2.14	-3.39	2.30	-2.48	2.14
		Left	-2.85	2.08	-2.60	1.99	-2.46	1.29
		Right	-2.38	1.84	-2.41	2.24	-2.30	2.90
Ongoing + $PM_{percept}$	Parietal	Midline	0.33	1.21	0.59	1.57	-0.23	1.16
		Left	0.02	1.13	0.59	1.31	0.02	0.59
		Right	0.25	0.95	0.95	1.15	0.53	0.92
	Inferior parietal	Left	-1.56	1.34	-1.81	2.43	-1.89	1.18
		Right	-1.41	1.20	-2.04	1.32	-1.13	1.05
	Occipital	Midline	-3.03	1.89	-3.20	2.64	-2.08	2.18
		Left	-2.89	1.67	-2.64	1.81	-2.57	2.06
		Right	-2.54	1.87	-2.28	2.47	-1.71	1.47
Ongoing + $PM_{concept}$	Parietal	Midline	0.24	1.25	0.74	1.57	-0.24	1.25
		Left	0.04	0.94	0.52	1.31	0.08	0.68
		Right	0.34	0.90	0.73	1.11	0.45	0.83

	Inferior parietal	Left	-1.55	0.94	-1.85	1.29	-1.27	1.11
		Right	-1.68	1.12	-1.65	1.36	-1.11	1.31
	Occipital	Midline	-3.16	2.18	-3.28	2.72	-2.63	1.98
		Left	-2.85	1.89	-2.31	1.58	-2.52	1.63
		Right	-2.36	2.14	-1.96	1.87	-1.86	1.56

Table F.4

Means and Standard Deviations of N2 ERP Latencies across Stimuli, Hemisphere, Cluster and Group.

			YA		OA		MCI	
Stimuli	**Cluster**	**Hemisphere**	**M (ms)**	**SD**	**M (ms)**	**SD**	**M (ms)**	**SD**
Ongoing-only	Parietal	Midline	201.03	33.22	180.72	36.74	206.00	41.91
		Left	186.66	31.60	185.55	37.14	198.19	38.49
		Right	191.41	35.10	180.20	35.40	183.18	34.37
	Inferior parietal	Left	189.87	32.50	200.25	34.03	193.26	32.12
		Right	195.59	30.76	200.14	33.94	196.18	29.55
	Occipital	Midline	197.27	25.08	194.39	32.74	197.16	38.70
		Left	187.50	22.10	189.56	24.02	195.72	31.49
		Right	185.76	23.04	184.62	23.47	189.35	28.63
Ongoing + $PM_{percept}$	Parietal	Midline	212.15	35.34	200.51	37.71	214.65	38.49
		Left	184.94	30.06	212.42	36.63	207.03	39.96
		Right	207.84	36.93	211.47	39.33	208.40	37.75
	Inferior parietal	Left	196.93	26.40	210.73	28.08	198.83	25.78
		Right	191.95	26.92	215.48	37.08	206.64	30.62
	Occipital	Midline	202.32	19.85	194.63	26.24	194.34	29.06
		Left	191.27	20.50	194.89	27.12	188.48	20.23

		Right	189.52	21.10	192.15	26.43	192.38	23.57
Ongoing $PM_{concept}$	+ Parietal	Midline	213.36	35.72	207.22	39.65	208.20	34.06
		Left	192.21	31.47	207.72	38.00	205.47	30.32
		Right	208.78	36.44	204.96	39.07	209.77	31.41
	Inferior parietal	Left	195.58	29.40	200.14	33.37	207.23	24.53
		Right	199.62	26.54	208.59	33.26	207.23	36.08
	Occipital	Midline	200.30	21.29	194.98	30.74	197.85	37.56
		Left	193.29	22.16	188.83	22.86	192.38	28.56
		Right	288.98	21.41	289.96	24.92	190.82	26.38

Table F.5

Descriptions of Early Frontal Positive (EFP) Amplitudes across Stimuli, Hemisphere, Cluster and Group

			YA		OA		MCI	
Stimuli	**Cluster**	**Hemisphere**	**M (μv)**	**SD**	**M (μv)**	**SD**	**M (μv)**	**SD**
Ongoing-only	Frontal	Midline	4.16	2.21	4.34	1.53	3.62	1.55
		Left	0.90	2.43	347	2.96	3.47	2.46
		Right	1.53	2.69	4.53	2.28	3.80	2.54
	Frontocentral	Left	3.97	1.81	4.37	1.50	3.93	1.36
		Right	3.93	1.43	4.31	1.59	3.63	1.82
	Central	Midline	3.10	1.25	3.87	1.75	3.35	1.09
		Left	2.70	1.07	3.16	1.90	3.20	1.30
		Right	2.75	1.40	2.82	1.41	3.21	1.61
	Frontotemporal	Left	3.29	1.32	3.22	2.61	2.48	2.19
		Right	2.52	1.27	2.59	1.45	2.57	2.00
Ongoing $PM_{percept}$	+ Frontal	Midline	3.59	1.46	3.86	1.58	2.90	1.48

		Left	1.00	2.83	2.54	2.16	3.81	3.76
		Right	0.85	1.81	3.32	1.24	3.50	3.59
	Frontocentral	Left	3.97	1.81	4.37	1.50	3.93	1.36
		Right	3.93	1.43	4.31	1.59	3.63	1.82
	Central	Midline	3.07	1.26	3.90	1.83	2.84	1.06
		Left	2.65	1.12	3.45	2.00	2.53	1.10
		Right	2.54	1.24	3.54	2.03	2.78	1.26
	Frontotemporal	Left	2.25	1.43	2.14	1.78	1.93	1.57
		Right	2.16	1.44	2.68	2.21	2.14	1.51
Ongoing + $PM_{concept}$	Frontal	Midline	3.58	1.37	3.72	1.93	2.82	1.88
		Left	1.03	2.17	3.28	2.00	2.79	1.90
		Right	0.98	2.01	3.33	2.34	3.47	3.52
	Frontocentral	Left	3.80	1.21	3.84	1.69	3.10	1.79
		Right	3.57	1.22	3.87	1.65	3.14	1.86
	Central	Midline	2.98	1.22	3.47	1.65	3.20	2.38
		Left	2.52	0.88	3.09	1.65	2.43	1.61
		Right	2.59	1.03	3.29	1.25	2.90	2.11
	Frontotemporal	Left	2.34	1.29	2.49	1.94	2.09	1.76
		Right	2.10	1.41	2.34	1.56	2.52	1.36

Table F.6

Means and Standard Deviations of Late Frontal Positive (LFP) Amplitudes across Stimuli, Hemisphere, Cluster and Group

			YA		**OA**		**MCI**	
Stimuli	**Cluster**	**Hemisphere**	**M (μv)**	**SD**	**M (μv)**	**SD**	**M (μv)**	**SD**

Ongoing-only	Frontal	Midline	1.52	3.14	3.06	2.46	3.45	3.63
		Left	3.09	2.87	3.55	4.54	3.30	3.94
		Right	4.43	5.83	5.90	4.64	4.37	3.55
	Frontocentral	Left	2.27	3.36	3.22	4.06	3.51	4.04
		Right	3.76	1.53	4.98	2.20	4.02	2.44
	Central	Midline	3.53	2.70	3.37	1.86	3.65	2.60
		Left	2.66	2.26	3.05	3.99	3.14	3.61
		Right	4.50	1.80	4.78	2.70	3.80	2.31
	Frontotemporal	Left	1.84	3.53	2.82	5.30	1.10	2.88
		Right	3.29	4.81	3.21	3.38	2.39	5.08
Ongoing + $PM_{percept}$	Frontal	Midline	0.93	2.11	2.98	2.50	1.91	2.19
		Left	5.32	5.04	3.94	3.88	2.80	4.31
		Right	5.45	5.43	5.54	4.17	3.74	2.19
	Frontocentral	Left	2.84	3.25	2.97	2.50	19.69	3.13
		Right	3.27	3.22	5.28	3.39	3.20	1.34
	Central	Midline	3.53	2.70	3.37	1.86	3.65	2.60
		Left	2.66	2.57	3.05	3.99	3.14	3.61
		Right	4.50	1.80	4.78	2.70	3.80	2.31
		Left	3.32	3.68	1.85	4.76	1.14	2.25
		Right	3.09	3.49	2.88	3.20	2.25	2.32

Ongoing $PM_{concept}$	+	Frontal	Midline	0.88	2.07	3.70	3.16	2.85	3.33
			Left	6.03	5.29	4.80	5.13	3.57	3.64
			Right	4.74	4.91	6.34	5.04	4.90	5.33
		Frontocentral	Left	2.47	2.91	4.15	5.13	2.67	3.14
			Right	2.76	1.54	5.33	3.04	3.31	2.87
		Central	Midline	2.53	1.75	3.61	3.47	3.92	3.96
			Left	2.19	1.93	2.59	4.00	1.90	2.91
			Right	2.87	1.47	4.09	3.07	3.48	2.72
		Frontotemporal	Left	3.46	4.51	1.79	3.64	-0.39	2.57
			Right	3.35	3.98	3.04	2.96	2.38	3.73