

**SUBJECTIVE AND OBJECTIVE SPATIAL MEMORY  
AND NAVIGATION ABILITIES IN AGING AND AMNESIA**

SARA PISHDADIAN

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## Abstract

Compared to the extensive research on how older adults evaluate their memory abilities, the evaluation of subjective spatial navigation abilities is understudied. This dissertation was guided by four research objectives: 1) Investigate the psychometric properties of a subjective spatial navigation questionnaire to assess the nature and extent of self-reported changes to spatial navigation in neurotypical aging; 2) Determine the relationship among subjective assessments of spatial navigation and of memory and how they relate to psychological distress and objective memory performance; 3) Understand the impact of hippocampal damage on subjective awareness of areas of spared and impaired episodic and spatial memory; and 4) Identify more precisely the conditions in which spatial memory and navigation depend on hippocampal integrity. In study 1, multidimensional item response theory was used to evaluate the factor structure and item reliability of the novel Changes in Navigation Questionnaire (CNQ) in a community sample of older adults. Results showed that the CNQ has a reliable factor structure, with items falling under *typical* and *atypical* changes. In study 2, the relationship between subjective spatial navigation and metamemory in aging was investigated using structural equation modeling. Findings showed that the subjective spatial navigation and metamemory constructs had a positive, weak correlation. Objective episodic memory performance did not load onto metamemory, and allocentric spatial memory performance had a weak loading onto spatial navigation abilities. Psychological distress symptoms had stronger loadings on metamemory than spatial navigation abilities. In study 3, two individuals with hippocampal amnesia completed questionnaires assessing metamemory and spatial navigation abilities and were compared to age-, gender-, and education-matched controls. The individuals with amnesia reported sound awareness of metamemory and spatial navigation difficulties. Lastly, in study 4, these individuals' performance on a videogame wayfinding measure was compared with that of thousands of well-matched controls. The individuals showed distinct patterns of impairment and preservation on the tasks. These dissertation results show that subjective spatial navigation abilities can be reliably captured with questionnaires, are weakly related to metamemory, and that accurate self-evaluation is not contingent on intact episodic memory. The findings also highlight specific aspects of navigation that are hippocampal dependent.

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## Table of Contents

Abstract .....	ii
Acknowledgments.....	iii
Table of Contents.....	v
List of Tables .....	x
List of Figures.....	xi
CHAPTER 1 .....	1
Episodic Memory .....	2
Spatial Navigation in Typical Aging, Atypical Aging, and Hippocampal Amnesia.....	3
Subjective Cognitive Decline and Risk Factors for Dementia.....	5
Subjective Episodic Memory Abilities in Individuals with Amnesia .....	7
Subjective Spatial Abilities in Aging and in Individuals with Amnesia .....	7
Overview of Studies .....	9
CHAPTER 2 .....	11
Objective Spatial Memory and Navigation Abilities.....	12
Subjective Spatial Navigation Abilities .....	12
Current Study .....	14
Method .....	15
Questionnaire Development .....	15
Participants.....	16
Materials .....	17
Procedure .....	18
Data Analysis .....	19
Results.....	19
Discussion .....	24
Table 2.1.....	30
Table 2.2.....	31
Table 2.3.....	32
Table 2.4.....	33
Table 2.5.....	34
Table 2.6.....	35

Table 2.7.....	36
Table 2.8.....	37
Table 2.9.....	38
Table 2.10.....	39
Table 2.11.....	40
Figure 2.1 .....	41
Figure 2.2 .....	42
CHAPTER 3 .....	43
Subjective Spatial Navigation Abilities .....	44
Subjective Memory Abilities .....	45
Current Study .....	47
Method .....	47
Participants.....	47
Materials .....	47
Procedure .....	48
Data Analysis .....	48
Results.....	48
Descriptive Statistics .....	48
Correlation Matrix.....	48
Path Analyses.....	49
Discussion .....	50
Subjective Spatial Navigation Abilities.....	51
Changes in Navigation Questionnaire .....	52
Spatial Navigation Abilities and Metamemory.....	53
Objective Memory & Psychological Distress.....	54
Limitations and Future Directions .....	56
Conclusion .....	57
Table 3.1.....	58
Table 3.2.....	59
Table 3.3.....	60
Table 3.4.....	61

Figure 3.1 .....	62
Figure 3.2 .....	63
Figure 3.3 .....	64
Figure 3.4 .....	65
Figure 3.5 .....	66
Figure 3.5 .....	66
Figure 3.6 .....	67
CHAPTER 4.....	68
Method .....	71
Participants.....	71
Materials .....	72
Procedure .....	73
Data Analysis .....	73
Results.....	73
DA’s Task Performance and Response Profile.....	73
BL’s Task Performance and Response Profile .....	75
Discussion .....	76
Objective Memory Performance .....	76
Subjective Memory Abilities .....	77
Subjective Spatial Navigation Abilities.....	79
Anosognosia.....	81
Implications for Memory Theories .....	82
Conclusion.....	83
Table 4.1.....	84
Table 4.2.....	85
Table 4.3.....	87
Table 4.4.....	88
Figure 4.1 .....	89
Figure 4.2 .....	90
Figure 4.3 .....	91
Figure 4.4 .....	92

Figure 4.5 .....	93
Figure 4.6 .....	94
CHAPTER 5 .....	95
Method .....	98
Participants.....	98
Materials .....	98
Procedure .....	99
Data Analysis .....	99
Results.....	100
Wayfinding Levels .....	100
Path Integration .....	103
Discussion .....	103
Table 5.1 .....	109
Table 5.2 .....	110
Table 5.3 .....	111
Table 5.4 .....	112
Table 5.5 .....	113
Table 5.6 .....	115
CHAPTER 6 .....	116
Summary of Studies.....	116
Subjective Changes in Spatial Navigation Ability .....	118
Relationship Between Subjective Memory and Subjective Spatial Navigation Abilities .....	120
Objective Episodic Associative and Spatial Memory .....	122
Relationship between Objective and Subjective Metrics.....	123
Sex Differences .....	125
The Role of the Hippocampus in Spatial Memory and Navigation .....	127
Psychological Distress .....	129
Anosognosia and Learning of Deficits .....	131
Clinical Implications.....	133
Limitations and Future Directions.....	135
Conclusion.....	138

Bibliography .....	139
Appendix A. Attention Checks.....	200
Appendix B. Study Questionnaires.....	201
Changes in Navigation Questionnaire (CNQ).....	201
Santa Barbara Sense of Direction Questionnaire (SBSOD) .....	203
Navigational Strategies Questionnaire (NSQ) .....	206
Wayfinding Questionnaire (WQ) .....	209
Survey of Autobiographical Memory Event (Episodic) Subscale .....	213
Multifactorial Memory Questionnaire (MMQ).....	214
Patient Health Questionnaire-9 (PHQ-9) .....	223
Generalized Anxiety Disorder-7 (GAD-7) .....	224
Appendix C. Sample Stimuli.....	225
Appendix D. Sea Hero Quest Map Levels .....	227
Appendix E. Acronyms.....	230
Appendix F. Older Adult Sample Self-Reported Nationality .....	231
Appendix G. Correlation Matric by Sex .....	232

## List of Tables

Table 2.1.	Sample Demographics .....	30
Table 2.2.	Scale Description & Descriptive Statistics .....	31
Table 2.3.	CNQ Descriptive Statistics by Item .....	32
Table 2.4.	CNQ Descriptive Statistics by Sex .....	33
Table 2.5.	CNQ Qualitative Coding .....	34
Table 2.6.	EFA Results – Number of Factors .....	35
Table 2.7.	Two-factor EFA Results – Factor Loadings & Commonalities .....	36
Table 2.8.	CFA Results– Factor Loadings & Commonalities .....	37
Table 2.9.	CFA Results by Sex .....	38
Table 2.10.	CFA Item Fit .....	39
Table 2.11.	Threshold Parameters .....	40
Table 3.1.	Correlation Matrix .....	58
Table 3.2.	Model 1 loadings and fit indices .....	59
Table 3.3.	Model 2 loadings and fit indices .....	60
Table 3.4.	Model 3 loadings and fit indices .....	61
Table 4.1.	DA Neuropsychological Test Results .....	84
Table 4.2.	BL Neuropsychological Test Results .....	85
Table 4.3.	DA Performance on Study Measures .....	87
Table 4.4.	BL Performance on Study Measures .....	88
Table 5.1.	Wayfinding Level Descriptions .....	109
Table 5.2.	DA Wayfinding Results .....	110
Table 5.3.	BL Wayfinding Results .....	111
Table 5.4.	First Turn Accuracy .....	112
Table 5.5.	Qualitative Scoring .....	113
Table 5.6.	Path Integration Levels - Flare Accuracy .....	115

## List of Figures

Figure 2.1. CNQ Total Score Distribution .....	41
Figure 2.2. CNQ Category of Changes .....	42
Figure 3.1. Prediction of Subjective Spatial Ability by CNQ Factor 1.....	62
Figure 3.2. Prediction of Subjective Spatial Ability by CNQ Factor 2 .....	63
Figure 3.3. Prediction of Subjective Spatial Ability by WQ Subscale .....	64
Figure 3.4. Model 1 Path Diagram - Metamemory & Spatial Navigation Abilities ..	65
Figure 3.5. Model 2 Path Diagram - Addition of Objective Memory .....	66
Figure 3.6. Model 3 Path Diagram - Addition of Psychological Distress .....	67
Figure 4.1. DA MRI .....	89
Figure 4.2. BL MRI .....	90
Figure 4.3. DA Responses on the CNQ .....	91
Figure 4.4. BL Responses on the CNQ .....	92
Figure 4.5. DA loadings on CNQ factor 1 & 2 .....	93
Figure 4.6. BL loadings on CNQ factor 1 & 2 .....	94

# CHAPTER 1

## General Introduction

Numerous studies have linked hippocampal structural and functional integrity to autobiographical episodic memory deficits, with evidence from older adults, individuals with hippocampal amnesia, and individuals diagnosed with Mild Cognitive Impairment (MCI) and Alzheimer's disease & related dementias (ADRD) (Leal & Yassa, 2015; Terry et al., 2015; Pishdadian & Rosenbaum, 2021). The studies converge on the finding that a broad network of brain regions that includes the hippocampus and regions of the neocortex is critical to both spatial and episodic memory (Kühn & Gallinat, 2014; Li & King, 2019; Moscovitch et al., 2016; Murphy et al., 2008; Small et al., 1999; Spreng et al., 2009).

An overlapping network that includes the hippocampus at its core underlies spatial memory<sup>1</sup> and spatial navigation<sup>2</sup>. Spatial memory and navigation decline have been given greater attention recently as an early, clinical marker of ADRD (Coughlan et al., 2018; Iachini et al., 2009; Laczó et al., 2017; Lithfous et al., 2013). Spatial memory is more easily verifiable than autobiographical episodic memory (i.e., detailed memories about one's personal experiences) and possibly more amenable to intervention. However, the aspects of spatial memory that change as individuals experience hippocampal compromise in relation to neurotypical aging and neurological trauma or disease are under debate. Also unclear is whether objective changes to spatial memory and navigation are noticed by those experiencing the changes (i.e., subjective spatial memory and navigation), and whether this relationship between subjective report and objective changes in spatial memory corresponds to the relationship between subjective report and objective changes in episodic memory (Burmester et al., 2016; McWhirter et al., 2020), which are impacted by intraindividual factors such as psychological distress (Mourao et al., 2016; Peters et al., 2019; van Harten et al., 2018).

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<sup>1</sup> Spatial memory refers to the learning, storage, and retrieval of spatial information, often relevant to spatial navigation. Examples include allocentric spatial representations (cognitive maps), knowledge of environmental landmarks, and navigational routes.

<sup>2</sup> Spatial navigation refers to the process of moving through a particular environment to reach a goal location. Successful spatial navigation involves multiple computations and subprocesses, which include but also extend beyond spatial memory.

In this dissertation, I aim to examine the relationships among subjective and objective episodic memory, and subjective and objective spatial memory and navigation. I address four main research objectives:

1. Investigate the psychometric properties of a subjective spatial navigation questionnaire to assess the nature and extent of self-reported changes to spatial memory and navigation in neurotypical aging;

2. Determine the relationship between among subjective assessment of spatial memory and of episodic memory and how they, in turn, relate to psychological distress and objective memory performance;

3. Understand the impact of hippocampal damage on subjective awareness of areas of spared and impaired episodic and spatial memory; and

4. Identify more precisely the conditions in which spatial memory and navigation depend on hippocampal integrity.

Before describing these dissertation studies in greater detail, I will briefly review the role of the hippocampus in episodic memory and spatial navigation, with a focus on these processes in aging and in individuals with hippocampal compromise. I will draw attention to different factors that have been shown to influence spatial memory and navigation as well as considerations for assessing these abilities. Then, I will present findings on how subjective memory and spatial abilities are typically evaluated and their relevance to the clinical syndromes of MCI and ADRD. I will also highlight the gap in the literature on subjective memory in individuals with hippocampal amnesia. Lastly, the review will provide a rationale for investigating the subjective evaluation of spatial navigation abilities in typical aging and in individuals with hippocampal amnesia.

### **Episodic Memory**

The medial temporal lobes (MTLs) and the hippocampus specifically are implicated in episodic memory, with non-episodic, semantic information shown to be dependent on other brain regions (Nadel & Moscovitch, 1997; Moscovitch et al., 2005, 2006, 2016; Patterson et al., 2007; Petersen et al., 2000). Episodic memory has classically been defined by the recollection of rich, perceptual details specific to a time and place (Renoult & Rugg, 2020; Tulving, 2002). The hippocampus is thought to be particularly critical for rich perceptual and spatial details in episodic memory and autobiographical episodic memory (Hassabis & Maguire, 2007; B. Levine

et al., 2002; Moscovitch et al., 2016; Picard et al., 2013). Individuals with reduced hippocampal functioning due to a variety of reasons (including typical aging, ADRD spectrum, hippocampal amnesia) generate fewer episodic details in their memories (Grilli et al., 2018; B. Levine et al., 2002; Murphy et al., 2008; Pishdadian & Rosenbaum, 2021). While recent research has refined the classic episodic-semantic distinction in memory (Renoult et al., 2012, 2019), the hippocampus continues to be critical for the recollection of episodic information.

### **Spatial Navigation in Typical Aging, Atypical Aging, and Hippocampal Amnesia**

In addition to episodic memory, the hippocampus also appears to be essential for supporting rich, detailed representations in spatial memory. Cognitive map theory (CMT) claims that the hippocampus supports allocentric mental representations of the environment, whether the representations were formed recently or long ago (Burgess et al., 2002; O'Keefe, 1990; O'Keefe & Dostrovsky, 1971). Studies of individuals with hippocampal damage have found deficits in the recollection of vivid, detailed aspects of familiar environments, but find intact knowledge of the coarser, gist-like aspects of those environments (Herdman et al., 2015; Robin et al., 2019; Rosenbaum et al., 2000; Winocur et al., 2005). In typical aging, there is also reduced detail and richness in allocentric or map-based memory (Ekstrom et al., 2018b; Hirshhorn et al., 2011; Iaria et al., 2009; Rosenbaum et al., 2012). Corresponding with reduced detail in their allocentric memory, older adults also tend to rely less on allocentric-based mapping strategies (Colombo et al., 2017; Klencklen et al., 2012). Findings from individuals with hippocampal amnesia and aging support the view that the hippocampus is central to supporting rich, detailed representations in spatial memory, particularly when these representations are allocentric.

There are known declines in hippocampal functioning in healthy or typical aging. These include structural changes in the form of reduced hippocampal volume as well as functional changes in hippocampal activity and connectivity (Bettio et al., 2017; Driscoll et al., 2003; Jack et al., 2000; Raz & Rodrigue, 2006; Nordin et al., 2018), though there is substantial individual variability (Lupien et al., 2007; Van Petten, 2004). Associated with these changes are age-related declines in associative memory, episodic memory, and aspects of spatial memory (Carr et al., 2017; Old & Naveh-Benjamin, 2008; Shing et al., 2011; Van Petten, 2004).

In clinical conditions where there is reduced MTL and hippocampal functioning, there are well-established impairments in allocentric spatial memory. Individuals with amnesic Mild Cognitive Impairment (aMCI) and ADRD take longer to form a cognitive map and have worse

performance on allocentric spatial tasks in new and familiar environments (Caffò et al., 2020; da Costa et al., 2021; Hort et al., 2007; Keynejad et al., 2018; Laczó et al., 2009; Lithfous et al., 2013; Schöberl et al., 2020; Tu et al., 2017; Tuena et al., 2021). The spatial learning deficits seen in aMCI are consistent with navigation-related brain region volume and network inefficiencies; affected regions include the retrosplenial cortex, precuneus, posterior parietal cortex and MTLs, including the hippocampus, which overlap with areas subject to atrophy in early ADRD (Antonova et al., 2009; Aguirre et al., 2019; Claessen & van der Ham, 2017; Coughlan et al., 2018; T.F. Levine et al., 2020; Visser et al., 2002; Weniger et al., 2011). Despite evidence of spatial memory decline, more extreme instances of impaired spatial navigation, such as spatial disorientation or “getting lost” behaviours, are rare in typical aging (Laczó et al., 2017; Lithfous et al., 2013).

Some, but not all, aspects of spatial memory and spatial navigation are affected in neurotypical aging. Navigating in familiar environments and from egocentric frames of reference are thought to be less hippocampally dependent and show less decrement with age (Laczó et al., 2017; Lester et al., 2017; Moffat, 2009). Since effective spatial navigation is a multicomponent process, there are several ways it can be impacted by atypical aging and in individuals diagnosed with ADRD beyond deficits in allocentric spatial memory. One aspect of navigation is path integration, which involves referring to one’s starting location and requires the translation from allocentric to egocentric frames (Ekstrom et al., 2018b). Path integration is thought to rely on posterior parietal and retrosplenial cortex integrity (Chrastil et al., 2015; Epstein, 2008; Vann et al., 2009), regions of the brain that are compromised in aMCI and ADRD (Lithfous et al., 2013). Consistently, individuals with these conditions show deficits on certain path integration paradigms (Ruggiero et al., 2018; Tu et al., 2015, 2017). Spatial navigation is a process which recruits multiple brain regions, some of which are unaffected in typical aging but that are negatively affected in clinical conditions of aMCI and ADRD.

Spatial memory and navigation difficulties have been argued to be a valuable early marker of ADRD pathology in aging (Allison et al., 2016; Costa et al., 2020; Coughlan et al., 2018; 2019; Laczó et al., 2017; Lithfous et al., 2013; Moffat, 2009). Research has shown that multiple spatial memory tasks are sensitive to detecting deficits in individuals on the ADRD spectrum (Salimi et al., 2018; Serino et al., 2014). Allocentric spatial memory tasks have shown sensitivity to cerebrospinal fluid (CSF) levels of tau/ $\beta$ -amyloid in individuals with aMCI,

important biomarkers of Alzheimer's Disease (AD) pathology (Allison et al., 2019; Chan et al., 2016). Allocentric spatial memory tasks have also been shown to predict conversion to ADRD better than CSF tau/ $\beta$ -amyloid markers, hippocampal volume, and standardized neuropsychological memory tests (Wood et al., 2016).

Sea Hero Quest (SHQ) is a videogame task with wayfinding and path integration components in new environments that has been shown to be sensitive to *APOE* status (Coughlan et al., 2019; Coughlan et al., 2020) and to the condition of ADRD (Puthusseryppady et al., 2022b). Since SHQ is on a virtual platform it also allows for detailed information on performance, which can address questions related to the importance of precision for spatial navigation (Coutrot et al., 2018; Ekstrom & Yonelinas, 2020). Research with the SHQ paradigm is promising as it demonstrates that virtual measurement of spatial navigation abilities may be sensitive to hippocampal and MTL dysfunction seen in aMCI and ADRD.

Spatial navigation difficulties are often present in ADRD and influenced by individual, neural, and clinical factors (He & Hegarty, 2020; Wolbers & Hegarty, 2010). Getting lost and wandering behaviours are reported by up to 70% of the care partners of individuals with ADRD, with a higher incidence of the behaviours in newer environments (Henderson et al., 1989; Pai & Jacobs, 2004; Rodriguez et al., 2020). With greater illness progression and cognitive deficits, as well as cardiovascular pathology (Yatawara et al., 2019), these behaviours are known to increase in familiar environments (Pai & Lee, 2016; Rodriguez et al., 2020; Yatawara et al., 2017). Objective (and subjective) spatial navigation abilities also tend to differ by biological sex and/or gender (Andersen et al., 2012; Nazareth et al., 2019; Turano et al., 2009), and appear related to sociocultural environment and geographical experience, including urban versus rural living (Coutrot et al., 2018, 2022). If deficits in spatial navigation are to be used as a marker of brain integrity and potential progression to ADRD, then it is important to first understand the intraindividual variability in spatial navigation in typical aging (Spiers et al., 2021; Tractenberg & Pietrzak, 2011).

### **Subjective Cognitive Decline and Risk Factors for Dementia**

Typical aging differs from the clinical syndrome of MCI which is defined by objective cognitive decline with preserved independent functioning (Petersen et al., 2001, 2018). The condition of aMCI refers to MCI with objective decline in the domain of memory (American Psychiatric Association, 2013). Individuals with aMCI are at higher risk of developing ADRD as

well as other dementias (Bondi et al., 2014; Cheng et al., 2017; Sperling et al., 2011). The prevalence of MCI in the older adult population is difficult to estimate due to multiple operational definitions, with estimates ranging from 3-42% for MCI and 0.5-31.9% for aMCI, (Cheng et al., 2017; Ward et al., 2012).

The condition of subjective cognitive decline (SCD) is described as self-reported memory decline that is not seen on objective cognitive testing (Cheng et al., 2017; Jessen et al., 2014; Jessen et al., 2020a). SCD can be assessed with brief questions (“Do you feel your memory is becoming worse?”) and responses of concern (“Yes it worries me.”; Jessen et al., 2010) or with longer questionnaires (Rami et al., 2014; Troyer & Rich, 2018; see Wasef et al., 2021 for a review). There is substantial variability in how SCD is measured (L.A. Rabin et al., 2015). Overall, individuals with SCD are at a greater risk of developing the conditions of aMCI and ADRD which makes metamemory<sup>3</sup> and subjective memory concerns or complaints of clinical and research interest (Ball et al., 2020; Buckley et al., 2016; Hohman et al., 2011; Jessen et al., 2020a, 2020b, 2022; Mitchell et al., 2014).

Older individuals with cardiovascular risk factors, mood disorders, and neuropsychiatric (or psychological distress) symptoms are at a higher risk of developing ADRD and other dementias (Angevaere et al., 2022; Cherbuin et al., 2015; Fillit et al., 2008, Peters et al., 2019; Mourao et al., 2016; Sannemann et al., 2020). Both depression symptoms and SCD are independent predictors of dementia and also highly correlated, with SCD related more to depression symptoms than to objective cognitive performance (Burmester et al., 2016, see Chu et al., 2017 for individuals with major depression history). Anxiety symptoms have also been shown to influence the incidence of SCD (Norman et al., 2020; Pavusic et al., 2021). While the relative contribution of these risk factors is difficult to disentangle, modifiable risk factors and age (S. Gao et al., 1998) are among the strongest contributors to ADRD incidence (Peters et al., 2019), with neuropathological evidence showing most ADRD cases have vascular pathology (L.A. Rabin et al., 2017; Toledo et al., 2013). Since SCD is a heterogenous condition, research is

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<sup>3</sup> Metamemory refers to how individuals evaluate or judge their own memory abilities. This may include evaluations of episodic memory abilities, general memory skills and memory satisfaction. It can also include the frequency and use of memory strategies.

still ongoing on the best approach to define it (Diaz-Galvan et al., 2021). To date, SCD has almost exclusively focused on memory and other cognitive complaints which do not encompass spatial memory and navigation.

### **Subjective Episodic Memory Abilities in Individuals with Amnesia**

While there has been an abundance of research into the subtle and unique patterns of objective memory loss in the face of amnesia due to hippocampal compromise, the field has largely neglected these individuals' subjective experience or insight into their memory deficits (Pishdadian & Rosenbaum, 2021). Anecdotal evidence suggests that individuals with hippocampal amnesia do have a general insight into their anterograde amnesia (Corkin, 2013; Klein et al., 1996). However, to the best of my knowledge, this has never been formally tested with objective measures, limiting our understanding of the nature and extent of these individuals' insight into their memory loss.

Compared to controls, individuals with hippocampal amnesia have intact self-referential encoding (Kurczek et al., 2015; Sui & Humphreys, 2013) and similar biases in temporal self-appraisal (Halilova et al., 2020) which may be attributable to intact introspection processes (Juskenaitė et al., 2016). These findings predict that individuals with amnesia would have accurate assessments of their memory abilities. However, previous studies have shown that individuals with hippocampal amnesia have impaired recollection of personal events (Steinvorth et al., 2005) and also generate fewer personal semantic memories, particularly for trait-based self-statements (Grilli & Verfaellie, 2015).

Whereas personal semantic memory for personality trait knowledge appears intact in individuals with hippocampal amnesia, their own personality ratings appear to relate more to their preinjury traits than their current traits (Garland et al., 2021) and also lack accuracy and reliability (Wank et al., 2022). Consequently, even if general self-concept is intact, individuals with amnesia may have incomplete knowledge of their memory and spatial navigation abilities (Renoult et al., 2012, 2019).

### **Subjective Spatial Abilities in Aging and in Individuals with Amnesia**

The assessment of subjective episodic memory in aging and in individuals with memory decline is an area of active research (Jessen et al., 2022; Wasef et al., 2021). However, the best measures to assess the subjective evaluation of spatial memory and navigation in aging and in individuals with memory decline are under researched.

There are several existing subjective (self-report) questionnaires on spatial navigation ability. Self-report questionnaires of spatial navigation have different aims or constructs they intend to measure. The most commonly used questionnaire in the field measures self-perceived navigation ability, confidence, and style (Santa Barbara Sense of Direction Questionnaire, SBSOD; Hegarty et al., 2002). Other questionnaires focus on strategy use during navigation (Navigational Strategies Questionnaire or NSQ, Brunec et al., 2018; Lawton's Wayfinding Strategy Scale, Lawton & Kalli, 2002) while another questionnaire aims to capture perceived spatial abilities and anxiety during navigation (Wayfinding Questionnaire, WQ; Claessen et al., 2016b; De Rooij et al., 2019; van der Ham et al., 2013; van der Kuil et al. 2021). There is another questionnaire in the field which measures specific symptoms of disorientation accounting for environmental familiarity (Questionnaire on Everyday Navigational Ability; Pai et al., 2012). More recently, two questionnaires have been designed which query perceived differences or difficulties in navigational abilities (Allison et al., 2019; Cerman et al., 2018). One of these measures, which focuses on self-reported changes (more difficulties) in spatial navigation abilities, found responses correlated with AD biomarkers for older individuals on the preclinical AD spectrum (Allison et al., 2019).

Across these various subjective spatial navigation questionnaires, differences in self-reported ability have been identified in younger adults (Brunec et al., 2018; Hegarty et al., 2022), individuals across the adult lifespan or who have had a stroke or acquired brain injury (ABI) (van der Ham et al., 2021; van der Kuil et al., 2021), and individuals with aMCI as well as AD (Allison et al., 2019; Cerman et al., 2018; Pai et al., 2012). No prior research has looked at subjective spatial navigation abilities in individuals with hippocampal amnesia, despite extensive research into these individuals' objective spatial memory and spatial navigation abilities (Ekstrom et al., 2018b; Herdman et al., 2015; Pishdadian & Rosenbaum, 2021). While all these spatial navigation questionnaires have different reported aims, it remains unclear how related or distinct the questionnaires are to one another.

Despite mood and personality factors being related to subjective memory evaluation (L.A. Rabin et al., 2017), the influence of personality or psychological distress (i.e., anxiety and depression symptoms) has generally not been considered in the subjective evaluation of spatial navigation abilities. The exception to this is a recent investigation of the SBSOD, the most frequently used self-report measure of spatial navigation abilities (Hegarty et al., 2002).

Researchers found that SBSOD scores are largely explained by personality traits of conscientiousness, emotional stability, extraversion as well as intellect (Condon et al., 2015). Recent work has found that responses on the SBSOD do not significantly decline in aging or correlate with biomarkers of ADRD, specifically CSF levels of tau and amyloid (T.F. Levine et al., 2021). These results are concerning for the SBSOD's sensitivity to declining abilities in typical aging as opposed to personality features (Kuzma et al., 2011). No other spatial navigation ability questionnaire has been investigated for personality contributions. One measure has been studied for its relationship with psychological distress in older adults and findings were inconsistent (Cerman et al., 2018; Sheardova et al., 2015). Overall, there is a need for subjective spatial navigation measures in the field to be investigated for their correlates, particularly psychological distress, and personality.

Diagnosing aMCI and ADRD involves gathering client, and often collateral, reports of declining cognitive skills to supplement objective cognitive testing (AACN Board of Directors, 2007; American Psychiatric Association, 2013). It is not common practice for objective spatial navigation abilities to be included in assessments (L.A. Rabin et al., 2016), despite evidence of the sensitivity of these measures to further cognitive decline, sometimes better than measures of episodic memory (Allison et al., 2019; Wood et al., 2016). Subjective assessment of spatial navigation abilities can supplement objective measurement and may be a valid and simple way to measure decline for a particular individual. An approach focused on subjective assessment of skills, including on changes in spatial navigation abilities, would be consistent with how other cognitive abilities are assessed in the clinic and possibly reduce the reliance on highly interindividual objective skills.

## **Overview of Studies**

The current dissertation investigates outstanding questions related to objective spatial navigation and subjective appraisal of spatial navigation abilities in aging and in two individuals with anterograde amnesia due to MTL damage. In the following chapters, I will describe studies which investigate the influences on and utility of objective and subjective measures of spatial navigation in older adults and in individuals with hippocampal compromise.

The first study of this dissertation explores the psychometric properties of a novel questionnaire measuring subjective changes in spatial navigation ability in typically aging older adults. The findings from the study will also help characterize older adults' perceptions of spatial

navigation challenges, sex differences in performance, and show the value of gathering qualitative information to understand these changes.

In the second study of this dissertation, correlations and structural equation modeling are used to further the understanding of the relationship between metamemory and subjective spatial navigation abilities in aging, and to investigate the influence of psychological distress and objective memory abilities on these constructs.

In the third study, two well-characterized individuals with anterograde amnesia due to bilateral hippocampal compromise are tested. Their insight into their memory and spatial navigation abilities is investigated through evaluating their responses on established questionnaires compared to control participants. Also considered are the responses by these individuals on the novel questionnaire from studies 1 and 2.

In the fourth and last study of this dissertation, the contributions of the MTL and specifically the hippocampus to the complex process of wayfinding and path integration is investigated. New spatial learning is assessed in the same two individuals with memory loss from study 3 using an immersive, ecologically valid videogame test, with comparisons in performance to normative ‘big data’.

The studies described in this dissertation will inform theoretical models of the contribution of the hippocampus to spatial memory, evaluate the psychometric properties of a subjective questionnaire designed to assess decline in spatial navigation abilities, and provide a greater understanding into the relationship between subjective episodic memory and spatial navigation in aging and in individuals with anterograde amnesia.

## CHAPTER 2

### Study 1: Psychometric Investigation of the Changes in Navigation Questionnaire in Aging

A growing literature suggests that spatial memory and navigation difficulties in older adults hold diagnostic value as preclinical markers for cognitive decline associated with ADRD (Coughlan et al., 2018; Lithfous et al., 2013; Tuena et al., 2021). This claim is based on multiple studies employing experimental spatial learning tasks which have found worse performance in older adults compared to young adults, and in individuals with aMCI and early ADRD compared to cognitively intact controls and other individuals with dementia (Bird et al., 2010; Chan et al., 2016; Delpolyi et al., 2007; Fernandez-Baizan et al., 2019; Meneghetti et al., 2018; Rusconi et al., 2015; Wang et al., 2012). Neuroimaging and biomarker data also indicate that spatial memory deficits are sensitive to neuroanatomical changes associated with ADRD, including, but not exclusive to, the integrity of the hippocampus, a brain structure that is viewed as critical to both episodic memory and spatial navigation (Laczó et al., 2017; Ramanoël et al., 2019; Rosenbaum et al., 2008; Schöberl et al., 2020; Sodoma et al., 2021; Wood et al., 2016).

While many studies have assessed subjective memory decline in aging (Burmester et al., 2016; Mitchell et al., 2014), there is far less research on how to best measure potential subjective declines in spatial navigation that may be indicative of aMCI and early ADRD. This study investigates the psychometric properties of a novel questionnaire on changes in spatial navigation abilities in neurotypical older adults, elucidating subjective awareness of spatial navigation changes in typical aging.

Subjective cognitive complaints, especially for memory abilities, are common in the older adult population (25-76%; Ginó et al., 2010; Jonker et al., 2000). Subjective cognitive complaints only have weak to moderate correlations with objective memory performance (Brailean et al., 2019; Burmester et al., 2016; Crumley et al., 2014; Herrmann 1982). The lack of a strong relationship with objective memory performance should not lead to dismissal of these complaints, since subjective cognitive complaints and the condition of SCD are related to ADRD neuropathology and associated with an increased risk of developing ADRD (Amariglio et al., 2012; Diaz-Galvan et al., 2021; Jessen et al., 2020b; Numbers et al., 2021; Parfenov et al., 2020). The diagnosis of aMCI or ADRD also requires subjective or informant (particularly with increasing illness progression) report of memory decline (American Psychiatric Association,

2013; Edmonds et al., 2018). Overall, subjective cognitive complaints are necessary to consider in clinical work and are related to an increased risk of ADRD.

### **Objective Spatial Memory and Navigation Abilities**

A number of individual factors can influence spatial navigation abilities. There appears to be declines in aging for both objective spatial memory and navigation abilities, declines which begin to emerge in midlife (Spiers et al., 2021; Van der Ham et al., 2021; Yu et al., 2021).

The type of navigation strategy adopted by an individual appears to moderate objective ability. A flexible, map-based (allocentric) strategy is generally viewed as more optimal than a route-based (egocentric) strategy (Brunec et al., 2018, 2019; Hegarty et al., 2022). Compared to their younger peers, older individuals are less likely to rely on allocentric strategies or spatial frames of reference during spatial navigation (Colombo et al., 2017; Lopez et al., 2018) as are individuals with aMCI (Parizkova et al., 2018). This difference in strategy use may directly impact individuals' wayfinding accuracy and efficiency, including the likelihood of taking shortcuts (Harris & Wolbers, 2014). Strategy use appears to interact with age to account for differences in objective spatial navigation abilities.

There also appears to be sex-based differences in spatial navigation ability which are possibly mediated by strategy use. Males are more likely to use allocentric strategies than females; these differences may be due, in part, to sociocultural factors, including economic stability and gender inequality (Boone et al., 2018; Coutrot et al., 2018; Tascón et al., 2018; Ulrich et al., 2019). A recent meta-analysis indicated better spatial navigation performance in large-scale and small-scale environments in males over females, with performance disparities attributable to differences in neural recruitment, spatial anxiety, and strategy use (Yuan et al., 2019). Sex-based differences in navigation ability and strategy use appear to favour better performance in males.

### **Subjective Spatial Navigation Abilities**

A review of the literature on subjective spatial navigation abilities based on a wide range of questionnaires suggests that in typical aging there is less self-reported reliance on allocentric strategies, greater spatial anxiety, and lower ratings of general spatial abilities in both familiar and unfamiliar environments (Cerman et al., 2018; Lester et al., 2017; Pai et al., 2012; van der Ham et al., 2021; Yu et al., 2021). These subjective spatial navigation abilities have positive (weak) correlations with objective spatial skills (Allison et al., 2019; van der Ham et al., 2021)

and incidents of getting lost behaviour (Pai et al., 2012). Past work has shown that there is a larger discrepancy between subjective evaluations and objective spatial navigation skills in males than in females (van der Ham et al., 2021).

Almost all subjective spatial navigation questionnaires measure subjective evaluation of current skills or abilities in different domains. Researchers then summarize responses from individuals, who may be older adults or individuals diagnosed with different clinical conditions such as aMCI and ADRD, to create normative data (i.e., descriptive statistics) of responses on questionnaires or questionnaire subscales. The domains captured vary across questionnaires and include navigation confidence, landmark recognition, spatial orientation, and spatial anxiety (Allison et al., 2019; Brunec et al., 2018; Cerman et al., 2018; Hegarty et al., 2002; Pai et al., 2012; van der Ham et al., 2013).

The subjective evaluation of general spatial navigation abilities across different domains may not be the most sensitive way to measure subjective spatial navigation abilities in aging. For example, recent work has found that scores on the SBSOD do not correlate with ADRD biomarkers (T.F. Levine et al., 2021). However, subjective reports of increased difficulty in spatial navigation ability are associated with AD biomarkers for individuals on the preclinical AD spectrum (Allison et al., 2019). Another study with a subjective spatial navigation questionnaire focusing on difficulties in navigation found that 55-64% of individuals diagnosed with MCI and 72% of individuals with AD had complaints about their spatial navigation skills (Cerman et al., 2018). These studies underscore the potential sensitivity of measuring subjective changes or increasing difficulty in spatial navigation ability in aging and preclinical AD instead of the evaluation of general spatial navigation abilities.

Despite well-established normative age-related changes in spatial navigation abilities, no subjective spatial navigation questionnaire is divided across what would be expected or normative in the population of typical aging individuals. In typical aging, instances of forgetting the geographical layout in familiar environments, getting lost frequently, or a general loss of independence in navigating would be considered atypical and seen in clinical syndromes of topographical disorientation, aMCI or ADRD (Aguirre & D'Esposito, 1999; Claessen & van der Ham, 2017; Laczó et al., 2017; Lithfous et al., 2013; Lopez et al., 2018). A measure that is designed to capture typical versus atypical changes in spatial navigation abilities may be more

useful to clinicians aiming to capture spatial navigation changes seen on the preclinical ADRD spectrum (Denney & Prigatano, 2019).

There are several ways which current subjective measures of spatial navigation ability may not be optimally designed for the clinical assessment of spatial navigation difficulties in the older adult population. Most spatial navigation questionnaires focus on the evaluation of current skills, instead of the evaluation of changes in ability, which are the most clinically relevant given interindividual variability. To my knowledge, no existing questionnaires gather information regarding temporal onset, but instead query more general skill evaluation or impose a timeframe for individuals to rate their abilities. For example, the questionnaire designed by Cerman and colleagues (2018) asks participants about difficulties in spatial navigation over the last 3 months. It is unclear what timeframe of changes is best to query, with research indicating a gradual decline in spatial abilities is expected in typical aging. Existing questionnaires also neglect to query incidents of getting lost behaviour, instead focusing on specific errors which may contribute to these incidents. Since spatial navigation deficits and getting lost behaviour may be indicative of vascular pathology (Chi et al., 2021; Yatawara et al., 2019), which relates to  $\beta$ -amyloid pathology in ADRD (Attems & Jellinger, 2014; J.S. Rabin et al., 2021), it is of clinical significance to assess the presence of specific incidents of getting lost behaviour in addition to other subjective changes in spatial navigation ability. An ideal measure designed for use in the clinical assessment of spatial navigation difficulties would classify the type, frequency, and timeframe of reported changes and/or increased difficulties in spatial navigation.

### **Current Study**

Informed by the literature on the changes to spatial navigation which occur in aging and with the aim of designing a clinically useful measure to capture subjective changes to spatial navigation in aging, I created a novel questionnaire: The Changes in Navigation Questionnaire (CNQ). Instead of focusing on participants' views of their current spatial navigation abilities, the questionnaire asks participants to reflect on perceived changes in spatial navigation abilities that they have experienced, including when those changes occurred. The questionnaire (and written items) was designed to capture aspects of spatial navigation that are most likely to change in typical aging versus those that are most likely to change in preclinical ADRD.

To investigate the latent variable structure (items querying changes that are *typical* versus *atypical* in aging) and internal reliability of items on the questionnaire, multidimensional item

response theory analyses were conducted in a large sample of neurotypical older adults without a diagnosis of MCI or dementia. The item response theory (IRT) approach evaluates the relationship between item responses and underlying constructs or item structure of a scale, drawing from and expanding on Classical Test Theory to provide specific information about items on a measure to inform latent variable structure and item reliability (Cappelleri et al., 2014; Edelen & Reeve, 2007). Using IRT in this study to investigate the measure's psychometric properties is ideal as it offers information on the relationship of each item on the CNQ to underlying constructs. The information obtained from IRT analyses can then be used to modify the CNQ items. Future work can then investigate the overall measure's psychometric properties, using methods from Classical Test Theory.

The results of the current study will help shed light on the types of changes in spatial navigation ability that are reported in typical aging. They will also serve as a benchmark for future studies measuring changes in spatial navigation ability in atypical aging and in preclinical ADRD populations.

## **Method**

### **Questionnaire Development**

The CNQ was developed based on a comprehensive literature review of the types of spatial navigation difficulties experienced in neurotypical aging and in ADRD, and questionnaires that are currently used to assess subjective awareness of these difficulties (including those described below), with a focus on potential areas of change that are not captured by these questionnaires. Ten items were generated, some that relate to expected changes in typical aging (items 1-5) and others that relate to *atypical* changes (items 6-10). The *typical* aging items address reduced confidence in navigating and reliance on GPS. The *atypical* aging items focus on navigation errors that are not normative in aging and increased reliance on other people to navigate, as seen on the preclinical ADRD spectrum. The questionnaire was designed with clinical utility in mind and gathers both quantitative and qualitative information on the changes noticed by the examinee.

The CNQ is available in Appendix B. The CNQ's first 10 items ask individuals to rate the amount of change experienced in different spatial abilities followed by a timeline of when the changes were first noticed. The timeframe of the changes is meant to inform clinical case conceptualization regarding etiology and course. Participants are requested to elaborate if they

select the timeframe response “after a specific event.” Participants are then asked two-open ended questions. The first item queries any general changes that they have noticed in navigation. The second item asks whether they have had any experiences of disorientation or getting lost.

In-person pilot testing with approximately 20 neurotypical older adults and 10 older individuals with neuropsychologically characterized memory impairment led to item changes, including altering item phrasing and length for clarity.

## **Participants**

Ethics approval was obtained from the Research Ethics Boards at Baycrest Health Sciences and York University to conduct this study. A sample of 747 older adults was recruited from Prolific, a United Kingdom-based online participant platform (<https://prolific.co/>). Testing was completed on the online survey platform Qualtrics (<https://www.qualtrics.com/>). Recruitment criteria was for individuals without neurological or other medical conditions who were fluent in English and between 60-80 years of age.

Participants were excluded due to duplicate IP addresses ( $N = 42$ ), taking more than 2 hours ( $N = 12$ ) or less than 25 minutes ( $N = 42$ ) to complete the study, being over 80 years of age ( $N = 2$ ), and failing attention checks ( $N = 13$ ; see Appendix A for specific items). Individuals were also excluded from the sample based on generated comments provided at the end of the study which would suggest inaccurate information, such as an individual explicitly stating that they did not enter accurate information ( $N = 16$ ). Participants were also removed if they reported significant vision difficulties, including diabetic retinopathy, floaters, detached retinas, partial blindness or uncorrected cataracts ( $N = 35$ ) or if they achieved less than 50% accuracy (i.e., chance performance) on an associative episodic memory task ( $N = 2$ ). An additional 11 individuals were removed for self-disclosing a history of stroke. This resulted in a final sample of 587 individuals. Demographics of these participants are available in Table 2.1. The sample’s self-reported nationality is available in Appendix F. The majority of participants (68.48%) reported the United Kingdom and British Isles as their nationality. The second largest percentage of participants (20.95%) reported the United States of America as their nationality. Only 1.87% of participants reported Canada as their nationality.

Responses to the CNQ are reported in the entire sample of 587 participants. Due to missing data across questionnaires, a subsample of 533 individuals’ performance is reported on the objective memory, psychological distress symptoms, and the subjective memory and

subjective spatial navigation measures. Demographic information for these 533 individuals is available in Table 2.1; the subsample and larger sample do not statistically differ on the demographic variables.

## **Materials**

### ***Attention Checks***

Multiple attention checks were distributed throughout the experiment. These included selecting specific answers among multiple choice responses and typing in specified answers into open-ended questions. Specific items are available in Appendix A.

### ***Objective Memory Measures***

Objective memory abilities were assessed with two tasks that include an encoding phase followed by a recognition phase. Sample stimuli and a schematic of each task is available in Appendix C.

Objective spatial memory was assessed with the Four Mountains Task, an allocentric memory test that involves encoding 20 images of mountains followed by a forced-choice recognition task where the target (studied) mountain image and three distractor (unstudied) mountain images have been rotated (task adapted from Burles & Iaria, 2020). The task used in this study is based on a similar task that is sensitive to deficits in performance in older adults and individuals on the preclinical ADRD spectrum (Bird et al., 2010; Chan et al., 2016).

Objective episodic memory was assessed with an associative episodic memory task which pairs faces and names, aptly named the Face-Name Task (Troyer et al., 2011, 2012). Overall percent accuracy and accuracy of previously studied faces with recombined names were calculated, the latter appearing to be more sensitive to age-related associative memory difficulties (Fan et al., 2020; Troyer et al., 2012).

### ***Psychological Distress Measures***

Symptoms of psychological distress were assessed with two commonly used self-report symptom measures that map onto the DSM-5 diagnostic criteria for Major Depressive Disorder and Generalized Anxiety Disorder (American Psychiatric Association, 2013). The Patient Health Questionnaire-9 (PHQ-9) was used to capture depression symptomatology and Generalized Anxiety Disorder 7-item (GAD-7) scale was used to capture general anxiety symptomatology (Kroenke et al., 2001; Spitzer et al., 1990; Spitzer et al., 2006). See Appendix B for questionnaires.

### ***Subjective Memory and Spatial Navigation Measures***

All subjective episodic memory and spatial navigation measures are available in Appendix B.

Participants were administered metamemory measures to establish their general impressions of memory ability to compare with spatial navigation abilities. Subjective trait memory abilities were assessed with the Survey of Autobiographical Memory (SAM) Event (Episodic) subscale (Fan et al., 2021; Palombo et al., 2013; Sheldon et al., 2016). The three subscales of the Multifactorial Memory Questionnaire (MMQ) were used to capture subjective memory satisfaction, memory abilities, and strategy use (Troyer & Rich, 2018). This measure has been utilized in older adult populations, including in individuals with subjective memory complaints, aMCI, severe pain, and diabetes (Troyer & Rich, 2018). It has a reliable factor structure and is sensitive to real-world activity levels in SCD (Rotenberg et al., 2020; Shaikh et al., 2021).

Subjective spatial navigation abilities were measured with four questionnaires. The SBSOD was used to assess general navigation ability, confidence, and style (Hegarty et al., 2002). Allocentric strategy use during navigation was measured with the NSQ from Brunec and colleagues (2018, 2019); responses on the NSQ have been shown to relate to hippocampal volume in young adults. The WQ was used to measure general spatial abilities and levels of spatial anxiety. This questionnaire's psychometric properties have been investigated across the adult lifespan and in individuals with stroke and ABI; WQ subscales are also weakly correlated with objective spatial ability (Claessen et al., 2016b; De Rooij et al., 2019; van der Ham et al., 2013, 2021). Subjective changes in spatial navigation abilities were measured with the CNQ.

### **Procedure**

All participants gave informed written consent and were provided with monetary compensation for their time. Testing procedures involved providing consent, filling out demographics and medical history followed by a random distribution of the subjective episodic memory and spatial navigation measures and objective tasks, and finally administration of symptom measures of mood and anxiety, followed by general mental health resources. Participants were provided with an opportunity to provide feedback on the study and given a study debriefing form.

## Data Analysis

The data were analyzed using R version 4.2.0 (R Core Team, 2013). Descriptive statistics were run using the *psych* package (Revelle & Revelle, 2015). Sex differences were investigated with parametric or non-parametric tests based on data distributions. Given that there was only one individual who identified their sex as “other” and another who identified as “nonbinary”, these individuals were excluded from statistical analyses divided by biological sex and included in all IRT analyses. Scoring for qualitative responses on the final two items of the CNQ were discussed with an experienced research assistant who scored all responses. Responses were scored on several metrics to capture transcript quality, domains of difficulty, and a subjective characterization of severity.

All IRT analyses were run with the *mirt* package (Chalmers et al., 2012) which address the psychometric structure of the CNQ, specifically the latent structure of the measure and item internal reliability. All IRT analyses were conducted with a graded response model given the Likert-type scale items on the CNQ. The *lavaan* package (Rosseel, 2012) was used to conduct exploratory factor analysis (EFA) to investigate the factorial structure of the CNQ and to run a two-factor model of the data based on theoretical constructs of *typical* and *atypical* age-related changes in spatial memory and navigation.

Informed by EFA findings, confirmatory factor analysis (CFA) was then used to confirm the factor structure of the CNQ including item loadings. CFA was also used to account for biological sex differences. Item fit analyses were used to measure CNQ item responses relationship (or overall fit) to the model, specifically comparative fit index (CFI), tucker-lewis index (TLI), root mean square error of approximation (RMSEA), Akaike information criterion (AIC), sample-size-adjusted Bayesian information criterion (SABIC).

## Results

### Descriptive Statistics & Qualitative Findings

#### *Objective Memory*

Objective memory results, presented in Table 2.2, show that older adult participants performed well above chance on all objective memory measures. Participants performed better on the Face-Name Task than the Four Mountains Task. Consistent with past research, older adults’ performance accuracy was lowest on the recombined condition of the Face-Name Task (Troyer et al., 2011; Fan et al., 2020).

There were no sex differences in performance on the Four Mountains Task,  $t(554) = 0.24$ ,  $p = 0.81$ , 95% CI (-0.02, 0.02). Females performed better ( $M = 0.99$ ,  $SD = 0.1$ ) than males ( $M = 0.88$ ,  $SD = 0.1$ ) on overall accuracy on the Face-Name Task,  $t(560) = -5.52$ ,  $p < .001$ , 95% CI (-0.06, -0.03). Females ( $M = 0.69$ ,  $SD = 0.2$ ) also performed better than males ( $M = 0.78$ ,  $SD = 0.2$ ) on the recombined condition of the Face-Name Task,  $t(564) = -4.52$ ,  $p < .001$ , 95% CI (-0.12, -0.05).

### ***Psychological Distress***

Participants' PHQ-9 responses (see Table 2.2) indicate mild depressive symptomatology with a positive skew, showing a bias towards lower symptom endorsement. Females ( $M = 4.0$ ,  $SD = 4.7$ ) reported significantly higher levels of depression symptoms than males ( $M = 3.3$ ,  $SD = 4.0$ ) on the PHQ-9,  $t(583) = -2.17$ ,  $p = 0.03$ , 95% CI (-1.45, -0.07).

Similar to responses on the PHQ-9, participants' GAD-7 responses (see Table 2.2) also indicate low levels of anxiety and a positive skew showing a bias towards lower symptomatology. A Wilcoxon signed-rank test indicated that there was no significant difference in anxiety levels between females ( $M = 3.2$ ,  $SD = 4.5$ ) and males ( $M = 2.4$ ,  $SD = 3.3$ ),  $W = 39343$ ,  $p = 0.08$ .

### ***Established Subjective Memory and Spatial Navigation Measures***

Average scores on each MMQ subscale were rounded to the nearest whole number and T-scores were calculated based on available normative data, described in detail below (Troyer & Rich, 2018). Responses indicated that the sample, as a whole, viewed themselves as having high memory ability, were typically satisfied with their memory, and did not use many strategies, a metamemory profile consistent with typical aging.

Specifically, responses were in the average range on the MMQ Satisfaction subscale (T-score = 54), high average range on the MMQ Ability subscale (T-score = 58), and low average range on the MMQ Strategy subscale (T-score = 40) (Guilmette et al., 2020; Troyer & Rich, 2018). Sex differences in endorsement were found on the MMQ Strategy subscale, with females ( $M = 28.8$ ,  $SD = 11.4$ ) reporting greater use of strategies than males ( $M = 26.0$ ,  $SD = 10.8$ ),  $t(582) = -2.99$ ,  $p = 0.003$ , 95% CI (-4.53 -0.94). No sex differences were found on the MMQ Ability [ $t(568) = -0.70$ ,  $p = 0.48$ , 95% CI (-2.60, 1.23)] or MMQ Satisfaction subscales [ $t(582) = 0.27$ ,  $p = 0.79$ , 95% CI (-1.78, 2.35)].

Participants' responses on the SAM Episodic subscale are in the typical range compared to past research with the measure across the adult lifespan (Palombo et al., 2013). Females reported significantly higher ( $M = 101.6$ ,  $SD = 14.2$ ) scores than males ( $M = 98.9$ ,  $SD = 13.9$ ),  $t(578) = -2.37$ ,  $p = 0.02$ , 95% CI(-5.02, -0.47). This indicates that females in this sample view their episodic memory capabilities as better than males.

Participants' responses on the WQ indicate self-reported spatial ability and spatial anxiety within normal limits based on a cut-off method for the lowest 5% of scores, an approach that has been previously applied with this questionnaire (De Rooij et al., 2019). Mean responses on all subscales were well above cut-offs ( $54 > 32$  for the Navigation Orientation subscale,  $13 > 6$  for the Distance Estimation subscale, and  $27 > 20$  for the Spatial Anxiety subscale). Scores are also similar to a Dutch healthy control sample that was previously administered the WQ (Claessen et al., 2016b).

On the WQ Navigation Orientation subscale females had significantly lower ( $M = 4.7$ ,  $SD = 1.2$ ) scores than males ( $M = 5.2$ ,  $SD = 1.0$ ),  $t(572) = 6.76$ ,  $p < .001$ , 95% CI (0.43, 0.79). Females also had significantly lower ( $M = 3.8$ ,  $SD = 1.7$ ) scores than males ( $M = 5.0$ ,  $SD = 1.2$ ) on the WQ Distance Estimation subscale,  $t(561) = 9.91$ ,  $p < .001$ , 95% CI (0.91, 1.35). Females had significantly higher ( $M = 3.8$ ,  $SD = 1.5$ ) scores than males ( $M = 3.0$ ,  $SD = 1.2$ ) on the WQ Spatial Anxiety subscale,  $t(574) = -6.93$ ,  $p < .001$ , 95% CI (-0.97, -0.53).

On the SBSOD, females had significantly lower ( $M = 4.1$ ,  $SD = 1.1$ ) scores than males ( $M = 4.8$ ,  $SD = 0.9$ ),  $t(576) = 8.19$ ,  $p < .001$ , 95% CI (0.51, 0.83). Comparison of SBSOD scores to a recently published older adult baseline sample ( $M = 5.1$ ,  $SD = 1.0$ ) that was collected as part of a longitudinal study in the United States of America shows a significant difference between the participant samples,  $t(489) = 10.27$ ,  $p < .001$ , 95% CI (0.63, 0.92), with this sample's ratings being lower ( $M = 4.4$ ,  $SD = 1.1$ ) (T.F. Levine et al., 2021).

Scores on the NSQ are derived from comparing responses on items of map-based versus non-map-based strategy use. Higher scores indicate more map-based (allocentric) strategy use. Results show an approximately normal distribution of scores on the NSQ in this sample of participants. There is no available normative data for older adult populations, and, to the best of my knowledge, this is the first time that this measure has been administered in an older adult sample. There were significant differences between scores in this sample ( $M = 0.6$ ,  $SD = 4.9$ ) compared to younger adults ( $M = 4.1$ ,  $SD = 4.3$ ),  $t(74) = -5.81$ ,  $p < .0001$ , 95% CI (-4.73, -2.31)

(Brunec et al., 2019), with less self-reported allocentric strategy use in this, older adult, sample. Females had significantly different scores on the NSQ ( $M = -1.0$ ,  $SD = 5.1$ ) compared to males ( $M = 2.4$ ,  $SD = 4.0$ ), indicating less allocentric strategy use,  $t(577) = 8.75$ ,  $p < .001$ , 95% CI (2.57, 4.06).

### *Changes in Navigation Questionnaire*

Quantitative descriptive statistics by item on the CNQ are available in Table 2.3. Results show that all item responses are highly positively skewed, with different patterns of endorsement between amount of change noticed and timeframe of change. Figure 2.1 shows the distribution of total scores on the CNQ. In terms of item endorsement, items 3 and 5 are the most endorsed while items 9 and 10 are the least endorsed (forgetting indoor environments and others commenting on individual getting lost, respectively).

Item endorsement divided by self-reported sex assigned at birth is available in Table 2.4. Females' average responses are higher than male's responses for items 1-4 (confidence navigating) and item 6 (reliance on others), for both amount of change noticed and timing of the change.

Findings from qualitative scoring of items 11 and 12 are available in Table 2.5. A total of 199 responses (33.90% of the sample) were coded for item 11, and 100 responses (17.03% of sample) were coded for item 12.

Qualitative scoring of responses on item 11 (i.e., any noticed changes in navigation), included assigning a score on the general quality, severity or concerning nature, and emotional valence (positivity, negativity) of the described change. Participants' responses were also characterized based on the general theme of the changes described. Figure 2.2 presents a graphical depiction of the findings. The results show a wide range of changes described by participants, with none of the participants describing positive changes in their navigation ability, and most participants reporting negative changes. The most common domains of change reported were increased reliance on GPS, avoiding navigation at night, reduced confidence navigating, and reduced overall sense of direction.

Qualitative scoring of responses on item 12 (i.e., getting lost incidents) included assigning a score for general quality, frequency, severity, environmental familiarity, physical environment, transportation modality, and change positivity. The results show a wide range of incidents in different physical environments, levels of environmental familiarity, and

transportation modalities, with difficulties with nighttime navigation and navigation inside buildings being most prominent.

### **Exploratory Factor Analysis (EFA)**

Given the novelty of the CNQ, an EFA was utilized to investigate the factorial structure of the scale, specifically the number of factors that is most appropriate. Four models with an increasing number of factors (1,2,3,4) were run with GRM IRT using the *mirt* package. Results are available in Table 2.6. Fit statistics (AIC, SABIC, BIC) indicate a comparable model fit between 2-, 3-, and 4-factor models, indicating no benefit of more than two factors for the model.

A two-factor EFA model was subsequently run for the first 10 items. Factor loadings and communalities for questionnaire items are available in Table 2.7. Results show that items 1-4 (confidence in abilities) load heavily on factor 1, and items 7-10, particularly 8-10 (forgetting layout or environments, others commenting on getting lost), load heavily on factor 2. These item loadings on the two factors overall align well with the hypothesized *typical* and *atypical* aging constructs that the measure was intended to capture. Items 5 and 6 have similar loadings on both factors, with item 5 having the lowest commonality of all items.

### **Confirmatory Factor Analysis (CFA)**

Based on the two-factor EFA results described above, a 2-factor multidimensional CFA was then run. Items 1-6 were constrained under factor 1, and items 5-10 were constrained under factor 2. Items 5 and 6 were loaded onto both factors 1 and 2. Factor loadings are available in Table 2.8.

The results show strong item loadings based on the assigned factors, with items 5 and 6 loading similarly onto both factors. All model fit indices were within acceptable limits (CFI = 1, TLI = 1.01, SRMR = 0.07) based on previously reported standards of CFI  $\geq$  .90, TLI  $\geq$  0.95, RMSEA & SRMR < 0.08 (Kline, 2015; Hooper et al., 2008). The EFA and CFA models have similar fits, AIC = 7171.56 versus 7141.87 and SABIC = 7231.82 versus 7209.08, respectively.

To investigate any differences in responses due to biological sex, a multiple group graded response IRT analysis was conducted. Factor loadings per item divided by biological sex are available in Table 2.9. Results between a constrained and equated IRT analysis show a significant difference based on biological sex ( $X^2(4) = 59.52, p < .0001$ ), conditioning on sex improving model fit (BIC of 7393.82 versus 7359.63, SABIC of 7225.57 versus 7178.69, respectively). This is demonstrated by higher loadings and variance accounted for by the female

group (loadings:  $f_1 = 3.15$ ,  $f_2 = 3.68$ , variance:  $f_1 = 0.32$ ,  $f_2 = 0.37$ ) on both factors over the male group (loadings:  $f_1 = 2.78$ ,  $f_2 = 3.30$ , variance:  $f_1 = 0.28$ ,  $f_2 = 0.33$ ). Male group raw coefficients (Mean = 0.45, covariance = 1.48) and female group raw coefficients (M = -0.34, covariance = 1.18) also show corresponding differences. Overall, the results indicate different response patterns on the CNQ based on sex.

Lastly, item fit analyses were conducted. This S-X<sup>2</sup> goodness of fit analysis included family-wise correction; S-X<sup>2</sup> is best equipped for multidimensional IRT and reduces the incidence of Type-I error (Kang & Chen, 2008). Findings show adequate item fit for all items, with RMSEA values below recommended cut-offs (< .08), and all items fail to reject the null hypothesis with chi-square testing ( $p > .05$ ). Results are available in Table 2.10. Unstandardized threshold parameters, which can be interpreted as indicating response difficulty, are also available in Table 2.11.

## Discussion

In this study, I aimed to investigate the psychometric properties of a novel questionnaire for detecting the subjective experience of changes in spatial navigation abilities in neurotypical older adults. I found that the CNQ has a reliable 2-factor structure in a large, community-dwelling older adult population, with loadings on the theorized *typical* and *atypical* navigation constructs. Exceptions to this were two items that were found to load onto both constructs. Results showed acceptable item fit for all items, a metric of the CNQ's internal reliability. Overall, the findings show that community-dwelling older adults with age-normative memory satisfaction and objective memory performance endorse few changes in their navigation ability on the CNQ. This low endorsement of change and positively skewed distribution on the CNQ is consistent with two other measures that are used in the field that focus on difficulty or change in navigation abilities, one questionnaire has a moderately positively skewed distribution in individuals with preclinical AD (Allison et al., 2019) and the other questionnaire has a distribution that appears to be extremely positively skewed in typical aging and moderately positively skewed in individuals with aMCI (Cerman et al., 2018).

This study extends past work by being the first to measure self-evaluations of changes in spatial navigation ability within the context of subjective and objective assessment of episodic and spatial memory and navigation ability. Objective memory performance on both the Face-Name and Four Mountains tasks in this sample of older adults was in the typical range for aging

(Burles & Iaria, 2020; Troyer et al., 2012). The sample's metamemory evaluations, as measured by the MMQ and SAM Episodic subscale, are also consistent with what has been reported in typical aging (Palombo et al., 2013; Troyer et al., 2012). Also consistent with typical aging is the sample's evaluation of their general spatial navigation abilities and spatial anxiety as measured on the WQ (van der Ham et al., 2021). By contrast, this sample's general spatial navigation abilities, as assessed by the SBSOD, was significantly lower than those of a group of American older adults tested in a previous study (T.F. Levine et al., 2021). This difference may be due to the current study's sample being predominantly from the United Kingdom and/or the lack of screening for cognitive decline and ADRD risk factors (cognitive or biomarker), unlike in T.F. Levine and colleagues' study.

To the best of my knowledge, this the first administration of the NSQ to an older adult sample which quantifies allocentric strategy use. Scores on the NSQ in this older adult sample were significantly lower when compared to younger adults (Brunec et al., 2019). The finding of reduced self-reported allocentric strategy use in this aging sample is consistent with experimental findings (Colombo et al., 2017; Lopez et al., 2018) and offer initial support for the measure's use in the older adult population. Overall, the sample's profile of metamemory and subjective spatial navigation abilities is consistent with typical aging.

Quantitative responses on the CNQ diverged from these other spatial navigation measures, seeming to capture a different construct than general spatial memory, anxiety, or strategy use. The CNQ also appears to provide valuable information on the type of spatial changes noticed in typical aging. Spatial navigation changes that were most endorsed in this sample were in comfort and anxiety when navigating. It is worth noting that not all CNQ items explicitly orient participants to negative changes in spatial navigation. The negative directionality of changes could be investigated explicitly by altering items to query negative changes, though this framing could reduce participants' willingness to endorse changes to spatial memory and navigation that they have experienced.

The pattern of endorsed responses and qualitative data on the CNQ are consistent with the literature on older adults' self-reported decline in certain domains and not others (Cerman et al., 2018; Lester et al., 2017). Specifically, fewer participants endorsed *atypical* changes, specifically items addressing getting lost, forgetting the layout of familiar spaces or difficulties navigating. This low endorsement of *atypical* changes when navigating aligns with previous

findings which suggest that declines in spatial navigation abilities may be a good marker of pathological as opposed to typical aging and expands on it by specifying the types of difficulties that may be experienced in typical aging (Coughlan et al., 2018; Laczó et al., 2017). Although responses to items were not of sufficient length to allow for a full qualitative analysis, categorization of responses show that a small but significant subgroup of individuals report some incidents of disorientation and getting lost in both familiar and unfamiliar environments. These responses highlight the potential benefits of supplementing quantitative data with qualitative data when assessing spatial navigation difficulties. Overall, the results corroborate and extend past research on subjective declines in navigation and changes in strategy use in aging by elaborating on the types of changes in navigation that older adults subjectively experience and are aware of (Colombo et al., 2017; Van der Ham et al., 2021). The next dissertation chapter will evaluate the relationship between the CNQ and the other study questionnaires and objective tasks in more detail using structural equation modeling.

While item fit analyses indicate acceptable fit of all items, CNQ items 5 and 6 were best modeled as loading onto both the *typical* and *atypical* constructs. Item 5 queries participants on increased GPS reliance. There are several possible reasons why this item loads onto both the constructs. GPS use may indicate a need for an external compensatory tool due to declining spatial navigation skills. However, GPS use is also relatively novel and therefore increased reliance over the recent years may indicate GPS integration into daily life. There are recent data suggesting that GPS reliance may be detrimental to spatial memory over time (Dahmani & Bohbot, 2020). Therefore, the item loading onto the *atypical* construct may be more relevant to greater future vulnerability to spatial navigation deficits due to greater reliance on GPS. The CNQ's current structure does not gather sufficient information to distinguish between these hypotheses; a solution may be to reframe the item to specify whether individuals would be comfortable navigating without GPS in familiar and unfamiliar areas, and what prompted their increased reliance on GPS.

Item 6 on the CNQ also loaded onto both the *typical* and *atypical* constructs. Item 6 queries participants on whether they rely more on others for assistance when navigating. Increased reliance on others may be considered pathological, indicating a loss of independence, or alternatively, it may be attributable to reduced confidence in navigating new environments as is seen in typical aging (van der Ham et al., 2021) and on other CNQ item responses (items 1-4).

The CNQ does not differentiate environmental familiarity in its items; a revision of the CNQ could include items that ask participants to complete items for familiar environments separately from unfamiliar environments, similar to the questionnaire designed by Pai and colleagues (2012).

In this study there were notable sex differences on both self-report and objective experimental measures. Compared to males, females reported less allocentric strategy use and worse spatial navigation abilities on all questionnaires. Females also reported higher levels of spatial anxiety. For metamemory, females reported better episodic memory skills (SAM Episodic subscale) and more memory strategy use (MMQ Strategy subscale) but similar ability and satisfaction skills to males (MMQ Ability and MMQ Satisfaction subscales).

Females had better associative episodic performance than males as measured by the Face-Name Task. There were no sex differences in allocentric spatial memory performance as measured on the Four Mountains Task. The latter is consistent with the (at most) small-to-moderate differences in objective spatial navigation abilities between the sexes across the lifespan, with the most pronounced differences in pointing recall and distance estimation (Nazareth et al., 2019; Yu et al., 2021); the Four Mountains Task does not fall within either of these categories. The most extreme sex-differences in objective ability (i.e., moderate effect sizes) are in mental rotation abilities, with males outperforming females. These sex differences increase with age (Silverman et al., 2007; Newcombe, 2020). While the Four Mountains Task does have a rotation element, past work shows that performance on this task does not relate to general mental rotation abilities (Burles & Iaria, 2020) and, instead, it is best conceptualized as a hippocampally based allocentric task (Bird et al., 2010). Overall, the current findings appear to be consistent with research showing that males, particularly with increasing age, are more likely to overestimate their objective spatial memory abilities than females (Yu et al., 2021).

Consistent with previous empirical evidence of biological sex differences in objective spatial memory and navigation abilities, strategy use, and self-reported skills (Andersen et al., 2012; Boone et al., 2018; Nazareth et al., 2019), there were differences in item endorsement on the CNQ as a function of sex. Specifically, in this participant sample females endorsed greater changes in their ability and over a longer period of time for the CNQ *typical* items than males. It is common in clinical practice to divide neuropsychological test norms by sex, including verbal episodic memory (Bleecker et al., 1988; Brunet et al., 2020; Irwing et al., 2012; Schmidt et al.,

2000) and there is evidence that aMCI diagnostic accuracy improves when considering sex (Sundermann et al., 2019). The current results suggest that it may be beneficial to use sex-divided norms for the CNQ, particularly the *typical* items, similar to other subjective spatial navigation measures in the field (Condon et al., 2015; van der Ham et al., 2021).

Participants in this study reported psychological distress that was overall in the low range and differed by sex (Manea et al., 2012; Spitzer et al., 1990). Females reported significantly higher depression, but not anxiety, symptoms than males. It is worth noting data collection occurred during the COVID-19 pandemic which had a profound negative impact on mood and may have impacted these findings (Salari et al., 2020). Psychological distress is one explanation for the sex-based findings reported in this study (Altemus et al., 2014; Pavisic et al., 2021). Other explanations include hormonal fluctuations (Barel & Tzischinsky, 2018; Hamson et al., 2011), strategy use (Boone et al., 2018; Yuan et al., 2019), and sociocultural variables (Coutrot et al., 2018; Spiers et al., 2021). Further research is needed to pull apart these influences. For now, sex-divided norms on subjective spatial navigation ability measures may be adequate.

There are several notable limitations to this first investigation into the psychometric properties of the CNQ. While internal consistency and item reliability is addressed in these analyses, I did not establish test-retest reliability, a critical psychometric property essential to any test and particularly significant to clinical care (Calamia et al., 2013).

Furthermore, while the older adult sample in this study was large and divided by biological sex, the sample was not characterized with neuropsychological tests. Given the population incidence of aMCI, it is possible that some individuals in this sample are on the preclinical ADRD spectrum (Ward et al., 2012). However, this is less likely based on the high degree of memory satisfaction, relatively high scores on objective tasks and online recruitment methodology. These variables, coupled with the demographic characteristics of the sample (i.e., high education levels), and participant exclusion based on attentional checks, may have led to a bias towards a higher-functioning sample, affecting generalizability of the findings. Future work will need to investigate CNQ performance in neuropsychologically characterized older adults with and without aMCI to further investigate the measure's psychometric properties and sensitivity to more subtle navigation dysfunction.

The sample's international recruitment of English-speaking older adults may be considered a strength for the generalizability of results. However, caution is warranted in extending findings

to individuals outside of the United States or the United Kingdom and British Isles, especially since IRT analyses by nationality were not possible and objective spatial navigation abilities may differ by nationality (Coutrot et al., 2018).

Overall, this study provides an initial investigation of the CNQ's psychometric properties in aging. The results contribute to a small but growing literature on the measurement of the subjective changes or recent difficulties in spatial navigation abilities (Allison et al., 2019; Cerman et al., 2018). Future work should investigate the CNQ's clinical utility and psychometric properties in a more diverse sample of older adults and in individuals on the preclinical ADRD spectrum. With further research, the CNQ may be best used as an addition to current subjective measures of general ability and spatial anxiety with large normative data (van der Kuil et al. 2021; Yu et al., 2021) to better characterize and contextualize individuals' navigation abilities.

**Table 2.1****Sample Demographics**

	<i>Initial Sample</i>	<i>Final Sample</i>
	<i>N = 587</i>	<i>N = 533</i>
<b>Age</b>	<i>M = 65.5, SD = 4.6</i>	<i>M = 65.5, SD = 4.6</i>
<b>Education</b>	<i>N = 195 high school, N = 241 college, N = 134 masters, professional, doctoral, N = 19 other*</i>	<i>N = 167 high school, N = 229 college, N = 119 masters, professional, doctoral, N = 17 other*</i>
<b>Sex</b>	274M, 311F (47% Male)	250M, 281F (47% Male)
<b>Gender</b>	<i>N = 1 identifying as nonbinary, N = 1 identifying as other</i>	<i>N = 1 identifying as nonbinary, N = 1 identifying as other</i>
<b>English as first language</b>	92%	93%
<b>English language used most often</b>	97%	97%

*Note.* “M” indicates Male, “F” indicates female.

*M* = mean, *SD* = standard deviation.

\*Other indicates individuals who were not comfortable sharing their education and either left this section blank or provided insufficient information for coding, such as “apprenticeship”

**Table 2.2***Scale Description & Descriptive Statistics*

<b>Measures</b>	<b>Description</b>	<b>Mean (SD)   Skew, Range</b>
<b>Objective Memory Measures</b>		
Four Mountains Task, %	↑ scores = ↑ ability	51 (13)   1, 20-90
Face-Name Task Overall Accuracy, %	↑ scores = ↑ ability	84 (9)   -8, 48-96
Face-Name Task Old Recombined Accuracy, %	↑ scores = ↑ ability	73 (22)   -9, 0-100
<b>Subjective Memory &amp; Spatial Measures</b>		
Survey of Autobiographical Memory Event (Episodic) Subscale	↑ scores = ↑ ability	100.2 (14.1)   0.5, 73-136.9
Multifactorial Memory Questionnaire		
Satisfaction Subscale	↑ scores = ↑ satisfaction	49.8 (12.7)   -0.5, 7-72
Ability Subscale	↑ scores = ↑ ability	57.8 (11.7)   -0.5, 21-80
Strategy Subscale	↑ scores = ↑ strategy use	27.4 (11.2)   0.2, 0-60
Santa Barbara Sense of Direction Questionnaire	↑ scores = ↑ spatial ability	4.4 (1.1)   -0.6, 1.6-6.3
Navigational Strategies Questionnaire	↑ scores = ↑ map strategy	0.6 (4.9)   -0.3, -12-13
Wayfinding Questionnaire		
Navigation/Orientation Subscale	↑ scores = ↑ ability	4.9 (1.2)   -0.6, 1-7
Distance Estimation Subscale	↑ scores = ↑ ability	4.3 (1.5)   -0.4, 1-7
Spatial Anxiety Subscale	↑ scores = ↑ anxiety	3.3 (1.4)     0.4, 1-7
Changes in Navigation Questionnaire (CNQ)	↑ scores = ↑ changes	4.5 (5.7)   2.0, 0-35
CNQ Factor 1	↑ scores = ↑ changes	2.5 (3.3)   1.7, 0-16
CNQ Factor 2	↑ scores = ↑ changes	0.7 (1.8)   4.4, 0-16
<b>Mood</b>		
Patient Health Questionnaire-9 (PHQ-9)	↑ scores = ↑ depression	3.7 (4.3)   1.7, 0-22
Generalized Anxiety Disorder-7 (GAD-7)	↑ scores = ↑ anxiety	2.8 (4.0)   2.0, 0-21

**Table 2.3*****CNQ Descriptive Statistics by Item***

<b>Items</b>	<b>Mean (Standard Deviation), Skew</b>
1.1	0.35 (0.84), 2.61
1.2	0.72 (1.14), 1.55
1.3	1.26 (1.34), 0.68
1.4	0.27 (0.76), 3.10
1.5	0.96 (1.32), 1.11
1.6	0.42 (0.93), 2.34
1.7	0.40 (0.84), 2.41
1.8	0.09 (0.44), 5.81
1.9	0.11 (0.49), 5.34
1.10	0.10 (0.48), 5.99
2.1	0.78 (1.69), 1.95
2.2	1.60 (2.13), 0.80
2.3	2.56 (2.29), 0.03
2.4	0.59 (1.55), 2.48
2.5	1.93 (2.28), 0.53
2.6	0.94 (1.80), 1.61
2.7	0.93 (1.74), 1.61
2.8	0.17 (0.71), 4.70
2.9	0.24 (0.95), 4.34
2.10	0.20 (0.92), 4.88

*Note.* See Appendix B for CNQ items.

Items 1.1-1.10 refer to amount of change noticed, rated on 0-4 scale with 4 indicating most amount of change. Items 2.1-2.10 refer to timeframe of change noticed, with 0-8 ratings.

**Table 2.4***CNQ Descriptive Statistics by Sex*

<b>Item</b>	<b>Males</b>	<b>Females</b>
1.1	0.3 (0.7), 3.1	0.4 (0.9), 2.3
1.2	0.4 (0.9), 2.1	1.0 (1.3), 1.1
1.3	0.9 (1.1), 1.0	1.6 (1.4), 0.4
1.4	0.3 (0.7), 3.3	0.3 (0.8), 2.9
1.5	1.0 (1.3), 1.0	0.9 (1.4), 1.2
1.6	0.3 (0.8), 2.5	0.5 (1.1), 2.1
1.7	0.4 (0.8), 2.3	0.4 (0.9), 2.5
1.8	0.1 (0.4), 5.0	0.1 (0.4), 6.5
1.9	0.1 (0.5), 5.1	0.1 (0.5), 5.5
1.10	0.1 (0.5), 5.4	0.1 (0.4), 6.6
2.1	0.6 (1.5), 2.4	1.0 (1.8), 1.6
2.2	1.2 (1.97), 1.2	1.9 (2.2), 0.5
2.3	2.0 (2.3), 0.5	3.0 (2.2), -0.3
2.4	0.5 (1.3), 2.9	0.7 (1.7), 2.2
2.5	2.1 (2.3), 0.3	1.7 (2.3), 0.7
2.6	0.8 (1.7), 1.7	1.0 (1.9), 1.5
2.7	1.0 (1.8), 1.4	0.9 (1.7), 1.8
2.8	0.2 (0.7), 4.9	0.2 (0.7), 4.5
2.9	0.3 (1.0), 4.2	0.2 (0.9), 4.4
2.10	0.2 (0.9), 4.3	0.2 (1.0), 5.2

*Note.* See Appendix B for CNQ items. Values per group are mean (standard deviation), skew. Items 1.1-1.10 refer to amount of change noticed, rated on 0-4 scale with 4 indicating most amount of change. Items 2.1-2.10 refer to timeframe of change noticed, with 0-8 ratings.

**Table 2.5**

***CNQ Qualitative Coding***

	<b>Number, Mean (SD), Skew</b>
<b>CNQ– Item 11 Responses</b>	
<i>Item 11: “Please use the space below to describe any changes you have noticed in navigating”</i>	
Description Quality	<i>N</i> = 199, 1.8 (0.7), 0.21
Severity	<i>N</i> = 199, 2.0, (0.9), 0.69, 3 unclear
Positivity in Changes Described	<i>N</i> = 123 negative, <i>N</i> = 24 stable, <i>N</i> = 82 unclear
<b>CNQ – Item 12 Responses</b>	
<i>Item 12: “If you have had an experience of being disoriented or lost or confused while navigating a physical environment (while driving, walking or inside dwellings), please describe this experience in detail”</i>	
Description Quality	<i>N</i> = 100, 2.0 (0.8), -0.02
Frequency	<i>N</i> = 100, 2.8 (1.3), 0.11 <i>N</i> = 32 (1), <i>N</i> = 21 (2), <i>N</i> = 10 (3), <i>N</i> = 34 (4), <i>N</i> = 3 (5)
Severity	<i>N</i> = 100, 2.6 (1.0), 0.47
Environmental Familiarity	<i>N</i> = 22 (1), <i>N</i> = 22 (2), <i>N</i> = 6 (3), <i>N</i> = 44 (4), <i>N</i> = 5 (5)
Physical Environment	<i>N</i> = 60 (0), <i>N</i> = 2 (1), <i>N</i> = 17 (2), <i>N</i> = 1(3), <i>N</i> = 16 (4), <i>N</i> = 3(5) 1(6)
Transportation	<i>N</i> = 29 (1), <i>N</i> = 29 (2), <i>N</i> = 42 (4)

*Note.*

**Description Quality Scale:** 1= Basic description, 3 = Detailed description

**Severity:** 1 to 5 scale, with 1 = No worry, 5 = Very worrisome

**Positivity in Changes Described:** 1 = negative change, 2 = stable, 3 = unclear, 4 = positive change

**Frequency** 1 = 1 time, 2 = several, 3 = lifetime, 4 = general, 5 = many times

**Environmental Familiarity:** 1 = new, 2 = familiar, 3 = highly familiar, 4 = unclear, 5 = both new & familiar

**Physical Environment:** 0 = no category, 1 = parking, 2 = nighttime/low visibility, 3 = home, 4 = building, 5 = woods/countryside, 6 = crowds, 7 = bus/subway stations

**Transportation Modality:** 1 = walking, 2 = driving, 3 = transit, 4 = unspecified, 5 = biking

**Table 2.6*****EFA Results – Number of Factors***

	<b>AIC</b>	<b>SABIC</b>	<b>BIC</b>	<b>LogLik</b>	<b>X<sup>2</sup></b>	<b>df</b>	<b><i>p</i></b>
1 factor model	7254.24	7311.02	7466.57	-3578.12	NA	NA	NA
2 factor model	7141.87	7209.08	7393.20	-3512.93	130.38	9	< .001
3 factor model	7141.93	7218.40	7427.92	-3504.96	15.94	8	0.043
4 factor model	7124.44	7209.03	7440.77	-3489.22	31.48	7	< .001

*Note.* AIC = Akaike information criterion, SABIC = Sample-size-adjusted Bayesian information criterion, LogLik= Log Likelihood of observed data.

**Table 2.7*****Two-factor EFA Results – Factor Loadings & Commonalities***

	<b>Factor 1 Loadings</b>	<b>Factor 2 Loadings</b>	<b>h<sup>2</sup></b>
Item 1 <i>Confidence traveling familiar places alone</i>	0.87	-0.03	0.79
Item 2 <i>Confidence traveling unfamiliar places alone</i>	1.00	0.09	0.91
Item 3 <i>Confidence traveling at night/reduced visibility</i>	0.77	0.01	0.59
Item 4 <i>Confidence giving directions to other people</i>	0.57	-0.28	0.58
Item 5 <i>How much rely on GPS or other technology for navigation (rely more)</i>	0.34	-0.32	0.35
Item 6 <i>How much rely on others for navigation aid/assistance (rely more)</i>	0.50	-0.41	0.65
Item 7 <i>Making more mistakes when going places</i>	0.44	-0.54	0.76
Item 8 <i>Forgetting the layout inside familiar buildings or homes</i>	-0.09	-0.93	0.77
Item 9 <i>Forgetting (becoming confused) about where doors lead to in buildings or homes</i>	0.01	-0.92	0.86
Item 10 <i>Family members or others commenting on your getting lost</i>	0.04	-0.87	0.80

*Note.* h<sup>2</sup> refers to commonality or total variance the factors account for in the model. All CNQ items begin with ‘Have you noticed any changes in..’

**Table 2.8*****CFA Results – Factor Loadings & Commonalities***

	<b>Factor 1 Loadings</b>	<b>Factor 2 Loadings</b>	<b>h<sup>2</sup></b>
Item 1 <i>Confidence traveling familiar places alone</i>	0.90	0.00	0.81
Item 2 <i>Confidence traveling unfamiliar places alone</i>	0.93	0.00	0.87
Item 3 <i>Confidence traveling at night/reduced visibility</i>	0.77	0.00	0.59
Item 4 <i>Confidence giving directions to other people</i>	0.76	0.00	0.58
Item 5 <i>How much rely on GPS or other technology for navigation (rely more)</i>	0.22	0.45	0.25
Item 6 <i>How much rely on others for navigation aid/assistance (rely more)</i>	0.43	0.57	0.51
Item 7 <i>Making more mistakes when going places</i>	0.00	0.90	0.80
Item 8 <i>Forgetting the layout inside familiar buildings or homes</i>	0.00	0.80	0.64
Item 9 <i>Forgetting (becoming confused) about where doors lead to in buildings or homes</i>	0.00	0.88	0.77
Item 10 <i>Family members or others commenting on your getting lost</i>	0.00	0.87	0.77

*Note.* h<sup>2</sup> refers to commonality or total variance accounted for in the model. All CNQ items begin with ‘Have you noticed any changes in...’

**Table 2.9*****CFA Results by Sex***

	Males			Females		
	F1	F2	h <sup>2</sup>	F1	F2	h <sup>2</sup>
Item 1 <i>Confidence traveling familiar places alone</i>	0.84	0.00	0.71	0.89	0.00	0.79
Item 3 <i>Confidence traveling at night/reduced visibility</i>	0.74	0.00	0.54	0.80	0.00	0.64
Item 4 <i>Confidence giving directions to other people</i>	0.69	0.00	0.47	0.76	0.00	0.57
Item 5 <i>How much rely on GPS or other technology for navigation (rely more)</i>	0.17	0.45	0.23	0.19	0.51	0.30
Item 6 <i>How much rely on others for navigation aid/assistance (rely more)</i>	0.43	0.52	0.45	0.48	0.56	0.54
Item 7 <i>Making more mistakes when going places</i>	0.00	0.88	0.77	0.00	0.91	0.83
Item 8 <i>Forgetting the layout inside familiar buildings or homes</i>	0.00	0.78	0.60	0.00	0.83	0.68
Item 9 <i>Forgetting (becoming confused) about where doors lead to in buildings or homes</i>	0.00	0.85	0.73	0.00	0.89	0.79
Item 10 <i>Family members or others commenting on your getting lost</i>	0.00	0.86	0.74	0.00	0.89	0.80

*Note.* F1= Factor 1 Loadings, f2 = Factor 2 Loadings. All CNQ items begin with “Have you noticed any changes in...”

**Table 2.10*****CFA Item Fit***

	<b>S_X<sup>2</sup></b>	<b>RMSEA.S_X<sup>2</sup></b>	<b>p.S_X<sup>2</sup></b>
Item 1 <i>Confidence traveling familiar places alone</i>	27.82	0.00	0.75
Item 2 <i>Confidence traveling unfamiliar places alone</i>	20.17	0.00	0.84
Item 3 <i>Confidence traveling at night/reduced visibility</i>	45.35	0.02	0.75
Item 4 <i>Confidence giving directions to other people</i>	30.82	0.01	0.75
Item 5 <i>How much rely on GPS or other technology for navigation (rely more)</i>	68.11	0.03	0.15
Item 6 <i>How much rely on others for navigation aid/assistance (rely more)</i>	21.49	0.00	0.84
Item 7 <i>Making more mistakes when going places</i>	40.35	0.03	0.15
Item 8 <i>Forgetting the layout inside familiar buildings or homes</i>	10.31	0.00	0.75
Item 9 <i>Forgetting (becoming confused) about where doors lead to in buildings or homes</i>	9.49	0.00	0.83
Item 10 <i>Family members or others commenting on your getting lost</i>	7.95	0.00	0.75

*Note.* RMSEA = Root Mean Square Error of Approximation. All CNQ items begin with “Have you noticed any changes in...”

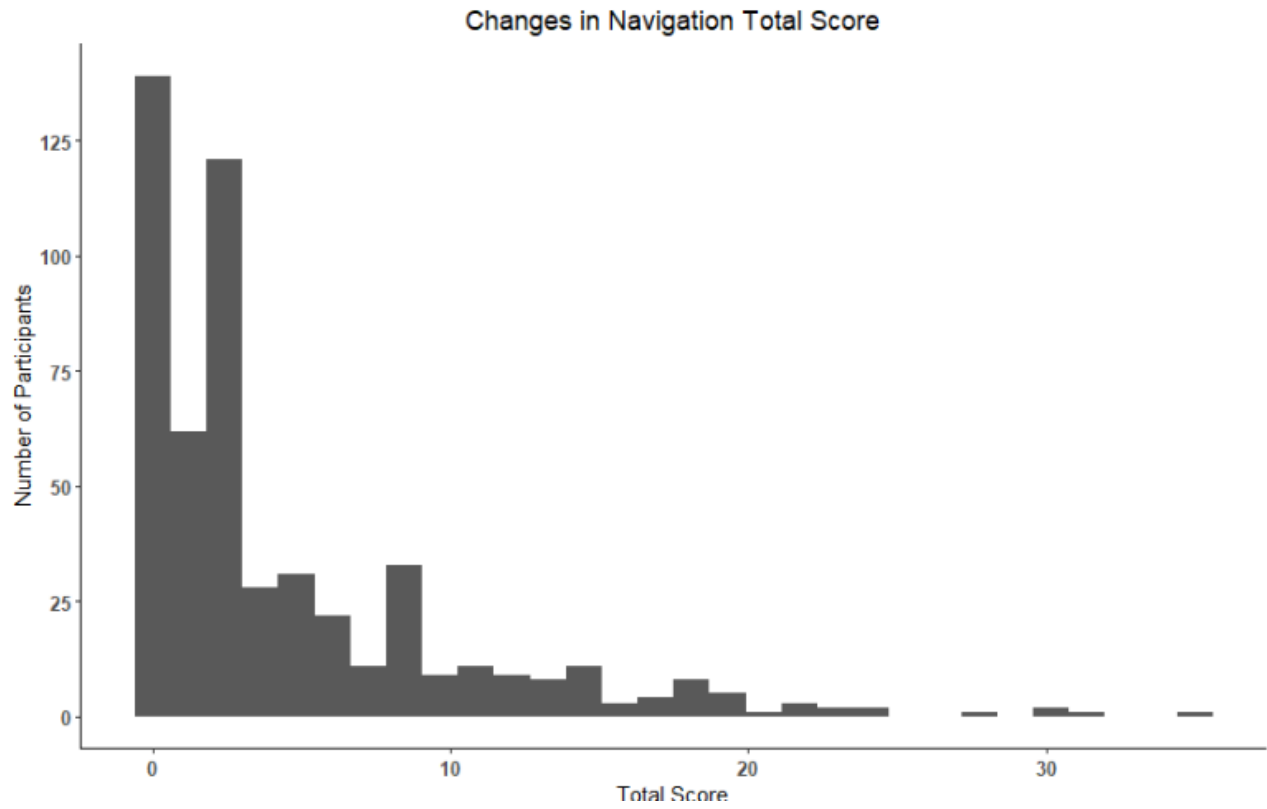
**Table 2.11*****Threshold Parameters***

	<b>R1</b>	<b>R2</b>	<b>R3</b>	<b>R4</b>	<b>R5</b>	<b>R6</b>
Item 1 <i>Confidence traveling familiar places alone</i>	3.49	0.00	-3.41	-4.85	-6.47	-8.69
Item 2 <i>Confidence traveling unfamiliar places alone</i>	4.33	0.00	-1.46	-3.84	-5.90	-8.02
Item 3 <i>Confidence traveling at night/reduced visibility</i>	2.05	0.00	0.53	-0.77	-2.04	-3.77
Item 4 <i>Confidence giving directions to other people</i>	1.99	0.00	-2.79	-3.80	-4.78	-6.18
Item 5 <i>How much rely on GPS or other technology for navigation (rely more)</i>	0.43	0.87	-0.36	-1.08	-2.13	-2.95
Item 6 <i>How much rely on others for navigation aid/assistance (rely more)</i>	1.05	1.40	-2.22	-3.25	-4.56	-5.96
Item 7 <i>Making more mistakes when going places</i>	0.00	3.42	-2.45	-4.86	-6.69	-8.47
Item 8 <i>Forgetting the layout inside familiar buildings or homes</i>	0.00	2.26	-4.51	-5.69	-7.74	NA
Item 9 <i>Forgetting (becoming confused) about where doors lead to in buildings or homes</i>	0.00	3.08	-5.21	-7.05	-8.05	-9.68
Item 10 <i>Family members or others commenting on your getting lost</i>	0.00	3.07	-5.69	-7.13	-8.19	-9.16

*Note.* R = Response. Item 8 response 6 had no responses. All CNQ items begin with “Have you noticed any changes in...”

**Figure 2.1**

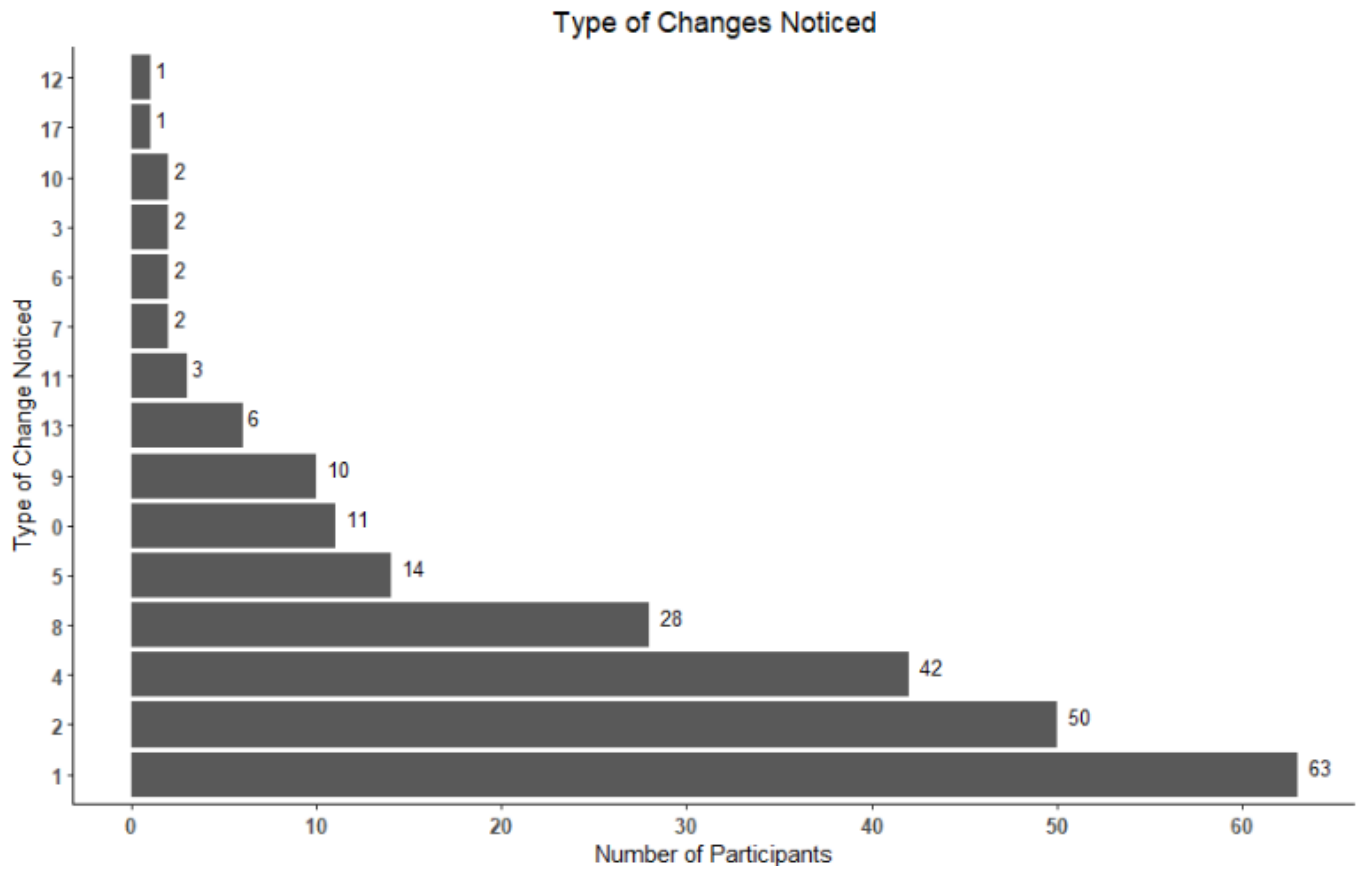
*CNQ Total Score Distribution*



*Note.* Higher scores mean more changes in spatial navigation ability.

**Figure 2.2**

*CNQ Category of Changes*



*Note.* 0 = normal, 1 = reliance on GPS, 2 = avoiding nighttime /vision, 3 = familiar streets only, 4 = less comfort/less confidence, 5 = forgetting known navigation info, 6 = overall memory worse, 7 = difficulty with verbal directions, 8 = sense of direction/overall navigation, 9 = attention issues, 10 = issues visualizing known locations, 11 = issues with route changes, 12 = confuse new routes with old, 13 = issues navigating new routes, 14 = rely on other people, 15 = improved navigation, 16 = buildings, 17 = issues with navigating while walking

## CHAPTER 3

### Study 2: Investigating the relationship between subjective spatial navigation & memory abilities

In the previous chapter, I characterized a typical aging sample on common spatial navigation questionnaires used in the field and investigated the psychometric properties, specifically the internal reliability and item structure, of the CNQ. It is unclear how responses to different subjective spatial navigation measures relate to one another and whether performance on these questionnaires is associated with other aspects of memory. This is important to understanding how perceived spatial navigation abilities change with age and relate to clinical variables such as psychological distress and objective memory abilities. In this study, correlation analyses and structural equation modeling were used to evaluate relationships among responses on questionnaires assessing spatial navigation ability and metamemory, and measures of psychological distress, and objective memory abilities.

Like most fluid cognitive abilities, including episodic and associative memory, objective spatial navigation memory abilities decline as individuals age (LaPlume et al., 2022). Objective spatial memory is often measured with tasks such as cognitive map learning, landmark recognition and ordering, and distance estimation (Keynejad et al., 2018; Techentin et al., 2014; van der Ham et al., 2021). There are numerous studies that have investigated the overlap between spatial memory and navigation abilities and episodic memory, driven by the shared neural substrate of the hippocampus (Buzsáki & Moser, 2013; Ekstrom & Ranganath, 2017; Hassabis & Maguire, 2007; Moscovitch et al., 2016). It is proposed that the hippocampus offers a perceptual framework of vivid, detailed information that links both episodic and spatial processes (Ekstrom & Yonelinas, 2020; Gilboa & Moscovitch, 2021; Hassabis & Maguire, 2007).

The hippocampus is implicated in a broader spatial navigation network (Aguirre et al., 2019; Antonova et al., 2009; Delpolyi et al., 2007). Navigation changes or difficulties related to reduced hippocampal functioning in aging include learning new routes, forming a comprehensive cognitive map and generally effective versatile, non-habit-based navigation (Coughlan et al., 2018; Lester et al., 2017). Importantly, hippocampal integrity appears to contribute to spatial disorientation and navigation difficulties seen in individuals diagnosed with aMCI and ADRD (Coughlan et al., 2018; Ekstrom et al., 2018b; Giannakopoulos et al., 2000). Research investigating individual differences using the SAM, a subjective memory measure, has found that episodic and spatial abilities dissociate as independent constructs (Fan et al., 2021). A study

in young adults found similar results, showing that episodic memory as measured by the SAM was separate from self-reported spatial abilities on the SBSOD (Clark & Maguire, 2020). These results suggest a dissociation between self-reported spatial navigation and episodic memory, which contrasts with theories that propose a shared underlying substrate (Buzsáki & Moser, 2013; Ekstrom & Ranganath, 2017). It is unclear whether the subjective evaluation of spatial navigation abilities would relate to metamemory (subjective memory ability) or objective memory abilities in the aging population when using different and more comprehensive measures.

### **Subjective Spatial Navigation Abilities**

Multiple questionnaires exist to assess the subjective evaluation of spatial navigation abilities. The relationship between these different classes of questionnaires has not been formally assessed, including the extent to which they capture different aspects of the spatial navigation experience. Understanding the relationship between these measures can inform researchers and clinicians' selection of measures and reduce redundancy in assessment.

The SBSOD is a 15-item questionnaire with a 7-point Likert scale designed as a “measure of environmental spatial ability” and initially developed for use with younger adults (Hegarty et al., 2002; see Appendix B for the questionnaire). It is the most commonly used measure of spatial navigation abilities in the field, with the original paper being cited over 950 times (Hegarty et al., 2002). Factor-analytic work finds the measure captures orientation, engagement with maps, engagement with directions, and allocentric processing, and finds that responses on the measure are strongly influenced by personality traits (Condon et al., 2015). The SBSOD has been used in many behavioural and neuroimaging studies on spatial memory, spatial navigation and driving, including in older adults (Allison et al., 2018; Merriman et al., 2016; Turano et al., 2009). Recent longitudinal work has indicated the measure may not be sensitive to important metrics (amyloid and tau biomarkers or *APOE* genotype) of preclinical ADRD (T.F. Levine et al., 2021). The SBSOD has laid the groundwork in the field of subjective spatial navigation abilities, but it may not be the best measure to capture subjective spatial navigation abilities in aging and preclinical ADRD.

The WQ is a more recently developed subjective measure of spatial navigation abilities and spatial anxiety (van der Ham et al., 2013). The measure has 22 items each with a 7-point Likert scale and 3 subscales: the Distance Estimation subscale, Navigation Orientation subscale, and

Spatial Anxiety subscale (Claessen et al., 2016b; see Appendix B for the questionnaire). Findings show that individuals who have experienced a stroke or ABI report reduced wayfinding ability (i.e., Distance Estimation and Navigation Orientation subscale scores) and higher spatial anxiety on the WQ (De Rooij et al., 2019; van der Ham et al., 2013; van der Kuil et al. 2021). A similar pattern of lower responses on the WQ has been observed in older adults compared to younger adults and WQ scores are weakly related to objective spatial measures (van der Ham et al., 2021; Yu et al., 2021). The WQ is a promising measure of subjective spatial navigation ability for use in aging and in individuals with cognitive impairment which expands on the SBSOD by including the construct of spatial anxiety.

Both the WQ and SBSOD questionnaires have items which refer to the use and manipulation of cognitive maps. There has been increasing interest into how (allocentric) strategies used during spatial navigation may mediate performance on objective navigation tasks, including sex differences in performance (Boone et al., 2018; Harris & Wolbers, 2014; Hegarty et al., 2022). The NSQ is a 15-item questionnaire with 2-3 response choices per item which results in a single score quantifying allocentric strategy use (Brunec et al., 2018, 2019; see Appendix B for the questionnaire). Responses to the NSQ have been linked to hippocampal engagement in young adults (Brunec et al., 2018; 2019). While the NSQ has only been previously used in young adults, its sensitivity to hippocampal integrity and focus on allocentric strategy use may increase our understanding of spatial navigation abilities in aging.

The last class of spatial navigation questionnaires query individuals about perceived changes in ability. There are two recently published questionnaires that focus on changes or increased difficulty in spatial navigation ability. These questionnaires have been used samples of older adults and individuals on the ADRD spectrum (Allison et al., 2019; Cerman et al., 2018). The CNQ described in study 1 is such as a measure and was designed to have a 2-factor structure of *typical* and *atypical* changes in navigation ability.

In this study I included different established questionnaires on spatial navigation ability and investigated the relationship between them. I also included the CNQ to see how it relates to other questionnaires used in the field.

### **Subjective Memory Abilities**

In contrast to emerging nature of the research on the extent and quality of declines in subjective spatial navigation abilities in aging, there is an extensive body of work on the

subjective evaluation of memory ability or metamemory, in aging and in individuals diagnosed with aMCI and ADRD (Mitchell et al., 2014). It is common for older adults to have increased memory dissatisfaction and subjective cognitive complaints (Jonker et al., 2000; Ginó et al., 2010). These memory complaints have weak to moderate negative correlations with objective memory performance, with weaker correlations in aMCI and MCI (Brailean et al., 2019; Fyock & Hampstead, 2015; Herrmann, 1982). Despite the discrepancy between subjective complaints and objective performance, poor metamemory or high memory dissatisfaction shows a positive significant relationship to ADRD biomarker pathology, including hippocampal integrity (Amariglio et al., 2012; Cantero et al., 2016; Parfenov et al., 2020; Saykin et al., 2006).

Subjective memory complaints and SCD are multi-faceted in the demographic and clinical features which account for them. They have been shown to be moderated by personality traits (L.A. Rabin et al., 2017), sociodemographic factors (Flatt et al., 2021; Gupta et al., 2021), and most significantly, psychological symptoms of depression and anxiety (Peters et al., 2019; Yates et al., 2017). The latter is particularly important because psychological distress is associated with an increased risk of aMCI and ADRD (Mourao et al., 2016; Sannemann et al., 2020). There is also a historic exclusion of individuals with psychiatric comorbidity in medical research studies, including in studies of individuals with ADRD, which presents an issue to the generalizability of many research findings (Humphreys et al., 2015; Keynejad et al., 2018). If subjective spatial navigation abilities are to be routinely measured in clinical assessment, it will be important to investigate their relationship to metamemory and also the contributors to individuals' evaluation of these abilities, including psychological distress.

There are multiple measures available to assess subjective memory complaints and metamemory in aging, each with subtle differences (Broadbent, 1982; Gilewskiet al., 1990; Wasef et al. 2021). The MMQ is a measure that stands out for its sound psychometric properties and for being used in typical aging, in older individuals with subjective cognitive complaints, and in individuals diagnosed with aMCI (Troyer & Rich, 2018; Shaikh et al., 2021). Metamemory evaluations using the SAM have been related to MTL connectivity in young adults (Palombo et al., 2013; Sheldon et al., 2016) and the measure has been used in aging to investigate subjective memory mistakes (Fan et al., 2020). In this study, I used both the MMQ and the SAM Episodic subscale to measure older adult participants' subjective evaluation of their memory abilities.

## **Current Study**

The present study was motivated by four research questions. First, what is the relationship among different spatial navigation questionnaires, and to what extent do they load onto the same latent variable? Second, what is the relationship between the CNQ and other established measures of subjective spatial navigation? Third, what is the strength of the relationship between metamemory and subjective spatial navigation abilities? And fourth, do objective memory (associative episodic and spatial) and psychological distress have the same relationships with spatial navigation abilities and metamemory?

I aimed to address these questions by integrating multiple sources of information, approximating clinical situations where a clinician is asked to integrate subjective, objective, and psychiatric information to determine the significance of subjective complaints. In this study, I administered multiple questionnaires assessing spatial navigation and psychological distress, along with objective tests of episodic and spatial memory. I then used structural equation modeling to investigate the relationships between performance on these tasks. The results have the potential to inform theoretical models on the relationship between episodic memory and spatial navigation abilities and offer information on the best measures to assess subjective spatial navigation abilities in aging.

## **Method**

### **Participants**

The older adult participant sample of 587 individuals is described in study 1. A subset of 533 individuals were included in the current analyses. Demographic information for these individuals is provided in Table 2.1.

### **Materials**

Study materials are described in Chapter 2. Objective memory measures included the Four Mountains Task (Burlles & Iaria, 2020) and Face-Name Task (Troyer et al., 2011).

Subjective memory and spatial navigation abilities were measured with the MMQ, the SAM Episodic subscale, the SBSOD, the NSQ, the WQ and novel CNQ (Brunec et al., 2018; Hegarty et al., 2002; Palombo et al., 2013; Troyer & Rich, 2018; van der Ham et al., 2013).

Symptoms of psychological distress were measured with the PHQ-9 and GAD-7 (Kroenke et al., 2001; Spitzer et al., 1990; Spitzer et al., 2006).

## **Procedure**

Participant recruitment, data collection and data cleaning procedures are described in Chapter 2.

## **Data Analysis**

Data were analyzed using R version 4.2.0 (R Core Team, 2013). Descriptive statistics were run using the *psych* package (Revelle & Revelle, 2015). Correlations were run from base R and the *Hmisc* package (Harrell & Harrell, 2019). Due to the non-normal distributions for several of the variables, nonparametric statistics, specifically Spearman rank-order correlations, were calculated. Correlations divided by sex are available in Appendix G. Structural equation modeling analyses were run with the *lavaan* package (Rosseel, 2012). Unfortunately, the sample size was not sufficient to run separate structural equation models for females and males.

Assigning labels to the strength of correlational relationships based on cut-offs is arbitrary and often inconsistent (Schober et al., 2018). Instead of using cut-offs, it is best practice to contextualize the relationships within the literature and standards of the field. Nevertheless, these labels are beneficial for descriptive and interpretative purposes. In this study, I described relationships as *weak* when coefficients were between 0.1-0.3, *moderate* when between 0.4-0.6, and *strong* when between 0.7-0.9 (Akoglu, 2018; Ratner, 2009; Schober et al., 2018).

## **Results**

### **Descriptive Statistics**

Descriptive statistics and scale descriptions for all of the study measures are available in Table 2.2. Interpretation of descriptive statistics is available in Chapter 2.

### **Correlation Matrix**

Zero-order correlations and corresponding statistical significance between study measures are available in Table 3.1. Results show statistically significant correlations among almost all questionnaires, ranging in strength. The exception to this was the NSQ and MMQ Strategy Subscale which had weaker, and more selective relationships with other questionnaires. Measures of psychological distress were significantly correlated with almost all study questionnaires and with each other. The Face-Name Task had no significant correlations with other study variables, with the exception of the Four Mountains Task. The Four Mountains Task

had statistically significant relationships with the MMQ Ability subscale, the NSQ, the SBSOD, the WQ Spatial Anxiety subscale, the WQ Navigation Orientation subscale and the GAD-7.

### **Path Analyses**

To investigate the four research questions detailed above, a series of structural equation models or path analyses were conducted. Three models were constructed in total, with each building on the previous model. Given the two-factor structure of the CNQ found in the previous chapter, the questionnaire was modeled in all path analyses with 2 factors. The cross loading of items 5 and 6 led to the omission of these items from the factors. The alternative would have been to load each item onto one factor over the other which would disregard study 1 structural equation modeling findings that these items are best modeled as cross-loading.

Model 1 investigated the relationship between metamemory and subjective spatial navigation abilities. The three MMQ subscales were loaded onto a *Metamemory* construct and all four spatial questionnaires, divided by subscales when appropriate, were loaded onto a (subjective) *Spatial Navigation Abilities* construct. Factor loadings are available in Table 3.2 and graphical depiction is available in Figure 3.4. Model 1 results show a weak positive and significant relationship between Metamemory and Spatial Navigation Abilities. There are moderate to strong loadings from all predictors on both latent variables, with the exception of the CNQ factors, which had negative (due to item framing) weak to moderate loadings. The CNQ factor 1 had a stronger loading (-0.39) than CNQ factor 2 (-0.21) on Spatial Navigation Abilities.

Model 1 had evidence of suboptimal fit, including a significant chi-square statistic ( $\chi^2 < .001$ ) and fit statistics below or above recommended cut-offs (TLI = 0.83, SRMR = 0.10, RMSEA = 0.13). Diagnostic investigation of latent variables and the predictors revealed a heteroscedastic prediction of the Spatial Navigation Abilities construct for the two CNQ factors, as depicted in Figures 3.1 and 3.2. All other latent variable loadings had appropriate linear relationships (see Figure 3.3 for an example of the WQ Navigation Orientation subscale). This suggests that model fit is negatively impacted by the CNQ loadings. Critically, the poor model fit does not prevent interpretation between latent variables or their model loadings.

Model 2 included the addition of the study's two objective memory measures, the Face-Name Task (old-recombined accuracy) and the Four Mountains Task (overall accuracy). Factor loadings and fit statistics are available in Table 3.3 and graphical depiction is available in Figure 3.5. Model 2 findings show that the objective memory tasks have a weak and significant positive

correlation with one another. The Four Mountains Task had a weak but significant loading onto Spatial Navigation Abilities. The Face-Name Task did not significantly load onto Metamemory. The relationship between Metamemory and Spatial Navigation Abilities, or between questionnaires/subscale loadings onto either construct was not altered in significance from the previous model. Like Model 1, Model 2 also had evidence of suboptimal fit, including a significant chi-square statistic ( $\chi^2 < .001$ ), and fit statistics below or above recommended cut-offs (TLI = 0.8, SRMR = 0.09, RMSEA = 0.11).

Model 3 included the two psychological distress measures, the PHQ-9 and GAD-7, measuring depression and anxiety, respectively. Both measures were loaded onto the latent variables, Metamemory and Spatial Navigation Abilities, and also correlated with one another as latent variables. Factor loadings and fit statistics are available in Table 3.4 and graphical depiction is available in Figure 3.6.

Model 3 results show that depression and anxiety scores were strongly, positively correlated with each other. Both psychological distress measures also had significant weak loadings onto Metamemory. Only anxiety symptoms had a significant, weak loading onto Spatial Navigation Abilities. There were no changes in Model 3 from Model 2 relationships between Metamemory and Spatial Navigation Abilities, objective memory tasks, or questionnaire/subscale loadings onto either construct. The exception to this is the Four Mountains Task which no longer had a statistically significant loading onto Spatial Navigation Abilities. Like the previous models, Model 3 also had evidence of suboptimal fit, including a significant chi-square statistic ( $\chi^2 < .001$ ), and fit statistics below or above recommended cut-offs (TLI = 0.85, SRMR = 0.08, RMSEA = 0.10).

### **Discussion**

This study aimed to investigate the relationship between different spatial navigation measures, and between metamemory and spatial navigation abilities in a typical aging population, while exploring relationships with psychological distress and objective memory abilities. Findings offer a more nuanced understanding of the relationship between metamemory and subjective spatial navigation abilities in aging by quantifying this relationship with structural equation modeling. By providing specific information on the relationships between questionnaires, results also offer considerations for selecting measures to evaluate subjective spatial navigation abilities.

In this discussion, I will revisit the four research questions posed at the start of this chapter, share study limitations, and propose future directions for research.

### **Subjective Spatial Navigation Abilities**

To the best of my knowledge, this study is the first and most comprehensive investigation of the relationship between different subjective spatial navigation questionnaires, and in an aging sample.

Using structural equation modeling, results show that different, established spatial navigation questionnaires (SBSOD, WQ, and NSQ) have moderate to strong loadings onto the same latent construct. Questionnaires and subscales of more general spatial navigation ability (SBSOD, WQ Navigation Orientation subscale, WQ Distance Estimation subscale) have strong positive loadings onto the latent variable of Spatial Navigation Abilities, showing significant overlap between these questionnaires and subscales.

The NSQ was the measure that had the fewest number of significant zero-order correlations with other spatial navigation questionnaires and had a moderate loading on the latent variable of Spatial Navigation Abilities. These findings suggest that allocentric strategy use, as measured by the NSQ, is at least partly distinct from evaluations of general spatial navigation ability. This finding is notable since there are items on the other measures that ask about allocentric spatial strategy use. It may be that the NSQ is particularly sensitive to hippocampal integrity (Brunec et al., 2018; 2019). Regardless, it appears better subjective general spatial navigation abilities are not synonymous with more self-reported allocentric spatial strategy use. This suggests caution in simplifying better navigation abilities as to whether individuals use more allocentric spatial strategies (Caffò et al., 2020; Colombo et al., 2017; Ekstrom et al., 2014). Instead, it appears allocentric spatial strategy use is but one element contributing to how individuals rate their subjective spatial navigation abilities.

The WQ Spatial Anxiety subscale had a moderate (bordering on strong) negative loading on the latent variable of Spatial Navigation Abilities. The negative directionality is due to higher scores on the WQ Spatial Anxiety subscale indicating greater difficulty. This subscale measures the less commonly assessed construct of spatial anxiety. The WQ Spatial Anxiety subscale's significant moderate loading supports its relevance to, and divergence from, general spatial navigation abilities (Hund & Minarik, 2006; van der Ham et al., 2021).

Overall, the results confirm that established spatial navigation questionnaires of general spatial ability are highly related. The findings further suggest that there may be utility in including measures that assess spatial anxiety and strategy use as they offer different information from estimates of general spatial navigation skills.

### **Changes in Navigation Questionnaire**

The second study question centered on the relationship of the CNQ with other classes of spatial navigation questionnaires. The CNQ's skewed distribution presented an issue for overall model fit in structural equation modeling. Non-parametric correlations showed a weak relationship of CNQ total score with other spatial navigation measures. I would hypothesize that in a different population, such as in individuals on the preclinical ADRD spectrum, more items would be endorsed and there would be less skew in responses, as seen on other measures focusing on changing or increased difficulty in spatial navigation abilities (Cerman et al., 2018; Allison et al., 2019).

In all models, the CNQ factors had negative weak-moderate loadings on the latent variable Spatial Navigation Abilities. The CNQ factor 1 *typical* changes had a higher loading on Spatial Navigation Abilities than the *atypical* CNQ factor 2. This shows a greater divergence of atypical changes than typical changes from subjective spatial navigation skills as captured on other questionnaires. This is consistent with the CNQ's item creation which was based on past data of normative age-related changes in spatial navigation (Laczó et al., 2017; Lithfous et al., 2013; Lopez et al., 2018; Yu et al., 2021). These findings also show that lower self-reported spatial navigation abilities are related to a higher number of typical changes on the CNQ. While correlational, results suggest that older individuals with generally lower spatial navigation abilities prior to aging may be more susceptible to the increased spatial navigation changes in aging.

Overall results provide evidence, for the first time, on the relationship between subjective changes in spatial navigation ability and general spatial navigation abilities. Findings indicate there is unique information provided by measuring changes in navigation ability. Since individuals rate themselves according to internal standards instead of the hypothetical general population, and subjective general spatial navigation abilities are highly related to personality characteristics, as captured by the SBSOD (Condon et al., 2015), measuring changes in spatial

navigation ability may be a more sensitive way to measure atypical versus typical spatial navigation abilities in aging.

### **Spatial Navigation Abilities and Metamemory**

The third study question focused on the relationship between Metamemory and Subjective Spatial Navigation Abilities. In all three study models, the latent variables Spatial Navigation Abilities and Metamemory were weakly positively related.

This finding is partially consistent with the proposed shared dependence of episodic memory and spatial memory on the hippocampus (Buzsáki & Moser, 2013; Ekstrom & Ranganath, 2018; Hassabis & Maguire, 2007). However, the strength of the relationship supports the notion that these are distinct constructs, as posited by others (Fan et al., 2021, Clark & Maguire, 2020). This would be consistent with findings that the overlap between the spatial navigation network and episodic memory network is not complete and that there may be differences within the spatial memory network in older versus younger adults (Ekstrom et al., 2017, 2018b; Herweg & Kahana, 2018; Lester et al., 2017; Ramanoël et al., 2019). Overall, results appear to support that the evaluation of memory and spatial abilities are largely separate.

Still, the weak positive relationship found between metamemory, and spatial navigation abilities in this study is stronger than in a previous study that used the SAM Episodic and Spatial subscales and found the loadings on the subscales to be independent (Fan et al., 2021). The metamemory questionnaire used in this study, the MMQ, is longer in length than the SAM Episodic subscale and gathers information on memory satisfaction, memory abilities, and strategy use with items framed for the older adult population (Troyer & Rich, 2018). This is different from the shorter SAM Episodic subscale which is designed to capture a more general trait estimate of memory ability and has primarily been examined in younger adults for individual differences and for its relationships to the MTLs and neuroanatomical functioning (Palombo et al., 2013; Sheldon et al., 2016). Another explanation for the (marginally) stronger relationship between spatial navigation abilities and metamemory found in this study is the inclusion of multiple spatial navigation questionnaires and subscales (including measuring spatial anxiety and allocentric strategy use), instead of only the SBSOD or SAM Spatial subscale. Overall, while findings of a weak relationship are largely consistent with past research, results underscore the importance of study methodology and questionnaires used.

## **Objective Memory & Psychological Distress**

The fourth research question surrounded the relationships of objective memory abilities and psychological distress with subjective Spatial Navigation Abilities and Metamemory. First, I will discuss the results related to objective memory abilities, followed by the results related to psychological distress.

### ***Objective Memory***

Structural equation modeling results showed that performance on the two objective memory measures, the Four Mountains Task and Face-Name Task, was weakly related with one another and had weak loadings onto Spatial Navigation Abilities and Metamemory.

The weak loading of the Four Mountains Task onto spatial navigation abilities was statistically significant in Model 2 but not Model 3. Past research has found the subjective evaluation of spatial navigation ability is weakly but significantly associated with objective spatial navigation ability (Clark & Maguire, 2020; van der Ham et al., 2021; Selarka et al., 2019). This is the first use of this version of Four Mountains Task in a neurotypical older adult population. A similar version of this allocentric spatial memory task has been administered to individuals with developmental topographical disorientation (Burles & Iaria, 2020), and other versions have been found to be sensitive to deficits seen in individuals with aMCI and preclinical ADRD (Bird et al., 2010; Chan et al., 2016). The Four Mountains Task therefore has past evidence of being sensitive to hippocampal functioning and difficulties with real-world spatial navigation.

In this study, the Four Mountains Task's strongest relationship (albeit weak) with a subjective spatial navigation questionnaire was with the NSQ, a measure which focuses on allocentric strategy use (Brunec et al., 2018; 2019). It may be that the Four Mountains Task's weak significant relationship to the construct Spatial Navigation Abilities is due to the task's greater reliance on hippocampal functioning, which is only one aspect of subjective spatial navigation abilities.

The lack of a significant loading of the objective episodic associative memory performance on the Face-Name Task on the Metamemory construct is largely consistent with past literature showing, at most, a weak relationship between subjective and objective memory and that, generally, individuals evaluate themselves according to internal benchmarks (Brailean et al., 2019; Crumley et al., 2014). Other work has shown that subjective memory complaints on the

Memory Function Questionnaire do predict associative memory performance even when age, sex, mood, and *APOE*  $\epsilon$ 4 status is accounted for (Horn et al., 2018). The MMQ was not designed to be related to objective associative episodic memory, and past investigations of its relationships to objective skills have focused on neuropsychological measures of memory (Troyer & Rich, 2018). Overall, the Face-Name Task's distinctiveness from Metamemory is generally consistent with past research.

These findings highlight the importance of gathering subjective and objective information on memory and spatial navigation/memory abilities as they are largely independent.

### ***Psychological Distress***

In addition to objective memory, the fourth research question also aimed to investigate the relationship of psychological distress to Metamemory and Spatial Navigation Abilities.

In this study, anxiety and depression symptoms (i.e., psychological distress) were strongly positively related with each other and had significant, weak loadings onto metamemory. This concurs with past literature indicating a positive relationship between subjective cognitive complaints (negative metamemory evaluations) and symptoms of anxiety and depression (Buckley et al., 2016; Burmester et al., 2016; Cherbuin et al., 2015; Norman et al., 2020).

The influence of psychological distress has generally not been considered in the subjective evaluation of spatial abilities and, to my knowledge, has never been investigated with structural equation modeling. Model results showed that anxiety symptoms, but not depression symptoms, had a weak significant negative loading onto Spatial Navigation Abilities. This is consistent with the negative relationship between spatial anxiety and navigation skills, particularly for females (Hund & Minarik, 2006; Lawton & Kalli, 2002; Yuan et al., 2019).

These findings suggest that symptoms of psychological distress may have a different, weaker relationship with spatial navigation abilities than with metamemory. This work expands on the two past studies which I am aware of that investigated psychological distress in older participants in relation to subjective changes (or increased difficulty) in spatial navigation abilities. Cerman and colleagues (2018) found group differences in self-reported depression symptoms between individuals with SCD, aMCI, and non-amnesic MCI compared to control participants, and also found group differences in self-reported changes in spatial navigation abilities. However, they did not find a significant relationship between depression or anxiety symptoms with reports of changing spatial navigation abilities. Using the same measure, Sheardova and colleagues (2015)

found anxiety, but not depression, symptoms were related to subjective navigation complaints in an older adult sample. If the results from this study are replicated and psychological distress relates less to subjective spatial navigation abilities than metamemory this may have implications for its clinical use. Specifically, these abilities may be less influenced by the construct-irrelevant information of psychological distress or personality, and better reflect the evaluation of everyday objective skills instead of personality judgment.

Future work can elaborate on these results by including more comprehensive mood and anxiety measurements, such as diagnostic interviewing, and personality metrics for a more thorough investigation into the contributions of psychological factors to subjective spatial navigation abilities.

### **Limitations and Future Directions**

A strength of this work is the large sample size and use of multiple, established spatial navigation measures to investigate the relationship among the Spatial Navigation Abilities and Metamemory constructs with path analyses.

A limitation of this study was that the sample size was not sufficient to investigate sex differences with structural equation modeling. Findings from study 1 and correlations (Appendix G), combined with past literature suggest dividing analyses by sex may have subtly changed the relationships between subjective and objective episodic and spatial memory measures. Specifically, there may be stronger correlations between objective task performance and subjective abilities in females than in males (Crumley et al., 2014; van der Ham et al., 2021). Due to sex-differences in item endorsement, relationships among metamemory and subjective spatial navigation abilities may also have been altered.

Future research should investigate these relationships in individuals who are characterized with neuropsychological measures and in individuals with documented memory impairment attributable to neurodegenerative processes, such as in preclinical ADRD. In the next chapter, individuals with anterograde amnesia were administered the same measures of subjective and objective episodic and spatial memory in order to understand the relationship between impaired episodic memory and hippocampal functioning with metamemory and subjective spatial navigation abilities.

## Conclusion

The results of this study show that commonly used questionnaires of spatial navigation ability are strongly related to one another when capturing general trait evaluations of navigation ability. The findings further investigate the CNQ's psychometric properties by evaluating its relationship to other spatial navigation questionnaires. Models and correlations indicate that CNQ scores have a negative, weak relationship with general spatial navigations abilities and there is a difference depending on the factor, providing more evidence for the *atypical* and *typical* factor structure of the measure. Subjective spatial navigation abilities were found to be weakly related to metamemory judgments and weakly related to objective spatial memory. Symptoms of psychological distress were more related to metamemory than subjective spatial navigation abilities.

These study findings show that the measurement of subjective spatial navigation abilities is likely to offer additional information over and above metamemory evaluations. When measuring spatial navigation abilities in aging, multiple questionnaires may be beneficial, with a comprehensive battery aiming to capture general ability, strategy use, spatial anxiety, and changes to abilities.

Table 3.1

*Correlation Matrix*

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	
1. MMQ Satisfaction	1.00															
2. MMQ Ability	0.63	1.00														
3. MMQ Strategy	-0.35	-0.56	1.00													
4. SAM Episodic	0.43	0.42	-0.15	1.00												
5. NSQ	0.05	0.08	-0.10	0.02	1.00											
6. SBSOD	0.34	0.31	-0.18	0.39	0.55	1.00										
7. WQ Spatial Anxiety	-0.24	-0.25	0.21	-0.21	-0.45	-0.58	1.00									
8. WQ Navigation Orientation	0.27	0.23	-0.13	0.41	0.52	0.81	-0.58	1.00								
9. WQ Distance Estimation	0.18	0.15	-0.10	0.28	0.39	0.56	-0.44	0.65	1.00							
10. CNQ Total	-0.33	-0.38	0.24	-0.27	-0.17	-0.33	0.34	-0.30	-0.23	1.00						
11. CNQ Factor 1	-0.30	-0.35	0.24	-0.23	-0.17	-0.33	0.37	-0.30	-0.27	0.90	1.00					
12. CNQ Factor 2	-0.24	-0.31	0.14	-0.20	-0.14	-0.23	0.24	-0.22	-0.13	0.60	0.48	1.00				
13. PHQ-9	-0.36	-0.35	0.21	-0.16	-0.08	-0.18	0.23	-0.14	-0.14	0.21	0.22	0.19	1.00			
14. GAD-7	-0.33	-0.33	0.24	-0.14	-0.14	-0.23	0.30	-0.18	-0.12	0.26	0.27	0.24	0.71	1.00		
15. Face-Name Task	0.00	0.07	0.01	0.00	0.01	-0.01	-0.04	-0.01	-0.03	0.02	0.05	-0.03	0.01	1.00		
16. Four Mountains Task	0.07	0.09	-0.01	-0.05	0.15	0.11	-0.13	0.09	0.08	0.01	-0.01	-0.08	-0.02	0.00	1.00	
														-0.09	0.10	

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

*Note.* Values indicate strength of relationship between variables with Spearman's

$\rho$  non-parametric test statistic.

**Table 3.2***Model 1 loadings and fit indices.*

<b>Latent Variables &amp; Loadings</b>	<b>Estimate</b>	<b>Standard Error</b>	<b><i>p</i>-value</b>	<b>Standardized Coefficients</b>
Metamemory & Spatial Navigation Ability	0.32	0.04	< 0.001	0.32
<b>Metamemory</b>				
MMQ Ability Subscale	10.96	0.49	< 0.001	0.94
MMQ Satisfaction Subscale	8.93	0.55	< 0.001	0.70
MMQ Strategy Subscale	-6.76	0.49	< 0.001	-0.60
<b>Spatial Navigation Ability</b>				
SBSOD	0.94	0.04	< 0.001	0.89
NSQ	3.21	0.20	< 0.001	0.65
CNQ Factor 1	-1.29	0.14	< 0.001	-0.39
CNQ Factor 2	-0.37	0.08	< 0.001	-0.21
WQ Navigation/Orientation	1.06	0.04	< 0.001	0.92
WQ Distance Estimation	1.07	0.06	< 0.001	0.70
WQ Spatial Anxiety	-0.96	0.05	< 0.001	-0.69
$\chi^2 (45) = 340.63, p < .0001, CFI = 0.87, RMSEA = 0.13$				

*Note.* MMQ = Multifactorial Memory Questionnaire, SBSOD = Santa Barbara Sense of Direction Questionnaire, NSQ = Navigational Strategies Questionnaire, CNQ = Changes in Navigation Questionnaire, WQ = Wayfinding Questionnaire

**Table 3.3***Model 2 loadings and fit indices.*

<b>Latent Variables &amp; Loadings</b>	<b>Estimate</b>	<b>Standard Error</b>	<b><i>p</i>-value</b>	<b>Standardized Coefficients</b>
Metamemory & Spatial Navigation Ability	0.32	0.04	< 0.001	0.32
Face-Name Task & Four Mountains Task	0.05	0.03	0.028	0.10
<b>Metamemory</b>				
MMQ Ability Subscale	11.14	0.50	< 0.001	0.96
MMQ Satisfaction Subscale	8.85	0.57	< 0.001	0.69
MMQ Strategy Subscale	-6.79	0.50	< 0.001	-0.60
Face-Name Task	0.06	0.04	0.175	0.06
<b>Spatial Navigation Ability</b>				
SBSOD	0.93	0.04	< 0.001	0.89
NSQ	3.17	0.20	< 0.001	0.65
CNQ Factor 1	-1.34	0.15	< 0.001	-0.40
CNQ Factor 2	-0.39	0.08	< 0.001	-0.21
WQ Navigation/Orientation	1.05	0.04	< 0.001	0.91
WQ Distance Estimation	1.06	0.06	< 0.001	0.70
WQ Spatial Anxiety	-0.97	0.06	< 0.001	-0.69
Four Mountains Task	0.07	0.03	0.009	0.12
$\chi^2 (52) = 349.90, p < .0001, CFI = 0.87, RMSEA = 0.11$				

*Note.* MMQ = Multifactorial Memory Questionnaire, SBSOD = Santa Barbara Sense of Direction Questionnaire, NSQ = Navigational Strategies Questionnaire, CNQ = Changes in Navigation Questionnaire, WQ = Wayfinding Questionnaire

**Table 3.4***Model 3 loadings and fit indices.*

<b>Latent Variables &amp; Loadings</b>	<b>Estimate</b>	<b>Standard Error</b>	<b><i>p</i>-value</b>	<b>Standardized Coefficients</b>
Metamemory & Spatial Navigation Ability	0.33	0.05	< 0.001	0.33
Face-Name Task & Four Mountains Task	0.06	0.03	0.027	0.10
PHQ-9 & GAD-7	10.90	0.83	< 0.001	0.74
<b>Metamemory</b>				
MMQ Ability Subscale	10.74	0.48	< 0.001	0.92
MMQ Satisfaction Subscale	9.19	0.55	< 0.001	0.71
MMQ Strategy Subscale	-6.93	0.49	< 0.001	-0.61
Face-Name Task	0.05	0.05	0.256	0.05
PHQ-9	-1.42	0.21	< 0.001	-0.33
GAD-7	-1.13	0.19	< 0.001	-0.28
<b>Spatial Navigation Ability</b>				
SBSOD	0.93	0.04	< 0.001	0.89
NSQ	3.18	0.20	< 0.001	0.65
CNQ Factor 1	-1.35	0.15	< 0.001	-0.41
CNQ Factor 2	-0.40	0.08	< 0.001	-0.22
WQ Navigation/Orientation	1.04	0.04	< 0.001	0.91
WQ Distance Estimation	1.06	0.06	< 0.001	0.70
WQ Spatial Anxiety	-0.98	0.06	< 0.001	-0.69
Four Mountains Task	0.07	0.03	0.070	0.12
PHQ-9	-0.33	0.20	0.104	-0.08
GAD-7	-0.72	0.19	< 0.001	-0.18

$$\chi^2 (72) = 415.63, p < .0001, CFI = 0.88, RMSEA = 0.10$$

*Note.* MMQ = Multifactorial Memory Questionnaire, SBSOD = Santa Barbara Sense of Direction Questionnaire, NSQ = Navigational Strategies Questionnaire, CNQ = Changes in Navigation Questionnaire, WQ = Wayfinding Questionnaire, PHQ=9 = Patient Health Questionnaire-9, GAD-7 = Generalized Anxiety Disorder scale-7

Figure 3.1

*Prediction of Spatial Navigation Ability by CNQ Factor 1*

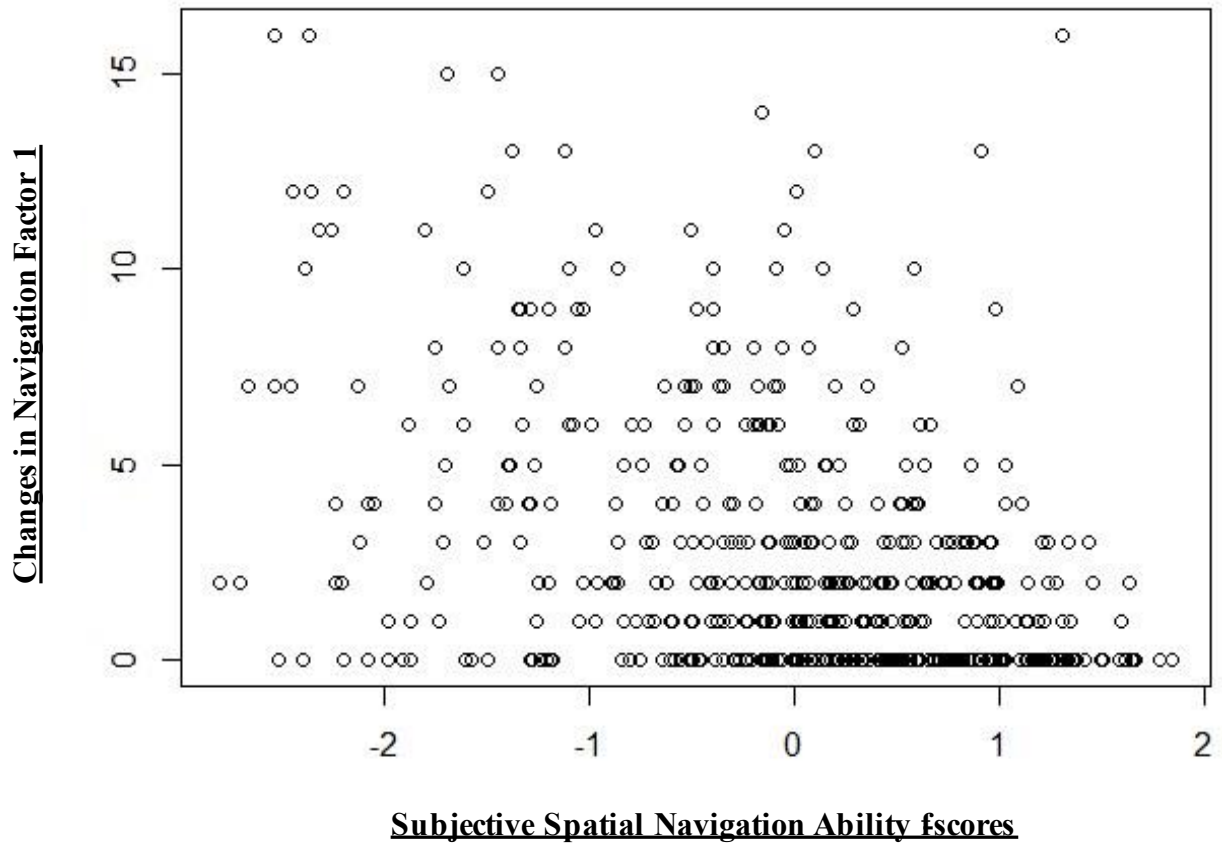
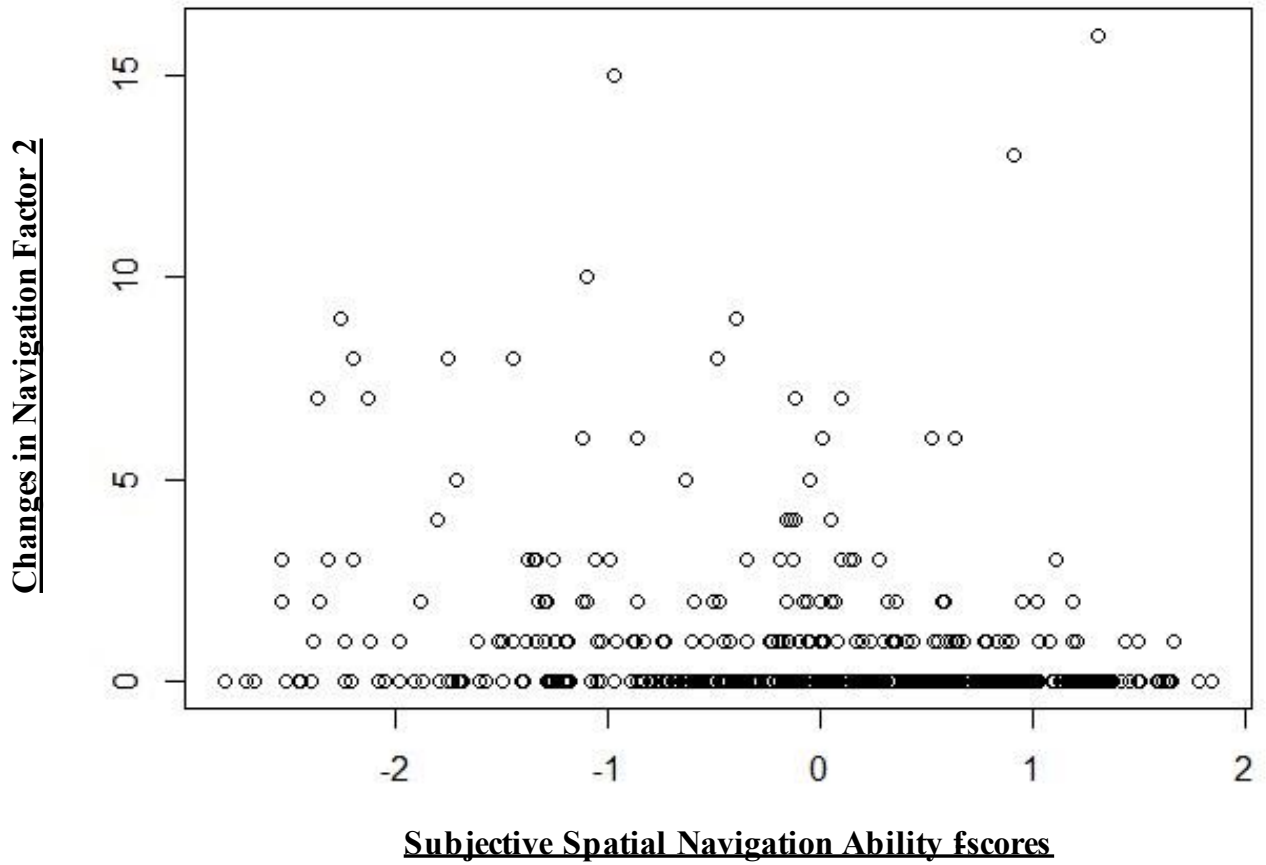


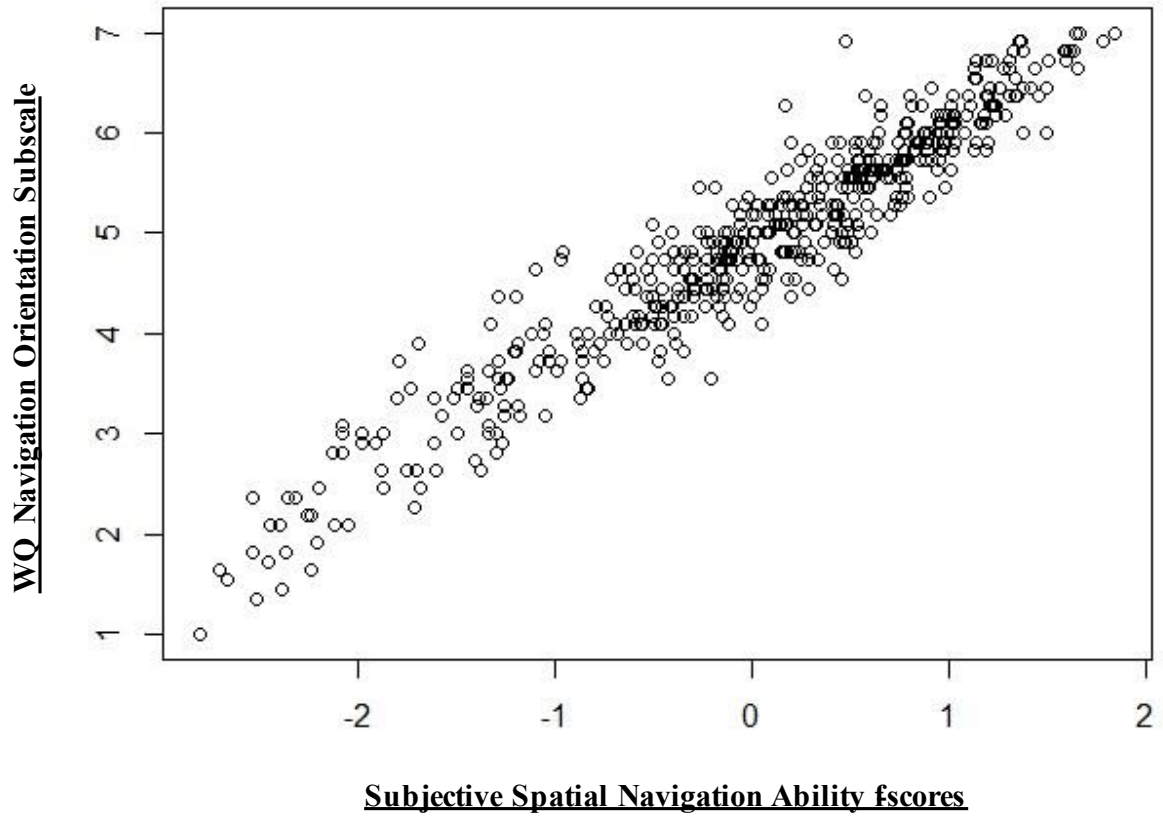
Figure 3.2

*Prediction of Spatial Navigation Ability by CNQ Factor 2*



**Figure 3.3**

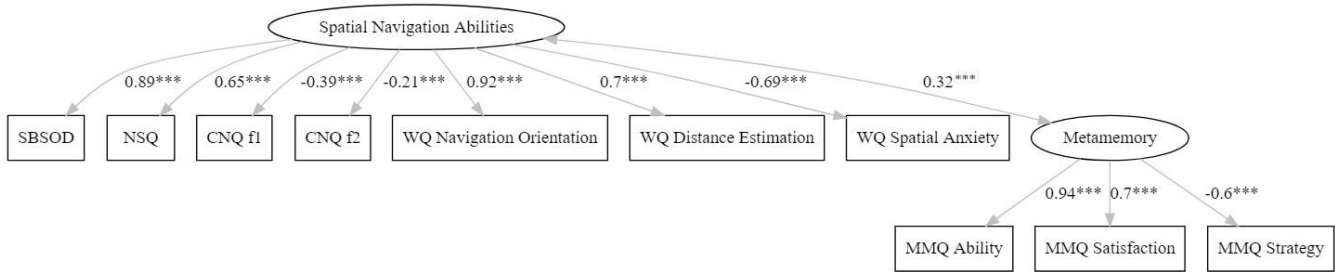
*Prediction of Spatial Navigation Ability by WQ Subscale*



*Note.* WQ = Wayfinding Questionnaire

**Figure 3.4**

**Model 1 Path Diagram – Metamemory & Spatial Navigation Abilities**

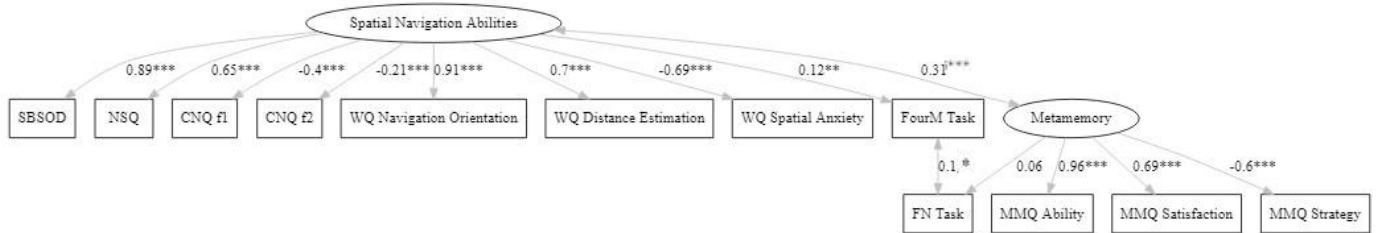


*Note.* MMQ = Multifactorial Memory Questionnaire, SBSOD = Santa Barbara Sense of Direction Questionnaire, NSQ = Navigational Strategies Questionnaire, CNQ\_f1 = CNQ Factor 1, CNQ\_f2 = CNQ Factor 2, CNQ = Changes in Navigation Questionnaire, WQ = Wayfinding Questionnaire.

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

**Figure 3.5**

**Model 2 Path Diagram– Addition of Objective Memory**

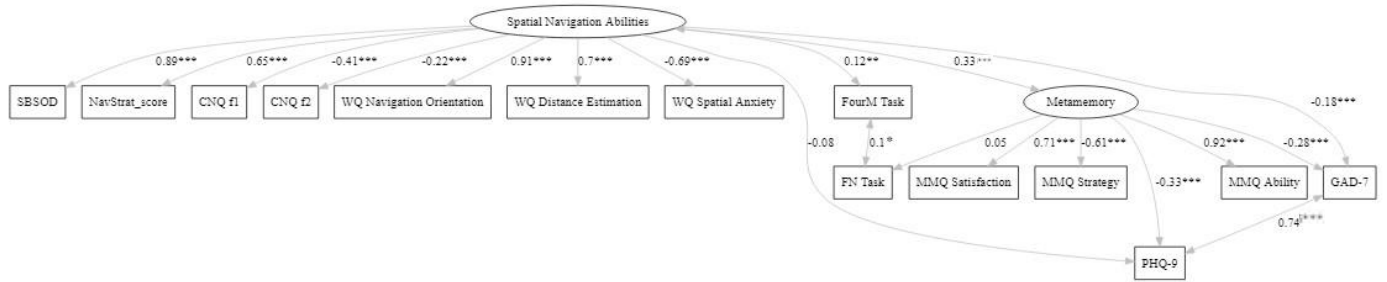


*Note.* MMQ = Multifactorial Memory Questionnaire, SBSOD = Santa Barbara Sense of Direction Questionnaire, NSQ = Navigational Strategies Questionnaire, CNQ\_f1 = CNQ Factor 1, CNQ\_f2 = CNQ Factor 2, CNQ = Changes in Navigation Questionnaire, WQ = Wayfinding Questionnaire.

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

**Figure 3.6**

**Model 3 Path Diagram – Addition of Psychological Distress**



*Note.* MMQ = Multifactorial Memory Questionnaire, SBSOD = Santa Barbara Sense of Direction Questionnaire, NSQ = Navigational Strategies Questionnaire, CNQ\_f1 = CNQ Factor 1, CNQ\_f2 = CNQ Factor 2, CNQ = Changes in Navigation Questionnaire, WQ = Wayfinding Questionnaire.

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

## CHAPTER 4

### Study 3: Subjective memory and spatial navigation abilities in individuals with hippocampal amnesia

Individuals with hippocampal lesions typically experience profound objective deficits in episodic memory and new spatial learning, which impacts spatial navigation (Pishdadian & Rosenbaum, 2021). In study 2, investigations using structural equation modeling showed that spatial navigation abilities and metamemory were weakly positively correlated and that there was a stronger loading for psychological distress measures onto metamemory than spatial navigation abilities. These findings suggest that while subjective navigation abilities are related to metamemory, they are not identical and should be assessed separately.

While researchers continue to investigate patterns of spared and impaired memory in the face of hippocampal compromise, the field has largely neglected the insight or subjective experience of memory deficits in individuals with amnesia. Anecdotal evidence suggests that individuals with hippocampal amnesia do have general insight into their anterograde amnesia (Corkin, 2013; Klein et al., 1996), though this has never been formally tested with standardized measures. In this study, I aimed to investigate the nature and extent of insight into memory loss and spatial navigation difficulties in individuals with hippocampal amnesia using established and novel measures. The results inform theories on the involvement of episodic memory in metamemory. Findings also have implications for the neural correlates of anosognosia, a condition where individuals lack insight into their cognitive deficits.

When asked, the most famous individual with amnesia, H.M., described himself as having “a lot of trouble remembering things” (Corkin, 2013). Building on these anecdotal reports, several studies have investigated the abilities of individuals with amnesia to acquire semantic knowledge post-injury and evaluate their pre- and post-morbid personality. Semantic knowledge after hippocampal damage was traditionally thought to be preserved (A.F. Gao et al., 2020; Rosenbaum et al., 2005b; Tulving et al., 1988; Westmacott & Moscovitch, 2001).

Recent research has shown that individuals with hippocampal amnesia not only have deficits recollecting details of personal events in episodic memory, but that they generate fewer details of personal semantic memories, including trait-based self-statements (Steinvorth et al., 2005; Grilli & Verfaellie, 2015). These findings have motivated a re-examination of the episodic-semantic distinction, introducing the concept of personal semantics, a subdivision of

autobiographical memory (Duff et al., 2020; Grilli & Verfaellie, 2014; Renoult et al., 2012, 2019). General, conceptual knowledge about personality appears to be intact in amnesia, but the updating of self-personality ratings appears to be impoverished, with personality ratings more closely related to preinjury than current traits and lacking reliability (Garland et al., 2021; Wank et al., 2022). An illustrative example of this incomplete learning in individuals with amnesia is individual K.C., who accurately reported that he had aged since his accident but thought that he was 10 years younger than his actual age (Rosenbaum et al., 2005b). It appears that for individuals with amnesia, memory impairment affects their self-knowledge and results in an inadequacy of specific details about the self, likely due to inadequate updating and consolidation processes (Gilboa & Moscovitch, 2021; Moscovitch et al., 2005).

Subjective assessment of cognitive decline is central to the diagnostic criteria of MCI, though it is not without controversy, particularly given the interindividual variability and multiple influences on self-reported deficits (Lenehan et al., 2012; Silva et al., 2014). Along with other brain regions associated with ADRD, subjective memory complaints have been linked to hippocampal integrity in neurotypical aging (Dauphinot et al., 2020; Saykin et al., 2006; Stewart et al., 2011; Striepens et al., 2010). In aMCI and preclinical ADRD, there are widespread brain changes that may affect insight into episodic memory or spatial navigation difficulties (Roberts et al., 2009; Rueda et al., 2015). These widespread brain changes make it challenging to know if individuals on the preclinical ADRD spectrum are unable to recall the nature of their deficits or lack insight (i.e., have anosognosia) due to other brain regions being affected by disease progression, including the prefrontal cortices (Harwood et al., 2005; Mondragón et al., 2019; Vogel et al., 2004, 2005).

As discussed in the previous chapters, there has been a proliferation of interest in investigating spatial navigation difficulties as a preclinical marker of ADRD (Coughlan et al., 2018; Laczó et al., 2017; Lithfous et al., 2013). There has also been interest in determining the best questionnaires to assess subjective spatial navigation abilities given the wide variability in objective navigation abilities. Investigating self-evaluations of episodic memory and spatial navigation in individuals with more circumscribed hippocampal lesions and/or cleaner functional dissociations within memory can offer causal information on the contribution of episodic memory deficits and the hippocampus to subjective memory and spatial navigation ability evaluations without the confounds of widespread disease processes seen in preclinical ADRD.

In summary, past work has indicated that individuals with amnesia have incomplete to impaired knowledge of self-related information. Unlike knowledge about personality or age which slowly changes over time, individuals with amnesia have pervasive deficits in memory and spatial navigation that are linked to a single event that is likely to be personally salient, and there are numerous opportunities for feedback or learning. These qualities would suggest that individuals with amnesia may have better awareness or insight into these abilities. Understanding the contributions to semantic or self-knowledge in the face of episodic memory impairment has implications for theories on the division of episodic and semantic memory (Renoult et al., 2019). Investigating these processes in individuals with hippocampal amnesia, who have stable and profound memory deficits, can also inform how other individuals with memory deficits understand and update information about themselves over time (Rosenbaum et al., 2014; Fyock & Hampstead, 2015).

In this study, I aimed to systematically investigate the subjective evaluation of memory and spatial navigation abilities in two individuals with anterograde amnesia due to hippocampal damage who are well characterized neuropsychologically. To accomplish this, first I measured the individuals' objective memory and spatial navigation abilities with hippocampally-dependent experimental tasks. I selected an associative episodic memory and an allocentric spatial memory task which have demonstrated sensitivity to hippocampal functioning, memory impairment, and spatial navigation difficulties (Bird et al., 2010; Burles & Iaria, 2020; Troyer et al., 2011, 2012). To assess metamemory, two subjective memory measures were administered which capture subjective memory ability, satisfaction, and strategy use (Palombo et al., 2013; Troyer & Rich, 2018). To measure subjective spatial navigation abilities, I administered standardized measures of general spatial skill, strategy use, and spatial anxiety (Brunec et al., 2018; Claessen et al., 2016b; Hegarty et al., 2002; van der Kuil et al., 2021). To test if individuals with amnesia are aware of their changed spatial navigation abilities, I administered the CNQ and asked individuals to anchor their ratings of changes from before their amnesic accident. I hypothesized that, given amnesic individuals' intact introspection processes, that more objective impairment would be related to worse ratings of memory and spatial navigation ability, and more memory strategy use. I further hypothesized that their memory satisfaction could be explained by considering both objective memory abilities and symptoms of psychological distress.

## Method

### Participants

Informed consent was gathered from all study participants and all participants were tested online for this study. Control testing procedures are described in study 1. Individuals with amnesia were tested online with an experimenter available through video or by phone to assist with instructions.

### *Individuals with amnesia*

Two individuals with amnesia, who are well-characterized based on extensive neuroanatomical and neuropsychological assessment, participated in the current study. They vary in the extent of their lesion and neuropsychological profiles, but both have in common hippocampal damage and deficits within episodic and spatial memory based on comprehensive testing.

The first individual with amnesia tested is DA. He is a 68-year-old, right-handed male with 17 years of education who developed amnesia as a result of herpes encephalitis (Kwan et al., 2013; Rosenbaum et al., 2008). He has bilateral MTL damage that is more severe in his right hemisphere (see Figure 4.1) and additional volume reduction in posterior temporal, ventral frontal, and occipital regions, as well as in the anterior cingulate cortex and posterior thalamus.

His neuropsychological profile is characterized by high-average intelligence, graded retrograde amnesia, severe anterograde amnesia, deficient episodic details in autobiographical memory, and otherwise intact cognitive functioning (Kwan et al., 2013; Pishdadian, 2018; Rosenbaum et al., 2008). Neuropsychological test results are presented in Table 4.1. DA has previously been shown to have difficulty learning to navigate in newly encountered spatial environments and has a loss of detailed but not schematic memory for remote spatial environments, consistent with his hippocampal amnesia (Herdman et al., 2015; Pishdadian & Rosenbaum, 2021; Robin et al., 2019).

The second individual with amnesia tested is BL. He is a 59-year-old, right-handed male with 13 years of education who experienced anoxia in relation to cardiac arrest following an electrical accident (Baker et al., 2016). He has bilateral loss of the dentate gyrus (DG) and, to a lesser extent, CA3 subregion of the hippocampus, and additional volume loss in left superior parietal lobe and right precuneus (Baker et al., 2016; see Figure 4.2 for Magnetic Resonance Imaging (MRI) image showing BL's DG/CA3 lesions).

BL's neuropsychological profile is characterized by average intelligence, mild-moderate anterograde amnesia, and weaknesses in processing speed and complex attention (Baker et al., 2016; Mitchnick et al., 2022). Neuropsychological test results are presented in Table 4.2. Interviews with BL and his care team reveal that BL's navigation is restricted to familiar environments learned long ago, and there have been incidents of disorientation even in these familiar environments.

### ***Controls***

A subset of the older adult sample described in study 1 served as controls for BL and DA. These individuals were matched to each case in terms of sex, level of education, and age within 5 years. A total of 54 college-educated males were included as control participants for DA, with a comparable but lower mean age ( $M = 63.06$ ,  $SD = 2.27$ ). A total of 48 high-school educated males were included as controls for BL, with a higher but comparable mean age ( $M = 63.96$ ,  $SD = 2.71$ ).

### **Materials**

All study measures are described in study 1. Objective memory measures included the Four Mountains Task and Face-Name Task (Burles & Iaria, 2020; Troyer et al., 2011). Subjective memory evaluations were measured with the MMQ and SAM Episodic Subscale (Palombo et al., 2013; Troyer & Rich, 2018). Subjective spatial navigation abilities were measured with the SBSOD, the NSQ, the WQ, and the novel CNQ (Brunec et al., 2018; Hegarty et al., 2002; van der Ham et al., 2013).

The CNQ is available in Appendix B. The questionnaire consists of 10 items and a higher total score means more perceived changes in spatial navigation ability. Study 1 multidimensional IRT analyses found items 1-4 loaded on factor 1, conceptualized as *typical* aging changes in spatial navigation and items 7-10 loaded onto factor 2, conceptualized as the *atypical* aging changes in spatial navigation. Items 5 and 6 were found to load onto both factors.

Psychological distress symptoms were assessed with the PHQ-9 and GAD-7 (Kroenke et al., 2001; Spitzer et al., 2006). These symptom measures have been used previously in aging samples (Phelan et al., 2010; Wild et al., 2014) and in individuals with traumatic brain injuries (TBIs) (Teymoori et al., 2020).

## **Procedure**

Ethics approval was obtained from the research ethics boards at Baycrest Health Sciences and York University to conduct this study.

## **Data Analysis**

The data were analyzed using R version 4.2.0 (R Core Team, 2013). Descriptive statistics were run using the *psych* package (Revelle & Revelle, 2015). Individuals with amnesia were compared to controls based on *Z*-scores, and, when available, as has been done previously in the literature, *T*-scores ( $M = 50$ ,  $SD = 10$ ) were calculated based on published norms (Robin et al., 2019; Wank et al., 2022). This method is also consistent with a person-centered approach used in personality assessment (Borkenau & Leising, 2016). Descriptive labels were assigned according to Guilmette and colleagues (2020) American Academy of Clinical Neuropsychology consensus guidelines on labeling of performance of test scores, which is adaptation of this labeling to self-report measures.

On the PHQ-9 and GAD-7, individuals are described based on severity (Kroenke et al., 2001; Spitzer et al., 1990; Spitzer et al., 2006). Due to the skewed distribution on the CNQ, *Z*-scores were not calculated. On the CNQ, performance was described qualitatively, and response patterns and *F*-scores were calculated according to study 2's CFA-model unstandardized parameters to calculate each individuals' loadings on the two factors. Graphs are also used to illustrate performance.

## **Results**

### **DA's Task Performance and Response Profile**

Scale descriptions for all study measures are available in study 1, Table 2.2. All of DA's task performance and questionnaire results are available in Table 4.3.

### ***Objective Memory***

The results show DA had very poor performance ( $< 2.5 SD$ ) compared to controls on all Face-Name Task memory metrics. His performance was more comparable to controls (35% accuracy,  $z = -1.29$ ) on the Four Mountains Task, where chance performance is 25%. Overall, DA's poor performance on objective memory measures is consistent with his neuropsychological test results and clinical presentation of severe anterograde amnesia.

### ***Established Subjective Memory and Spatial Navigation Questionnaires***

DA's metamemory evaluations as captured by the MMQ indicate a profile of significant self-reported memory dysfunction compared to controls and normative data, demonstrating intact insight (Troyer & Rich, 2018). Responses on the MMQ indicate memory satisfaction and ability subscale scores are below average ( $T = 32$ ,  $T = 34$ ) and strategy use is exceptionally high ( $T = 70$ ) (Guilmette et al., 2020). Episodic memory evaluation as measured by the SAM Episodic subscale also indicates perceived lower memory abilities compared to those of controls and to the measure's normal distribution ( $z = -1.58$ ). Overall, metamemory results indicate DA has a moderate to high degree of insight into his poor memory abilities and reports using a high number of compensatory memory strategies.

There is a more nuanced profile of performance for DA's subjective spatial navigation abilities. Specifically, he reports lower overall abilities compared to controls on the SBSOD ( $z = -1.58$ ) and WQ Navigation Orientation subscale ( $z = -1.25$ ). He also reports increased spatial anxiety compared to controls, as captured by the WQ Spatial Anxiety subscale ( $z = 1.27$ ). However, his performance on the WQ Distance Estimation subscale ( $z = 0.45$ ) and NSQ ( $z = -0.11$ ) is comparable to that of controls, indicating relatively good evaluation of distance estimation spatial abilities and tendency towards allocentric strategy use.

### ***Changes in Navigation Questionnaire***

Without prompting, DA referred to his encephalitic injury as an orienting event for his changing spatial abilities on the CNQ and responded to all items with this timeframe in mind. DA endorsed most CNQ items, and his responses are depicted in Figure 4.3.

His response pattern on factor 1 *typical* aging items (1-4) was: 1,4,3,0. His response pattern on factor 2 *atypical* aging items (7-10) was: 4,1,3,2. Lastly, his response pattern on the CNQ items (5,6) loading onto both factors was: 0,4.

DA's loadings on the CNQ's Factor 1 and Factor 2 are depicted graphically in Figure 4.5. His performance was compared to the older adult sample in which the CNQ's psychometric properties were investigated in study 1. He had high loadings on both Factor 1 ( $f1 = 1.67$ , standard error = 0.29) and Factor 2 ( $f2 = 2.47$ , standard error = 0.27). It is clear from the graphical depiction and factor loadings that DA's loadings are extreme compared to the general sample's responses, indicating a high number of perceived changes.

On the open-ended item 11 asking about any changes noticed in navigating, DA wrote, “I really rely on my sense of what is north, south, east, west to know where I am and how to reposition myself to know my way home; could be dropped off in the city of Toronto and find my way home; See where I am, major street name, and find my way home.”

### ***Psychological Distress***

DA endorsed mild levels of depression symptomatology which was greater than that of controls (Manea et al., 2012; Spitzer et al., 1990). He did not report elevated levels of anxiety symptoms, similar to control participants (Plummer et al., 2016; Spitzer et al., 1990; Wild et al., 2014).

### **BL’s Task Performance and Response Profile**

All of BL’s task performance and questionnaire results are available in Table 4.4.

### ***Objective Memory***

On both the Face-Name Task intact ( $z$ -score = -0.25) and recombined condition metrics ( $z$ -score = -1.57), BL had performance comparable to controls. On all remaining objective memory measure metrics, BL had poor performance ( $< 1.5 SD$ ) compared to controls. Consistent with his neuropsychological profile of mild-moderate anterograde amnesia, BL has better objective memory performance (as indicated by  $Z$ -scores) than DA.

### ***Established Subjective Memory and Spatial Navigation Questionnaires***

BL’s metamemory evaluations as captured by the MMQ indicate a profile of moderate self-reported memory dysfunction compared to that of controls and normative data (Troyer & Rich, 2018). His MMQ Satisfaction subscale score is average ( $T = 45$ ), MMQ Ability subscale score is below average ( $T = 32$ ), and MMQ Strategy subscale score is exceptionally high ( $T = 70$ ) (Guilmette et al., 2020). Episodic memory evaluation as measured by the SAM Episodic subscale shows lower memory abilities compared to controls and to the measure’s normal distribution ( $z = -0.83$ ). The results suggest that BL has a good degree of insight into his memory deficits and reports using a high number of compensatory memory strategies, though he is generally satisfied with his abilities.

BL’s responses on subjective spatial navigation questionnaires show lower overall abilities compared to controls ( $< 1.5 SD$ ), with the exception of the WQ Spatial Anxiety subscale which is within one standard deviation compared to controls ( $z = 0.85$ ). He also reports less allocentric strategy use ( $NSQ = -8.00$ ) than DA ( $NSQ = 3.00$ ).

### ***Changes in Navigation Questionnaire***

On the CNQ, BL was oriented by the examiner to his injury as the anchoring event for any perceived changes. BL's responses are depicted in Figure 4.4. BL endorsed all questionnaire items.

His response pattern on factor 1 *typical* aging items (1-4) was: 4, 4, 4,4. His response pattern on factor 2 *atypical* aging items (7-10) was: 3, 2, 3, 3. Lastly, his response pattern on items (5,6) loading onto both factors was: 4,1.

BL's loadings on the CNQ's Factor 1 and Factor 2 are depicted graphically in Figure 4.6. He had very high loadings on both Factor 1 ( $f1 = 2.79$ , standard error = 0.40) and Factor 2 ( $f2 = 2.53$ , standard error = 0.26). It is clear from the graphical depiction and loadings that BL's responses are extreme compared to the general sample, indicating a high number of perceived changes.

### ***Psychological Distress***

BL endorsed moderately severe depression and mild anxiety symptoms, both of which were greater than control participants (Plummer et al., 2016; Spitzer et al., 1990; Wild et al., 2014).

## **Discussion**

In this study, I aimed to investigate the subjective evaluation of memory and spatial navigation abilities in two well-characterized individuals with different degrees of anterograde amnesia and MTL damage, both with lesions to the hippocampus. Both individuals' item endorsement on standardized questionnaires indicate insight into their episodic memory and spatial navigation difficulties. Discrepancies between objective ability and self-reported abilities, and between the two individuals with amnesia, included judgments related to distance estimation, spatial strategy use, spatial anxiety, and memory satisfaction. These findings speak to how individual differences may impact the subjective evaluation of memory and spatial navigation abilities and the role of the hippocampus in anosognosia.

### **Objective Memory Performance**

Consistent with their clinical presentations and neuropsychological profiles, DA and BL had poor objective memory performance on the Four Mountains and Face-Name Tasks. Similar deficits in associative episodic memory and new spatial learning have been seen in other individuals with amnesia (see Pishdadian & Rosenbaum, 2021 for a review). The pattern of

reduced performance has also been seen in neurotypical aging, SCD, and aMCI, where reduced hippocampal integrity positively correlates with associative memory and new allocentric spatial learning task performance (Caillaud et al., 2020; Schöberl et al., 2020; Shing et al., 2011; Striepens et al., 2010; Troyer et al., 2012; Zheng et al., 2017).

On both objective memory tasks DA performed poorly. However, his performance was better compared to controls on the Four Mountains Task ( $Z$ -score = -1.29) than on the Face-Name Task ( $Z$ -score = -3.44). It is worth noting that controls had lower accuracy on the Four Mountains Task ( $M = 53\%$ ,  $SD = 14\%$ , chance = 25%) compared to the Face-Name Task ( $M = 83\%$ ,  $SD = 9\%$ , chance = 50%). The difference in controls' performance on the tasks may therefore explain DA's relatively better performance on the Face-Name Task.

Overall, BL's objective memory performance showed a pattern of deficits that was less severe than DA's and compared to matched controls. This corresponds with his milder anterograde amnesia. His performance on recognition trials on the Face-Name Task was comparable to controls ( $Z$ -score = -0.25). This better performance corresponds to BL's mild-moderate amnesia and intact parahippocampal cortex, a region critical to familiarity processes on tests of recognition memory (Bennett et al., 2019; Brown et al., 2010; Eichenbaum et al., 2007). Past research has shown that BL is impaired on tests of mnemonic discrimination in recognition memory, consistent with his DG/CA3 volume loss (Baker et al., 2016; see also Bennet et al., 2019).

Overall, both DA and BL have poor performance on objective memory tasks which is consistent with their neuropsychological profiles and MTL damage.

### **Subjective Memory Abilities**

To my knowledge, the current study offers the first formal examination of insight into memory difficulties and metamemory in individuals with amnesia. Both DA and BL rated their memory abilities as worse than controls on standardized measures, specifically on the MMQ Ability and SAM Episodic subscales (Palombo et al., 2013; Troyer & Rich, 2018). They also both reported exceptionally high memory strategy use on the MMQ. Past research has indicated the DA spontaneously uses strategies during relational learning which improves his performance, corroborating his responses on the MMQ Strategy subscale (Ryan et al., 2013). Overall, this profile of responses indicates intact insight into poor memory abilities and corresponding compensation for poor memory with strategies (Troyer & Rich, 2018).

The results reported here on DA and BL's evaluation of their memory abilities is partially consistent with past literature. The findings expand on anecdotal evidence (Corkin, 2013; Rosenbaum et al., 2005b) to show that individuals with amnesia can learn of their post-amnesia memory deficits. These findings are also consistent with past work showing that amnesic individuals have intact self-referential encoding (Kurczek et al., 2015; Sui & Humphreys, 2013) and similar biases in temporal self-appraisal compared to controls (Halilova et al., 2020). The findings diverge from research in individuals with ADRD, which shows that hippocampal integrity negatively relates to metamemory judgments (Mondragón et al., 2019; Morris & Mograbi, 2013). This divergence is likely due to the DA and BL's selective lesions and the absence of widespread neurodegenerative processes.

The two individuals with amnesia in this study share some commonalities and differ in other ways which impact the generalizability of these findings. Both individuals with amnesia in this study presented with chronic amnesia (>20 years). They have also been participating in research experiments for many years, and as such have had many opportunities to learn about their memory deficits. It is unclear how much insight or learning would be present for individuals with more recently amnesic events. Individuals DA and BL differ in several ways which increase the likelihood of these findings extending to other individuals with amnesia. Specifically, they differ in the severity of their anterograde amnesia, extent of hippocampal lesions, and premorbid intelligence estimates. Future research should aim to replicate and expand on these findings with other individuals with anterograde amnesia.

An important moderator of accurate reporting of memory deficits may be memory satisfaction, which is related to mental well-being and personality features (Zuniga et al., 2016; Pearman & Storandt, 2004). Memory satisfaction has an emotional valence that distinguishes it from evaluations of general memory ability or strategy use (Troyer & Rich, 2018). Mood symptoms are known to be an important contributor to memory satisfaction (Buckley et al., 2016; Burmester et al., 2016; Topiwala et al., 2021) and accompany objective and SCD (Brailean et al., 2019).

The two individuals with amnesia tested in this study differed in their memory satisfaction and psychological distress. One individual, DA, had a MMQ Satisfaction score that was extremely low, while BL's MMQ Satisfaction score was within the average range. DA's mild levels of depression symptoms correspond with his very low memory satisfaction and severity of

his anterograde amnesia. In contrast, BL had elevated symptoms of both anxiety and depression. BL's elevated psychological distress and average memory satisfaction present an incongruity that requires further consideration. It may be psychologically protective for BL to maintain a coherent self-image and not admit his memory dissatisfaction (Conway, 2005). It is also possible that given the long length of time since his injury (>20 years) and co-occurring natural aging processes, BL has learned to accept his current (and milder than DA's) memory difficulties. Another non-mutually exclusive explanation is that BL's premorbid cognitive abilities may not have been as strong and so he is more satisfied with his current skills than DA, who had a higher estimated premorbid functioning and has more severe amnesia, making the discrepancy between his current ability and self-image starker. Further research with more individuals with amnesia should investigate how time since amnesia onset, degree of memory impairment, personality factors, and coping strategies may mediate memory satisfaction.

### **Subjective Spatial Navigation Abilities**

Both individuals with amnesia rated their general spatial navigation abilities as lower than that of controls, consistent with their objective navigation difficulties. To expand on the accuracy of these subjective evaluations, a more thorough investigation of DA and BL's objective spatial navigation abilities is available in the following chapter.

BL's subjective spatial navigation scores were uniformly poor and disparate from controls on all measures, with the exception of spatial anxiety, which was only marginally elevated compared to controls. His low spatial anxiety is congruent with his high memory satisfaction, suggesting that the construct of spatial anxiety may be more related to the satisfaction aspect of metamemory (van der Ham et al., 2021).

DA reported higher levels of spatial anxiety but similar allocentric strategy use and distance estimation skills as controls. DA's scores may represent a decline relative to how he would have assessed his skills prior to his injury. Since the WQ Distance Estimation subscale does not specify environmental familiarity, it is also possible that DA responded based on his ability to navigate remote, familiar environments, which has been shown to be largely intact (Herdman et al., 2015).

Another explanation for DA's responses on strategy use and distance estimation comes from considering the literature on personal semantics and general, trait-level evaluations in amnesia. Specifically, it may be that within subjective views of spatial navigation, there is a division

between more general impressions of ability that have become part of self-knowledge or personal semantic information (Garland et al., 2021; Grilli & Verfaellie, 2015; Prebble et al., 2013) and specific experiential or “experience-near” judgments of skill, such as actual strategy use and particular navigation skills like distance estimation (Wank et al., 2022). Due to episodic memory deficits, these latter judgments may not be updated over time and thus are based on an individuals’ general or pre-injury evaluations. It follows that DA, who has semantic knowledge of his amnesic condition, is also able to learn over the decades of repeated difficulties with navigation that his general spatial abilities are impaired. Due to his severe amnesia, the more experientially based and specific information of distance estimation and strategy use are less accessible to him and so he relies on available preinjury information that is consistent with his self-trait information (Funder et al., 2012; Wank et al., 2022). As a contrast to DA and illustrating this, BL has less severe amnesia to impact new experiential learning and reports lower allocentric spatial strategy use and distance estimation skills.

DA and BL’s responses on the CNQ provide unique information on the degree of change perceived in spatial navigation abilities since their amnesic onset. Both individuals’ responses on the CNQ diverged from a large sample of neurotypical older adults and their matched controls, providing further evidence of intact insight into current spatial navigation abilities.

Interestingly, on select CNQ items, both DA and BL had lower scores or less reported change. DA endorsed a high degree of change since his amnesia onset on most CNQ items, with the exception of items 1, 4, 5, and 8. Item 5 refers to GPS use, and DA’s low endorsement of change on this item may be attributed to his inability to independently use computer or smartphone technology due to his amnesia. The remaining three items (1, 4, and 8) refer to confidence or navigation in familiar environments. DA’s report of little change on these items likely reflects his trait evaluations of high premorbid spatial abilities and is consistent with his reported allocentric strategy use and strong distance estimation skills. BL endorsed all items on the CNQ and with a pattern of lower endorsement on the *atypical* items. His lowest endorsement was on item 6 which asks about reliance on others for navigation. Possible explanations for BL’s low endorsement of item 6 include that he lives and navigates alone in environments that are highly familiar. This means that BL does not have a reliable other on whom he can rely for navigation assistance and has also maintained greater independence in navigating. These items of

low endorsement on the CNQ highlight the individual characteristics and circumstances which can affect item responses.

Overall, the individuals with amnesia responses on the CNQ provide unique evidence of the measure's sensitivity to real-world spatial navigation difficulties in individuals with memory problems. The measure also more clearly captures these individuals' subjective experience of their changed abilities since their accidents.

### **Anosognosia**

The current results offer considerations for the role of the hippocampus in anosognosia and particularly for individuals with memory impairment.

Past research has found conflicting evidence for the importance of the hippocampus for anosognosia. Severity of anosognosia in individuals with aMCI and AD has implicated the hippocampus both bilaterally and laterally on the right side (Flores-Vázquez et al., 2021; Tondelli et al., 2018). A review of the literature on the relationship between MTL structural integrity and (cognitive) self-awareness in individuals with AD found involvement of the bilateral hippocampus, and perirhinal and posterior parahippocampal cortices (Chavoix & Insausti, 2017). Recent work with individuals with AD using the Measurement of Anosognosia Instrument, which compares individuals with AD's insight into their deficits to that of informants (e.g., significant others), found memory anosognosia to be associated with reduced volume of the anterior cingulate cortex, lingual gyrus, fusiform gyrus, thalamus, and frontal lobes (Valera-Bermejo et al., 2020). Since these authors did find associations between hippocampal volume and anosognosia scores they argue that MTL structures provide supportive as opposed to causal input (Valera-Bermejo et al., 2020). Functional connectivity analyses have linked anosognosia severity to the extent of disconnection of the medial temporal subsystem from the default mode network (Antoine et al., 2019). This latter finding may explain the inconsistent results on the role of the hippocampus in anosognosia.

Our study findings of mostly intact insight into memory and spatial navigation difficulties in individuals with anterograde amnesia due to hippocampal damage offer causal evidence that while the hippocampus may be involved in anosognosia in cases of memory loss, it is not critical. It may be that the role of the hippocampus in reduced insight may be more tied to specific recollection of deficits as opposed to the lack of ability to register cognitive deficits, the latter seen in individuals with psychosis spectrum illness (Pijnenborg et al., 2020). Future

research can build on these findings by characterizing individuals with amnesia's level of insight and relating this to functional network-level disruptions (Argyropoulos et al., 2019).

### **Implications for Memory Theories**

These findings may be interpreted within the context of prominent episodic and semantic memory theories and help to extend them. The current results suggest that after decades of individuals with hippocampal amnesia experiencing poor memory and spatial navigation, their Personal Database of memory and spatial navigation skills are updated due to an intact Metacognitive Awareness System or prefrontally mediated introspection processes (Juskenaite et al., 2016; Morris & Mograbi, 2013; Sui & Humphreys, 2013). From a memory systems perspective, the finding of incomplete, partial learning of certain specific spatial abilities by DA is consistent with the critical role of the hippocampus and episodic processes for updating and consolidating new information (Gilboa & Moscovitch, 2021; Renoult et al., 2019; Moscovitch et al., 2005).

The overall high level of insight demonstrated by DA and BL in the current study contrasts with past work on personality in amnesia, which emphasizes that individuals with amnesia have impairments in updating knowledge about the self (Garland et al, 2021; Grilli & Verfaellie, 2015, for contradictory evidence see Rosenbaum et al., 2005b). Both individuals with amnesia also reported very high memory strategy use, likely indicating a perceived need to compensate for deficient abilities. This is aligned with past research in future decision-making which shows that individuals with amnesia are not “stuck in time” and plan for the future similarly to controls (Craver et al., 2014). Thus, the ability to update self-knowledge about memory abilities and compensate for deficits in individuals with anterograde amnesia may deserve additional consideration in theoretical models. Specifically, why might some individuals with amnesia have insight into changes to their spatial navigation and memory abilities but not their personality?

Anecdotally, during testing DA happily shared details with me about his young granddaughter which is wife confirmed as accurate. This included her name, age, and the date of her upcoming second birthday. I hypothesize the personal salience and meaning attached to details about his granddaughter may have accelerated his learning. The repetition of his granddaughter's name and potential cues around the home may have also aided this learning. More thorough investigations of insight and personal learning in individuals with amnesia could be pursued with qualitative interviews with the individuals and reliable informants. This would

expand on current findings and may reveal subtle deficits in their understanding of their impairments, or alternatively, a greater comprehension than was previously hypothesized.

### **Conclusion**

The current results provide the first quantitative evidence that individuals with adult-onset amnesia due to hippocampal compromise do have good overall insight into their episodic memory and spatial navigation deficits, though premorbid self-concept also plays a role. These findings expand our understanding of the mental lives of individuals with amnesia and show that individuals are learning about their memory difficulties and differ in their memory satisfaction. The individuals' stable cognitive and spatial navigation deficits and high endorsements of change on the CNQ suggest that the measure may be sensitive to objective spatial navigation difficulties, offering a basis for the questionnaire's utility in individuals with memory impairment, including individuals with aMCI.

In the next chapter of this dissertation, DA and BL's objective spatial navigation skills were investigated using mobile-game technology, further elaborating on the role of episodic memory and the hippocampus in spatial navigation abilities.

**Table 4.1*****DA Neuropsychological Test Results***

	<b>Scores</b>	<b>Score Label</b>
<b>General Intellectual Functioning</b>		
WAIS-R <sup>a</sup> Full-scale Intellectual Quotient, <i>Standard Score</i>	117	High Average
WAIS-R <sup>a</sup> Verbal Intellectual Quotient, <i>Standard Score</i>	121	Above Average
WAIS-R <sup>a</sup> Performance Intellectual Quotient, <i>Standard Score</i>	106	Average
<b>Attention &amp; Executive Functioning</b>		
WAIS-R <sup>a</sup> Digits, <i>Scaled Score</i>	13	High Average
Wisconsin Card Sorting Test (WCST) Categories, <i>raw score /6</i>	6	Within Normal Limits
WCST Perseverative Responses, <i>Z-score</i>	-0.5	Average
Letter Fluency <sup>b</sup> , <i>Scaled Score</i>	8	Average
<b>Memory</b>		
California Verbal Learning Test (CVLT) Acquisition, <i>T-score</i>	9	Low Average
CVLT Short Delay Free Recall, <i>Z-score</i>	-4	Exceptionally Low
CVLT Long Delay Free Recall, <i>Z-score</i> ,	-4	Exceptionally Low
CVLT Recognition Discrimination, <i>Z-score</i>	-4	Exceptionally Low
WMS-R <sup>b</sup> Logical Memory I, <i>percentile</i>	15 <sup>th</sup>	Low Average
WMS-R <sup>b</sup> Logical Memory II, <i>percentile</i>	<1 <sup>st</sup>	Exceptionally Low
Rey Osterrieth Complex Figure Delayed recall, <i>raw score /36</i>	0	Exceptionally Low
<b>Perception/Visuospatial Abilities</b>		
Rey Osterrieth Complex Figure Copy, <i>raw score /36</i>	35	Within Normal Limits
<b>Language</b>		
Boston Naming Test, <i>raw score /60</i>	56	Within Normal Limits
Semantic Fluency <sup>d</sup> , <i>Scaled Score</i>	12	High Average

*Note.* Score labels were assigned according to Guilmette et al., 2020.

<sup>a</sup> Wechsler Adult Intelligence Scale–Revised (WAIS-R)

<sup>b</sup> Score is based on the total number of words produced for the letters *F*, *A*, and *S* when given 1 minute for each.

<sup>c</sup> Wechsler Memory Scale–Revised (WMS-R)

<sup>d</sup> Score is based on the number of animal names produced in 1 minute

**Table 4.2**

***BL Neuropsychological Test Results***

	<b>Scores</b>	<b>Score Label</b>
<b>General Intellectual Functioning</b>		
WASI-II <sup>a</sup> Similarities Subscale, <i>percentile</i>	53 <sup>rd</sup>	Average
WASI-II <sup>a</sup> Vocabulary Subscale, <i>percentile</i>	53 <sup>rd</sup>	Average
WASI-II <sup>a</sup> Matrix Reasoning Subscale, <i>percentile</i>	39 <sup>th</sup>	Average
WASI-II <sup>a</sup> 2-factor Intellectual Quotient, <i>percentile</i>	45 <sup>th</sup>	Average
<b>Processing Speed</b>		
WAIS-IV <sup>b</sup> Symbol Search, <i>percentile</i>	9 <sup>th</sup> , 1 error	Low Average
WAIS-IV <sup>b</sup> Coding, <i>percentile</i>	9 <sup>th</sup> , 0 errors	Low Average
WAIS-IV <sup>b</sup> Processing Speed Index, <i>percentile</i>	6 <sup>th</sup>	Below Average
D-KEFS <sup>c</sup> Colour Naming, <i>percentile</i>	5 <sup>th</sup> , 0 errors	Below Average
D-KEFS <sup>c</sup> Word Reading, <i>percentile</i>	9 <sup>th</sup> , 0 errors	Low Average
<b>Attention &amp; Executive Functioning</b>		
Wisconsin Card Sorting Test (WCST), <i>Scaled Score</i>	6	Low Average
WAIS-IV <sup>b</sup> Digit span Forward, <i>percentile</i>	50 <sup>th</sup>	Average
D-KEFS <sup>c</sup> Verbal fluency phonemic, <i>percentile</i>	63 <sup>rd</sup> , 0 errors	Average
D-KEFS <sup>c</sup> Verbal fluency semantic, <i>percentile</i>	50 <sup>th</sup> , 0 errors	Average
D-KEFS <sup>c</sup> Colour-word inhibition, <i>percentile</i>	1 <sup>st</sup> , 0 errors	Exceptionally low
D-KEFS <sup>c</sup> Colour-word switching, <i>percentile</i>	1 <sup>st</sup> , 0 errors	Exceptionally low
D-KEFS <sup>c</sup> Trails visual scanning, <i>percentile</i>	5 <sup>th</sup> , 0 errors	Below average
D-KEFS <sup>c</sup> Trails number sequencing, <i>percentile</i>	16 <sup>th</sup> , 0 errors	Low average
D-KEFS <sup>c</sup> Trails letter sequencing, <i>percentile</i>	2 <sup>nd</sup> , 0 errors	Exceptionally low
D-KEFS <sup>c</sup> Trails switching, <i>percentile &amp; Time Discontinue errors</i>	<1 <sup>st</sup> , 2 errors 5 TD <sup>f</sup> errors	Exceptionally low
<b>Memory</b>		
Rey Osterrieth Complex Figure Delayed Recall, <i>Scaled Score</i>	5	Below Average
WMS-IV <sup>d</sup> LM-I, <i>Scaled Score</i>	8	Average
WMS-IV <sup>d</sup> LM-II, <i>Scaled Score</i>	6	Low Average
CVLT-3 <sup>e</sup> Verbal Learning, <i>percentiles (raw score trials)</i>	1 <sup>st</sup> , (3,5,4,4,5)	Exceptionally Low
CVLT-3 <sup>e</sup> Short Delay Free Recall, <i>percentile</i>	2 <sup>nd</sup>	Below Average
CVLT-3 <sup>e</sup> Short Delay Cued Recall, <i>percentile</i>	5 <sup>th</sup>	Below Average
CVLT-3 <sup>e</sup> Long Delay Free recall, <i>percentile</i>	5 <sup>th</sup>	Below Average
CVLT-3 <sup>e</sup> Long Delay Cued Recall <i>percentile</i>	9 <sup>th</sup>	Low Average
CVLT-3 <sup>e</sup> Long Delay free recall vs. T5 learning, <i>percentile</i>	25 <sup>th</sup>	Average
CVLT-3 <sup>e</sup> Recognition Hits, <i>percentile</i>	50 <sup>th</sup>	Average
CVLT-3 <sup>e</sup> Recognition False Positives, <i>percentile</i>	<1 <sup>st</sup>	Exceptionally Low
CVLT-3 <sup>e</sup> Recognition Discriminability (d'), <i>percentile</i>	5 <sup>th</sup>	Below average
<b>Perception/Visuospatial Abilities</b>		
Rey Osterrieth Complex Figure Copy, <i>Scaled Score</i>	6	Low Average

	<b>Scores</b>	<b>Score Label</b>
Judgement of Line Orientation, <i>percentile</i>	11-18 <sup>th</sup>	Low Average

*Note.* Score labels assigned according to Guilmette et al., 2020.

<sup>a</sup> Wechsler Abbreviated Scale of Intelligence II (WASI-II)

<sup>b</sup> Wechsler adult intelligence scale-IV (WAIS-IV)

<sup>c</sup> Delis-Kaplan Executive Function System (D-KEFS)

<sup>d</sup> Wechsler Memory Scale IV (WMS-IV)

<sup>e</sup> California Verbal Learning Test-3 (CVLT-3)

<sup>f</sup> TD – time discontinue errors

**Table 4.3*****DA Performance on Study Measures***

<b>Study Measure</b>	<b>DA</b>	<b>Control Mean (SD)</b>	<b>DA Z-score</b>	<b>T-score</b>
<b>Objective Memory Measures</b>				
Four Mountains Task, % Accuracy	0.35	0.53 (0.14)	-1.29	-
Face-Name Task, Intact % Accuracy	0.38	0.92 (0.11)	-4.91	-
Face-Name Task, Recombined % Accuracy	0.63	0.70 (0.22)	-2.55	-
Face-Name Task, New % Accuracy	0.63	0.97 (0.07)	-4.86	-
Face-Name Task, Overall % Accuracy	0.52	0.83 (0.09)	-3.44	-
<b>Subjective Memory Measures</b>				
MMQ Satisfaction Subscale	19.00	51.69 (12.39)	-2.64	32
MMQ Ability Subscale	31.00	61.19 (11.71)	-2.58	34
MMQ Strategy Subscale	58.00	24.33 (9.75)	3.45	70
SAM Event (Episodic) Subscale	78.00	102.34 (15.38)	-1.58	-
<b>Subjective Spatial Navigation Measures</b>				
SBSOD	3.47	4.91 (0.91)	-1.58	-
NSQ	3.00	3.39 (3.69)	-0.11	-
CNQ	20.00	3.06 (4.43)	-	-
WQ Navigation Orientation Subscale	4.01	5.56 (1.24)	-1.25	-
WQ Distance Estimation Subscale	5.67	5.19 (1.07)	0.45	-
WQ Spatial Anxiety Subscale	4.63	2.94 (1.33)	1.27	-
<b>Mood Measures</b>				
PHQ-9 Total Score	7.00	3.43 (5.03)	-	-
GAD-7 Total Score	3.00	2.33 (3.40)	-	-

*Note.* *MMQ* = Multifactorial Memory Questionnaire, *SAM* = Survey of Autobiographical Memory, *SBSOD* = Santa Barbara Sense of Direction Questionnaire, *NSQ* = Navigational Strategies Questionnaire (*NSQ*), *CNQ* = Changes in Navigation Questionnaire, *WQ* = Wayfinding Questionnaire (*WQ*), *PHQ-9* = Patient Health Questionnaire-9, *GAD-7* = Generalized Anxiety Disorder-7

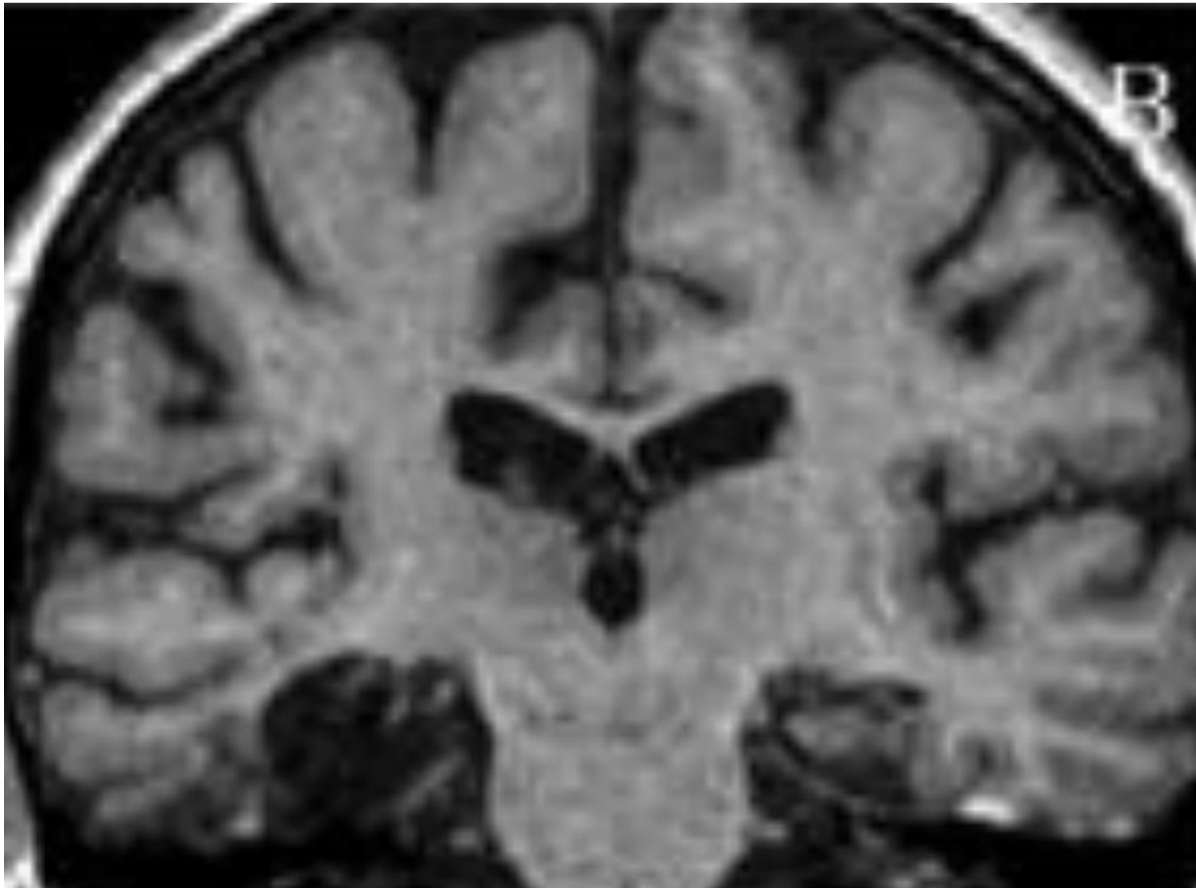
**Table 4.4*****BL Performance on Study Measures***

<b>Study Measure</b>	<b>BL</b>	<b>Control Mean (SD)</b>	<b>BL Z-score</b>	<b>T- score</b>
<b>Objective Memory Measures</b>				
Four Mountains Task, % Accuracy	0.25	0.53 (0.14)	-1.98	-
Face-Name Task, Intact % Accuracy	0.88	0.90 (0.11)	-0.25	-
Face-Name Task, Recombined % Accuracy	0.38	0.72 (0.22)	-1.57	-
Face-Name Task, New % Accuracy	0.75	0.97 (0.09)	-2.41	-
Face-Name Task, Overall % Accuracy	0.64	0.83 (0.09)	-2.11	
<b>Subjective Memory Measures</b>				
MMQ Satisfaction Subscale	37.00	48.19 (12.03)	-0.93	45
MMQ Ability Subscale	29.00	56.25 (13.17)	-2.07	32
MMQ Strategy Subscale	58.00	24.90 (9.69)	3.42	70
SAM Event (Episodic) Subscale	85.93	95.39 (11.47)	-0.83	-
<b>Subjective Spatial Navigation Measures</b>				
SBSOD	2.13	4.35 (0.95)	-2.34	-
NSQ	-8.00	1.10 (4.80)	-1.90	-
CNQ	32.00	3.37 (4.10)	-	-
WQ Navigation Orientation Subscale	2.82	5.56 (0.75)	-3.65	-
WQ Distance Estimation Subscale	1.67	5.06 (1.26)	-2.69	-
WQ Spatial Anxiety Subscale	3.86	2.83 (1.21)	0.85	-
<b>Mood Measures</b>				
PHQ-9 Total Score	15.00	2.69 (3.21)	-	-
GAD-7 Total Score	8.00	1.78 (2.91)	-	-

*Note.* MMQ = Multifactorial Memory Questionnaire, SAM = Survey of Autobiographical Memory, SBSOD = Santa Barbara Sense of Direction Questionnaire, NSQ = Navigational Strategies Questionnaire (NSQ), CNQ = Changes in Navigation Questionnaire, WQ = Wayfinding Questionnaire (WQ), PHQ-9 = Patient Health Questionnaire-9, GAD-7 = Generalized Anxiety Disorder-7

**Figure 4.1**

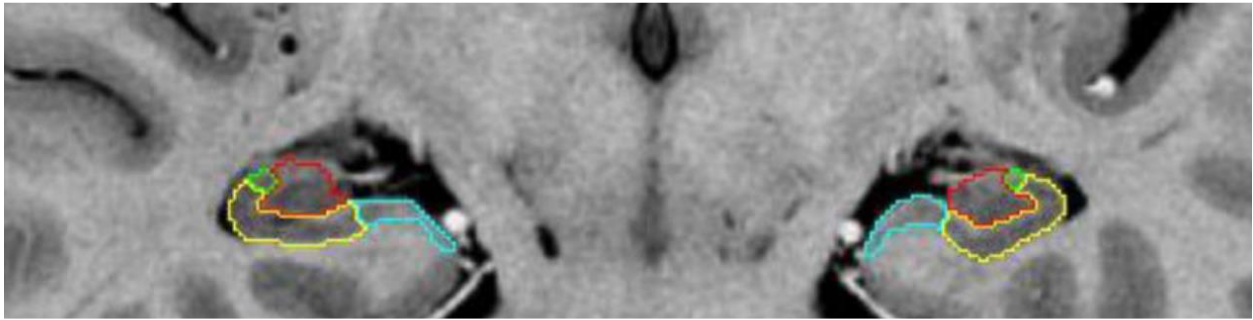
*DA MRI*



*Note.* MRI of DA's Medial Temporal Lobes (MTLs). Image adapted from Kwan and colleagues (2013)

**Figure 4.2**

*BL MRI*



*Note.* MRI of BL's Medial Temporal Lobes (MTL), with hippocampal segmentation. Image adapted from Baker and colleagues (2016)

**Figure 4.3**

*DA Responses on the CNQ*

	How much change you have noticed. (Please rate 0-4).					If you noticed changes, please select when you noticed them.								Please elaborate on the event ONLY if you selected 'After a specific Event'
	0	1	2	3	4	No changes	Last few weeks	Last 6 months	Last 1 year	Last 2 years	Last 5 years	Last 10 years	After a Specific Event	After a specific Event
1. Have you noticed any changes in your confidence travelling to familiar places alone?	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
2. Have you noticed any changes in your confidence travelling to unfamiliar places alone?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
3. Have you noticed any changes in your confidence travelling to places at night / reduced visibility?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
4. Have you noticed any changes in your confidence giving directions to other people?	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
5. Have you noticed any changes in how much you rely on GPS or other technology for navigation? (Do you rely more on them?)	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
6. Have you noticed any changes in how much you rely on others for navigation aid/ assistance? (Do you rely more on them?)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
7. Have you noticed any changes in making more mistakes when going places?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
8. Have you noticed any changes in forgetting the layout inside familiar buildings or homes?	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
9. Have you noticed any changes in forgetting (becoming confused) about where doors lead to in buildings or homes?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
10. Have you noticed any changes in family members or others commenting on you getting lost?	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>

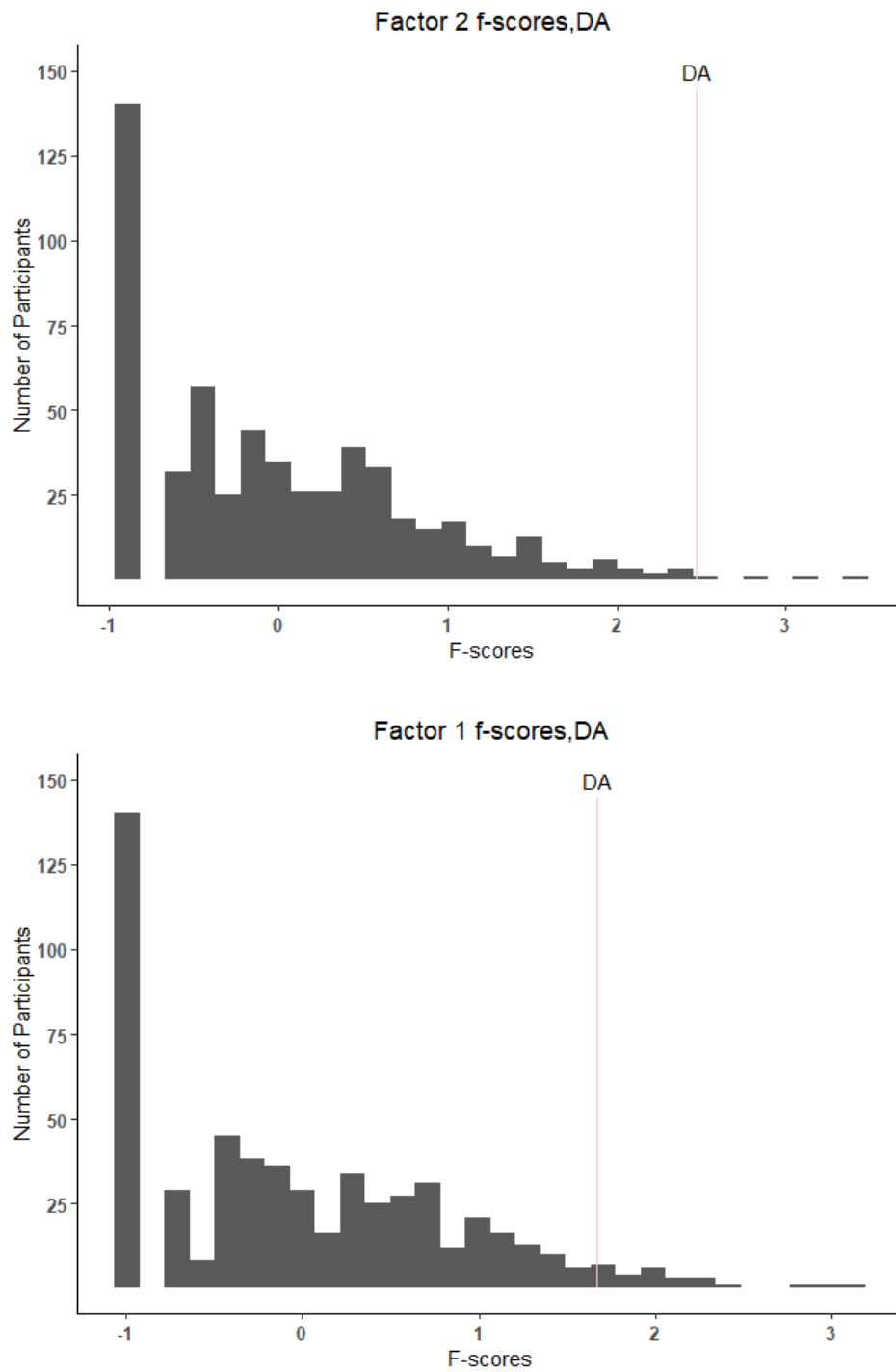
**Figure 4.4**

*BL Responses on the CNQ*

	How much change you have noticed. (Please rate 0-4).					If you noticed changes, please select when you noticed them.								Please elaborate on the event ONLY if you selected 'After a specific Event'
	0	1	2	3	4	No changes	Last few weeks	Last 6 months	Last 1 year	Last 2 years	Last 5 years	Last 10 years	After a Specific Event	After a specific Event
1. Have you noticed any changes in your confidence travelling to familiar places alone?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
2. Have you noticed any changes in your confidence travelling to unfamiliar places alone?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
3. Have you noticed any changes in your confidence travelling to places at night / reduced visibility?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
4. Have you noticed any changes in your confidence giving directions to other people?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
5. Have you noticed any changes in how much you rely on GPS or other technology for navigation? (Do you rely more on them?)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
6. Have you noticed any changes in how much you rely on others for navigation aid/ assistance? (Do you rely more on them?)	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
7. Have you noticed any changes in making more mistakes when going places?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
8. Have you noticed any changes in forgetting the layout inside familiar buildings or homes?	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
9. Have you noticed any changes in forgetting (becoming confused) about where doors lead to in buildings or homes?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>
10. Have you noticed any changes in family members or others commenting on you getting lost?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	<input type="text"/>

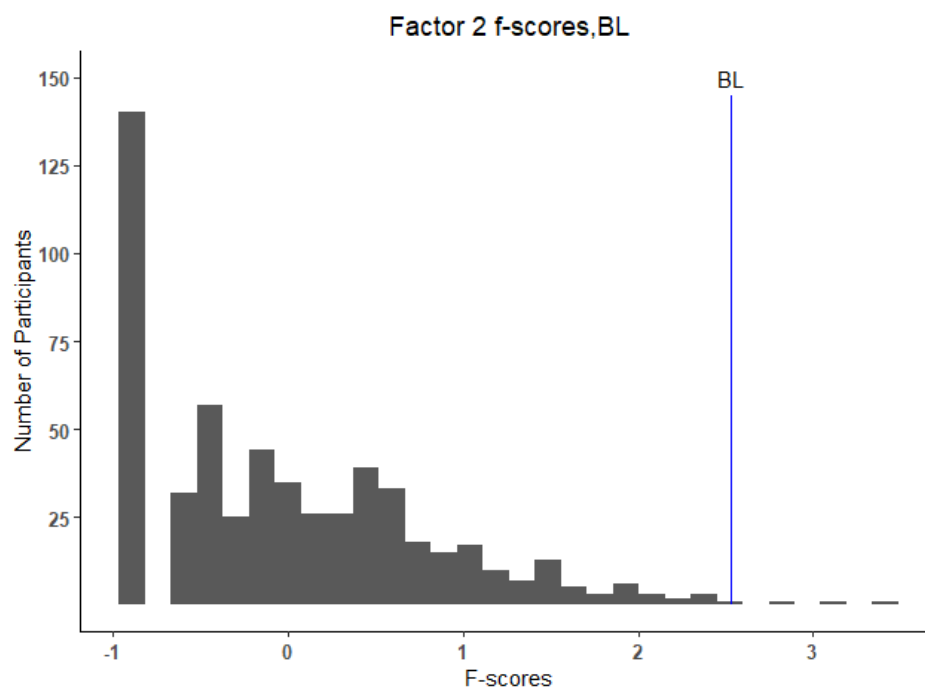
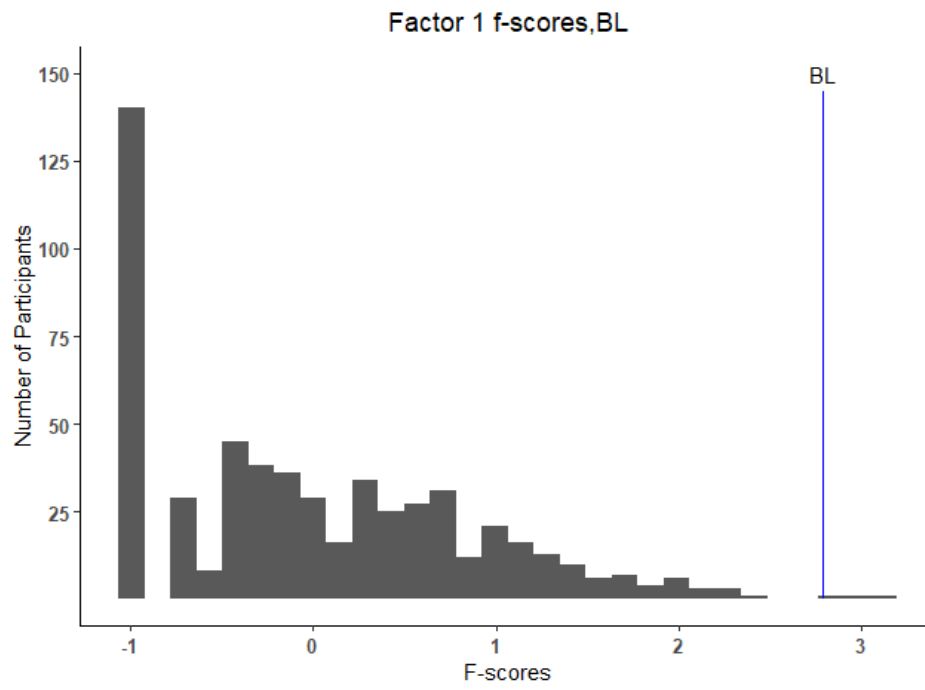
**Figure 4.5**

**DA loadings on CNQ factors 1 & 2**



**Figure 4.6**

*BL loadings on CNQ factors 1 & 2*



## CHAPTER 5

### Study 4: Big data meet deep data: Characterizing spatial navigation in hippocampal amnesia

The first two studies of this dissertation showed that performance on objective tests of associative and spatial memory may, at most, weakly relate to the subjective appraisal of one's spatial navigation abilities in typical aging. However, findings from the third study showed subjective appraisal of episodic memory and spatial navigation deficits in individuals with hippocampal amnesia to be largely consistent with objective evidence of impaired function. These results suggest a need to further understand how memory compromise in individuals with amnesia relates to objective spatial navigation abilities. The current study integrates deep data from individuals with amnesia with 'big data' to reconcile discrepancies in the spatial navigation literature while reinforcing the case study method as a gold-standard approach to understanding brain-behaviour relations.

The very existence of functional dissociations in memory arose from studying individuals with amnesia, leading to a paradigm shift away from the initial dominant view that memory is a unitary system, towards a multiple memory view that recognized distinctions between implicit and explicit memory and between episodic and semantic memory (Corkin, 2002; Rosenbaum et al., 2001, 2005a, 2005b, 2014; Pishdadian & Rosenbaum, 2021). The patient-lesion approach compares the behavioural performance of a single individual, ideally with a well-characterized brain lesion, to that of a group of control participants who are without brain lesions. Differences in performance between the brain-lesioned individual and control participants are then causally attributed to the brain region.

Like all methodologies, the patient-lesion approach has its limitations. Case studies typically include a relatively small number of controls who are not always closely matched on key variables, including age, education, and, in the case of studies on spatial navigation, geographic experience. This may lead to overly general or inappropriate interpretations of data. The value of the patient-lesion approach should not be diminished by these shortcomings but, rather, improved upon, especially given the limitations of averaging group-level performance at the expense of individual-level variability (Fisher et al., 2018; Tibon et al., 2022). When the deep data that are available from extensively studied individuals with amnesia is combined with large, well-matched control samples available from the 'big data' approach, results are more likely to

advance our understanding of human cognition and memory than when either method is used alone.

The view that the hippocampus is needed to support allocentric spatial memories, viewpoint-independent representations of relations among items contained within an environment, was founded on the discovery of place cells that fire maximally when a rodent occupies a particular location (O'Keefe & Dostrovsky, 1971). This view formed the basis of CMT, recognized this past decade by a Nobel Prize, which predicted impaired allocentric spatial memory in rodents and in humans following hippocampal lesions (O'Keefe & Dostrovsky, 1971). The hippocampus was not believed to be required for egocentric (viewpoint-dependent) spatial representations, nor for path-integration, which involves referencing back to one's previous location in relation to both allocentric and egocentric coordinates (Ekstrom et al., 2018a; Epstein, 2008).

Initial findings from lesion studies appeared to be in line with predictions from CMT (P. Banta Lavenex et al., 2006; Burgess et al., 2002; Guderian et al., 2015; Holdstock et al., 2000; Kessels et al., 2001; Morris, 1982; Parslow et al., 2004). This includes evidence that an individual with amnesia due to selective bilateral lesions was more impaired at recalling the position of a light from an allocentric frame of reference than from an egocentric frame of reference (Holdstock et al., 2000) and that monkeys with lesioned hippocampi could not effectively use allocentric spatial representations to navigate (Lavenex et al., 2006). However, there are also notable exceptions to findings of impaired allocentric learning following hippocampal lesions. Examples include H.M.'s ability to reproduce the basic floor plan of a house he lived in following the bilateral resection of his hippocampus (Corkin, 2002) and find a hidden sensor from multiple start locations in a human analog of the Morris Water Maze (Bohbot & Corkin, 2007). Impaired performance on the latter task appears to be associated with more extensive MTL lesions that include the right parahippocampal cortex rather than the hippocampus specifically (Bohbot et al., 1998).

Research has shown there are certain patterns to spatial navigation deficits in the face of hippocampal compromise. When deficits do emerge following hippocampal lesions, they tend to occur when greater distances need to be traveled and/or are reflected in greater time taken to navigate and lack of precision, such that destinations are reached circuitously, if at all (Ekstrom & Yonelinas, 2020; Goodrich-Hunsaker et al., 2010; Holdstock et al., 2000; Kim et al., 2013;

Kolarik et al., 2016, 2018; Rosenbaum et al., 2015). This resembles findings in remote spatial memory, where gist-like representations of environments learned long ago appear to be largely intact in hippocampal amnesia despite the loss of memory for more precise details contained within the same environments (Herdman et al., 2015; Rosenbaum et al., 2000, 2001, 2005a, 2005b). Overall, spatial navigation depends on multiple computations, beyond those that are allocentric in nature and may implicate the hippocampus, even when cognitive maps seem to be required for task performance.

To specify the contribution of the hippocampus to complex, real-world spatial navigation in this study, spatial learning was examined in two well-characterized individuals with amnesia compared to a very large number of carefully curated and well-matched controls. The mobile video game SHQ has been administered to over 4 million people globally and measures path integration and allocentric mapping abilities across different levels of environmental complexity and scaffolding (Coutrot et al., 2018). SHQ performance has been found to correlate with real-world navigation and is sensitive to national-level income and gender inequality (Coutrot et al., 2018, 2019). By using the SHQ paradigm in this study, results can expand on theoretical models of the contribution of the hippocampus to spatial navigation and provide guidance for integrating detailed information available in individual case studies with large, well-matched sample sizes.

Performance on the SHQ has been found to distinguish individuals based on *APOE*  $\epsilon 4$  status who are at higher genetic risk of developing ADRD (Coughlan et al., 2020) and relate to incidence of disorientation in individuals with AD (Puthusserypady et al., 2022b), supporting the view that spatial navigation difficulties hold utility as a diagnostic marker of hippocampal compromise and neurodegenerative disease (Allison et al., 2016; Coughlan et al., 2018; Laczó et al., 2017; Lithfous et al., 2013). A challenge of studying spatial navigation in individuals with or at-risk for memory compromise due to neurodegenerative disease is the potential for evolving underlying disease processes. Individuals with amnesia have circumscribed lesions and therefore more stable memory impairment. Testing these individuals provides the opportunity to better understand the contribution of the hippocampus and MTL to spatial navigation. This is particularly important as performance on the spatial navigation tasks are hypothesized to differ based on task demands on anterograde memory and precision. To investigate this hypothesis, the two individuals tested in this study differ in their nature and degree of their anterograde amnesia.

The results from this study data provide a new standard for clinicians to assess performance in more subtle cases of memory decline in preclinical AD and in other neurological conditions.

## **Method**

### **Participants**

Two individuals with anterograde amnesia, DA and BL, were included in this study. Details of their neuropsychological profiles are provided in study 3.

DA's neuropsychological test results are available in Table 4.1 and an MRI scan showing his anterior and MTL damage is available in Figure 4.1. DA's neuropsychological profile is characterized by high average intelligence, graded retrograde amnesia, severe anterograde amnesia, and otherwise intact cognitive functioning (Kwan et al., 2013; Pishdadian, 2018). Due to his amnesia, DA struggles to use newer technology and so was repeatedly provided with prompts for using an iPad during testing.

BL's neuropsychological test results are available in Table 4.2 and an MRI scan of his hippocampal lesions is available in Figure 4.2. His neuropsychological profile is characterized by average intelligence, mild-moderate anterograde amnesia, and weaknesses in processing speed and complex attention (Baker et al., 2016; Mitchnick et al., 2022).

Control groups were formed from subsets of the SHQ benchmark data (Coutrot et al., 2018, 2019; Spiers et al., 2021). All control participants were matched with individuals with amnesia based on practice level performance as well as country of origin (Canada), age (+/3 years) and sex. DA was matched with a possible 7,439 individuals. Patient BL was matched with a possible 10,295 individuals. The number of participants matched to DA and BL for each wayfinding level are available in Table 5.2 and Table 5.3, respectively.

### **Materials**

Both wayfinding and path integration ("flare") levels were administered from SHQ gameplay.

#### ***Wayfinding Levels***

The SHQ wayfinding levels have different characteristics which are detailed in Table 5.1. On each wayfinding level participants are asked to navigate to a specified number of buoys in a particular order.

Participants are shown a map of each wayfinding level before navigating (images available in Appendix D). These maps may fully or partially depict the environment and are

always from an allocentric viewpoint (Table 5.1). A full map depiction shows the environment outline and the number of buoys which themselves are numbered. A partial map depiction displays the number and position of buoys but not the entire map outline, which is partially faded.

Wayfinding levels also differ in environmental layout. This includes whether a level is open or closed. An open layout has all buoys in one space (see Appendix D, level 6 for an example). A closed layout has buoys along different paths. In neither the open nor closed layouts are all buoys visible from any one point.

Another environmental element differing across wayfinding levels is whether there is a decision point at the start of navigation (the participants' first turn) that lead to different buoys (see Appendix D, level 11 for an example).

Participants are asked to visit buoys in a specified order to successfully complete a wayfinding level. The number and order of buoys also varies across wayfinding levels (Table 5.1). There is a range of 3-5 buoys depending on the level. The ordering and distance between buoys also differ across levels.

### ***Path Integration Levels***

Path integration or "Flare" levels require participants to navigate a level to a single location where a flare is located (Coutrot et al., 2018). These levels differ in the number of turns taken before reaching the flare location. Once participants reach the flare location, they are then asked to send the flare back to the level's starting location. They are given three options to choose from and provided with feedback afterwards by seeing the flare sent to the specified location. The number of turns on each flare level is available in Table 5.6.

### **Procedure**

Individuals with amnesia were tested individually on select SHQ levels on a tablet with technical assistance available by a researcher or personal support worker. Controls were tested independently through SHQ gameplay (Coutrot et al., 2018).

### **Data Analysis**

The data were analyzed using R version 4.2.0 (R Core Team, 2013). Descriptive statistics were run using the *psych* package (Revelle & Revelle, 2015). The individuals with amnesia were compared to controls using percentiles for distance traveled and time taken to complete each level (duration). Performance was also averaged across all levels and divided by whether maps

presented prior to each level were fully visible or partially visible (see Table 5.1 for level descriptions). On appropriate levels, the accuracy (correct or incorrect) of the first decision point was also coded. Path integration levels were coded for accuracy; chance performance is 33% given that there were three options to choose from.

To better contextualize participants' performance on each level, qualitative scoring was conducted by two trained research assistants who were blind to group membership (i.e., individual with amnesia vs. control). Videos of the individuals with amnesia's performance on each level were compared to 10 randomly selected controls, for a total of 20 controls. Videos and map levels are available for download at <https://osf.io/mydwa/>. Scoring categories included longest dwell time (i.e., pause) in a given level, number of returns to a previous location that is not relevant to the goal of navigation (i.e., backtracking), and an overall subjective rating of navigation quality. In case of a discrepancy between scorers, which were minor (within one point), participants were given the benefit of the doubt and were not penalized. Whenever possible on wayfinding levels, Z-scores comparing individuals to amnesia to controls were calculated to show relative performance.

## Results

### Wayfinding Levels

#### *DA Performance*

Due to his dense anterograde amnesia, DA has not effectively learned to use an iPad or computer technology. This resulted in him forgetting the iPad commands (dragging versus swiping his finger) multiple times during testing and, at times, moving forward tightly in one area, unable to effectively maneuver to the exact correct spot. An experimenter was present to remind DA of technology instructions, but he was still less accurate as reflected by longer level durations. He also had a style of slower, more deliberate navigation that appeared separate from any technical difficulty. On certain levels that were particularly difficult due to technical challenges (levels 7, 13, and 18), indicated in Table 5.2, duration metrics were excluded from the mean and standard deviation calculations listed below.

DA's performance, when averaged across the 13 available wayfinding levels, was in the average range for distance traveled ( $M = 39.15\%$ ,  $SD = 32.09\%$ ) and low-average range for duration or time taken ( $M = 16.20\%$ ,  $SD = 20.90\%$ ) (Guilmette et al., 2020). Level 21 is omitted

from calculations. Quantitative data is unavailable on the level as DA quit to significant task and technical difficulties.

When considering performance in the context of map visibility, DA's distance performance was worse for partial map ( $M = 20.67\%$ ,  $SD = 34.06\%$ ) than full map ( $M = 44.70\%$ ,  $SD = 31.09\%$ ) levels. The data show that duration was also longer in partial map ( $M = 1\%$ ) than full-map levels ( $M = 20.00\%$ ,  $SD = 21.53\%$ ). This latter comparison should be interpreted cautiously as only 2 levels are available for the calculation for the partial-map conditions.

There was a wide variability in performance across levels, with DA performing better than 25% of controls on 8 of 13 wayfinding levels. This calls for greater consideration into what map characteristics may have contributed to task performance.

DA appears to have performed best on closed map levels, defined as maps where navigation is occurring in a tight space. DA's first decision point or turn accuracy can also help explain his performance. First decision point may be indicative of the level of encoding of the map presented before navigating. DA made the correct decision on 3 of the 5 levels where there is a clear decision point early in the level (see Table 5.4).

Another consideration for performance differences is the order of buoys on a wayfinding level. On level 11, DA makes an incorrect decision at the first decision point and overall has much poorer performance (5% distance, 1% duration). Level 11's buoys are out of order, which requires DA to return to a previous location and the first buoy he passes. In contrast, on level 12 he makes a correct judgment at the first decision point and does not need to return to the first buoy he passes. His performance on this level is in the average range (69% distance, 53% duration). The exception to the explanatory value of decision points is level 7 where DA makes a correct decision at the first point but does poorly overall. Level characteristics can help explain this performance. In addition to being an open map level, level 7's buoys are also out of order or not in set sequence so DA must return to previous buoys during navigation.

Overall, it appears that when DA must remember and return to the previously visited buoys, he is more likely to perform poorly compared to control participants. This may also relate to more time spent navigating as levels with buoys out of order are longer and more time passes since map encoding.

Additional qualitative scoring information from blinded review of videos is available in Table 5.5. This includes counts of backtracking, overall navigation ratings and longest pause. In

this table is DA's performance, control performance and calculated Z-scores for each level when available. When Z-score calculations were not possible due to no standard deviation (no variability in controls), a label of 'comparable' or 'elevated' was assigned.

Overall, DA had a higher incidence of backtracks ( $M = 3.17$ ,  $SD = 1.87$ ) than control participants ( $M = 1.53$ ,  $SD = 1.75$ ). Ratings of overall quality of navigation were also lower for DA ( $M = 4.39$ ,  $SD = 2.92$ ) than for control participants ( $M = 8.08$ ,  $SD = 1.22$ ). DA's longest pauses, calculated in seconds, were also much longer ( $M = 31.56$ ,  $SD = 22.43$ ) than control participants ( $M = 0.5$ ,  $SD = 0.57$ ), the majority of whom did not have any pauses during navigation.

### ***BL Performance***

BL's performance was averaged across 14 available wayfinding levels and is available in Table 5.3. Performance was in the low-average range for distance traveled ( $M = 24.14\%$ ,  $SD = 32.97\%$ ) and duration of navigation ( $M = 10.09\%$ ,  $SD = 18.90\%$ ) (Guilmette et al., 2020).

Considering map visibility, BL performed better for both distance ( $M = 58.67\%$ ,  $SD = 37.54\%$ ) and duration ( $M = 54\%$ ,  $SD = 34.04\%$ ) on the three levels in which maps were partially visible.

BL's best wayfinding performance was on levels 12, 18, and 22. These levels differ in map visibility but share the characteristic of a closed map style. Some other characteristics make navigating these levels easier. Specifically, level 18 has all buoys in a set sequence, level 22 has an island in the centre that participants can navigate around, and level 12 has both buoys in order and an island in the centre to navigate around. The islands in the centre may offer a cue for navigation in open map levels. Like DA, BL performs best and more comparably to controls when he is not required to return to previous locations, as this places fewer demands on learning.

Additional qualitative information from review of videos by trained scorers who were blind to group membership is available in Table 5.5. In addition to DA's performance, this table also includes BL's performance, BL control's performances, and calculated Z-scores for each level. When Z-score calculations were not possible due to a lack of variability in control performance, a label of 'comparable' or 'elevated' was assigned for each level.

Overall, BL had a higher incidence of backtracks ( $M = 5.11$ ,  $SD = 6.90$ ) than control participants ( $M = 1.50$ ,  $SD = 1.73$ ). BL also had a higher average number of backtracks ( $M = 5.11$ ,  $SD = 6.90$ ) than DA ( $M = 3.17$ ,  $SD = 1.87$ ).

Ratings of overall quality of navigation were lower for BL ( $M = 4.72$ ,  $SD = 3.31$ ) than controls ( $M = 8.11$ ,  $SD = 1.20$ ). BL's overall navigation was rated as similar to that of DA and worse than that of controls. Duration of pauses was similar for BL ( $M = 0.67$ ,  $SD = 1.03$ ) and control participants ( $M = 0.68$ ,  $SD = 0.93$ ). His dwell times were comparable to controls and much lower than DA's. This suggests that BL has a more direct navigation style than DA.

### **Path Integration**

Performance accuracy on each of the 7 path integration levels is presented in Table 5.6 for both DA and BI and their respective matched controls.

DA did not navigate directly to the flare on 2 of the 7 levels (44, 49), which are indicated with asterisks in Table 5.6. On these levels, he navigated backwards, seeming to forget the task instructions, and performing as if he was on a wayfinding level. DA's performance was accurate on 2 of the 7 (28.57%) flare levels that he had completed. His performance was accurate on 1 of the 5 (25%) levels where he navigated directly to the flare. Controls matched to DA showed higher accuracy on each of the 7 flare levels ( $M = 51.49\%$ ,  $SD = 0.05\%$ ).

BL took a direct path on all flare levels. His performance was accurate on 3 of the 7 (42.86 %) levels, whereas controls were slightly more accurate ( $M = 58.46\%$ ,  $SD = 0.07$ ).

### **Discussion**

Using the mobile video game SHQ, wayfinding and path integration behaviours were scrutinized in two well-characterized individuals with amnesia and compared to those of thousands of controls selected from a pool of over 4 million participants to identify the conditions in which the hippocampus contributes to human spatial memory. The two individuals with amnesia performed poorly on several, but not all, SHQ wayfinding levels, indicating that their spatial learning is not universally impaired. Instead, performance differed based on clinical profiles and on wayfinding level complexity, operationalized by environment characteristics (open versus closed) and memory demands (number and order of buoys). The individual with more extensive MTL damage (DA) performed worse than controls on path integration levels than the individual with more selective MTL and hippocampal damage (BL). These findings expand on a growing area of research showing preservation in spatial learning and memory in individuals with hippocampal amnesia (P.A. Banta Lavenex et al., 2014; Herdman et al., 2015; Kolarik et al., 2018; McAvan et al., 2022; Parslow et al., 2005). The results appear to confer with CMT's proposition that the hippocampus is critical to allocentric spatial memory given the poor

performance shown by both individuals on most trials. However, the results extend CMT by showing that navigation deficits may be more linked to general deficits in learning, given that minimal learning demands in an environment do not necessarily interfere with navigation, even on levels that appear to require allocentric spatial processing. These findings also demonstrate the value of combining the patient-lesion method with ‘big data’ to understand brain-behaviour relations.

The SHQ paradigm used in this study provides information on the spatial navigation abilities of individuals with amnesia in different virtual environments that vary in memory demands. The results showed that individuals performed worse, as evidenced by needing to return to a previously visited location and therefore a less direct navigation path, when there was a greater demand for anterograde memory during navigation. Increased time needed on certain levels likely further taxed anterograde memory (Gilboa & Moscovitch, 2021; Pishdadian & Rosenbaum, 2021). Unlike controls, the two individuals with amnesia demonstrated significant ‘backtracking’ behaviour, defined as unnecessary revisiting of previous locations. Analyses of backtracking to previous locations have been used in studies of sex-differences in virtual and real-world environments, with females showing more revisits compared to males (Gagnon et al., 2018; Munion et al., 2019). The more extreme nature of the backtracking observed in individuals with amnesia likely indicates rapid forgetting or deficient learning of environmental characteristics, consistent with their episodic memory deficits (Pishdadian & Rosenbaum, 2021). Future research in individuals with different cognitive profiles is needed to understand whether backtracking during navigation is pathognomonic of anterograde memory impairment.

The SHQ levels also differed in terms of map visibility, allowing for different opportunities for encoding the overall layout of the environment prior to navigation. For these maps to be useful for navigating the wayfinding levels, individuals would also need to translate the encoded maps between a bird’s-eye view and ground-level perspective (Ekstrom et al., 2018b; Vann et al., 2009). Control participants generally performed worse on partially visible map trials compared to trials in which completely visible maps were presented. For individuals with amnesia, results showed that BL, but not DA, performed more similarly to controls and better on levels with partially visible maps. This is at least partly attributable to some of the differences in memory demands on partial map levels compared to fully visible map levels. It may also indicate that BL is not making effective use of visible maps, whether fully or partially available, making

his performance more similar to that of controls on partial map trials. Future work using the SHQ paradigm could assess the effects of map visibility to investigate if it aids or interferes with navigation for individuals with anterograde amnesia.

Qualitative analyses show the influence of individual style of navigation on wayfinding performance. Despite DA's more severe anterograde amnesia, he did not perform much worse than BL on wayfinding levels and had fewer instances of backtracking. He also paused longer during navigation than BL, which may be interpreted as indicative of a slower and more deliberate navigation style. It is unclear whether DA is rehearsing or otherwise using any strategies during this additional time. This difference in navigational style may correspond with DA's subjective report of greater everyday reliance on allocentric strategies and better distance estimation skills compared to matched controls and BL (study 3). Individual style of navigation may be an important moderator to objective performance on the SHQ.

The individuals' clinical profiles and detailed neuropsychological testing may provide insight into some of the described differences in performance seen between DA and BL. While BL's memory impairment is milder than DA's, he has weaknesses in processing speed and complex attention whereas DA has intact abilities in these areas. Past research has shown that BL has difficulty with fine-grained perceptual discrimination, which may be linked to his DG/CA3 lesions (Baker et al., 2016; Mitchnick et al., 2022). This may have contributed to his difficulty with learning map details or effectively attending to details when navigating wayfinding levels on the SHQ (Kolarik et al., 2016; McAvan et al., 2022). This may also explain his extreme backtracking performance. These findings highlight the attentional and perceptual contributions to spatial navigation performance, including the ability to learn from a partially visible map (Javadi et al., 2017; Kim et al., 2013; Patai & Spiers, 2021). Overall, DA and BL's navigation styles and different profiles of cognitive deficits may interact to produce differences in navigational performance.

The two individuals with amnesia performed better on the closed than the open wayfinding levels. On closed levels, DA and BL were able to stay close to the boundaries and appeared to benefit from the restricted navigation options, with fewer opportunities to make errors. Open levels more closely resemble a Morris water maze-like environment since all buoys are in one space and not along different paths (Bohbot et al., 1998; Coughlan et al., 2019; McAvan et al., 2022; Morris, 1982). The current findings confirm that open environments may be particularly

demanding on the MTLs and specifically the hippocampus, likely due to a higher dependency on precision of allocentric spatial processes (Guderian et al., 2015; Holdstock et al., 2000; Lavenex et al., 2006). Unlike in the rodent literature or human analogs of the Morris water maze, none of the SHQ levels have the entire environment visible to participants. That said, investigating the line of sight during navigation may help explain some differences in performance across the closed and open environments, for example due to differences in the visibility of distal cues (Goodrich-Hunsaker et al., 2010; McElhinney et al., 2022).

Traditionally, wayfinding tasks drawing on allocentric spatial relations were thought to be dependent on the hippocampus. Findings from the current study show that hippocampal involvement may depend more on anterograde memory demands originating from map characteristics. Other work hypothesizes that the role of the hippocampus in allocentric spatial relations may be more about precision and/or flexibility of use (Ekstrom & Yonelinas, 2020; Kolarik et al., 2016, 2018). The findings of poor performance in BL, who has difficulties with fine-perceptual discrimination but less severe anterograde amnesia, support the importance of precision (Mitchnick et al., 2022). These results help to refine predictions of CMT, suggesting that the role of the hippocampus may be driven by anterograde memory and precision more than by allocentric spatial processing per se.

Path integration, which involves some degree of egocentric-to-allocentric translation, is believed to depend on the retrosplenial cortex to a greater degree than the hippocampus, though some studies have suggested otherwise (Hunsaker & Kesner, 2018; Kim et al., 2013; Shrager et al., 2008; Urgolites et al., 2016; Whishaw et al., 1997). These findings show worse path integration in both individuals with amnesia compared to each of their control groups. Individual DA performed worse than BL, which may relate to more extensive hippocampal/MTL damage and severe anterograde amnesia. This is consistent with findings of hippocampal contributions to path integration in a rodent study (Sapiurka et al., 2016). It is important to note, however, that the timeframe of each of the path integration levels in this study were likely beyond the limits of working memory, which may explain the performance deficits seen in DA and BL (Shrager et al., 2008). Interpretation of path integration performance is also more tentative than that for wayfinding given the relatively small number of trials. However, given the large and well-matched control samples, it is difficult to completely rule out the role of the hippocampus/MTLs

in path integration, which has been suggested in previous research, including in individuals on the ADRD spectrum (Burgess, 2006; Coutrot et al., 2019; Lowry et al., 2020).

Examination of wayfinding and path integration on the SHQ in two individuals with different degrees of anterograde amnesia provides information on the SHQ's sensitivity to memory impairment and encourages future research to assess its clinical utility in assessing the nature of spatial navigation. The complexity of environments and breadth of wayfinding and path integration levels available for testing on the SHQ, coupled with the ease of digital administration and availability of 'big data' in the form of global samples of diverse controls, adds to the appeal of this task as a neuropsychological measure. The data presented in this study provide clinicians and researchers with an in-depth view of spatial navigation integrity on the SHQ in individuals with well-characterized, real-world spatial memory impairment in relation to hippocampus and MTL damage. These findings in turn can be used as a benchmark for assessing spatial learning in milder cases of memory compromise and as a contrast to those who are genetically at risk of developing ADRD (e.g., Coughlan et al., 2018).

It is important to note that DA and BL have volume loss outside of the hippocampus and MTLs that may have contributed to their task performance, but that is largely unavoidable in patient-lesion research (Kwan et al., 2013; McAvan et al., 2022; Rosenbaum et al., 2014). The findings of significant overlap in areas of spared and impaired performance despite different locations and extents of extra-MTL volume loss allows for stronger conclusions to be drawn about hippocampal involvement. Importantly, both individuals with amnesia in this study have seemingly intact structural integrity of other regions known to be necessary for different aspects of spatial memory and navigation, including the striatum, posterior parietal cortex, and retrosplenial cortex (Chersi & Burgess, 2015; Chrastil et al., 2015; Ciaramelli et al., 2010; Epstein, 2008; McDonald & White, 1994; Rosenbaum et al., 2008). To better understand the contributions of the hippocampus, MTL, and extra-MTL regions to spatial navigation, future studies are needed to assess SHQ performance in individuals with focal lesions to these regions.

Overall, the current investigation of wayfinding and path integration on the SHQ provides a unique approach to understanding the contributions of the hippocampus to spatial navigation by combining in-depth examination of single individuals with 'big data'. The results show that hippocampal damage and anterograde amnesia do not necessarily translate to an all-encompassing allocentric spatial memory deficit. Wayfinding is possible, and particularly

benefits from ‘closed’ environments and fewer demands on anterograde memory and precision of performance.

These results expand on past research on the spatial navigation abilities of individuals with amnesia. This includes anecdotal reports of skills (Rosenbaum et al., 2005b; Corkin et al., 2013), performance on table-top tests of memory (Smith & Milner, 1989; Hartley et al., 2007), and performance on allocentric spatial tasks in environments with few distal cues and only a single goal (Bohbot et al., 1998; Goodrich-Hunsaker et al., 2010). Since the spatial navigation network extends beyond the hippocampus (Maguire et al., 1998; Ramanoël et al., 2019), results have implications not only for individuals with hippocampal compromise on the ADRD clinical spectrum (Coughlan et al., 2018; Puthusseryppady et al., 2022b), but also for individuals who present with topographical disorientation due to neurological conditions affecting other regions within and beyond the MTL (Aguirre & D’Esposito, 1999; Claessen & van der Ham, 2017; Goulter et al., 2021; Hamre et al., 2020), or have lifelong deficient spatial navigation abilities without a clear etiology (i.e., developmental topographical disorientation; Burles & Iaria, 2020; Conson et al., 2018). The current work also highlights the utility of the SHQ and identifies task levels that are most sensitive to memory deficits and that may be considered within the context of a more comprehensive assessment of spatial navigation abilities.

**Table 5.1*****Wayfinding Level Descriptions***

Map Level	Difficulty	Map Description	Number of Buoys	Map Visibility
6	Easy	Open	3	Yes
7	Easy	Open-Island	3	Yes
8	Moderate	Closed – Decision Point	3	Partial
11	Easy	Closed- Decision Point	3	Yes
12	Easy	Closed	3	Yes
13	Easy	Closed- Decision Point	3	Yes
16	Moderate	Closed- Decision Point	3	Yes
17	Easy	Closed- Decision Point	3	Yes
18	Moderate	Closed	3- in order	Partial
21	Moderate	Closed – 2 islands	3	Yes
22	Moderate	Closed – 1 island	3	Partial
43	Hard	Closed	4	Yes
46	Hard	Closed	3	Yes
56	Hard	Closed	5	Yes

*Note.* Difficulty was assigned by subjective judgment into three characterizations: ‘Easy’, ‘Moderate’ and ‘Difficult’. These were determined based on map description, number of buoys visible and overall map complexity. Map visibility was not accounted for in assigning difficulty.

**Table 5.2*****DA Wayfinding Results***

Map Level	DA Distance	DA Duration	Number of Controls
6	30%	48%	5389
7	100%	NA – stuck in front of buoy	5060
8	1%	2%	4713
11	5%	1%	3745
12	69%	53%	3392
13	68%	1% – stuck in one location	3068
16	1%	0%	1993
17	23%	6%	1869
18	60%	2% – stuck in one location	1702
21	Quit	Quit	-
22	1%	0%	1327
43	44%	0%	425
46	44%	21%	315
56	63%	31%	208

*Note.* Percentiles indicated in the table, with higher numbers indicating better performance.

**Table 5.3*****BL Wayfinding Results***

Map Level	BL Distance	BL Duration	Number of Controls
6	13%	5%	7978
7	17%	18%	7647
8	18%	17%	7247
11	1%	0%	5774
12	90%	64%	5237
13	13%	15%	4709
16	2%	2%	3106
17	0%	0%	2875
18	92%	84%	2611
21	20%	3%	2168
22	66%	61%	2006
43	4%	3%	580
46	1%	1%	447
56	1%	0%	295

*Note.* Percentiles indicated in the table, with higher numbers indicating better performance.

**Table 5.4***First Turn Accuracy*

Level	Correct decision direction	BL Accuracy	DA Accuracy
7	Left	Yes	No
11	Left	Yes	No
12	Right	Yes	Yes
13	Right	Yes	Yes
17	Right	No	Yes

**Table 5.5*****Qualitative Scoring***

Level	Category	BL	BL Controls	BL Z-score	DA	DA Controls	DA Z-score
11	Navigation Rating	1.5	8.15 (2.30)	-2.89	2.5	8.7 (1.44)	-4.31
	Backtracks	6	0.95 (1.24)	4.07	3	0.55 (0.83)	2.95
	Longest Dwell	2	0.95 (2.27)	0.46	9	0.4 (0.66)	13.03
13	Navigation Rating	7	8.75 (2.14)	-0.82	10	7.8 (1.74)	1.26
	Backtracks	1	0.65 (1.38)	0.25	0	1.4 (1.58)	-0.89
	Longest Dwell	0	0.90 (2.85)	-0.32	43.5	0	elevated
16	Navigation Rating	3.5	8.67 (2.00)	-2.59	3	9.70 (0.35)	-19.14
	Backtracks	3	0.78 (1.46)	1.52	4*	0.10 (0.32)	12.18
	Longest Dwell	1.5	0.28 (0.67)	1.82	25	0.50 (1.27)	19.29
17	Navigation Rating	2.5	9.55 (0.50)	-14.19	8	8.65 (1.13)	-0.58
	Backtracks	6	0.3 (0.48)	11.88	2	0.85 (0.58)	1.98
	Longest Dwell	0	0	comparable	10	1.7 (5.38)	1.54
18	Navigation Rating	9.5	8.45 (1.01)	1.04	1.5	8.25 (1.34)	-5.04
	Backtracks	0	1.1 (1.02)	-1.08	2	0.95 (0.93)	1.13
	Longest Dwell	0	0.1 (0.32)	-0.31	40.5	0.35 (0.75)	53.33
21	Navigation Rating	3	7.35 (2.02)	-2.15	NA	-	-
	Backtracks	2	2.55 (2.33)	-0.24	NA	-	-
	Longest Dwell	1	0	comparable	NA	-	-
22	Navigation Rating	9	8.7 (0.68)	0.44	2.5	8.55 (0.80)	-7.56
	Backtracks	0	0.75 (0.79)	-0.95	4	0.85 (1.03)	3.06
	Longest Dwell	0	0	-	24	0.3 (0.95)	24.95
43	Navigation Rating	2	6.65 (2.74)	-1.70	3	7.45 (1.01)	-4.41
	Backtracks	7	2.85 (2.47)	1.68	5	2.9 (1.47)	1.43

Level	Category	BL	BL Controls	BL Z-score	DA	DA Controls	DA Z-score
	Longest Dwell	2.5	2.95 (8.98)	-0.05	71.5	0	elevated
46	Navigation Rating	6.5	8.4 (0.81)	-1.70	6	8.35 (1.65)	-1.42
	Backtracks	1	0.45 (0.37)	1.49	2	0.5 (0.75)	2.00
	Longest Dwell	0	0.25 (0.79)	-0.32	54	1.15 (3.64)	14.52
56	Navigation Rating	1	5.65 (2.43)	-1.91	3	5.3 (2.06)	-1.12
	Backtracks	22	5.65 (4.03)	4.06	6	5.7 (4.38)	0.07
	Longest Dwell	0	0.7 (1.27)	-0.55	6.5	0.1 (0.32)	20.00

*Note.* Mean and Standard Deviation indicated for control participants. Level 21 is unavailable as DA could not complete the level. The asterisk on level 16 indicates that DA struggled to use the ipad on this level and so had to return to the buoy as he had not gotten close enough.

**Category Labels:**

*Navigation Rating:* Likert rating (1 to 10) given by blinded scorers on the effectiveness of the navigation, with 10 being highest possible rating

*Backtracks:* Count of revisits to previous location which is not relevant to navigation

*Longest Dwell:* Longest number of seconds of a stop or pause during navigation.

**Table 5.6*****Path Integration Levels - Flare Accuracy***

Flare Level	Number of Turns	BL Accuracy	BL Control Accuracy %	DA Accuracy	DA Control Accuracy %
4	1	0	70.9 (0.45)	0	55.31 (0.50)
9	1	0	59.7 (0.49)	0	55.89 (0.50)
14	1	1	65.06 (0.48)	0	57.32 (0.49)
24	1	1	52.2 (0.50)	0	47.31 (0.50)
44	2	0	53.3 (0.50)	1*	44.65 (0.50)*
49	2	1	53.49 (0.50)	0*	50.15 (0.50)*
54	2	0	54.57 (0.50)	1	49.81 (0.50)

*Note:* There are three possible options presented for each flare level. A score of “1” indicates accurate choice while a score of “0” indicates inaccurate choice. Asterisks indicate levels where DA did not navigate directly to the buoy.

## CHAPTER 6

### General Discussion

This dissertation addresses the integrity of spatial memory and navigation in neurotypical aging and following hippocampal damage. It also focuses on the relationship between subjective assessment and objective performance as well as with other factors known to affect these, specifically episodic memory and psychological distress. Specific aims included:

1. Investigating the psychometric properties of a subjective spatial navigation questionnaire to assess the nature and extent of self-reported changes to spatial memory and navigation in neurotypical aging;

2. Determining the relationship between subjective assessment of spatial memory and of episodic memory and how they, in turn, relate to psychological distress and objective memory performance;

3. Understanding the impact of hippocampal damage on subjective awareness of areas of spared and impaired episodic and spatial memory; and

4. More precise identification of the conditions in which spatial memory and navigation depend on hippocampal integrity.

The results of this dissertation have both theoretical and clinical implications and provide directions for future research on memory, aging, and amnesia.

#### **Summary of Studies**

In study 1, I developed and investigated the psychometric properties of a novel self-report questionnaire, the CNQ, which assesses different types of changes in spatial navigation that may be experienced by neurotypical older adults. Responses to the questionnaire were considered in the context of objective memory performance, metamemory, and subjective spatial navigation abilities on established measures (Brunec et al., 2019; Hegarty et al., 2002; Palombo et al., 2013; Troyer & Rich, 2018; van der Ham et al., 2013).

The results from study 1 showed that the CNQ has a reliable factor structure, consistent with the measure's design, that divides most questionnaire items according to *typical* and *atypical* spatial navigation changes. Two items loaded on both factors and require additional consideration; these items focused on technology use and environmental familiarity. Overall, the sample reported few changes in their abilities, particularly on items designed to capture *atypical* changes for normative aging. Changes were described as occurring over several years, which is

consistent with the literature that suggests a gradual decline in spatial navigation abilities in typical aging (Yu et al., 2021; van der Ham et al., 2021). There were sex differences in item endorsement on all metamemory and spatial navigation questionnaires. On the CNQ, females reported more changes in their abilities and over a longer time period than men. Study 1 showed that the CNQ has a reliable factor structure and provides unique qualitative data about subjective spatial navigation abilities, the latter of which, to my knowledge, had not been previously investigated.

In study 2, structural equation modeling was used to examine the relationship between the constructs of Metamemory and subjective Spatial Navigation Abilities along with Psychological Distress and Objective Memory. The findings showed a positive weak, yet statistically significant, relationship between Metamemory and subjective Spatial Navigation Abilities. The relationships among different spatial navigation questionnaires, including the CNQ, were examined with correlations and by considering the questionnaires' loadings on the latent variable Spatial Navigation Abilities. General spatial ability questionnaires and subscales loaded most strongly on the Spatial Navigation Abilities construct, followed by distance estimation, spatial anxiety, and allocentric strategy use. The CNQ had negative, weak loadings on Spatial Navigation Abilities, demonstrating its divergence from other questionnaires. Both objective memory measures had weak loadings on Metamemory and Spatial Navigation Abilities. Symptoms of psychological distress had stronger loadings on Metamemory than Spatial Navigation Abilities. Overall, the results show that, in typical aging, there are differences between spatial navigation measures, a weak relationship between Metamemory and Spatial Navigation Abilities, a strong divergence between objective and subjective metrics, and different relationship of Psychological distress with Metamemory and Spatial Navigation Abilities.

Study 3 took a patient-lesion approach to examine how episodic memory impairment affects metamemory and subjective spatial navigation abilities. Self-assessment of memory and strategy use in two individuals with memory impairment due to hippocampal compromise was compared to that of controls matched in age, education, and sex. Across most questionnaires, both individuals rated their metamemory and spatial navigation abilities as worse than controls, consistent with objective memory performance, indicating that they had good insight into their episodic memory, daily memory, and spatial navigation difficulties. Both individuals also reported substantial changes to their spatial navigation abilities since the onset of their amnesia

on the CNQ. These data indicate that anterograde amnesia does not necessarily impede learning of declines in episodic memory and spatial navigation abilities. These results also provide a deeper understanding of the role of premorbid skills and psychological distress in the subjective evaluation of these abilities.

In the fourth and final study reported in this dissertation, wayfinding and path integration abilities were investigated in the same two individuals with hippocampal amnesia described in study 3. Performance was compared to that of a large sample of closely matched controls. The results showed that there was not a universal impairment on all wayfinding levels. Instead, performance differed based on level characteristics (closed versus open environments) and anterograde memory demands. One of the individuals with amnesia (DA) performed worse on path integration levels than the other individual (BL), indicating the impact that the extent of MTL damage and associated anterograde amnesia has on performance. The results of study 4 highlight the specific environmental features and wayfinding demands that result in poor navigation performance in individuals with amnesia. This study also showed an approach to combining ‘big data’ from an accessible mobile navigation game with classic neuropsychological patient-lesion methodology to better understand spatial memory and navigation.

### **Subjective Changes in Spatial Navigation Ability**

Previously established intraindividual differences in subjective spatial navigation and memory abilities helped motivate my investigation into subjective changes in spatial navigation abilities (Mourao et al., 2019; L.A. Rabin et al., 2017; Yu et al., 2021). The work presented in this dissertation is the first to compare changes in spatial memory and navigation ability to ratings of general spatial navigation ability and strategy use. The findings from studies 1, 2 and 3 show that subjective evaluations of changing abilities are related but not identical to subjective evaluations of overall spatial navigation abilities.

The results from study 1 are aligned with past work indicating that typically aging older adults experience few significant changes in general spatial ability and are unlikely to be disoriented, although they do report changes in their navigation confidence (Laczó et al., 2017; Lithfous et al., 2013; Lopez et al., 2018; Markova et al., 2017; Pai & Lee, 2016; Rodriguez et al., 2020; Yatawara et al., 2017; Yu et al., 2021). Qualitative information from the CNQ provided novel information on the types of changes in navigation ability that occur in typical aging

(Allison et al., 2019; Cerman et al., 2018), which, to my knowledge, represents the first time self-reported changes to navigation in neurotypical aging have been documented to this extent. The results show that older adults report greater reliance on GPS, avoidance of navigation during nighttime or if experiencing difficulties to vision, increased difficulty traveling on familiar streets, and a general reduction in comfort and confidence when navigating.

One of the dissertation research objectives was to investigate the psychometric properties of the CNQ. Integrating findings across studies, the CNQ was shown to have items with acceptable fit, a latent factor structure of *typical* and *atypical* changes for most items, and to diverge from other measures of general spatial navigation ability and strategy use in aging. Individuals with hippocampal amnesia endorsed more premorbid to postmorbid changes (reflected in higher scores) on the CNQ than controls, supporting the measure's sensitivity to objective impairment in spatial navigation.

Multidimensional item response analyses indicated that CNQ items 5 and 6 may need additional consideration. These may include removing the questions from the scale or revising them. For example, the CNQ does not address environmental familiarity like another subjective spatial navigation measure that is used in the field, the Questionnaire on Everyday Navigational Ability (Pai et al., 2012). Environmental familiarity may be an important consideration for CNQ item 5, which references GPS technology use. This item could be reframed to account for environmental familiarity or separated into two questions asking about GPS use in familiar versus unfamiliar environments.

Determining the validity of a measure is an ongoing process that needs to be specific to the intended purpose and the population of interest (AERA, APA, & NCME, 2014). The results presented here provide initial support for use of the CNQ to detect spatial navigation changes in typical aging and in individuals with longstanding memory impairment. Future work will need to investigate if the measure is appropriate for detecting clinically significant spatial navigation changes in individuals on the preclinical ADRD spectrum.

Overall, these dissertation findings on subjective changes in spatial navigation abilities expand on the potential utility of treating decline in spatial navigation abilities as a marker of atypical aging and ADRD by providing specific information on the type and timeframe of changes experienced by typically aging individuals (Costa et al., 2020; Coughlan et al., 2018, 2019; Laczó et al., 2017; Lithfous et al., 2013; Moffat, 2009).

## **Relationship Between Subjective Memory and Subjective Spatial Navigation Abilities**

In addition to investigating changes in subjective spatial navigation ability in this dissertation I also explored the relationship between metamemory and subjective spatial navigation abilities. Objective episodic memory and spatial navigation are proposed to rely on similar neurocognitive processes or share the same neural substrate (Buzsáki & Moser, 2013; Ekstrom & Ranganath, 2017). This shared underpinning includes the hippocampus, which contributes to detailed, perceptually rich and subjectively recalled information in episodic memory and spatial memory (Moscovitch et al., 2016; Renoult & Rugg, 2020; Tulving, 2002). This shared relationship has been critiqued in recent work on the subjective evaluation of these abilities (Fan et al., 2021). The findings from this dissertation show that subjective spatial navigation abilities are weakly positively related to metamemory and subjective episodic memory abilities in typical aging (study 2). However, the findings from studies 3 and 4 suggest greater alignment between these subjective appraisals, as individuals with amnesia report both poor metamemory and spatial navigation abilities.

The results of the current studies build on the findings from the few past studies that had examined the relationship between subjective episodic memory and spatial memory in aging. This research, which was predominantly in young and middle-aged participant samples, has relied on the SAM Episodic and Spatial Subscales, the SBSOD Questionnaire, and the Subjective Memory Questionnaire. The results indicated weak but significant relationships between subjective episodic memory and spatial memory (Clark & Maguire, 2020; Fan et al., 2021). A longitudinal study involving community-dwelling older adults found that subjective cognitive complaints were related to both depression and spatial orientation abilities; however, there are very few reports of poor spatial orientation in the sample, and other subjective spatial navigation skills were not assessed (Markova et al., 2017). Findings of weak relationships between the constructs in the current dissertation provide the most compelling evidence of this relationship to date in aging due to the use of structural equation modeling and comprehensive measurement of subjective spatial navigation and metamemory. These results support previous findings of a discrepancy between these subjective abilities.

There are several reasons why the relationship between metamemory and subjective spatial navigation abilities may be stronger in individuals with memory impairment due to hippocampal compromise, who, in this study, were also older in age. Meta-analytic research

shows that the hippocampus may be differentially involved in episodic memory and spatial navigation networks (Kühn & Gallinat, 2014), and that individual differences in the default mode (memory) network may become more extreme with aging (Staffaroni et al., 2018). Longitudinal work shows that baseline, but not current hippocampal volume mediates the relationship between the hippocampus and subjective memory complaints, with differences in memory ability becoming more apparent to individuals as they age (Stewart et al., 2011). Correlational results from ‘SuperAgers’, defined as individuals over 80 years of age with episodic memory performance comparable to that of individuals who are 2-3 decades younger, show a strong pairing of episodic memory with spatial navigation abilities when they are better than expected given the participant’s age (Zhou et al., 2022). It may be that subjective memory and spatial navigation abilities are more likely to be related when there is more variability present in a sample, such as in older age or individuals with deficient memory. While the current results provide evidence that there are significant differences between subjective episodic memory and spatial navigation, the findings also emphasize the importance of the measurement tools used (i.e., questionnaires, neurocognitive tasks) and the populations being studied.

The differences found between subjective spatial navigation abilities and metamemory are likely not attributable to the unique characteristics of the sample given that subjectively rated abilities were largely aligned with past work in aging (T.F. Levine et al., 2021; Palombo et al., 2013; Troyer & Rich, 2018; van der Ham et al., 2021). Sample characteristics are still worth considering for future work. Specifically, it is important to note that the majority of the older adult sample recruited in this study reported their country of nationality to be the United Kingdom followed by the United States. This is different from the MMQ and SAM norms, which are based on Canadian samples. When mean scores (as opposed to T-scores or Z-scores) are considered, the older adult sample that was tested in this dissertation reported higher satisfaction and ability, and less strategy use compared to the Canadian MMQ sample (Troyer & Rich, 2018). Since metamemory is of global interest, this finding does encourage future researchers to look at whether nationality is a moderator of metamemory in aging. This would extend research that finds differences in neuropsychological test scores based on cultural background and ethnicity (Pedraza & Mungas, 2008; Rosselli & Ardila, 2003). There may be global or national-level patterns to metamemory that are tied to sociocultural factors, which may or may not resemble differences seen in objective spatial navigation abilities (Spiers et al., 2021).

In summary, subjective episodic memory and metamemory, and subjective spatial memory and navigation, relate to one another but appear to be more separate in aging than in individuals with memory impairment due to hippocampal compromise. Separate consideration of subjective evaluations of these different types of abilities in cognitive assessment in aging is likely to be fruitful.

### **Objective Episodic Associative and Spatial Memory**

In typical aging there are known declines in episodic memory and in spatial memory (Becker et al., 2015; Clark et al., 2018; LaPlume et al., 2022; Old & Naveh-Benjamin, 2008; van der Ham et al., 2021; Yu et al., 2021), with corresponding declines in hippocampal volume and function (Bettio et al., 2017; Driscoll et al., 2003; Raz & Rodrigue, 2006; Nordin et al., 2017; Zheng et al., 2017). The results from the studies reported in this dissertation indicate reduced performance on tests of associative episodic (or relational memory) and spatial memory in individuals with hippocampal amnesia and typically aging older adults, particularly when considered in the context of past findings in younger adults.

Older adult participants' reduced performance on objective tests of associative episodic memory (Face-Name Task) and spatial memory (Four Mountains Task) was similar in pattern (although not in extent) to that seen in the individuals with amnesia tested in the current dissertation, DA and BL. As people get older, the hippocampus is vulnerable to a host of changes in structural and functional integrity and to age-related neurological conditions, including ischemic lesions, which occurred for BL. The older adults tested in the current set of studies performed better on the Face-Name Task in the overall condition than the recombined condition; this pattern of performance was similar to that seen in BL, who has bilateral hippocampal damage limited to the DG and part of the CA3 subfield (Nordin et al., 2017; Old & Naveh-Benjamin, 2008). BL also showed similar performance to controls and to typically aging older adults on the Face-Name Task intact condition, whereas DA did not, mirroring DA's more extensive MTL damage (Brown et al., 2010; Old & Naveh-Benjamin, 2008). These findings are consistent with the idea that the hippocampus is critical to recollecting context/source information as opposed to familiarity of items/content, with the latter engaging extra-hippocampal MTL regions, including the perirhinal cortex (Bowles et al., 2007; Brown et al., 2010; Eichenbaum et al., 2007; Pishdadian & Rosenbaum, 2021; Thakral et al., 2022). The similarities and differences in the patterns of results between the older adults and individuals

with amnesia in this work suggest declines in aging may be partly, but not fully, due to age-related changes to hippocampal function, which impacts associative memory and relational binding of details (Olsen et al., 2012; Ryan et al., 2000; Shing et al., 2011; Troyer et al., 2011), possibly through less precision in memory (Ekstrom & Yonelinas, 2020).

Older adults' performance appeared to be worse on the test of allocentric spatial memory than associative (episodic) memory, tasks which are weakly related in path analyses (studies 1 and 2). In addition to differences in task difficulty, performance differences between the allocentric and associative episodic memory tasks may reflect the differential use of compensatory strategies, which may be easier to implement in the Face-Name Task given the availability of verbal labels. Self-initiated strategy use has been shown to engage brain regions outside the MTLs and mediate objective episodic and associative memory performance (Cohn et al., 2008; Frankenmolen et al., 2018; Guerrero et al., 2019; Kirchoff et al., 2014). Taken together, older adults and individuals with amnesia had reduced performance on episodic associative and spatial memory tasks known to rely on MTL and hippocampal integrity, though to varying degrees, in line with previous literature.

### **Relationship between Objective and Subjective Metrics**

The findings from this dissertation have implications for the relationship between objective and subjective evaluation of memory and spatial abilities. Past research in aging has shown that the subjective evaluation of memory abilities is weakly but significantly related to objective memory abilities (Brailean et al., 2019; Burmester et al., 2016; Crumley et al., 2014; McWhirter et al., 2020). Similarly, studies have found a weak but significant positive relationship between subjective and objective spatial navigation abilities (Clark & Maguire, 2020; Selarka et al., 2019; van der Ham et al., 2021; Weisberg et al., 2014). This discrepancy resembles the differences between self and observer ratings of personality (Connolly et al., 2007) and is similar to objective assessment of other cognitive abilities, such as executive functions, which tend to be weakly related, if at all, to subjective evaluations (Gardner et al., 2017; Howlett et al., 2022; Hutchinson et al., 2012). The results from study 2 are consistent with discrepancies between subjective and objective evaluation of memory and spatial abilities in aging.

Past research has mainly focused on the relationship between objective and subjective memory abilities in individuals with memory impairment who are on the preclinical ADRD spectrum and therefore known to experience widespread brain changes that extend beyond the

hippocampus and MTLs (Allison et al., 2019; Cerman et al., 2018; Dauphinot et al., 2020). The findings from studies 3 and 4 of this dissertation provide the first formal investigation of the relationship between objective and subjective memory and spatial abilities in individuals with episodic memory impairment due to relatively selective hippocampal/MTL damage. The individuals with hippocampal amnesia reported poor, and therefore largely accurate, spatial navigation and memory skills. This suggests a clearer relationship between objective and subjective abilities in individuals with memory impairment than in typical aging (study 2).

While the individuals with amnesia overall evaluated their subjective memory and spatial navigation abilities as poor, this was not universal. For example, DA rated his allocentric strategy use and distance estimation abilities as comparable to controls. The results from study 3 showed that DA had deficits on both objective memory and spatial tasks compared to controls. The findings from study 4 indicate that DA had comparable performance to controls on certain SHQ levels and an approach to navigating that was more precise and deliberate than BL's, despite his more extensive lesions. Past research shows that DA has intact remote spatial memory abilities (Herdman et al., 2015) as well as instances of compensatory strategy use (Ryan et al., 2013). Therefore, DA's subjective evaluation of his spatial navigation abilities may reflect his premorbid abilities, his remote spatial navigation abilities, and/or his navigational style. Another possibility is that DA's subjective evaluation indicates a deficit in "experience-near" learning that is linked to deficient anterograde memory and rich episodic details (Wank et al., 2022). What may be concluded from DA's report of his subjective abilities and performance on objective tasks is that even in the face of extreme, long-standing objective memory difficulties, subjective reporting of abilities appears to be largely accurate.

BL's objective memory performance was generally consistent with the subjective evaluation of his general spatial and memory abilities as well as reported strategy use. However, his memory satisfaction was higher and spatial anxiety lower than expected given his objectively assessed performance on tasks. Elevated psychological distress may explain this pattern; BL may be more psychologically defended or, alternatively, more accepting of his deficits. This response pattern draws attention to the importance of psychological factors on subjective reporting of spatial navigation ability and metamemory.

Overall, the results of this dissertation are consistent with previous studies showing discrepancies between subjective and objective metrics of memory and cognition in aging. The

findings from individuals with hippocampal amnesia suggest a stronger relationship between subjective and objective metrics in the face of memory compromise and also highlight the importance of considering intraindividual factors, including strategy use and psychological distress.

### **Sex Differences**

In addition to psychological distress and strategy use, sex is an important intraindividual factor that has been shown to interact with episodic and spatial memory (Boone et al., 2018; Zheng et al., 2017). Several findings from this dissertation speak to the importance of accounting for sex (and/or gender, depending, in part, on how study questions are framed) when investigating metamemory, objective memory, and subjective and objective spatial navigation abilities in aging. Since both individuals with amnesia were males, it was not possible to draw conclusions about sex differences in the context of hippocampal amnesia.

### ***Objective Performance***

In study 1, females performed better on the associative episodic memory task (i.e., Face-Name Task) than males. This is consistent with past research showing that females tend to have better verbal associative memory and face recognition than males (LaPlume et al., 2022; Nordin et al., 2017). This builds on neuroimaging work, which finds that greater hippocampal volume and integrity predict differences in associative memory performance in females but not males (Zheng et al., 2017).

In contrast to the Face-Name Task, no sex differences were found on the Four Mountains Task, a perspective-taking allocentric spatial memory test. The most extreme sex differences (moderate effect sizes) in objective abilities reported in the literature are observed on tests of mental rotation, with males outperforming females and sex differences increasing with age (Newcombe, 2020; Silverman et al., 2007). Sex differences in objective spatial memory abilities have small-to-moderate effect sizes across the lifespan, with the largest sex differences reported on tests of pointing recall and distance estimation (Nazareth et al., 2019; Yu et al., 2021). Wayfinding abilities have also been shown to differ by sex and/or gender, including on the SHQ task (Coutrot et al, 2018; Gagnon et al., 2018; Munion et al., 2019). The Four Mountains Task is neither a pointing task nor a distance estimation task, and while the task does have a rotation element, it appears to be best conceptualized as an allocentric spatial memory task that has been shown to rely on hippocampal integrity (Bird et al., 2010; Burles & Iaria, 2020). Therefore, the

lack of sex differences on the Four Mountains Task may be explained by the task's processing demands.

Consideration of past research on the Four Mountains Task may also help in understanding the lack of sex-differences in performance. This precise version of the Four Mountains Task had not been used in a typical aging older adult sample prior to this dissertation. Performance on a similar version of this task with more trials was found to be sensitive to group differences between controls and individuals with developmental topographical disorientation, the latter tested in a female-dominated younger sample (Mean age = 35.6,  $SD = 12.2$ ) (Burles & Iaria, 2020). The results from that same study indicated a sex advantage in performance, favouring males (Burles & Iaria, 2020). Sex differences were not noted in another version of this task that was administered to older adults, individuals with preclinical ADRD, and individuals with amnesia (Bird et al., 2010; Chan et al., 2016; Hartley et al., 2007). The (abbreviated) version of the Four Mountains Task used in this dissertation might not be sufficiently sensitive to sex differences, or females and males with age-related decline in hippocampal functioning might not differ on the form of allocentric memory assessed by this task (Burles & Iaria, 2020; Chan et al., 2016).

In this dissertation, objective memory performance on hippocampally mediated tasks appears on tests of (verbal) associative memory, but not allocentric spatial memory, in a manner largely consistent with past literature.

### ***Subjective Performance***

Sex differences in subjective reports of memory integrity did not fully align with objective performance, further demonstrating the discrepancy between objective and subjective metrics. Despite no objective differences in performance in allocentric spatial memory (i.e., on the Four Mountains Task), females reported significantly worse subjective spatial navigation abilities across all subjective measures than males (study 1). These subjective results are consistent with past findings (He & Hegarty, 2020; Nazareth et al., 2019; Yu et al., 2021). Females also reported less reliance on allocentric spatial strategies than males, a known contributor to suboptimal objective spatial navigation (Andersen et al., 2012; Boone et al., 2018; Coutrot et al., 2018; Ulrich et al., 2019). Females also reported higher spatial anxiety than males. Higher spatial anxiety is related to more spatial navigation errors (Hund & Minarik, 2006; Lawton et al., 1996) and reduced feelings of personal safety, which is lower in females (Lawton

& Kalli, 2002). It is possible that personal safety and gender equality are overlooked in their influence on spatial navigation abilities. Indeed, on a global level, gender equality has been found to positively relate to objective wayfinding performance (Coutrot et al., 2018; Lawton & Kallai, 2002; Spiers et al., 2021).

There were no sex differences in self-reported memory on the MMQ Ability or Satisfaction subscales despite females performing better than males on the Face-Name Task (Troyer & Rich, 2018; study 1). However, females had higher scores on the MMQ Strategy and SAM Episodic subscales. This latter finding concurs with females reporting greater memory strategy use and memory efficacy than males (Hertzog et al., 2019). Findings of higher scores on the MMQ Strategy and SAM Episodic subscales suggest that sex differences in strategy use should be considered as a possible mediator of objective memory performance.

There are data to suggest that subjective memory complaints are more common in females than males (Tomita et al., 2014), though this may be at least partly attributable to personality differences between the sexes (Jonker et al., 2000; Slavin et al., 2010). Other findings have indicated that the quality of complaints may differ across sex, with females' subjective reports of cognitive decline more likely to have elements of worry and also be more predictive of subsequent dementia (Heser et al., 2019; Hopper et al., 2022). In the older adult participants tested in the current dissertation, females reported significantly higher depression symptoms, but not anxiety symptoms, than males. It appears that sex overlaps with mood and personality to influence metamemory evaluations.

In summary, females appear to report higher levels of spatial anxiety, that they rely less on allocentric spatial strategies, and have worse spatial navigation abilities than males. Females also report greater strategy use and better episodic memory abilities, but do not report better general memory ability or greater memory satisfaction than males. The findings from this dissertation emphasize the prominence of sex differences in objective and subjective spatial navigation and metamemory, which should be considered in theory and practice.

### **The Role of the Hippocampus in Spatial Memory and Navigation**

The results of this dissertation help to inform our understanding of the importance of the MTLs, and specifically the hippocampus, in episodic memory and spatial navigation. Older adults may be viewed as a model of declining hippocampal function in research on episodic and spatial memory (Addis et al., 2008; Hirshhorn et al., 2011; B. Levine et al., 2002; Rosenbaum et

al., 2012). However, it is not possible to draw conclusions regarding the direct role of the hippocampus in different forms of memory based on behavioural studies in older adults. In this dissertation, examining the performance of two individuals with different extents of hippocampal damage provides more conclusive evidence of how the hippocampus contributes to episodic and spatial memory, and how these forms of memory relate to one another. The specific pattern of results in the two individuals with hippocampal amnesia extends previous findings and informs theories that view the hippocampus as critical for allocentric spatial memory, such as CMT (O'Keefe, 1990; O'Keefe & Dostrovsky, 1971; Burgess et al., 2002).

Despite differences in etiology and extent of lesions within and beyond the hippocampus, DA and BL both performed worse than controls on the Four Mountains Task in study 3 and most SHQ wayfinding levels in study 4. Moreover, both individuals showed intact performance on certain SHQ trials. Performance on the SHQ appeared to be moderated by map characteristics and anterograde memory demands, specifically the number and order of buoys (Coutrot et al., 2022; Daugherty & Raz, 2017). This extends past work, which has found that navigation in individuals with hippocampal amnesia is imprecise, by specifying the environmental characteristics that might influence performance by increasing demands on memory (Kolarik et al., 2018). Overall, the results show, on the one hand, that allocentric spatial memory may be vulnerable to even partial bilateral hippocampal lesions that are relatively limited to the dentate gyrus and part of CA3 (BL), but, on the other hand, that even more extensive bilateral hippocampal lesions (DA) do not necessarily result in a universal impairment in wayfinding or path integration abilities. The findings also speak to the sensitivity of the SHQ to spared and impaired performance in the face of hippocampal compromise (Coutrot et al., 2018; Herdman et al., 2015).

Study 3 and 4 findings from this dissertation are consistent with a growing body of work which questions the emphasis on the role of the hippocampus in spatial navigation, specifically in allocentric spatial representations (Ekstrom et al., 2014; Ekstrom & Ranganath, 2018; Sapiurk et al., 2016; Shrager et al., 2008). Indeed, there is previous evidence of preserved spatial memory abilities in the presence of hippocampal lesions in learning newly encountered environments (Banta-Lavenex et al., 2014; McAvan et al., 2022; Parslow et al., 2004). There is also research showing intact remote spatial memory in individuals with hippocampal amnesia, including DA who was included in this dissertation (Corkin et al., 2013; Herdman et al., 2015; Maguire et al.,

2006; Rosenbaum et al., 2000, 2012). For example, in this dissertation, DA's better performance on visible as opposed to partially visible map levels suggests that he derived some benefit to navigation from allocentric spatial representations, particularly if it was within the confines of working memory (Shrager et al., 2008). The areas of intact performance shown by BL and DA may also be due to reliance on non-allocentric forms of spatial memory. It may also be tied to reliance on some non-detailed or imprecise form of allocentric spatial memory that are tied to schema knowledge outside of MTLs (Farzanfar et al., in press; Ghosh & Gilboa, 2014). Overall, while the results may be taken to support the role of the hippocampus in allocentric spatial memory as predicted by CMT, they suggest that the theory might require fine-tuning to accommodate findings that the hippocampus is most critical when the environment is newly learned and for more detailed or precise representations (Ekstrom & Yonelinas, 2020; Moscovitch et al., 2005; Rosenbaum et al., 2001).

The areas of intact performance by BL and DA emphasize the importance of considering a broader 'spatial navigation' network. This network extends beyond the hippocampus to include regions that are closely connected to the hippocampus, such as the retrosplenial cortex, posterior parietal cortex, prefrontal cortex, and other MTL regions (Chrastil et al., 2015; Ekstrom et al., 2014, 2018b; Maguire et al., 1998; Patai & Spiers, 2021; Ramanoël et al., 2019). For example, the translation of maps encoded prior to each SHQ level to egocentric navigation during a level is likely to engage the retrosplenial cortex, while remembering previously visited buoys is likely to engage prefrontal cortex regions. Overall, these dissertation results suggest ways to refine CMT. Specifically, the role of the hippocampus should be attributable to demands on learning and precision (detail), particularly when representing large-scale space for real-world navigation.

### **Psychological Distress**

There are multiple intraindividual factors that can impact both objective and subjective abilities. The influence of psychological distress on Metamemory and subjective Spatial Navigation abilities was investigated in studies 2 and 3. In study 2, I used structural equation modeling to investigate the influence of psychological distress on Metamemory and subjective Spatial Navigation Abilities in aging. The results from this study showed that psychological distress had negative relationships with both Metamemory and subjective Spatial Navigation Abilities, with stronger loadings on Metamemory than Spatial Navigation Abilities. These findings are consistent with research showing that older adults' subjective memory complaints

are positively and significantly related to psychological distress (Brigola et al., 2015; Edmonds et al., 2014; Lenehan et al., 2012; Reynolds et al., 2022; Silva et al., 2014).

The influence of psychological distress on subjective spatial navigation abilities is less clear than its influence on metamemory. Previous research has looked at the relationship between mood symptoms and subjective spatial navigation abilities in aging, aMCI, and ADRD in a correlational manner and has not found a significant relationship (Cerman et al., 2018). A separate study found that anxiety symptoms, but not depression symptoms, relate to complaints about spatial navigation abilities in aging (Sheardova et al., 2015). Consistent with results from this study, path analyses in study 2 indicated that anxiety symptoms, but not depression symptoms, loaded significantly on Spatial Navigation Abilities. Both psychological distress symptom measures loaded less strongly onto Spatial Navigation Abilities than Metamemory. These findings suggest that subjective spatial navigation abilities in aging may be less affected than metamemory by psychological distress, and in particular depression symptoms. Psychological distress may be considered construct-irrelevant information if the goal of measuring subjective spatial navigation abilities is to understand objective declines in spatial navigation (AERA, APA, & NCME, 2014). Future research is needed to pull apart the influence of psychological distress on metamemory versus subjective spatial navigation abilities.

The results from study 3 showed that individuals with hippocampal amnesia mostly reported accurate spatial navigation and memory abilities even though there was evidence for elevated psychological distress, particularly for BL. Despite decades of research involving individuals with hippocampal amnesia, there are few reports of mood or anxiety symptoms in these individuals (Pishdadian & Rosenbaum, 2021).

While past work on the relationship between psychological distress and subjective spatial navigation abilities is limited, there is research documenting the influence of psychological distress on objective spatial navigation and hippocampal integrity. Past research shows that individuals with depression have worse objective spatial navigation abilities compared to individuals without depression, and performance corresponds with MTL functional activity (Cornwell et al., 2010). Meta-analytic research indicates that major depressive disorder is associated with global hippocampal atrophy (Santos et al., 2018). These findings bolster the importance of considering psychological distress, and in particular depression symptoms, when studying spatial navigation abilities, particularly in individuals with hippocampal compromise.

Research on self-reported cognitive function in individuals with TBIs and ABIs, which can affect the anterior temporal lobes/MTLs, can be informative on how psychological distress may impact subjective reporting. In individuals with mild to moderate and acute (i.e., 6 months post injury) TBIs, depression symptoms are the best predictor of cognitive deficits and relate to a higher likelihood of subjective cognitive complaints (Chamelian & Feinstein, 2006). There is evidence that in individuals 10 years post-injury with mild-to-very severe TBIs emotional state is related to subjective reports of cognitive change since TBI, again supporting the importance of accounting for mood symptoms (Draper & Ponsford, 2009). Other work in individuals with TBI indicates that as the time since injury increases (up to 36 months), factors such as somatic symptoms, stress, communication difficulties, and age become the most important predictors of subjective memory complaints (Bay et al., 2012). For the individuals with amnesia tested in this study many years (i.e., more than 20) have passed since their ABIs and lesion onset. Therefore, while it is likely that symptoms of psychological distress are impacting DA's and BL's subjective reporting of abilities, there is also research suggesting that the length of time since DA's and BL's hippocampal/MTL damage may lessen the significance of their psychological distress symptoms. Future work in individuals with amnesia should document and incorporate the influence of psychological distress on task performance and consider time since lesion onset.

Overall, the results from studies 2 and 3 emphasize the importance of accounting for psychological distress in subjective evaluations of ability, albeit to a greater extent for metamemory than for subjective spatial navigation, and possibly more in typical aging than in chronic neurological conditions associated with hippocampal amnesia.

### **Anosognosia and Learning of Deficits**

The neurological condition of anosognosia, or unawareness of deficits, presents an obstacle to accurate subjective assessment of cognitive abilities and is common in the conditions of aMCI and ADRD (Acharya & Sánchez-Manso, 2021). Past research has shown that hippocampal integrity, and in particular right hippocampal integrity, is an important correlate of anosognosia in aging, aMCI, and ADRD (Chavoix & Insausti, 2017; Flores-Vázquez et al., 2021; Marshall et al., 2004; Tondelli et al., 2018). However, the findings from studies 3 and 4 indicate that individuals with anterograde amnesia due to more selective hippocampal damage have good overall awareness of pre- and postmorbid spatial navigation and memory abilities, suggesting a relative absence of anosognosia. This is notable in DA as he has extensive damage to his MTLs

bilaterally (Kwan et al., 2013; Rosenbaum et al., 2008). The intact knowledge is consistent with findings of relative preservation of semantic memory in the face of hippocampal damage (Pishdadian & Rosenbaum, 2021). These results therefore suggest that damage to the hippocampus/MTLs, and associated episodic memory impairment, is not essential for the condition of anosognosia.

Subjective awareness of cognitive abilities in individuals with hippocampal amnesia have been observed (e.g., Corkin, 2013; Klein et al., 1996; Rosenbaum et al., 2005b) but, to my knowledge, had not been formally tested until the current studies. The results from this dissertation suggest that self-knowledge of premorbid and postmorbid memory and spatial navigation abilities may be retained and/or learned over time even in severe forms of anterograde amnesia. This contrasts with work on learning of personality traits in amnesia, which appears to be incomplete (Kurczek et al., 2015; Wank et al., 2022). It may be that learning about memory and spatial navigation difficulties is easier and more personally salient to individuals with amnesia than personality ratings given the link to their severe ABIs and presence in their daily lives (Juskenaite et al., 2016; Kurczek et al., 2015; Sui & Humphreys, 2013). There is some evidence that certain aspects of subjective knowledge of spatial navigation, such as distance estimation abilities or strategy use (as apparent in DA's self-reports), are less likely to be integrated into self-information (Garland et al., 2021; Wank et al., 2022). However, DA's remote spatial memory abilities suggest this reporting is relatively accurate. The results from study 4 encourage re-examination of theories of personal semantics to account for knowledge of one's spatial and memory abilities, instead of focusing primarily or exclusively on autobiographical or general current self-knowledge (Renoult et al., 2012, 2019). These can, in turn, be used to inform theories on anosognosia in other individuals with memory impairment.

Research in individuals with other neurological conditions that are known to affect memory has suggested that the relationship between episodic memory deficits and decreased self-awareness might not be as strong as originally believed. A recent study in individuals with temporal lobe epilepsy did not find a significant relationship between episodic memory performance and self-awareness of cognitive function, instead implicating seizure frequency and psychological distress in decreased self-awareness (Zimmermann et al., 2020). In individuals with aMCI, unawareness of deficits was not found to be related to memory impairment or to performance on specific neuropsychological tests (Piras et al., 2016). Dissertation findings build

on these results to show that moderate-to-severe deficits in episodic memory in relation to MTL dysfunction does not prohibit awareness into spatial navigation or memory abilities.

The insight demonstrated by individuals with anterograde amnesia due to hippocampal/MTL lesions points to the importance of other brain regions to learning and awareness of cognitive deficits. Past work has indicated that lesions to bilateral medial prefrontal cortices are associated with inaccurate personality trait evaluations (Philippi et al., 2017; Marquine et al., 2016). In individuals with psychosis spectrum illness, anosognosia is linked to reduced frontal lobe integrity and diverse brain-wide changes, including total brain volume (Pia & Tamietto, 2006; Pijnenborg et al., 2020). In studies of individuals with aMCI, anosognosia was related to brain glucose metabolism and  $\beta$ -amyloid load in the posterior cingulate cortex, bilateral MTLs, and right lateral temporal lobes (i.e., the default mode network) (Hanseeuw et al., 2019; Mondragón et al., 2019; Therriault et al., 2018). Longitudinal research of self-awareness of memory deficits in individuals with aMCI who convert to ADRD implicates midline brain structures, including the anterior cingulate, the inferior frontal cortex, and cerebellar vermis (Ries et al., 2007; Spalletta et al., 2014). Anosognosia is therefore related to widespread changes in the brain that extend beyond the hippocampus, even in individuals with memory impairment (Antoine et al., 2019; Fyock & Hampstead, 2015; Valera-Bermejo et al., 2020).

Overall, the findings from this dissertation concur with the importance of widespread brain changes to the learning of memory deficits and anosognosia.

### **Clinical Implications**

In addition to contributing to our understanding of anosognosia, findings from this dissertation may inform other aspects of clinical assessment and care.

This preliminary investigation into the CNQ's psychometric properties shows that it has a reliable factor structure in aging, diverges from other established measures in hypothesized ways, and provides rich qualitative information. The responses on the CNQ by individuals with amnesia offer evidence of the measure's sensitivity to spatial navigation difficulties in the context of hippocampal compromise (studies 3 and 4). At this time, CNQ scores can only be compared to a typically aging sample or to individuals with hippocampal amnesia. It is not currently clear whether the measure is sensitive to actual spatial navigation changes seen in aMCI or ADRD. The CNQ's psychometric properties, including the two items which load on

both factors, also needs to be investigated in older adults characterized with neurocognitive measures before it is put to clinical use in aging.

The current findings provide suggestions for clinicians selecting questionnaires or querying spatial navigation abilities either in aging or in individuals with longstanding memory impairment. The findings show that there is a weak relationship between metamemory and subjective spatial navigation abilities, suggesting that querying older adults on these abilities is likely to yield different information. It is also best for clinicians not to assume that a high number of metamemory complaints or psychiatric symptoms will necessarily mean dissatisfaction in spatial navigation abilities. Instead, psychological distress appears to relate more to metamemory than subjective spatial navigation abilities. Clinicians should also expect females, on average, to report greater spatial anxiety and worse spatial navigation abilities than males. Importantly, the findings from this dissertation suggest that memory impairment does not prohibit accurate reporting of current or changing spatial navigation abilities, at least in individuals with long-term memory difficulties due to neurological compromise.

These results indicate that it may be worthwhile to query the subjective evaluation of general spatial skill, strategy use, and spatial anxiety, as these may provide different kinds of information. The WQ is likely to be useful as it measures both general skill and spatial anxiety and has norms and cut-offs available, including divisions by sex (Claessen et al., 2016b; van der Kuil et al., 2021). However, the WQ does not measure changes in ability. Therefore, using multiple questionnaires is advised for a fuller picture of subjective spatial navigation abilities.

Some other considerations for clinicians querying spatial navigation abilities in aging include being attentive to recent as opposed to gradual changes, and to occurrence of specific events of disorientation, particularly inside buildings or in highly familiar environments. The current data indicate that these are infrequent in typical aging. Although a greater reliance on wayfinding technology (GPS) might not be adaptive in the long-term (Dahmani & Bohbot, 2020), these data indicate it should not necessarily be taken as a sign of declining spatial memory and hippocampal function.

This dissertation also provides suggestions for the assessment of spatial navigation abilities in aging and in individuals with memory loss. Decades of research into the most sensitive objective measures to capture real-world spatial navigation difficulties and topographical disorientation in aging and in individuals with memory impairment has yielded a plethora of

measures that differ in their ease, mode of administration (e.g., tabletop, virtual reality, real-world), and accessibility (e.g., technology, individualization) (Caffò et al., 2020; Cogné et al., 2017; Hartley et al., 2007; Laczó et al., 2009; Lopez et al., 2020; Schöberl et al., 2020; Tu et al., 2017; Wang et al., 2012; Wood et al., 2016). The ecological validity of tasks versus accessibility of administration has been a consistent issue in past work (Burles & Iaria, 2020; Chan et al., 2016; Cogné et al., 2017; Descloux & Maurer, 2018; Grewe et al., 2014; Rosenbaum et al., 2012; Taillade et al., 2016). The mobile video game SHQ used in study 4 may provide a compromise between accessibility and ecological validity (Coutrot et al., 2019), with the added benefit of large amounts of benchmark data (Coughlan et al., 2020; Coutrot et al., 2018, 2019). In this dissertation, I investigated the sensitivity of the SHQ to extreme memory dysfunction due to hippocampal compromise and showed that it provides valuable information that corresponds to individuals' neuropsychological profiles. These findings support future research on the utility of the SHQ in clinical settings.

Virtual reality paradigms have been used to improve spatial navigation abilities in different populations, including in individuals with stroke, multiple sclerosis, epilepsy, and on the ADRD spectrum (Claessen et al., 2016a; Montana et al., 2019). Although the current studies did not assess a rehabilitative intervention, the results indicate that individuals with amnesia perform worse in open spatial environments and when greater precision and demands on new learning are required. Designing wayfinding strategies to assist individuals with memory impairment should thus consider the incorporation of environments that are 'closed', less stringent criteria for how a goal location is defined, and shorter task durations to place fewer demands on anterograde memory.

### **Limitations and Future Directions**

There are several limitations and unanswered questions from this dissertation. A limitation of this work is that a young adult sample was not available for direct comparison to the older adult samples. Wherever possible, comparisons were made with previous study findings, with reference to young and older adult samples. Future work should directly compare the performance of older adults to that of young adults to better understand the effects of aging.

Another limitation of these studies is that data from all older adult and control samples were collected online or through mobile technology without an experimenter present. Online administration allowed for data to be collected from individuals in different countries during the

COVID-19 pandemic. However, this prevented participants from asking clarifying questions and prevented observation of participants during task performance to ensure task compliance. It is also important to consider all these findings in the context of the COVID-19 pandemic, which has been associated with increased psychological distress (Salari et al., 2020).

Only study 4 had control data based on geography available for comparison with the individuals with amnesia who reside in Canada. Overall, these data can only be generalized to individuals living in Canada, the United States, and the United Kingdom. The importance of geographic location for spatial navigation abilities was emphasized in a recent study that used the SHQ to test participants. These findings indicate that individuals with experience navigating in the United States and Canada have comparable spatial navigation abilities and are among the best navigators globally, with individuals from the United Kingdom falling slightly below (Coutrot et al., 2018). Future work should aim to replicate and expand on these findings with in-person testing, geographically matched control samples, and in individuals outside of the countries represented in the sample, ideally including countries that do not share the common linguistic and socio-cultural features of the three predominantly English-speaking, highly developed countries surveyed (Statucka & Cohn, 2019).

An essential follow-up to this investigation of the psychometric properties of the CNQ would be administering the measure to neuropsychologically characterized older adults, including individuals diagnosed with aMCI, and relating performance to volume of the hippocampus/MTLs and other brain regions known to be involved in spatial navigation. Given the role of insight into subjective evaluation of cognitive abilities, the volumes and functionality of prefrontal cortex regions, including the medial prefrontal cortex, should also be considered (Harwood et al., 2005; Marquine et al., 2016). It would also be useful to account for genetic factors, lifestyle factors, and other metrics of ADRD disease burden (i.e.,  $\beta$ -amyloid and tau levels) (Hanseeuw et al., 2019; Kametani & Hasegawa, 2018; Peters et al., 2019; Vromen et al., 2022). Lastly, longitudinal follow-up of these well-characterized older adult participants would be needed to consider the predictive utility of measuring subjective changes in spatial navigation abilities for progression to ADRD.

Given that disorientation or difficulty navigating is not exclusive to memory disorders, it would also be useful for the CNQ to be administered to older adults without memory problems to determine the measure's sensitivity to memory. For example, individuals who have experienced

strokes do not typically have predominant impairments in memory but do report lower spatial navigation ability on the WQ (Claessen et al., 2016b; De Rooij et al., 2019). Critically, these investigations would expand on the CNQ's specificity for spatial navigation difficulties in individuals with memory compromise and ADRD.

The current studies only compared subjective spatial navigation abilities to an objective allocentric spatial memory task in aging. Future research should investigate whether evaluations of subjective spatial navigation abilities have predictive validity for daily real-world navigation. Predictive validity could also be investigated by including a wayfinding measure that has been shown to correlate with real-world performance, such as the SHQ. Combining questionnaires with momentary assessments of navigation or daily tracking of incidents of disorientation or navigational difficulties could also be used to investigate the predictive validity of the measures. These assessments have been conducted using GPS in individuals with psychosis (Parrish et al., 2020) and, more recently, in individuals with AD to understand spatial disorientation and navigation tendencies (Ghosh et al., 2022; Puthusseryppady et al., 2022a; Puthusseryppady et al., 2022b).

An important objective measure of spatial navigation abilities in aging and preclinical ADRD is driving abilities. In aging, driving abilities are typically examined in relation to objective neurocognitive performance and diagnosis, but not the subjective evaluation of spatial navigation abilities (Davis et al., 2012; Hird et al., 2016). Future studies could evaluate whether subjective judgments of strategy use, general navigation ability, and changes to navigation ability relate to spatial disorientation when driving and how this intersects with real-world navigation.

Other areas of future research could be inspired by the findings from the studies involving the two individuals with amnesia, BL and DA (studies 3 and 4). The studies provided data regarding whether the hippocampus and adjacent MTL structures are necessary for different aspects of spatial memory and navigation along with insight into spared and impaired function. A next step is to use resting-state and/or task-based fMRI to understand the role of other brain structures in supporting areas of preserved function as well as impaired function, which may reflect disconnection from the hippocampus/MTL rather than hippocampal/MTL damage per se (Argyropoulos et al., 2019). Given that research into subjective evaluations of cognitive ability in hippocampal amnesia has focused on personality judgments (Grilli & Verfaellie, 2015; Tulving

et al., 1998; Wank et al., 2022), it would also be worthwhile investigating BL's and DA's personality judgments and the accuracy of those judgments in relation to self-reported episodic and spatial memory reported in the current study. Both individuals reported a high reliance on memory strategies; an important follow-up would be to investigate these individuals' actual daily memory strategy use. Quantitative informant reports of memory and spatial abilities would be helpful to quantify insight (Allison et al., 2019; Pai et al., 2012), as only qualitative information from informants was available in this dissertation. Asking individuals to evaluate their performance during navigation would speak to more immediate knowledge and learning of abilities. Finally, to bolster the generalizability of findings, testing additional cases of hippocampal amnesia would be beneficial, especially females and individuals with amnesia in more acute stages of recovery. Testing opportunities are, unfortunately, likely to be accessible given the recent increase in cases of opioid induced amnesia (Barash et al., 2020).

## **Conclusion**

This dissertation reports four studies aimed at increasing our understanding of metamemory and spatial navigation abilities in aging and in individuals with memory impairment due to hippocampal lesions, with a focus on the subjective report of spatial navigation abilities and their correlates. To answer my research questions in older adults and in individuals with memory compromise, I relied on online study methods, advanced statistical modeling, classical neuropsychological lesion methodology, 'big data', and mobile-game technology. Although the literature suggests that spatial navigation abilities are a unique and sensitive marker of abnormal aging, few studies have formally tested the extent of this claim or self-report of changes to these abilities in the context of existing subjective and objective measures. I examined variables (i.e., objective memory abilities, psychological distress) that may interact with the subjective spatial navigation abilities construct to better characterize this construct in aging and in individuals with memory loss. These findings inform theories of hippocampal function by suggesting that the anterograde memory demands of the tasks and precision of the response are critical determinants of hippocampal contributions to wayfinding. Overall, the results of this dissertation suggest that subjective and objective measures of spatial memory and navigation, including questionnaires assessing self-reported changes and mobile games with 'big' normative data, should be considered in the assessment of aging and hippocampal amnesia.

## Bibliography

- Acharya, A. B., & Sánchez-Manso, J. C. (2021). Anosognosia. In *StatPearls [Internet]*. StatPearls Publishing. <https://www.ncbi.nlm.nih.gov/books/NBK513361/>
- Addis, D. R., Wong, A. T., & Schacter, D. L. (2008). Age-related changes in the episodic simulation of future events. *Psychological science, 19*(1), 33-41. <https://doi.org/10.1111/j.1467-9280.2008.02043.x>
- Aguirre, G. K., & D'Esposito, M. (1999). Topographical disorientation: a synthesis and taxonomy. *Brain, 122*, 1613-1628. <https://doi.org/10.1093/brain/122.9.1613>
- Aguirre, N., Costumero, V., Marin-Marin, L., Escudero, J., Belloch, V., Parcet, M. A., & Ávila, C. (2019). Activity in memory brain networks during encoding differentiates mild cognitive impairment converters from non-converters. *Journal of Alzheimer's Disease, 71*(3), 1049-1061. <https://doi.org/10.3233/JAD-190421>
- Akoglu, H. (2018). User's guide to correlation coefficients. *Turkish journal of emergency medicine, 18*(3), 91-93. <https://doi.org/10.1016/j.tjem.2018.08.001>
- Allison, S. L., Fagan, A. M., Morris, J. C., & Head, D. (2016). Spatial navigation in preclinical Alzheimer's disease. *Journal of Alzheimer's Disease, 52*(1), 77-90. <https://doi.org/10.3233/JAD-150855>
- Allison, S., Babulal, G. M., Stout, S. H., Barco, P. P., Carr, D. B., Fagan, A. M., ... & Head, D. (2018). Alzheimer's disease biomarkers and driving in clinically normal older adults: Role of spatial navigation abilities. *Alzheimer disease and associated disorders, 32*(2), 101. <https://doi.org/10.1097/WAD.0000000000000257>
- Allison, S. L., Rodebaugh, T. L., Johnston, C., Fagan, A. M., Morris, J. C., & Head, D. (2019).

- Developing a spatial navigation screening tool sensitive to the preclinical Alzheimer disease continuum. *Archives of Clinical Neuropsychology*, 34(7), 1138-1155.  
<https://doi.org/10.1093/arclin/acz019>
- Altemus, M., Sarvaiya, N., & Epperson, C. N. (2014). Sex differences in anxiety and depression clinical perspectives. *Frontiers in neuroendocrinology*, 35(3), 320-330.  
<https://doi.org/10.1016/j.yfrne.2014.05.004>
- Amariglio, R. E., Becker, J. A., Carmasin, J., Wadsworth, L. P., Lorus, N., Sullivan, C., ... & Rentz, D. M. (2012). Subjective cognitive complaints and amyloid burden in cognitively normal older individuals. *Neuropsychologia*, 50(12), 2880-2886.  
<https://doi.org/10.1016/j.neuropsychologia.2012.08.011>
- American Educational Research Association, American Psychological Association, & National Council on Measurement in Education (Eds.). (2014). *Standards for educational and psychological testing*. American Educational Research Association.
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). <https://doi.org/10.1176/appi.books.9780890425596>
- Argyropoulos, G. P., Loane, C., Roca-Fernandez, A., Lage-Martinez, C., Gurau, O., Irani, S. R., & Butler, C.R. (2019). Network-wide abnormalities explain memory variability in hippocampal amnesia. *Elife*, 8, e46156. <https://doi.org/10.7554/eLife.46156>
- Andersen, N. E., Dahmani, L., Konishi, K., & Bohbot, V. D. (2012). Eye tracking, strategies, and sex differences in virtual navigation. *Neurobiology of learning and memory*, 97(1), 81-89. <https://doi.org/10.1016/j.nlm.2011.09.007>
- Angevaere, M. J., Vonk, J. M., Bertola, L., Zahodne, L., Watson, C. W. M., Boehme, A., ... &

- Manly, J. J. (2022). Predictors of Incident Mild Cognitive Impairment and Its Course in a Diverse Community-Based Population. *Neurology*, *98*(1), e15-e26.  
<https://doi.org/10.1212/WNL.00000000000013017>
- Antoine, N., Bahri, M. A., Bastin, C., Collette, F., Phillips, C., Balteau, E., ... & Salmon, E. (2019). Anosognosia and default mode subnetwork dysfunction in Alzheimer's disease. *Human brain mapping*, *40*(18), 5330-5340. <https://doi.org/10.1002/hbm.24775>
- Antonova, E., Parslow, D., Brammer, M., Dawson, G. R., Jackson, S. H. D., & Morris, R. G. (2009). Age-related neural activity during allocentric spatial memory. *Memory*, *17*(2), 125-143. <https://doi.org/10.1080/09658210802077348>
- Attems, J., & Jellinger, K. A. (2014). The overlap between vascular disease and Alzheimer's disease-lessons from pathology. *BMC medicine*, *12*(1), 1-12.  
<https://doi.org/10.1186/s12916-014-0206-2>
- Baker, S., Vieweg, P., Gao, F., Gilboa, A., Wolbers, T., Black, S. E., & Rosenbaum, R. S. (2016). The human dentate gyrus plays a necessary role in discriminating new memories. *Current Biology*, *26*(19), 2629-2634.  
<https://doi.org/10.1016/j.cub.2016.07.081>
- Ball, H. A., McWhirter, L., Ballard, C., Bhome, R., Blackburn, D. J., Edwards, M. J., ... & Carson, A. J. (2020). Functional cognitive disorder: dementia's blind spot. *Brain*, *143*(10), 2895-2903. <https://doi.org/10.1093/brain/awaa224>
- Banta Lavenex, P., Amaral, D. G., & Lavenex, P. (2006). Hippocampal Lesion Prevents Spatial Relational Learning in Adult Macaque Monkeys. *Journal of Neuroscience*, *26*(17), 4546-4558. <https://doi.org/10.1523/jneurosci.5412-05.2006>
- Banta Lavenex, P. A., Colombo, F., Ribordy Lambert, F., & Lavenex, P. (2014). The human

- hippocampus beyond the cognitive map: evidence from a densely amnesic patient. *Frontiers in human neuroscience*, 8, 711.  
<https://doi.org/10.3389/fnhum.2014.00711>
- Barash, J. A., Whitley, J., Watson, C. J., Boyle, K., Lim, C., Lev, M. H., ... & Ganetsky, M. (2020). Opioid-associated amnesic syndrome: description of the syndrome and validation of a proposed definition. *Journal of the Neurological Sciences*, 417, 117048.  
<https://doi.org/10.1016/j.jns.2020.117048>
- Barel, E., & Tzischinsky, O. (2018). Age and sex differences in verbal and visuospatial abilities. *Advances in Cognitive Psychology*, 2(14), 51. <https://doi.org/10.5709/acp-0238-x>
- Bay, E., Kalpakjian, C., & Giordani, B. (2012). Determinants of subjective memory complaints in community-dwelling adults with mild-to-moderate traumatic brain injury. *Brain Injury*, 26(7-8), 941-949. <https://doi.org/10.3109/02699052.2012.666365>
- Becker, N., Laukka, E. J., Kalpouzos, G., Naveh-Benjamin, M., Bäckman, L., & Brehmer, Y. (2015). Structural brain correlates of associative memory in older adults. *NeuroImage*, 118, 146–153. <https://doi.org/10.1016/j.neuroimage.2015.06.00>
- Bennett, I. J., Stark, S. M., & Stark, C. E. (2019). Recognition memory dysfunction relates to hippocampal subfield volume: a study of cognitively Normal and mildly impaired older adults. *The Journals of Gerontology: Series B*, 74(7), 1132-1141.  
<https://doi.org/10.1093/geronb/gbx181>
- Bettio, L. E., Rajendran, L., & Gil-Mohapel, J. (2017). The effects of aging in the hippocampus and cognitive decline. *Neuroscience & Biobehavioral Reviews*, 79, 66-86.  
<https://doi.org/10.1016/j.neubiorev.2017.04.030>
- Bird, C. M., Chan, D., Hartley, T., Pijnenburg, Y. A., Rossor, M. N., & Burgess, N. (2010).

- Topographical short-term memory differentiates Alzheimer's disease from frontotemporal lobar degeneration. *Hippocampus*, 20(10), 1154-1169.  
<https://doi.org/10.1002/hipo.20715>
- Bleecker, M. L., Bolla-Wilson, K., Agnew, J., & Meyers, D. A. (1988). Age-related sex differences in verbal memory. *Journal of clinical psychology*, 44(3), 403-411.  
[https://doi.org/10.1002/1097-4679\(198805\)44:3<403::AID-JCLP2270440315>3.0.CO;2-0](https://doi.org/10.1002/1097-4679(198805)44:3<403::AID-JCLP2270440315>3.0.CO;2-0)
- Board of Directors. (2007). American Academy of Clinical Neuropsychology (AACN) practice guidelines for neuropsychological assessment and consultation. *The Clinical Neuropsychologist*, 21(2), 209-231. <https://doi.org/10.1080/13825580601025932>
- Bohbot, V. D., Kalina, M., Stepankova, K., Spackova, N., Petrides, M., & Nadel, L. Y. N. N. (1998). Spatial memory deficits in patients with lesions to the right hippocampus and to the right parahippocampal cortex. *Neuropsychologia*, 36(11), 1217-1238.  
[https://doi.org/10.1016/S0028-3932\(97\)00161-9](https://doi.org/10.1016/S0028-3932(97)00161-9)
- Bohbot, V. D., & Corkin, S. (2007). Posterior parahippocampal place learning in \ HM. *Hippocampus*, 17(9), 863-872. <https://doi.org/10.1002/hipo.20313>
- Bondi, M. W., Edmonds, E. C., Jak, A. J., Clark, L. R., Delano-Wood, L., McDonald, C. R., ... & Alzheimer's Disease Neuroimaging Initiative. (2014). Neuropsychological criteria for mild cognitive impairment improves diagnostic precision, biomarker associations, and progression rates. *Journal of Alzheimer's Disease*, 42(1), 275-289.  
<https://doi.org/10.3233/JAD-140276>
- Boone, A. P., Gong, X., & Hegarty, M. (2018). Sex differences in navigation strategy and efficiency. *Memory & cognition*, 46(6), 909-922. <https://doi.org/10.3758/s13421-018-0811-y>

- Borkenau, P., & Leising, D. (2016). A more complete picture of personality: What analyses of trait profiles have told us about personality judgment—So far. *Current Directions in Psychological Science*, 25(4), 228-232. <https://doi.org/10.1177/0963721416651960>
- Bowles, B., Crupi, C., Mirsattari, S. M., Pigott, S. E., Parrent, A. G., Pruessner, J. C., ... & Köhler, S. (2007). Impaired familiarity with preserved recollection after anterior temporal-lobe resection that spares the hippocampus. *Proceedings of the National Academy of Sciences*, 104(41), 16382-16387. <https://doi.org/10.1073/pnas.070527310>
- Brailean, A., Steptoe, A., Batty, G. D., Zaninotto, P., & Llewellyn, D. J. (2019). Are subjective memory complaints indicative of objective cognitive decline or depressive symptoms? Findings from the English Longitudinal Study of Ageing. *Journal of psychiatric research*, 110, 143-151. <https://doi.org/10.1016/j.jpsychires.2018.12.005>
- Brigola, A. G., Manzini, C. S. S., Oliveira, G. B. S., Ottaviani, A. C., Sako, M. P., & Vale, F. A. C. (2015). Subjective memory complaints associated with depression and cognitive impairment in the elderly: A systematic review. *Dementia & Neuropsychologia*, 9, 51-57. <https://doi.org/10.1590/S1980-57642015DN91000009>
- Broadbent, D. E., Cooper, P. F., FitzGerald, P., & Parkes, K. R. (1982). The cognitive failures questionnaire (CFQ) and its correlates. *British journal of clinical psychology*, 21(1), 1-16. <https://doi.org/10.1111/j.2044-8260.1982.tb01421.x>
- Brown, M. W., Warburton, E. C., & Aggleton, J. P. (2010). Recognition memory: material, processes, and substrates. *Hippocampus*, 20(11), 1228-1244. <https://doi.org/10.1002/hipo.20858>
- Brunec, I. K., Bellana, B., Ozubko, J. D., Man, V., Robin, J., Liu, Z. X., ... & Moscovitch, M. (2018). Multiple scales of representation along the hippocampal anteroposterior axis in humans. *Current Biology*, 28(13), 2129-2135. <https://doi.org/10.1016/j.cub.2018.05.016>

- Brunec, I. K., Robin, J., Patai, E. Z., Ozubko, J. D., Javadi, A. H., Barense, M. D., ... & Moscovitch, M. (2019). Cognitive mapping style relates to posterior–anterior hippocampal volume ratio. *Hippocampus*, 29(8), 748-754.  
<https://doi.org/10.1002/hipo.23072>
- Brunet, H. E., Caldwell, J. Z., Brandt, J., & Miller, J. B. (2020). Influence of sex differences in interpreting learning and memory within a clinical sample of older adults. *Aging, Neuropsychology, and Cognition*, 27(1), 18-39.  
<https://doi.org/10.1080/13825585.2019.1566433>
- Buckley, R. F., Maruff, P., Ames, D., Bourgeat, P., Martins, R. N., Masters, C. L., ... & Ellis, K. A. (2016). Subjective memory decline predicts greater rates of clinical progression in preclinical Alzheimer's disease. *Alzheimer's & Dementia*, 12(7), 796-804.  
<https://doi.org/10.1016/j.jalz.2015.12.013>
- Burgess, N., Maguire, E. A., & O'Keefe, J. (2002). The human hippocampus and spatial and episodic memory. *Neuron*, 35(4), 625-641. [https://doi.org/10.1016/S0896-6273\(02\)00830-9](https://doi.org/10.1016/S0896-6273(02)00830-9)
- Burgess, N. (2006). Spatial memory: how egocentric and allocentric combine. *Trends Cogn. Sci.* 10, 551–557. <https://doi.org/10.1016/j.tics.2006.10.005>
- Burles, F., & Iaria, G. (2020). Behavioural and cognitive mechanisms of Developmental Topographical Disorientation. *Scientific reports*, 10(1), 1-11.  
<https://doi.org/10.1038/s41598-020-77759-8>
- Burmester, B., Leathem, J., & Merrick, P. (2016). Subjective cognitive complaints and objective cognitive function in aging: a systematic review and meta-analysis of recent cross-sectional findings. *Neuropsychology Review*, 26(4), 376-393.  
<https://doi.org/10.1007/s11065-016-9332-2>

- Buzsáki, G., & Moser, E. I. (2013). Memory, navigation and theta rhythm in the hippocampal-entorhinal system. *Nature neuroscience*, *16*(2), 130-138. <https://doi.org/10.1038/nn.3304>
- Caffò, A. O., Lopez, A., Spano, G., Stasolla, F., Serino, S., Cipresso, P., ... & Bosco, A. (2020). The differential effect of normal and pathological aging on egocentric and allocentric spatial memory in navigational and reaching space. *Neurological Sciences*, *41*(7), 1741-1749. <https://doi.org/10.1007/s10072-020-04261-4>
- Caillaud, M., Hudon, C., Boller, B., Brambati, S., Duchesne, S., Lorrain, D., ... & Belleville, S. (2020). Evidence of a relation between hippocampal volume, white matter hyperintensities, and cognition in subjective cognitive decline and mild cognitive impairment. *The Journals of Gerontology: Series B*, *75*(7), 1382-1392. <https://doi.org/10.1093/geronb/gbz120>
- Calamia, M., Markon, K., & Tranel, D. (2013). The robust reliability of neuropsychological measures: Meta-analyses of test–retest correlations. *The Clinical Neuropsychologist*, *27*(7), 1077-1105. <https://doi.org/10.1080/13854046.2013.809795>
- Cantero, J. L., Iglesias, J. E., Van Leemput, K., & Atienza, M. (2016). Regional hippocampal atrophy and higher levels of plasma amyloid-beta are associated with subjective memory complaints in nondemented elderly subjects. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*, *71*(9), 1210-1215. <https://doi.org/10.1093/gerona/glw022>
- Cappelleri, J. C., Lundy, J. J., & Hays, R. D. (2014). Overview of classical test theory and item response theory for the quantitative assessment of items in developing patient-reported outcomes measures. *Clinical therapeutics*, *36*(5), 648-662. <https://doi.org/10.1016/j.clinthera.2014.04.006>
- Carr, V. A., Bernstein, J. D., Favila, S. E., Rutt, B. K., Kerchner, G. A., & Wagner, A. D. (2017).

- Individual differences in associative memory among older adults explained by hippocampal subfield structure and function. *Proceedings of the National Academy of Sciences*, 114(45), 12075-12080. <https://doi.org/10.1073/pnas.1713308114>
- Cerman, J., Ross, A., Laczo, J., Martin, V., Zuzana, N., Ivana, M., ... & Jakub, H. (2018). Subjective spatial navigation complaints-a frequent symptom reported by patients with subjective cognitive decline, mild cognitive impairment and alzheimer's disease. *Current Alzheimer Research*, 15(3), 219-228. <https://doi.org/10.2174/1567205014666171120145349>
- Chalmers, R. P. (2012). mirt: A multidimensional item response theory package for the R environment. *Journal of statistical Software*, 48(1), 1-29. <https://doi.org/10.18637/jss.v048.i06>
- Chamelian, L., & Feinstein, A. (2006). The effect of major depression on subjective and objective cognitive deficits in mild to moderate traumatic brain injury. *The Journal of neuropsychiatry and clinical neurosciences*, 18(1), 33-38. <https://doi.org/10.1176/jnp.18.1.33>
- Chan, D., Gallaher, L. M., Moodley, K., Minati, L., Burgess, N., & Hartley, T. (2016). The 4 mountains test: A short test of spatial memory with high sensitivity for the diagnosis of pre-dementia Alzheimer's disease. *JoVE (Journal of Visualized Experiments)*, (116), e54454. <https://doi.org/10.3791/54454>
- Chavoix, C., & Insausti, R. (2017). Self-awareness and the medial temporal lobe in neurodegenerative diseases. *Neuroscience & Biobehavioral Reviews*, 78, 1-12. <https://doi.org/10.1016/j.neubiorev.2017.04.015>
- Cheng, Y. W., Chen, T. F., & Chiu, M. J. (2017). From mild cognitive impairment to subjective cognitive decline: conceptual and methodological evolution. *Neuropsychiatric disease*

- and treatment*, 13, 491. <https://doi.org/10.2147/NDT.S123428>
- Cherbuin, N., Kim, S., & Anstey, K. J. (2015). Dementia risk estimates associated with measures of depression: a systematic review and meta-analysis. *BMJ open*, 5(12).  
<http://dx.doi.org/10.1136/bmjopen-2015-008853>
- Chersi, F., & Burgess, N. (2015). The cognitive architecture of spatial navigation: hippocampal and striatal contributions. *Neuron*, 88(1), 64-77.  
<https://doi.org/10.1016/j.neuron.2015.09.021>
- Chi, L., Zhào, H., Huang, Y., Zhang, Y., & Tian, H. (2021). Spatial Navigation Is Impaired in Elderly Patients With Cerebral Small Vessel Disease. *Frontiers in neurology*, 1246.  
<https://doi.org/10.3389/fneur.2021.608797>
- Chrastil, E. R., Sherrill, K. R., Hasselmo, M. E., & Stern, C. E. (2015). There and back again: hippocampus and retrosplenial cortex track homing distance during human path integration. *Journal of Neuroscience*, 35(46), 15442-15452.  
<https://doi.org/10.1523/JNEUROSCI.1209-15.2015>
- Chu, C. S., Sun, I. W., Begum, A., Liu, S. I., Chang, C. J., Chiu, W. C., ... & Stewart, R. (2017). The association between subjective memory complaint and objective cognitive function in older people with previous major depression. *PloS one*, 12(3), e0173027.  
<https://doi.org/10.1371/journal.pone.0173027>
- Ciaramelli, E., Rosenbaum, R. S., Solcz, S., Levine, B., & Moscovitch, M. (2010). Mental space travel: damage to posterior parietal cortex prevents egocentric navigation and reexperiencing of remote spatial memories. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 36(3), 619. <https://doi.org/10.1037/a0019181>
- Claessen, M. H., van der Ham, I. J., Jagersma, E., & Visser-Meily, J. M. (2016a). Navigation

- strategy training using virtual reality in six chronic stroke patients: a novel and explorative approach to the rehabilitation of navigation impairment. *Neuropsychological rehabilitation*, 26(5-6), 822-846. <https://doi.org/10.1080/09602011.2015.1045910>
- Claessen, M. H. G., Visser-Meily, J. M., de Rooij, N. K., Postma, A., & van der Ham, I. J.M. (2016b). The wayfinding questionnaire as a self-report screening instrument for navigation-related complaints after stroke: internal validity in healthy respondents and chronic mild stroke patients. *Archives of Clinical Neuropsychology*, 31(8), 839-854. <https://doi.org/10.1093/arclin/acw044>
- Claessen, M. H. G., & van der Ham, I. J. M. (2017). Classification of navigation impairment: A systematic review of neuropsychological case studies. *Neuroscience and Biobehavioral Reviews*, 73, 81-97. <https://doi.org/10.1016/j.neubiorev.2016.12.015>
- Clark, R., Hazeltine, E., Freedberg, M., & Voss, M. W. (2018). Age differences in episodic associative learning. *Psychology and Aging*, 33(1), 144-157. <https://doi.org/10.1037/pag0000234>
- Clark, I. A., & Maguire, E. A. (2020). Do questionnaires reflect their purported cognitive functions?. *Cognition*, 195, 104114. <https://doi.org/10.1016/j.cognition.2019.104114>
- Cogné, M., Taillade, M., N’Kaoua, B., Tarruella, A., Klinger, E., Larrue, F., ... & Sorita, E. (2017). The contribution of virtual reality to the diagnosis of spatial navigation disorders and to the study of the role of navigational aids: A systematic literature review. *Annals of physical and rehabilitation medicine*, 60(3), 164-176. <https://doi.org/10.1016/j.rehab.2015.12.004>
- Cohn, M., Emrich, S. M., & Moscovitch, M. (2008). Age-Related Deficits in Associative Memory: The Influence of Impaired Strategic Retrieval. *Psychology and Aging*, 23(1), 93–103. <https://doi.org/10.1037/0882-7974.23.1.93>

- Colombo, D., Serino, S., Tuena, C., Pedroli, E., Dakanalis, A., Cipresso, P., & Riva, G. (2017). Egocentric and allocentric spatial reference frames in aging: A systematic review. *Neuroscience & Biobehavioral Reviews*, *80*, 605-621. <https://doi.org/10.1016/j.neubiorev.2017.07.012>
- Condon, D. M., Wilt, J., Cohen, C. A., Revelle, W., Hegarty, M., & Uttal, D. H. (2015). Sense of direction: General factor saturation and associations with the Big-Five traits. *Personality and Individual Differences*, *86*, 38-43. <https://doi.org/10.1016/j.paid.2015.05.023>
- Connolly, J. J., Kavanagh, E. J., & Viswesvaran, C. (2007). The convergent validity between self and observer ratings of personality: A meta-analytic review. *International Journal of Selection and Assessment*, *15*(1), 110-117. <https://doi.org/10.1111/j.1468-2389.2007.00371.x>
- Conson, M., Bianchini, F., Quarantelli, M., Boccia, M., Salzano, S., Di Vita, A., & Guariglia, C. (2018). Selective map-following navigation deficit: a new case of developmental topographical disorientation. *Journal of Clinical and Experimental Neuropsychology*, *40*(9), 940-950. <https://doi.org/10.1080/13803395.2018.1451493>
- Conway, M. A. (2005). Memory and the self. *Journal of memory and language*, *53*(4), 594-628. <https://doi.org/10.1016/j.jml.2005.08.005>
- Corkin, S. (2002). What's new with the amnesic patient HM?. *Nature reviews neuroscience*, *3*(2), 153-160. <https://doi.org/10.1038/nrn726>
- Corkin, S. (2013). *Permanent present tense: The unforgettable life of the amnesic patient, HM*. Basic Books (AZ).
- Cornwell, B. R., Salvatore, G., Colon-Rosario, V., Latov, D. R., Holroyd, T., Carver, F. W., ...

- & Grillon, C. (2010). Abnormal hippocampal functioning and impaired spatial navigation in depressed individuals: evidence from whole-head magnetoencephalography. *American Journal of Psychiatry*, *167*(7), 836-844. <https://doi.org/10.1176/appi.ajp.2009.09050614>
- Costa, R. Q. M. D., Pompeu, J. E., Viveiro, L. A. P. D., & Brucki, S. M. D. (2020). Spatial orientation tasks show moderate to high accuracy for the diagnosis of mild cognitive impairment: a systematic literature review. *Arquivos de Neuro-Psiquiatria*, *78*, 713-723. <https://doi.org/10.1590/0004-282X20200043>
- Coughlan, G., Laczó, J., Hort, J., Minihane, A. M., & Hornberger, M. (2018). Spatial navigation deficits—overlooked cognitive marker for preclinical Alzheimer disease?. *Nature Reviews Neurology*, *14*(8), 496-506. <https://doi.org/10.1038/s41582-018-0031-x>
- Coughlan, G., Coutrot, A., Khondoker, M., Minihane, A. M., Spiers, H., & Hornberger, M. (2019). Toward personalized cognitive diagnostics of at-genetic-risk Alzheimer's disease. *Proceedings of the National Academy of Sciences*, *116*(19), 9285-9292. <https://doi.org/10.1073/pnas.1901600116>
- Coughlan, G., Puthusseryppady, V., Lowry, E., Gillings, R., Spiers, H., Minihane, A. M., & Hornberger, M. (2020). Test-retest reliability of spatial navigation in adults at-risk of Alzheimer's disease. *Plos one*, *15*(9), e0239077. <https://doi.org/10.1371/journal.pone.0239077>
- Coutrot, A., Silva, R., Manley, E., de Cothi, W., Sami, S., Bohbot, V. D., ... & Spiers, H. J. (2018). Global determinants of navigation ability. *Current Biology*, *28*(17), 2861-2866. <https://doi.org/10.1016/j.cub.2018.06.009>
- Coutrot, A., Schmidt, S., Coutrot, L., Pittman, J., Hong, L., Wiener, J. M., ... & Spiers, H. J.

- (2019). Virtual navigation tested on a mobile app is predictive of real-world wayfinding navigation performance. *PloS one*, *14*(3), e0213272.  
<https://doi.org/10.1371/journal.pone.0213272>
- Coutrot, A., Manley, E., Goodroe, S., Gahnstrom, C., Filomena, G., Yesiltepe, D., ... & Spiers, H. J. (2022). Entropy of city street networks linked to future spatial navigation ability. *Nature*, *604*(7904), 104-110. <https://doi.org/10.1038/s41586-022-04486-7>
- Craver, C. F., Kwan, D., Steindam, C., & Rosenbaum, R. S. (2014). Individuals with episodic amnesia are not stuck in time. *Neuropsychologia*, *57*, 191-195.  
<https://doi.org/10.1016/j.neuropsychologia.2014.03.004>
- Crumley, J. J., Stetler, C. A., & Horhota, M. (2014). Examining the relationship between subjective and objective memory performance in older adults: a meta-analysis. *Psychology and Aging*, *29*(2), 250. <https://doi.org/10.1037/a0035908>
- da Costa, R. Q. M., Pompeu, J. E., Moretto, E., Silva, J. M., Dos Santos, M. D., Nitrini, R., & Brucki, S. M. D. (2021). Two Immersive Virtual Reality Tasks for the Assessment of Spatial Orientation in Older Adults with and Without Cognitive Impairment: Concurrent Validity, Group Comparison, and Accuracy Results. *Journal of the International Neuropsychological Society*, 1-13. <https://doi.org/10.1017/S1355617721000655>
- Dahmani, L., & Bohbot, V. D. (2020). Habitual use of GPS negatively impacts spatial memory during self-guided navigation. *Scientific reports*, *10*(1), 1-14.  
<https://doi.org/10.1038/s41598-020-62877-0>
- Daugherty, A. M., & Raz, N. (2017). A virtual water maze revisited: Two-year changes in navigation performance and their neural correlates in healthy adults. *NeuroImage*, *146*, 492-506. <https://doi.org/10.1016/j.neuroimage.2016.09.044>
- Dauphinot, V., Bouteloup, V., Mangin, J. F., Vellas, B., Pasquier, F., Blanc, F., ... & Krolak-

- Salmon, P. (2020). Subjective cognitive and non-cognitive complaints and brain MRI biomarkers in the MEMENTO cohort. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, 12(1), e12051. <https://doi.org/10.1002/dad2.12051>
- Davis, J. D., Papandonatos, G. D., Miller, L. A., Hewitt, S. D., Festa, E. K., Heindel, W. C., & Ott, B. R. (2012). Road test and naturalistic driving performance in healthy and cognitively impaired older adults: does environment matter?. *Journal of the American Geriatrics Society*, 60(11), 2056-2062. <https://10.1111/j.1532-5415.2012.04206.x>.
- Delpolyi, A. R., Rankin, K. P., Mucke, L., Miller, B. L., & Gorno-Tempini, M. L. (2007). Spatial cognition and the human navigation network in AD and MCI. *Neurology*, 69(10), 986-997. <https://doi.org/10.1212/01.wnl.0000271376.19515.c6>
- Denney, D. A., & Prigatano, G. P. (2019). Subjective ratings of cognitive and emotional functioning in patients with mild cognitive impairment and patients with subjective memory complaints but normal cognitive functioning. *Journal of Clinical and Experimental Neuropsychology*, 41(6), 565-575.  
<https://doi.org/10.1080/13803395.2019.1588229>
- De Rooij, N. K., Claessen, M. H. G., van der Ham, I. J., Post, M. W. M., & Visser-Meily, J. M. (2019). The Wayfinding Questionnaire: A clinically useful self-report instrument to identify navigation complaints in stroke patients. *Neuropsychological rehabilitation*, 29(7), 1042-1061. <https://doi.org/10.1080/09602011.2017.1347098>
- Descloux, V., & Maurer, R. (2018). Cognitive map recall test: A new specific test to assess topographical disorientation. *Applied Neuropsychology: Adult*, 25(2), 91-109.  
<https://doi.org/10.1080/23279095.2016.1247094>
- Diaz-Galvan, P., Ferreira, D., Cedres, N., Falahati, F., Hernández-Cabrera, J. A., Ames, D., ... &

- Westman, E. (2021). Comparing different approaches for operationalizing subjective cognitive decline: impact on syndromic and biomarker profiles. *Scientific reports*, 11(1), 1-15. <https://doi.org/10.1038/s41598-021-83428-1>
- Draper, K., & Ponsford, J. (2009). Long-term outcome following traumatic brain injury: a comparison of subjective reports by those injured and their relatives. *Neuropsychological Rehabilitation*, 19(5), 645-661. <https://doi.org/10.1080/17405620802613935>
- Driscoll, I., Hamilton, D. A., Petropoulos, H., Yeo, R. A., Brooks, W. M., Baumgartner, R. N., & Sutherland, R. J. (2003). The aging hippocampus: cognitive, biochemical and structural findings. *Cerebral cortex*, 13(12), 1344-1351. <https://doi.org/10.1093/cercor/bhg081>
- Duff, M. C., Covington, N. V., Hilverman, C., & Cohen, N. J. (2020). Semantic memory and the hippocampus: Revisiting, reaffirming, and extending the reach of their critical relationship. *Frontiers in Human Neuroscience*, 13, 471. <https://doi.org/10.3389/fnhum.2019.00471>
- Edelen, M. O., & Reeve, B. B. (2007). Applying item response theory (IRT) modeling to questionnaire development, evaluation, and refinement. *Quality of life research*, 16(1), 5-18. <https://doi.org/10.1007/s11136-007-9198-0>
- Edmonds, E. C., Delano-Wood, L., Galasko, D. R., Salmon, D. P., & Bondi, M. W. (2014). Subjective cognitive complaints contribute to misdiagnosis of mild cognitive impairment. *Journal of the International Neuropsychological Society*, 20(8), 836-847. <https://doi.org/10.1017/S135561771400068X>
- Edmonds, E. C., Weigand, A. J., Thomas, K. R., Eppig, J., Delano-Wood, L., Galasko, D. R., ... & Bondi, M. W. (2018). Increasing inaccuracy of self-reported subjective cognitive complaints over 24 months in empirically derived subtypes of mild cognitive impairment. *Journal of the International Neuropsychological Society*, 24(8), 842-853.

<https://doi.org/10.1017/S135561771400068X>

Eichenbaum, H., Yonelinas, A. P., & Ranganath, C. (2007). The medial temporal lobe and recognition memory. *Annu. Rev. Neurosci.*, *30*, 123-152.

<https://doi.org/10.1146/annurev.neuro.30.051606.094328>

Ekstrom, A. D., Arnold, A. E., & Iaria, G. (2014). A critical review of the allocentric spatial representation and its neural underpinnings: toward a network-based perspective. *Frontiers in human neuroscience*, *8*, 803.

<https://doi.org/10.3389/fnhum.2014.00803>

Ekstrom, A. D., Huffman, D. J., & Starrett, M. (2017). Interacting networks of brain regions underlie human spatial navigation: a review and novel synthesis of the literature. *Journal of neurophysiology*, *118*(6), 3328-3344. <https://doi.org/10.1152/jn.00531.2017>

Ekstrom, A. D., & Ranganath, C. (2018a). Space, time, and episodic memory: The hippocampus is all over the cognitive map. *Hippocampus*, *28*(9), 680-687.

<https://doi.org/10.1002/hipo.22750>

Ekstrom, A. D., Spiers, H. J., Bohbot, V. D., & Rosenbaum, R. S. (2018b). *Human spatial navigation*. Princeton University Press.

Ekstrom, A. D., & Yonelinas, A. P. (2020). Precision, binding, and the hippocampus: Precisely what are we talking about?. *Neuropsychologia*, *138*, 107341.

<https://doi.org/10.1016/j.neuropsychologia.2020.107341>

Epstein, R. A. (2008). Parahippocampal and retrosplenial contributions to human spatial navigation. *Trends in cognitive sciences*, *12*(10), 388-396.

<https://doi.org/10.1016/j.tics.2008.07.004>

Fan, C. L., Romero, K., & Levine, B. (2020). Older adults with lower autobiographical memory

- abilities report less age-related decline in everyday cognitive function. *BMC geriatrics*, 20(1), 1-12. <https://doi.org/10.1186/s12877-020-01720-7>
- Fan, C. L., Abdi, H., & Levine, B. (2021). On the relationship between trait autobiographical episodic memory and spatial navigation. *Memory & Cognition*, 49(2), 265-275. <https://doi.org/10.3758/s13421-020-01093-7>
- Farzanfar, D., Spiers, H. J., Moscovitch, M., Rosenbaum, R. S., (in press) From Cognitive Maps to Spatial Schemas. *Nature Neuroscience Reviews*.
- Fernandez-Baizan, C., Diaz-Caceres, E., Arias, J. L., & Mendez, M. (2019). Egocentric and allocentric spatial memory in healthy aging: performance on real-world tasks. *Brazilian Journal of Medical and Biological Research*, 52. <https://doi.org/10.1590/1414-431X20198041>
- Flatt, J. D., Cicero, E. C., Lambrou, N. H., Wharton, W., Anderson, J. G., Bouldin, E. D., ... & Taylor, C. A. (2021). Subjective cognitive decline higher among sexual and gender minorities in the United States, 2015–2018. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, 7(1), e12197. <https://doi.org/10.1002/trc2.12197>
- Flores-Vázquez, J. F., Ramírez-García, G., Marrufo-Meléndez, O. R., Alcalá-Lozano, R., Lietz, M. P., Rodríguez-Agudelo, Y., ... & Sosa-Ortiz, A. L. (2021). Anosognosia in Amnesic Mild Cognitive Impairment Is Related to Diminished Hippocampal Volume Comparable to Alzheimer's Disease Dementia: Preliminary MRI Findings. *Frontiers in aging neuroscience*, 13. <https://doi.org/10.3389/fnagi.2021.739422>
- Fillit, H., Nash, D. T., Rundek, T., & Zuckerman, A. (2008). Cardiovascular risk factors and dementia. *The American journal of geriatric pharmacotherapy*, 6(2), 100-118. <https://doi.org/10.1016/j.amjopharm.2008.06.004>
- Fisher, A. J., Medaglia, J. D., & Jeronimus, B. F. (2018). Lack of group-to-individual

- generalizability is a threat to human subjects research. *Proceedings of the National Academy of Sciences*, *115*(27), E6106-E6115. <https://doi.org/10.1073/pnas.1711978115>
- Frankenmolen, N. L., Fasotti, L., Kessels, R. P., & Oosterman, J. M. (2018). The influence of cognitive reserve and age on the use of memory strategies. *Experimental Aging Research*, *44*(2), 117-134. <https://doi.org/10.1080/0361073X.2017.1422472>
- Funder, D. C. (2012). Accurate personality judgment. *Current Directions in Psychological Science*, *21*(3), 177-182. <https://doi.org/10.1177/0963721412445309>
- Fyock, C. A., & Hampstead, B. M. (2015). Comparing the relationship between subjective memory complaints, objective memory performance, and medial temporal lobe volumes in patients with mild cognitive impairment. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, *1*(2), 242-248. <https://doi.org/10.1016/j.dadm.2015.03.002>
- Gagnon, K. T., Thomas, B. J., Munion, A., Creem-Regehr, S. H., Cashdan, E. A., & Stefanucci, J. K. (2018). Not all those who wander are lost: Spatial exploration patterns and their relationship to gender and spatial memory. *Cognition*, *180*, 108-117. <https://doi.org/10.1016/j.cognition.2018.06.020>
- Gao, S., Hendrie, H. C., Hall, K. S., & Hui, S. (1998). The relationships between age, sex, and the incidence of dementia and Alzheimer disease: a meta-analysis. *Archives of general psychiatry*, *55*(9), 809-815. <https://doi.org/10.1001/archpsyc.55.9.809>
- Gao, A.F., Keith, J.L., Gao, F.Q., Black, S.E., Moscovitch, M., Rosenbaum, R.S., (2020). Neuropathology of a remarkable case of memory impairment informs human memory. *Neuropsychologia*, *140*, 107342. <https://doi.org/10.1016/j.neuropsychologia.2020.107342>
- Gardner, R. C., Langa, K. M., & Yaffe, K. (2017). Subjective and objective cognitive function

- among older adults with a history of traumatic brain injury: A population-based cohort study. *PLoS medicine*, *14*(3), e1002246. <https://doi.org/10.1371/journal.pmed.1002246>
- Garland, M. M., Vaidya, J. G., Tranel, D., Watson, D., & Feinstein, J. S. (2021). Who Are You? The Study of Personality in Patients With Anterograde Amnesia. *Psychological Science*, *32*(10), 1649-1661. <https://doi.org/10.1177/09567976211007463>
- Ghosh, V. E., & Gilboa, A. (2014). What is a memory schema? A historical perspective on current neuroscience literature. *Neuropsychologia*, *53*, 104-114. <https://doi.org/10.1016/j.neuropsychologia.2013.11.010>
- Ghosh, A., Puthusserypady, V., Chan, D., Mascolo, C., & Hornberger, M. (2022). Machine learning detects altered spatial navigation features in outdoor behaviour of Alzheimer's disease patients. *Scientific Reports*, *12*(1), 1-13. <https://doi.org/10.1038/s41598-022-06899-w>
- Giannakopoulos, P., Gold, G., Duc, M., Michel, J. P., Hof, P. R., & Bouras, C. (2000). Neural substrates of spatial and temporal disorientation in Alzheimer's disease. *Acta neuropathologica*, *100*(2), 189-195. <https://doi.org/10.1007/s004019900166>
- Gilboa, A., & Moscovitch, M. (2021). No consolidation without representation: Correspondence between neural and psychological representations in recent and remote memory. *Neuron*, *109*(14), 2239-2255. <https://doi.org/10.1016/j.neuron.2021.04.025>
- Gilewski, M. J., Zelinski, E. M., & Schaie, K. W. (1990). The Memory Functioning Questionnaire for assessment of memory complaints in adulthood and old age. *Psychology and aging*, *5*(4), 482. <https://doi.org/10.1037/0882-7974.5.4.482>
- Ginó, S., Mendes, T., Maroco, J., Ribeiro, F., Schmand, B. A., De Mendonça, A., & Guerreiro, M. (2010). Memory complaints are frequent but qualitatively different in young and elderly healthy people. *Gerontology*, *56*(3), 272-277. <https://doi.org/10.1159/000240048>

- Goodrich-Hunsaker, N. J., & Hopkins, R. O. (2010). Spatial memory deficits in a virtual radial arm maze in amnesic participants with hippocampal damage. *Behavioral Neuroscience*, *124*(3), 405–413. <https://doi.org/10.1037/a0019193>
- Grewe, P., Lahr, D., Kohsik, A., Dyck, E., Markowitsch, H. J., Bien, C. G., ... & Piefke, M. (2014). Real-life memory and spatial navigation in patients with focal epilepsy: ecological validity of a virtual reality supermarket task. *Epilepsy & Behavior*, *31*, 57-66. <https://doi.org/10.1016/j.yebeh.2013.11.014>
- Grilli, M. D., & Verfaellie, M. (2014). Personal semantic memory: insights from neuropsychological research on amnesia. *Neuropsychologia*, *61*, 56-64. <http://dx.doi.org/10.1016/j.neuropsychologia.2014.06.012>
- Grilli, M. D., & Verfaellie, M. (2015). Supporting the self-concept with memory: insight from amnesia. *Social cognitive and affective neuroscience*, *10*(12), 1684-1692. <https://doi.org/10.1093/scan/nsv056>
- Grilli, M.D., Wank, A.A., Berchel, J.J., Ryan, L. (2018). Evidence for Reduced Autobiographical Memory Episodic Specificity in Cognitively Normal Middle-Aged and Older Individuals at Increased Risk for Alzheimer's Disease Dementia. *J Int Neuropsychol Soc*, *23*, 1-11. <https://doi.org/10.1017/S1355617718000577>
- Guerrero, L., Bouazzaoui, B., Burger, L., Froger, C., Isingrini, M., & Tacconat, L. (2019). Optimizing memory strategy use in young and older adults: The role of metamemory and internal strategy use. *Acta Psychologica*, *192*, 73–86. <https://doi.org/10.1016/j.actpsy.2018.11.002>
- Guilmette, T. J., Sweet, J. J., Hebben, N., Koltai, D., Mahone, E. M., Spiegler, B. J., ... & Conference Participants. (2020). American Academy of Clinical Neuropsychology consensus conference statement on uniform labeling of performance test scores. *The*

*Clinical Neuropsychologist*, 34(3), 437-453.

<https://doi.org/10.1080/13854046.2020.1722244>

Goulter, J. R., Fitzpatrick, L. E., & Crowe, S. F. (2021). An analysis of distinct navigational domains and topographical disorientation syndromes in ABI: A meta-analysis. *Journal of clinical and experimental neuropsychology*, 43(5), 449-468.

<https://doi.org/10.1080/13803395.2021.1926933>

Guderian, S., Dzieciol, A. M., Gadian, D. G., Jentschke, S., Doeller, C. F., Burgess, N., Mishkin, M., & Vargha-Khadem, F. (2015). Hippocampal Volume Reduction in Humans Predicts Impaired Allocentric Spatial Memory in Virtual-Reality Navigation. *Journal of Neuroscience*, 35(42), 14123–14131.

<https://doi.org/10.1523/jneurosci.0801-15.2015>

Gupta, S. (2021). Racial and ethnic disparities in subjective cognitive decline: A closer look, United States, 2015–2018. *BMC public health*, 21(1), 1-12.

<https://doi.org/10.1186/s12889-021-11068-1>

Halilova, J. G., Addis, D. R., & Rosenbaum, R. S. (2020). Getting better without memory. *Social Cognitive and Affective Neuroscience*, 15(8), 815-825.

<https://doi.org/10.1093/scan/nsaa105>

Hamre, C., Fure, B., Helbostad, J. L., Wyller, T. B., Ihle-Hansen, H., Vlachos, G., ... & Tangen, G. G. (2020). Impairments in spatial navigation during walking in patients 70 years or younger with mild stroke. *Topics in Stroke Rehabilitation*, 27(8), 601-609.

<https://doi.org/10.1080/10749357.2020.1755814>

Hamson, D. K., Roes, M. M., & Galea, L. A. (2011). Sex hormones and cognition: neuroendocrine influences on memory and learning. *Comprehensive Physiology*, 6(3), 1295-1337.

<https://doi.org/10.1002/cphy.c150031>

Hanseuw, B. J., Betensky, R. A., Jacobs, H. I., Schultz, A. P., Sepulcre, J., Becker, J. A., ... &

- Johnson, K. (2019). Association of amyloid and tau with cognition in preclinical Alzheimer disease: a longitudinal study. *JAMA neurology*, *76*(8), 915-924.  
<https://doi.org/10.1001/jamaneurol.2019.1424>
- Harrell Jr, F. E., & Harrell Jr, M. F. E. (2019). Package ‘hmisc’. *CRAN2018, 2019*, 235-236.
- Harris, M. A., & Wolbers, T. (2014). How age-related strategy switching deficits affect wayfinding in complex environments. *Neurobiology of aging*, *35*(5), 1095-1102.  
<https://doi.org/10.1016/j.neurobiolaging.2013.10.086>
- Hartley, T., Bird, C. M., Chan, D., Cipolotti, L., Husain, M., Vargha-Khadem, F., & Burgess, N. (2007). The hippocampus is required for short-term topographical memory in humans. *Hippocampus*, *17*(1), 34-48. <https://doi.org/10.1002/hipo.20240>
- Harwood, D. G., Sultzer, D. L., Feil, D., Monserratt, L., Freedman, E., & Mandelkern, M. A. (2005). Frontal lobe hypometabolism and impaired insight in Alzheimer disease. *The American Journal of Geriatric Psychiatry*, *13*(11), 934-941.  
<https://doi.org/10.1097/00019442-200511000-00003>
- Hassabis, D., & Maguire, E. A. (2007). Deconstructing episodic memory with construction. *Trends in cognitive sciences*, *11*(7), 299-306.  
<https://doi.org/10.1016/j.tics.2007.05.001>
- He, C., & Hegarty, M. (2020). How anxiety and growth mindset are linked to navigation ability: Impacts of exploration and GPS use. *Journal of Environmental Psychology*, *71*, 101475.  
<https://doi.org/10.1016/j.jenvp.2020.101475>
- Hegarty, M., Richardson, A. E., Montello, D. R., Lovelace, K., & Subbiah, I. (2002). Development of a self-report measure of environmental spatial ability. *Intelligence*, *30*(5), 425-447. [https://doi.org/10.1016/S0160-2896\(02\)00116-2](https://doi.org/10.1016/S0160-2896(02)00116-2)
- Hegarty, M., He, C., Boone, A. P., Yu, S., Jacobs, E. G., & Chrastil, E. R. (2022). Understanding

- Differences in Wayfinding Strategies. *Topics in Cognitive Science*.  
<https://doi.org/10.1111/tops.12592>
- Henderson, V. W., Mack, W., & Williams, B. W. (1989). Spatial disorientation in Alzheimer's disease. *Archives of neurology*, 46(4), 391-394.  
<https://doi.org/10.1001/archneur.1989.00520400045018>
- Herdman, K. A., Calarco, N., Moscovitch, M., Hirshhorn, M., & Rosenbaum, R. S. (2015). Impoverished descriptions of familiar routes in three cases of hippocampal/medial temporal lobe amnesia. *Cortex*, 71, 248-263. <https://doi.org/10.1016/j.cortex.2015.06.008>
- Herrmann, D. J. (1982). Know thy memory: The use of questionnaires to assess and study memory. *Psychological Bulletin*, 92(2), 434. <https://doi.org/10.1037/0033-2909.92.2.434>
- Hertzog, C., Small, B. J., McFall, G. P., & Dixon, R. A. (2019). Age, cohort, and period effects on metamemory beliefs. *Psychology and Aging*, 34(8), 1077–1089.  
<https://doi.org/10.1037/pag0000384>
- Herweg, N. A., & Kahana, M. J. (2018). Spatial representations in the human brain. *Frontiers in human neuroscience*, 12, 297. <https://doi.org/10.3389/fnhum.2018.00297>
- Heser, K., Kleineidam, L., Wiese, B., Oey, A., Roehr, S., Pabst, A., ... & Wagner, M. (2019). Subjective cognitive decline may be a stronger predictor of incident dementia in females than in men. *Journal of Alzheimer's Disease*, 68(4), 1469-1478.  
<https://doi.org/10.3233/JAD-180981>
- Hird, M. A., Egeto, P., Fischer, C. E., Naglie, G., & Schweizer, T. A. (2016). A systematic review and meta-analysis of on-road simulator and cognitive driving assessment in Alzheimer's disease and mild cognitive impairment. *Journal of Alzheimer's disease*, 53(2), 713-729. <https://doi.org/10.3233/JAD-160276>
- Hirshhorn, M., Newman, L., & Moscovitch, M. (2011). Detailed descriptions of routes traveled,

- but not map-like knowledge, correlates with tests of hippocampal function in older adults. *Hippocampus*, 21(11), 1147-1151. <https://doi.org/10.1002/hipo.20871>
- Hohman, T. J., Beason-Held, L. L., Lamar, M., & Resnick, S. M. (2011). Subjective cognitive complaints and longitudinal changes in memory and brain function. *Neuropsychology*, 25(1), 125. <https://doi.org/10.1037/a0020859>
- Holdstock, J. S., Mayes, A. R., Cezayirli, E., Isaac, C. L., Aggleton, J. P., & Roberts, N. (2000). A comparison of egocentric and allocentric spatial memory in a patient with selective hippocampal damage. *Neuropsychologia*, 38(4), 410–425. [https://doi.org/10.1016/s0028-3932\(99\)00099-8](https://doi.org/10.1016/s0028-3932(99)00099-8)
- Hooper, D., Coughlan, J., & Mullen, M. (2008, September). Evaluating model fit: a synthesis of the structural equation modelling literature. In *7th European Conference on research methodology for business and management studies* (pp. 195-200).
- Hopper, S., Hammond, N. G., Taler, V., & Stinchcombe, A. (2022). Biopsychosocial Correlates of Subjective Cognitive Decline and Related Worry in the Canadian Longitudinal Study on Aging. *Gerontology*, 1-14. <https://doi.org/10.1159/000524280>
- Horn, M. M., Kennedy, K. M., & Rodrigue, K. M. (2018). Association between subjective memory assessment and associative memory performance: Role of ad risk factors. *Psychology and Aging*, 33(1), 109–118. <https://doi.org/10.1037/pag0000217>
- Hort, J., Laczó, J., Vyhnálek, M., Bojar, M., Bureš, J., & Vlček, K. (2007). Spatial navigation deficit in amnesic mild cognitive impairment. *Proceedings of the National Academy of Sciences*, 104(10), 4042-4047. <https://doi.org/10.1073/pnas.0611314104>
- Howlett, C. A., Wewege, M. A., Berryman, C., Oldach, A., Jennings, E., Moore, E., Karran, E. L., Szeto, K., Pronk, L., Miles, S., & Moseley, G. L. (2022). Back to the Drawing Board—The Relationship Between Self-Report and Neuropsychological Tests of

- Cognitive Flexibility in Clinical Cohorts: A Systematic Review and Meta-Analysis.  
*Neuropsychology*. Advance online publication. <http://dx.doi.org/10.1037/neu0000796>
- Humphreys, K., Blodgett, J. C., & Roberts, L. W. (2015). The exclusion of people with psychiatric disorders from medical research. *Journal of Psychiatric Research*, *70*, 28-32.  
<https://doi.org/10.1016/j.jpsychires.2015.08.005>
- Hund, A. M., & Minarik, J. L. (2006). Getting from here to there: Spatial anxiety, wayfinding strategies, direction type, and wayfinding efficiency. *Spatial cognition and computation*, *6*(3), 179-201. [https://doi.org/10.1207/s15427633scc0603\\_1](https://doi.org/10.1207/s15427633scc0603_1)
- Hunsaker, M. R., & Kesner, R. P. (2018). Unfolding the cognitive map: The role of hippocampal and extra-hippocampal substrates based on a systems analysis of spatial processing. *Neurobiology of Learning and Memory*, *147*, 90-119.  
<https://doi.org/10.1016/j.nlm.2017.11.012>
- Hutchinson, A. D., Hosking, J. R., Kichenadasse, G., Mattiske, J. K., & Wilson, C. (2012). Objective and subjective cognitive impairment following chemotherapy for cancer: a systematic review. *Cancer treatment reviews*, *38*(7), 926-934.  
<https://doi.org/10.1016/j.ctrv.2012.05.002>
- Iachini, T., Iavarone, A., Senese, V. P., Ruotolo, F., & Ruggiero, G. (2009). Visuospatial memory in healthy elderly, AD and MCI: a review. *Current aging science*, *2*(1), 43-59.  
<https://doi.org/10.2174/1874609810902010043>
- Iaria, G., Palermo, L., Committeri, G., & Barton, J. J. (2009). Age differences in the formation and use of cognitive maps. *Behavioural brain research*, *196*(2), 187-191.  
<https://doi.org/10.1016/j.bbr.2008.08.040>
- Irwing, P. (2012). Sex differences in g: An analysis of the US standardization sample of the

WAIS-III. *Personality and Individual Differences*, 53(2), 126-131.

<https://doi.org/10.1016/j.paid.2011.05.001>

Jack, C. R., Petersen, R. C., Xu, Y., O'Brien, P. C., Smith, G. E., Ivnik, R. J., ... & Kokmen, E.

(2000). Rates of hippocampal atrophy correlate with change in clinical status in aging and AD. *Neurology*, 55(4), 484-490. <https://doi.org/10.1212/WNL.55.4.484>

Javadi, A. H., Emo, B., Howard, L. R., Zisch, F. E., Yu, Y., Knight, R., ... & Spiers, H. J. (2017).

Hippocampal and prefrontal processing of network topology to simulate the future. *Nature communications*, 8(1), 1-11. <https://doi.org/10.1038/ncomms14652>

Jessen, F., Wiese, B., Bachmann, C., Eifflaender-Gorfer, S., Haller, F., Kölsch, H., ... & Bickel,

H. (2010). Prediction of dementia by subjective memory impairment: effects of severity and temporal association with cognitive impairment. *Archives of general psychiatry*, 67(4), 414-422. <https://doi.org/10.1001/archgenpsychiatry.2010.30>

Jessen, F., Amariglio, R. E., Van Boxtel, M., Breteler, M., Ceccaldi, M., Chételat, G., ... &

Glodzik, L. (2014). A conceptual framework for research on subjective cognitive decline in preclinical Alzheimer's disease. *Alzheimer's & dementia*, 10(6), 844-852.

<https://doi.org/10.1016/j.jalz.2014.01.001>

Jessen, F., Amariglio, R. E., Buckley, R. F., van der Flier, W. M., Han, Y., Molinuevo, J. L., ...

& Wagner, M. (2020a). The characterisation of subjective cognitive decline. *The Lancet Neurology*, 19(3), 271-278. [https://doi.org/10.1016/S1474-4422\(19\)30368-0](https://doi.org/10.1016/S1474-4422(19)30368-0)

Jessen, F., Kleineidam, L., Wolfsgruber, S., Bickel, H., Brettschneider, C., Fuchs, A., ... &

Wagner, M. (2020b). Prediction of dementia of Alzheimer type by different types of subjective cognitive decline. *Alzheimer's & Dementia*, 16(12), 1745-1749.

<https://doi.org/10.1002/alz.12163>

Jessen, F., Wolfsgruber, S., Kleineidam, L., Spottke, A., Altenstein, S., Bartels, C., ... & Düzel,

- E. (2022). Subjective cognitive decline and stage 2 of Alzheimer disease in patients from memory centers. *Alzheimer's & Dementia*. <https://doi.org/10.1002/alz.12674>
- Jonker, C., Geerlings, M. I., & Schmand, B. (2000). Are memory complaints predictive for dementia? A review of clinical and population-based studies. *International journal of geriatric psychiatry*, *15*(11), 983-991. [https://doi.org/10.1002/1099-1166\(200011\)15:11<983::AID-GPS238>3.0.CO;2-5](https://doi.org/10.1002/1099-1166(200011)15:11<983::AID-GPS238>3.0.CO;2-5)
- Juskenaite, A., Quinette, P., Laisney, M., Eustache, M. L., Desgranges, B., Viader, F., & Eustache, F. (2016). Preserved self-evaluation in amnesia supports access to the self through introspective computation. *Frontiers in Human Neuroscience*, *10*, 462. <https://doi.org/10.3389/fnhum.2016.00462>
- Kametani, F., & Hasegawa, M. (2018). Reconsideration of amyloid hypothesis and tau hypothesis in Alzheimer's disease. *Frontiers in neuroscience*, *12*, 25. <https://doi.org/10.3389/fnins.2018.00025>
- Kang, T., & Chen, T. T. (2008). Performance of the generalized S-X2 item fit index for polytomous IRT models. *Journal of Educational Measurement*, *45*(4), 391-406. <https://doi.org/10.1111/j.1745-3984.2008.00071.x>
- Kessels, R. P., de Haan, E. H., Kappelle, L. J., & Postma, A. (2001). Varieties of human spatial memory: a meta-analysis on the effects of hippocampal lesions. *Brain Research Reviews*, *35*(3), 295-303. [https://doi.org/10.1016/S0165-0173\(01\)00058-3](https://doi.org/10.1016/S0165-0173(01)00058-3)
- Keynejad, R. C., Marková, H., Šiffelová, K., Kumar, N., Vlček, K., Laczó, J., ... & Kopelman, M. D. (2018). Spatial navigation deficits in amnesic mild cognitive impairment with neuropsychiatric comorbidity. *Aging, Neuropsychology, and Cognition*, *25*(2), 277-289. <https://doi.org/10.1080/13825585.2017.1290212>
- Kim, S., Sapiurka, M., Clark, R. E., & Squire, L. R. (2013). Contrasting effects on path

- integration after hippocampal damage in humans and rats. *Proceedings of the National Academy of Sciences*, *110*(12), 4732–4737. <https://doi.org/10.1073/pnas.1300869110>
- Kirchhoff, B. A., Gordon, B. A., & Head, D. (2014). Prefrontal gray matter volume mediates age effects on memory strategies. *NeuroImage*, *90*, 326–334. <https://doi.org/10.1016/j.neuroimage.2013.12.052>
- Klein, S. B., Loftus, J., & Kihlstrom, J. F. (1996). Self-knowledge of an amnesic patient: toward a neuropsychology of personality and social psychology. *Journal of Experimental Psychology: General*, *125*(3), 250. <https://doi.org/10.1037/0096-3445.125.3.250>
- Klencklen, G., Després, O., & Dufour, A. (2012). What do we know about aging and spatial cognition? Reviews and perspectives. *Ageing research reviews*, *11*(1), 123-135. <https://doi.org/10.1016/j.arr.2011.10.001>
- Kline, R. B. (2015). *Principles and practice of structural equation modeling*. Guilford publications.
- Kolarik, B. S., Shahlaie, K., Hassan, A., Borders, A. A., Kaufman, K. C., Gurkoff, G., Yonelinas, A. P., & Ekstrom, A. D. (2016). Impairments in precision, rather than spatial strategy, characterize performance on the virtual Morris Water Maze: A case study. *Neuropsychologia*, *80*, 90–101. <https://doi.org/10.1016/j.neuropsychologia.2015.11.013>
- Kolarik, B. S., Baer, T., Shahlaie, K., Yonelinas, A. P., & Ekstrom, A. D. (2018). Close but no cigar: Spatial precision deficits following medial temporal lobe lesions provide novel insight into theoretical models of navigation and memory. *Hippocampus*, *28*(1), 31-41. <https://doi.org/10.1002/hipo.22801>
- Kroenke, K., Spitzer, R. L., & Williams, J. B. (2001). The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine*, *16*(9), 606-613. <https://doi.org/10.1046/j.1525-1497.2001.016009606.x>

- Kühn, S., & Gallinat, J. (2014). Segregating cognitive functions within hippocampal formation: A quantitative meta-analysis on spatial navigation and episodic memory. *Human Brain Mapping, 35*(4), 1129-1142. <https://doi.org/10.1002/hbm.22239>
- Kurczek, J., Wechsler, E., Ahuja, S., Jensen, U., Cohen, N. J., Tranel, D., & Duff, M. (2015). Differential contributions of hippocampus and medial prefrontal cortex to self-projection and self-referential processing. *Neuropsychologia, 73*, 116-126. <https://doi.org/10.1016/j.neuropsychologia.2015.05.002>
- Kuzma, E., Sattler, C., Toro, P., Schönknecht, P., & Schröder, J. (2011). Premorbid personality traits and their course in mild cognitive impairment: results from a prospective population-based study in Germany. *Dementia and Geriatric Cognitive Disorders, 32*(3), 171-177. <https://doi.org/10.1159/000332082>
- Kwan, D., Craver, C. F., Green, L., Myerson, J., & Rosenbaum, R. S. (2013). Dissociations in future thinking following hippocampal damage: evidence from discounting and time perspective in episodic amnesia. *Journal of Experimental Psychology: General, 142*(4), 1355. <https://doi.org/10.1037/a0034001>
- Laczó, J., Vlček, K., Vyhnálek, M., Vajnerová, O., Ort, M., Holmerová, I., ... & Hort, J. (2009). Spatial navigation testing discriminates two types of amnesic mild cognitive impairment. *Behavioural brain research, 202*(2), 252-259. <https://doi.org/10.1016/j.bbr.2009.03.041>
- Laczó, J., Andel, R., Nedelska, Z., Vyhnalek, M., Vlcek, K., Crutch, S., ... & Hort, J. (2017). Exploring the contribution of spatial navigation to cognitive functioning in older adults. *Neurobiology of aging, 51*, 67-70. <https://doi.org/10.1016/j.neurobiolaging.2016.12.003>
- LaPlume, A. A., Anderson, N. D., McKetton, L., Levine, B., & Troyer, A. K. (2022). When I'm

- 64: Age-related variability in over 40,000 online cognitive test takers. *The Journals of Gerontology: Series B*, 77(1), 104-117. <https://doi.org/10.1093/geronb/gbab207>
- Lavenex, P. B., Amaral, D. G., & Lavenex, P. (2006). Hippocampal lesion prevents spatial relational learning in adult macaque monkeys. *Journal of Neuroscience*, 26(17), 4546-4558. <https://doi.org/10.1523/JNEUROSCI.5412-05.2006>
- Lawton, C. A., Charleston, S. I., & Zieles, A. S. (1996). Individual-and gender-related differences in indoor wayfinding. *Environment and Behavior*, 28(2), 204-219. <https://doi.org/10.1177/0013916596282003>
- Lawton, C. A., & Kallai, J. (2002). Gender differences in wayfinding strategies and anxiety about wayfinding: A cross-cultural comparison. *Sex Roles*, 47(9/10), 389-401. <https://doi.org/10.1023/A:1021668724970>
- Leal, S. L., & Yassa, M. A. (2015). Neurocognitive aging and the hippocampus across species. *Trends in neurosciences*, 38(12), 800-812. <https://doi.org/10.1016/j.tins.2015.10.003>
- Lenehan, M. E., Klekociuk, S. Z., & Summers, M. J. (2012). Absence of a relationship between subjective memory complaint and objective memory impairment in mild cognitive impairment (MCI): is it time to abandon subjective memory complaint as an MCI diagnostic criterion?. *International Psychogeriatrics*, 24(9), 1505-1514. <https://doi.org/10.1017/S1041610212000695>
- Lester, A. W., Moffat, S. D., Wiener, J. M., Barnes, C. A., & Wolbers, T. (2017). The aging navigational system. *Neuron*, 95(5), 1019-1035. <https://doi.org/10.1016/j.neuron.2017.06.037>
- Levine, B., Svoboda, E., Hay, J. F., Winocur, G., & Moscovitch, M. (2002). Aging and

- autobiographical memory: dissociating episodic from semantic retrieval. *Psychology and aging*, 17(4), 677. <https://doi.org/10.1037/0882-7974.17.4.677>
- Levine, T. F., Allison, S. L., Stojanovic, M., Fagan, A. M., Morris, J. C., & Head, D. (2020). Spatial navigation ability predicts progression of dementia symptomatology. *Alzheimer's & Dementia*, 16(3), 491-500. <https://doi.org/10.1002/alz.12031>
- Levine, T. F., Roe, C. M., Babulal, G. M., Fagan, A. M., & Head, D. (2021). Limited Longitudinal Change in Self-reported Spatial Navigation Ability in Preclinical Alzheimer Disease. *Alzheimer Disease and Associated Disorders*. <https://doi.org/10.1097/WAD.0000000000000487>
- Li, A. W. Y., & King, J. (2019). Spatial memory and navigation in ageing: A systematic review of MRI and fMRI studies in healthy participants. *Neuroscience and Biobehavioral Reviews*, 103, 33–49. <https://doi.org/10.1016/j.neubiorev.2019.05.005>
- Lithfous, S., Dufour, A., & Després, O. (2013). Spatial navigation in normal aging and the prodromal stage of Alzheimer's disease: insights from imaging and behavioral studies. *Ageing research reviews*, 12(1), 201-213. <https://doi.org/10.1016/j.arr.2012.04.007>
- Lopez, A., Caffò, A. O., & Bosco, A. (2018). Topographical disorientation in aging. Familiarity with the environment does matter. *Neurological Sciences*, 39(9), 1519-1528. <https://doi.org/10.1007/s10072-018-3464-5>
- Lopez, A., Caffò, A. O., & Bosco, A. (2020). Memory for familiar locations: The impact of age, education and cognitive efficiency on two neuropsychological allocentric tasks. *Assessment*, 27(7), 1588-1603. <https://doi.org/10.1177/1073191119831780>
- Lowry, E., Puthusseryppady, V., Coughlan, G., Jeffs, S., & Hornberger, M. (2020). Path

- integration changes as a cognitive marker for vascular cognitive impairment?—A pilot study. *Frontiers in Human Neuroscience*, *14*, 131.  
<https://doi.org/10.3389/fnhum.2020.00131>
- Lupien, S. J., Evans, A., Lord, C., Miles, J., Pruessner, M., Pike, B., & Pruessner, J. C. (2007). Hippocampal volume is as variable in young as in older adults: implications for the notion of hippocampal atrophy in humans. *Neuroimage*, *34*(2), 479-485.  
<https://doi.org/10.1016/j.neuroimage.2006.09.041>
- Maguire, E. A., Burgess, N., Donnett, J. G., Frackowiak, R. S., Frith, C. D., & O'Keefe, J. (1998). Knowing where and getting there: a human navigation network. *Science*, *280*(5365), 921-924. <https://doi.org/10.1126/science.280.5365.921>
- Maguire, E. A., Nannery, R., & Spiers, H. J. (2006). Navigation around London by a taxi driver with bilateral hippocampal lesions. *Brain*, *129*(11), 2894-2907.  
<https://doi.org/10.1093/brain/awl286>
- Manea, L., Gilbody, S., & McMillan, D. (2012). Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): a meta-analysis. *Cmaj*, *184*(3), E191-E196. <https://doi.org/10.1503/cmaj.110829>
- Markova, H., Andel, R., Stepankova, H., Kopecek, M., Nikolai, T., Hort, J., ... & Vyhnaek, M. (2017). Subjective cognitive complaints in cognitively healthy older adults and their relationship to cognitive performance and depressive symptoms. *Journal of Alzheimer's Disease*, *59*(3), 871-881. <https://doi.org/10.3233/JAD-160970>
- Marquine, M. J., Grilli, M. D., Rapcsak, S. Z., Kaszniak, A. W., Ryan, L., Walther, K., & Glisky, E. L. (2016). Impaired personal trait knowledge, but spared other-person trait knowledge, in an individual with bilateral damage to the medial prefrontal

cortex. *Neuropsychologia*, 89, 245-253.

<https://doi.org/10.1016/j.neuropsychologia.2016.06.021>

Marshall, G. A., Kaufer, D. I., Lopez, O. L., Rao, G. R., Hamilton, R. L., & DeKosky, S. T. (2004). Right subiculum amyloid plaque density correlates with anosognosia in Alzheimer's disease. *Journal of Neurology, Neurosurgery & Psychiatry*, 75(10), 1396-1400. <http://dx.doi.org/10.1136/jnnp.2003.030007>

McAvan, A. S., Wank, A. A., Rapcsak, S. Z., Grilli, M. D., & Ekstrom, A. D. (2022). Largely intact memory for spatial locations during navigation in an individual with dense amnesia. *Neuropsychologia*, 170, 108225.

<https://doi.org/10.1016/j.neuropsychologia.2022.108225>

McDonald, R. J., & White, N. M. (1994). Parallel information processing in the water maze: evidence for independent memory systems involving dorsal striatum and hippocampus. *Behavioral and neural biology*, 61(3), 260-270.

[https://doi.org/10.1016/S0163-1047\(05\)80009-3](https://doi.org/10.1016/S0163-1047(05)80009-3)

McElhinney, S., Zisch, F., Hornsberger, M., Coutrot, A., Spiers, H., & Hanna, S. (2022, June). Exosomatic Route Choice in Navigation: Evidence from video game player data. In *Proceedings of the 13th Space Syntax Symposium*.

<https://discovery.ucl.ac.uk/id/eprint/10150148>

McWhirter, L., Ritchie, C., Stone, J., & Carson, A. (2020). Functional cognitive disorders: a systematic review. *The Lancet Psychiatry*, 7(2), 191-207. [https://doi.org/10.1016/S2215-0366\(19\)30405-5](https://doi.org/10.1016/S2215-0366(19)30405-5)

Meneghetti, C., Muffato, V., Borella, E., & De Beni, R. (2018). Map learning in normal aging: the role of individual visuo-spatial abilities and implications. *Current Alzheimer Research*, 15(3), 205-218. <https://doi.org/10.2174/1567205014666171030113515>

- Merriman, N. A., Ondřej, J., Roudaia, E., O'Sullivan, C., & Newell, F. N. (2016). Familiar environments enhance object and spatial memory in both younger and older adults. *Experimental Brain Research*, 234(6), 1555-1574. <https://doi.org/10.1007/s00221-016-4557-0>
- Mitchell, A. J., Beaumont, H., Ferguson, D., Yadegarfar, M., & Stubbs, B. (2014). Risk of dementia and mild cognitive impairment in older people with subjective memory complaints: meta-analysis. *Acta Psychiatrica Scandinavica*, 130(6), 439-451. <https://doi.org/10.1111/acps.12336>
- Mitchnick, K. A., Ahmad, Z., Mitchnick, S. D., Ryan, J. D., Rosenbaum, R. S., & Freud, E. (2022). Damage to the human dentate gyrus impairs the perceptual discrimination of complex, novel objects. *Neuropsychologia*, 108238. <https://doi.org/10.1016/j.neuropsychologia.2022.108238>
- Moffat, S. D. (2009). Aging and spatial navigation: what do we know and where do we go?. *Neuropsychology review*, 19(4), 478. <https://doi.org/10.1007/s11065-009-9120-3>
- Mondragón, J. D., Maurits, N. M., & De Deyn, P. P. (2019). Functional neural correlates of anosognosia in mild cognitive impairment and Alzheimer's disease: a systematic review. *Neuropsychology review*, 29(2), 139-165. <https://doi.org/10.1007/s11065-019-09410-x>
- Montana, J. I., Tuena, C., Serino, S., Cipresso, P., & Riva, G. (2019). Neurorehabilitation of spatial memory using virtual environments: a systematic review. *Journal of clinical medicine*, 8(10), 1516. <https://doi.org/10.3390/jcm8101516>
- Morris, R. G., Garrud, P., Rawlins, J. N., & O'Keefe, J. (1982). Place navigation impaired in rats with hippocampal lesions. *Nature*, 297, 681–683. <https://doi.org/10.1038/297681a0>
- Morris, R.G., Mograbi, D.C., (2013). Anosognosia, autobiographical memory and self

- knowledge in Alzheimer's disease. *Cortex*, 49, 1553–1565.  
<https://doi.org/10.1016/j.cortex.2012.09.006>
- Moscovitch, M., Rosenbaum, R. S., Gilboa, A., Addis, D. R., Westmacott, R., Grady, C., ... Nadel, L. (2005). Functional neuroanatomy of remote episodic, semantic and spatial memory: a unified account based on multiple trace theory. *Journal of Anatomy*, 207(1), 35–66. <https://doi.org/10.1111/j.1469-7580.2005.00421.x>
- Moscovitch, M., Nadel, L., Winocur, G., Gilboa, A., & Rosenbaum, R. S. (2006). The cognitive neuroscience of remote episodic, semantic and spatial memory. *Current opinion in neurobiology*, 16(2), 179-190. <https://doi.org/10.1016/j.conb.2006.03.013>
- Moscovitch, M., Cabeza, R., Winocur, G., & Nadel, L. (2016). Episodic memory and beyond: the hippocampus and neocortex in transformation. *Annual review of psychology*, 67, 105-134. <https://doi.org/10.1146/annurev-psych-113011-143733>
- Mourao, R. J., Mansur, G., Malloy-Diniz, L. F., Castro Costa, E., & Diniz, B. S. (2016). Depressive symptoms increase the risk of progression to dementia in subjects with mild cognitive impairment: systematic review and meta-analysis. *International journal of geriatric psychiatry*, 31(8), 905-911. <https://doi.org/10.1002/gps.4406>
- Munion, A. K., Stefanucci, J. K., Rovira, E., Squire, P., & Hendricks, M. (2019). Gender differences in spatial navigation: Characterizing wayfinding behaviors. *Psychonomic bulletin & review*, 26(6), 1933-1940. <https://doi.org/10.3758/s13423-019-01659-w>
- Murphy, K. J., Troyer, A. K., Levine, B., & Moscovitch, M. (2008). Episodic, but not semantic, autobiographical memory is reduced in amnesic mild cognitive impairment. *Neuropsychologia*, 46(13), 3116-3123.  
<https://doi.org/10.1016/j.neuropsychologia.2008.07.004>
- Nadel, L., & Moscovitch, M. (1997). Memory consolidation, retrograde amnesia and the

- hippocampal complex. *Current opinion in neurobiology*, 7(2), 217-227.  
[https://doi.org/10.1016/S0959-4388\(97\)80010-4](https://doi.org/10.1016/S0959-4388(97)80010-4)
- Nazareth, A., Huang, X., Voyer, D., & Newcombe, N. (2019). A meta-analysis of sex differences in human navigation skills. *Psychonomic bulletin & review*, 26(5), 1503-1528.  
<https://doi.org/10.3758/s13423-019-01633-6>
- Newcombe, N. S. (2020). The puzzle of spatial sex differences: Current status and prerequisites to solutions. *Child Development Perspectives*, 14(4), 251-257.  
<https://doi.org/10.1111/cdep.12389>
- Nordin, K., Herlitz, A., Larsson, E. M., & Söderlund, H. (2017). Overlapping effects of age on associative memory and the anterior hippocampus from middle to older age. *Behavioural Brain Research*, 317, 350-359. <https://doi.org/10.1016/j.bbr.2016.10.002>
- Nordin, K., Persson, J., Stening, E., Herlitz, A., Larsson, E. M., & Söderlund, H. (2018). Structural whole-brain covariance of the anterior and posterior hippocampus: Associations with age and memory. *Hippocampus*, 28(2), 151-163.  
<https://doi.org/10.1002/hipo.22817>
- Norman, A. L., Woodard, J. L., Calamari, J. E., Gross, E. Z., Pontarelli, N., Socha, J., ... & Armstrong, K. (2020). The fear of Alzheimer's disease: mediating effects of anxiety on subjective memory complaints. *Aging & Mental Health*, 24(2), 308-314.  
<https://doi.org/10.1080/13607863.2018.1534081>
- Numbers, K., Lam, B. C., Crawford, J. D., Kochan, N. A., Sachdev, P. S., & Brodaty, H. (2021). Increased reporting of subjective cognitive complaints over time predicts cognitive decline and incident dementia. *International journal of geriatric psychiatry*, 36(11), 1739-1747. <https://doi.org/10.1002/gps.5594>
- O'Keefe, J., & Dostrovsky, J. (1971) The hippocampus as a spatial map: Preliminary evidence

- from unit activity in the freely-moving rat. *Brain Research*, 34(1), 171-175.  
[https://doi.org/10.1016/0006-8993\(71\)90358-1](https://doi.org/10.1016/0006-8993(71)90358-1)
- O'Keefe, J. (1990). A computational theory of the hippocampal cognitive map. *Progress in brain research*, 83, 301-312. [https://doi.org/10.1016/S0079-6123\(08\)61258-3](https://doi.org/10.1016/S0079-6123(08)61258-3)
- Old, S. R., & Naveh-Benjamin, M. (2008). Differential effects of age on item and associative measures of memory: a meta-analysis. *Psychology and aging*, 23(1), 104.  
<https://doi.org/10.1037/0882-7974.23.1.104>
- Olsen, R. K., Moses, S. N., Riggs, L., & Ryan, J. D. (2012). The hippocampus supports multiple cognitive processes through relational binding and comparison. *Frontiers in Human Neuroscience*, 6, 146–146. <https://doi.org/10.3389/fnhum.2012.00146>
- Pai, M. C., & Jacobs, W. J. (2004). Topographical disorientation in community-residing patients with Alzheimer's disease. *International journal of geriatric psychiatry*, 19(3), 250-255. <https://doi.org/10.1002/gps.1081>
- Pai, M. C., Lee, C. C., Yang, Y. C., Lee, Y. T., Chen, K. C., Lin, S. H., ... & Cheng, P. J. (2012). Development of a questionnaire on everyday navigational ability to assess topographical disorientation in Alzheimer's disease. *American Journal of Alzheimer's Disease & Other Dementias®*, 27(1), 65-72. <https://doi.org/10.1177/1533317512436805>
- Pai, M. C., & Lee, C. C. (2016). The incidence and recurrence of getting lost in community-dwelling people with Alzheimer's disease: A two and a half-year follow-up. *PLoS one*, 11(5), e0155480. <https://doi.org/10.1371/journal.pone.0155480>
- Palombo, D. J., Williams, L. J., Abdi, H., & Levine, B. (2013). The survey of autobiographical memory (SAM): A novel measure of trait mnemonics in everyday life. *Cortex*, 49(6), 1526-1540. <https://doi.org/10.1016/j.cortex.2012.08.023>
- Parfenov, V. A., Zakharov, V. V., Kabaeva, A. R., & Vakhnina, N. V. (2020). Subjective

- cognitive decline as a predictor of future cognitive decline: a systematic review. *Dementia & Neuropsychologia*, 14, 248-257. <https://doi.org/10.1590/1980-57642020dn14-030007>
- Parizkova, M., Lerch, O., Moffat, S. D., Andel, R., Mazancova, A. F., Nedelska, Z., ... & Laczó, J. (2018). The effect of Alzheimer's disease on spatial navigation strategies. *Neurobiology of aging*, 64, 107-115. <https://doi.org/10.1016/j.neurobiolaging.2017.12.019>
- Parrish, E. M., Depp, C. A., Moore, R. C., Harvey, P. D., Mikhael, T., Holden, J., ... & Granholm, E. (2020). Emotional determinants of life-space through GPS and ecological momentary assessment in schizophrenia: What gets people out of the house?. *Schizophrenia research*, 224, 67-73. <https://doi.org/10.1016/j.schres.2020.10.002>
- Parslow, D. M., Rose, D., Brooks, B., Fleminger, S., Gray, J. A., Giampietro, V., Brammer, M. J., Williams, S., Gasston, D., Andrew, C., Vythelingum, G. N., Ioannou, G., Simmons, A., & Morris, R. G. (2004). Allocentric Spatial Memory Activation of the Hippocampal Formation Measured With fMRI. *Neuropsychology*, 18(3), 450–461. <https://doi.org/10.1037/0894-4105.18.3.450>
- Parslow, D. M., Morris, R. G., Fleminger, S., Rahman, Q., Abrahams, S., & Recce, M. (2005). Allocentric spatial memory in humans with hippocampal lesions. *Acta Psychologica*, 118(1-2), 123–147. <https://doi.org/10.1016/j.actpsy.2004.10.006>
- Patai, E. Z., & Spiers, H. J. (2021). The Versatile Wayfinder: Prefrontal Contributions to Spatial Navigation. *Trends in cognitive sciences*. <https://doi.org/10.1016/j.tics.2021.02.010>
- Patterson, K., Nestor, P. J., & Rogers, T. T. (2007). Where do you know what you know? The representation of semantic knowledge in the human brain. *Nature reviews neuroscience*, 8(12), 976-987. <https://doi.org/10.1038/nrn2277>

- Pavisc, I. M., Lu, K., Keuss, S. E., James, S. N., Lane, C. A., Parker, T. D., ... & Schott, J. M. (2021). Subjective cognitive complaints at age 70: associations with amyloid and mental health. *Journal of Neurology, Neurosurgery & Psychiatry*, 92(11), 1215-1221. <http://dx.doi.org/10.1136/jnnp-2020-325620>
- Pearman, A., & Storandt, M. (2004). Predictors of subjective memory in older adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, 59(1), P4-P6. <https://doi.org/10.1093/geronb/59.1.P4>
- Pedraza, O., & Mungas, D. (2008). Measurement in cross-cultural neuropsychology. *Neuropsychology review*, 18(3), 184-193. <https://doi.org/10.1007/s11065-008-9067-9>
- Peters, R., Booth, A., Rockwood, K., Peters, J., D'Este, C., & Anstey, K. J. (2019). Combining modifiable risk factors and risk of dementia: a systematic review and meta-analysis. *BMJ open*, 9(1), e022846. <http://dx.doi.org/10.1136/bmjopen-2018-022846>
- Petersen, R. C., Jack, C. R., Xu, Y. C., Waring, S. C., O'brien, P. C., Smith, G. E., ... & Kokmen, E. (2000). Memory and MRI-based hippocampal volumes in aging and AD. *Neurology*, 54(3), 581-581. <https://doi.org/10.1212/WNL.54.3.581>
- Petersen, R. C., Doody, R., Kurz, A., Mohs, R. C., Morris, J. C., Rabins, P. V., ... & Winblad, B. (2001). Current concepts in mild cognitive impairment. *Archives of neurology*, 58(12), 1985-1992. <https://doi.org/10.1001/archneur.58.12.1985>
- Petersen, R. C., Lopez, O., Armstrong, M. J., Getchius, T. S., Ganguli, M., Gloss, D., ... & Rae-Grant, A. (2018). Practice guideline update summary: Mild cognitive impairment: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*, 90(3), 126-135. <https://doi.org/10.1212/WNL.0000000000004826>
- Phelan, E., Williams, B., Meeker, K., Bonn, K., Frederick, J., LoGerfo, J., & Snowden, M.

- (2010). A study of the diagnostic accuracy of the PHQ-9 in primary care elderly. *BMC family practice*, *11*(1), 1-9. <https://doi.org/10.1186/1471-2296-11-63>
- Philippi, N., Roquet, D., Ben Malek, H., Noblet, V., Botzung, A., Cretin, B., & Blanc, F. (2017). Henry, where have you lost your Self? *Cortex*, *95*, 37e50. <https://doi.org/10.1016/j.cortex.2017.06.019>
- Pia, L., & Tamietto, M. (2006). Unawareness in schizophrenia: neuropsychological and neuroanatomical findings. *Psychiatry and Clinical Neurosciences*, *60*(5), 531-537. <https://doi.org/10.1111/j.1440-1819.2006.01576.x>
- Picard, L., Mayor-Dubois, C., Maeder, P., Kalenzaga, S., Abram, M., Duval, C., ... & Piolino, P. (2013). Functional independence within the self-memory system: New insights from two cases of developmental amnesia. *Cortex*, *49*(6), 1463-1481. <https://doi.org/10.1016/j.cortex.2012.10.003>
- Pijnenborg, G. H. M., Larabi, D. I., Xu, P., Hasson-Ohayon, I., de Vos, A. E., Ćurčić-Blake, B., ... & Van der Meer, L. (2020). Brain areas associated with clinical and cognitive insight in psychotic disorders: A systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews*, *116*, 301-336. <https://doi.org/10.1016/j.neubiorev.2020.06.022>
- Piras, F., Piras, F., Orfei, M. D., Caltagirone, C., & Spalletta, G. (2016). Self-awareness in Mild Cognitive Impairment: Quantitative evidence from systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews*, *61*, 90-107. <https://doi.org/10.1016/j.neubiorev.2015.10.002>
- Pishdadian, S. (2018) The Effects of Prior Knowledge on Mnemonic Discrimination in Young and Older Adults, and in Hippocampal Amnesia. *York University*. <http://hdl.handle.net/10315/35565>
- Pishdadian, S., & Rosenbaum, R.S., (2021) Memory and Amnesia. In: Della Sala, S. (Ed.),

*Encyclopedia of Behavioral Neuroscience*, vol. 2. Elsevier, pp. 413–424.

<https://dx.doi.org/10.1016/B978-0-12-819641-0.00133-X>

Plummer, F., Manea, L., Trepel, D., & McMillan, D. (2016). Screening for anxiety disorders with the GAD-7 and GAD-2: a systematic review and diagnostic metaanalysis. *General hospital psychiatry*, 39, 24-31. <https://doi.org/10.1016/j.genhosppsych.2015.11.005>

Prebble, S. C., Addis, D. R., & Tippett, L. J. (2013). Autobiographical memory and sense of self. *Psychological Bulletin*, 139(4), 815–840. <https://doi.org/10.1037/a0030146>

Puthusseryppady, V., Morrissey, S., Aung, M. H., Coughlan, G., Patel, M., & Hornberger, M. (2022a). Using GPS Tracking to Investigate Outdoor Navigation Patterns in Patients With Alzheimer Disease: Cross-sectional Study. *JMIR aging*, 5(2), e28222. <https://doi.org/10.2196/28222>

Puthusseryppady, V., Morrissey, S., Spiers, H. Patel, M., Hornberger, M. (2022b) Predicting real world spatial disorientation in Alzheimer’s disease patients using virtual reality navigation tests. *Sci Rep* 12, 13397. <https://doi.org/10.1038/s41598-022-17634-w>

Rabin, J. S., Schultz, A. P., Hedden, T., Viswanathan, A., Marshall, G. A., Kilpatrick, E., ... & Chhatwal, J. P. (2018). Interactive associations of vascular risk and  $\beta$ -amyloid burden with cognitive decline in clinically normal elderly individuals: findings from the Harvard Aging Brain Study. *JAMA neurology*, 75(9), 1124-1131. <https://doi.org/10.1001/jamaneurol.2018.1123>

Rabin, J. S., Pruzin, J. J., Schultz, A. P., Scott, M. R., Hampton, O. L., Hsieh, S., ... & Chhatwal, J. P. (2021). The combined influence of beta-amyloid and vascular risk on prospective brain atrophy in clinically normal individuals. *Alzheimer's & Dementia*, 17, e049730. <https://doi.org/10.1002/alz.049730>

Rabin, L. A., Smart, C. M., Crane, P. K., Amariglio, R. E., Berman, L. M., Boada, M., ... &

- Sikkas, S. A. (2015). Subjective cognitive decline in older adults: an overview of self-report measures used across 19 international research studies. *Journal of Alzheimer's Disease*, 48(s1), S63-S86. <https://doi.org/10.3233/JAD-150154>
- Rabin, L. A., Paolillo, E., & Barr, W. B. (2016). Stability in test-usage practices of clinical neuropsychologists in the United States and Canada over a 10-year period: A follow-up survey of INS and NAN members. *Archives of Clinical Neuropsychology*, 31(3), 206-230. <https://doi.org/10.1093/arclin/acw007>
- Rabin, L. A., Smart, C. M., & Amariglio, R. E. (2017). Subjective cognitive decline in preclinical Alzheimer's disease. *Annual review of clinical psychology*, 13, 369-396. <https://doi.org/10.1146/annurev-clinpsy-032816-045136>
- Rami, L., Mollica, M. A., García-Sánchez, C., Saldaña, J., Sanchez, B., Sala, I., ... & Molinuevo, J. L. (2014). The subjective cognitive decline questionnaire (SCD-Q): a validation study. *Journal of Alzheimer's Disease*, 41(2), 453-466. <https://doi.org/10.3233/JAD-132027>
- Ramanoël, S., York, E., Le Petit, M., Lagrené, K., Habas, C., & Arleo, A. (2019). Age-related differences in functional and structural connectivity in the spatial navigation brain network. *Frontiers in neural circuits*, 13, 69. <https://doi.org/10.3389/fncir.2019.00069>
- Ratner, B. (2009). The correlation coefficient: Its values range between +1/-1, or do they?. *Journal of targeting, measurement and analysis for marketing*, 17(2), 139-142. <https://doi.org/10.1057/jt.2009.5>
- Raz, N., & Rodrigue, K. M. (2006). Differential aging of the brain: patterns, cognitive correlates and modifiers. *Neuroscience & Biobehavioral Reviews*, 30(6), 730-748. <https://doi.org/10.1016/j.neubiorev.2006.07.001>
- Renoult, L., Davidson, P. S., Palombo, D. J., Moscovitch, M., & Levine, B. (2012). Personal

- semantics: At the crossroads of semantic and episodic memory. *Trends in Cognitive Sciences*, 16(11), 550e558. <https://doi.org/10.1016/j.tics.2012.09.003>
- Renoult, L., Irish, M., Moscovitch, M., & Rugg, M. D. (2019). From knowing to remembering: the semantic–episodic distinction. *Trends in Cognitive Sciences*, 23(12), 1041-1057. <https://doi.org/10.1016/j.tics.2019.09.008>
- Renoult, L., & Rugg, M. D. (2020). An historical perspective on Endel Tulving's episodic-semantic distinction. *Neuropsychologia*, 139, 107366. <https://doi.org/10.1016/j.neuropsychologia.2020.107366>
- Revelle, W., & Revelle, M. W. (2015). Package ‘psych’. *The comprehensive R archive network*, 337, 338. <https://cran.rstudio.org/web/packages/psych/psych.pdf>
- Reynolds, G. O., Manning, L., Kirn, D., Klein, H., Hampton, O., Burke, O., ... & Amariglio, R. E. (2022). Subjective Cognitive Decline in a Registry Sample: Relation to Psychiatric History, Loneliness, and Personality. *The Journal of Prevention of Alzheimer's Disease*, 1-6. <https://doi.org/10.14283/jpad.2022.31>
- Ries, M. L., Jabbar, B. M., Schmitz, T. W., Trivedi, M. A., Gleason, C. E., Carlsson, C. M., ... & Johnson, S. C. (2007). Anosognosia in mild cognitive impairment: relationship to activation of cortical midline structures involved in self-appraisal. *Journal of the International Neuropsychological Society*, 13(3), 450-461. <https://doi.org/10.1017/S1355617707070488>
- Roberts, J. L., Clare, L., & Woods, R. T. (2009). Subjective memory complaints and awareness of memory functioning in mild cognitive impairment: a systematic review. *Dementia and geriatric cognitive disorders*, 28(2), 95-109. <https://doi.org/10.1159/000234911>
- Robin, J., Rivest, J., Rosenbaum, R. S., & Moscovitch, M. (2019). Remote spatial and

- autobiographical memory in cases of episodic amnesia and topographical disorientation. *Cortex*, *119*, 237-257. <https://doi.org/10.1016/j.cortex.2019.04.013>
- Rodriguez, F. S., Pabst, A., Hesel, K., Kleineidam, L., Hajek, A., Eisele, M., ... & Riedel-Heller, S. G. (2020). Risk for disorientation: Longitudinal evidence from three old-age cohorts in Germany (AgeDifferent. de) Epidemiology/Risk and protective factors in MCI and dementia. *Alzheimer's & Dementia*, *16*, e039676. <https://doi.org/10.1002/alz.039676>
- Rosenbaum, R. S., Priselac, S., Köhler, S., Black, S. E., Gao, F., Nadel, L., & Moscovitch, M. (2000) Remote spatial memory in an amnesic person with extensive bilateral hippocampal lesions. *Nature Neuroscience*, *3*(10), 1044-1048. <https://doi.org/10.1038/79867>
- Rosenbaum, R. S., Winocur, G., & Moscovitch, M. (2001). New views on old memories: Re-evaluating the role of the hippocampal complex. *Behavioural Brain Research*, *127*(1-2), 183-197. [https://doi.org/10.1016/S0166-4328\(01\)00363-1](https://doi.org/10.1016/S0166-4328(01)00363-1)
- Rosenbaum, R. S., Gao, F., Richards, B., Black, S. E., & Moscovitch, M. (2005a). "Where to?" Remote memory for spatial relations and landmark identity in former taxi drivers with Alzheimer's disease and encephalitis. *Journal of Cognitive Neuroscience*, *17*(3), 446-462. <https://doi.org/10.1162/0898929053279496>
- Rosenbaum, R. S., Köhler, S., Schacter, D. L., Moscovitch, M., Westmacott, R., Black, S. E., ... & Tulving, E. (2005b). The case of KC: contributions of a memory-impaired person to memory theory. *Neuropsychologia*, *43*(7), 989-1021. <https://doi.org/10.1016/j.neuropsychologia.2004.10.007>
- Rosenbaum, R. S., Moscovitch, M., Foster, J. K., Schnyer, D. M., Gao, F., Kovacevic, N., ... & Levine, B. (2008). Patterns of autobiographical memory loss in medial-temporal lobe amnesic patients. *Journal of Cognitive Neuroscience*, *20*(8), 1490-1506.

- <https://doi.org/10.1162/jocn.2008.20105>
- Rosenbaum, R. S., Winocur, G., Binns, M. A., & Moscovitch, M. (2012). Remote spatial memory in aging: all is not lost. *Frontiers in aging neuroscience*, 4, 25. <https://doi.org/10.3389/fnagi.2012.00025>
- Rosenbaum, R. S., Gilboa, A., & Moscovitch, M. (2014). Case studies continue to illuminate the cognitive neuroscience of memory. *Annals of the New York Academy of Sciences*, 1316(1), 105-133. <https://doi.org/10.1111/nyas.12467>
- Rosenbaum, R. S., Cassidy, B. N., & Herdman, K. A. (2015). Patterns of preserved and impaired spatial memory in a case of developmental amnesia. *Frontiers in human neuroscience*, 9, 196. <https://doi.org/10.3389/fnhum.2015.0019>
- Rosseel, Y. (2012). lavaan: An R package for structural equation modeling. *Journal of statistical software*, 48, 1-36. <https://doi.org/10.18637/jss.v048.i02>
- Rosselli, M., & Ardila, A. (2003). The impact of culture and education on non-verbal neuropsychological measurements: A critical review. *Brain and cognition*, 52(3), 326-333. [https://doi.org/10.1016/S0278-2626\(03\)00170-2](https://doi.org/10.1016/S0278-2626(03)00170-2)
- Rotenberg, S., Maeir, A., & Dawson, D. R. (2020). Changes in activity participation among older adults with subjective cognitive decline or objective cognitive deficits. *Frontiers in neurology*, 10, 1393. <https://doi.org/10.3389/fneur.2019.01393>
- Rueda, A. D., Lau, K. M., Saito, N., Harvey, D., Risacher, S. L., Aisen, P. S., ... & Alzheimer's Disease Neuroimaging Initiative. (2015). Self-rated and informant-rated everyday function in comparison to objective markers of Alzheimer's disease. *Alzheimer's & Dementia*, 11(9), 1080-1089. <https://doi.org/10.1016/j.jalz.2014.09.002>
- Ruggiero, G., Iavarone, A., & Iachini, T. (2018). Allocentric to egocentric spatial switching:

- Impairment in aMCI and Alzheimer's Disease patients?. *Current Alzheimer Research*, 15(3), 229-236. <https://doi.org/10.2174/1567205014666171030114821>
- Rusconi, M. L., Suardi, A., Zanetti, M., & Rozzini, L. (2015). Spatial navigation in elderly healthy subjects, amnesic and non amnesic MCI patients. *Journal of the neurological sciences*, 359(1-2), 430-437. <https://doi.org/10.1016/j.jns.2015.10.010>
- Ryan, J. D., Althoff, R. R., Whitlow, S., & Cohen, N. J. (2000). Amnesia is a deficit in relational memory. *Psychological science*, 11(6), 454-461. <https://doi.org/10.1111/1467-9280.00288>
- Ryan, J. D., Moses, S. N., Barense, M., & Rosenbaum, R. S. (2013). Intact learning of new relations in amnesia as achieved through unitization. *Journal of Neuroscience*, 33(23), 9601-9613. <https://doi.org/10.1523/JNEUROSCI.0169-13.2013>
- Salari, N., Hosseinian-Far, A., Jalali, R., Vaisi-Raygani, A., Rasoulpoor, S., Mohammadi, M., ... & Khaledi-Paveh, B. (2020). Prevalence of stress, anxiety, depression among the general population during the COVID-19 pandemic: a systematic review and meta-analysis. *Globalization and health*, 16(1), 1-11. <https://doi.org/10.1186/s12992-020-00589-w>
- Salimi, S., Irish, M., Foxe, D., Hodges, J. R., Piguet, O., & Burrell, J. R. (2018). Can visuospatial measures improve the diagnosis of Alzheimer's disease?. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, 10, 66-74. <https://doi.org/10.1016/j.dadm.2017.10.004>
- Sannemann, L., Schild, A. K., Altenstein, S., Bartels, C., Brosseron, F., Buerger, K., ... & Jessen, F. (2020). Neuropsychiatric symptoms in at-risk groups for AD dementia and their association with worry and AD biomarkers—results from the DELCODE

- study. *Alzheimer's research & therapy*, 12(1), 1-11. <https://doi.org/10.1186/s13195-020-00701-7>
- Santos, M. A. O., Bezerra, L. S., Carvalho, A. R. M. R., & Brainer-Lima, A. M. (2018). Global hippocampal atrophy in major depressive disorder: a meta-analysis of magnetic resonance imaging studies. *Trends in Psychiatry and Psychotherapy*, 40, 369-378. <https://doi.org/10.1590/2237-6089-2017-0130>
- Sapiurka, M., Squire, L. R., & Clark, R. E. (2016). Distinct roles of hippocampus and medial prefrontal cortex in spatial and nonspatial memory. *Hippocampus*, 26(12), 1515-1524. <https://doi.org/10.1002/hipo.22652>
- Saykin, A. J., Wishart, H. A., Rabin, L. A., Santulli, R. B., Flashman, L. A., West, J. D., ... & Mamourian, A. (2006). Older adults with cognitive complaints show brain atrophy similar to that of amnesic MCI. *Neurology*, 67(5), 834-842. <https://doi.org/10.1212/01.wnl.0000234032.77541.a2>
- Schmidt, S. L., Oliveira, R. M., Rocha, F. R., & Abreu-Villaca, Y. (2000). Influences of handedness and gender on the grooved pegboard test. *Brain and cognition*, 44(3), 445-454. <https://doi.org/10.1006/brcg.1999.1204>
- Schober, P., Boer, C., & Schwarte, L. A. (2018). Correlation coefficients: appropriate use and interpretation. *Anesthesia & Analgesia*, 126(5), 1763-1768. <https://doi.org/10.1213/ANE.0000000000002864>
- Schöberl, F., Pradhan, C., Irving, S., Buerger, K., Xiong, G., Kugler, G., ... & Zwergal, A. (2020). Real-space navigation testing differentiates between amyloid-positive and-negative aMCI. *Neurology*, 94(8), e861-e873. <https://doi.org/10.1212/WNL.0000000000008758>
- Selarka, D., Rosenbaum, R. S., Lapp, L., & Levine, B. (2019). Association between self-reported

- and performance-based navigational ability using internet-based remote spatial memory assessment. *Memory*, 27(5), 723-728. <https://doi.org/10.1080/09658211.2018.1554082>
- Serino, S., Cipresso, P., Morganti, F., & Riva, G. (2014). The role of egocentric and allocentric abilities in Alzheimer's disease: a systematic review. *Ageing research reviews*, 16, 32-44. <https://doi.org/10.1016/j.arr.2014.04.004>
- Shaikh, K. T., Tatham, E. L., Rich, J. B., & Troyer, A. K. (2021). Examining the factor structure of the Multifactorial Memory Questionnaire. *Memory*, 29(2), 255-260. <https://doi.org/10.1080/09658211.2021.1874995>
- Sheardova, K., Laczó, J., Vyhnalek, M., Mokrisova, I., Telensky, P., & Andel, R. (2015). Spatial navigation complaints are associated with anxiety regardless of the real performance in non-demented elderly. *J Depress Anxiety*, 4(4), 1000205. <http://dx.doi.org/10.4200/2167-1044.1000205>
- Sheldon, S., Farb, N., Palombo, D. J., & Levine, B. (2016). Intrinsic medial temporal lobe connectivity relates to individual differences in episodic autobiographical remembering. *Cortex*, 74, 206–216. <https://doi.org/10.1016/j.cortex.2015.11.005>
- Shing, Y. L., Rodrigue, K. M., Kennedy, K. M., Fandakova, Y., Bodammer, N., Werkle-Bergner, M., ... & Raz, N. (2011). Hippocampal subfield volumes: age, vascular risk, and correlation with associative memory. *Frontiers in aging neuroscience*, 3, 2. <https://doi.org/10.3389/fnagi.2011.00002>
- Shrager, Y., Kirwan, C. B., & Squire, L. R. (2008). Neural basis of the cognitive map: Path integration does not require hippocampus or entorhinal cortex. *Proceedings of the National Academy of Sciences*, 105(33), 12034–12038. <https://doi.org/10.1073/pnas.0805414105>
- Silva, D., Guerreiro, M., Faria, C., Maroco, J., Schmand, B. A., & Mendonça, A. D. (2014).

- Significance of subjective memory complaints in the clinical setting. *Journal of Geriatric Psychiatry and Neurology*, 27(4), 259-265. <https://doi.org/10.1177/0891988714532018>
- Silverman, I., Choi, J., & Peters, M. (2007). The hunter-gatherer theory of sex differences in spatial abilities: Data from 40 countries. *Archives of sexual behavior*, 36(2), 261-268. <https://doi.org/10.1007/s10508-006-9168-6>
- Slavin, M. J., Brodaty, H., Kochan, N. A., Crawford, J. D., Trollor, J. N., Draper, B., & Sachdev, P. S. (2010). Prevalence and predictors of “subjective cognitive complaints” in the Sydney Memory and Ageing Study. *The American Journal of Geriatric Psychiatry*, 18(8), 701-710. <https://doi.org/10.1097/JGP.0b013e3181df49fb>
- Small, S. A., Perera, G. M., DeLaPaz, R., Mayeux, R., & Stern, Y. (1999). Differential regional dysfunction of the hippocampal formation among elderly with memory decline and Alzheimer's disease. *Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society*, 45(4), 466-472. [https://doi.org/10.1002/1531-8249\(199904\)45:4<466::AID-ANA8>3.0.CO;2-Q](https://doi.org/10.1002/1531-8249(199904)45:4<466::AID-ANA8>3.0.CO;2-Q)
- Smith, M. L., & Milner, B. (1989). Right hippocampal impairment in the recall of spatial location: encoding deficit or rapid forgetting?. *Neuropsychologia*, 27(1), 71-81. [https://doi.org/10.1016/0028-3932\(89\)90091-2](https://doi.org/10.1016/0028-3932(89)90091-2)
- Sodoma, M. J., Cole, R. C., Sloan, T. J., Hamilton, C. M., Kent, J. D., Magnotta, V. A., & Voss, M. W. (2021). Hippocampal acidity and volume are differentially associated with spatial navigation in older adults. *NeuroImage*, 245, 118682. <https://doi.org/10.1016/j.neuroimage.2021.118682>
- Spalletta, G., Piras, F., Piras, F., Sancesario, G., Iorio, M., Fratangeli, C., ... & Orfei, M. D. (2014). Neuroanatomical correlates of awareness of illness in patients with amnesic mild cognitive impairment who will or will not convert to Alzheimer's disease. *Cortex*, 61,

183-195. <https://doi.org/10.1016/j.cortex.2014.10.010>

- Sperling, R. A., Aisen, P. S., Beckett, L. A., Bennett, D. A., Craft, S., Fagan, A. M., ... & Park, D. C. (2011). Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & dementia*, 7(3), 280-292. <https://doi.org/10.1016/j.jalz.2011.03.003>
- Spiers, H. J., Coutrot, A., & Hornberger, M. (2021). Explaining World-Wide Variation in Navigation Ability from Millions of People: Citizen Science Project Sea Hero Quest. *Topics in Cognitive Science*. <https://doi.org/10.1111/tops.12590>
- Spitzer, R.L., Williams, J.B.W., Kroenke, K. (1990) Instruction Manual: Instructions for Patient Health Questionnaire (PHQ) and GAD-7 Measures. PHQ and GAD-7 Instructions. <http://www.phqscreeners.com>
- Spitzer, R. L., Kroenke, K., Williams, J. B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of internal medicine*, 166(10), 1092-1097. <https://doi.org/10.1001/archinte.166.10.1092>
- Spreng, R. N., Mar, R. A., & Kim, A. S. (2009). The common neural basis of autobiographical memory, prospection, navigation, theory of mind, and the default mode: a quantitative meta-analysis. *Journal of Cognitive Neuroscience*, 21(3), 489-510. <https://doi.org/10.1162/jocn.2008.21029>
- Staffaroni, A. M., Brown, J. A., Casaletto, K. B., Elahi, F. M., Deng, J., Neuhaus, J., ... & Kramer, J. H. (2018). The longitudinal trajectory of default mode network connectivity in healthy older adults varies as a function of age and is associated with changes in episodic memory and processing speed. *Journal of Neuroscience*, 38(11), 2809-2817. <https://doi.org/10.1523/JNEUROSCI.3067-17.2018>

- Statucka, M., & Cohn, M. (2019). Origins matter: Culture impacts cognitive testing in Parkinson's disease. *Frontiers in human neuroscience, 13*, 269.  
<https://doi.org/10.3389/fnhum.2019.00269> **Error! Hyperlink reference not valid.**
- Steinvorth, S., Levine, B., & Corkin, S. (2005). Medial temporal lobe structures are needed to re-experience remote autobiographical memories: evidence from HM and WR. *Neuropsychologia, 43*(4), 479-496.  
<https://doi.org/10.1016/j.neuropsychologia.2005.01.001>
- Stewart, R., Godin, O., Crivello, F., Maillard, P., Mazoyer, B., Tzourio, C., & Dufouil, C. (2011). Longitudinal neuroimaging correlates of subjective memory impairment: 4-year prospective community study. *The British Journal of Psychiatry, 198*(3), 199-205.  
<https://doi.org/10.1192/bjp.bp.110.078683>
- Striepens, N., Scheef, L., Wind, A., Popp, J., Spottke, A., Cooper-Mahkorn, D., ... & Jessen, F. (2010). Volume loss of the medial temporal lobe structures in subjective memory impairment. *Dementia and geriatric cognitive disorders, 29*(1), 75-81.  
<https://doi.org/10.1159/000264630>
- Sui, J., & Humphreys, G. W. (2013). Self-referential processing is distinct from semantic elaboration: Evidence from long-term memory effects in a patient with amnesia and semantic impairments. *Neuropsychologia, 51*(13), 2663-2673.  
<https://doi.org/10.1016/j.neuropsychologia.2013.07.025>
- Sundermann, E. E., Maki, P., Biegon, A., Lipton, R. B., Mielke, M. M., Machulda, M., ... & Alzheimer's Disease Neuroimaging Initiative. (2019). Sex-specific norms for verbal memory tests may improve diagnostic accuracy of amnesic MCI. *Neurology, 93*(20), e1881-e1889. <https://doi.org/10.1212/WNL.00000000000008467>
- Taillade, M., N'Kaoua, B., & Sauz\_eon, H. (2016). Age-related differences and cognitive

- correlates of self-reported and direct navigation performance: The effect of real and virtual test conditions manipulation. *Frontiers in Psychology*, 6. Article ID 2034.  
<https://doi.org/10.3389/fpsyg.2015.02034>
- Tascón, L., Castillo, J., León, I., & Cimadevilla, J. M. (2018). Walking and non-walking space in an equivalent virtual reality task: Sexual dimorphism and aging decline of spatial abilities. *Behavioural brain research*, 347, 201-208.  
<https://doi.org/10.1016/j.bbr.2018.03.022>
- Team, R. C. (2013). R: A language and environment for statistical computing.
- Techentin, C., Voyer, D., & Voyer, S. D. (2014). Spatial abilities and aging: A meta-analysis. *Experimental aging research*, 40(4), 395-425.  
<https://doi.org/10.1080/0361073X.2014.926773>
- Terry, D. P., Sabatinelli, D., Puente, A. N., Lazar, N. A., & Miller, L. S. (2015). A meta-analysis of fMRI activation differences during episodic memory in Alzheimer's disease and mild cognitive impairment. *Journal of neuroimaging*, 25(6), 849-860.  
<https://doi.org/10.1111/jon.12266>
- Teymoori, A., Gorbunova, A., Haghish, F. E., Real, R., Zeldovich, M., Wu, Y. J., ... & v. Steinbüchel, N. (2020). Factorial structure and validity of depression (PHQ-9) and anxiety (GAD-7) scales after traumatic brain injury. *Journal of clinical medicine*, 9(3), 873. <https://doi.org/10.3390/jcm9030873>
- Thakral, P. P., Yu, S. S., & Rugg, M. D. (2022). Sensitivity of the hippocampus to objective but not subjective episodic memory judgments. *Cognitive Neuroscience*, 1-6.  
<https://doi.org/10.1080/17588928.2022.2033713>
- Therriault, J., Ng, K. P., Pascoal, T. A., Mathotaarachchi, S., Kang, M. S., Struyfs, H., ... &

- Alzheimer's Disease Neuroimaging Initiative. (2018). Anosognosia predicts default mode network hypometabolism and clinical progression to dementia. *Neurology*, *90*(11), e932-e939. <https://doi.org/10.1212/WNL.00000000000005120>
- Tibon, R., Geerligs, L., & Campbell, K. (2022). Bridging the big (data) gap: levels of control in small-and large-scale cognitive neuroscience research. *Trends in Neurosciences*. <https://doi.org/10.1016/j.tins.2022.03.011>
- Toledo, J. B., Arnold, S. E., Raible, K., Brettschneider, J., Xie, S. X., Grossman, M., ... & Trojanowski, J. Q. (2013). Contribution of cerebrovascular disease in autopsy confirmed neurodegenerative disease cases in the National Alzheimer's Coordinating Centre. *Brain*, *136*(9), 2697-2706. <https://doi.org/10.1093/brain/awt188>
- Tomita, T., Sugawara, N., Kaneda, A., Okubo, N., Iwane, K., Takahashi, I., ... & Yasui-Furukori, N. (2014). Sex-specific effects of subjective memory complaints with respect to cognitive impairment or depressive symptoms. *Psychiatry and clinical neurosciences*, *68*(3), 176-181. <https://doi.org/10.1111/pcn.12102>
- Tondelli, M., Barbarulo, A. M., Vinceti, G., Vincenzi, C., Chiari, A., Nichelli, P. F., & Zamboni, G. (2018). Neural correlates of anosognosia in Alzheimer's disease and mild cognitive impairment: a multi-method assessment. *Frontiers in Behavioral Neuroscience*, *12*, 100. <https://doi.org/10.3389/fnbeh.2018.00100>
- Topiwala, A., Suri, S., Allan, C., Zsoldos, E., Filippini, N., Sexton, C. E., ... & Ebmeier, K. P. (2021). Subjective cognitive complaints given in questionnaire: relationship with brain structure, cognitive performance and self-reported depressive symptoms in a 25-year retrospective cohort study. *The American Journal of Geriatric Psychiatry*, *29*(3), 217-226. <https://doi.org/10.1016/j.jagp.2020.07.002>
- Tractenberg, R. E., & Pietrzak, R. H. (2011). Intra-individual variability in Alzheimer's disease

- and cognitive aging: definitions, context, and effect sizes. *PLoS One*, 6(4), e16973.  
<https://doi.org/10.1371/journal.pone.0016973>
- Troyer, A. K., D'Souza, N. A., Vandermorris, S., & Murphy, K. J. (2011). Age-related differences in associative memory depend on the types of associations that are formed. *Aging, Neuropsychology, and Cognition*, 18(3), 340–352.  
<https://doi.org/10.1080/13825585.2011.553273>
- Troyer, A. K., Murphy, K. J., Anderson, N. D., Craik, F. I., Moscovitch, M., Maione, A., & Gao, F. (2012). Associative recognition in mild cognitive impairment: Relationship to hippocampal volume and apolipoprotein E. *Neuropsychologia*, 50(14), 3721-3728.  
<https://doi.org/10.1016/j.neuropsychologia.2012.10.018>
- Troyer, A. K., & Rich, J. B. (2018). Multifactorial Memory Questionnaire.
- Tu, S., Wong, S., Hodges, J. R., Irish, M., Piguet, O., & Hornberger, M. (2015). Lost in spatial translation—A novel tool to objectively assess spatial disorientation in Alzheimer's disease and frontotemporal dementia. *Cortex*, 67, 83-94.  
<https://doi.org/10.1016/j.cortex.2015.03.016>
- Tu, S., Spiers, H. J., Hodges, J. R., Piguet, O., & Hornberger, M. (2017). Egocentric versus Allocentric Spatial Memory in Behavioral Variant Frontotemporal Dementia and Alzheimer's Disease. *Journal of Alzheimer's Disease*, 59(3), 883-892.  
<https://doi.org/10.3233/JAD-160592>
- Tuena, C., Mancuso, V., Stramba-Badiale, C., Pedroli, E., Stramba-Badiale, M., Riva, G., & Repetto, C. (2021). Egocentric and allocentric spatial memory in mild cognitive impairment with real-world and virtual navigation tasks: A systematic review. *Journal of Alzheimer's Disease*, 79(1), 95-116. <https://doi.org/10.3233/JAD-201017>
- Tulving, E., Schacter, D. L., Mclachlan, D. R., & Moscovitch, M. (1988). Priming of semantic

- autobiographical knowledge: A case study of retrograde amnesia. *Brain and cognition*, 8(1), 3-20. [https://doi.org/10.1016/0278-2626\(88\)90035-8](https://doi.org/10.1016/0278-2626(88)90035-8)
- Tulving, E. (2002). Episodic memory: From mind to brain. *Annual review of psychology*, 53(1), 1-25. <https://doi.org/10.1146/annurev.psych.53.100901.135114>
- Turano, K. A., Munoz, B., Hassan, S. E., Duncan, D. D., Gower, E. W., Roche, K. B., ... & West, S. K. (2009). Poor sense of direction is associated with constricted driving space in older drivers. *Journals of Gerontology: Series B*, 64(3), 348-355. <https://doi.org/10.1093/geronb/gbp017>
- Ulrich, S., Grill, E., & Flanagin, V. L. (2019). Who gets lost and why: A representative cross-sectional survey on sociodemographic and vestibular determinants of wayfinding strategies. *PloS one*, 14(1), e0204781. <https://doi.org/10.1371/journal.pone.0204781>
- Urgolites, Z. J., Kim, S., Hopkins, R. O., & Squire, L. R. (2016). Map reading, navigating from maps, and the medial temporal lobe. *Proceedings of the National Academy of Sciences*, 113(50), 14289–14293. <https://doi.org/10.1073/pnas.1617786113>
- Valera-Bermejo, J. M., De Marco, M., Mitolo, M., McGeown, W. J., & Venneri, A. (2020). Neuroanatomical and cognitive correlates of domain-specific anosognosia in early Alzheimer's disease. *Cortex*, 129, 236-246. <https://doi.org/10.1016/j.cortex.2020.04.026>
- van der Ham, I. J., Kant, N., Postma, A., & Visser-Meily, J. M. (2013). Is navigation ability a problem in mild stroke patients? Insights from self-reported navigation measures. *Journal of rehabilitation medicine*, 45(5), 429-433. <https://doi.org/10.2340/16501977-1139>
- van der Ham, I. J., van der Kuil, M. N., & Claessen, M. H. (2021). Quality of self-reported cognition: Effects of age and gender on spatial navigation self-reports. *Aging & mental health*, 25(5), 873-878. <https://doi.org/10.1080/13607863.2020.1742658>
- van der Kuil, M. N. A., Visser-Meily, J. M. A., Evers, A. W. M., & van der Ham, I. J. M.

- (2021). Navigation ability in patients with acquired brain injury: A population-wide online study. *Neuropsychological rehabilitation*, 1-24.  
<https://doi.org/10.1080/09602011.2021.1893192>
- van Harten, A. C., Mielke, M. M., Swenson-Dravis, D. M., Hagen, C. E., Edwards, K. K., Roberts, R. O., ... & Petersen, R. C. (2018). Subjective cognitive decline and risk of MCI: The Mayo Clinic Study of Aging. *Neurology*, 91(4), e300-e312.  
<https://doi.org/10.1212/WNL.0000000000005863>
- Vann, S. D., Aggleton, J. P., & Maguire, E. A. (2009). What does the retrosplenial cortex do?. *Nature reviews neuroscience*, 10(11), 792-802. <https://doi.org/10.1038/nrn2733>
- Van Petten, C. (2004). Relationship between hippocampal volume and memory ability in healthy individuals across the lifespan: review and meta-analysis. *Neuropsychologia*, 42(10), 1394-1413. <https://doi.org/10.1016/j.neuropsychologia.2004.04.006>
- Visser, P. J., Verhey, F. R. J., Hofman, P. A. M., Scheltens, P., & Jolles, J. (2002). Medial temporal lobe atrophy predicts Alzheimer's disease in patients with minor cognitive impairment. *Journal of Neurology, Neurosurgery & Psychiatry*, 72(4), 491-497.  
<http://dx.doi.org/10.1136/jnnp.72.4.491>
- Vogel, A., Stokholm, J., Gade, A., Andersen, B. B., Hejl, A. M., & Waldemar, G. (2004). Awareness of deficits in mild cognitive impairment and Alzheimer's disease: do MCI patients have impaired insight?. *Dementia and geriatric cognitive disorders*, 17(3), 181-187. <https://doi.org/10.1159/000076354>
- Vogel, A., Hasselbalch, S. G., Gade, A., Ziebell, M., & Waldemar, G. (2005). Cognitive and functional neuroimaging correlate for anosognosia in mild cognitive impairment and Alzheimer's disease. *International journal of geriatric psychiatry*, 20(3), 238-246.  
<https://doi.org/10.1002/gps.1272>

- Vromen, E. M., de Boer, S., Teunissen, C. E., Rozemuller, A., Sieben, A., Bjerke, M., ... & Alzheimer's Disease Neuroimaging Initiative. (2022). Biomarker A+ T-: is this Alzheimer's disease or not? A combined CSF and pathology study. *Brain*.  
<https://doi.org/10.1093/brain/awac158>
- Wang, T. Y., Kuo, Y. C., Ma, H. I., Lee, C. C., & Pai, M. C. (2012). Validation of the route map recall test for getting lost behavior in Alzheimer's disease patients. *Archives of clinical neuropsychology*, 27(7), 781-789. <https://doi.org/10.1093/arclin/acs073>
- Wank, A. A., Robertson, A., Thayer, S. C., Verfaellie, M., Rapcsak, S. Z., & Grilli, M. D. (2022). Autobiographical memory unknown: Pervasive autobiographical memory loss encompassing personality trait knowledge in an individual with medial temporal lobe amnesia. *Cortex*, 147, 41-57. <https://doi.org/10.1016/j.cortex.2021.11.013>
- Ward, A., Arrighi, H. M., Michels, S., & Cedarbaum, J. M. (2012). Mild cognitive impairment: disparity of incidence and prevalence estimates. *Alzheimer's & Dementia*, 8(1), 14-21. <https://doi.org/10.1016/j.jalz.2011.01.002>
- Wasef, S., Laksono, I., Kapoor, P., Tang-Wei, D., Gold, D., Saripella, A., ... & Chung, F. (2021). Screening for subjective cognitive decline in the elderly via subjective cognitive complaints and informant-reported questionnaires: a systematic review. *BMC anesthesiology*, 21(1), 1-9. <https://doi.org/10.1186/s12871-021-01493-5>
- Weisberg, S. M., Schinazi, V. R., Newcombe, N. S., Shipley, T. F., & Epstein, R. A. (2014). Variations in cognitive maps: understanding individual differences in navigation. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 40(3), 669  
<https://doi.org/10.1037/a0035261>
- Weniger, G., Ruhleder, M., Lange, C., Wolf, S., & Irle, E. (2011). Egocentric and allocentric

- memory as assessed by virtual reality in individuals with amnesic mild cognitive impairment. *Neuropsychologia*, 49(3), 518-527.  
<https://doi.org/10.1016/j.neuropsychologia.2010.12.031>
- Westmacott, R., & Moscovitch, M. (2001). Names and words without meaning: incidental postmorbidity semantic learning in a person with extensive bilateral medial temporal damage. *Neuropsychology*, 15(4), 586. <https://doi.org/10.1037/0894-4105.15.4.586>
- Whishaw, I. Q., McKenna, J. E., & Maaswinkel, H. (1997). Hippocampal lesions and path integration. *Current opinion in neurobiology*, 7(2), 228-234.  
[https://doi.org/10.1016/S0959-4388\(97\)80011-6](https://doi.org/10.1016/S0959-4388(97)80011-6)
- Wild, B., Eckl, A., Herzog, W., Niehoff, D., Lechner, S., Maatouk, I., ... & Löwe, B. (2014). Assessing generalized anxiety disorder in elderly people using the GAD-7 and GAD-2 scales: results of a validation study. *The American journal of geriatric psychiatry*, 22(10), 1029-1038. <https://doi.org/10.1016/j.jagp.2013.01.076>
- Winocur, G., Moscovitch, M., Fogel, S., Rosenbaum, R. S., & Sekeres, M. (2005). Preserved spatial memory after hippocampal lesions: effects of extensive experience in a complex environment. *Nature neuroscience*, 8(3), 273-275. <https://doi.org/10.1038/nn1401>
- Wolbers, T., & Hegarty, M. (2010). What determines our navigational abilities?. *Trends in cognitive sciences*, 14(3), 138-146. <https://doi.org/10.1016/j.tics.2010.01.001>
- Wood, R. A., Moodley, K. K., Lever, C., Minati, L., & Chan, D. (2016). Allocentric spatial memory testing predicts conversion from mild cognitive impairment to dementia: an initial proof-of-concept study. *Frontiers in neurology*, 7, 215.  
<https://doi.org/10.3389/fneur.2016.00215>
- Yatawara, C., Lee, D. R., Lim, L., Zhou, J., & Kandiah, N. (2017). Getting lost Behavior in

- Patients with Mild Alzheimer's Disease: a cognitive and anatomical Model. *Frontiers in medicine*, 4, 201. <https://doi.org/10.3389/fmed.2017.00201>
- Yatawara, C., Ng, K. P., Lim, L., Chander, R., Zhou, J., & Kandiah, N. (2019). Cerebrovascular Disease Is a Risk for Getting Lost Behavior in Prodromal Dementia. *American Journal of Alzheimer's Disease & Other Dementias*®, 34(5), 344-352. <https://doi.org/10.1177/1533317519852864>
- Yates, J. A., Clare, L., Woods, R. T., & MRC CFAS. (2017). Subjective memory complaints, mood and MCI: a follow-up study. *Aging & mental health*, 21(3), 313-321. <https://doi.org/10.1080/13607863.2015.1081150>
- Yu, S., Boone, A. P., He, C., Davis, R. C., Hegarty, M., Chrastil, E. R., & Jacobs, E. G. (2021). Age-related changes in spatial navigation are evident by midlife and differ by sex. *Psychological Science*, 32(5), 692-704. <https://doi.org/10.1177/0956797620979185>
- Yuan, L., Kong, F., Luo, Y., Zeng, S., Lan, J., & You, X. (2019). Gender differences in large-scale and small-scale spatial ability: A systematic review based on behavioral and neuroimaging research. *Frontiers in Behavioral Neuroscience*, 13, 128. <https://doi.org/10.3389/fnbeh.2019.00128>
- Zheng, Z., Li, R., Xiao, F., He, R., Zhang, S., & Li, J. (2017). Sex matters: hippocampal volume predicts individual differences in associative memory in cognitively normal older females but not men. *Frontiers in Human Neuroscience*, 11, 93. <https://doi.org/10.3389/fnhum.2017.00093>
- Zhou, R., Belge, T., & Wolbers, T. (2022). Reaching the Goal: Superior Navigators in Late Adulthood Provide a Novel Perspective into Successful Cognitive Aging. *Topics in Cognitive Science*. <https://doi.org/10.1111/tops.12608>
- Zimmermann, N., Castro-Pontes, M., Barqueta, R., Goes, P., Mufarrej, G., Meira, I. D. A., ... &

Prigatano, G. P. (2020). Self-awareness and underestimation of cognitive abilities in patients with adult temporal lobe epilepsy after surgical treatment. *Epilepsy & Behavior, 112*, 107463. <https://doi.org/10.1016/j.yebeh.2020.107463>

Zuniga, K. E., Mackenzie, M. J., Kramer, A., & McAuley, E. (2016). Subjective memory impairment and well-being in community-dwelling older adults. *Psychogeriatrics, 16*(1), 20-26. <https://doi.org/10.1111/psyg.12112>

## **Appendix A. Attention Checks**

### **Demographics Section**

Please write “NA” in the box below.

Please type the number “78” in the box below.

Please select ‘No’ to the following question and write “memory” in the box after.

### **Navigational Strategies Questionnaire**

Question 8 –

Please write navigation in the box.

### **Multifactorial Memory Questionnaire (MMQ)**

Question 19 -

Please select the option rarely for this question.

### **Generalized Anxiety Disorder-7 (GAD-7)**

Question 6 -

To answer this question, please choose option number 3, “neither agree nor disagree”

### **Patient Health Questionnaire-9 (PHQ-9)**

Question 3 -

Please select option ‘several days’ in response to this question

# Appendix B. Study Questionnaires

## Changes in Navigation Questionnaire (CNQ)

### Changes in Navigation Questionnaire

The first column asks a series of questions about whether you have noticed changes in your spatial navigation.

The second column asks how much change you noticed. Responses are on a "0" to "4" scale, with "0" indicating no changes and "4" indicating significant changes.

0	1	2	3	4
No changes				Significant Changes

The third column is for how long ago you noticed these changes.

The fourth column is only if you selected 'After a specific event.'

	How much change you have noticed. (Please rate 0-4).					If you noticed changes, please select when you noticed them.							Please elaborate on the event ONLY if you selected 'After a specific Event' After a specific Event	
	0	1	2	3	4	No changes	Last few weeks	Last 6 months	Last 1 year	Last 2 years	Last 5 years	Last 10 years		After a Specific Event
1. Have you noticed any changes in your confidence travelling to familiar places alone?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
2. Have you noticed any changes in your confidence travelling to unfamiliar places alone?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
3. Have you noticed any changes in your confidence travelling to places at night / reduced visibility?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
4. Have you noticed any changes in your confidence giving directions to other people?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
5. Have you noticed any changes in how much you rely on GPS or other technology for navigation? (Do you rely more on them?)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
6. Have you noticed any changes in how much you rely on others for navigation aid/ assistance? (Do you rely more on them?)	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
7. Have you noticed any changes in making more mistakes when going places?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
8. Have you noticed any changes in forgetting the layout inside familiar buildings or homes?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
9. Have you noticed any changes in forgetting (becoming confused) about where doors lead to in buildings or homes?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>
10. Have you noticed any changes in family members or others commenting on you getting lost?	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="text"/>

Please double check your answers above, you will not be able to go back once you click the next button.

11. Please use the space below to describe any changes you have noticed in navigating. If you have had no such experiences please write "NA" in the box below.

---

12. If you have had an experience of being disoriented or lost or confused while navigating a physical environment (while driving, walking or inside dwellings), please describe this experience in detail.

If you have had no such experiences please write "NA" in the box below.

# Santa Barbara Sense of Direction Questionnaire (SBSOD)

## Santa Barbara Sense of Direction Scale

This questionnaire consists of several statements about your spatial and navigational abilities, preferences, and experiences.

After each statement, you should choose a number to indicate your level of agreement with the statement.

Choose "1" if you strongly agree that the statement applies to you, "7" if you strongly disagree, or some number in between if your agreement is intermediate.

Choose "4" if you neither agree nor disagree.

---

1. I am very good at giving directions.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

---

2. I have a poor memory for where I left things.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

---

3. I am very good at judging distances.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

---

4. My "sense of direction" is very good.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

5. I tend to think of my environment in terms of cardinal directions (N, S, E, W).

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

---

6. I very easily get lost in a new city.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

---

7. I enjoy reading maps.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

---

8. I have trouble understanding directions.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

---

9. I am very good at reading maps.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

10. I don't remember routes very well while riding as a passenger in a car.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

---

11. I don't enjoy giving directions.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

---

12. It's not important to me to know where I am.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

---

14. I can usually remember a new route after I have traveled it only once.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

---

13. I usually let someone else do the navigational planning for long trips.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

---

15. I don't have a very good "mental map" of my environment.

Strongly Agree 1	2	3	4	5	6	Strongly Disagree 7
---------------------	---	---	---	---	---	------------------------

# Navigational Strategies Questionnaire (NSQ)

## Navigational Strategies Questionnaire

This questionnaire contains questions about your experience navigating, the strategies you use, and what helps you to navigate.

Select the answer for each question that best describes how you navigate, or describe your answer in the space beside "Other" if neither applies.

---

1. When planning a route, do you picture a map of your route or do you picture scenes of what you will see along the way?

Map

Scenes

Other (please explain)

---

2. Do you consider yourself a good navigator?

Yes

No

---

3. Do you find it easy to read and use maps?

Yes

Somewhat

No

---

4. How often do you get disoriented while finding your way around?

Very often

Somewhat often

Very rarely

5. When thinking about a familiar street, how well can you picture the buildings along it?

Very clearly

Somewhat clearly

Hardly at all

6. Would you give directions to a friend in terms of landmarks (i.e. when you see the subway stop, turn left?) or in terms of map directions (i.e. walk north four blocks, then turn left)?

Landmarks

Map Directions

Other

7. Do you picture travelling a route on street level or from a bird's eye view?

Street-level

Bird's eye view

Other

9. When navigating in an area you know well, do you usually just know where to go or do you need to look around at the surroundings to decide (e.g. coming out of a subway station)?

Know it

Some of each

Need to look around

10. When travelling along a new route, do you usually remember what buildings you've passed?

Yes

Somewhat

Rarely

11. Would you prefer to navigate using a list of directions or a map?

Directions

Map

No preference

12. Do you use landmarks (i.e. familiar buildings) to orient yourself when navigating?

Often

Sometimes

Rarely

13. Do you find you're flexible navigating along routes (i.e. you can take new shortcuts easily), or do you prefer to follow the same path every time?

Flexible

Somewhat flexible

Prefer the same route

14. How easily could you draw a map of an area of the city that you know well?

Very easily

Somewhat easily

Not easily

15. Do you think that you navigate by following a mental map, or working on one scene at a time?

Maps

Scene at a time

Other

# Wayfinding Questionnaire (WQ)

## Wayfinding Questionnaire

The following 22 statements are about navigation ability. For each of these statements, please select the number that best describes your ability to navigate. The numbers 1 to 7 represent the following:

1	2	3	4	5	6	7
Not at all applicable to me	Almost never applicable to me	Rarely applicable to me	Sometimes applicable to me	Often applicable to me	Almost always applicable to me	Fully applicable to me

1. When I am in a building for the first time, I can easily point to the main entrance of this building.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

2. If I see a landmark (building, monument, intersection) multiple times, I know exactly from which side I have seen that landmark before.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

3. In an unknown city I can easily see where I need to go when I read a map on an information board.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

4. Without a map, I can estimate the distance of a route I have walked well, when I walk it for the first time.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

5. I can estimate well how long it will take me to walk a route in an unknown city when I see the route on a map (with a legend and scale).

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

6. I can always orient myself quickly and correctly when I am in an unknown environment.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

---

7. I always want to know exactly where I am (meaning, I am always trying to orient myself in an unknown environment).

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

8. I am afraid of losing my way somewhere.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

---

9. I am afraid of getting lost in an unknown city.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

---

10. In an unknown city, I prefer to walk in a group rather than by myself

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

---

11. When I get lost, I get nervous.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

How uncomfortable are you in the following situations (items 12, 13 and 14):

12. Deciding where to go when you are just exiting a train, bus, or subway station.

Not uncomfortable at all 1	2	3	4	5	6	Very uncomfortable 7
-------------------------------------	---	---	---	---	---	----------------------------

---

13. Finding your way in an unknown building (for example a hospital).

Not uncomfortable at all 1	2	3	4	5	6	Very uncomfortable 7
-------------------------------------	---	---	---	---	---	----------------------------

---

14. Finding your way to a meeting in an unknown city or part of a city.

Not uncomfortable at all 1	2	3	4	5	6	Very uncomfortable 7
-------------------------------------	---	---	---	---	---	----------------------------

---

15. I find it frightening to go to a destination I have not been before.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
--	---	---	---	---	---	-----------------------------------

16. I can usually recall a new route after I have walked it once.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

---

17. I am good at estimating distances (for example, from myself to a building I can see).

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

---

18. I am good at understanding and following route descriptions.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

---

19. I am good at giving route descriptions (meaning, explaining a known route to someone).

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

---

20. When I exit a store, I do not need to orient myself again to determine where I have to go.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

---

21. I enjoy taking new routes (for example shortcuts) to known destinations.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

---

22. I can easily find the shortest route to a known destination.

Not at all applicable to me 1	2	3	4	5	6	Fully applicable to me 7
----------------------------------	---	---	---	---	---	-----------------------------

## Survey of Autobiographical Memory Event (Episodic) Subscale

### Episodic (Event) Memory

Please indicate the strength of your agreement with each of the following statements.

	<b>Strongly Disagree</b>	<b>Disagree Somewhat</b>	<b>Neither Agree nor Disagree</b>	<b>Agree Somewhat</b>	<b>Strongly Agree</b>
1. Specific events are difficult for me to recall.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. When I remember events, I have a hard time determining the order of details in the event.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. When I remember events, in general I can recall objects that were in the environment.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. When I remember events, in general I can recall what I was wearing.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. I am highly confident in my ability to remember past events.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. To answer this question, please choose option number three, "neither agree nor disagree."	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. When I remember events, I remember a lot of details.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. When I remember events, in general I can recall which day of the week it was.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. When I remember events, in general I can recall people, what they looked like, or what they were wearing.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

## Multifactorial Memory Questionnaire (MMQ)

### How I Feel About My Memory

In this questionnaire, there are statements about feelings that people may have about their memory. Read each statement and think about your feelings over the past **two weeks**. Then, select the response that best describes how much you agree or disagree.

---

1. I am generally pleased with my memory ability.

Strongly  
Agree

Agree

Undecided

Disagree

Strongly  
Disagree

---

2. There is something seriously wrong with my memory.

Strongly  
Agree

Agree

Undecided

Disagree

Strongly  
Disagree

---

3. If something is important, I will probably remember it.

Strongly  
Agree

Agree

Undecided

Disagree

Strongly  
Disagree

---

4. When I forget something, I fear that I may have a serious memory problem, like Alzheimer's disease.

Strongly  
Agree

Agree

Undecided

Disagree

Strongly  
Disagree

---

5. My memory is worse than most other people my age.

Strongly  
Agree

Agree

Undecided

Disagree

Strongly  
Disagree

6. I have confidence in my ability to remember things.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
----------------	-------	-----------	----------	-------------------

---

7. I feel unhappy when I think about my memory ability.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
----------------	-------	-----------	----------	-------------------

---

8. I worry that others will notice that my memory is not very good.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
----------------	-------	-----------	----------	-------------------

---

9. When I have trouble remembering something, I'm not too hard on myself.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
----------------	-------	-----------	----------	-------------------

---

10. I am concerned about my memory.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
----------------	-------	-----------	----------	-------------------

---

11. My memory is really going downhill lately.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
----------------	-------	-----------	----------	-------------------

---

12. I am generally satisfied with my memory ability.

Strongly Agree	Agree	Undecided	Disagree	Strongly Disagree
----------------	-------	-----------	----------	-------------------

---

13. I don't get upset when I have trouble remembering something.

Strongly  
Agree

Agree

Undecided

Disagree

Strongly  
Disagree

---

14. I worry that I will forget something important.

Strongly  
Agree

Agree

Undecided

Disagree

Strongly  
Disagree

---

15. I am embarrassed about my memory ability.

Strongly  
Agree

Agree

Undecided

Disagree

Strongly  
Disagree

---

16. I get annoyed or irritated with myself when I am forgetful.

Strongly  
Agree

Agree

Undecided

Disagree

Strongly  
Disagree

---

17. My memory is good for my age.

Strongly  
Agree

Agree

Undecided

Disagree

0 Strongly  
Disagree

---

18. I worry about my memory ability.

Strongly  
Agree

Agree

Undecided

Disagree

Strongly  
Disagree

## Memory Mistakes

In this questionnaire there is a list of common memory mistakes that people make. Decide how often you have done each one in the last **two weeks**. Then, select the option for the appropriate response.

---

1. Forgot to pay a bill on time.

All the time

Often

Sometimes

Rarely

Never

---

2. Misplace something you use daily, like your keys or glasses.

All the time

Often

Sometimes

Rarely

Never

---

3. Have trouble remembering a telephone number you just looked up.

All the time

Often

Sometimes

Rarely

Never

---

4. Not recall the name of someone you just met.

All the time

Often

Sometimes

Rarely

Never

---

5. Leave something behind when you meant to bring it along with you.

All the time

Often

Sometimes

Rarely

Never

---

6. Forget an appointment.

All the time

Often

Sometimes

Rarely

Never

7. Forget what you were just about to do; for example, walk into a room and forget what you went there to do.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

8. Forget to run an errand.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

9. In conversation, have difficulty coming up with a specific word that you want.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

10. Have trouble remembering details from a newspaper or magazine article you read earlier that day.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

11. Forget to take medication.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

12. Not recall the name of someone you have known for some time.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

13. Forget to pass on a message.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

14. Forget what you were going to say in conversation.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

15. Forget a birthday or anniversary that you used to know well.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

16. Forget a telephone number you use frequently.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

17. Retell a story or joke to the same person because you forgot you already told him or her.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

18. Misplace something that you put away a few days ago.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

19. Please select the option rarely for this question.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

20. Forgot to buy something you intended to buy.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

21. Forget details about a recent conversation.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

## Use of Memory Strategies

Attention is the ability to focus on 1 task at a time, and not get distracted. People often use different tricks or strategies to help them remember things. Several strategies are listed in this questionnaire. Decide how often you used each one in the **last two weeks**. Then select the appropriate response.

---

1. Use a timer or alarm to remind you when to do something.

All the time

Often

Sometimes

Rarely

Never

---

2. Ask someone to help you remember something or to remind you to do something.

All the time

Often

Sometimes

Rarely

Never

---

3. Create a rhyme out of what you want to remember.

All the time

Often

Sometimes

Rarely

Never

---

4. In your mind, create an image of something you want to remember, like a name and face.

All the time

Often

Sometimes

Rarely

Never

---

5. Write things on a calendar, such as appointments or things you need to do.

All the time

Often

Sometimes

Rarely

Never

---

6. Go through the alphabet one letter at a time to see if it sparks a memory for a name or word.

All the time

Often

Sometimes

Rarely

Never

---

7. Organize information you want to remember; for example, organize your grocery list according to food groups.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

8. Say something out loud in order to remember it, such as a phone number you just looked up.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

9. Use a routine to remember important things, like checking that you have your wallet and keys when you leave home.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

10. Make a list, such as a grocery list or a list of things to do.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

11. Mentally elaborate on something you want to remember; for example focus on a lot of the details.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

12. Put something in a prominent place to remind you to do something, like putting your umbrella by the front door so you will remember to take it with you.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

13. Repeat something to yourself at increasingly longer and longer intervals so you will remember it.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

14. Create a story to link together information you want to remember.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

15. Write down in a notebook things that you want to remember.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

---

16. Create an acronym out of the first letters in a list of things to remember, such as carrots, apples, and bread (cab).

All the time	Often	Sometimes	Rarely	Never
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17. Intentionally concentrate hard on something so that you will remember it.

All the time	Often	Sometimes	Rarely	Never
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18. Write a note or reminder for yourself (other than on a calendar or in a notebook).

All the time	Often	Sometimes	Rarely	Never
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19. Mentally retrace your steps in order to remember something, such as the location of a misplaced item.

All the time	Often	Sometimes	Rarely	Never
--------------	-------	-----------	--------	-------

## Patient Health Questionnaire-9 (PHQ-9)

Over the past 2 weeks, how often have you been bothered by any of the following problems?

	Not at all 0	Several days 1	More than half the days 2	Nearly every day 3
1. Little interest or pleasure in doing things	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. Feeling down, depressed, or hopeless	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. Please select option 'several days' in response to this question	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. Trouble falling or staying asleep, or sleeping too much	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. Feeling tired or having little energy	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
	Not at all 0	Several days 1	More than half the days 2	Nearly every day 3
6. Poor appetite or overeating	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. Feeling bad about yourself - or that you are a failure or have let yourself or your family down	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. Trouble concentrating on things, such as reading the newspaper or watching television	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. Moving or speaking so slowly that other people could have noticed? Or the opposite - being so fidgety and restless that you have been moving around a lot more than usual	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. Thoughts you would be better off dead or of hurting yourself in some way	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

## Generalized Anxiety Disorder-7 (GAD-7)

Generalized Anxiety Disorder 7-item (GAD-7)

Over the last 2 weeks, how often have you been bothered by the following problems?

	Not at all	Several days	Over half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. Not being able to stop or control worrying	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. Worrying too much about different things	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. Please choose option 'nearly every day' for this item	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. Trouble relaxing	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. Being so restless that it's hard to sit still	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. Becoming easily annoyed or irritable	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. Feeling afraid as if something awful might happen	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

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If you checked off any problems, how difficult have these made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all

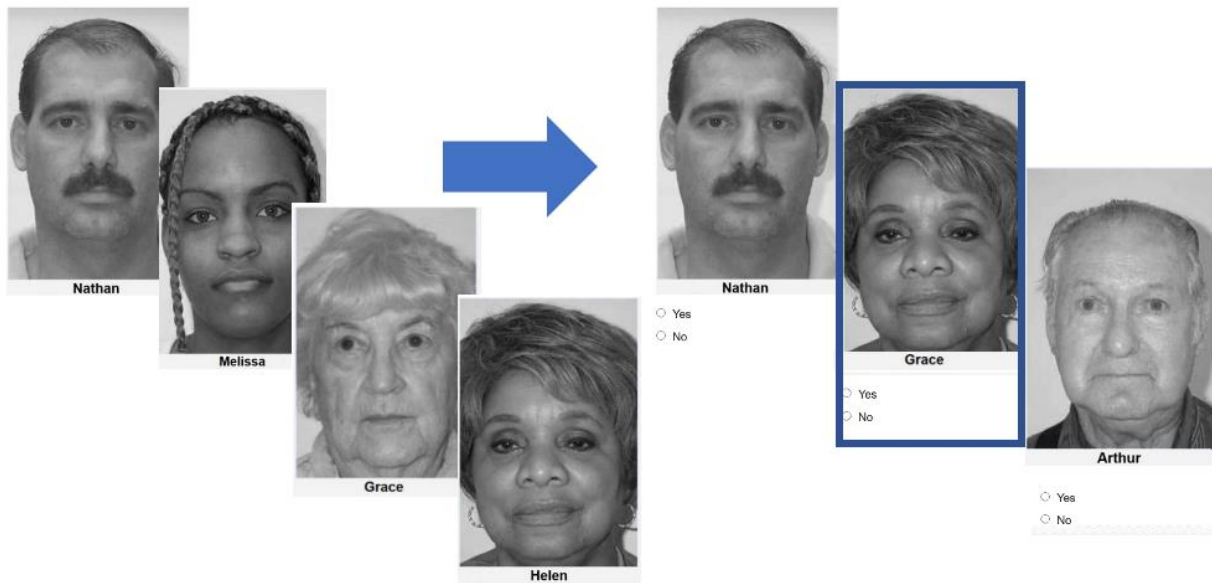
Somewhat difficult

Very difficult

Extremely Difficult

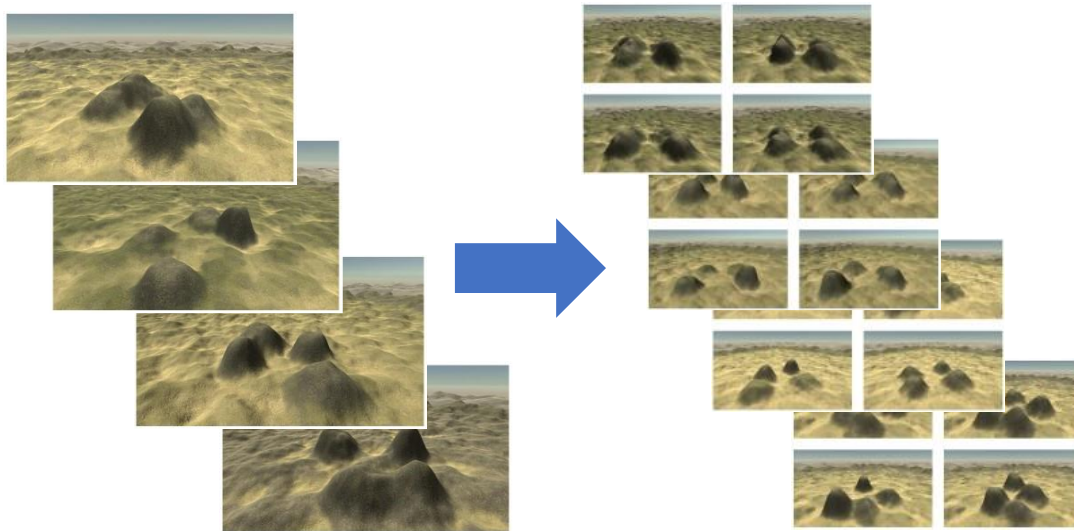
## Appendix C. Sample Stimuli

### Face-Name Task Schematic, Encoding & Retrieval



*Note.* On the left side of arrow is an example of four encoding trials, which consist of grayscale faces and names. On the right side of arrow are example of three retrieval trials. There is an example of an *intact* trial (old face and old name), a *recombined* trial (new face, old name) and lastly a *new* trial (new face, new name).

## Four Mountains Task Schematic, Encoding & Retrieval



*Note.* On the left side of arrow is an example of four encoding trials, which each consist of a mountain landscape. On the right side of arrow are examples of four retrieval trials. On each retrieval trial four mountain landscapes are presented, one of which was previously shown and is now rotated.

## Appendix D. Sea Hero Quest Map Levels







## **Appendix E. Acronyms**

Acquired Brain Injury (ABI)

Alzheimer's Disease (AD)

Alzheimer's Disease and Related Dementias (ADRD)

Amnesic Mild Cognitive Impairment (aMCI)

Changes in Navigation Questionnaire (CNQ)

Cerebrospinal Fluid (CSF)

Cognitive Map Theory (CMT)

Generalized Anxiety Disorder scale -7 (GAD-7)

Item Response Theory (IRT)

Magnetic Resonance Imaging (MRI)

Medial Temporal Lobes (MTLs)

Multifactorial Memory Questionnaire (MMQ)

Navigational Strategies Questionnaire (NSQ)

Patient Health Questionnaire-9 (PHQ)

Santa Barbara Sense of Direction Questionnaire (SBSOD)

Sea Hero Quest (SHQ)

Subjective Cognitive Decline (SCD)

Survey of Autobiographical Memory (SAM)

SAM Event (Episodic) Subscale

Traumatic Brain Injury (TBI)

Wayfinding Questionnaire (WQ)

## Appendix F. Older Adult Sample Self-Reported Nationality

Nationality	Number of Participants
British	378
American	123
Broader United Kingdom	24
Canadian	11
Italian	5
Australian	4
Polish	4
Greek	3
French	3
Dutch	3
German	3
Cuban	2
South African	2
Maltese	2
Hungarian	2
New Zealander	1
Mexican	1
Portuguese	1
Finnish	1
Norwegian	1
Bangladeshi	1
Brazilian	1
Czech	1
Swedish	1
Nigerian	1

*Note.* Seven individuals listed multiple nationalities and were grouped under the first one listed. Eight individuals provided information on either ethnicity or race and are not included in this table.

*Correlation Matrix, Males*

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. MMQ Satisfaction	1.00														
2. MMQ Ability	0.63	1.00													
3. MMQ Strategy	-0.36	-0.59	1.00												
4. SAM Episodic	0.48	0.50	-0.16	1.00											
5. NSQ	0.03	0.07	-0.02	0.04	1.00										
6. SBSOD	0.42	0.39	-0.14	0.04	0.32	1.00									
7. WQ Spatial Anxiety	-0.24	-0.22	0.14	0.04	-0.29	-0.47	1.00								
8. WQ Navigation Orientation	0.32	0.27	-0.07	0.04	0.34	0.74	-0.46	1.00							
9. WQ Distance Estimation	0.24	0.20	-0.03	0.04	0.25	0.46	-0.42	0.59	1.00						
10. CNO Total	-0.29	-0.32	0.15	0.04	-0.10	0.28	0.25	-0.23	-0.19	1.00					
11. CNO Factor 1	-0.25	-0.30	0.14	0.04	-0.05	-0.24	0.27	-0.20	-0.25	0.83	1.00				
12. CNO Factor 2	-0.23	-0.26	0.12	-0.10	-0.12	-0.19	0.14	-0.15	-0.10	0.60	0.45	1.00			
13. PHQ-9	-0.34	-0.37	0.23	-0.15	-0.01	-0.17	0.22	-0.10	-0.11	0.22	0.22	0.18	1.00		
14. GAD-7	-0.30	-0.28	0.20	-0.12	-0.02	-0.12	0.25	-0.09	-0.09	0.26	0.27	0.25	0.73	1.00	
15. Face-Name Task	-0.02	0.06	-0.03	-0.13	0.10	0.03	-0.04	0.01	0.01	0.00	0.02	0.00	-0.01	0.00	1.00
16. Four Mountains Task	0.10	0.02	0.02	-0.06	0.15	0.17	-0.18	0.16	0.16	0.01	-0.03	-0.03	-0.03	-0.06	0.06

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

Note. Values indicate strength of relationship between variables with Spearman's rho non-parametric test statistic.

*Correlation Matrix, Females*

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. MMQ Satisfaction	1.00														
2. MMQ Ability	0.63	1.00													
3. MMQ Strategy	-0.34	-0.54	1.00												
4. SAM Episodic	0.38	0.36	-0.18	1.00											
5. NSQ	0.08	0.11	-0.08	0.09	1.00										
6. SBSOD	0.32	0.30	-0.18	0.40	0.64	1.00									
7. WQ Spatial Anxiety	-0.25	-0.30	0.23	-0.27	-0.48	-0.62	1.00								
8. WQ Navigation Orientation	0.25	0.23	-0.13	0.46	0.59	0.84	-0.60	1.00							
9. WQ Distance Estimation	0.17	0.16	-0.08	0.39	0.36	0.54	-0.36	0.64	1.00						
10. CNQ Total	-0.36	-0.45	0.29	-0.32	-0.18	-0.35	0.39	-0.33	-0.22	1.00					
11. CNQ Factor 1	-0.35	-0.43	0.28	-0.28	-0.17	-0.33	0.39	-0.30	-0.20	0.95	1.00				
12. CNQ Factor 2	-0.26	-0.36	0.18	-0.30	-0.20	-0.32	0.36	-0.31	-0.20	0.64	0.55	1.00			
13. PHQ-9	-0.39	-0.35	0.18	-0.19	-0.10	-0.15	0.22	-0.14	-0.12	0.21	0.20	1.00			
14. GAD-7	-0.36	-0.38	0.27	-0.17	-0.22	-0.30	0.34	-0.24	-0.12	0.26	0.27	0.25	1.00		
15. Face-Name Task	0.01	0.06	0.01	0.07	0.05	0.05	-0.14	0.07	0.06	0.01	-0.01	-0.02	0.70	1.00	
16. Four Mountains Task	0.05	0.14	-0.02	-0.02	0.13	0.07	-0.10	0.03	0.01	0.00	0.01	-0.14	-0.02	-0.02	1.00

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

*Note.* Values indicate strength of relationship between variables with Spearman's  $\rho$  non-parametric test statistic.