# Cognitive and neural mechanisms of sense of self in neurodegenerative disorders

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# List of abbreviations

| | |
|---|---|
| ABM | Autobiographical memory |
| ACC | Anterior cingulate cortex |
| ACE-III | Addenbrooke's Cognitive Examination-Third Edition |
| ACE-R | Addenbrooke's Cognitive Examination-Revised |
| AD | Alzheimer's disease |
| AI | Autobiographical Interview |
| AMI | Autobiographical Memory Interview |
| ANCOVA | Analysis of Covariance |
| ANOVA | Analysis of Variance |
| ATL | Anterior temporal lobe |
| bvFTD | Behavioural variant of frontotemporal dementia |
| C9orf72 | Chromosome 9 open reading frame 72 |
| CBI | Cambridge Behavioural Inventory |
| DMN | Default mode network |
| EBQ | Egocentric Behaviour Questionnaire |
| EE | Extended Episode details |
| EXT-EVT | External Event details |
| fMRI | Functional magnetic resonance imaging |
| FA | Fractional anisotropy |
| FSL | Functional MRI of the Brain Software Library |
| FTD | Frontotemporal dementia |
| FTD-FRS | Frontotemporal Dementia Functional Rating Scale |
| FWE | Familywise error |
| GLM | General Linear Model |
| GS | General Semantic details |
| IFG | Inferior frontal gyrus |
| IRI | Interpersonal Reactivity Index |
| MANCOVA | Multivariate Analysis of Covariance |
| MNI | Montreal Neurological Institute |

| | |
|---|---|
| mPFC | Medial prefrontal cortex |
| MTL | Medial temporal lobe |
| MRI | Magnetic resonance imaging |
| NExt | New External details taxonomy |
| OFC | Orbitofrontal cortex |
| PCC | Posterior cingulate cortex |
| PET | Positron emission tomography |
| PS | Personal Semantic details |
| PT | Perspective Taking |
| RAVLT | Rey Auditory Verbal Learning Test |
| RCF | Rey Complex Figure |
| SD | Semantic dementia |
| SE | Specific Episode details |
| SEM | Semantic details |
| SNQ | Social norms questionnaire |
| SPM | Statistical Parametric Mapping |
| SYDBAT | Sydney Language Battery |
| TDP | TAR DNA binding protein |
| TFCE | Threshold-free cluster enhancement |
| TMT | Trail Making Test |
| ToM | Theory of mind |
| TPJ | Temporoparietal junction |
| VBM | Voxel-based morphometry |
| VPT | Visual perspective taking |

# List of publications and presentations

The following first-author publications form a major part of this thesis. Author contributions are outlined for each instance.

Chapter 1 contains material published in:

Strikwerda-Brown, C., Grilli, M. D., Andrews-Hanna, J. R., Irish, M. (2019). "All is not lost" – Rethinking the nature of memory and the self in dementia. *Ageing Research Reviews, 54*, 100932.

CSB conducted the critical review of the literature. MI designed the concept. All authors contributed to the drafting of the manuscript and critical revision of the final piece.

Chapters 1 and 6 contain material published in:

Strikwerda-Brown, C., Ramanan, S., Irish, M. (2019). Neurocognitive mechanisms of theory of mind impairments in neurodegeneration: A transdiagnostic approach. *Neuropsychiatric Disease and Treatment, 15*, 557-573.

CSB & SR completed the critical review of the literature. All authors contributed to the article conceptualisation, drafting of the manuscript, and critical revision of the final piece.

Chapter 3 contains material published in:

Strikwerda-Brown, C., Mothakunnel, A., Hodges, J. R., Piguet, O., Irish, M. (2018). External details revisited – A new taxonomy for coding 'non-episodic' content during autobiographical memory retrieval. *Journal of Neuropsychology, 13*(3), 371-397.

CSB designed the study, completed data scoring, analysis, and interpretation, and wrote the paper. AM assisted with scoring and data management. MI contributed to study design. MI and OP provided input into data interpretation, drafting and revision of the paper. JRH and OP facilitated the original research project from which the data was taken.

In addition to the statements above, in cases where I am not the corresponding author of a published item, permission to include the published material has been granted by the corresponding author.

Cherie Strikwerda-Brown
Date: 31/12/2019

As supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

Associate Professor Muireann Irish
Date: 11/12/2019

Results from this thesis have also been presented in the form of conference presentations, listed below:

Chapter 1:

Strikwerda-Brown, C. (March 2019). *The self in dementia: A neurocognitive approach.* Invited Seminar, Cognition and Circuits Series, Montreal Neurological Institute, McGill University, Canada.

Strikwerda-Brown, C. (February 2019). *The episodic-semantic continuum: A new approach to examining the content of autobiographical narratives.* Invited Seminar, University of Ottawa, Canada.

Strikwerda-Brown, C. (February 2019). *Reconsidering the episodic-semantic distinction in past and future thinking: A new classification system.* Invited Seminar, Psychology Department Brownbag Series, University of Toronto, Canada.

Strikwerda-Brown, C. (December 2018). *When the self breaks down – Self-related cognition in frontotemporal dementia.* Oral Presentation at the Australasian Society for Philosophy and Psychology (ASPP) Conference Symposium on 'The temporally extended self – from development to degeneration', Sydney.

Chapter 3:

Strikwerda-Brown, C. (March 2019). *The episodic-semantic interplay in autobiographical memory and future thinking.* Oral Presentation at the Cognitive Neuroscience Society (CNS) Annual Meeting Symposium on 'From knowing to re-experiencing – The semantic-episodic distinction 47 years on', San Francisco, CA, USA.

Strikwerda-Brown, C. (March 2019). *The self in dementia: A neurocognitive approach.* Invited Seminar, Cognition and Circuits Series, Montreal Neurological Institute, McGill University, Canada.

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Strikwerda-Brown, C., Mothakunnel, A., Hodges, J. R., Piguet, O., Irish, M. (April 2018). *Events, facts, and everything in between – A fine-grained analysis of 'non-episodic' autobiographical memory in dementia syndromes.* Oral Presentation at the International Conference on Learning and Memory (L&M), Huntington Beach, CA, USA.

Strikwerda-Brown, C. (April 2018). *What can dementia tell us about the representation of the 'self' in the brain?* Invited Seminar at University of Arizona, Tucson, AZ, USA.

Strikwerda-Brown, C., Mothakunnel, A., Hodges, J. R., Piguet, O., Irish, M. (March 2018). *The episodic-semantic continuum in autobiographical memory – A new classification system*. Oral Presentation at the Australian Research Council Centre of Excellence in Cognition and its Disorders (CCD) Annual Memory Program Meeting, Sydney.

Strikwerda-Brown, C., Mothakunnel, A., Hodges, J. R., Piguet, O., Irish, M. (October 2017). *Autobiographical memory in Alzheimer's disease and semantic dementia – A detailed examination of episodic and semantic content.* Poster Presentation at the Brain and Mind Centre (BMC) Symposium, Sydney.

Chapter 4:

Strikwerda-Brown, C. (March 2019). *The episodic-semantic interplay in autobiographical memory and future thinking.* Oral Presentation at the Cognitive Neuroscience Society (CNS) Annual Meeting Symposium on 'From knowing to re-experiencing – The semantic-episodic distinction 47 years on', San Francisco, CA, USA.

Strikwerda-Brown, C., Hodges, J. R., Piguet, O., & Irish, M. (March 2019). *"Blurred lines": 'Non-episodic' content of future thinking narratives challenges a strict episodic-semantic distinction.* Poster Presentation at the Cognitive Neuroscience Society (CNS) Annual Meeting, San Francisco, CA, USA.

Strikwerda-Brown, C. (March 2019). *The self in dementia: A neurocognitive approach.* Invited Seminar, Cognition and Circuits Series, Montreal Neurological Institute, McGill University, Canada.

Strikwerda-Brown, C. (February 2019). *The episodic-semantic continuum: A new approach to examining the content of autobiographical narratives.* Invited Seminar, University of Ottawa, Canada.

Strikwerda-Brown, C. (February 2019). *Reconsidering the episodic-semantic distinction in past and future thinking: A new classification system.* Invited Seminar, Psychology Department Brownbag Series, University of Toronto, Canada.

Strikwerda-Brown, C. (December 2018). *When the self breaks down – Self-related cognition in frontotemporal dementia.* Oral Presentation at the Australasian Society for Philosophy and Psychology (ASPP) Conference Symposium on 'The temporally extended self – from development to degeneration', Sydney.

Chapter 5:

Strikwerda-Brown, C. (March 2019). *The self in dementia: A neurocognitive approach.* Invited Seminar, Cognition and Circuits Series, Montreal Neurological Institute, McGill University, Canada.

Strikwerda-Brown, C., Goldberg, Z. L., Hodges, J. R., Piguet, O., & Irish, M. (November 2018). *Right or wrong? Reduced emotional response to moral conflict in bvFTD is associated with loss of social knowledge.* Invited talk at Behavioural Management Pre-Conference Workshop at the International Conference on Frontotemporal Dementias (ICFTD), Sydney, Australia.

Strikwerda-Brown, C., Goldberg, Z. L., Hodges, J. R., Piguet, O., & Irish, M. (November 2018). *Right or wrong? Reduced emotional response to moral conflict in bvFTD is associated with loss of social knowledge.* Poster Presentation at the International Conference on Frontotemporal Dementias (ICFTD), Sydney, Australia.

Strikwerda-Brown, C. (November 2018). *Show no mercy: Reduced emotional response to morally conflictual dilemmas in frontotemporal dementia* Oral Presentation at the Sydney Postgraduate Psychology Conference (SPPC), Sydney (awarded best Clinical Oral Presentation).

Strikwerda-Brown, C., Goldberg, Z. L., Hodges, J. R., Piguet, O., & Irish, M. (November 2018). *No remorse: Reduced emotional response to morally conflictual dilemmas in frontotemporal dementia.* Poster Presentation at the Brain and Mind Centre (BMC) Symposium, Sydney.

Strikwerda-Brown, C., Goldberg, Z. L., Hodges, J. R., Piguet, O., & Irish, M. (October 2018). *No regrets: Lack of remorse following morally conflictual decisions is associated with loss of social*

*knowledge in frontotemporal dementia.* Poster Presentation at the Australian Research Council Centre of Excellence in Cognition and its Disorders (CCD) Annual Workshop, Sydney.

Strikwerda-Brown, C., Goldberg, Z. L., Hodges, J., Piguet, O., Irish, M. (July 2018). *For the greater good? Reduced emotional response to morally conflicting dilemmas in frontotemporal dementia.* Oral Presentation at the International Neuropsychological Society (INS) Conference, Prague, Czech Republic.

Strikwerda-Brown, C. (April 2018). *What can dementia tell us about the representation of the 'self' in the brain?* Invited Seminar at University of Arizona, Tucson, AZ, USA.

Strikwerda-Brown, C., Goldberg, Z. L., Mothakunnel., A., Piguet, O., Irish, M. (November 2017). *Do no harm- Exploring mechanisms of moral reasoning in frontotemporal dementia.* Oral Presentation at Australasian Cognitive Neuroscience Society (ACNS) Conference, Adelaide (awarded Student Travel Grant).

Chapter 6:

Strikwerda-Brown, C., Piguet, O., & Irish, M. (November 2019). *Try to see if my way: Distinct neural correlates of different forms of perspective taking in dementia.* Oral Presentation at the Australasian Cognitive Neuroscience Society (ACNS) Conference, Launceston (awarded Student Travel Grant).

Strikwerda-Brown, C. (March 2019). *The self in dementia: A neurocognitive approach.* Invited Seminar, Cognition and Circuits Series, Montreal Neurological Institute, McGill University, Canada.

Strikwerda-Brown, C. (December 2018). *When the self breaks down – Self-related cognition in frontotemporal dementia.* Oral Presentation at the Australasian Society for Philosophy and Psychology (ASPP) Conference Symposium on 'The temporally extended self – from development to degeneration', Sydney.

# Statement of originality

This is to certify that to the best of my knowledge, the content of this thesis is my own work. This thesis has not been submitted for any degree or other purposes. I certify that the intellectual content of this thesis is the product of my own work and that all the assistance received in preparing this thesis and sources have been acknowledged.

The work undertaken during my PhD was performed under the supervision of Associate Professor Muireann Irish and Professor Olivier Piguet. The studies contained within this thesis were conducted within the FRONTIER Frontotemporal Dementia Research Clinic, at the Brain and Mind Centre, the University of Sydney. The standardised neuropsychological assessment battery described in Chapter 2 was predominantly collected by research assistants at FRONTIER. The data contained within Chapters 3 and 4 was also collected by FRONTIER research assistants, though I performed the novel scoring and analyses for these studies.

All data was collected through direct contact with participants, with written informed consent obtained from all participants or their person responsible. In accordance with the Declaration of Helsinki, ethical approval was obtained from the Human Research Ethics Committee of the South Eastern Sydney Local Health District at the University of New South Wales (HREC 10/126 and HREC 13/177).

Cherie Strikwerda-Brown

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# Abstract

The ability to maintain a coherent and continuous 'sense of self' is a fundamental component of being human, enabling us to interact and function successfully in everyday life. While a sense of self is commonly accepted to involve both 'extended' (i.e., memories) and 'interpersonal' (i.e., social) elements, the precise cognitive and neural mechanisms underlying these aspects of the self remain poorly understood. This thesis draws upon theory and methods from contemporary cognitive neuroscience to examine the neurocognitive underpinnings of the extended and interpersonal self in Alzheimer's disease (AD), semantic dementia (SD), and the behavioural variant of frontotemporal dementia (bvFTD): neurodegenerative disorders involving progressive cognitive and behavioural change as the result of degeneration to distinct brain networks.

Employing a novel experimental method (the 'NExt' taxonomy), Part 1 of the thesis (Chapters 3 and 4) reveals how a full spectrum of episodic and semantic memory representations may be drawn upon to support one's past and future life stories, giving rise to a sense of continuity of the extended self. Part 2 (Chapters 5 and 6) illustrates how the complex social interactions that comprise the interpersonal self may be deconstructed into several distinct, yet interacting, psychological components. Furthermore, neuroimaging analyses uncover widespread neural regions to be associated with both the extended and interpersonal aspects of the self, incorporating brain networks beyond those typically implicated in self-related processing. The improved neurocognitive characterisation of the self provided by this thesis highlights the complex, multifaceted nature of this construct. Moreover, from a clinical perspective, distinct profiles of the self unveiled across AD, SD, and bvFTD reveal how ultimately, 'all is not lost' in neurodegeneration.

# Chapter 1

# Introduction

This chapter contains material from the following two published manuscripts:

Strikwerda-Brown, C., Grilli, M. D., Andrews-Hanna, J. R., Irish, M. (2019). "All is not lost" – Rethinking the nature of memory and the self in dementia. *Ageing Research Reviews, 54*, 100932.

Strikwerda-Brown, C., Ramanan, S., Irish, M. (2019). Neurocognitive mechanisms of theory of mind impairments in neurodegeneration: A transdiagnostic approach. *Neuropsychiatric Disease and Treatment, 15*, 557-573.

One of the fundamental qualities of the human experience is the ability to maintain a coherent and continuous 'sense of self' (Mauss, 1985). This feeling that we exist as a distinct and unique person (Prebble, Addis, & Tippett, 2013) enables us to interact and function successfully in everyday life (Clare et al., 2013; Rathbone, Holmes, Murphy, & Ellis, 2015; Vanderveren, Bijttebier, & Hermans, 2017). For over two thousand years, the 'self' has been the subject of keen interest and in-depth inquiry by philosophers, psychologists, and neuroscientists alike. While various theoretical models have been proposed, it is generally accepted that a sense of self comprises both 'extended' (i.e., memories and life stories) and 'interpersonal' (i.e., personality traits, social interactions) elements (S. Gallagher, 2013; Harré, 1991; Neisser, 1988). Despite substantial progress in defining and conceptualising the construct, however, the precise cognitive and neural mechanisms underlying a sense of self remain poorly understood. This is likely attributable, at least in part, to the disconnect between the empirical investigation of the self and the latest conceptual and methodological developments in cognitive neuroscience. While these theoretical and technological advances have the potential to significantly improve the characterisation of the self, studies marrying these two separate lines of research remain scarce.

Alzheimer's disease (AD), semantic dementia, (SD), and the behavioural variant of frontotemporal dementia (bvFTD) are three distinct neurodegenerative disorders of the brain, involving progressive cognitive and behavioural change as a result of the selective and systematic degeneration of large-scale neural networks (Seeley, Crawford, Zhou, Miller, &

Greicius, 2009). While AD and SD are characterised by impairments in episodic and semantic memory, respectively (Gorno-Tempini et al., 2011; McKhann et al., 2011), bvFTD manifests as a disorder of social interaction, comprising striking changes in personality and behaviour (Piguet, Hornberger, Mioshi, & Hodges, 2011; Rascovsky et al., 2011). Accordingly, these syndromes offer a unique opportunity to inform understanding of the neurocognitive architecture of the extended and interpersonal aspects of the self.

This thesis draws upon contemporary cognitive neuroscientific methods and theory to investigate the cognitive and neural mechanisms of the extended self in AD and SD (Part 1), and the interpersonal self in bvFTD (Part 2), with the overall aim of improving characterisation of the self. Chapter 1 provides an overview of theoretical models of the self; current cognitive neuroscience understanding of the extended and interpersonal self; the AD, SD, and bvFTD syndromes; and research to date investigating the extended and interpersonal self in these disorders. In Section 1.1., theoretical models of the self are reviewed, with particular focus on the Neisser framework. Section 1.2. outlines Part 1 of the thesis, by providing an overview of the cognitive neuroscience literature on the extended self. The clinical syndromes of AD and SD are described, followed by a review of the studies on the extended self in AD and SD. The aims and structure of Part 1 of the thesis are then presented. Next, Section 1.3. outlines Part 2 of the thesis, reviewing the interpersonal self from a cognitive neuroscience perspective, the syndrome of bvFTD, and the current knowledge about the interpersonal self in bvFTD. The aims and structure of Part 2 of the thesis are then provided. Finally, the overall justification and aims of the thesis are presented in Section 1.4.

## 1.1. Theoretical models of the self

Since the 19$^{th}$ century, numerous philosophical and psychological models of the self have been proposed. A common thread underlying many of these theories is the notion that the self is not a unitary construct, but instead comprises multiple distinct components. Early models (James, Burkhardt, Bowers, & Skrupskelis, 1890; Mead, 1934), influenced by the ancient Greek philosophy of Socrates and Plato, distinguished between the self as the experiencer, or subject, of ongoing consciousness (the 'I' self) and the self as the object of this awareness (the 'me' self). This distinction has remained dominant in theoretical

conceptualisations of the self, as well as forming the launchpad for several extensions (reviewed by Morin, 2006). Such elaborations of the model propose several additional aspects of the self, based on the type and complexity of self-referential information (Neisser, 1988; Newen & Vogeley, 2003), and its temporal nature (i.e., in the present moment versus extended across time; S. Gallagher, 2000; Neisser, 1988; Prebble et al., 2013). The Neisser (1988) model, which proposes five kinds of self-knowledge, has been particularly dominant (see section 1.1.1.). In addition to incorporating many of the elements proposed by other influential models (i.e., consciousness, self-awareness, temporal dimension), the components of the Neisser (1988) model are tangible and as such, objectively measurable. Accordingly, this theoretical framework is suited to form the basis of empirical research, and is particularly recommended for studies of the self in dementia syndromes (Caddell & Clare, 2013).

### 1.1.1. Neisser model

Neisser (1988) proposes that the self comprises five aspects, so distinct from one another that each represents a different 'self'. These components vary in terms of their developmental histories, contribution to human interaction and functioning, and susceptibility to pathology. Neisser's (1988) five selves include: the *ecological self,* the *interpersonal self,* the *extended self,* the *private self,* and the *conceptual self.* While the ecological self refers to the self as perceived with respect to the physical environment, the interpersonal self is the self engaged in social interaction. The extended self is based on memories of the past and anticipations of the future, the private self refers to experiences not shared with other people, and the conceptual self regards the knowledge we hold about ourselves. While each of these five selves may be affected to varying degrees in neurodegeneration (Seeley & Miller, 2005), the extended and interpersonal aspects are those most prominently impacted in the syndromes of AD, SD, and bvFTD. Furthermore, these two components are recognised across multiple theoretical frameworks of the self (e.g., S. Gallagher, 2013; Harré, 1991), and therefore will form the focus of this thesis.

## 1.2. Part 1: The extended self

*"Memory alone… 'tis to be considered… as the source of personal identity"*

Hume (1739)

Scottish Enlightenment Philosopher

The extended self is defined by Neisser (1988) as the self experienced over time, based on our memories of the past and anticipations of the future. This provides a sense of continuity of the self across time[1], enabling both stability and growth in who one is as a person (Conway, 2005; Locke, 1690; Ricoeur, 2010). The extended self first emerges early in childhood (by age three), corresponding to the development of memory for past events (Todd & Perlmutter, 1980) and routines (Nelson, 1986).

### 1.2.1. Cognitive neuroscience of the extended self

***Contributions of episodic and semantic memory***

While the importance of memory for the extended self is well-recognised (James et al., 1890; Locke, 1690; Neisser, 1988; Squire & Kandel, 2009), less attention has been paid to the relative contributions of different forms of memory in supporting a sense of self-continuity. Traditionally, the extended self was understood with reference to episodic memory (i.e., memory for events from one's past) (Neisser, 1988), though contemporary theoretical refinements also recognise the contribution of semantic memory (i.e., conceptual knowledge) in supporting self-continuity over past, present, and future (Addis & Tippett, 2008; Haslam, Jetten, Haslam, Pugliese, & Tonks, 2011; Prebble et al., 2013). These two forms of memory were initially proposed to be interdependent (Tulving, 1972), however, a tendency to consider episodic and semantic memory as representing distinct systems, with dissociable contributions to the extended self, has since pervaded the literature (see Conway, 2005; Renoult & Rugg, 2019). Nonetheless, more recently, the interactions and overlap between episodic and semantic memory have returned to the spotlight (Burianová & Grady, 2007; Greenberg & Verfaellie, 2010; Renoult, Irish, Moscovitch, & Rugg, 2019), for recollecting one's past, as well as imagining the personal future (Irish, 2016; Irish & Piguet, 2013). As such, both

[1] 'In this thesis, 'self-continuity' will be used interchangeably with the 'extended self'.

episodic and semantic memory are proposed to support the extended self across temporal contexts, in ways that are both distinct and overlapping (Figure 1.1.; Prebble et al., 2013). Episodic memory is proposed to provide a sense of *subjective* continuity of the self, that is, the ability to mentally project to the past or future to re-experience (or 'pre-experience') episodes, otherwise known as autonoetic consciousness (Tulving, 1972; Wheeler, Stuss, & Tulving, 1997). This gives rise to a feeling that the present self is an extension of who one was (or will be) at the time of the event, allowing a sense of agency (Metcalfe, Snellenberg, DeRosse, Balsam, & Malhotra, 2012), aiding in future decision making (Hershfield, 2011), contributing to growth of the self over time (D'Argembeau, Lardi, & Van der Linden, 2012), and benefiting social relationships (Alea & Bluck, 2003). On the other hand, semantic memory is thought to underlie the objective, narrative continuity of the self, experienced via 'noetic' (i.e., 'knowing') consciousness (Tulving, 1972). This allows for the creation of a meaningful life story connecting past, present, and future selves. Personal facts and experiences may be weaved together via common themes, providing a narrative which one can retell, update, and create new meaning from (McAdams, 2001). Both forms of self-continuity, therefore, crucially contribute to an individual's functioning and wellbeing (Rathbone et al., 2015; Vanderveren et al., 2017).

Empirical studies of the contribution of episodic and semantic memory to continuity of the extended self have thus far been scarce (see Prebble et al., 2013). Of the limited studies to date, one approach has involved measurement of the self independently from episodic and/or semantic memory, with the relationship between the two subsequently explored (e.g., Addis & Tippett, 2004; Naylor & Clare, 2008). Reliable assessment of the abstract construct of the 'self', however, is inherently challenging (Caddell & Clare, 2010), and existing measures do not necessarily fit within proposed theoretical frameworks of the self, including the Neisser (1988) model (see Caddell & Clare, 2013). Substantial insights into the processes underlying subjective and narrative continuity may nonetheless be gleaned from studies of episodic and semantic memory on their own. In the following sections, the utility of contemporary memory measures for informing the characterisation of the extended self will be explored, including metrics of event specificity, contextual detail, the subjective phenomenological experience of remembering, and knowledge of autobiographical facts.

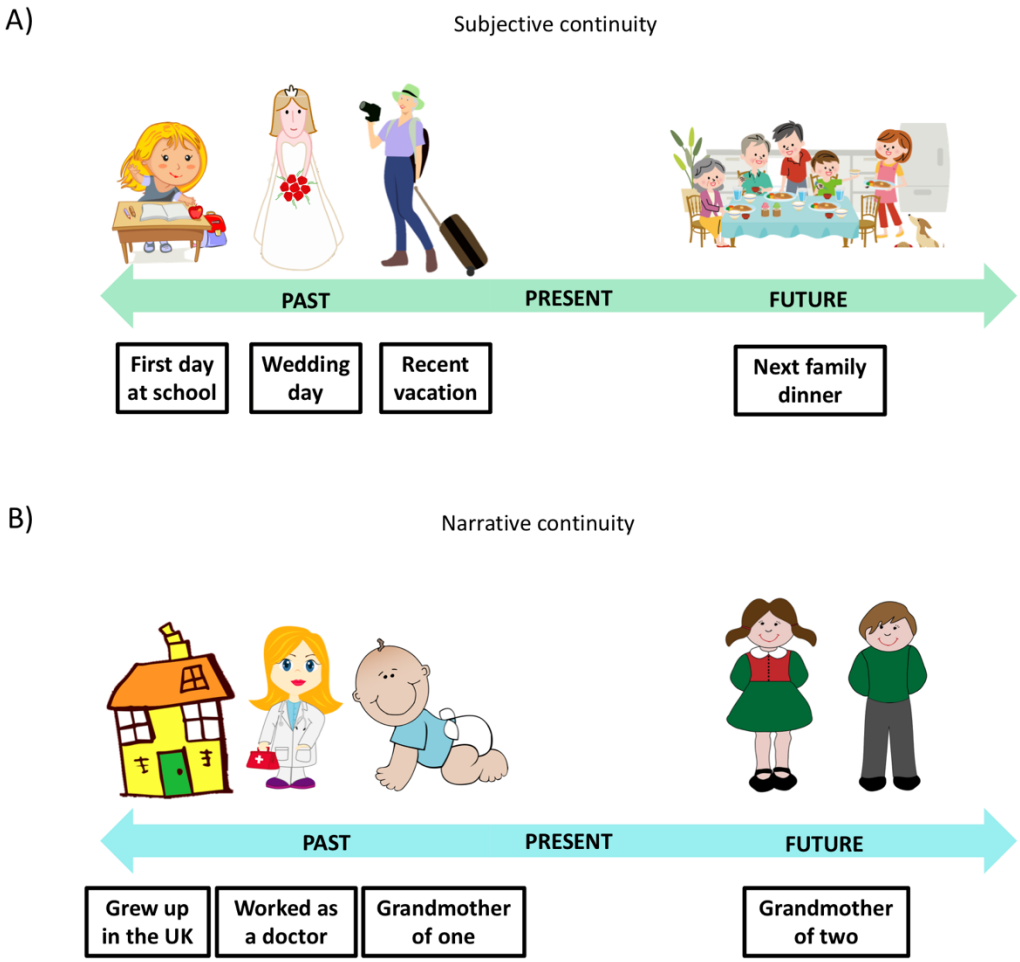



*Figure 1.1.* Theoretical model of the relationship between episodic and semantic memory and subjective and narrative continuity, as proposed by Addis and Tippett (2008); Haslam et al. (2011); Prebble et al. (2013). (A) Episodic re-experiencing of significant autobiographical events (e.g., first day at school, wedding day, a recent holiday) and pre-experiencing of potential self-relevant future occurrences (e.g., next family dinner) are proposed to give rise to a subjective sense of continuity of the extended self across time. (B) The weaving of personal facts from across the lifespan into a life story for one's past (e.g., grew up in the UK, worked as a doctor, and have one grandchild) and imagined future (e.g., becoming a grandmother of two) is believed to provide a sense of narrative continuity of the extended self, spanning past, present, and future.

### *"I was" – remembering the personal past*

Autobiographical memory (ABM) is defined as the recollection of personally-relevant past memories (Conway & Rubin, 1993). ABM involves rich sensory-perceptual and emotional episodic information, such as the specific details of one's wedding day, as well as abstracted semantic knowledge not specific to time or place, for example, the names of one's children (Greenberg & Verfaellie, 2010; Grilli & Verfaellie, 2014; Irish & Piguet, 2013; Renoult, Davidson, Palombo, Moscovitch, & Levine, 2012). To date, the majority of studies of ABM have focused on the episodic component, in recognition of its proposed importance for subjective self-continuity (Prebble et al., 2013). Traditionally, episodic ABM has been quantified by the specificity of a recollected past, personal event (i.e., whether it occurred at a specific time and place; e.g., the Autobiographical Memory Interview, AMI, Kopelman, Wilson, & Baddeley, 1989; TEMPau, Piolino, Desgranges, & Eustache, 2000). Scores on these tasks, however, are constrained by the limited range of the scoring systems, which are unable to distinguish between highly detailed, vivid episodic memories, versus those that are less detailed, but nonetheless specific (Barnabe, Whitehead, Pilon, Arsenault-Lapierre, & Chertkow, 2012). Furthermore, healthy participants often score at ceiling on the AMI (see Dritschel, Williams, Baddeley, & Nimmo-Smith, 1992), which may confound the results of patient-control comparison studies. Accordingly, more recent studies of ABM draw upon uncapped scoring systems (e.g., the Autobiographical Interview, AI, Levine, Svoboda, Hay, Winocur, & Moscovitch, 2002), which credit participants for the total number of episodic details generated, in acknowledgement of the central role of contextual details in vivid re-experiencing, and consequently, subjective continuity of the self. Such tools have been immensely popular and useful in advancing the understanding of episodic ABM (Levine, 2019). In addition to the amount of contextual details, however, insights into the subjective feeling of autonoetic reliving can also be gained from self-reports of the phenomenological experience of remembering (Irish, Lawlor, O'Mara, & Coen, 2008, 2011; Piolino, Desgranges, et al., 2003). As such, subjective reports of the degree of re-experiencing, the visual perspective of the memory (i.e., remembered through one's own eyes or from an observer perspective), and the emotional valence of retrieved memories can be used alongside measures of event specificity and level of detail to comprehensively assess subjective self-continuity.

While episodic expressions of ABM have received the most attention in relation to the extended self, the semantic component of ABM is also integral to self-continuity, by providing an 'objective' store of all that is known about the self (Klein, Loftus, & Kihlstrom, 2002). These semantic elements provide a sense of *narrative* self-continuity over time (Thomsen, 2009). Importantly, narrative self-continuity can be drawn upon to support the extended self even when its subjective counterpart is impoverished, for example in patients with amnesia (Grilli & Verfaellie, 2015; Ogden & Corkin, 1991; Rathbone, Moulin, & Conway, 2009). Accordingly, semantic memory can provide a sense of continuity of the extended self across time, without a need for autonoetic reliving, by creating a personal life story encompassing facts about oneself and abstractions of one's experiences (Prebble et al., 2013; Tippett, Prebble, & Addis, 2018). For example, such a narrative could incorporate that one grew up in the UK, moved to Australia, has three children, and enjoys classical music. Recent theoretical updates, however, contend that semantic ABM is not necessarily a unitary entity, but rather comprises subcomponents that vary in their relative degree of 'episodicity' or 'semanticity'. By this view, episodic and semantic memory lie at opposite ends of a continuum, with memories of repeated or extended episodes ('general event' memories), and highly abstracted knowledge regarding personal traits and facts about oneself ('personal semantics'), falling in between these two extremes (Figure 1.2., Grilli & Verfaellie, 2014; Renoult et al., 2012) (see also Conway's 'self memory system' model, Conway & Pleydell-Pearce, 2000). General event memories refer to episodes that have been repeated a number of times (e.g., "I used to go dancing every Friday") (also known as 'summarised events', Barsalou, 1988; or 'repisodes', Neisser, 1981), or span an extended time period (e.g., "I worked in the city for a few years") (also known as 'lifetime periods', Conway & Pleydell-Pearce, 2000). Both general events and personal semantics may draw upon either episodic or semantic memory for their retrieval (Grilli & Verfaellie, 2016), which may explain the relative ease of access to this form of autobiographical information (Conway, 1996). Importantly, each of the dimensional elements of semantic memory impart crucial contributions to narrative continuity of the extended self (Conway & Pleydell-Pearce, 2000; Grilli & Verfaellie, 2015; Prebble et al., 2013).

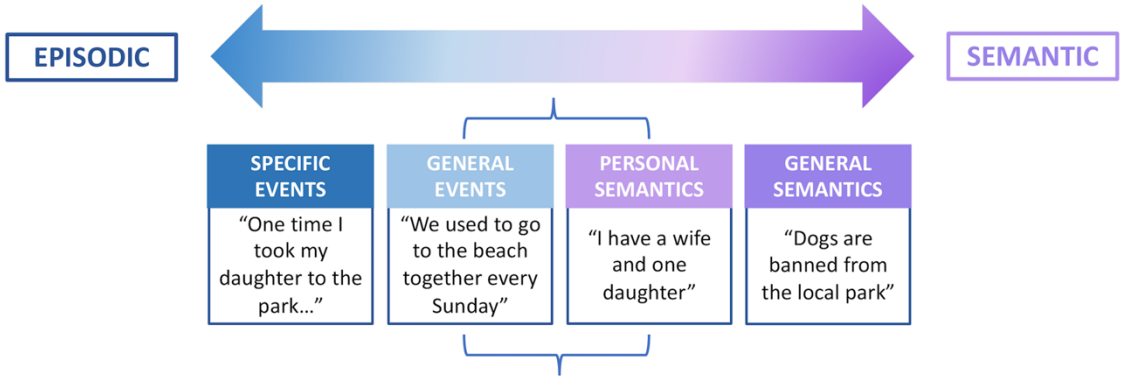



*Figure 1.2.* The episodic-semantic-continuum of autobiographical memory (ABM), informed by Grilli and Verfaellie (2014); Renoult et al. (2012). General events (i.e., repeated or extended episodes) and personal semantics (i.e., trait knowledge and autobiographical facts) lie at the intersection of episodic and semantic ABM (represented by brackets), and may draw upon either, or both, forms of memory for their retrieval.

Studies of general event memory typically examine the specificity of recollected personal episodes (e.g., on the AMI, Kopelman et al., 1989), with the provision of more general, abstract events (i.e., not occurring at a specific time or place) interpreted as reflecting spared general event ABM. Personal semantic memory, on the other hand, is usually measured via the direct probing of autobiographical facts or personal traits, for example, asking where one went to school (Kopelman et al., 1989), or whether they are a kind person (Wiggins, 1995). The intact recall of personal semantic facts or general events alone, however, is not sufficient to provide a sense of self-continuity, which also requires integration of this information into a coherent narrative (McAdams, 2001). Accordingly, ecologically valid measures, incorporating naturalistic autobiographical narratives, are likely to provide the most sensitive and comprehensive characterisation of narrative continuity of the extended self.

***"I will be" – imagining the personal future***

While Neisser's (1988) original framework clearly articulates that the self extends into the future, the majority of empirical studies of the extended self exclusively focus on memory for the past. This is despite much of our waking life consisting of planning and imagining our personal future, simulating hypothetical situations, and foreseeing different outcomes (Andrews-Hanna, Reidler, Huang, & Buckner, 2010). From an evolutionary perspective, the

ability to envisage personally-relevant future events is of great adaptive value (Suddendorf, Addis, & Corballis, 2009), and provides a sense of temporal persistence of the self that is integral for wellbeing (Chandler, Lalonde, Sokol, & Hallett, 2003). Furthermore, projecting oneself into the future via the simulation of self-relevant events can be used to define the extended self across time (D'Argembeau et al., 2012; Rathbone, Conway, & Moulin, 2011), with imagined future events considered even more important for fostering one's sense of self than memories for past events (Berntsen & Bohn, 2010). Indeed, in the cognitive neuroscientific literature, the last decade has seen growing interest in the processes underlying the imagination of future events. The most popular tool for assessing episodic future thinking is the Past-Future task (Addis, Wong, & Schacter, 2008), which employs the Autobiographical Interview (AI, Levine et al., 2002) scoring method to examine the amount and type of detail provided across both remembered past and imagined future events. Studies employing this method have revealed striking parallels between episodic memory and episodic future thinking, including overlapping cognitive and neural mechanisms (Addis, Wong, & Schacter, 2007; Hassabis, Kumaran, Vann, & Maguire, 2007; Szpunar, Watson, & McDermott, 2007). Furthermore, patients with episodic memory impairments display significant difficulty with imagining future events, including amnesic patients with medial temporal lobe (MTL) damage (Race, Keane, & Verfaellie, 2011), mild cognitive impairment (Gamboz et al., 2010), and Alzheimer's disease (Addis, Sacchetti, Ally, Budson, & Schacter, 2009; Irish, Addis, Hodges, & Piguet, 2012a, considered further in Section 1.2.3., below). Collectively, these findings reveal the crucial importance of episodic memory in the simulation of future events, leading to the proposal of the 'constructive episodic simulation hypothesis' (Schacter & Addis, 2007a, 2007b). By this view, imagining novel, self-relevant future events involves the flexible recombination of contextual details from previous experiences in order to create a new simulation.

More recent findings, however, have also uncovered a pivotal role for semantic memory in supporting the capacity to envisage future events (reviewed by Irish & Piguet, 2013). Individuals with developmental amnesia have been demonstrated to retain the ability to imagine future events, notwithstanding profound deficits in episodic memory (Hurley, Maguire, & Vargha-Khadem, 2011; Maguire, Vargha-Khadem, & Hassabis, 2010). Even more strikingly, patients with semantic dementia, despite displaying preserved recall of recent

events, experience marked impairments in imagining future episodes on the Past-Future task (Duval, Desgranges, et al., 2012; Irish, Addis, et al., 2012a; Irish, Addis, Hodges, & Piguet, 2012b, described in detail in Section 1.2.3., below). These findings have led to the development of the 'semantic scaffolding hypothesis', which proposes that the imagination of personally-relevant future episodes draws upon semantic scripts, representations, and schemas (i.e., higher-order knowledge structures), which guide one along a prescribed path of typical life events (Irish, 2016; Irish & Piguet, 2013). In doing so, these semantic representations provide a scaffold for the generation of self-relevant future events that may plausibly occur. Accordingly, while there has been a tendency to view subjective self-continuity for the past as predominantly reliant upon episodic memory, this line of research suggests that semantic representations may be equally important as their episodic counterpart for simulating future events, and perhaps, therefore, for subjectively experiencing the self in the future (see also Klein, 2013). Such a view challenges the episodic-subjective/semantic-narrative dichotomy of self-continuity previously proposed (Addis & Tippett, 2008; Prebble et al., 2013). In comparison to studies of episodic future thinking, however, there has been less empirical investigation into the objective, narrative experience of the self in the future, that is, imagining one's prospective life story (e.g., becoming a grandmother of two; Figure 1.1.). Moreover, the limited existing research on this topic has predominantly involved the direct probing of personal roles or traits that may emerge in the future, and associated potential future events (Chessell, Rathbone, Souchay, Charlesworth, & Moulin, 2014; Rathbone et al., 2011), rather than capturing the ability to weave facts about the self into a coherent future narrative. As such, developing and employing naturalistic measures of narrative self-continuity will be of utmost importance for improving the characterisation of the extended self, across both past and future.

***The neural signature of the extended self***

Traditionally, the endeavour of cognitive neuroscience was to localise psychological processes to specific brain regions (Downing, Jiang, Shuman, & Kanwisher, 2001; Kanwisher, McDermott, & Chun, 1997). This approach, incorporating both neuroimaging and patient lesion studies, has been extremely valuable in helping delineate the functions of discrete brain areas. For example, the famous case of H.M., in which surgical removal of the bilateral hippocampi rendered the patient amnesic (Scoville & Milner, 1957), was seminal in advancing

our understanding of the crucial role of the MTL in episodic memory. In more recent years, however, neuroscientific research has undergone a paradigmatic shift, away from examining the function of isolated brain areas, and toward investigating how the integrated activity of entire neural networks gives rise to complex psychological processes (Bressler & Menon, 2010). One of the most well-known functional brain networks is the so-called 'default mode network' (DMN), which comprises frontal and parietal cortical midline regions, medial and lateral temporal lobes, and lateral parietal cortex (Buckner, Andrews-Hanna, & Schacter, 2008; Buckner & DiNicola, 2019). The DMN was initially discovered by chance, via the observation of coherent and consistent patterns of brain activity during resting periods in functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) studies (Greicius, Krasnow, Reiss, & Menon, 2003; Raichle et al., 2001). Since this time, however, rigorous research efforts have focused on uncovering the function of the DMN, ultimately revealing its central role in self-related cognition (Andrews-Hanna, 2012). Neuroimaging studies reveal reliable activation of the DMN during tasks involving the processing of self-relevant information, including ABM and episodic future thinking, moral reasoning, and theory of mind (Spreng, Mar, & Kim, 2009). Furthermore, activity of the DMN at rest has been demonstrated to scale with the degree to which one reports internally-directed thoughts while lying in the scanner (Mason et al., 2007). Together, these findings point to an important contribution of the DMN to the representation of the self in the brain.

Given the robust activation of the DMN during both episodic autobiographical retrieval and episodic future thinking (Spreng et al., 2009), this network may be assumed to support subjective continuity of the self. Indeed, this same set of brain regions has been previously described as the 'autobiographical retrieval' (Maguire, 2001) or 'episodic recollection' (Rugg & Vilberg, 2013) network. While some differences have been elicited in DMN activations during past retrieval versus future simulation, it is thought these are in fact attributable to differences in the amount and familiarity of details comprising the event, rather than its temporal orientation *per se* (Addis & Schacter, 2008; Addis, Wong, et al., 2007). Specific regions of the DMN have been ascribed unique functions in supporting both past and future thinking. The hippocampus has long been recognised as critical for supporting episodic memory (Scoville & Milner, 1957), and more recently, episodic future thinking (Hassabis et al., 2007). Its precise role in these endeavours, however, remains debated, with leading views

proposing the hippocampus may be involved in constructing a spatially-coherent scene in one's mind's eye (Hassabis & Maguire, 2007), and/or the flexible, relational processing of disparate information into event simulations (Schacter & Addis, 2007a). Cortical midline structures, namely medial prefrontal (mPFC) and posterior cingulate cortices (PCC) are argued to play a key role in self-referential processing in general, which also extends to episodic ABM and simulation (Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010; Northoff & Bermpohl, 2004). The anterolateral temporal cortex is believed to contribute the semantic component to episodic construction (Irish, Addis, et al., 2012a), while the angular gyrus may play a role in the contextual integration (Ramanan, Piguet, & Irish, 2018; Rugg & King, 2018) and/or controlled retrieval of the content of the simulation (Cabeza, Ciaramelli, Olson, & Moscovitch, 2008).

Emerging views, however, propose the parcellation of the DMN into two subsystems, which each play a distinct role in episodic ABM and future simulation (Ranganath & Ritchey, 2012; Robin & Moscovitch, 2017; Sheldon & Levine, 2016). This perspective is informed by the divergent profiles of structural and functional connectivity of the anterior versus posterior hippocampus (Adnan et al., 2016), together with the graded functional specialisation of this structure along its long axis (Poppenk, Evensmoen, Moscovitch, & Nadel, 2013). By this view, the anterior hippocampus, together with the anterior temporal lobes (ATLs) and mPFC, are thought to contribute coarse, global representations, such as the semantic and schematic elements of events (Mack, Love, & Preston, 2016; McCormick, St-Laurent, Ty, Valiante, & McAndrews, 2013). By contrast, the posterior hippocampus is tightly connected to posterior cortical regions associated with perceptual processing, such as medial and lateral parietal regions, including PCC, precuneus, and angular gyrus. Collectively, the posterior DMN is proposed to lend the fine-grained, sensory-perceptual episodic details during event retrieval or imagination (Adnan et al., 2016; McCormick et al., 2013). Such anterior-posterior distinctions form a useful heuristic, however the additional roles of these brain regions (described above) should also be considered when conceptualising the neurocognitive contributions to subjective continuity of the self.

While the neural signature of episodic ABM and future simulation has been relatively well established, the brain regions supporting different forms of semantic ABM, and therefore

narrative continuity of the self, have received comparatively less attention (reviewed by Renoult et al., 2012). Nonetheless, emerging evidence suggests autobiographical facts, self-knowledge, and repeated events may all rely upon mPFC and lateral temporal lobes (Addis, McIntosh, Moscovitch, Crawley, & McAndrews, 2004; Addis, Moscovitch, Crawley, & McAndrews, 2004; Gilboa et al., 2005; Holland, Addis, & Kensinger, 2011; Levine et al., 2004; Maguire & Frith, 2003; Maguire & Mummery, 1999; Schroeter, Ettrich, Menz, & Zysset, 2010; Zysset, Huber, Samson, Ferstl, & von Cramon, 2003). This is consistent with the established role of the mPFC in self-referential processing (Northoff et al., 2006), and the importance of the ATLs for semantic memory (Binder, Desai, Graves, & Conant, 2009), along with the implication of both of these regions in the representation of schemas (Gilboa & Marlatte, 2017). Along with the mPFC and ATLs, however, knowledge of personal traits is thought to also recruit the precuneus and lateral parietal lobes (Schroeter et al., 2010; Zysset et al., 2003), while mPFC, ATL, medial temporal and lateral parietal regions are all involved in the retrieval of repeated events (Addis, McIntosh, et al., 2004; Addis, Moscovitch, et al., 2004; Holland et al., 2011; Levine et al., 2004). Of note, the regions implicated in different forms of personal semantic memory intersect with those associated with episodic ABM and future thinking (described above), further reinforcing the overlap and interplay between the episodic and semantic memory systems.

### 1.2.2. Neurodegenerative lesion models of the extended self: Clinical and neuroimaging profiles

Alzheimer's disease (AD) and semantic dementia (SD) are contrasting disorders, characterised by stark impairments in episodic and semantic memory, respectively. As such, these syndromes permit the examination of how changes in these distinct forms of memory affect the extended self. The following section outlines the clinical, pathological, and neuroimaging characteristics of AD and SD.

#### *Alzheimer's disease (AD)*

*Clinical presentation*

Alzheimer's disease (AD) is the most common cause of dementia (Brown, Hansnata, & La, 2016). While most patients with AD present with an amnestic syndrome, other, less common

non-amnestic variants of AD also exist, characterised by prominent deficits in language (i.e., logopenic progressive aphasia), visuospatial abilities (i.e., posterior cortical atrophy), or executive function (i.e., dysexecutive AD) (McKhann et al., 2011). In this thesis, however, only the amnestic form of AD will be considered further. Clinically, patients with typical AD present with pronounced deficits in episodic memory, involving an impaired ability to encode and store recently learnt information (Salmon & Bondi, 2009), along with varying degrees of semantic, visuospatial, and executive dysfunction (McKhann et al., 2011). By contrast, socioemotional functioning is generally preserved in the early stages of AD (F. Zhang, Ho, & Fung, 2015).

*Neuropathological and neuroimaging features*

Neuropathologically, AD is characterised by extracellular plaques and intracellular neurofibrillary tangles, caused by the abnormal accumulation of beta-amyloid and tau, respectively (Braak & Braak, 1991). The distribution and spread of these pathological abnormalities occurs in a coordinated manner, beginning in the MTLs (namely transentorhinal, entorhinal, and hippocampal areas), before reaching more widespread neocortical regions (Braak & Braak, 1991). Consistent with this pathological progression, structural neuroimaging reveals initial atrophy in AD in hippocampal and transentorhinal regions, which progresses to lateral temporal, medial and lateral parietal (i.e., PCC and precuneus), and frontal brain regions (Karas et al., 2004; Vemuri et al., 2008) (Figure 1.3.). By contrast, the earliest functional changes are apparent in inferior parietal lobule and precuneus, with hypometabolism in these regions observed using fluorodeoxyglucose (FDG)-PET imaging (Schroeter, Stein, Maslowski, & Neumann, 2009). Of note, many of the regions affected by AD form part of the DMN. Reduced resting-state functional connectivity has been found within this network in AD (Buckner et al., 2005; Zhou et al., 2010), particularly its posterior components (Jones et al., 2016). Importantly, the structural and functional changes that occur with the progression of AD map closely to the trajectory of cognitive decline (Buckner et al., 2005; Thompson et al., 2007).

### *Semantic dementia (SD)*

*Clinical presentation*

Semantic dementia (SD), also known as the semantic-variant of primary progressive aphasia, falls under the umbrella of frontotemporal dementia (FTD), a collection of syndromes involving atrophy of the frontal and/or temporal lobes. SD is one of two language variants of FTD, and is characterised by a fluent aphasia, which reflects a progressive, amodal disruption of conceptual or semantic knowledge (Gorno-Tempini et al., 2011). This presents as impairments in confrontation naming and single-word comprehension (Hodges & Patterson, 2007). Episodic memory, by contrast, remains relatively intact in SD, specifically when non-verbal stimuli are employed (Irish, Bunk, et al., 2016; Simons, Graham, & Hodges, 2002). Behavioural changes, such as interpersonal difficulties and rigidity, can arise in SD with disease progression (Snowden et al., 2001), particularly with progression of atrophy from the left to right hemispheres (see further below).

*Neuropathological and neuroimaging features*

From a neuropathological perspective, the majority of cases of SD are produced by the deposition of TAR DNA binding protein 43 (TDP-43) (Chare et al., 2014; Hodges et al., 2004). Brain atrophy and hypometabolism are asymmetric and primarily circumscribed to the ATLs, incorporating the temporal pole, fusiform gyrus, and perirhinal cortex, but also extend postero-medially into the insula, and MTLs, including anterior hippocampus and amygdala (Chapleau, Aldebert, Montembeault, & Brambati, 2016; Rosen et al., 2002) (Figure 1.3.). As such, SD predominantly affects anterior DMN regions, with the posterior subnetwork relatively spared. Most patients with SD present with disproportionate atrophy of the left hemisphere (Galton et al., 2001), which encroaches into the right hemisphere with disease progression (Kumfor, Landin-Romero, et al., 2016). A subset (~25%) of SD patients harbour predominantly right-sided atrophy early in the disease course (Hodges et al., 2009), though for the purposes of this thesis, only the canonical left-sided patients will be included.

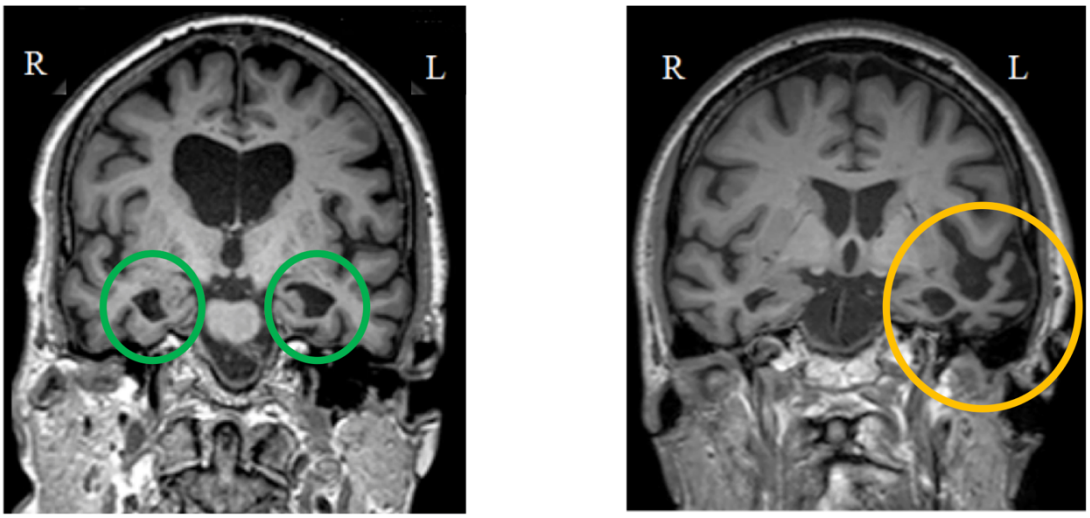



*Figure 1.3.* Coronal magnetic resonance imaging (MRI) scans displaying typical patterns of atrophy, most pronounced in the bilateral medial temporal lobes in Alzheimer's disease (AD; left) and left anterior temporal lobe in semantic dementia (SD; right). R = right; L = left.

### 1.2.3. The extended self in Alzheimer's disease and semantic dementia

Studies examining ABM and episodic future thinking in AD and SD will now be reviewed. Particular consideration will be given to the potential of these findings to inform understanding of the contribution of episodic and semantic memory to subjective and narrative self-continuity, and the neural networks involved. Importantly, along with the memory metrics outlined in Section 1.2.1., convergent evidence regarding observable manifestations of the extended self (i.e., actions, preferences, and interactions) in AD and SD will also be drawn upon to support these claims.

#### *"I was" – remembering the past*

In addition to deficits in learning and recalling new information, patients with AD have well-established difficulties with retrieving personally-relevant events from their past (i.e., episodic ABM). The precise nature of these impairments, however, has proven difficult to decipher, given discrepancies in the profiles of episodic ABM in AD, contingent upon the assessment method employed. When the AMI (Kopelman et al., 1989) is used, the majority of studies suggest a temporal gradient of event recall in AD, with impaired retrieval of recent events (i.e., in the past year), in the context of relatively intact remote recall (Barnabe et al.,

2012; De Simone et al., 2016; Graham & Hodges, 1997; J. W. D. Greene, Hodges, & Baddeley, 1995; Irish et al., 2006; Irish, Lawlor, et al., 2011; Kirk & Berntsen, 2018; Leyhe, Muller, Milian, Eschweiler, & Saur, 2009; Müller et al., 2013; Naylor & Clare, 2008; Piolino, Desgranges, et al., 2003; Seidl, Lueken, Thomann, Geider, & Schroder, 2011). Such findings are in accordance with Ribot's law, which suggests that in amnesia, recent memories are more likely to be lost than more remote ones (Ribot, 1881). Using the uncapped scoring system of the AI (Levine et al., 2002), by contrast, fails to produce this temporal gradient, with a relatively flat profile of episodic ABM impairment found across all lifetime periods in AD (Addis et al., 2009; Barnabe et al., 2012; Irish, Hornberger, et al., 2014; Irish, Hornberger, et al., 2011; Irish et al., 2018). As discussed in Section 1.2.2., this measure is likely to provide a more valid assessment of subjective self-continuity than the AMI, given its emphasis on the contextual details thought necessarily for vivid re-experiencing. Indeed, findings on the AI are consistent with the marked alterations in the phenomenological experience of remembering in AD, which are apparent for all lifetime periods. AD patients report no longer mentally reliving their past memories, instead stating that they simply "know" the events to have taken place (Piolino, Desgranges, et al., 2003). Other elements of autonoetic re-experiencing are also compromised in AD, including first-person self-referential imagery and emotional salience (Irish, Lawlor, et al., 2011). Accordingly, memories of pivotal experiences from across the lifespan, such as one's wedding day, birth of a child, or death of a parent, become impoverished in detail, and lack a sense of having lived through the event. Taken together, these findings suggest that subjective self-continuity for the past may be impaired across all time periods in AD.

Although SD primarily involves the progressive deterioration of the conceptual knowledge base, studying this group nonetheless provides insights into the relationship between episodic ABM and subjective continuity of the extended self. In contrast to AD, recent episodic retrieval is relatively intact in SD, with these patients typically displaying detailed recollection of recent episodes, regardless of the assessment method employed (i.e., AMI versus AI; Graham & Hodges, 1997; Hou, Miller, & Kramer, 2005; Irish, Hornberger, et al., 2011; Piolino, Desgranges, et al., 2003). Furthermore, SD patients report a preserved sense of mental reliving for these recent events (Piolino, Belliard, Desgranges, Perron, & Eustache, 2003; Piolino, Desgranges, et al., 2003). By contrast, memory for remote episodes is largely

impoverished in specificity and detail in SD (Graham & Hodges, 1997; Hou et al., 2005; Irish, Hornberger, et al., 2011), interpreted as reflecting the semanticisation of episodic experiences that can occur with the passage of time (Moscovitch, Nadel, Winocur, Gilboa, & Rosenbaum, 2006). While SD patients report autonoetically re-experiencing these remote events, the validity of such accounts is questionable given they are unable to provide sufficient contextual details to adequately justify this sense of remembering (Piolino, Belliard, et al., 2003; Piolino, Desgranges, et al., 2003). As such, a degree of subjective continuity of the extended self appears retained in SD, though this is likely limited to a narrow temporal window (i.e., the past year). Intriguingly, this temporal tapering of the subjective self in SD as uncovered by studies of ABM is also supported by behavioural observations in these patients. Individuals with SD are commonly reported to display rigid and stereotypical behaviours (Ahmed et al., 2014; Perry et al., 2001; Rosen et al., 2006), and often develop a strong preference for routine, such as wearing the same clothes, or insisting on attending the same café, and eating the same lunch, at the same time, every day. This over-reliance on recent events to guide behaviour in SD may stem from the ability to subjectively re-experience the self exclusively within the recent past. Together, the findings in SD suggest that episodic and semantic ABM may differentially contribute to subjective continuity of the self for the past, contingent upon the time period in question. While the subjective experience of the self in the recent past may predominantly draw upon episodic ABM, the additional contribution of semantic ABM may be particularly important for subjective self-continuity for the remote past.

With regard to semantic ABM, direct probing of personal semantic information reveals impaired retrieval of autobiographical facts in AD (e.g., Barnabe et al., 2012; Graham & Hodges, 1997; Irish et al., 2006; Irish, Lawlor, et al., 2011), but relatively preserved knowledge of personal traits (Addis & Tippett, 2004; M. L. Eustache et al., 2013; Klein, Cosmides, & Costabile, 2003; Rankin, Baldwin, Pace-Savitsky, Kramer, & Miller, 2005; Ruby et al., 2009). Temporal gradients are evident for both types of personal semantics in AD, such that self-knowledge about the recent past is particularly impaired, including being unable to recall recent facts about oneself (e.g., having new grandchildren; Kazui et al., 2000), or recent changes to one's personality that have been reported by close others (e.g., becoming less self-assured; Hehman, German, & Klein, 2005; Klein et al., 2003). Nonetheless, knowledge

about the self from the distant past, such as the location of their childhood home, the university they attended, and their premorbid personality, remains relatively resilient in AD (Hou et al., 2005; Rankin, Baldwin, et al., 2005). General event memory is also typically found to be preserved in AD (Irish, Lawlor, et al., 2011; Philippi et al., 2015). For example, an individual with AD can recall that they went dancing every Friday during their twenties, despite being unable to provide a detailed description of one particular instance. Taken together, this literature suggests that AD patients retain some access to the semantic elements required to provide narrative continuity of the self, though this is predominantly limited to remote time periods, leading to an extended self that is largely anchored on the remote past (i.e., childhood & early adulthood periods, see Addis & Tippett, 2004; Tippett et al., 2018). Intriguingly, the relative preservation of remote personal semantics, coupled with the episodic encoding impairments in AD, results in a mismatch between the period of life they believe they are in, and objective reality. For example, AD patients may rate their current age as younger than they actually are (M. L. Eustache et al., 2013), and fail to recognise themselves in a mirror (Biringer & Anderson, 1992). Behavioural observations of patients returning to previous life roles (e.g., a former doctor continuing to write reports) or mistaking family members (e.g., looking for their young children, who are in fact now grown up) (B. E. Harrison, Therrien, & Giordani, 2005) provide convincing illustrations of how the extended self is not lost in AD *per se*. Rather, the individual may revert to an older iteration of the self that is incongruent with their present experience and surroundings. Together, the extant findings in AD suggest that, as for subjective self-continuity, the relative contribution of episodic and semantic memory to narrative self-continuity for the past may vary depending upon the particular epoch in question. Specifically, while narrative self-continuity for the remote past may predominantly rest upon semantic memory, episodic memory may be particularly important for narrative continuity for the recent past, in order to lay down new facts about oneself. When episodic memory is impaired, as is the case in AD, narrative continuity of the self for the recent period is subsequently disrupted.

Unsurprisingly, the gross semantic impairments in SD extend to the retrieval of autobiographical facts (e.g., where they went to school), resulting in 'step function', such that recent facts are better preserved than those from the remote past (Graham & Hodges, 1997; Hou et al., 2005; Nestor, Graham, Bozeat, Simons, & Hodges, 2002). Although this evidence

suggests some preservation of 'personal semantic' memory in SD for the recent past, it has been proposed that these so called 'facts' may actually instead reflect the retrieval of recent experiences (e.g., remembering the conversation in which they were told a new grandchild's name), and therefore draw upon predominantly episodic, rather than semantic, memory representations (Graham, Lambon Ralph, & Hodges, 1997; McKinnon, Black, Miller, Moscovitch, & Levine, 2006; Snowden, Griffiths, & Neary, 1994; Westmacott & Moscovitch, 2003). Nonetheless, these memories likely touch on activities, people, or places that can provide a sense of continuity with the recent past, at a factual level. Preserved recent episodic ABM may therefore support a degree of narrative continuity in SD, though this is restricted to the recent period. These observations marry well with those in AD, suggesting an increased importance of episodic ABM for narrative continuity for the recent, but not remote, past.

***"I will be" – imagining the future***

Despite the established importance of imagining the future for maintaining a sense of self-continuity (D'Argembeau et al., 2012), surprisingly little empirical research has been conducted on this topic in AD and SD. Of the limited studies to date, the deficits in episodic retrieval for the past in AD have been found to extend to the imagination of future events, in line with the constructive episodic simulation hypothesis (Addis et al., 2009; Irish, Addis, et al., 2012a). In the context of such striking alterations in the content of future simulations in AD, however, the phenomenological components of these events have proven more difficult to decipher. Interestingly, subjective quality ratings of vividness and level of detail for future events do not differ between AD and control participants (Addis et al., 2009; Irish, Addis, et al., 2012b). Nonetheless, the impoverished episodic content of future simulations implies a narrowing of the temporal window of subjective continuity of the extended self in AD. This assertion is supported by the impairments in prospective memory (Kamminga, O'Callaghan, Hodges, & Irish, 2014; van den Berg, Kant, & Postma, 2012), planning, and adaptive decision making (Gleichgerrcht, Ibanez, Roca, Torralva, & Manes, 2010) observed in AD. Collectively, the findings in AD further suggest an important role for episodic memory in subjective-self continuity for the future.

Interestingly, however, despite preserved recall of recent episodes in SD, future thinking is compromised in these patients (Duval, Desgranges, et al., 2012) at a level comparable to that

seen in AD (Irish, Addis, et al., 2012a, 2012b). This reveals the central importance of semantic memory in imagining future episodes (Irish, 2016; Irish & Piguet, 2013), and therefore, subjectively experiencing the self in the future. As for AD, subjective quality ratings of simulated future events do not differ between SD and controls (Irish, Addis, et al., 2012b). When attempting to imagine the future, however, SD patients frequently 're-cast' entire events from one's past, that is, they describe exact events that they have already experienced (Irish, 2016; Irish, Addis, et al., 2012a, 2012b). Any apparent preservation of autonoetic continuity for future simulations in SD may therefore stem from having already experienced the event in the recent past. As such, while individuals with SD retain some sense of subjective self-continuity for the recent past, this heavily influences their experience of the self in the future. This meshes well with the aforementioned behavioural rigidity in this condition. Further supporting this notion, impaired prospection has been associated with increased stereotypical and repetitive behaviours in SD (Kamminga et al., 2014). Importantly, changes to subjective continuity of the future self may significantly impact mental wellbeing, potentially to an even greater degree than for the past. A pertinent case study by Hsiao, Kaiser, Fong, and Mendez (2013) describes a patient with SD who loses the ability to imagine his future self, leading to marked distress and suicidality as he questions, "What am I going to do for the rest of my life?" (p 3). Taken together, the evidence from AD and SD points to distinct mechanisms underlying the extended self for past versus future epochs (Figure 1.4.). Namely, while subjective self-continuity for the recent past may predominantly depend upon episodic memory, semantic representations may additionally be particularly important for remote past and future time periods. Moreover, narrative self-continuity for the remote past may largely require semantic memory, with episodic memory also especially important for the recent past.

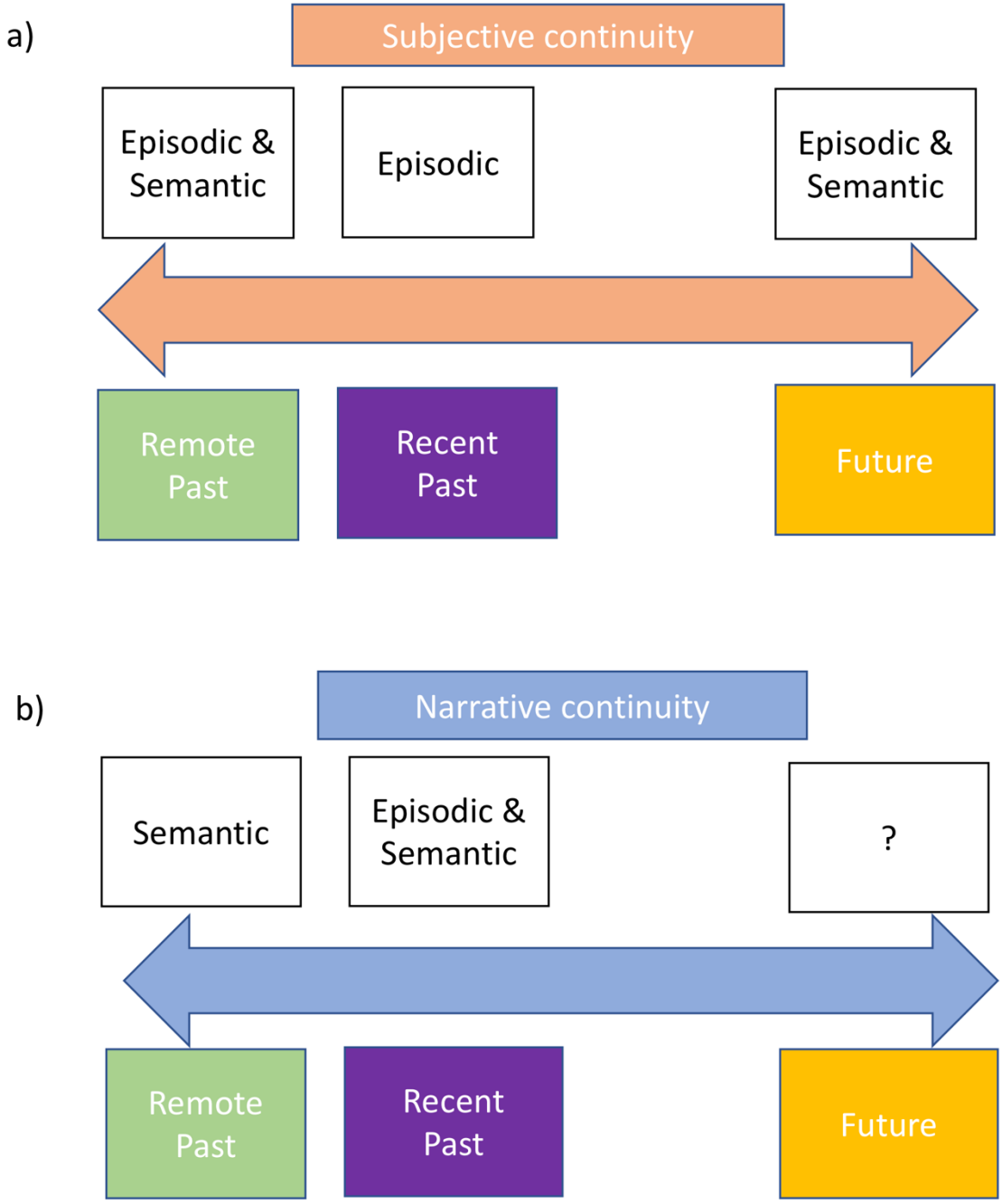



*Figure 1.4.* Updated model of the relationship between episodic and semantic memory and a) subjective and b) narrative continuity of the extended self, based on the extant literature in Alzheimer's Disease (AD) and semantic dementia (SD). a) While subjective continuity for the recent past may predominantly draw upon episodic memory, semantic representations may additionally be particularly important for this form of self-continuity for remote past and future time periods. b) Narrative continuity for the remote past is proposed to principally

require semantic memory, although episodic memory may also be especially involved for the recent past. Narrative self-continuity for the future remains to be examined.

***Neural correlates of the extended self in AD and SD***

In AD, impairments in episodic ABM have been associated with atrophy to the MTLs (Gilboa et al., 2005). Specifically, smaller hippocampal volumes correspond to worse episodic ABM in AD, for both recent and remote periods (Meulenbroek, Rijpkema, Kessels, Rikkert, & Fernandez, 2010; Philippi et al., 2012). In addition, atrophy to other nodes of the DMN, namely left lateral temporoparietal, and posterior cingulate cortices, along with extra-DMN regions such as bilateral frontal lobes, have been linked to impairments in recent episodic ABM in AD (Irish, Addis, et al., 2012a). A decline in both remote and recent episodic ABM over time in AD is also related to progressive cortical thinning in lateral temporal cortex (Irish et al., 2018), likely reflecting semanticisation of episodic ABMs in AD. In conjunction with these patterns of atrophy, increased recruitment of frontal regions is observed during autobiographical retrieval in AD, including mPFC and left inferior frontal gyrus (IFG) in an fMRI study (Meulenbroek et al., 2010), and bilateral lateral prefrontal cortices in a PET study (F. Eustache et al., 2004), potentially in attempt to compensate for degradation to other brain regions. By contrast, no studies to date have examined the neural correlates of semantic ABM in AD. Overall, the regions implicated in episodic ABM in AD span regions typically associated with both episodic and semantic memory, which underscores the coalescing of these elements in subjective continuity of the self for the past. On the other hand, in line with the proposed importance of episodic memory for the imagination of future events, deficits in episodic future thinking in AD are predominantly associated with atrophy to the DMN, namely medial temporal and posteromedial regions (Irish, Addis, et al., 2012a).

In SD, impairments in remote episodic ABM are often attributed to progressive atrophy to the ATLs, reflective of the semanticisation of memories over time (Westmacott, Leach, Freedman, & Moscovitch, 2001), though this has not been directly examined. A single case study suggested that when episodic ABM is intact in SD, such as for recent memories, it is underpinned by a similar network to that employed by healthy controls (i.e., medial and lateral temporal, mFPC, posterior medial and lateral cortical regions) (Maguire, Kumaran, Hassabis, & Kopelman, 2010). Finally, in a group of SD, AD, and bvFTD patients combined, the

structural integrity of the ATLs was related to remote episodic ABM retrieval (Irish, Hornberger, et al., 2014). Taken together, albeit preliminary, this evidence suggests that the brain regions necessary for subjective continuity of the self may vary contingent upon the time period in question, with the ATLs likely more pertinent for the remote versus recent past. Similar to AD, the neural networks involved in semantic ABM in SD remain to be explored. With regard to future thinking, impairments in SD have been associated with atrophy to anterior and lateral temporal lobes in SD (Irish, Addis, et al., 2012a), consistent with the emerging importance of semantic memory for subjective continuity of the self in the future. Atrophy to the anterior hippocampus and bilateral superior medial frontal gyrus, and hyperactivation in frontal and occipital regions during fMRI, have also been related to episodic future thinking impairments in SD, though the task used in this study provided pre-determined cues for each simulated event, generated by the patients' informants (Viard et al., 2014). In doing so, this removed the requirement to invoke a semantic scaffold (Irish, 2016), rendering it difficult to compare these findings to others using the traditional, un-cued future thinking task. Taken together, the neuroimaging findings in AD and SD support the behavioural findings reviewed above, by suggesting that the neural networks involved in subjective continuity of the self for the past and future incorporate brain regions typically implicated in both episodic and semantic memory, with particular support for involvement of semantic networks for the remote past and future.

### 1.2.4. Summary and aims of Part 1

The studies of AD and SD reviewed thus far emphasise the complex relationship between episodic and semantic memory and the subjective and narrative components of the extended self, which appears to vary across different lifetime periods. Based on this literature, an update to the Prebble et al. (2013) model is proposed in Figure 1.4. A number of outstanding theoretical and methodological issues, however, remain, which constrain current conceptualisations of the extended self. First, previous work on ABM and episodic future thinking, including in AD and SD, has typically dissected episodic from semantic elements, treating these constructs as dissociable entities. This tendency to fractionate episodic and semantic memory, however, overlooks the many ways in which the two memory systems interact during ABM retrieval and future thinking (Greenberg & Verfaellie, 2010; Irish & Piguet, 2013; Renoult et al., 2019). Second, despite recent theoretical updates proposing a

continuum between episodic and semantic memory (Grilli & Verfaellie, 2014; Renoult et al., 2012), no single measure exists which enables empirical investigation of this framework. Third, while semantic ABM has often been assessed via the direct probing of personal facts, some integration of this information into a coherent life story is required to provide a sense of narrative self-continuity (McAdams, 2001). Finally, compared with its subjective counterpart, understanding of the cognitive and neural mechanisms underlying narrative self-continuity for both the past and future lags well behind, given the dearth of studies on the topic. Part 1 of this thesis, therefore, aims to address these limitations, drawing upon the syndromes of AD and SD to refine the understanding of the relationship between episodic and semantic memory and narrative continuity of the self, across past, present, and future. Accordingly, Chapter 3 presents the development of a new approach for examining narrative self-continuity, involving a novel method for scoring the full range of episodic to semantic information enmeshed within naturalistic autobiographical narratives. This scoring tool is then validated in AD and SD. In Chapter 4, the new scoring method is applied to narratives of imagined future events in AD and SD, and the neural correlates of narrative continuity explored. In doing so, Part 1 of this thesis aims to draw upon contemporary theory and methods in cognitive neuroscience to improve the characterisation of the extended self.

## 1.3. Part 2: The interpersonal self

*"I am because we are, and since we are, therefore I am"*

Mbiti (1969)

Kenyan Philosopher

According to Neisser (1988), the interpersonal self refers to the self as engaged in social interaction (see also Mead, 1934). This aspect of the self first appears in early infancy, observable by the automatic co-ordination of actions with another person's (e.g., becoming attuned to one's mother's affect) (Trevarthen, 1984). In early childhood (between two and four years of age), the interpersonal self further develops to incorporate the understanding of other people's mental states (i.e., 'theory of mind') (Leslie, 1987), knowledge which facilitates social engagement with others.

### 1.3.1. Cognitive neuroscience of the interpersonal self

The relatively newborn study of 'social cognition' has begun to enable the delineation of the neurocognitive processes underlying social interactions (Adolphs, 1999; Frith & Frith, 2007). Two of the crucial socio-cognitive functions that give rise to the interpersonal self are morality and perspective taking. An individual's moral traits, or in other words their judgements of right and wrong, their kindness, and empathy, crucially affect their social interactions, and are considered some of the most defining characteristics of the self (Strohminger & Nichols, 2014, 2015). Further, the ability to shift from one's own perspective, to adopt that of an another, forms the foundation for successful interpersonal relations (Mead, 1934).

#### *Moral reasoning*

The cognitive and neuroscientific study of morality has primarily centered on moral reasoning, defined as the ability to evaluate social situations in terms of moral criteria (Pizarro, 2007). In turn, these judgements of right and wrong guide subsequent behaviour. Traditionally, the empirical analysis of moral reasoning was informed by the ideas of 18$^{th}$ century philosophers (Hume, 1751; Kant, 1785/2002), regarding the relative contributions of emotional versus rational processes to moral judgements. The earliest work in this area focused on the development of moral reasoning abilities in childhood, with multiple stages proposed (Kohlberg, 1963; Piaget, 1932). The understanding of moral rules is thought to come online between ages seven to 10, with the capacity to judge moral scenarios also developing around age 10 (Piaget, 1932). The reasoning behind moral judgements is another critical skill which develops in childhood (Kohlberg, 1963).

While this seminal work by Piaget (1932) and Kohlberg (1963) set the stage for understanding moral development, arguably the most profound influence on the bourgeoning study of moral reasoning has been the introduction of the 'trolley problem' (Foot, 1967). This, and related moral dilemmas, have since been used extensively in experimental studies of moral reasoning. In the trolley problem, participants are presented with a scenario of a runaway train heading towards five railway workers. The five workers will be killed by the train, unless the participant decides to hit a switch directing the train onto another track, though this would instead kill another worker. A choice to hit the switch represents the 'utilitarian' decision, with the ultimate outcome providing benefit to 'the greater good'. By contrast,

refusing to hit the switch reflects a 'deontological' decision, in that the action itself is believed to be wrong (i.e., 'do no harm'). A variant of this dilemma, known as the 'footbridge problem', introduces a personal factor to the scenario. In this case, the five workers can only be saved if the participant chooses to physically push a bystander off a nearby footbridge onto the tracks, halting the train but killing the bystander (Thomson, 1976). Unlike the trolley problem, however, in which most people state they would hit the switch, the majority of respondents refuse to push the bystander in the footbridge problem (80-90% versus 10-35% of utilitarian responses, respectively; J. D. Greene, 2014; Hauser, Cushman, Young, Kang-Xing Jin, & Mikhail, 2007). As will be discussed in the following sections, this dissociation has been fundamental in advancing the understanding of the relative contribution of emotional versus rational processes to moral decision making.

*Neurocognitive mechanisms*

A pivotal study by J. D. Greene, Sommerville, Nystrom, Darley, and Cohen (2001) provided the first empirical cognitive neuroscience investigation of moral dilemmas. Based on a hypothesis that dilemmas like the footbridge problem engage more emotional processing than trolley-type problems, due to their 'personal' nature (i.e., they require personally inflicting direct harm), the study employed fMRI to examine the neural correlates of 'personal' versus 'impersonal' moral dilemmas. Compared with impersonal dilemmas, increased activation was observed during the personal moral dilemmas in regions typically associated with emotional processing, namely mPFC, PCC, and bilateral angular gyrus (Kosslyn et al., 1996; Maddock, 1999; Reiman, 1997; Reiman et al., 1997). By contrast, impersonal moral dilemmas preferentially activated frontoparietal regions associated with controlled cognitive processing and working memory (Cohen et al., 1997; E. E. Smith & Jonides, 1997). The findings are interpreted as reflecting a dual-process account of moral reasoning, such that the emotional and rational subsystems compete during moral decision making, with emotional versus rational processes more commonly drawn upon for personal versus impersonal moral dilemmas, respectively. This view has been highly influential on subsequent cognitive neuroscientific research into moral reasoning.

Ensuing research has supported the dual-process account, uncovering deficits specific to personal moral reasoning in clinical populations with impaired emotion processing and

lesions to brain regions integral for emotion (e.g., mPFC; Ciaramelli, Muccioli, Làdavas, & di Pellegrino, 2007; Koenigs et al., 2007; Mendez, Anderson, & Shapira, 2005). Namely, these patients provide an elevated amount of utilitarian responses to personal, but not impersonal, moral dilemmas, suggesting a suppression of the normal emotional response to moral conflict that tends to produce a deontological response to personal dilemmas in healthy individuals. Furthermore, manipulation of emotional state affects personal moral judgements in behavioural studies (Valdesolo & DeSteno, 2006; Wheatley & Haidt, 2005), and a wealth of neuroimaging evidence from fMRI studies reveals activation of emotional regions during personal moral reasoning, including amygdala, hippocampus, orbitofrontal cortex (OFC), and insula, in addition to mFPC, PCC, and angular gyrus/temporoparietal junction (TPJ; reviewed by Pascual, Rodrigues, & Gallardo-Pujol, 2013). Along with emotion, however, it is increasingly apparent that other neurocognitive processes are involved in personal moral decision making (Figure 1.5.). For example, in recognition of their overlap with the DMN (B. J. Harrison et al., 2008; Spreng et al., 2009), the brain regions commonly associated with personal moral reasoning (i.e., mPFC, PCC, angular gyrus/TPJ, hippocampus) are not exclusively implicated in emotional responses, but also in theory of mind (Young, Cushman, Hauser, & Saxe, 2007), self-referential processing (Northoff et al., 2006), and simulation of scenarios beyond the here and now (Buckner & Carroll, 2007). Specifically, mPFC and TPJ are thought to support personal moral reasoning via inferences about others' mental states, in order to judge the social consequences of the moral decision (Roberts, Henry, & Molenberghs, 2019). Cortical midline regions (i.e., mPFC and PCC) are proposed to lend the self-reflective component of personal moral decisions (Reniers et al., 2012), while the hippocampus is suggested to support the construction of a mental scene of the hypothetical dilemma (Craver et al., 2016; McCormick, Rosenthal, Miller, & Maguire, 2016). In addition to these DMN regions, the anterior cingulate (ACC) and dorsolateral prefrontal cortices are postulated to play an integral role in resolving the cognitive conflict that arises between the emotional and rational responses toward personal moral dilemmas (J. D. Greene, Nystrom, Engell, Darley, & Cohen, 2004). Finally, the bilateral superior and anterior temporal lobes are speculated to process and represent social information during personal moral reasoning, including conceptual knowledge about social rules and norms (Allison, Puce, & McCarthy, 2000; J. Moll, Zahn, de Oliveira-Souza, Krueger, & Grafman, 2005), though experimental evidence for this role remains lacking.

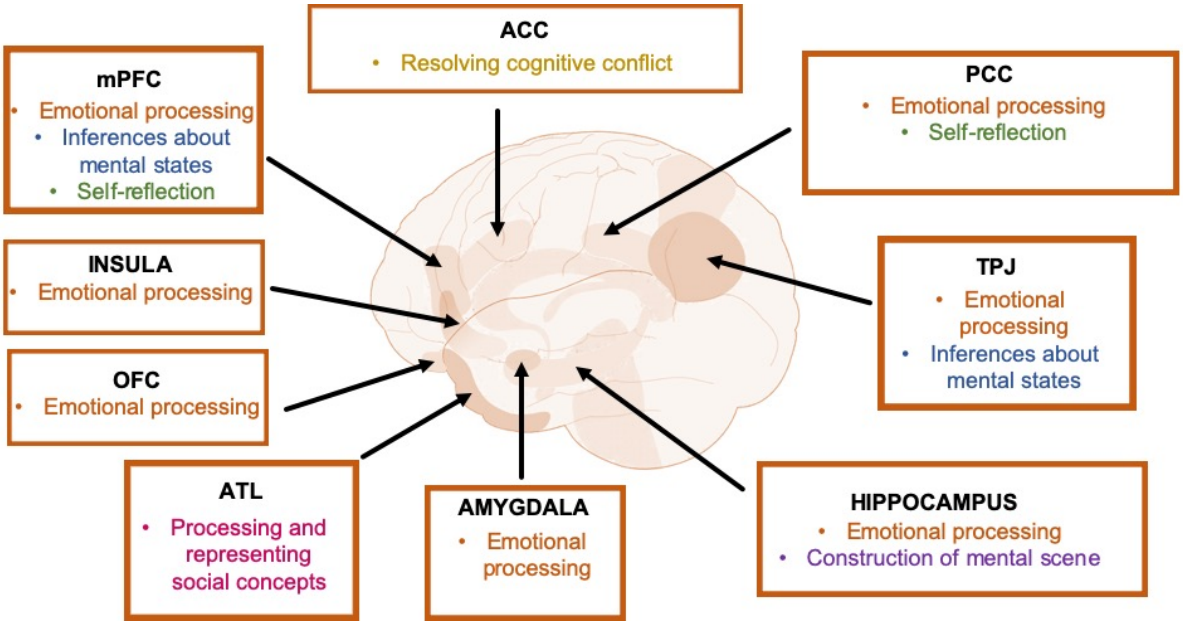



*Figure 1.5.* Brain regions typically implicated in personal moral reasoning, and their purported roles. ACC = anterior cingulate cortex; ATL = anterior temporal lobe; mPFC = medial prefrontal cortex; OFC = orbitofrontal cortex; PCC = posterior cingulate cortex; TPJ = temporoparietal junction.

*Methodological issues*

One criticism of the original distinction between personal and impersonal moral dilemmas made by J. D. Greene et al. (2001) is the large variability in the scenarios considered as personal moral dilemmas. In fact, a subset of these dilemmas consistently elicit a deontological response in healthy individuals, while the remainder are more divisive, even in control participants. Accordingly, Koenigs et al. (2007) proposed a new categorisation of personal moral dilemmas into low- and high-conflict scenarios. While the low-conflict dilemmas involve rather inexcusable actions often rejected by healthy people (e.g., committing cannibalism to save oneself and others), the high-conflict scenarios (e.g., killing a fellow hostage so that oneself and others may escape from terrorists) involve competing considerations of inflicting direct personal harm versus benefiting the aggregate welfare, and produce varying responses in the general population. Separating scenarios in this manner has revealed that the abnormal response to personal moral dilemmas in patients with mPFC lesions is specific to the high-conflict scenarios (Koenigs et al., 2007). This improved sensitivity of the low-/high-conflict distinction in differentiating between patients and controls also

extends to other lesion populations, including amnesic individuals with MTL damage (McCormick et al., 2016). Not all research into moral dilemmas, however, has adopted this distinction (see Friesdorf, Conway, & Gawronski, 2015), leading to widespread methodological differences between studies (Christensen & Gomila, 2012). Another limitation of previous work is that the majority of evidence for the emotional contribution to personal moral decision making is inferred from neuroimaging and lesion studies that implicate emotional brain regions, rather than direct experimental manipulation. Taken together, the current literature review indicates that future studies employing the high- and low- conflict distinction, empirically examining the contribution of emotion and social conceptual knowledge to personal moral reasoning, and their corresponding neural correlates, are clearly warranted, in order to improve the characterisation of the cognitive and neural processes underpinning this aspect of the interpersonal self.

### *Perspective taking*

*Visual perspective taking (VPT)*

Visual perspective taking (VPT) is defined as the capacity to see the world from another person's perspective (Flavell, 1977). As with moral reasoning, the earliest empirical work on perspective taking focused on the development of this ability across childhood, most notably by Piaget. In his theory of cognitive development, Piaget (1924) proposed that during the 'preoperational' stage, between the ages of two and seven, children's thoughts and communications are 'egocentric'. That is, children are unable to see a situation from another person's perspective. Experimentally, these difficulties with VPT have been revealed using the Three Mountains Task, with young children assuming that other people see the same view of the three mountains as they do (Piaget & Inhelder, 1956). While some studies have criticised the methodology of this task, a general consensus has been reached that VPT comes online around age three to four (Borke, 1975; Flavell, Flavell, Green, & Wilcox, 1980). Other evidence, however, supports the existence of two kinds of VPT, each with distinct developmental trajectories (Flavell, Everett, Croft, & Flavell, 1981; Masangkay et al., 1974). Level 1 VPT refers to the understanding that someone else may see different things from yourself, for example that someone else's view may be obstructed and thus they cannot see the horse you are looking at. This ability is thought to develop as early as 14 months of age (Sodian, Thoermer, & Metz, 2007; Sommer et al., 2010). Level 2 VPT, by contrast, is the

understanding that others may see the same things as yourself, but in a different way (Flavell, 1992), for example, from the other person's point of view, they can see the back of the horse, whereas you can only see the front. This ability is not believed to be fully developed until age four to four and-a-half years (H. Moll, Meltzoff, Merzsch, & Tomasello, 2013).

*Neurocognitive processes of VPT*

In addition to following different developmental trajectories, Level 1 and Level 2 VPT may also involve somewhat distinct neurocognitive processes. Namely, Level 2 VPT requires more complex spatial processing than its Level 1 counterpart, given its requirement of mentally rotating oneself to adopt the viewpoint of another person (Zacks & Tversky, 2005). This ability, however, has been dissociated from the capacity to mentally rotate an object relative to the self, as measured by classic mental rotations tasks (Inagaki et al., 2002; Wraga, Creem, & Proffitt, 2000; Zacks, 2008). In terms of their neural correlates, a meta-analysis of neuroimaging studies revealed both Level 1 and Level 2 VPT to activate TPJ, precuneus, and lateral prefrontal cortex (i.e., inferior frontal gyrus; IFG), though precuneal activations were stronger for Level 1 VPT tasks (Schurz, Aichhorn, Martin, & Perner, 2013). Each of these regions are proposed to play distinct roles in VPT (Figure 1.6.). While the TPJ is thought to represent the taking/adoption of different perspectives (McCleery, Surtees, Graham, Richards, & Apperly, 2011), the IFG is proposed to inhibit one's own perspective (Ramsey, Hansen, Apperly, & Samson, 2013), consistent with its role in cognitive control. Finally the precuneus is responsible for representing visuospatial imagery in general (Fletcher et al., 1995), although its specific role in VPT has not been explicitly discussed.

*Theory of mind (ToM)*

In addition to difficulties with imagining another person's *visual* perspective, young children also assume others perceive, think, and feel exactly the same as themselves (Piaget, 1924). Around the age of four, children begin to be able to adopt another's perspective at this conceptual level, via the development of 'theory of mind' (ToM) (Wimmer & Perner, 1983). This ability, also known as mentalising, refers to the capacity to attribute and infer the mental states of oneself and others, and encompasses the understanding of feelings, thoughts, beliefs, and intentions (Baron-Cohen, 1995; Premack & Woodruff, 1978). The original and most commonly used test of ToM is the false belief task, which requires the understanding

that others may not possess the same knowledge as oneself, and can hold a belief that is different from reality (e.g., recognising that since a character in a story did not see their chocolate bar moved to another cupboard, they will search for it in its original location) (Wimmer & Perner, 1983). A variety of other experimental tasks have since been developed, in particular attempting to fractionate affective ToM (i.e., feelings and emotions) from its cognitive counterpart (i.e., thoughts, beliefs, and intentions) (see Poletti, Enrici, & Adenzato, 2012). This distinction, however, is not necessarily clear-cut, given cognitive and affective ToM are themselves multifaceted constructs. Moreover, the conceptualisation of affective ToM overlaps with the related construct of empathy, which involves the basic recognition and understanding of another person's affective state, in addition to the *sharing* of this emotional experience (Decety & Jackson, 2004). These definitional blurs reflect the inherent difficulty in attempting to parcellate complex social interactions into exclusive categories (McDonald, Flanagan, Rollins, & Kinch, 2003). As such, combining formal laboratory measures of ToM with observations of an individual's social behaviour in daily life (e.g., Davis, 1983) is likely to provide the most thorough and ecologically valid representation of this ability.

*Neurocognitive processes of ToM*

The centrality of the mPFC for ToM has long been established (H. Gallagher, Jack, Roepstorff, & Frith, 2002; McCabe, Houser, Ryan, Smith, & Trouard, 2001; Stuss, Gallup, & Alexander, 2001). More recent research, however, has also revealed the importance of a more distributed neural network in supporting this ability, which partially overlaps with the DMN. In addition to medial prefrontal regions, this includes the bilateral posterior superior temporal sulcus (i.e., the TPJ), precuneus, and IFG (reviewed by Schurz, Radua, Aichhorn, Richlan, & Perner, 2014). Each of these regions have been ascribed unique functions in the service of successful ToM performance (Figure 1.6.). The mPFC is thought to be responsible for the 'decoupling' from current reality to imagine alternative circumstances (H. Gallagher & Frith, 2003), as well as playing a general role in processing emotionally or socially relevant information about others (Saxe & Powell, 2006). In addition, this region is also strongly implicated in processing information about the self, with one view proposing that self-reflecting upon one's own mental state allows us to simulate and understand the minds of others (Frith & Frith, 2006). Two competing hypotheses have emerged to explain the consistent activation of the TPJ in ToM. While some authors argue the TPJ is involved in the

orienting of attention to different mental states (Young, Dodell-Feder, & Saxe, 2010), others propose a more specific role in representing mental states and perspectives, irrespective of the particular task demands (Perner, Aichhorn, Kronbichler, Staffen, & Ladurner, 2006). The broad role of the precuneus in visual imagery is also presumed to extend to ToM, in the visual representation of another's perspective in the absence of external stimuli (Cavanna & Trimble, 2006). Finally, via the mirror neuron system, the IFG appears to play a specific role in ToM in identifying the actions and emotional expressions of others (Keysers & Gazzola, 2007).

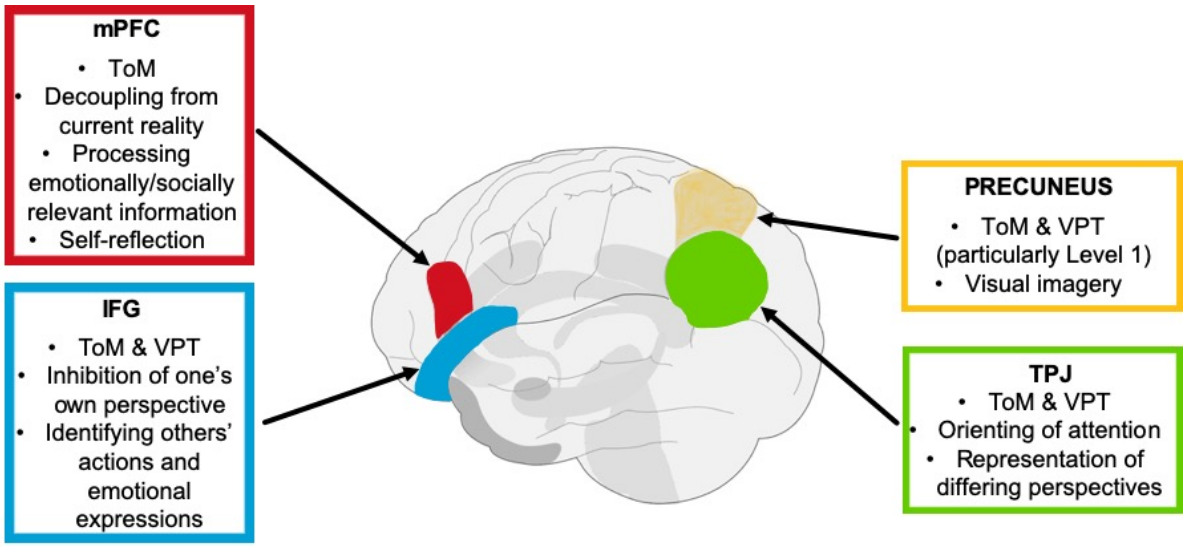



*Figure 1.6.* Brain regions implicated in visual perspective taking and theory of mind, and their purported roles. IFG = inferior frontal gyrus; mPFC = medial prefrontal cortex; ToM = theory of mind; TPJ = temporoparietal junction; VPT = visual perspective taking.

*Are VPT and ToM related?*

While the study of VPT and ToM has largely proceeded in parallel (see Schurz et al., 2013), it is apparent that these two types of perspective taking share a number of similarities in their developmental trajectory, proposed cognitive mechanisms, and neural correlates. Namely, Level 2 VPT and ToM emerge at a similar age (i.e., four years of age; H. Moll et al., 2013; Wimmer & Perner, 1983), and ToM abilities in children predict their performance on Level 2 VPT tasks (Hamilton, Brindley, & Frith, 2009). Furthermore, impairments in both Level 1 and

Level 2 VPT have been uncovered in neurodevelopmental conditions characterised by prominent deficits in ToM, such as autism (Hamilton et al., 2009; Schwarzkopf, Schilbach, Vogeley, & Timmermans, 2014; Yirmiya, Sigman, & Zacks, 1994), schizophrenia (Eack, Wojtalik, Keshavan, & Minshew, 2017; Langdon, Coltheart, Ward, & Catts, 2001), psychopathy (Drayton, Santos, & Baskin-Sommers, 2018), and specific language impairment (Farrant, Fletcher, & Maybery, 2006). Compellingly, VPT performance has been found to correlate with the ability to understand other's thoughts and feelings in these syndromes (Farrant et al., 2006; Hamilton et al., 2009; Langdon et al., 2001). As such, it has been proposed that VPT impairment may underlie the deficits in ToM in these syndromes, via an inability to simulate alternative perspectives (Langdon & Coltheart, 2001).

Overlap between ToM and VPT should not be surprising, given that both require an understanding of 'perspective' (i.e., that different people may hold different views/beliefs about the same situation), and as well as the deliberate switching to this other perspective. Furthermore, in addition to drawing upon spatial information (i.e., the position of the self, the other person, and the objects in relation to oneself and the other) (Kessler & Thomson, 2010), VPT requires a level of social processing. Namely, successful VPT involves understanding that oneself and the other person have different perspectives, i.e., technically, it requires some degree of 'theory of mind' (Aichhorn, Perner, Kronbichler, Staffen, & Ladurner, 2006). This representation of different perspectives, that is common to both VPT and ToM, is proposed to be mediated by the TPJ (Aichhorn et al., 2006; Perner & Leekam, 2008). In support of this notion, the TPJ emerged in a recent meta-analysis of functional neuroimaging studies as the primary site of activation overlap between VPT and ToM tasks (Schurz et al., 2013).

Despite these apparent intersections, however, VPT and ToM do indeed diverge in a number of ways, with one view proposing they reflect entirely distinct abilities (Leslie, 1987). For example, unlike the majority of ToM tasks, VPT does not require the consideration of behavioural or emotional consequences, which is proposed to be driven by the mPFC (Aichhorn et al., 2006). In line with this theory, medial prefrontal activation does not consistently emerge in neuroimaging studies of VPT (Schurz et al., 2013). In addition, some studies have found entirely distinct patterns of brain activation for VPT versus ToM (David et

al., 2008). How the mechanisms underlying Level 1 and Level 2 VPT diverge, and relate to those supporting ToM, is also unclear, given these two types of VPT have different developmental trajectories, and sometimes dissociate from one another, or from ToM, in clinical populations (e.g., psychopathy, Drayton et al., 2018; and autism, Pearson, Ropar, & Hamilton, 2013). The exact nature of the relationship between Level 1 VPT, Level 2 VPT, and ToM, therefore, remains poorly defined, in particular whether the cognitive and neural mechanisms underlying these aspects of the interpersonal self are distinct or overlapping. Additionally, the extant evidence for the neural mechanisms underlying VPT stems predominantly from neuroimaging studies of healthy individuals. As of yet, no lesion studies have been performed in populations with discrete brain damage, to determine which brain regions are not only involved, but *necessary* for these functions.

### 1.3.2. A neurodegenerative disorder of the interpersonal self: Clinical and neuroimaging profile of the behavioural variant of frontotemporal dementia

The behavioural variant of frontotemporal dementia (bvFTD) is the prototypical disorder of the interpersonal self (Wong, Irish, & Hornberger, 2018). Characterised by profound alterations in social functioning and interpersonal relationships, this syndrome permits examination of how alterations in social cognition affect the interpersonal self. This section outlines the clinical, pathological, and neuroimaging characteristics of bvFTD.

#### *Behavioural variant of frontotemporal dementia (bvFTD)*

*Clinical presentation*

Alongside semantic dementia (SD; described above), the behavioural variant of frontotemporal dementia (bvFTD) is another subtype of FTD. bvFTD is characterised by striking changes in personality and behaviour. Namely, patients present with disinhibition, apathy, reduced empathy, stereotypical behaviour, a decline in personal hygiene, and eating changes, and notably, lack insight into the presence of these symptoms (Neary, Snowden, Northen, & Goulding, 1988; Piguet et al., 2011; Rascovsky et al., 2011). Personality is often starkly altered from early in the disease course, involving clear deviations from the individuals' premorbid traits and interests (B. L. Miller et al., 2001). In terms of cognition, current diagnostic criteria incorporate a dysexecutive neuropsychological profile, with

relative sparing of episodic memory and visuospatial function (Rascovsky et al., 2011). Many patients, however, may actually perform normally on neuropsychological assessment (Mioshi et al., 2007), including on tests of executive function (Gregory, Serra-Mestres, & Hodges, 1999), particularly in early stages of the disease (Ranasinghe et al., 2016). Moreover, episodic memory can indeed be impaired in early bvFTD (Hornberger & Piguet, 2012; Hornberger, Piguet, Graham, Nestor, & Hodges, 2010). Accordingly, increased emphasis is being placed on social cognitive, rather than neuropsychological, deficits in the differential diagnosis of bvFTD (Johnen & Bertoux, 2019).

*Neuropathological and neuroimaging features*

Unlike in AD and SD, the neuropathology of bvFTD is heterogeneous. Most cases of bvFTD are associated with either tau or TDP-43 protein depositions, with small subset of patients harbouring the RNA-binding protein fused in sarcoma (FUS) (Chare et al., 2014; Hodges et al., 2004). The clinical features of bvFTD predominantly reflect atrophy to the frontal lobe, in particular orbitofrontal, medial prefrontal, and frontoinsular regions (Figure 1.7.; Seeley, 2008). With disease progression, atrophy encroaches into dorsolateral prefrontal cortex, anterior and medial temporal lobes, and basal ganglia (Rabinovici et al., 2007; Rosen et al., 2002). The white matter tracts connecting frontal to more posterior regions of the brain are also affected (Lam, Halliday, Irish, Hodges, & Piguet, 2014). Regarding functional networks, bvFTD has consistently been associated with reduced functional connectivity within the 'salience network' (Day et al., 2013; Zhou et al., 2010). This network incorporates anterior insula and ACC, along with striatum and amygdala, and is thought responsible for detecting behaviourally relevant internal and external stimuli, and mobilising the brain's response to these stimuli (Uddin, 2015). Around 10-15% of FTD cases are caused by a genetic mutation, the most common of these being in the chromosome 9 open reading frame 72 (*C9orf72*), progranulin (*GRN*), and microtubule-associated protein tau (*MAPT*) genes (Greaves & Rohrer, 2019). Indeed, the patterns of atrophy in these genetic variants do differ somewhat from the sporadic (i.e., non-genetic) cases. While all bvFTD patients display medial prefrontal atrophy, anterior temporal degeneration is more pronounced in *MAPT*, with *GRN* and *c9orf72* also affecting posterior cortical regions including posterior cingulate and lateral parietal cortices (Whitwell et al., 2012).

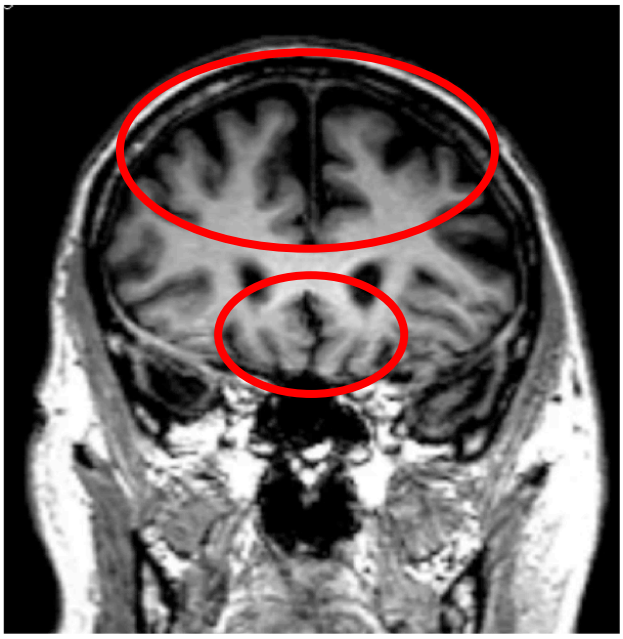


*Figure 1.7.* Coronal MRI scan displaying the typical frontal lobe atrophy in the behavioural variant of frontotemporal dementia (bvFTD).

### 1.3.3. The interpersonal self in the behavioural variant of frontotemporal dementia

Socially disruptive and inappropriate behaviours are often the first presenting symptom of bvFTD (Piguet, Kumfor, & Hodges, 2017), which represent a clear departure from the individuals' premorbid tendencies. For example, previously law-abiding, socially conforming, affectionate individuals may begin behaving inappropriately (e.g., aggression, urinating in public), making rude comments to strangers (e.g., crass jokes, sexist remarks), and displaying a seeming lack of empathy for other people (e.g., indifference to death of a family member, disinterest in other's concerns). Given the pervasive lack of insight in bvFTD, these reports will often come from family members and close others, who report the patient to lack warmth (Dermody et al., 2016), and show poor awareness of social norms, reduced tact, and an apparent disregard and disinterest in others (Barsuglia et al., 2014; Mendez et al., 2014). Importantly, bvFTD patients display a breakdown in the synchronous social interactions that characterise Neisser's (1988) interpersonal self (Barsuglia et al., 2014), ultimately leading to deterioration in interpersonal relationships in these patients (Hsieh, Irish, Daveson, Hodges, & Piguet, 2013; Takeda et al., 2019). Given such behaviours in bvFTD represent striking transgressions from societal values about how its members should behave, they are often described as sociopathic, or 'immoral' (Mendez, Chen, Shapira, & Miller, 2005). In some cases,

the alterations in moral behaviour in bvFTD can even result in criminal offences. Estimates of criminality in bvFTD range from 37-54%, with crimes including theft, violence, hypersexuality, traffic violations, and even homicide reported in these patients (Liljegren et al., 2015). In fact, for some individuals, law-breaking represents the first-noticed symptom of the disease. These extreme moral transgressions in bvFTD place a significant burden on the patients, families, care facilities, as well as society more broadly (Liljegren et al., 2015).

Of further significance for the interpersonal self, the bvFTD syndrome leads to alterations in many of the fundamental characteristics that define the person. For example, preferences, values, traits, and interests can markedly change in bvFTD, including style of dress, sense of humour, sexual preferences, and even political and religious ideologies (B. L. Miller et al., 2001). Of note, the patients themselves typically display no concern regarding these major transformations of the self, in fact, they are often are unaware that any changes have occurred (Rankin, Baldwin, et al., 2005; Ruby et al., 2009). This is in contrast to the significant distress reported by family members, who perceive the individual with bvFTD as a 'fundamentally different person' from who they were prior to illness onset, in some even cases describing them as a 'stranger' (Strohminger & Nichols, 2015). These perceptions are particularly responsible for the relationship breakdowns that ensue (Strohminger & Nichols, 2015).

As a result of these striking behavioural observations of changes to the interpersonal self in bvFTD, a wealth of studies have endeavoured to empirically examine social cognition in these patients (reviewed by Johnen & Bertoux, 2019). Using an array of experimental tasks, unsurprisingly, deficits have been revealed in bvFTD across all aspects of emotional and social processing, including perceiving, expressing, and responding to emotion; reward processing and affective decision making; knowledge of social norms and rules; moral reasoning (reviewed in detail in Chapter 5); and theory of mind (reviewed in detail in Chapter 6). Such global impairments in socio-affective processing in bvFTD are attributed to the breakdown in the 'social brain', the large-scale brain network thought to be specialised for social and emotional functioning (Dunbar, 2012; Seeley, Zhou, & Kim, 2012), which incorporates mPFC, insula, amygdala, and ATLs.

### 1.3.4. Summary and aims of Part 2

Given the profound and characteristic alterations in social functioning in bvFTD, and concomitant degeneration to circumscribed neural networks, this syndrome provides the ideal test-bed upon which to refine our understanding of the neurocognitive underpinnings of the interpersonal self. In particular, while several studies of moral reasoning have been conducted in bvFTD (to be reviewed in detail in Chapter 5), the precise cognitive and neural mechanisms of this function are not yet fully understood. Chapter 5, therefore, employs up-to-date, theoretically driven experimental methods (i.e., high- versus low-conflict personal moral dilemmas) to examine how emotional processing and conceptual knowledge contribute to personal moral reasoning in bvFTD, and the corresponding neural correlates. Furthermore, despite well-established deficits in ToM in bvFTD (to be reviewed in detail in Chapter 6), no study has examined VPT in this syndrome. Thus, Chapter 6 comprehensively explores the relationship between, and neural corelates of, several aspects of perspective taking in bvFTD (Level 1 and Level 2 VPT, ToM, as well as real-world, behavioural manifestations of these functions), to adjudicate between the accounts that these represent distinct versus overlapping processes. In sum, Part 2 of the thesis aims to draw upon the syndrome of bvFTD in order to improve the characterisation of the interpersonal self, from a neurocognitive perspective.

## 1.4. Summary and overall thesis aims

Bringing the two parts together, this thesis draws upon contemporary theoretical frameworks, methodological advances in cognitive neuroscience, and neurodegenerative patient models in order to inform our understanding of the extended and interpersonal self. Ultimately, by combining objective psychological tools with traditionally-philosophical constructs, this body of work aims to inform cross-disciplinary knowledge about the self, as well as extend the clinical profile of AD, SD, and bvFTD.

# Chapter 2

# Experimental methods

This chapter describes the methods shared by the four experimental chapters, including participant recruitment, ethics, neuropsychological and clinical assessment, and structural and diffusion-weighted MRI acquisition and pre-processing procedures.

## 2.1. Participant recruitment

Patients and healthy control participants were recruited through FRONTIER, the frontotemporal dementia research clinic at the University of Sydney, Australia. Healthy control participants were friends or family of the patient or volunteers from the community.

Patient diagnosis was made by an experienced behavioural neurologist in consultation with a neuropsychologist and occupational therapist, based on clinical examination, neuropsychological assessment, and brain structural magnetic resonance imaging (MRI).

### 2.1.1. Inclusion criteria

All patients met current international consensus criteria for a diagnosis of AD (McKhann et al., 2011), SD (Gorno-Tempini et al., 2011), or bvFTD (Rascovsky et al., 2011). These diagnostic criteria are provided in Appendix A.

Briefly, AD patients met diagnostic criteria for probable, amnestic AD (McKhann et al., 2011), with deficits in episodic memory, including learning and recall of recently encountered information, and reductions in one or more of naming, visuospatial abilities, and executive function. Atrophy was typically present in the medial and lateral temporal and parietal lobes.

Patients with SD were required to meet diagnostic criteria for primary progressive aphasia, as well as the subtype classification criteria for SD (Gorno-Tempini et al., 2011). SD patients presented with a primary language disturbance, characterised by a progressive loss of conceptual knowledge, manifesting as anomia and deficits in confrontation naming and

single-word comprehension. Only patients with left-side predominant ATL atrophy were included.

Patients with bvFTD (possible or probable) typically presented with personality and/or behavioural changes including disinhibition, apathy, loss of empathy, perseverative behaviour, change in eating habits, and/or executive dysfunction. Those diagnosed with probable bvFTD additionally harboured atrophy in the frontal and anterior temporal lobes (Rascovsky et al., 2011).

### 2.1.2. Exclusion criteria

Exclusion criteria for all participants included a significant history of another psychiatric or neurological condition, significant vision or hearing loss, and alcohol or substance abuse. Participants were also required to have sufficient English proficiency to complete the neuropsychological and experimental tasks, and have attained a minimum of a primary school level of education (i.e., 6 years).

Control participants were required to score within the cognitively normal range, i.e., 88/100 or above, on a general cognitive screening measure, the Addenbrooke's Cognitive Examination-Revised (ACE-R) (Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006), or the updated Addenbrooke's Cognitive Examination-III (ACE-III) (Hsieh, Schubert, Hoon, Mioshi, & Hodges, 2013) (see Section 2.3.).

## 2.2. Ethics

Ethics approval was obtained for the study from the University of New South Wales and South Eastern Sydney Health Service ethics committees (HREC 10/126 and HREC 13/177). Informed consent was obtained from all participants or their person responsible in accordance with the Declaration of Helsinki. Participants volunteered their time and were reimbursed for their travel costs.

## 2.3. Neuropsychological assessment

All participants underwent a comprehensive battery of standardised neuropsychological assessment tasks. This included a measure of global cognition, as well as more detailed examination of specific cognitive domains including processing speed, attention, language, visuospatial abilities, verbal and non-verbal episodic memory, and executive function.

### 2.3.1. General cognitive screening

Participants completed the Australian version of the ACE-R (Mioshi et al., 2006) or the updated ACE-III (Hsieh, Schubert, et al., 2013) as a measure of general cognitive functioning. This task is scored out of 100 and comprises five subscales, briefly sampling the cognitive domains of Attention/Orientation, Memory, Fluency, Language, and Visuospatial abilities. A cut-off score of 88/100 on both versions offers excellent sensitivity and specificity for discriminating patients with dementia from healthy controls (Hsieh, Schubert, et al., 2013; Mioshi et al., 2006; So et al., 2018). The ACE-III correlates strongly with the ACE-R (Hsieh, Schubert, et al., 2013; So et al., 2018) as well as with performance on standardised neuropsychological tasks (Hsieh, Schubert, et al., 2013).

### 2.3.2. Processing speed

Speed of processing was assessed using Part A of the Trail Making Test (TMT; Reitan, 1958). This paper and pencil task requires participants to connect numbers, in order, as quickly as possible. Performance is measured by completion time (seconds).

### 2.3.3. Attention

Attention was measured using the Digit Span Forwards subtest from the Weschler Memory Scale-Third Edition (WMS-III; Wechsler, 1997). In this task, participants are read a string of digits aloud, and asked to repeat back the same string of digits. String length begins at 2 digits, and progresses to 9 digits, with two trials for each string length. If the participant makes errors on both trials of a given length, the task is discontinued. The achieved score represents the maximum string length repeated by the participant without errors, with a maximum score of 9.

### 2.3.4. Language

Language was assessed using the Naming and Comprehension subtests from the Sydney Language Battery (SYDBAT; Savage et al., 2013) and the ACE Fluency subscale (Mioshi et al., 2006).

SYDBAT Naming is a confrontation naming task involving 30 colour photographs. Participants are required to provide the name of the item shown in the photograph. Mispronunciations of the word due to phonemic, semantic, or phonological substitutions, as well as any omissions, are counted as errors. The maximum score is 30 points.

The SYDBAT Comprehension subtest consists of 30 trials, each displaying an array of seven colour photographs. Participants are asked to point to the photograph that matches a word said by the experimenter. Maximum score on this test is 30 points.

The ACE Fluency subscale comprises two subtests. The Letter Fluency subtest requires participants to generate as many words as possible starting with a given letter within the space of one minute. On the Semantic Fluency subtest, participants must generate as many animals as possible within one minute. For each of these subtests, correct words are counted to form a total score. Repeated words or those from an incorrect category are not counted toward this score. The total words are then converted to a score out of 7 (Figure 2.1.) for both Letter Fluency and Semantic Fluency. These are summed to form a total Fluency score, out of a maximum of 14 points.

| Letters: | |
|---|---|
| ≥18 | 7 |
| 14-17 | 6 |
| 11-13 | 5 |
| 8-10 | 4 |
| 6-7 | 3 |
| 4-5 | 2 |
| 2-3 | 1 |
| 0-1 | 0 |

| Animals: | |
|---|---|
| ≥22 | 7 |
| 17-21 | 6 |
| 14-16 | 5 |
| 11-13 | 4 |
| 9-10 | 3 |
| 7-8 | 2 |
| 5-6 | 1 |
| <5 | 0 |

*Figure 2.1.* Scoring procedure for the Addenbrooke's Cognitive Examination (ACE) Letter and Semantic (i.e., animal) Fluency subtests. For each subtest, the right column displays the score out of 7 corresponding to the total number of correct words generated (left column).

### 2.3.5. Visuospatial abilities

Visuospatial skills were measured using the ACE Visuospatial subscale and the Rey Complex Figure (RCF; Rey, 1941).

The ACE Visuospatial subscale contains four components, and is scored out of a total of 16 points. First, participants are asked to copy a design of two intersecting infinity loops, scored out of a total of 3 points. Next, they are required to draw the face of a clock, including all of the numbers, and set the time to ten past five. A total of 5 points is possible, including 1 point for the circle, 2 for the numbers, and 2 for the hands. The third component involves the presentation of four squares, containing randomly arranged dots. Participants must count the number of dots in the boxes, without pointing. Each correct box scores 1 point. Finally, participants must identify aloud four visually degraded letters (K, M, A, T), with one point awarded for each correct letter.

For the RCF, participants are presented with a complex geometric figure and required to copy it. One point is given for the accurate drawing, and one point for the correct placement, of each element, with a maximum score of 36.

### 2.3.6. Verbal episodic memory

Verbal episodic memory was assessed using the ACE Word Recall and Address Recall subtests from the ACE Memory subscale and the Rey Auditory Verbal Learning Test (RAVLT; Schmidt, 1996).

The ACE Word Recall subtest requires participants to recall three words they previously heard and repeated (as part of the Attention subscale), after a 1-2 minute delay. One point is awarded for each correctly retrieved word.

On the ACE Address Recall, participants are asked after an approximate 10-15 minute delay to recall a name and address that they previously repeated three times. The total score is out of 7.

The RAVLT requires participants to listen to a list of 15 words (List A) read aloud by an experimenter, and immediately recall as many words as possible. This process is repeated for 5 trials. A second list of 15 words (List B) is then read aloud, and recall tested. Next, recall for List A is again tested. After a 30-minute delay, recall of List A is tested once more. The number of words recalled at this 30-minute delay provides a measure of Delayed Free Recall, which forms the index of interest here.

### 2.3.7. Non-verbal episodic memory

The RCF (described in Section 2.3.5.) was used to measure non-verbal memory. After participants initially copy the figure, there is a 3-minute delay, following which participants are asked to reproduce the figure from memory. One point is given for the accurate drawing, and one point for the correct placement, of each element, with a maximum score of 36.

### 2.3.8. Executive functions

To assess executive functions, participants completed Digit Span Backwards (Wechsler, 1997), Hayling Sentence Completion test (Burgess & Shallice, 1997) and Trail Making Test Part B (TMT; Reitan, 1958).

Digit Span Backwards provides a measure of working memory. Similar to Digit Span Forwards, participants are read strings of numbers, of increasing length, and asked to recite the string in the reverse order to that said by the experimenter. The maximum possible span length is 8. The procedure is otherwise identical to Digit Span Forwards (described in Section 2.3.3.).

The Hayling Sentence Completion test is a measure of response inhibition. In Section 1 participants are read sentences aloud, and asked to complete the sentence as quickly as possible (e.g., "*It's hard to admit when one is…"*). In Section 2, participants must complete the sentence using a completely unrelated word, as quickly as possible (e.g., *"The captain wanted to stay with the sinking…*"). Related words (e.g., *"ship"*) and partly related words (e.g.,

*"aeroplane"*) are counted as Category A and Category B errors, respectively. The total number of each of these error types is calculated, and each is then converted to a scaled score (Figure 2.2.). These two scaled scores are then summed, forming a Total AB score, which is used as a measure of inhibition. Higher scores reflect greater disinhibition.

| Category A errors | |
|---|---|
| Errors | A score |
| 1 | 3 |
| 2 | 6 |
| 3 | 10 |
| 4 | 14 |
| 5 | 18 |
| 6 | 24 |
| 7 | 30 |
| 8 | 36 |
| 9 | 42 |
| 10 | 48 |
| 11 | 54 |
| 12 | 60 |
| 13 | 66 |
| 14 | 72 |
| 15 | 78 |

| Category B errors | |
|---|---|
| Errors | B score |
| 1 | 1 |
| 2 | 2 |
| 3 | 3 |
| 4 | 4 |
| 5 | 9 |
| 6 | 14 |
| 7 | 19 |
| 8 | 24 |
| 9 | 29 |
| 10 | 34 |
| >10 | 50 |

*Figure 2.2.* Scoring procedure for the Hayling test. The number of Category A (i.e., connected words) and Category B (i.e., partly connected words) errors (left column) are converted to A Scores and B scores respectively. These A and B scores are subsequently summed to form the Total AB score.

Set-switching was measured using the TMT Part B. Like Part A (see Section 2.3.2), participants are required to draw a line to connect circles as quickly as possible. This time, however, they must switch between numbers and letters (i.e., 1-A-2-B-3-C … etc). Completion time is

recorded in seconds. The difference in time between Part B and Part A is used as a measure of executive function, accounting for baseline processing speed.

## 2.4. Clinical assessment

Measures of disease duration, severity, and behavioural change were also collected for all patients.

### 2.4.1. Disease duration

Disease duration, used as an indicator of disease stage, was calculated as the months elapsed between the onset of first symptoms (reported by a knowledgeable informant) and the date of assessment.

### 2.4.2. Disease severity

Disease severity was assessed using the Frontotemporal Dementia Functional Rating Scale (FTD-FRS; Mioshi, Hsieh, Savage, Hornberger, & Hodges, 2010). The FTD-FRS is a 30-item questionnaire completed by carers, which measures the day-to-day functioning of patients. Raw scores are converted into a Rasch score, with lower numbers denoting greater functional impairments (Bond & Fox, 2007).

### 2.4.3. Behavioural change

Behavioural change was measured using the Cambridge Behavioural Inventory (CBI; Wedderburn et al., 2008). This 45-item carer questionnaire assesses behavioural and psychiatric symptoms, in areas of memory and orientation, everyday skills, self-care, abnormal behaviour, mood, beliefs, eating habits, sleep, stereotypical behaviours, and motivation. The frequency of behaviours is rated on a scale of 0 to 4. A total score is calculated (maximum 180), with higher values representing increased frequency of the behaviours. Control participants also completed a self-rated version of the questionnaire.

## 2.5. Statistical analysis

Behavioural analyses were performed using SPSS Version 24 (IBM). The specific statistical tests employed by the individual studies are outlined in each chapter.

Unless otherwise specified, parametric analyses were used for all studies. The suitability of variables for parametric analysis were examined using Kolmogorov-Smirnov (K-S) tests of normality. Logarithmic transformations were applied if variables were non-normally distributed in one or more of the patient groups (K-S test $p < .05$). All analyses were conducted and reported using the logarithmically transformed variables, where appropriate, but for ease of interpretation, figures display untransformed values.

Statistical significance was set at $p < .05$ for all behavioural analyses, unless otherwise indicated.

## 2.6. Structural MRI acquisition and pre-processing

Participants underwent structural MRI scans and voxel-based morphometry (VBM) was used to analyse the integrity of grey matter.

### 2.6.1. Image acquisition

Participants underwent $T_1$-weighted structural neuroimaging using a 3Tesla MRI scanner with standard quadrature head coil (eight channels). The 3D $T_1$-weighted images were acquired using the following sequences: coronal orientation, matrix 256 × 256, 200 slices, 1 × 1 mm in-plane resolution, slice thickness = 1mm, echo time/repetition = 2.6/5.8 ms, flip angle $\alpha = 8°$.

### 2.6.2. Data pre-processing

VBM analyses in Chapter 4 were conducted using SPM-VBM (Statistical Parametric Mapping 12, Wellcome Department of Cognitive Neurology, London, UK). Given additional neuroimaging analyses were conducted in Chapter 5 (i.e., diffusion tensor imaging), a different software program was employed for the VBM analyses in this chapter, in order to ensure compatibility between structural and diffusion analyses. For Chapter 5, FSL-VBM (Functional MRI of the Brain (FMRIB) Software Library; Ashburner & Friston, 2000) was employed, using the toolbox from the FMRIB software package (http://www.fmrib.ox.ac.uk/fsl/fslvbm/index.html; S. Smith et al., 2004). To maintain consistency in Part 2 of the thesis, FSL-VBM was also used in Chapter 6.

For pre-processing in SPM, images were first segmented into six tissue probability maps in the native space. A DARTEL template was then computed from the grey matter, white matter, and cerebrospinal fluid probability maps of all participants. The grey matter probability maps of each participant were spatially normalised to the Montreal Neurological Institute (MNI) space according to the transformation parameters from the DARTEL template. Images were modulated then smoothed with an 8mm full-width at half-maximum Gaussian filter.

For pre-processing in FSL, images were extracted using the Brain Extraction Tool (BET; S. Smith, 2002), then tissue was segmented into grey and white matter and cerebrospinal fluid using FMRIB's Automatic Segmentation Tool (FAST; Y. Zhang, Brady, & Smith, 2001). The resulting grey matter partial volume maps were aligned to the Montreal Neurological Institute standard space (MNI152) using the FMRIB Non-linear Image Registration Tool (FNIRT; Andersson, Jenkinson, & Smith, 2007) which uses a *b*-spline representation of the registration warp field (Rueckert et al., 1999). A study-specific template was then created from the resulting images, to which the native grey matter images were re-registered non-linearly. Modulation of the registered partial volume maps was conducted by dividing them by the Jacobian of the warp field. Finally, the modulated, segmented images were smoothed with an isotropic Gaussian kernel with a sigma of 3mm.

### 2.6.3. Voxel-based morphometry analyses

In each of the studies, group contrasts were first conducted, identifying regions of differing grey matter intensity (i.e., a proxy measure of brain atrophy). Next, correlations were explored between grey matter intensity and performance on the behavioural variable of interest. This analysis allows for the characterisation of the brain regions that are associated with different aspects of the self.

Details of the study-specific analyses are provided in Chapters 4, 5, and 6.

## 2.7. Diffusion-weighted MRI acquisition and pre-processing

Participants underwent diffusion-weighted MRI imaging and diffusion tensor imaging analyses were conducted to analyse white matter microstructure.

### 2.7.1. Image acquisition

Diffusion-weighted MRI was conducted using a 3Tesla MRI Scanner with a standard quadrature head coil (eight channels). Whole-brain echo planar images with 64 noncollinear gradient directions were collected using the following sequences: matrix 96 x 96mm, 55 slices, voxel size = 2.5mm$^3$ repetition time/echo time/inversion time: 8400/68/90msec, b-value = 1000 sec/mm$^2$, field of view = 240 x 240mm.

### 2.7.2. Data pre-processing

Tract-based Spatial Statistics (TBSS) in FSL were employed to perform a skeleton-based analysis of white matter fractional anisotropy (FA). Raw diffusion-weighted images for each participant were corrected for eddy-currents and co-registered using nonlinear registration to MNI standard space using their respective 3D $T_1$-weighted structural MR image. Given the coarse resolution of diffusion tensor imaging data (i.e., 2.5mm$^3$), this template was subsampled at 2mm$^3$. Following image registration, a tensor model was fitted to the diffusion-weighted image and FA maps generated for each participant. FA maps were then averaged to produce a group mean FA image. A skeletonised algorithm was applied to define a group template of the lines of maximum FA (S. Smith et al., 2006), corresponding to the centres of the white matter tracts. Finally, FA values for each participant were projected onto the group template skeleton.

### 2.7.3. Diffusion tensor imaging analyses

Group contrasts were first conducted, identifying regions of differing FA (i.e., a proxy measure of white matter integrity). Next, correlations were explored between FA and performance on the behavioural variable of interest.

Details of the study-specific analyses are provided in Chapter 5.

## 2.8. Summary

The comprehensive clinical characterisation of dementia patients, including the neurological, neuropsychological, and MRI assessments described in this chapter, ensures their accurate diagnosis in line with current consensus criteria. This approach, combined with the novel

experimental measures and neuroimaging analyses to be described in upcoming chapters, enables the detailed neurocognitive characterisation of sense of self across AD, SD, and bvFTD syndromes.

# Chapter 3

# NExt – A new approach to examining the extended self

This chapter is a revised version of:

Strikwerda-Brown, C., Mothakunnel, A., Hodges, J. R., Piguet, O., Irish, M. (2018). External details revisited – A new taxonomy for coding 'non-episodic' content during autobiographical memory retrieval. *Journal of Neuropsychology, 13*(3), 371-397.

## 3.1. Introduction

As discussed in Chapter 1, while autobiographical memory (ABM) encompasses both episodic and semantic elements, the majority of studies in this field have focused on clarifying the cognitive and neural substrates of the episodic component. While this emphasis has helped to advance the understanding of subjective continuity of the extended self, far less is known about semantic ABM, and its relevance for narrative continuity of the self. Indeed, it remains unclear whether strictly dissociating between event-based and conceptual information in ABM accurately captures the complexity of autobiographical narration, and therefore, the extended self.

In recent years, the Autobiographical Interview (AI; Levine et al., 2002) has become a popular tool for assessing ABM retrieval. This task requires participants to describe a past, personally experienced event, which occurred at a specific time and place, in as much detail as possible. Unlike other validated techniques which segregate episodic and semantic memory via the use of targeted subscales (Irish, Lawlor, et al., 2011; Kopelman et al., 1989; Piolino et al., 2000), the AI attempts to capture the naturalistic manner in which these two types of information are typically intertwined during autobiographical retrieval (see Barnabe et al., 2012). On the AI, narratives are scored in terms of the number and type of 'internal' (i.e., referring to the main event being described) and 'external' (i.e., any additional information provided) details, which are widely held to reflect episodic and semantic retrieval, respectively. Accordingly, this procedure permits the direct comparison of the constituent elements of ABM without imposing any constraints on their production (Barnabe et al., 2012).

To date, studies using the AI have predominantly focused on the internal details provided during ABM retrieval. This is unsurprising given internal details represent the primary outcome measure of the test, which was originally proposed to adjudicate between different theories regarding the hippocampal contribution to memory (i.e., standard consolidation versus multiple trace theories (Nadel & Moscovitch, 1997; Squire, Cohen, & Nadel, 1984). On the other hand, significantly less attention has been paid to the external details within the autobiographical narrative. These details often situate the retrieved event within the broader context of the individual's life story, and as such, can provide an ecologically valid window into narrative continuity of the self. Currently, however, the external details metric is rarely interpreted in this manner, for a combination of methodological and theoretical reasons. Importantly, the AI allows for external details to be further divided into subcategories including 'external events' (separate from the main event being described), 'semantic' detail, 'repetitions', and 'other', however, such segregation is not consistently performed. Instead, many studies have reported the total external details metric, without considering the constituent elements in more detail (e.g., Benjamin, Cifelli, Garrard, Caine, & Jones, 2015; Spreng et al., 2018), with others reporting only selective subcategories (e.g., Mair, Poirier, & Conway, 2017; Rensen et al., 2017), or failing to examine external details entirely (e.g., Baron & Bluck, 2009; Crete-Nishihata et al., 2012). In addition to their inconsistent reporting, there is a common tendency in the literature to consider the aggregated external details category as uniformly 'semantic' (e.g., Ally, Hussey, & Donahue, 2013; Zeman et al., 2016). By this approach, patient groups providing a relatively equal number of external details to healthy controls are considered to display intact semantic ABM. While no such claim was made in the original AI validation study (Levine et al., 2002), findings that elevated external details in healthy older adults are primarily driven by increased semantic information (Levine et al., 2002; St. Jacques & Levine, 2007) may have led to this erroneous conclusion.

A number of issues, however, are apparent with this tendency to equate the external detail category with semantic information. First, rather than exclusively representing semantic content, the external detail category can also contain episodic elements, as revealed by the inclusion of the external event subcategory in the original AI protocol (Levine et al., 2002). Furthermore, patients with SD have been found to produce elevated levels of external details during autobiographical retrieval (McKinnon et al., 2006) and episodic future thinking (Irish,

Addis, et al., 2012a, 2012b). Given the characteristic impairments in semantic memory in this syndrome, it is unlikely that this overproduction of external details is attributable to the provision of semantic content alone. Equating external details exclusively with 'semantic' retrieval, then, may obscure the true nature of information provided during ABM narration. Moreover, as discussed in Chapter 1, semantic ABM may be subdivided into discrete subcomponents, which vary in their relative degree of 'semanticity' or 'episodicity'. Namely, general events and personal semantics are proposed to lie in between the two extremes of the episodic-semantic continuum. No study, however, has disentangled these subcomponents of semantic ABM within the AI narrative.

Taken together, these findings highlight the need for a revised approach to studying the composition of external details during ABM retrieval, in order to refine the understanding of episodic and semantic contributions to narrative continuity of the extended self. On a practical level, providing a streamlined approach to the conceptualisation and scoring of external details will permit the direct comparison of findings across studies. In addition, from a theoretical perspective, incorporating contemporary knowledge on the episodic-semantic continuum will improve the characterisation of the full range of episodic and semantic elements contained within autobiographical narratives.

This study endeavours to achieve these goals, in two key stages. First, a literature review is undertaken of studies in which the AI scoring system was used as the main outcome measure to examine ABM. In doing so, the aim of Part 1 of this Chapter is to highlight the extensive variability in the reporting and interpreting of AI external details. It was hypothesised that marked inconsistencies in the breakdown of external details would be evident across studies of ABM, leading to divergent conclusions regarding the profile of these details during ABM narration. The findings from this literature review were then used to develop a new taxonomy for the fine-grained classification of external details on the AI. This new protocol (the 'NExt' taxonomy) is intended as an adjunct to the original AI method, allowing for a consistent approach to examining the components of external details. As outlined in Chapter 1, the syndromes of AD and SD provide an ideal test-bed for examining episodic and semantic ABM, and the extended self. Here, therefore, the NExt taxonomy is validated using previously collected AI data in AD and SD populations, compared with healthy older adults. In line with

their characteristic memory profiles, AD patients were predicted to provide more external details from the semantic end of the spectrum, whereas more episodic external details were expected in SD.

## 3.2. Part 1 – Review of existing ABM studies using the AI

### 3.2.1. Method

Studies using the AI scoring method to examine ABM were identified via a review of the literature.[2] An initial search was conducted in PubMed on 20th July 2017 using the term 'Autobiographical Interview', which returned 274 results. Upon reviewing these results, however, it was apparent that several studies had not explicitly used the Autobiographical Interview methodology in their study. Therefore, a search was instead conducted for articles citing the original AI validation study (Levine et al., 2002) in PubMed, Web of Science, Scopus and Google Scholar. These citation searches returned 152, 441, 487, and 733 articles, respectively. In order to ensure all relevant studies were included, the articles from the most comprehensive list were reviewed (i.e., that returned by Google Scholar). The key criteria for inclusion of studies were a primary outcome measure of ABM retrieval, and use of the AI scoring method to segregate details within the narrative of a self-referential, personally experienced event. Studies that were not published in peer-reviewed journals (e.g., conference abstracts, academic theses), not in English, were not primarily experimental (e.g., review papers, opinion pieces, book chapters), did not primarily focus on ABM (e.g., studies of future thinking), assessed memory for events occurring in an experimental setting rather than the participants' daily lives, or did not employ the AI as the primary measure of ABM, were excluded. Of the 733 articles returned by the citation search, 76 met criteria for inclusion. These studies were then classified based on their approach to reporting external details, and the population employed.

### 3.2.2. Results

Table 3.1. displays the studies included in the review, sorted by population, and their method of reporting AI external details. Of these 76 studies, 35 (46.1%) only reported results from the

[2] This literature review provides an adjunct to the main component of the study (i.e., the development and validation of the NExt method, reported in Part 2), and is therefore not intended to represent a formal systematic review or meta-analysis of previous studies.

total external details category, without any further information regarding external detail subcategories. Thirty (39.5%) studies segregated the overall external details into subcategories according to the AI scoring protocol. Of these studies, 21 reported results from three or more of the original Levine subcategories (external event, semantic, repetitions, and other). Further inconsistencies were noted, depending on the overall aims of the studies in question. For example, one study focused exclusively on the external event subcategory, whereas 8 studies reported only the semantic subcategory. Within the latter 8 studies, further variability was evident in that some studies focused only on semantic details and did not report total external details, whereas others adopted a modified scoring system wherein all details were classified as either episodic or semantic. The remaining 11 (14.5%) studies did not report any external detail results.

**Table 3.1.** Summary of studies using the Autobiographical Interview to examine autobiographical memory

| Reporting Method | Population | References |
|---|---|---|
| **Total external details (no breakdown of subcategories) (35)** | *Healthy Adults (8)* | Sheldon and Chu (2017) |
| | | Belfi, Karlan, and Tranel (2016) |
| | | Palombo, Alain, Soderlund, Khuu, and Levine (2015) |
| | | Barnier et al. (2014) |
| | | Ally et al. (2013) |
| | | Campbell, Nadel, Duke, and Ryan (2011) |
| | | Aizpurua and Koutstaal (2010) |
| | | Rudoy, Weintraub, and Paller (2009) |
| | *Healthy Aging (4)* | Spreng et al. (2018) |
| | | Aizpurua and Koutstaal (2015) |
| | | Ford, Rubin, and Giovanello (2014) [3] |
| | | Hohman, Peynircioglu, and Beason-Held (2013) |
| | *Medial Temporal Lobe Lesions/ Epilepsy (9)* | T. D. Miller et al. (2017) |
| | | Zeman, Byruck, Tallis, Vossel, and Tranel (2017)[4] |
| | | St-Laurent, Moscovitch, Tau, and McAndrews (2011) |
| | | Milton et al. (2010) |

[3] Reported internal details as a proportion of total details; external therefore inferred
[4] Only included raw values of external details in supplementary material, no statistical analysis

| | |
|---|---|
| | Milton, Butler, and Zeman (2011) |
| | Kirwan, Bayley, Galvan, and Squire (2008) |
| | Rosenbaum et al. (2008) |
| | Addis, Moscovitch, and McAndrews (2007) |
| | Gilboa et al. (2006) |
| *Neurodegeneration (8)* | (Irish et al., 2018) |
| | Ernst et al. (2016) |
| | Hsieh et al. (2016) |
| | Irish, Kamminga, et al. (2016) |
| | Benjamin et al. (2015) |
| | Miles, Fischer-Mogensen, Nielsen, Hermansen, and Berntsen (2013) |
| | Irish, Hornberger, et al. (2011) |
| | McKinnon et al. (2006) |
| *Other (parietal lesions) (1)* | Davidson et al. (2008) |
| *Paediatric (1)* | Gascoigne et al. (2013) |
| *Psychiatric (3)* | Parlar, Densmore, Hall, Lanius, and McKinnon (2017) |
| | Palombo et al. (2016) |
| | King et al. (2013) |

| | | |
|---|---|---|
| | *Traumatic Brain Injury (1)* | Esopenko and Levine (2017) |
| **Breakdown of external details subcategories (30)** | | |
| ***All subcategories (external event, semantic, repetitions, other) (21)*** | *Healthy Adults (5)* | Grysman (2017) |
| | | Hodgetts et al. (2017)[5] |
| | | Fuentes and Desrocher (2013) |
| | | Palombo, Williams, Abdi, and Levine (2013) |
| | | Fuentes and Desrocher (2011)[6] |
| | *Healthy Aging (2)* | St. Jacques and Levine (2007) |
| | | Levine et al. (2002) |
| | *Medial Temporal Lobe Lesions/Epilepsy (4)* | Munera et al. (2014)[7] |
| | | Levine, Svoboda, Turner, Mandic, and Mackey (2009) |
| | | St-Laurent, Moscovitch, Levine, and McAndrews (2009)[8] |
| | | Rosenbaum, McKinnon, Levine, and Moscovitch (2004) |

[5] Included modified external details subcategories: semantic, categorical, extended, repetitions, tangential, other
[6] External events were included in subcategory description but not results
[7] Did not include external event subcategory
[8] Did not include external event subcategory

| | | |
|---|---|---|
| | *Neurodegeneration (5)* | Bastin et al. (2013)<br>Barnabe et al. (2012)<br>Meulenbroek et al. (2010)<br>McKinnon et al. (2008)<br>Murphy, Troyer, Levine, and Moscovitch (2008) |
| | *Other (parietal lesions) (1)* | Berryhill, Phuong, Picasso, Cabeza, and Olson (2007) |
| | *Paediatric (2)* | Willoughby, McAndrews, and Rovet (2013)<br>Willoughby, Desrocher, Levine, and Rovet (2012) |
| | *Psychiatric (2)* | McKinnon et al. (2015)<br>Soderlund et al. (2014) |
| ***Only semantic subcategory (8)*** | *Healthy Aging (2)* | Mair et al. (2017)[9]<br>St. Jacques, Rubin, and Cabeza (2012)[10] |
| | *Medial Temporal Lobe Lesions/Epilepsy (1)* | Bayley, Hopkins, and Squire (2003)[11] |

[9] Only examined semantic subcategory, excluded external event subcategory, did not report total external details, or other subcategories
[10] Classified all details as either episodic or semantic
[11] Divided all details into either episodic, semantic, or repetitions

| | | |
|---|---|---|
| | *Neurodegeneration (1)* | Rensen et al. (2017)[12] |
| | *Paediatric (1)* | Gascoigne, Barton, Webster, Gill, and Lah (2015)[13] |
| | *Psychiatric (1)* | MacDougall, McKinnon, Herdman, King, and Kiang (2015)[14] |
| | *Traumatic Brain Injury (2)* | Wammes, Good, and Fernandes (2017)[15] |
| | | Palombo, Kapson, et al. (2015)[16] |
| ***Only external event subcategory (1)*** | *Medial Temporal Lobe Lesions/Epilepsy (1)* | Steinvorth, Levine, and Corkin (2005)[17] |
| **No results of external details reported (11)** | *Healthy Adults (3)* | LePort, Stark, McGaugh, and Stark (2015) |
| | | Rabin and Rosenbaum (2012) |
| | | Nadel, Campbell, and Ryan (2007) |
| | *Healthy Aging (1)* | Baron and Bluck (2009) |
| | *Medial Temporal Lobe Lesions/Epilepsy (1)* | Hornberger, Mohamed, et al. (2010) |

[12] Examined semantic subcategory in addition to total external details
[13] Only examined semantic subcategory, not total external details, or other subcategories
[14] Did not examine total external or other subcategories
[15] Divided all details into either episodic, semantic, or repetitions. Did not report total external details
[16] Classified all external details as either semantic or other
[17] Only examined external event details, external perceptual details and total external, no other subcategories

| | | |
|---|---|---|
| | *Neurodegeneration (5)* | Kumfor, Teo, et al. (2016) |
| | | Ernst et al. (2015) |
| | | (Irish, Hornberger, et al., 2014) |
| | | Crete-Nishihata et al. (2012) |
| | | Ernst et al. (2012) |
| | *Other (encephalopathy) (1)* | Zeman et al. (2016) |

### 3.2.3. Discussion

The current review of the ABM literature reveals large variability in the reporting of external details. It is apparent that, despite containing several subcomponents, the majority of studies either collectively aggregate the external details category or disregard this detail type entirely. Studies that explore external details subtypes further demonstrate inconsistencies in their approach, resulting in a lack of clarity regarding exactly what external details represent. Because of their variable reporting of external details, studies using the AI to examine external details cannot be directly compared.

As such, the current variability in the reporting and interpretation of external details may obscure the extent to which different forms of episodic and semantic information are enmeshed within the ABM narrative. A new taxonomy, providing a consistent method of reporting, as well as an accurate picture of the constituent elements that make up the external details category, therefore seems warranted.

## 3.3. Part 2 – The NExt taxonomy: A new classification system for AI external details

### 3.3.1. Method

#### *Participants*

AI data were re-analysed from 51 participants who had taken part in a previous study on ABM (Irish, Hornberger, et al., 2014; Irish, Hornberger, et al., 2011; Irish et al., 2018). Following the exclusion of one AD patient due to an unusually high score (94/100) on the ACE-R, the final sample for this study included 14 SD patients, 19 patients with AD, and 20 healthy Control participants. Control participants were selected from the original study cohort, matched to the patient groups as closely as possible for sex, age, and education. Chapter 2 provides further details of recruitment and neuropsychological assessment. In this study, ACE-R is included as a measure of global cognition, along with specific tests of verbal (ACE-R Address Recall and Word Recall subtests) and visual (RCF; Rey, 1941) episodic memory, language/semantic memory (ACE-R Fluency subscale; and SYDBAT Comprehension and Naming subtests; Savage et al., 2013), and executive function (Trail Making Test Part B-A; Tombaugh, 2004).

***Procedure***

Participants completed an abbreviated version of the Autobiographical Interview (AI; Levine et al., 2002) and provided detailed descriptions of personally experienced events from four different time periods: Teenage Years (11-17 years), Early Adulthood (18-34 years), Middle Adulthood (35-55 years) and Recent period (within the last year). In order to shorten the testing session and reduce the burden on patients, the Early Childhood epoch (up to 11 years) from the original test was not included in this study. If participants were unable to independently retrieve an event, they were presented with a list of typical events for each time period. In keeping with the standard protocol (see Levine et al., 2002 for further details), the task involved an initial Free Recall condition, in which participants described the event in question without guidance or time restrictions. This was followed by General (i.e., asking the participant if there are any further details they can provide) and Specific Probing (i.e., asking directly about event, time, place, perceptual, and emotion/thought details), to encourage greater recall of particular details. As the purpose of the current study was to examine the spontaneous provision of details within an unconstrained narrative, only the condition of low retrieval support is reported here (i.e., a combined index of Free Recall and General Probing).

All interviews were digitally recorded and subsequently transcribed. They were then scored using the original AI protocol (Levine et al., 2002), which segments autobiographical memories into 'internal' or 'external' details. Internal details are those that pertain directly to the main episode being described, whereas external details represent additional information provided in the narrative that is not specific to, or part of, this main event. The original AI protocol classifies these external details into subcategories of External Event (details of events, separate from the main episode being described), Semantic (factual information), Repetitions (details already provided during recall), and Other (metacognitive reflections about the event, comments on the current testing environment, etc.).

***NExt: A new taxonomy for external details***

A new scoring taxonomy was developed for use on the external content details of the AI (i.e., those external details initially classified as External Event or Semantic detail by the Levine et al., 2002 protocol). External details classified by the original protocol as Repetitions or Other were not considered in these analyses, as they do not provide any additional content.

The external content details were then re-classified into one of four categories: Specific Episodes (SE), Extended Episodes (EE), Personal Semantics (PS), and General Semantics (GS). The motivation for these categories was based on evidence for their potential cognitive and neurobiological parcellation (Conway & Pleydell-Pearce, 2000; Grilli & Verfaellie, 2014; Grilli & Verfaellie, 2016; Renoult et al., 2012; Renoult et al., 2016), and to capture the full episodic-semantic spectrum of external details (i.e., from highly specific episodes to over-general semantic detail). The re-coding into the four new subcategories was completed independent of their original classification as External Event or Semantic.

Specific Episodes (SE) were defined as events specific to time (i.e., lasting less than 24 hours) and place, that were separate from the defined main, internal event. Extended Episodes (EE) were also personally experienced memories, though less specific than SE (i.e., general events: either extended in time or repeated). Details classified as Personal Semantics (PS) were non-episodic but personally relevant facts. Finally, General Semantics (GS) included facts and knowledge about the world that were not directly autobiographically relevant. The full NExt scoring protocol, including examples of each detail type, is provided in Box 3.1., and an excerpt from a healthy Control's transcript scored using the NExt protocol is contained in Appendix B. Figure 3.1. also depicts the relationship between the NExt scoring system and the Levine et al. (2002) protocol, representing the intermediate status of the EE subcategory as reflecting an overlap between the original External Event and Semantic detail types.

**Box 3.1.** NExt External Details Scoring Protocol

**Specific Episodes (SE)**

Any details that are related to the memory of a specific event experienced by the participant but distinct from the central event described for this time period (i.e., the event which was scored predominantly in terms of 'internal' details). Although technically external to the main event being scored, this episode still fulfils the criteria of being a specific episodic, i.e., lasting no more than 24 hours in duration, and situated within a distinct spatiotemporal framework, yet falls in the external category as it is outside the scope of the main event.

*E.g., "My wife gave birth to our first child [internal event]. The next day, the people from the newspaper came and took a photo of us: me, my wife, and our child [external- SE]"; "One day I said to John, let's go to the Whitsundays"; "A couple of days later we travelled back home."*

**Extended Episodes (EE)**

This refers to personally experienced memories that lack the specificity of SE, but still contain some spatiotemporal information (i.e., general events). Specifically, they are one (or a combination) of the following:

- Extended in time (i.e., lasting greater than 24 hours, up to whole lifetime periods)

*E.g., "We stayed with my wife's family for a few days"; "I recovered from my illness"; "I built a house for my parents"; "I worked in the city for a few years"*

- Repeated (i.e., occurred a number of times, or involve the drawing upon of a number of events)

*E.g., "We went there every Christmas"; "We spent a lot of time there"; "Whenever I go back to Victoria…"; "We sometimes danced in the rain"; "I moved house many times"; "Normally we would go the opposite way"*

*Note: EE does not include memories that refer to something that the participant has not done, as this would not be based on any constituent episodes. *E.g., "I had never sailed*

*before"*; or *"I had not seen her for 30 years*" would instead fall under the category of Personal Semantics (PS; see below).

**Personal Semantics (PS)**

This includes details that are non-episodic in nature, i.e., they have been abstracted and are no longer linked to a specific episode, yet remain personally or autobiographically relevant. For example:

- Statements of personal roles

*E.g., "I was a dancer"*

- Statements of personal traits

*E.g., "I am more emotional these days"; "I'm good at reading maps"*

- Facts about oneself that are not linked to an episode

*E.g., "I have two brothers"; "I live in Sydney"*

- Personal thoughts and beliefs not related to an episode

*E.g., "I like sports"*

- Facts about other people if the statements are autobiographically relevant, i.e., are described in relation to oneself/one's own life

*E.g., "My father was a government public servant"; "My parents have a holiday home"; "My grandfather died before I was born"; "They were older than me"; "She was married to my sister"*

*Note PS does not include statements about other people (including family and friends) if the statement is no longer directly autobiographically relevant. *E.g., "Sam was my best friend"* would be classed as PS. However, "*Sam was always very shy"* would be classed as General Semantics (GS; see below). Similarly, *"My father remarried"* would be classed as PS, however *"My father's first wife died when she was 45"* would be GS (below).

**General Semantics (GS)**

This includes details that are non-episodic in nature and not explicitly self-relevant. For example:

- General knowledge (i.e., facts about the world and public events) including that which sets context for the event

*E.g., "Doctors have had years of training"; "The place is west of Port Lincoln"; "Long skirts were all the rage in those days"*

- Facts about other people (including family and friends) when the statements are not directly related to oneself

*E.g., "Uncle Sam was a very shy person"; "They have three children"*

- Events that happened to other people that the participant did not directly experience themselves

*E.g., "My sister-in-law gave birth to a daughter that same day"*

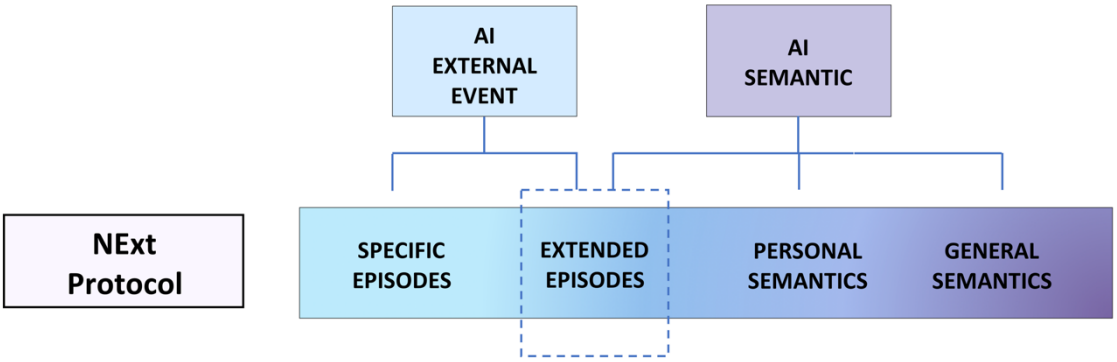



*Figure 3.1.* Comparison of the original (Levine et al., 2002; top) and NExt (bottom) taxonomies for classifying external details on the Autobiographical Interview (AI), demonstrating the episodic-semantic continuum captured by the NExt protocol, and the 'Extended Episode' (EE) subcategory reflecting an overlap between the original External Event and Semantic detail types.

The thesis author (CSB) scored all of the participants' transcripts using the NExt protocol. A second investigator (AM) re-scored a random sample of 40 of the memories (i.e., approximately 20% of the total, the accepted figure for establishing inter-rater reliability on narrative data; Syed & Nelson, 2015), blind to diagnosis and to the external detail coding completed by CSB. These transcripts were evenly distributed across each of the four time

periods and diagnostic groups. The two raters achieved excellent inter-rater reliability for overall external detail classifications (intraclass correlation coefficient: .95) and for each of the NExt subcategories (intraclass correlation coefficients: SE: .98, EE: .81, PS: .91, and GS: .99).

***Statistical analyses***

The AI variables of interest for the current study were Total Content details (i.e., internal and content-based external details combined), Internal details, External details (including only content details), and the newly created external detail categories of SE, EE, PS, and GS. The Levine et al. (2002) External detail subcategories of Semantic (SEM) and External Event (EXT-EVT) were also examined, in order to compare the original and new scoring systems. To investigate profiles across life epochs, a Remote period composite (i.e., average of Teenage, Early Adulthood, and Middle Adulthood) was examined separately from Recent memory performance (consistent with Addis et al., 2009; Irish, Hornberger, et al., 2011; Irish et al., 2018)[18]. Finally, Total scores were created for each external subcategory by summing performance across all time periods.

A series of one-way Analysis of Variance (ANOVAs) and Sidak *post hoc* tests were used to explore between-group differences (Control, SD, AD) on demographic variables and neuropsychological tasks, with independent samples t-tests employed for variables only collected in the patient groups. Chi-squared tests ($\chi^2$) were used to compare the frequency of dichotomous variables (i.e., sex). Univariate and multivariate analyses of covariance (MANCOVA) using the robust Pillai's trace multivariate statistic and Sidak *post hoc* tests were employed to compare groups on AI variables, adjusting for age. A multivariate, as opposed to repeated measures, approach was chosen given the data violated the assumption of sphericity (i.e., significant Mauchly's test) (O'Brien & Kaiser, 1985), the sample size was large relative to number of variables (Stevens, 1992), the NExt variables were not independent, and the primary research question related to between-group differences on, rather than the

[18] As 6 SD patients and 4 AD patients were reported to have onset of symptoms within the Middle Adulthood period (i.e., between 35-55 years), the potential effect of disease onset within this period on the profile of details provided for the epoch was explored. No significant relationships emerged. Results of these analyses are provided in Appendix B.

relationship between, the NExt variables. Effect sizes for the analyses of covariance were calculated using partial eta squared ($\eta^2$) values. Finally, the robust Spearman's correlation coefficient was used to explore associations between the new external detail subcategories and neuropsychological variables of interest in the patient groups.

### 3.3.2. Results

***Demographics and neuropsychological performance***

Table 3.2. displays participant demographics and neuropsychological performance. Groups did not differ significantly for sex ($p$ = .08) or years of education ($p$ = .99), but Control participants were significantly older than SD patients ($p$ = .02). Disease duration significantly varied between patient groups, with the SD group showing a longer disease duration compared with the AD group. Nonetheless, no significant differences were apparent between the two patient groups on the CBI ($p$ = .98) or FTD-FRS ($p$ = .47), indicating similar behavioural change and disease severity.

Both patient groups displayed characteristic cognitive profiles on the core neuropsychological tests. Briefly, relative to Controls, SD patients showed significant reductions in global cognitive functioning (ACE-R Total), verbal episodic memory (ACE-R Address Recall and Word Recall), and semantic memory (ACE-R Fluency, and SYDBAT Naming and Comprehension). This was in the context of relatively preserved visual episodic memory (RCF 3-minute Recall), and executive function (TMT B minus A). AD patients also showed impairments in global cognitive functioning, verbal episodic memory, and semantic memory (ACE-R Fluency, SYDBAT Naming and Comprehension); with additional impairments in visual episodic memory and executive function.

Direct comparison of the patient groups revealed disproportionate disruption of global cognitive functioning, Comprehension, and Naming in SD relative to AD, with worse visual episodic memory and executive function in AD compared with SD patients, in keeping with the hallmark clinical profiles of these syndromes.

**Table 3.2.** Demographics and clinical characteristics of the study cohort

| Variable | SD | AD | Control | F | Group effect | Post hoc test |
|---|---|---|---|---|---|---|
| N | 13 | 18 | 20 | | | |
| Sex (M/F) | 11/2 | 15/3 | 11/9 | $\chi^2$ = 5.09 | .08 | |
| Age (years) | 61.15 (8.39) | 66.17 (8.95) | 68.75 (5.22) | 4.03 | .02 | Controls > SD |
| Education (years) | 12.42 (2.75) | 12.58 (3.05) | 12.55 (3.31) | .01 | .99 | |
| Disease duration (years) | 5.17 (1.85) | 3.17 (2.20) | n/a | t = 2.59 | .02 | SD > AD |
| CBI Total (180) | 46.31 (21.78) | 43.53 (31.70) | 8.10 (8.79) | 16.35 | <.001 | SD & AD > Controls |
| FTD-FRS Rasch Score | 1.51 (1.34) | 1.14 (1.35) | n/a | t = .73 | .47 | |
| ACE-R (100) | 64 (12.54) | 74.61 (12.49) | 93.4 (3.35) | 37.47 | <.001 | Controls > SD & AD; AD > SD |
| ACE-R Address Recall (7) | 1.69 (1.60) | 1.44 (2.09) | 5.90 (1.07) | 43.59 | <.001 | Controls > SD & AD |
| ACE-R Word Recall (3) | 1.17 (1.03) | 1.22 (1.17) | 2.80 (0.41) | 19.02 | <.001 | Controls > SD & AD |
| ACE-R Fluency (14) | 5.33 (3.68) | 7.67 (3.20) | 11.55 (1.57) | 20.19 | <.001 | Controls > SD & AD |
| RCF 3 min recall (36) | 13.62 (8.19) | 4.10 (4.45) | 17.05 (4.45) | 22.24 | <.001 | Controls & SD > AD |

| | | | | | | |
|---|---|---|---|---|---|---|
| SYDBAT Compr. (30) | 21.46 (5.74) | 25.31 (4.27) | 29.25 (0.79) | 16.43 | <.001 | Controls > SD & AD; AD > SD |
| SYDBAT Naming (30) | 6.85(4.36) | 19.81(5.21) | 26.15(2.54) | 89.77 | <.001 | Controls > SD & AD; AD > SD |
| Trail Making Test B-A | 52.92 (32.71) | 94.91 (45.00) | 54.16 (31.61) | 5.46 | .008 | Controls & SD > AD |

*Notes:* Maximum test score depicted in brackets where appropriate. Values represent means and standard deviations for each group.

n/a: not applicable; ACE-R: Addenbrooke's Cognitive Examination-Revised; AD: Alzheimer's disease; CBI: Cambridge Behavioural Inventory; Compr: Comprehension; RCF: Rey Complex Figure; SD: semantic dementia; SYDBAT: Sydney Language Battery.

Disease duration not available for 1 SD patient; ACE-R variables aside from Total not available for 1 SD patient (Total score converted from ACE-III); CBI Total not available for 1 AD patient; FTD-FRS not available for 1 SD and 2 ADs; RCF not available for 3 ADs and 1 Control; SYDBAT Comprehension and Naming not available for 2 ADs; Trail Making Test not available for 7 ADs and 1 Control.

***Overall performance on the AI – standard protocol***

Detailed analysis of AI performance using the standard protocol is contained in Appendix B. Briefly, the current results replicated previous findings of impaired Internal details for SD and AD groups compared with Controls, both overall (i.e., all time periods combined), and for the Remote period. For the Recent period, while ADs again provided significantly fewer Internal details than Controls, SD patients performed at Control level.

***Fine-grained analysis of external details – NExt protocol***

Consistent with the original AI scoring protocol, the between-group external detail subcategory (SE, EE, PS, and GS) comparisons were adjusted for total narrative output. In the current study, this involved including Total Content details as a covariate in the analyses.

Figure 3.2. displays the profiles of NExt external detail subcategories provided by each group, summed across all time periods. Using Pillai's trace, a significant effect of group was found for the number of external details produced (V = .45, F(8, 88) = 3.23, $p$ = .003, partial $\eta^2$ = .23). Specifically, univariate ANCOVAs revealed significant main effects of group for Extended Episodes, Personal Semantics, and General Semantics (EE: F(2, 46) = 7.29, $p$ = .002, partial $\eta^2$ = .24; PS: F(2, 46) = 3.81, $p$ = .03, partial $\eta^2$ = .14; GS: F(2, 46) = 10.46, $p$ < .001, partial $\eta^2$ = .31), but not for Specific Episodes (SE: F(2, 46) = .31, $p$ = .74, partial $\eta^2$ = .01). Follow up Sidak *post hoc* comparisons uncovered distinct differences between the groups across the various external subcategories. SDs and ADs gave significantly more Extended Episodes ($p$ values = .04 & .002, respectively) and General Semantics (p values = .003 & <.001) relative to Controls. AD patients were further found to provide more Personal Semantics than Controls ($p$ = .03). No differences were apparent between the patient groups for any of the external detail subcategories (all $p$ values > .4).

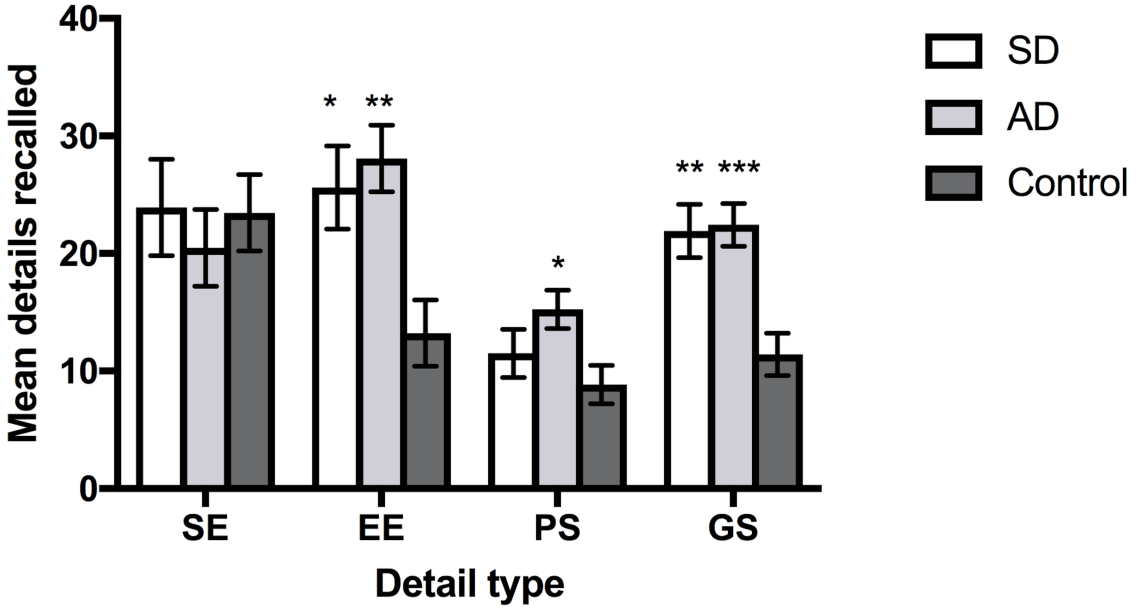



*Figure 3.2.* Breakdown of external details according to the NExt classification system summed across all time periods for each group (estimated marginal means controlling for age and Total Content; error bars represent standard error of the mean). AD: Alzheimer's disease; EE: Extended Episodes; GS: General Semantics; PS: Personal Semantics; SD: semantic dementia;

SE: Specific Episodes. Significant difference from Control performance at *$p < .05$, ** $p < .01$ and ***$p < .001$ respectively.

***Comparison between the AI original scoring method and the NExt taxonomy***

In order to compare the NExt taxonomy with the original protocol, profiles of the Levine et al. (2002) external detail subcategories of Semantic (SEM) and External Event (EXT-EVT) were examined across each group, summed across all time periods (Figure 3.3.). As with the NExt analyses, Total Content was included as a covariate. Using Pillai's trace, a significant effect of group was found for the number of external details produced ($V = .41$, $F(4, 92) = 5.92$, $p < .001$, partial $\eta^2 = .21$). Univariate ANCOVAs revealed a main effect of group for SEM details ($F(2, 46) = 11.68$, $p < .001$, partial $\eta^2 = .34$), with follow-up comparisons indicating AD patients provided more SEM than controls ($p < .001$). No significant differences were apparent between the number of SEM details recalled by SD and control groups ($p = .08$), or between the two patient groups ($p = .18$). Further, no significant between-group differences were observed for EXT-EVT details ($F(2, 46) = 1.62$, $p = .21$, partial $\eta^2 = .07$).

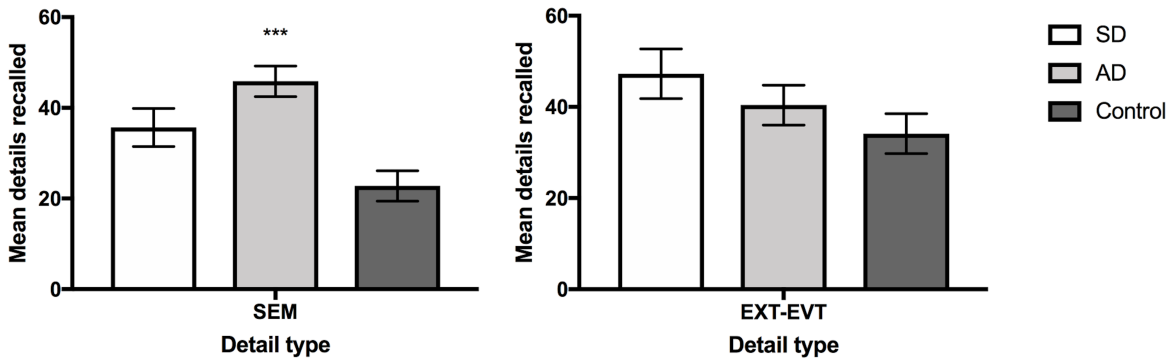



*Figure 3.3.* Breakdown of external details according to the original Levine et al. (2002) classification system summed across all time periods for each group (estimated marginal means controlling for age and Total Content, error bars represent standard error of the mean). AD: Alzheimer's disease; EXT-EVT: External Event; SEM: Semantic; SD: semantic dementia. Significant difference from control performance at *** $p < .001$.

***NExt external detail profiles by time period***

For the Remote period, Pillai's trace revealed a significant effect of group on the number of external details produced (V = .39, F(8, 88) = 2.65, $p$ = .01, partial $\eta^2$ = .19). Using univariate ANCOVAs, significant between-group effects emerged for Extended Episodes, Personal Semantics and General Semantic categories (EE: F(2, 46) = 6.30, $p$ = .004, partial $\eta^2$ = .22; PS: F(2, 46) = 4.28, $p$ = .02, partial $\eta^2$ = .16; GS: F(2, 46) = 4.10, $p$ = .02, partial $\eta^2$ = .15), with no main effect of group for Specific Episodes (F(2, 46) = .65, $p$ = .53, partial $\eta^2$ = .03). *Post hoc* analyses revealed that SD and AD provided increased Extended Episodes relative to Controls ($p$ values = .02 & .009, respectively). In addition, ADs provided a greater number of Personal Semantic and General Semantic details compared with Controls (PS: $p$ = .02, GS: $p$ = .03). Patient groups did not differ significantly in the provision of any of the external detail subtypes for the Remote period (all $p$ values > .56) (Figure 3.4.).

For the Recent period, Pillai's trace revealed a significant effect of group on the number of external details produced (V = .35, F(8, 88) = 2.65, $p$ = .03, partial $\eta^2$ = .17). Specifically, an effect of group was apparent for Extended Episodes (F(2, 46) = 4.05, $p$ = .02, partial $\eta^2$ = .15) and General Semantics (F(2, 46) = 3.53, $p$ = .04, partial $\eta^2$ = .13), such that AD patients provided more EE details than Controls ($p$ = .03) and SD patients gave more GS details than Controls ($p$ = .03). No significant differences were present between SD and AD patients on their provision of Extended Episodes ($p$ = .96) or General Semantics ($p$ = .49), and all groups provided similar amounts of Specific Episodes and Personal Semantics for the Recent period (SE: F(2, 46) = .23, $p$ = .79, partial $\eta^2$ = .01; PS: F(2, 46) = 1.69, $p$ = .20, partial $\eta^2$ = .07) (Figure 3.4.).

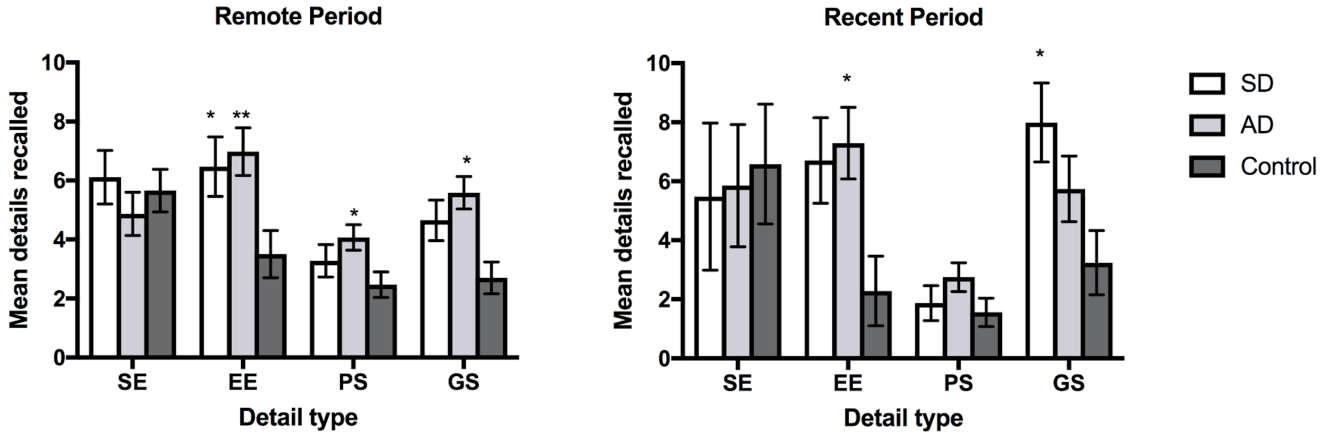



*Figure 3.4.* Breakdown of external details according to the NExt classification system for each group, for Remote (left) and Recent (right) periods (estimated marginal means controlling for age and Total Content; error bars represent standard error of the mean). AD: Alzheimer's disease; EE: Extended Episodes; GS: General Semantics; PS: Personal Semantics; SD: semantic dementia; SE: Specific Episodes. Significant difference from Control performance at *$p$ < .05 and **$p$ < .01 respectively.

***Correlations between Extended Episodes and episodic and semantic performance***

Given the proposed overlap of semantic and episodic elements within the Extended Episode subcategory (Grilli & Verfaellie, 2014; Renoult et al., 2012; Figure 3.1.), and the elevations in this detail type for both patient groups and time periods, the cognitive correlates of Extended Episodes were further explored. Spearman's correlations between neuropsychological measures of episodic and semantic memory and Extended Episode proportion scores (i.e., individual EE score divided by Total Content details) were performed separately in AD and SD, for Remote and Recent periods (Table 3.3.).

In SD, no significant correlations emerged for the Remote period, however Recent Extended Episodes were negatively correlated with independent measures of semantic processing (ACE-R Fluency: r = -.80, $p$ = .002; SYDBAT Naming: r = -.77, $p$ = .002). In AD, by contrast, a negative correlation between Extended Episodes and verbal episodic memory (Word Recall: r = -.48, $p$ = .04) was observed in the Remote period.

**Table 3.3.** Correlations between NExt Extended Episode (EE) details generated on the Autobiographical Interview (AI) and scores on neuropsychological tests of episodic and semantic memory for semantic dementia (SD) and Alzheimer's disease (AD) patients

| | SD | | AD | |
|---|---|---|---|---|
| | **Remote EE** | **Recent EE** | **Remote EE** | **Recent EE** |
| **Episodic Memory** | | | | |
| ACE-R Address Recall | .36 | -.40 | .08 | .46 |
| ACE-R Word Recall | .03 | -.31 | **-.48*** | .18 |
| RCF | .07 | -.37 | .01 | .38 |
| **Semantic Memory** | | | | |
| ACE-R Fluency | .17 | **-.80**** | -.28 | .02 |
| SYDBAT Comprehension | -.04 | -.49 | -.17 | -.03 |
| SYDBAT Naming | -.04 | **-.77**** | -.11 | -.16 |

*Notes:* ACE-R: Addenbrooke's Cognitive Examination-Revised; RCF: Rey Complex Figure; SYDBAT: Sydney Language Battery**.**

Asterisks denote significance at *$p < .05$ and **$p < .01$.

## 3.4. General Discussion

This study sought to characterise the variability in reporting and interpreting of external details on the AI, and use these findings to develop a new taxonomy to refine the understanding of the episodic and semantic information contained within autobiographical narratives. In turn, this study aimed to improve the characterisation of the mechanisms

underlying narrative continuity of the extended self. Motivated by recent theoretical frameworks emphasising the episodic-semantic continuum (Grilli & Verfaellie, 2014; Irish, 2020; Renoult et al., 2012), the new external details ('NExt') taxonomy yielded distinct profiles of the external detail subtypes for AD, SD, and healthy Controls, and for remote and recent epochs. The potential of this NExt classification system to help clarify the episodic and semantic elements underpinning narrative continuity of the self will now be discussed.

### 3.4.1. Sensitivity of the NExt taxonomy to differential profiles of ABM across groups

The NExt taxonomy successfully discriminated between AD, SD, and healthy Control participants, with distinct external detail profiles emerging in each clinical group. Overall, AD patients gave disproportionately greater amounts of Extended Episode, Personal Semantic, and General Semantic external details compared with Controls, whereas the SD group provided higher levels of Extended Episodes and General Semantics only. No between-group differences were apparent for Specific Episodes (i.e., details of specific events separate from the main episode being described). All groups, however, provided a nontrivial amount of this external detail type (> 22% of total external details) within their autobiographical narratives. This observation supports the hypothesis that, rather than representing strictly semantic content, the 'external' details in the autobiographical narrative also contain episodic elements, further highlighting the confluence of episodic and semantic processes in supporting narrative self-continuity. In addition, compared with the original AI scoring protocol (Levine et al., 2002), the NExt taxonomy demonstrated improved sensitivity to detect differences in external detail provision across patient groups, both in the present analyses, and with reference to past work in AD and SD (no difference in external details between patients and controls in most previous studies; Barnabe et al., 2012; Benjamin et al., 2015; Irish, Hornberger, et al., 2011; Irish et al., 2018; McKinnon et al., 2008; Meulenbroek et al., 2010). Direct comparison of external detail profiles across previous studies has also been impeded by the variability in how these details are reported, as demonstrated in Part 1 of this Chapter. The NExt taxonomy offers a theoretically informed approach to address these inconsistencies in the ABM literature, thus improving the characterisation of the episodic and semantic content contained within autobiographical narratives.

### 3.4.2. Composition of external details in AD

Distinct profiles of NExt details in AD patients compared with Controls emerged for remote and recent time periods. Regarding the remote epoch, AD patients provided a greater level of Extended Episodes, Personal Semantic, and General Semantic details compared to Controls, in the context of impaired episodic (Internal details) retrieval. The elevation of remote Personal Semantic and General Semantic details is consistent with the proposed importance of semantic information in supporting narrative self-continuity for the remote past, as outlined in Chapter 1. Further, these findings are in line with the study hypothesis of increased semantic external details in AD, and also mesh well with the relative preservation of remote semantic ABM in AD established using direct probing methods (see Chapter 1). Typically, the Extended Episode category is suggested to occupy an intermediate position on the episodic-semantic continuum, but to more closely resemble episodic, rather than semantic, memory (Renoult et al., 2012). Counter to this proposal, however, was the finding that elevated EE in AD during remote ABM narration correlated inversely with episodic memory in this group, such that worse episodic memory related to the provision of more EE details. Accordingly, the constituents of EE in AD may rely more heavily upon semanticised, rather than episodic, elements. Such an interpretation is consistent with the proposal by Grilli and Verfaellie (2016), that this detail type may in fact draw upon either episodic or semantic memory. Collectively, the external detail profile in AD supports the suggestions outlined in Chapter 1 that these patients may retain some degree of narrative continuity for the remote period. Importantly, however, the current findings extend those previous, by revealing how individuals with AD may weave personally-relevant details, spanning the full spectrum of semantic information, into a naturalistic narrative of their life story for the remote past. This life story, albeit outdated, may be retold and shared with others, to maintain some degree of persistence of the extended self in AD.

In contrast to their remote external detail profile, only Extended Episodes were elevated in AD for the recent period. Again, these details likely reflect AD patients' reliance on semantic and/or schematic facets of retrieved events when narrating their past. It is unclear, however, whether the EE details provided during recent ABM narration in AD referred to general events occurring within the past year, versus more remote time periods. Nonetheless, the abundance of this detail type during narration of the recent past in AD provides the first

evidence of some semblance of narrative continuity for these patients for the recent period, even if it reflects the attempted 'filling' of recent time periods with remote events. Taken together, the external detail profiles in AD revealed by the NExt taxonomy suggest that even in the absence of detailed event-based recollection and subjective self-continuity, semantic elements including general events, personal semantic facts, as well as general conceptual information, may still be harnessed to allow a degree of narrative continuity across remote and recent periods in these patients (see also Rathbone et al., 2019). While a previous study revealed the overall coherence of autobiographical narratives to be reduced in AD compared with healthy older adults, these somewhat simplified life stories are nonetheless sufficient to provide a sense of continuity across time in these patients (Tippett et al., 2018).

### 3.4.3. Composition of external details in SD

Similar to AD, the lifetime period in question appeared to play an important role in the resultant external details provided by SD patients, with divergent NExt profiles displayed for SD versus Controls in remote and recent epochs. Regarding remote retrieval, only the Extended Episode category was significantly elevated in SD, relative to Controls. By contrast, SD patients provided increased General Semantic details for the recent period, compared with Control participants. These elevations in seemingly semantic details are contrary to the study hypotheses, and at first glance, appear counterintuitive, given the characteristic semantic impairments in the disorder. As these details are inextricably bound to a specific event, however, they may have been acquired in an episodic manner, rather than reflecting truly abstracted semantic knowledge (Graham et al., 1997; Irish, Addis, et al., 2012b; McKinnon et al., 2006). For example, a qualitative review of the recent GS details provided by the SD group in this study suggested that the majority of these details, despite appearing as facts, could reasonably have been recently encoded (and retrieved) as part of an episodic event. For example, mentioning the distance of a location relative to one's home, while typically regarded as general semantic knowledge, could in fact reflect episodic recollection of a recent visit there. The proposal that external details in SD are more likely to be influenced by episodic, rather than general semantic, processes, is further supported by the finding of robust negative correlations between recent EE and measures of semantic memory in this group (*r* values larger than -.7). Unlike in AD, then, the Extended Episodes in SD may draw more heavily upon episodic, instead of semantic, representations. Irrespective of the origin

of such details, however, they may contribute to narrative continuity of the extended self in SD by providing relevant information for one's life story (Conway & Pleydell-Pearce, 2000), for both remote and recent time periods. It may be argued that this is the case even if the details are tangential to the main event being described (as seen in Seixas Lima et al., 2019), given they reflect self-relevant content that has been weaved into the personal narrative. Together these findings suggest a degree of narrative continuity of the extended self may be maintained in SD for both remote and recent periods. How the 'episodic-like' nature of this narrative manifests behaviourally, compared with the more 'semantic-like' life story seen in AD, will be interesting to explore. Studies examining the phenomenology (e.g., autonoetic consciousness, visual imagery) of the NExt detail types across patient groups will also be important in confirming their respective contributions to subjective versus narrative continuity.

### 3.4.4. Conclusions

The NExt taxonomy enables the fine-grained analysis of the episodic-semantic spectrum of external details, demonstrating improved sensitivity to differentiating between the ABM narratives of patient groups relative to healthy Controls. This allows for a refined understanding of the episodic and semantic contributions to narrative continuity of the extended self. Indeed, the distinct mechanisms underpinning external details outlined here in AD and SD, and across remote and recent epochs, highlight the varied ways in which narrative self-continuity for the past can be provided. Namely, details spanning the full episodic-semantic spectrum can be harnessed to provide narrative continuity for both remote and recent time periods. Intriguingly, the current findings suggest a preferential reliance on the most preserved memory type to support narrative continuity of the self, in the face of impairment to its counterpart (see also Irish, 2020). How the full range of episodic to semantic information contributes to narrative self-continuity for the future, however, remains to be uncovered, which forms the focus of Chapter 4.

# Chapter 4

# Applying NExt to the extended self in the future

## 4.1. Introduction

As outlined in Chapter 1, the extended self does not solely incorporate the personal past, but also extends into the future. The extant literature on episodic future thinking has uncovered how subjective continuity of the self for the future incorporates both episodic and semantic processes. The contribution of episodic and semantic memory to narrative self-continuity for the future, however, is not yet understood, given a paucity of studies on this topic.

In order to improve characterisation of narrative continuity for the past, Chapter 3 proposed a novel method (the 'NExt' taxonomy) for categorising the 'external' details provided within descriptions of personally-relevant past events, given these details often capture contextually-relevant background information for one's life story. The NExt taxonomy encompasses the full episodic-semantic spectrum of details provided within the ABM narrative, and as such, can examine the constituent elements of narrative self-continuity in a naturalistic manner. The distinct profiles of external details within ABM narratives in AD and SD, as revealed by the NExt taxonomy in Chapter 3, highlight how episodic and semantic processes may interact in the service of narrative continuity of the self for the past. It remains unclear whether this interplay also manifests for the future period.

Moreover, while the neural correlates of subjective self-continuity for both past and future are now relatively well-characterised, the brain regions underlying past and future narrative self-continuity are incompletely understood (see Chapter 1). The limited research to date has implicated medial prefrontal, medial and lateral temporal, precuneus, and lateral parietal regions in semantic ABM (reviewed by Renoult et al., 2012), but it is unclear whether a similar brain network extends to personal semantic processing in the future. The neurodegenerative disorders of AD and SD offer a unique opportunity to examine the neural correlates of these processes, given their characteristic atrophy to many of the regions implicated in semantic ABM, and their varying degrees of personal semantic memory impairment (see Chapters 1

and 3). Surprisingly, however, no studies to date have examined the neural underpinnings of narrative self-continuity in these syndromes.

This study employed the NExt taxonomy to explore the external content of episodic future thinking narratives, and their cognitive and neural correlates, with the aim to better characterise the neurocognitive mechanisms underlying narrative continuity for the future. Consistent with Chapter 3, NExt profiles were examined in patients with AD and SD, compared with healthy controls. In line with previous suggestions (Irish, 2020; Szpunar, 2010) and empirical findings (Chapter 3; Irish, Addis, et al., 2012b), the patterns of external details within future narratives were predicted to encompass the information that remains most accessible to the patients. Namely, AD patents were expected to draw predominantly upon intact semantic representations, whereas SD patients would primarily incorporate details from recent episodic memory. Similar patterns were hypothesised for the neural correlates, with patient groups predicted to draw upon the brain regions that remain relatively preserved (namely anterior DMN regions in AD, and posterior DMN regions in SD) in order to produce their external details, and in turn, narrative self-continuity for the future.

## 4.2. Method

### 4.2.1. Participants

Autobiographical past and future narratives were re-analysed for 39 participants who had previously taken part in a study on episodic future thinking (Irish, Addis, et al., 2012a, 2012b), including 11 AD and 13 SD patients, and 15 healthy Controls. Further details of recruitment and neuropsychological assessment are contained within Chapter 2. In this study, ACE-R is employed as a measure of global cognition, along with more specific tests of verbal (ACE-R Address Recall subtest) and non-verbal episodic memory (RCF; Rey, 1941), language/semantic memory (ACE-R Fluency; Mioshi et al., 2006; and SYDBAT Naming and Comprehension subtests; Savage et al., 2013), and executive function (Trail Making Test Part B-A; Tombaugh, 2004).

### 4.2.2. Procedure

Participants completed a modified version of the Past-Future task (Addis et al., 2009; Addis et al., 2008). Participants were required to describe in detail specific, personally relevant events that had occurred within the past year (Past), or that might occur over the next year (Future). In order to ensure suitability of the task for the dementia patients, the trials were limited to three Past and three Future events, with each involving the presentation of a cue word accompanied by a visual image. Two separate lists of 3 cue words were randomly allocated to Past or Future trials for each participant. The order of temporal condition (i.e., completing either 3 Past or 3 Future trials first) and the order of cue words within each list, was also randomised. The event generated, however, did not strictly need to involve the cued object, which instead acted as a general prompt. Specific probes from the AI (Levine et al., 2002) were provided throughout the interview to elicit event, time, place, perceptual, and emotion/thought details. As such, unlike the AI, the Past-Future task did not contain separate conditions for general recall and specific probing.

All interviews were digitally recorded and transcribed. The narratives were initially scored using the original AI protocol, in which narratives are segmented into internal and external details (see Chapter 3; and Levine et al., 2002 for the full scoring protocol).

### 4.2.3. NExt: New external details taxonomy

The NExt taxonomy (Chapter 3) was used to re-classify the external details that were predominantly content-based across Past and Future contexts, that is, those external details initially classified as External Event or Semantic according to the original AI scoring protocol (Levine et al., 2002). Content-based external details were reclassified into one of four categories: Specific Episodes (SE), Extended Episodes (EE), Personal Semantics (PS), and General Semantics (GS). An excerpt from a future event generated by a healthy Control, scored using the NExt protocol, is provided in Appendix C (see Chapter 3 for the full protocol). The thesis author (CSB) scored all of the transcripts using the NExt taxonomy. Excellent inter-rater reliability was established for this scoring system in Chapter 3.

### 4.2.4. Statistical analyses

The main variables of interest were as follows: Total Content details (i.e., internal and content-based external details combined), Internal details, content-based External details, as generated from the original AI scoring protocol, as well as the NExt protocol categories of SE, EE, PS, and GS. Detail scores were averaged across the three Past or three Future events. Consistent with the original AI protocol (Levine et al., 2002), and Chapter 3, the external detail subcategories (SE, EE, PS, GS) were adjusted for total narrative output, with Total content details included as a covariate in the analyses. Variables were all calculated separately for Past and Future narratives.

Between-group differences on demographic and background neuropsychological tasks were examined using one-way ANOVAs with Sidak *post hoc* tests. The frequencies of dichotomous variables (i.e., sex) were compared using chi-squared tests ($\chi^2$). To ensure consistency with Chapter 3, ANCOVAs and MANCOVAs using the robust Pillai's trace multivariate statistic and Sidak *post hoc* tests were employed to compare groups on Past-Future task variables, adjusting for age. Effect sizes were calculated using partial-eta squared ($\eta^2$) values. Finally, Spearman's correlations were used to examine associations between NExt subcategories and neuropsychological variables of interest in the patient groups.

**4.2.5. Neuroimaging analysis**

Thirty participants (11 AD, 10 SD, 9 Controls) were included in the voxel-based morphometry (VBM) analysis. Full details of MRI acquisition and pre-processing are outlined in Chapter 2.

For grey matter intensity, VBM analyses were employed using SPM12. Two-sample t-tests were employed to explore differences in grey matter intensity between groups, controlling for age and total intracranial volume. Next, correlation analyses with grey matter intensity were conducted for the NExt detail subtypes that were significantly elevated in patient groups compared with Controls, with age, total intracranial volume, and Total Content details entered as covariates of no interest. These analyses were conducted in the patient groups only (i.e., not including Controls). Positive t-contrasts were used, providing an index of association between higher grey matter intensity and greater external detail counts. Clusters were uncorrected at a threshold of $p < .001$, with a cluster extent threshold of 100 contiguous

voxels. This statistical approach takes into consideration the small sample size and balances the risk of Type I versus Type II errors (see Lieberman & Cunningham, 2009).

## 4.3. Results

### 4.3.1. Demographics and neuropsychological performance

Participant demographics and neuropsychological performance are displayed in Table 4.1. Groups did not differ significantly for sex ($p$ = .13), or education ($p$ = .27), but Controls were significantly older than SD patients ($p$ = .04). No significant difference between patient groups was apparent for disease severity (disease duration: $p$ = .60), behavioural change (CBI: $p$ = .41), or level of functional impairment (FTD-FRS: $p$ = .33).

AD and SD groups displayed characteristic cognitive profiles on standard neuropsychological tests (Table 4.1.). Briefly, relative to Controls, AD patients showed impairments in global cognitive functioning (ACE-R Total), fluency (ACE-R) and naming (SYDBAT), and verbal (ACE-R Address Recall) and non-verbal (RCF 3-minute recall) episodic memory, in the context of relatively intact semantic comprehension (SYDBAT), and executive function (TMT B minus A). SD patients displayed significant reductions in global cognitive functioning, fluency, naming, comprehension, and verbal episodic memory, in the context of relatively intact non-verbal episodic memory, and executive function.

In keeping with their hallmark neuropsychological profiles, non-verbal episodic memory was disproportionately disrupted in AD compared with SD patients, while fluency, naming, and comprehension were disproportionately impaired in SD relative to AD.

**Table 4.1.** Demographics and clinical characteristics of the study cohort

| Variable | AD | SD | Control | F | Group effect | *Post hoc* test |
|---|---|---|---|---|---|---|
| N | 11 | 13 | 15 | | | |
| Sex M/F | 9/2 | 11/2 | 8/7 | $X^2 = 4.13$ | ns | ns |
| Age (years) | 64.64 (6.10) | 63.00 (5.31) | 69.27 (7.10) | 3.78 | .03 | Controls > SD |
| Education (years) | 11.59 (3.63) | 12.69 (3.36) | 13.65 (2.56) | 1.35 | ns | ns |
| Disease duration (months) | 56.09 (29.19) | 61.92 (24.20) | - | .29 | ns | |
| CBI Total Frequency (180) | 44.82 (25.96) | 61.25 (38.72) | 4.55 (4.01) | 12.79 | < .001 | Controls > AD & SD |
| FTD-FRS Rasch Score | 1.32 (1.06) | .76 (1.56) | - | 1.00 | ns | |
| ACE-R Total (100) | 65.09 (21.58) | 57.15 (14.30) | 93.00 (3.76) | 35.67 | < .001 | Controls > AD & SD |
| ACE-R Address Recall (7) | 1.27 (1.62) | 1.23 (1.92) | 5.67 (1.40) | 33.14 | < .001 | Controls > AD & SD |
| ACE-R Fluency (14) | 7.27 (3.47) | 4.15 (3.63) | 11.73 (1.83) | 22.56 | < .001 | Controls > AD & SD; AD > SD |
| RCF 3-minute recall (36) | 5.78 (5.83) | 14.81 (5.95) | 16.47 (7.07) | 9.94 | < .001 | Controls & SD > AD |

| | | | | | | |
|---|---|---|---|---|---|---|
| SYDBAT Comprehension (30) | 23.91 (5.13) | 15.54 (5.39) | 28.20 (1.81) | 30.08 | < .001 | Controls & AD > SD |
| SYDBAT Naming (30) | 18.73 (6.99) | 5.00 (3.51) | 25.36 (1.96) | 95.16 | < .001 | Controls > AD & SD; AD > SD |
| Trail Making Test B-A | 88.00 (50.49) | 43.97 (70.92) | 51.00 (24.33) | 2.32 | ns | |

*Notes:* Maximum test score depicted in brackets. Values represent means and standard deviations for each group.

ACE-R = Addenbrooke's Cognitive Examination-Revised; AD = Alzheimer's disease; CBI = Cambridge Behavioural Inventory; FTD-FRS = Frontotemporal Dementia Functional Rating Scale; ns = nonsignificant; RCF = Rey Complex Figure; SD = semantic dementia; SYDBAT = Sydney Language Battery.

CBI not available for 1 SD patient and 4 Controls, FTD-FRS not available for 1 SD patient, RCF not available for 1 AD patient, SYDBAT Comprehension not available for 5 Controls, SYDBAT Naming not available for 4 Controls, Trail Making Test B-A not available for 1 SD and 5 AD patients.

### 4.3.2. Overall performance on the Past-Future task: standard AI protocol

Detailed analysis of Past-Future task performance using the standard scoring protocol is provided in Appendix C. Briefly, the current results reproduced previous findings (Irish, Addis, et al., 2012a, 2012b) with AD patients showing significantly reduced Internal details across Past and Future conditions relative to Controls, while SD patients displayed an asymmetric impairment of Future Internal details in the context of intact Past retrieval.

### 4.3.3. Fine-grained analysis of external details for Past and Future events: NExt protocol

Figure 4.1. displays the profiles of NExt external detail subcategories produced by each group for Past and Future events. For Past events, using Pillai's trace, a significant main effect of group was found for the number of external details produced (V = .48, $F(8, 64) = 2.54$, $p = .02$, partial $\eta^2 = .24$). Specifically, univariate ANCOVAs revealed a significant between-group effect

for GS ($F$(2, 34) = 5.06, $p$ = .01, partial $\eta^2$ = .23), reflecting increased provision of GS details in AD relative to Controls ($p$ = .01). No main effect of group was apparent for SE, EE, or PS categories (SE: $F$(2, 34) = 1.90, $p$ = .17, partial $\eta^2$ = .10; EE: $F$(2, 34) = 1.33, $p$ = .28, partial $\eta^2$ = .07; PS: $F$(2, 34) = 2.97, $p$ = .07, partial $\eta^2$ = .15). No significant differences between the external detail subtypes produced by SD versus Controls, or between the two patient groups, emerged for Past events (all $p$ values > .06).

For Future events, Pillai's trace revealed a significant effect of group for the number of external details produced (V = .67, $F$(8, 64) = 4.02, $p$ = .001, partial $\eta^2$ = .33). Looking at each NExt subcategory in turn, univariate ANCOVAs revealed significant group effects for SE ($F$(2, 34) = 7.71, $p$ = .002, partial $\eta^2$ = .31), EE ($F$(2, 34) = 7.14, $p$ = .003, partial $\eta^2$ = .30), GS ($F$(2, 34) = 5.58, $p$ = .008, partial $\eta^2$ = .25) but not for PS (F(2, 34) = .56, $p$ = .58, partial $\eta^2$ = .03). Relative to Controls, AD and SD patients provided more SE details ($p$ values = .009 and .002, respectively), while SD patients provided increased amounts of EE ($p$ = .002) and GS ($p$ = .008) details. Patient groups did not differ on the external detail subtypes produced for future events (all $p$ values > .27).

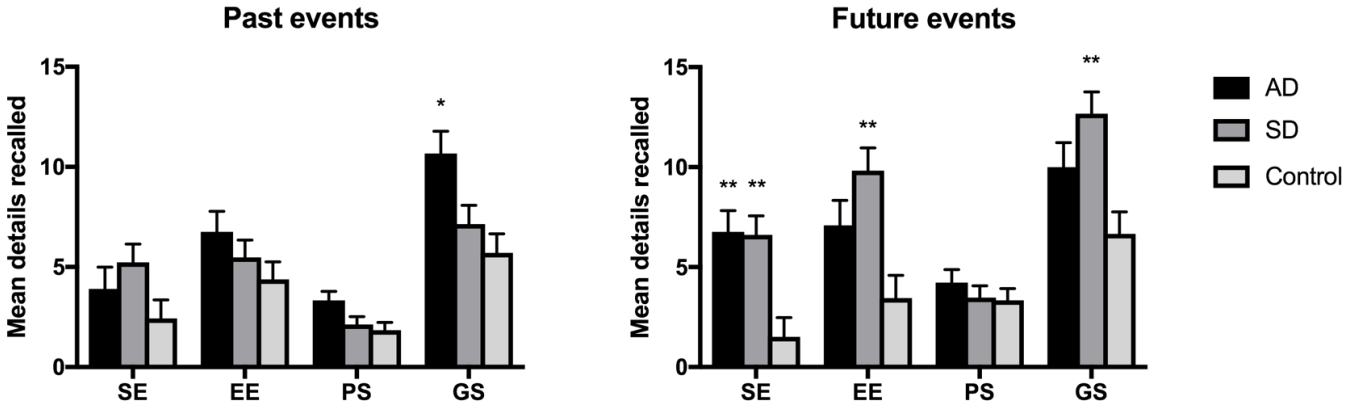



*Figure 4.1.* Breakdown of external details according to the NExt classification system for each group, for Past (left) and Future (right) events (estimated marginal means controlling for age and Total Content; error bars represent standard error of the mean). AD = Alzheimer's disease; EE = Extended Episodes; GS = General Semantics, PS = Personal Semantics; SD = semantic dementia; SE = Specific Episodes. Asterisks denote significant difference from Control performance at *$p$ < .05 and **$p$ < .01.

### 4.3.4. Association between Future NExt external detail subtypes and episodic and semantic performance

In order to examine the cognitive correlates of the Future NExt details, Spearman correlations were used to explore associations between the Future NExt subcategories that differed significantly between groups and neuropsychological measures of episodic and semantic memory. Correlations were performed using proportion scores (i.e. individual NExt scores divided by Total Content details) (Table 4.2.). In AD, future SE details were negatively correlated with episodic memory (RCF recall, r = -.67, $p$ = .04), suggesting that poorer episodic retrieval was associated with greater provision of SE details. In SD, a negative correlation emerged between future EE and semantic memory (SYDBAT comprehension, r = -.71, $p$ = .006), such that impairments in semantic processing related to increased provision of EE details.

**Table 4.2.** Correlations between NExt details generated for Future events and scores on episodic and semantic memory measures for Alzheimer's disease (AD) and semantic dementia (SD) patients

| | **AD** | | **SD** | |
|---|---|---|---|---|
| | Future Specific Episodes (SE) | Future Specific Episodes (SE) | Future Extended Episodes (EE) | Future General Semantics (GS) |
| **Episodic memory** | | | | |
| RCF recall | **-.67*** | .22 | .06 | .05 |
| **Semantic processing** | | | | |
| SYDBAT Comprehension | -.15 | .09 | **-.71**** | .33 |

*Notes:* RCF = Rey Complex Figure; SYDBAT = Sydney Language Battery

RCF missing for 1 AD patient

Asterisks denote significance at *$p$ < .05 and **$p$ < .01.

### 4.3.5. Voxel-based morphometry analyses

***Group differences in grey matter intensity***

Regional reductions in grey matter intensity between groups are displayed in Figure 4.2. Compared with Controls, widespread atrophy was apparent in AD, encompassing bilateral medial and lateral temporal lobes, incorporating the hippocampi, as well as bilateral frontal and posterior brain regions including the PCC and inferior parietal lobule. By contrast, SD patients presented with significant atrophy to the ATLs bilaterally, with a left>right hemisphere predominance, extending into frontoinsular regions primarily on the left. Direct comparison of the patient groups demonstrated a greater burden of atrophy in the AD group in bilateral medial and lateral parietal lobes, and frontal regions including the superior and middle frontal gyri. The reverse contrast revealed greater atrophy in bilateral ATLS, including left anterior hippocampus, and the left cerebellum in SD relative to AD. These patterns of atrophy are consistent with previous reports in AD (Karas et al., 2004) and SD (Rosen et al., 2002).

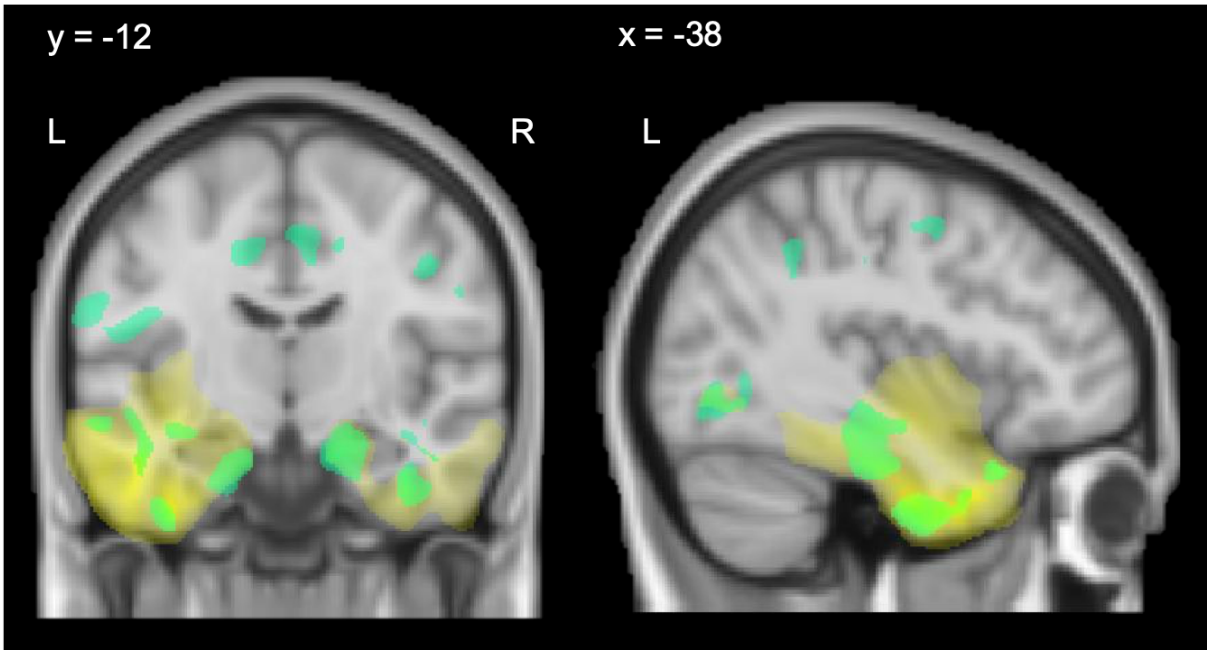



*Figure 4.2.* Voxel-based morphometry (VBM) analyses showing brain areas with decreased grey matter intensity in Alzheimer's disease (AD; green), and in semantic dementia (SD; yellow), compared with Controls. Coloured voxels emerged as significant in the analyses at $p < .001$ uncorrected with a cluster extent threshold of 100 contiguous voxels. Clusters are overlaid on the Montreal Neurological Institute (MNI) standard brain. L = Left; R = Right.

***Neural correlates of NExt subtypes***

For the neuroimaging correlation analysis, focus was constrained to those NExt detail subcategories in which significant elevations were evident in the patient groups relative to Controls during future simulation, namely SE details in AD patients, and SE, EE, and GS details in the SD group (Figure 4.3. and Table 4.3.). In AD, higher levels of SE details related to integrity of bilateral anterior frontal regions including the ventromedial, orbitofrontal, and dorsolateral prefrontal cortices and precentral gyri, along with the left posterior middle temporal gyrus. By contrast, in SD, increased SE details correlated with integrity of right occipital cortex and cerebellum, left precuneus, and left-lateralised posterior frontal regions including superior and middle frontal gyri and supplementary motor cortex. Furthermore, in SD, increased EE details were associated with grey matter intensity in left supramarginal and angular gyri, while increased GS details correlated with integrity of right supramarginal and postcentral gyri.

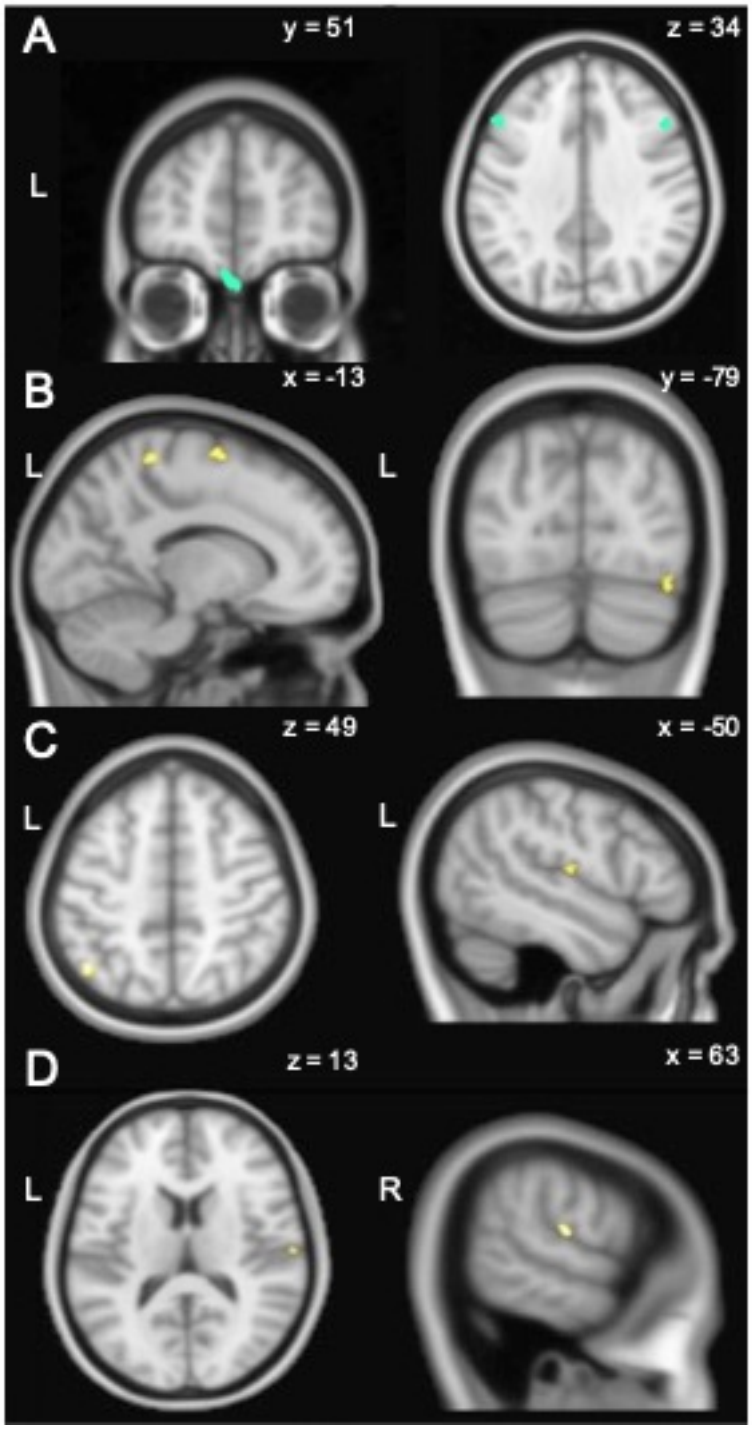



*Figure 4.3.* Voxel based morphometry (VBM) covariate analyses showing brain areas in which grey matter intensity positively correlates with NExt detail types in future thinking narratives for Alzheimer's disease (AD; green) and semantic dementia (SD; yellow) participants. A) Positive correlation between grey matter intensity and the provision of Future Specific Events (SE) in Alzheimer's disease. B) Positive correlation between grey matter intensity and the provision of Future Specific Events (SE) in semantic dementia. C) Positive correlation between

grey matter intensity and the provision of Future Extended Events (EE) in semantic dementia. D) Positive correlation between grey matter intensity and the provision of Future General Semantics (GS) in semantic dementia. All coloured voxels emerged as significant in the analyses at $p < .001$ uncorrected with a cluster extent threshold of 100 contiguous voxels. Clusters are overlaid on the Montreal Neurological Institute (MNI) standard brain. L = left; R = right.

**Table 4.3.** Voxel-based morphometry results showing regions of significant grey matter intensity increase that covary with increased provision of NExt external subtypes during future simulation

| Contrast | Regions | Side | Number of voxels | MNI coordinates | | | t-value |
|---|---|---|---|---|---|---|---|
| | | | | ***x*** | ***y*** | ***z*** | |
| AD | | | | | | | |
| ***Specific Episodes*** | Precentral gyrus, superior frontal gyrus, middle frontal gyrus | R | 1,016 | 31 | -16 | 64 | 14.72 |
| | Dorsolateral prefrontal cortex, middle frontal gyrus | L | 332 | -50 | 24 | 36 | 11.43 |
| | Precentral gyrus | R | 269 | 14 | -23 | 64 | 12.85 |
| | Ventromedial prefrontal cortex | B | 253 | 2 | 50 | -31 | 8.12 |
| | Dorsolateral prefrontal cortex, middle frontal gyrus | R | 227 | 48 | 21 | 32 | 34.23 |
| | Superior frontal gyrus, orbitofrontal cortex | R | 115 | 28 | 66 | -7 | 8.20 |
| | Posterior middle temporal gyrus | L | 114 | -53 | -70 | 17 | 9.04 |
| | Precentral gyrus | L | 112 | -30 | -18 | 58 | 12.42 |
| | Orbitofrontal cortex | R | 107 | 23 | 42 | -28 | 8.07 |
| SD | | | | | | | |
| ***Specific Episodes*** | Superior frontal gyrus, middle frontal gyrus | L | 485 | -22 | 7 | 58 | 17.02 |
| | Supplementary motor area, medial frontal gyrus, superior frontal gyrus | L | 200 | -7 | -8 | 67 | 10.31 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Occipital cortex, posterior fusiform gyrus, lingual gyrus, cerebellum | R | 123 | 43 | -80 | -22 | 19.31 |
| | Precuneus | L | 112 | -14 | -41 | 64 | 8.46 |
| ***Extended Episodes*** | Supramarginal gyrus | L | 289 | -50 | -14 | 11 | 9.32 |
| | Angular gyrus | L | 165 | -45 | -61 | 49 | 17.04 |
| ***General Semantics*** | Postcentral gyrus, supramarginal gyrus | R | 110 | 63 | -18 | 15 | 16.58 |

*Notes:* All clusters reported uncorrected using a strict threshold of $p < .001$ and cluster extent threshold of 100 contiguous voxels. Age, total intracranial volume, and Total Content details are included as covariates in all analyses. AD = Alzheimer's disease; B = Bilateral; L = left; MNI = Montreal Neurological Institute; R = right; SD = semantic dementia.

## 4.4. Discussion

This study aimed to explore the 'external' component of episodic future thinking narratives in order to elucidate the neurocognitive processes underlying narrative self-continuity into the future. Employing the NExt taxonomy, distinct profiles of external details within narratives of Past and Future events were uncovered in AD and SD, neurodegenerative disorders characterised by differential disruption of the episodic and semantic memory systems, respectively. These profiles appeared to be mediated by divergent cognitive and neural mechanisms for each group. This fine-grained analysis of the external content of future narratives reveals important insights into episodic and semantic contributions to narrative continuity of the self into the future.

### 4.4.1. External detail profiles in AD

The NExt taxonomy revealed distinct profiles of external details for Past and Future narratives in each clinical group, compared with Controls. Firstly, AD patients provided a significantly greater amount of General Semantic details when narrating events from the recent past, relative to Control participants. The elevation of GS details for past narratives in AD is in line with study hypotheses, and consistent with previous observations of preserved semantic ABM in these patients (Chapters 1 and 3). Indeed, findings from both the current study and

Chapter 3 suggest some semblance of narrative continuity is maintained for the recent past in AD. The precise nature of the external details provided by these patients during recent narration does, however, diverge between the studies, with elevations in Extended Episodes versus General Semantics uncovered in Chapters 3 and 4, respectively. Several methodological differences exist between the AI and Past-Future task that may account for these discrepancies. For example, the Past-Future task used here requires narratives of three, rather than one, event, in response to specific cue words, with more directed probing. Under these more demanding and constrained task conditions, AD patients may have difficulty retrieving more specific or personally-relevant details, and therefore default to providing generic semantic information. On the other hand, the one event and more general probing on the AI likely permits the retrieval of past experiences that remain easily accessible, albeit lacking in spatial and/or temporal specificity (i.e., Extended Episode details). These findings reinforce the importance of considering the nature of the assessment tool when attempting to characterise the processes underlying the extended self.

In the future condition, Specific Episodes, reflecting descriptions of events that are separate from the main future episode, were elevated in AD. The elevation of seemingly episodic details in a disorder typified by episodic memory loss is initially surprising. Upon closer inspection, however, it was apparent that many of the Specific Episodes described by AD patients when narrating the future referred to self-relevant, often emotionally salient, events from their past, that they were 're-casting' into the future (e.g., an important sporting match or family gathering). It is possible, therefore, that these descriptions of significant life events had been repeatedly rehearsed by the AD patients (see also Bright & Kopelman, 2004), whereby the essential information has been abstracted to form a schematised account. This observation is further supported by the strong negative correlation between these Specific Episode external details within future narratives, and episodic memory in AD, suggesting that the elevation in this detail type may reflect preserved semantic, rather than episodic, processes, at least in the AD group. Moreover, neuroimaging analyses revealed associations between future SE details in AD and the integrity of predominantly frontal regions, previously implicated in semantic, schematic processing (Gilboa & Marlatte, 2017; Sheldon, Farb, Palombo, & Levine, 2016), as well as emotional and self-relevance (Kumfor, Irish, Hodges, & Piguet, 2013; Lin, Horner, & Burgess, 2016), including ventromedial prefrontal cortex,

orbitofrontal cortex, and dorsolateral prefrontal cortex. Importantly, the regions emerging from the present analysis were distinct from those displaying significant atrophy in AD patients compared with Controls, suggesting that the *relative preservation* of specific anterior cortical regions in AD (including both DMN and extra-DMN areas) may allow for the harnessing of semanticised past memories when attempting to imagine the future, at least in early stages of the disease. As such, some degree of narrative continuity for the future appears to be present in AD, however, this is likely based upon preserved semantic representations of the past. Accordingly, the future self in AD may be lacking in the growth or change over time that forms a key element of the extended self (Locke, 1690; Ricoeur, 2010).

### 4.4.2. External detail profiles in SD

Turning attention to the findings in SD, no external detail types were elevated in these patients, compared with the other groups, during narration of recent events. This likely reflects the preserved episodic (internal) details for past events in SD, with no requirement for the compensatory provision of additional information. External detail profiles for recent events in SD diverged between the current study and that using the AI across the entire lifespan (Chapter 3), though as discussed above, this may be explained by methodological differences between the two tasks. In particular, the highly structured administration of the Past-Future task, involving the presentation of cue words and probing for specific details, may have reduced the tendency of SD patients to provide additional background information, as opposed to the more open-ended AI (resulting in increased General Semantic details for recent events). The increased structure of the Past-Future task may therefore have reduced the demands on executive function, with deficits in retrieval control and monitoring in SD proposed to contribute to the elevated external details on the AI in these patients (McKinnon et al., 2008). Notably, the pattern in SD contrasts from that seen in AD, whereby the task conditions of the Past-Future task lead to an increase in semantic details. The key difference between these groups, however, is the profile of internal details, with AD patients likely attempting to compensate for their impoverished internal details with semantic content. Taken together, these discrepancies highlight the need for future studies directly examining the effect of task requirements on the mechanisms underpinning narrative continuity, and how this may diverge across different patient groups.

Only one previous study has explored the nature of external details provided during future thinking narratives in SD, revealing striking elevations of External Event details using the traditional AI scoring method (Irish, Addis, et al., 2012b). The application of the sensitive NExt taxonomy, however, suggests that this inflation of External Event details in SD is driven by the increased provision of Specific Episodes, Extended Episodes, and General Semantic details compared with Controls. Consistent with findings in Chapter 3, the provision of future Extended Episodes in SD was negatively correlated with semantic memory performance, suggesting that these detail types (lying at an intermediate point on the episodic-semantic continuum) are more likely to reflect episodic, rather than semantic, processes in SD. In addition, taken together with Chapter 3, the present findings indicate that with increasing semantic impairment, the narratives of SD patients are more heavily weighted towards relative intact episodic representations, for both past and future epochs. Previous studies in SD have observed these patients to recapitulate previously experienced events into the future, describing these familiar events again in their entirety rather than generating a new scenario (Irish, 2016; Irish, Addis, et al., 2012a, 2012b). The current findings of elevations in both Specific and Extended Episode external details indicate that these recast events in SD likely comprise a combination of one-off (e.g., a specific concert) and repeated past occasions (e.g., regular family dinners). Furthermore, as discussed in Chapter 3, while the elevation in General Semantic details in SD may appear counterintuitive, these details can be intrinsically bound to event representations (Greenberg & Verfaellie, 2010; Tulving, 1972), with their production within future narratives potentially reflecting episodic-like processes. The suggestion that the external details provided by SD patients during future simulation (i.e., Specific Episode, Extended Episode, and General Semantic details) reflect intact episodic processing is supported on the neural level, with the integrity of posterior DMN regions, typically implicated in vivid episodic recall (Cavanna & Trimble, 2006; Gardini, Cornoldi, De Beni, & Venneri, 2006; Ramanan et al., 2018), associated with all of these detail types in our study. Thus, while both AD and SD patients produce an excess of Specific Episode external details within their future narratives, and seemingly share a 'static' future self, the mechanisms (semantic versus episodic) underlying narrative self-continuity for the future may diverge between the groups, dependent upon their relative profiles of memory impairment.

### 4.4.3. Conclusions

Here, the NExt taxonomy reveals that, as for the past, the future narratives of AD and SD patients also contain a spectrum of episodic and semantic content. These findings provide further evidence that external details represent a rich source of information regarding the processes underlying narrative continuity. Importantly, patient groups may preferentially rely upon the brain regions that remain relatively preserved in the disease, in order to imagine their personal future. The synergistic importance of the findings from Part 1 of the thesis (Chapters 3 and 4) for elucidating the neurocognitive mechanisms of the extended self will be discussed further in Chapter 7.

# Chapter 5

# Cognitive and neural mechanism of moral reasoning

## 5.1. Introduction

As reviewed in Chapter 1, morality forms a crucial facet of the interpersonal self, though its cognitive and neural mechanisms remain incompletely characterised. Namely, much of the understanding of the emotional contributions to personal moral reasoning is inferred from the implication of 'emotional' brain regions in lesion and neuroimaging studies, rather than experimental examination. In addition, despite early work on moral development revealing the importance of social rule understanding, the contribution of social conceptual knowledge to moral reasoning in adults has received comparatively less attention. This is likely due to the preponderance of studies examining moral reasoning in individuals with lesions to the mPFC (Ciaramelli et al., 2007; Koenigs et al., 2007; Taber-Thomas et al., 2014; Thomas, Croft, & Tranel, 2011). While such a focus has offered valuable insights into the necessity of the mPFC for personal moral decisions, the broader contributions of this research to the characterisation of the neurocognitive mechanisms of morality has remained limited.

The syndrome of bvFTD provides an ideal opportunity to extend current knowledge about the neural and cognitive processes supporting personal moral reasoning. In addition to demonstrating gross moral transgressions in daily life (see Chapter 1), these patients display impairments in both emotional and conceptual processes, which includes knowledge of socially acceptable behaviour (Carr et al., 2015; Panchal et al., 2016; Possin et al., 2013). Furthermore, as discussed in Chapter 1, bvFTD results in the systematic degeneration of whole brain networks specialised for socioemotional processing. As such, this syndrome allows for the examination of the contributions of emotional and conceptual processes to personal moral reasoning, and the corresponding large-scale neural networks involved.

Consistent with the trend in the field, the majority of studies examining personal moral reasoning in bvFTD have placed particular emphasis on emotional contributions. These studies have predominantly employed versions of the original moral reasoning paradigm developed by J. D. Greene et al. (2001), which distinguishes between personal and impersonal

moral dilemmas. On this task, bvFTD patients provide increased amounts of utilitarian responses to personal, but not impersonal, dilemmas, compared with healthy controls (Chiong et al., 2013; Fong et al., 2017; Mendez, Anderson, et al., 2005; Mendez & Shapira, 2009; Van den Stock et al., 2017), interpreted as reflecting impaired emotion processing. Further support for this notion stems from the reduced emotional responses reported by bvFTD patients toward their moral decisions on both personal (footbridge) and impersonal (trolley) dilemmas (Fong et al., 2017). Decreased autonomic arousal, as revealed by reduced skin conductance, was also observed in bvFTD during a personal moral dilemma (Fong et al., 2017). Moreover, utilitarian responses to personal moral dilemmas in bvFTD correlated with poor performance on a separate measure of facial emotion recognition, but affective responses toward the actual decision were not collected in this study (Van den Stock et al., 2017).

By contrast, only one study has examined the role of conceptual knowledge in moral reasoning in bvFTD. Employing one personal (footbridge) and one impersonal (trolley) dilemma, Fong et al. (2017) reported a correlation between self-reported emotional responses toward the moral dilemmas, and knowledge of socially acceptable behaviour in bvFTD, such that poorer knowledge of social norms was associated with a more positive (i.e., abnormal) affective reaction toward both the personal and impersonal dilemmas. The interpretation of this finding, however, is limited by the small number of dilemmas employed (i.e., only one dilemma of each type), and the failure to distinguish between low- and high-conflict personal moral dilemmas (see Chapter 1). In fact, only one study in bvFTD to date has employed this more sensitive distinction (high-/low-conflict), originally proposed by Koenigs et al. (2007). Interestingly, unlike the patterns revealed in other lesion groups (Koenigs et al., 2007; McCormick et al., 2016), Van den Stock et al. (2017) uncovered an elevation in utilitarian decisions for low-, but not high-conflict, personal dilemmas in bvFTD. This finding, though, was interpreted in terms of emotional contributions to personal moral reasoning, with the relevance of other socio-cognitive processes for low- versus high-conflict personal moral dilemmas yet to be explored.

Turning to the neuroimaging findings, structural and functional changes to frontal brain regions, including mPFC and insula, have been implicated in the abnormal responses to

personal moral dilemmas in bvFTD (Chiong et al., 2013; Van den Stock et al., 2017), particularly in the right hemisphere (Mendez & Shapira, 2009). In healthy individuals, the 'salience network', centered on the insula and ACC, is purported to identify the personal relevance of moral dilemmas, and subsequently recruit the DMN for their processing (Chiong et al., 2013). Such recruitment of the DMN in response to personal moral dilemmas is diminished in bvFTD (Chiong et al., 2013), likely due to the salience network aberrations in this disorder (Zhou et al., 2010). Finally, utilitarian responses to both personal and impersonal moral dilemmas were associated with reduced perfusion/metabolism to bilateral ATLs in one study in bvFTD (Mendez & Shapira, 2009), though a mechanistic account for this involvement was not examined.

This study aimed to address the methodological limitations of previous studies in order to comprehensively characterise the differential contributions of emotional and conceptual processes to personal moral reasoning in bvFTD, and their underlying brain networks. Specifically, a sensitive paradigm distinguishing between high- and low-conflict personal moral dilemmas was employed (Koenigs et al., 2007), along with ratings of emotional responses to the moral decisions, and a measure of social conceptual knowledge. Furthermore, advanced neuroimaging analyses were performed to examine the grey and white matter correlates of moral reasoning performance. In doing so, the current study aimed to help to further the understanding of the neurocognitive mechanisms underlying this crucial aspect of the interpersonal self. It was predicted that both emotional and conceptual functioning would relate to moral reasoning performance in bvFTD patients, which would be associated with integrity of the brain regions supporting these component processes (i.e., affective and salience networks, ATLs).

## 5.2. Method

### 5.2.1. Participants

Twenty-seven bvFTD patients and 22 healthy Control participants were recruited for this study. Details of recruitment procedures and neuropsychological assessment are outlined in Chapter 2. One of the bvFTD patients was excluded due to invalid responses on the Moral Reasoning task, leaving a final sample of 26. In this study, performance on the ACE-III is

reported as a measure of overall cognitive functioning, as well as additional tests of verbal attention and working memory (Digit Span Forward and Backward Maximum Span; Wechsler, 1997), verbal episodic memory (Rey Auditory Verbal Learning Test Delayed Recall; Schmidt, 1996), and executive function (Trail Making Test Part B-A; Tombaugh, 2004).

### 5.2.2. Moral reasoning task

Participants completed a moral reasoning task, adapted from Koenigs et al. (2007). Of the original 50 hypothetical scenarios, a subset of 14 were chosen for the current study. This reduced task length was chosen to accommodate the cognitive abilities of bvFTD patients.

The 14 scenarios fell into four categories. Neutral scenarios (n = 4) were practical dilemmas without a moral component (e.g., choosing whether to buy a new DVD player, or have your old one fixed, for the same price). These scenarios acted as a control condition to ensure appropriate task understanding and compliance. Impersonal moral dilemmas (n = 4) required a choice whether to sacrifice the life of one person in order to save multiple lives, via the deflection of an existing threat (e.g., the traditional 'trolley problem', whereby flicking a switch would divert a runaway train from the track with five people on it, to a track with one person; n = 2), or involved morally conflictual scenarios that did not require the infliction of direct personal harm (e.g., choosing whether to commit tax fraud; n = 2). Personal moral dilemmas, requiring a choice to personally harm somebody in order to save multiple lives, were divided into High (n = 4) and Low (n = 2) Conflict scenarios. While Personal Low Conflict moral dilemmas involve rather inexcusable actions, which are often rejected by healthy individuals (e.g., committing cannibalism to save oneself and others), Personal High Conflict moral dilemmas (e.g., killing a fellow hostage so that oneself and others may escape from terrorists) are more divisive in control participants (Koenigs et al., 2007). Scenarios in each category were selected at random from the larger Koenigs et al. (2007) database. The full text of all scenarios is provided in Appendix D.

Where necessary, phrasing of the scenarios was modified from the original task for cultural appropriateness (e.g., exchanging 'watchman' for 'security guard'). Scenarios were presented in pseudorandomised order in text format on a Microsoft PowerPoint presentation, and concurrently read aloud by the examiner.

Each of the 14 dilemmas, along with one practice dilemma, consisted of five slides. An example five-slide trial for a Personal High Conflict moral dilemma is depicted in Figure 5.1. The first slide displayed the scenario, ending with a yes/no question about the hypothetical action ("Would you … in order to …?"). No time limit was set, though if a response was not provided within approximately 15 seconds of the examiner reading the scenario, generic prompting was provided (e.g., re-reading of the question). Responses were classed as either Utilitarian (i.e., the maximising of aggregate welfare) or Deontological (i.e., a refusal to do harm). The percentage of Utilitarian decisions was calculated for each moral dilemma type (i.e., Impersonal, Personal Low Conflict, Personal High Conflict), for use in analysis.

In order to explore the mechanisms underlying moral decision making, the next four slides contained a series of follow-up questions regarding the decision-making process. Participants were required to rate "How sure are you about this decision?" (on a scale of 'Extremely Unsure' (1) to 'Extremely Sure' (5)), "How do you feel about your decision?" (on a scale of 'Extremely Bad' (1) to 'Extremely Good' (5)) and "How vividly did you picture this scenario in your mind's eye?" (on a scale of 'Not Vividly at All (1) to 'Extremely Vividly' (5)). The average certainty, feeling, and vividness ratings were calculated for each of the moral dilemma types.

Finally, in an attempt to qualitatively capture the moral decision-making process, for every trial participants were asked the open-ended question: "How did you make your decision?". During the practice trial at the beginning of the task, example responses to this question were provided (e.g., picturing the scene in the 'mind's eye'; emotions/gut reaction; knowledge of right/wrong; future consequences/outcome). In the main task, however, participants were encouraged to respond using their own words[19]. If the response was unclear, generic prompts were provided (e.g., "Can you tell me anything else about how you made your decision?"). Responses were later classed into either emotional (i.e., based on emotional reactions, or personal/societal beliefs about right and wrong) or rational (i.e., considering the outcome, or picturing the scene), consistent with McCormick et al. (2016). A proportion of emotional

[19] For the first 10 participants that were tested, individuals were required to choose from one of the example options (or the 'other' category) during the main task, in order to explain their decision-making process. The methodology was altered after observing that participants' responses did not always fit cleanly into one of the provided categories, and it was thought that an open-ended question would provide a broader and more accurate reflection of the decision-making process.

reasons was then calculated for each dilemma type, by dividing the number of emotional responses by the number of dilemmas.

The entire task lasted approximately 30-45 minutes.

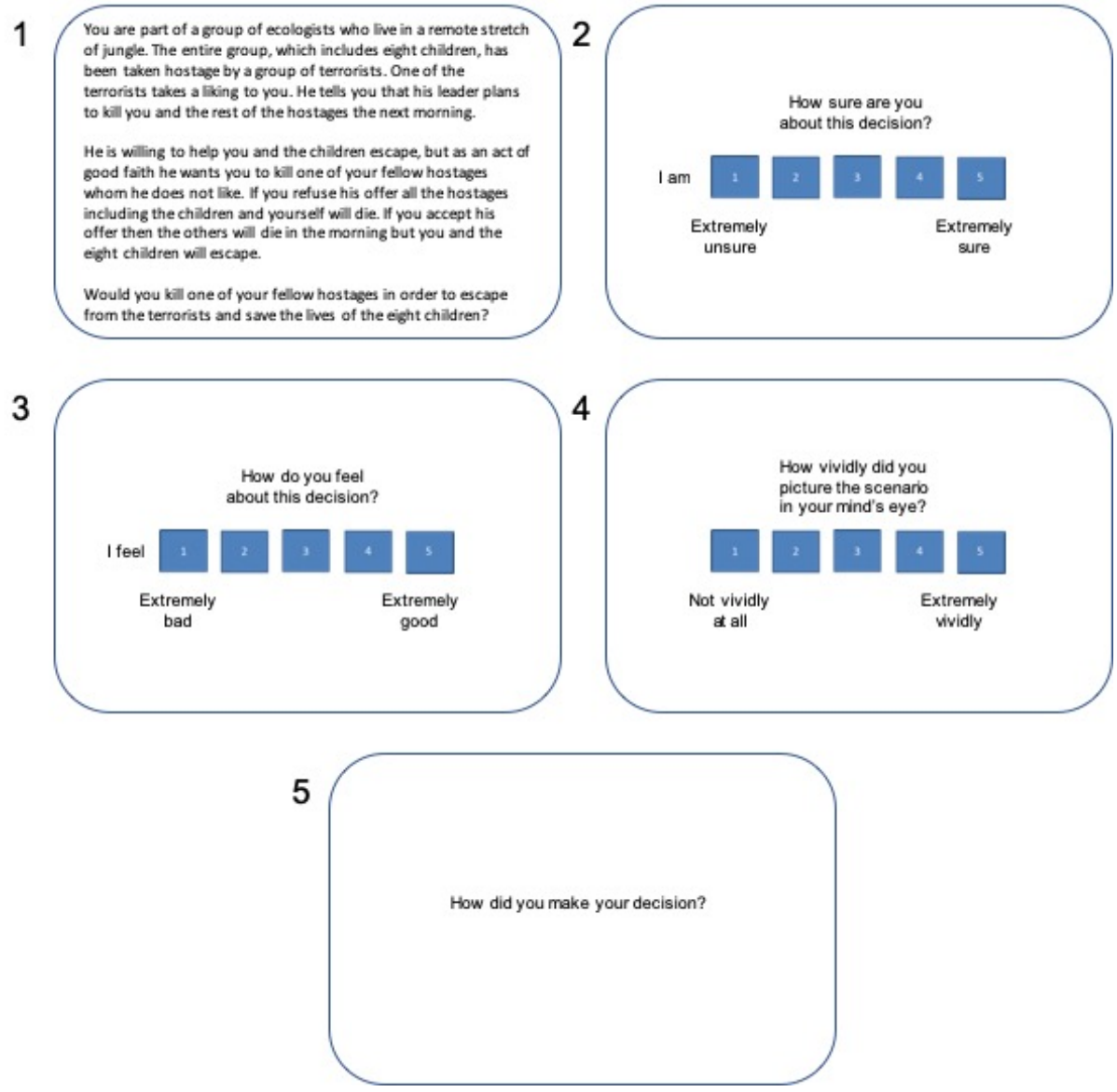



*Figure 5.1.* Example of a five-slide trial for a personal high-conflict moral dilemma.

### 5.2.3. Social norms questionnaire

To explore the effect of social conceptual knowledge on moral decision making, the Social Norms Questionnaire (SNQ; Possin et al., 2013) was administered. The SNQ measures the

ability to identify socially appropriate and inappropriate behaviours. For each of the 22 items, participants are required to respond yes or no as to whether a hypothetical behaviour would be considered socially appropriate in mainstream local culture. To ensure cultural appropriateness, slight modifications were made to the phrasing of the original version (e.g., switching 'sidewalk' for 'footpath'). Total number of errors were calculated, with higher values reflecting poorer social knowledge. Separate scores were also obtained for errors on the 'Break Norms' (rating socially unacceptable behaviours as acceptable, e.g., telling a stranger you don't like their hairstyle), and 'Overadherence' (rating socially acceptable behaviours as unacceptable, e.g., telling a stranger you like their hairstyle) subscales.

### 5.2.4. Statistical analyses

Independent samples t-tests were employed to assess group differences on demographic measures and neuropsychological tasks. The frequencies of dichotomous variables (i.e., sex) were compared using chi-squared tests ($\chi^2$). Given significant differences in Years of Education between bvFTD and Controls, repeated measures ANCOVAs with Sidak *post hoc* tests were used to investigate main effects of group (bvFTD, Control) and dilemma type (Impersonal, Personal Low-Conflict, Personal High-Conflict), and their interaction, on the percentage of Utilitarian responses provided, controlling for education. For the subjective ratings, non-parametric Mann Whitney *U* tests were run to examine group differences in average Certainty, Feeling and Vividness ratings. Univariate ANCOVA was used to investigate between-group differences in the proportion of emotional reasons given for the decisions. For the SNQ, a repeated-measures ANCOVA, with Sidak *post hoc* tests, was employed to explore main effects of group and error type (Rule Break, Overadhere), and their interaction, controlling for education. Finally, Spearman's correlations were employed to examine the relationship between moral reasoning and SNQ. The significance level was set at $p < .05$ for all analyses, and effect sizes were calculated using partial eta-squared ($\eta^2$) for parametric analyses and eta-squared ($\eta^2$) for nonparametric analyses.

### 5.2.5. Neuroimaging analysis

***Voxel-based morphometry***

Forty-five participants (22 Controls, 23 bvFTD) were included in the voxel-based morphometry (VBM) analysis. Full details of MRI acquisition and pre-processing are outlined in Chapter 2.

For analyses of grey matter intensity, permutation-based non-parametric testing was employed using unbiased whole-brain General Linear Models (GLM) in FSL, with 5000 permutations per contrast (Nichols & Holmes, 2002). Differences in grey matter intensity between bvFTD and Controls were assessed using *t*-tests, including age and education as covariates of no interest. Significant clusters were extracted using the threshold-free cluster enhancement (TFCE) method at a strict threshold of $p < .005$, corrected for multiple comparisons via familywise error (FWE) correction, with a cluster extent cut-off of 200 contiguous voxels.

Next, correlations between the moral reasoning variables that significantly differed between bvFTD and Controls (i.e., feeling rating for Personal High Conflict dilemmas) and grey matter intensity were investigated. For this analysis, a negative contrast was employed, providing an index of association between higher (i.e., more positive/more abnormal) feeling ratings and decreased grey matter intensity. Consistent with previous studies, these correlation analyses were performed on bvFTD patients combined with Controls, in order to provide greater variance in behaviour scores, and therefore increase the statistical power to detect brain-behaviour relationships (Sollberger et al., 2009). Age and education were included as covariates of no interest. Significant clusters were extracted using the TFCE method at a threshold of $p < .01$, FWE corrected, with a cluster extent cut-off of 200 contiguous voxels. Given the widespread neural networks that may be involved in social and affective functioning (Chapter 1), the statistical approach for the correlation analysis was more lenient than that employed for the between-group analysis, in order to increase the likelihood of detecting meaningful associations with behaviour.

Together, the statistical approaches for these neuroimaging analyses take into consideration the relatively large sample size and balance the risk of Type I versus Type II errors (see Lieberman & Cunningham, 2009).

Significant results were overlaid on the MNI standard brain, with maximum co-ordinates provided in MNI stereotaxic space. Anatomical labels were determined with reference to the Harvard-Oxford probabilistic cortical and subcortical atlases.

***Diffusion tensor imaging***

Diffusion-weighted MRI data were available for 40 participants (22 bvFTD; 19 Controls). Full details of acquisition and pre-processing are provided in Chapter 2.

Diffusion tensor imaging analyses were conducted to examine whole-brain changes in white matter microstructure (i.e., fractional anisotropy; FA). FA values were compared between groups using permutation-based non-parametric testing in FSL as outlined for the VBM analysis (above). Age and education were included as nuisance variables in this analysis. Significant clusters were extracted using the TFCE method and corrected for FWE at $p < .05$. The Johns Hopkins University probabilistic white matter atlas and the ICBM-DTI-WM atlas were used to determine anatomical labels.

Masks of selected white matter tracts of interest, namely the uncinate fasciculus and inferior longitudinal fasciculus, were created from the Johns Hopkins University probabilistic white matter atlas. Correlations between FA values of these tracts, extracted for each participant, and moral reasoning performance (i.e., feeling rating for Personal High Conflict moral dilemmas) were examined in the bvFTD group using one-way Spearman's correlations.

## 5.3. Results

### 5.3.1. Demographics and neuropsychological performance

Participant demographics and cognitive performance are displayed in Table 5.1. Groups did not significantly differ in age ($p = .88$) or sex ($p = .10$), but Controls were more educated than bvFTD patients ($p = .009$).

In keeping with their characteristic clinical profile, bvFTD patients showed impairments in behaviour (CBI), global cognitive functioning (ACE-III Total), attention (Digit Span Forward)

verbal episodic memory (RAVLT Delayed Recall), and executive function (Trails B-A). By contrast, verbal working memory (Digit Span Backwards) was relatively preserved.

**Table 5.1.** Demographics and clinical characteristics of the study cohort

| Variable | bvFTD | Control | *t* value | *p* value |
|---|---|---|---|---|
| N | 26 | 22 | | |
| Age | 62.96 (8.27) | 63.32 (7.20) | .16 | ns |
| Sex (M/F) | 21/5 | 13/9 | $X^2 = 2.71$ | ns |
| Education (Years) | 12.28 (3.12) | 14.77 (3.09) | 2.73 | .009 |
| Disease duration (Months) | 81.36 (60.26) | n/a | n/a | n/a |
| CBI Total Frequency (180) | 66.28 (35.67) | 8.71 (7.11) | -7.26 | < .001 |
| FTD-FRS Rasch Score | -.96 (1.53) | n/a | n/a | n/a |
| ACE-III Total (100) | 80.35 (10.84) | 94.82 (3.74) | 5.96 | < .001 |
| Digit Span Forwards Maximum Span (9) | 6.15 (1.52) | 7.36 (1.50) | 2.77 | .008 |
| Digit Span Backwards Maximum Span (8) | 4.46 (1.42) | 5.18 (1.33) | 1.80 | ns |
| RAVLT 30-minute Recall (15) | 5.08 (4.05) | 10.10 (2.21) | 5.07 | < .001 |

| | | | | |
|---|---|---|---|---|
| Trail Making Test Part B-A | 89.86 (104.18) | 42.67 (17.63) | -2.05 | .048 |

*Notes:* Maximum test score depicted in brackets. Values represent means and standard deviations for each group.

ACE-III = Addenbrooke's Cognitive Examination-III; CBI = Cambridge Behavioural Inventory; FTD-FRS = Frontotemporal Dementia Functional Rating Scale; ns = nonsignificant; RAVLT = Rey Auditory Verbal Learning Test.

Years of Education missing for 1 Control, Disease duration missing for 2 bvFTD patients, CBI Missing for 1 bvFTD patient and 1 Control, RAVLT missing for 1 bvFTD patient and 1 Control, Trail Making Test missing for 4 bvFTD and 1 Control.

### 5.3.2. Moral reasoning task performance

The majority of participants responded appropriately (i.e., provided the most logical response) to all Neutral dilemmas, confirming their understanding of the task and basic decision-making ability. Three Controls and one bvFTD patient responded counterintuitively to one out of four of the neutral scenarios, however their verbal explanations for these decisions indicated that these participants had nonetheless understood the dilemma (e.g., responding that they would rather save 15 minutes off a car trip than take the beautiful scenic route).

Figure 5.2. displays the average percentage of Utilitarian responses provided by bvFTD and Controls for each moral dilemma type. Mauchly's test indicated that the assumption of sphericity had been violated for the main effect of dilemma type ($\chi^2(2) = 10.23$, $p = .006$). Degrees of freedom were therefore corrected for this variable using Huynh-Feldt estimates of sphericity ($\varepsilon = .89$).

A significant main effect of dilemma type emerged ($F(1.79, 80.47) = 3.84$, $p = .03$, partial $\eta^2 = .08$), such that participants provided a greater percentage of Utilitarian responses for Impersonal moral dilemmas compared with Personal Low- and High Conflict dilemmas ($p < .001$ and .02, respectively). A higher percentage of Utilitarian responses was also observed

for Personal High- compared to Low-Conflict dilemmas ($p < .001$). This pattern of results is consistent with previous findings (Koenigs et al., 2007), confirming validity of the current task.

By contrast, no significant main effect of group ($F(1, 45) = 1.02$, $p = .32$, partial $\eta^2 = .08$), or interaction between group and dilemma type ($F(1.79, 80.47) = .73$, $p = .47$, partial $\eta^2 = .08$), on the responses to the moral dilemmas was observed (Figure 5.2.).

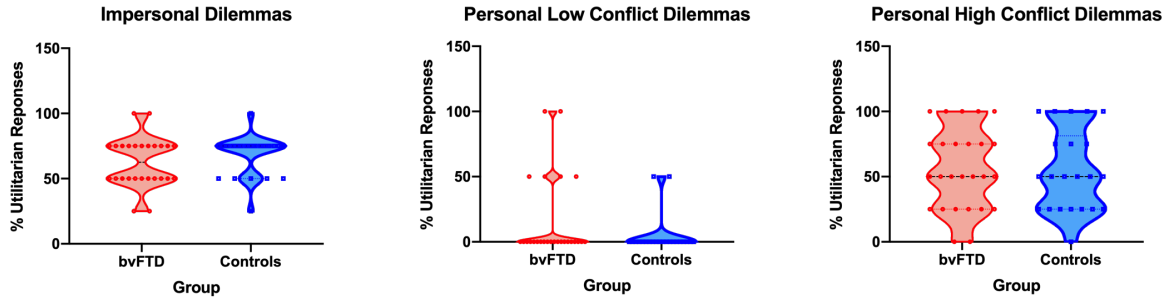



*Figure 5.2.* Violin plots representing the average percentage of Utilitarian responses provided by each group on each of the moral dilemma types. bvFTD = behavioural variant frontotemporal dementia.

Given the particular variability in responses to Personal High Conflict dilemmas across both groups (Figure 5.2.), and previous findings that these dilemmas differentiate between lesion patients and controls (Koenigs et al., 2007; McCormick et al., 2016), further analyses were conducted on the follow-up questions to Personal High Conflict dilemmas. No significant difference between groups was apparent for certainty (Mann Whitney U = 226.00, exact two-sided $p = .22$, $\eta^2 = .03$) or vividness ratings (Mann Whitney U = 247.50, exact two-sided $p = .42$, $\eta^2 = .01$). A significant between-group effect emerged, however, for feeling ratings (Mann Whitney U = 166.50, exact two-sided $p = .01$, $\eta^2 = .13$), such that bvFTD patients reported feeling *better* about their decisions on Personal High Conflict moral dilemmas than Controls (Figure 5.3.).

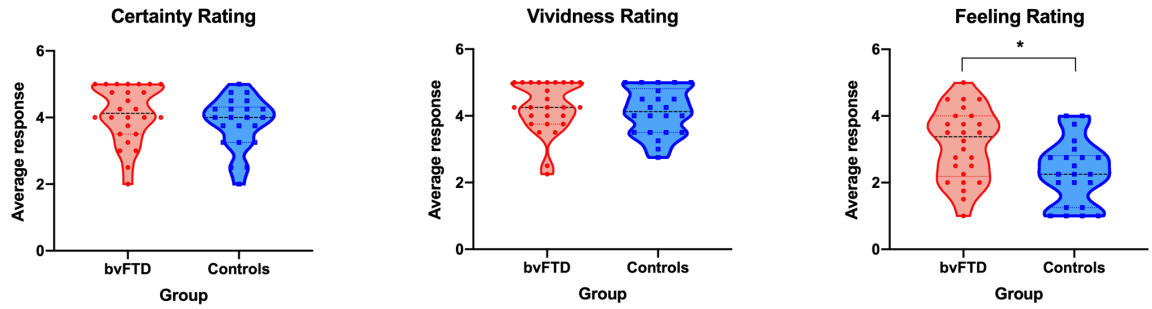



*Figure 5.3.* Violin plots representing the average certainty, vividness, and feeling ratings for the Personal High Conflict moral decisions provided by each group. bvFTD = behavioural variant frontotemporal dementia. Asterisk denotes significant difference between groups at $*p < .05$.

Finally, no significant differences were found between the groups in the reasons given for their moral decisions, with both groups providing relatively equal proportions of emotional (versus rational) reasons for their decisions on the Personal High Conflict moral dilemmas (bvFTD: M= .47, SD = .33: Control: M = .50, SD = .24) ($F(1, 45) = .11$, $p = .75$, partial $\eta^2 = .002$).

### 5.3.3. Social norms questionnaire (SNQ)

For the SNQ, a main effect of group emerged, such that bvFTD patients made more errors in social norm judgment, compared with Controls ($F(1, 45) = 6.63$, $p = .01$, partial $\eta^2 = .13$) (Figure 5.4.). By contrast, no main effect of error type (Rule Break, Overadhere) was observed ($F(1, 45) = 2.87$, $p = .10$, partial $\eta^2 = .06$), nor a significant interaction between group and error type ($F(1, 45) = .16$, $p = .69$, partial $\eta^2 = .004$), suggesting the impairment in social conceptual knowledge in bvFTD was not specific to, or driven by, either error type.

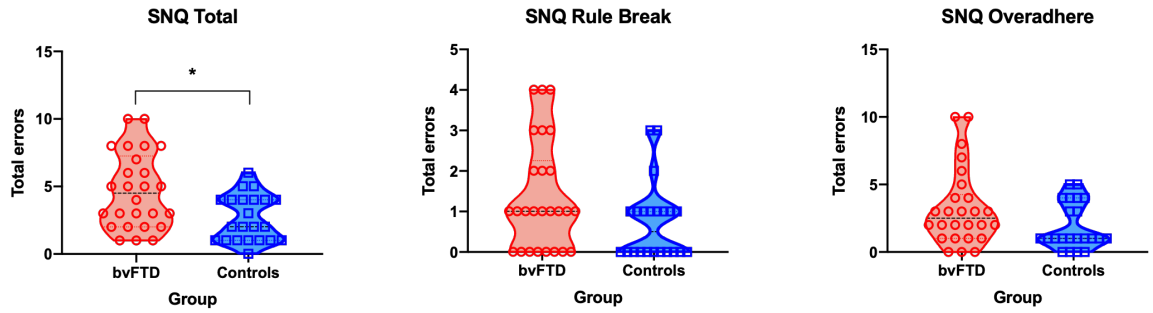



*Figure 5.4.* Violin plots representing (from left to right) Total errors, Rule Break errors, and Overadherence errors on the Social Norms Questionnaire. bvFTD = behavioural variant frontotemporal dementia, SNQ = Social Norms Questionnaire. Asterisks denote significant difference between groups at *$p$ < .05.

### 5.3.4. Correlations between emotional response to Personal High Conflict moral dilemmas and social conceptual knowledge

To examine the contribution of social conceptual knowledge to personal moral reasoning, the relationship between feeling ratings toward Personal High-Conflict moral dilemmas and performance on the SNQ was examined in the bvFTD group using Spearman's correlation coefficient. A significant negative correlation emerged, such that poorer social conceptual knowledge related to a reduced emotional response following Personal High-Conflict moral decisions (r = -.43, $p$ = .03).

### 5.3.5. Voxel-based morphometry analyses

#### *Group differences in grey matter intensity*

VBM analyses revealed a characteristic pattern of grey matter atrophy in the bvFTD group. Briefly, compared with Controls, bvFTD patients displayed reduced grey matter intensity in predominantly frontal and temporal lobes, including frontal pole, OFC, medial and lateral prefrontal cortex, extending into bilateral ATLs and MTLs and subcortical regions (e.g., basal ganglia, amygdala) (Figure 5.5.).

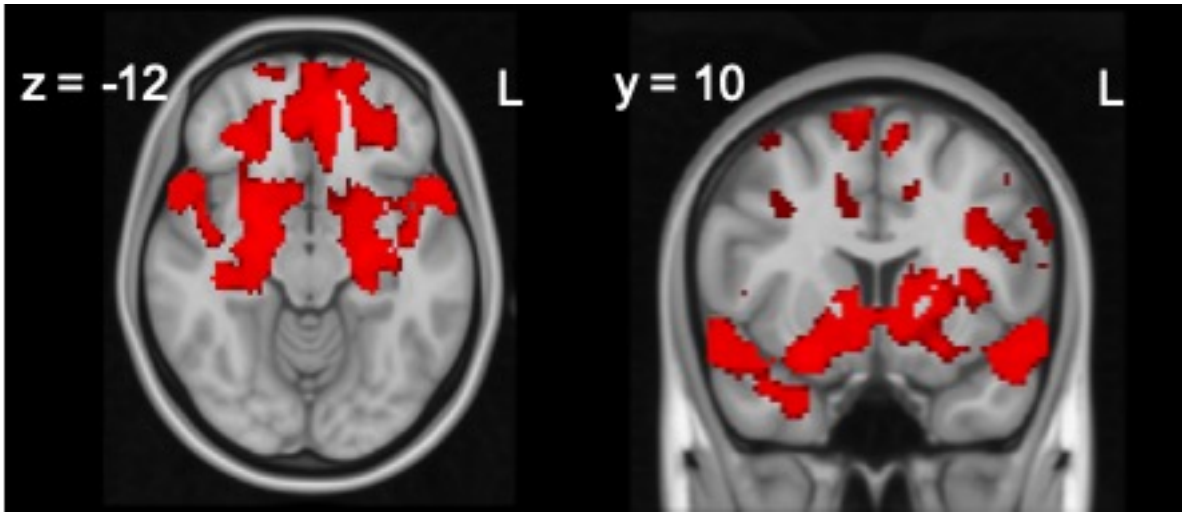



*Figure 5.5.* Voxel-based morphometry (VBM) analyses showing brain areas with decreased grey matter intensity in behavioural variant frontotemporal dementia (bvFTD) compared with Controls. Coloured voxels emerged as significant in a threshold-free cluster enhancement (TFCE) analysis at $p < .005$, corrected for familywise error, with a cluster extent threshold of 200 contiguous voxels. Clusters are overlaid on the Montreal Neurological Institute (MNI) standard brain. L = Left.

***Neural correlates of moral reasoning performance***

In bvFTD and Control participants combined, a more positive feeling rating toward Personal High Conflict moral dilemmas (i.e., a more abnormal emotional response) was associated with decreased grey matter intensity in frontal and subcortical regions including mPFC, OFC, dorsolateral prefrontal cortex, ACC, insula, amygdala, anterior hippocampus, and basal ganglia, as well as bilateral ATLs (Figure 5.6. and Table 5.2.).

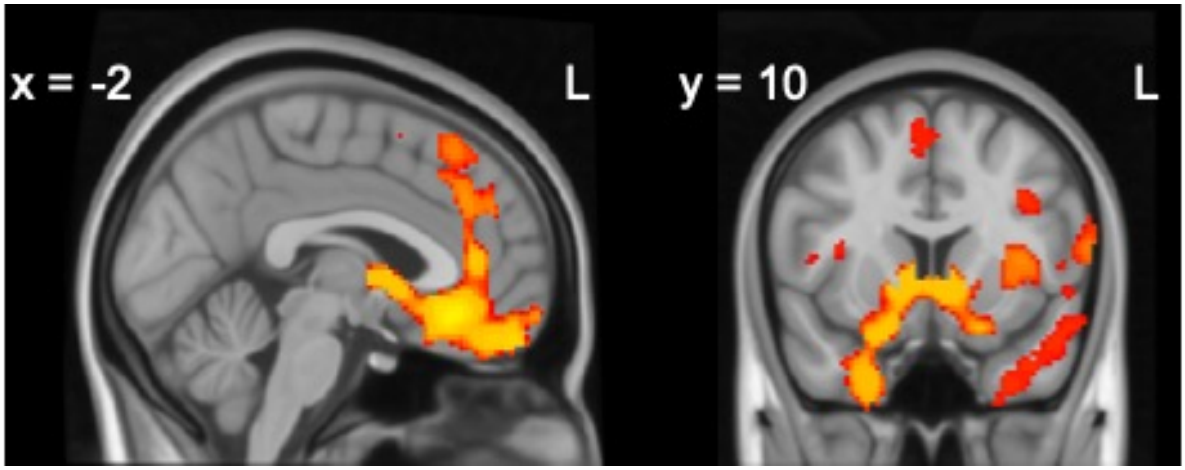



*Figure 5.6.* Voxel-based morphometry (VBM) correlation analyses showing brain areas in which grey matter intensity negatively correlates with emotional response to personal high conflict moral dilemmas in behavioural variant frontotemporal dementia (bvFTD) patients combined with Controls. Coloured voxels emerged as significant in a threshold-free cluster enhancement (TFCE) analysis at $p < .01$, corrected for familywise error, with a cluster extent threshold of 200 contiguous voxels. Clusters are overlaid on the Montreal Neurological Institute (MNI) standard brain. L = left.

**Table 5.2.** Voxel-based morphometry results showing regions of significant grey matter intensity that negatively correlate with emotional response to Personal High Conflict moral dilemmas

| **Regions** | **Hemisphere** | **Number of voxels** | **MNI coordinates** | | |
|---|---|---|---|---|---|
| | | | ***x*** | ***y*** | ***z*** |
| Bilateral frontal pole, medial prefrontal cortex, orbitofrontal cortex, anterior cingulate cortex, superior frontal gyrus, supplementary motor cortex, accumbens, caudate, putamen, pallidum, insula, amygdala, anterior hippocampus, parahippocampal gyrus, and temporal pole; extending into left central and frontal opercula, inferior frontal gyrus, precentral gyrus, and temporal fusiform cortex | B | 10305 | 6 | 30 | -16 |
| Insula, central operculum, putamen | R | 524 | 44 | -6 | 12 |

*Notes:* All t values ≥ .998. B = bilateral, MNI = Montreal Neurological Institute, R = right.

### 5.3.6. Diffusion tensor imaging analyses

DTI analyses revealed a typical profile of white matter atrophy in bvFTD patients compared with Controls, in the bilateral uncinate fasciculi, inferior fronto-occipital fasciculi, forceps minor, superior longitudinal fasciculi, and corpus callosum; and left cingulate, forceps major and inferior longitudinal fasciculus.

The uncinate fasciculus was chosen as the main white matter tract of interest given it is the primary tract connecting mPFC/OFC to ATL (Von Der Heide, Skipper, Klobusicky, & Olson, 2013): grey matter regions that correlated with moral reasoning performance in the VBM analyses (Figure 5.6. and Table 5.2.). Associations between emotional response to Personal High Conflict moral dilemmas and integrity of the bilateral uncinate fasciculi (i.e., mean FA) were examined within the bvFTD group. Negative correlations emerged for left and right uncinate fasciculi, such that reduced integrity of the tracts (i.e., lower FA values) was

associated with higher (i.e., an abnormal) feeling rating toward Personal High Conflict moral dilemmas (left: r = -.49, *p* = .01; right: r = -.50, *p* = .009) (Figure 5.7.).

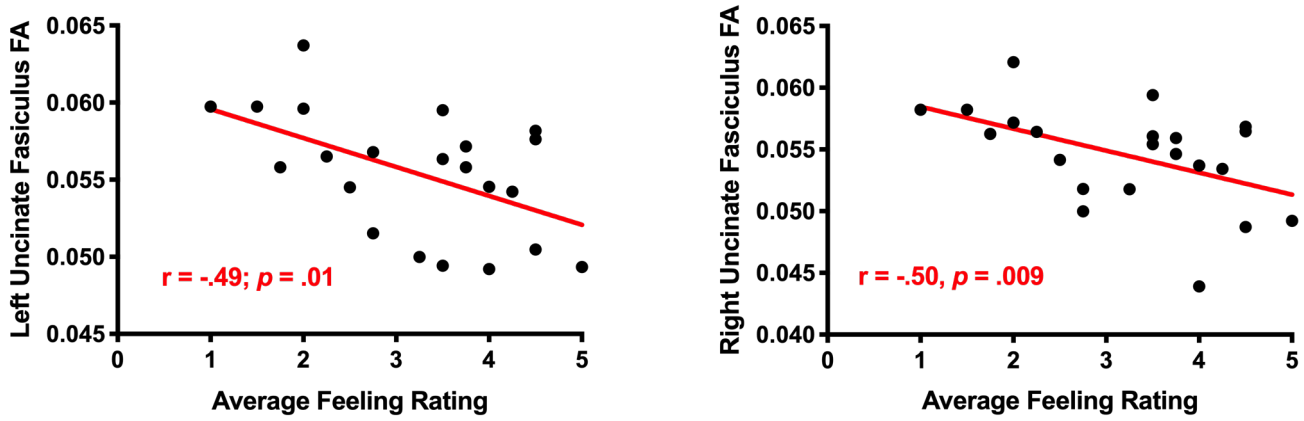



*Figure 5.7.* Relationship between Fractional Anisotropy (FA) values for the left and right uncincate fasciculi and feeling rating toward Personal High Conflict moral dilemmas in the behavioural variant of frontotemporal dementia (bvFTD).

The inferior longitudinal fasciculus, which connects the ATL to the occipital lobe, was chosen as a control white matter tract to examine the specificity of the current findings. No significant associations emerged between FA of the right or left inferior longitudinal fasciculus and feeling rating toward Personal High Conflict moral dilemmas in bvFTD patients (left: r = -.22, *p* = .17; right: -.28, *p* = .10).

## 5.4. Discussion

This study sought to employ contemporary updates in cognitive neuroscience, in order to comprehensively examine the neurocognitive mechanisms underlying personal moral reasoning in bvFTD, in turn informing the understanding of the interpersonal self. While no significant difference emerged between bvFTD and Controls for the actual moral decisions made, on personal high-conflict dilemmas, bvFTD patients displayed an attenuated emotional response toward their decision. This diminished emotional reaction further correlated with social conceptual knowledge, with worse knowledge of social norms associated with a more abnormal emotional response. Finally, a distributed network of frontal, subcortical, and temporal regions, and their white matter connections, were implicated in the impaired

emotional responding to highly conflictual moral dilemmas in bvFTD. These findings suggest multiple cognitive and neural processes likely interact in the service of personal moral reasoning, which will now be discussed in detail.

Regardless of group (i.e., bvFTD or Controls), the pattern of decisions made by participants across the different dilemma types was consistent with previous findings (Koenigs et al., 2007; McCormick et al., 2016), confirming the validity of the subset of dilemmas chosen for the current study. Overall, the utilitarian response was chosen more often than not (i.e., 65% of the time) for the impersonal moral dilemmas. By contrast, few utilitarian responses were made to personal low-conflict moral dilemmas. Personal high-conflict dilemmas proved more divisive, with the utilitarian response chosen approximately 50% of the time. Given this variation in responses, combined with previous findings that these dilemmas differentiate between lesion patients and controls (Koenigs et al., 2007; McCormick et al., 2016), personal high-conflict dilemmas represented the condition of interest for this study.

In contrast to findings in other patient groups (Koenigs et al., 2007; McCormick et al., 2016), no differences emerged between bvFTD and Controls in the percentage of utilitarian responses toward personal high-conflict dilemmas. Further, the groups did not significantly differ in their decisions for personal low-conflict or impersonal dilemmas. Previous studies in bvFTD have revealed increases in utilitarian decisions for personal moral dilemmas when the level of conflict is not specified (Chiong et al., 2013; Fong et al., 2017; Mendez, Anderson, et al., 2005; Mendez & Shapira, 2009), though the findings of Van den Stock et al. (2017) suggested this pattern of responses was specific to personal low-conflict dilemmas. In the present study, however, only a subset of bvFTD patients (6/26) provided a utilitarian response to one or more personal low-conflict dilemmas. As individual data points are not presented in Van den Stock et al. (2017), it is unclear whether this previous finding was driven by a subset of patients. Given that utilitarian decisions on personal low-conflict dilemmas involve the endorsement of highly unacceptable actions (e.g., committing cannibalism), it is possible the bvFTD patients providing these responses across both studies experienced a particular decline in knowledge of socially acceptable behaviour. It is interesting, then, that the patients included in the Van den Stock et al. (2017) study predominantly harboured atrophy to both left and right temporal poles: regions critically implicated in representing social conceptual

knowledge (Olson, McCoy, Klobusicky, & Ross, 2013)[20]. Unfortunately, the limited range of responses to personal low-conflict moral dilemmas in the present study precluded correlational analyses with social conceptual knowledge or brain atrophy. Future studies employing a larger bvFTD sample, and a broader range of atrophy profiles, may enable more in-depth exploration of the mechanisms underlying moral reasoning for personal low-conflict dilemmas.

Despite no between-group differences in the actual decisions made, analysis of the subjective ratings revealed a reduced emotional response to the personal high-conflict moral dilemmas in bvFTD, with these patients reporting more positive feelings about their decisions than Controls. As mentioned, these dilemmas are highly conflictual, as they require a choice between personally harming somebody, or indirectly causing the harm of many other people. As such, regardless of the chosen decision, participants are expected to experience some degree of negative emotional reaction, which was observed in the Control group. By contrast, the bvFTD patients appeared not to experience this affective response, instead commonly reporting they felt 'extremely good' about their decision. To date, the majority of the evidence for an emotional contribution to moral decision making is inferred from neuroimaging and lesion studies that implicate emotional brain regions, rather than drawing upon experimental investigation. The current findings in bvFTD, however, provide robust behavioural evidence for the importance of emotional processing in resolving moral dilemmas, specifically those of a highly conflictual, personal nature.

Consistent with study hypotheses, the current findings also reveal a contribution of social conceptual knowledge to personal high-conflict moral dilemmas. The abnormal emotional reaction to these dilemmas in bvFTD correlated with impaired knowledge of social norms, such that reduced knowledge of socially acceptable behaviour related to a more positive emotional response. This finding replicates that of Fong et al. (2017) in response to the footbridge dilemma, though in a larger sample of both patients and dilemmas. Despite early

[20] It is possible that the ATL atrophy also produced semantic comprehension deficits in these patients. It is unlikely, however, that the abnormal responding to personal low-conflict moral dilemmas in the Van Den Stock et al. (2017) study was exclusively attributable to difficulties understanding the scenarios, given the specificity of the findings to this dilemma type.

work on moral development revealing the importance of social rule understanding (Piaget, 1932), less focus has been placed on the contribution of social knowledge to moral reasoning in adults. Furthermore, conceptual, rational processes are typically only considered relevant for impersonal, and not personal, moral dilemmas, with the latter believed to predominantly rely upon emotion (J. D. Greene et al., 2001). The current findings demonstrate the importance of both emotional and social conceptual processes for personal moral decision making. Importantly, these appear to interact to produce an affective response to the dilemma under situations of high conflict.

The behavioural evidence for contributions of both emotional processing and social conceptual knowledge to personal high-conflict moral reasoning in the present study was further supported by the neuroimaging findings. The emotional response to personal high-conflict moral dilemmas correlated with grey matter intensity in frontal and subcortical brain areas typically associated with emotion and salience processing, including bilateral mPFC, OFC, ACC, insula, basal ganglia, amygdala, and hippocampus, with a more abnormal emotional response to the moral decision associated with reduced integrity of these regions. As discussed in Chapter 1, these regions have emerged in previous functional neuroimaging studies of personal moral reasoning, though this is the first patient study to implicate this widespread brain network in the emotional reaction to highly conflictual personal moral dilemmas. Intriguingly, in addition to these emotion and salience processing regions, grey matter integrity of the bilateral temporal poles was also related to emotional responses to personal high-conflict moral dilemmas. The ATLs have a well-established role in representing conceptual, semantic knowledge (see also Part 1 of this thesis), which is thought to extend to the storage of social concepts, including knowledge of social rules, norms, and socially appropriate behaviour (Carr et al., 2015; J. Moll et al., 2005; Panchal et al., 2016). This region has previously been activated in functional neuroimaging studies of moral reasoning (Pascual et al., 2013). Utilitarian responses to moral dilemmas in bvFTD have also been associated with reduced perfusion/metabolism to bilateral ATLs (Mendez & Shapira, 2009). The precise role of the ATLs in moral reasoning, however, has to date remained unclear. Interestingly, the implication of this region in the present study dovetails nicely with the behavioural finding of a correlation between knowledge of social norms and emotional response to personal high-conflict moral dilemmas in bvFTD. Taken together, the current behavioural and neuroimaging

findings suggest that the emotional response to personal high-conflict moral dilemmas is produced via a combination of emotional and social conceptual processes, arising from fronto-subcortical and anterior temporal brain regions, respectively.

In additional support of this hypothesis, white matter analyses revealed an association between the abnormal emotional response to personal high-conflict moral dilemmas in the bvFTD group and reduced integrity of the bilateral uncinate fasciculi, a tract connecting the OFC/mPFC to the ATLs. This relationship was not evident for the control tract, the inferior longitudinal fasciculus, suggesting its specificity to the uncinate. Indeed, it is tentatively proposed that the uncinate fasciculus may form the pathway by which social knowledge (from the ATLs) is transferred to the prefrontal cortex, where it is integrated with information from other frontal and subcortical regions to inform the emotional response to personal high-conflict moral dilemmas. Such directionality, however, cannot be inferred from the current analyses. As such, future studies examining the functional and effective connectivity between mPFC and ATLs, and its relationship with emotional and conceptual contributions to personal moral reasoning, will be of great interest.

Collectively, the current findings in bvFTD aid in clarifying the nature of the emotional and social conceptual contributions to the process of personal moral reasoning, and their corresponding brain regions. These findings have important implications for understanding the interpersonal self. Morality is one of the most defining traits of one's identity, both in terms of how an individual views themselves, as well as how others view them (Strohminger & Nichols, 2014, 2015). Moreover, given moral behaviour is defined by societal standards of right and wrong, it critically affects interpersonal interactions and relationships. While the majority of current understanding regarding morality stems from laboratory studies of moral reasoning, encouragingly, performance on these tasks is associated with various aspects of real-world moral behaviour (reviewed by Peng & Huashan, 2014). This includes caring for others (Latif, 2000), fulfilling commitments (Krebs & Rosenwald, 1977), aggression (Palmer, 2005) and even criminality (Palmer, 2003). As such, the present findings suggest that emotion and knowledge of right and wrong may be synergistically drawn upon to behave and interact appropriately with others in daily life, particularly in situations of high moral conflict. In bvFTD, the breakdown in both of these processes might help to explain the severe

interpersonal dysfunction in this syndrome (reviewed in Chapter 1). Namely, the absence of the normal affective response to highly conflictual moral scenarios in these patients may cause them to act in ways that are jarring to others, thereby damaging social relationships. For example, faced with a decision to go on a long-planned holiday, or stay home to look after a sick relative (everyday moral dilemma taken from Singer, Kreuzpointner, Sommer, Wüst, & Kudielka, 2019), a bvFTD patient may not experience the typical negative emotional response (e.g., guilt, shame) associated with the egoistic decision, and therefore choose the holiday, subsequently affecting social interactions with their family. Results from the current study suggest that this altered affective response may stem from impaired emotional processing, as well as loss of the conceptual knowledge that caring for family members is considered the 'right' thing to do, attributable to degeneration of a fronto-temporal-subcortical brain network. Evidently, drawing upon the syndrome of bvFTD provides valuable insights into the mechanisms underlying the interpersonal self, by revealing the dire consequences to social functioning when these processes break down (discussed further in Chapter 7).

# Chapter 6

# The neurocognitive relationship between visual perspective taking and theory of mind

This chapter includes revised material from:

Strikwerda-Brown, C., Ramanan, S., Irish, M. (2019). Neurocognitive mechanisms of theory of mind impairments in neurodegeneration: A transdiagnostic approach. *Neuropsychiatric Disease and Treatment, 15*, 557-573.

## 6.1. Introduction

As outlined in Chapter 1, the examination of visual versus more conceptual forms of perspective taking (i.e., ToM) have largely formed two separate lines of enquiry. A number of similarities, however, are apparent in terms of the developmental, cognitive and neural mechanisms underlying these two functions, though evidence also exists for their divergence. As such, whether VPT and ToM represent overlapping or distinct processes, remains unclear. The syndrome of bvFTD provides an exciting opportunity to help adjudicate between these two accounts. These patients present with pronounced deficits in understanding the thoughts, feelings, and beliefs of others (i.e., ToM), with the neurocognitive mechanisms of such impairments forming the focus of rigorous research efforts. By contrast, no study to date has examined more fundamental forms of perspective taking (i.e., VPT) in bvFTD. Examining VPT and ToM in bvFTD, and their cognitive and neural correlates, may therefore aid in clarifying the nature of the relationship between these two forms of perspective taking, and the brain regions involved.

bvFTD is characteristically a disorder of social interaction (Mendez et al., 2014) (see also Chapters 1 and 5). Considerable parallels between the social difficulties displayed in bvFTD and in individuals with autism provided an early clue that ToM may be altered in this dementia syndrome (John R Hodges, personal communication). Pervasive deficits have since been revealed across all aspects of ToM in bvFTD, including the basic decoding of emotion from visual cues (Torralva, Gleichgerrcht, Torres Ardila, Roca, & Manes, 2015) and understanding others' false beliefs about the world (Gregory et al., 2002), to the more complex functions of

attributing intentions in social interaction (Cotelli et al., 2018), and detecting social faux pas (Brioschi Guevara et al., 2015). Importantly, these impairments are dissociable from general cognitive decline in bvFTD (Bertoux, O'Callaghan, Dubois, & Hornberger, 2015), implying a specific difficulty in this social aspect of perspective taking. Carer reports of behavioural disruption in bvFTD reveal the extensive ToM deficits found in the laboratory in these patients also extend to the real world, manifesting in difficulties adopting other people's perspectives in everyday life (Dermody et al., 2016). Indeed, ToM impairments on formal measures are strongly correlated with carer ratings of behavioural disturbance (Gregory et al., 2002) and empathy (Synn et al., 2018) in bvFTD , suggesting that performance on laboratory measures may accurately capture functionally relevant impairments in this syndrome.

Deficits in bvFTD are commonly attributed to early structural and functional abnormalities in the mPFC (Adenzato, Cavallo, & Enrici, 2010). Converging evidence reveals clear associations between atrophy (Gregory et al., 2002; Synn et al., 2018) and reduced functional connectivity (Caminiti et al., 2015) of the mPFC and poor performance on various ToM tasks in bvFTD. Further, transcranial direct current simulation of this region has been demonstrated to improve ToM accuracy in bvFTD, suggesting a causal role of the mPFC in ToM performance (Cotelli et al., 2018). Emerging evidence, however, points to a distributed network of brain regions, beyond the mPFC, underpinning ToM impairments in bvFTD. With disease progression, atrophy in this syndrome encroaches into the anterior and superior lateral temporal lobes (Moller et al., 2016), and parietal cortices including precuneus and TPJ (Whitwell et al., 2015). Importantly, atrophy to these temporoparietal regions in bvFTD has also been shown to correlate with impaired ToM performance (Brioschi Guevara et al., 2015; Cerami et al., 2014; Eslinger et al., 2007; Irish, Hodges, & Piguet, 2014), suggesting a crucial contribution of regions beyond the mPFC.

In contrast to the abundant literature on ToM in bvFTD, no studies to date have assessed VPT in this syndrome. This may be attributable to the well-documented preservation of visuospatial functioning in bvFTD (Salimi et al., 2018), including mental rotation abilities (Binetti, Locascio, Corkin, Vonsattel, & Growdon, 2000), well into late stages of the disease. Nonetheless, deficits in VPT have been documented in other neuropsychiatric conditions characterised by impaired ToM, such as autism and schizophrenia (see Chapter 1). Further,

the VPT deficits in these syndromes have been found to correlate with, and therefore are proposed to underlie, their impairments in ToM (Farrant et al., 2006; Hamilton et al., 2009; Langdon et al., 2001). As such, a similar mechanism may be predicted in bvFTD, a hypothesis supported by the atrophy to key brain regions associated with VPT in this syndrome (i.e., IFG, along with TPJ and precuneus later in the disease course). On the other hand, the association between VPT and ToM has not consistently been revealed, with some studies supporting their dissociation (David et al., 2008; Drayton et al., 2018; Pearson et al., 2013) (reviewed in Chapter 1). Moreover, the precise relationship between different forms of VPT, namely Level 1 (i.e., understanding *what* someone else sees) and Level 2 (i.e., understanding *how* someone else sees the world), and ToM remains poorly understood, in particular whether their neurocognitive mechanisms are overlapping or distinct. The functional implications of Level 1 and Level 2 VPT impairments also remain unclear, as their behavioural manifestations in the real-world have not yet been explored.

The current study aimed to examine Level 1 and Level 2 VPT, ToM, and real-world perspective taking in bvFTD. The relationships between these functions, with other cognitive processes, and with underlying brain integrity were explored, in order to compare and contrast the cognitive and neural underpinnings of each of these forms of perspective taking. In doing so, this study endeavoured to discern whether VPT and ToM form discrete or overlapping components of the interpersonal self, and how this manifests in the real world. Despite their preserved spatial abilities, bvFTD patients were predicted to display impairments in both types of VPT, consistent with previous findings in other social disorders. In turn, these deficits were expected to correlate with ToM performance and perspective taking in daily life, and atrophy to a core perspective taking network (i.e., IFG, TPJ, and precuneus).

## 6.2. Method

### 6.2.1. Participants

Sixteen bvFTD patients and 15 healthy Control participants were recruited for this study (an independent sample from that included in Chapter 5). Details of recruitment procedures and neuropsychological assessment are outlined in Chapter 2. One bvFTD patient was excluded due to invalid responding on both VPT tasks, leaving a final sample of 15 in each group.

Genetic information was available for the bvFTD sample, revealing a *C9orf72* mutation in 5 out of 15 patients. In this study, ACE-III performance is reported as a measure of general cognitive functioning, along with specific tests of processing speed (Trail Making Test Part A; Tombaugh, 2004), visuospatial ability (Rey Complex Figure Copy; Rey, 1941) and ACE-III Visuospatial subscale, and executive functions of inhibition (Hayling test; Burgess & Shallice, 1997) and set-switching (Trail Making Test Part B minus A). FTD-FRS was not available for this sample, but disease duration and CBI Total provide alternative measures of disease staging.

### 6.2.2. Procedure

Participants completed a comprehensive battery of perspective taking tasks, including tasks of Level 1 and Level 2 VPT and ToM, as well as questionnaires capturing behavioural manifestations of perspective taking in everyday life. A mental rotation task was also completed, to assess the potential effect of mental rotation abilities on performance on the Level 2 VPT task.

#### *Level 1 VPT task*

Participants completed a computerised Level 1 VPT task, assessing the ability to imagine what someone else may see. The task was modified from Samson, Apperly, Braithwaite, Andrews, and Bodley Scott (2010) to ensure suitability for the cognitive abilities of bvFTD patients. Stimuli were presented using E-Prime software, with reaction times and accuracy recorded for each trial.

During the task, participants were presented with pictures of a human avatar in the centre of a room, with the left, back, and right walls visible (Figure 6.1.). Red dots were present on the left, right, or both walls, and the avatar faced either the left (50% trials) (Figure 6.1.A, D) or right (50% trials) (Figure 6.1.B, C) wall. The dots were positioned such that on 50% of the trials, the avatar saw the same number of dots as the participant completing the task (Consistent perspective condition; Figure 6.1.A, B). On the remaining 50% of trials, the avatar was unable to see some of the dots that were visible to the participant (i.e., the dots were positioned on the wall behind the avatar; Inconsistent perspective condition) (Figure 6.1.C, D).

For each trial, participants were presented with a picture of a room, with a question at the top of the screen indicating the perspective to be taken (Self or Other), and the number of dots to be verified (0-3 dots), for example, “Do YOU see a total of 1 dot?” (Self condition), or “Does HE see a total of 3 dots?” (Other condition) (Figure 6.1.). Participants were required to respond YES or NO to the question, using labelled buttons on the computer keyboard. While the original Samson et al. (2010) task presented the perspective (self/other), dots to be verified, and picture of the room across three successive screens, this information was condensed into a single screen for the current task, to reduce demands on memory. Furthermore, participants were encouraged to respond as quickly as possible, however given the characteristic reductions in processing speed in bvFTD patients (Ranasinghe et al., 2016), there was no time cut-off for the responses.

The task consisted of 72 main trials: 36 Self trials requiring participants to judge their own perspective (18 Consistent and 18 Inconsistent perspective trials), and 36 Other trials where participants were asked to judge the perspective of the avatar (18 Consistent and 18 Inconsistent perspective trials). The proportion of Matching (i.e., correct response of yes) and Mismatching (i.e., correct response of no) trials was equally distributed across these conditions. Eight filler trials were also presented, where no dots were displayed on the wall (consisting of an equal number of Self, Other, Matching, and Mismatching trials), though these were not included in the analysis (see Samson et al., 2010).

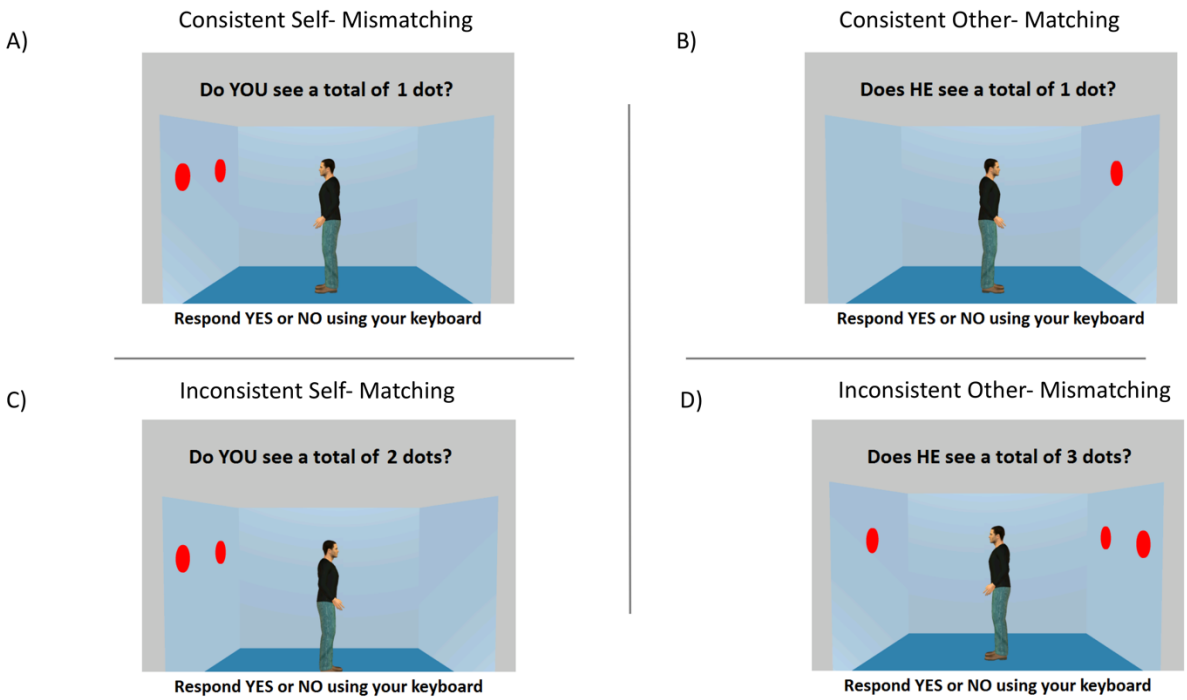



*Figure 6.1.* Examples of the main trial types for the Level 1 Visual Perspective Taking (VPT) task. A) Consistent Self Mismatching Trial: The participant sees the same number of dots as the avatar, must respond with respect to their own perspective, and the correct response is 'no'. B) Consistent Other Matching Trial: The participant sees the same number of dots as the avatar, must respond with respect to the avatar's perspective, and the correct response is 'yes'. C) Inconsistent Self Matching Trial: The participant sees a different number of dots to the avatar, must respond with respect to their own perspective, and the correct response is 'yes'. Incorrect responses on Inconsistent Self trials reflect 'altercentric' errors. D) Inconsistent Other Mismatching Trial: The participant sees a different number of dots to the avatar, must respond with respect to the avatar's perspective, and the correct response is 'no'. Incorrect responses on Inconsistent Other trials reflect 'egocentric' errors.

*Note:* Each condition (Consistent Self, Consistent Other, Inconsistent Self, Inconsistent Other) contains an equal number of Matching and Mismatching trials.

Following a practice block of 10 trials, the test trials were presented in four blocks, separated by a self-paced break. The order of trials within each block was pseudorandomised and consistent across participants.

The primary measures of interest in the current study were egocentric errors (i.e., the total number of errors on Inconsistent Other perspective trials, involving a projection of one's own viewpoint onto the avatar, Figure 6.1.D), and altercentric errors (i.e., the total number of errors on Inconsistent Self perspective trials, involving the adoption of the avatar's viewpoint as one's own, Figure 6.1.C). To ensure basic compliance with the task, error rates on Consistent perspective trials were also analysed (Figure 6.1.A, B).

As secondary measures of interest, reaction times were analysed, specifically indices of egocentric interference (i.e., the mean difference in response time between Inconsistent Other and Consistent Other perspective trials) and altercentric interference (i.e., the mean difference in response time between Inconsistent Self and Consistent Self perspective trials) (see Drayton et al., 2018). For these interference measures, outlying trials (i.e., a *z*-score of +/- 2 from the participant's mean score for the trial type), as well as incorrect trials, were removed from the analysis.

For reaction time analyses, only Matching trials were included. This is due to the unbalanced nature of the Mismatching trials, with Mismatching Consistent trials being particularly easy to process compared with the other trial types. Specifically, on Mismatching trials (i.e., a correct response of 'no') in the Inconsistent perspective condition, the number of dots to be verified was that seen by the irrelevant perspective (i.e., the number seen by the avatar when asked to judge one's own perspective, and the number seen by oneself when asked to judge the avatar's perspective) (e.g., Figure 6.1.D). On Mismatching trials in the Consistent perspective condition, however, participants were required to verify a number of dots that did not correspond to either one's own, or the avatar's, perspective (e.g., Figure 6.1.A). Accordingly, as the egocentric and altercentric interference measures required a direct comparison of reaction time between Inconsistent and Consistent trials, Mismatching trials were excluded from reaction time analyses (see Samson et al., 2010).

***Level 2 VPT task***

A simple, novel, computerised task was designed to examine Level 2 VPT, measuring the ability to imagine how a scene may look from a viewpoint different from one's own. Stimuli

were presented using E-Prime software, with reaction times and accuracy recorded for each trial.

On each trial, participants were shown a picture of a room created using Planner 5d interior design software (https://planner5d.com) (Figure 6.2.). The left, right, and back walls of the room were visible, and each contained 2 items of furniture and an avatar. Below the picture of the room was the question: "How does the room look from HIS perspective?". Underneath, three different rooms were presented (numbered 1-3), with the instruction "Choose the most correct option using numbers 1-3 on your keyboard". One of these options was the correct picture of the room as viewed by the avatar, one was an egocentric foil (i.e., a picture of the room from the participant's perspective), and one was a spatial foil (i.e., the picture was taken from the opposite side of the room from which the avatar is standing, see Figure 6.2.A option 2; or the furniture was located on the opposite side of the room see Figure 6.2.B option 1). Participants selected their response using the number keys 1-3 on the keyboard. While the onscreen instructions at the beginning of the task stated to respond as quickly as possible, participants were advised that accuracy was more important than speed for this task.

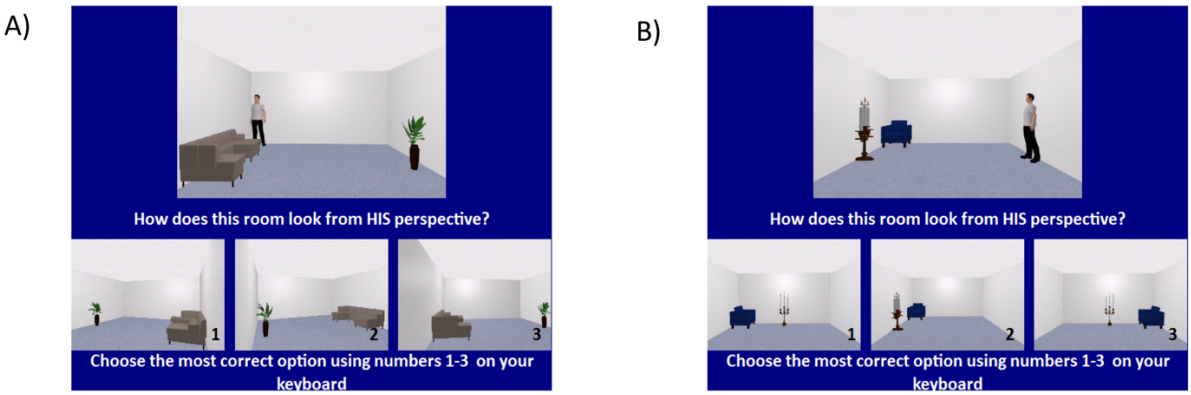



*Figure 6.2.* Example trials for the Level 2 Visual Perspective Taking (VPT) task. A) A mental rotation of 180° is required. In this trial, option 1 represents the correct response, with options 2 and 3 representing the spatial and egocentric foils, respectively. B) A mental rotation of 90° is required. In this trial, option 3 represents the correct response, with options 1 and 2 representing the spatial and egocentric foils, respectively.

Six practice trials were presented, followed by two blocks of 18 trials each. The correct responses and egocentric and spatial errors were equally distributed across the three response options. The position of the avatar in the room was also equivalently distributed across four locations (i.e., the two back corners, and the two side walls) so that half of the trials involved an imagined rotation of 180 degrees (Figure 6.2.A), and the other half a rotation of 90 degrees (Figure 6.2.B). The order of these trials was pseudorandomised and consistent across participants.

The primary measure of interest was egocentric errors on the task, with spatial errors and reaction times included as secondary measures.

One bvFTD patient could not complete the Level 2 VPT task due to cognitive impairment, leaving a final sample of 14 bvFTD and 15 healthy Controls completing this task.

***Theory of mind task***

ToM ability was examined using a cartoon mental state attribution task (Irish, Hodges, et al., 2014; Lough et al., 2006). Participants were presented with two sets of 10 cartoons, depicting scenarios requiring either (i) understanding of physical humour (e.g., a bucket of water falling on a man's head after walking into a joke shop), or (ii) the inference of mental states (i.e., ToM; e.g., escaped prisoners unknowingly tunnelling into a police station), respectively (Figure 6.3.). The physical and ToM cartoons were presented in pseudorandom order, consistent across participants, with participants required to describe the intended joke in the cartoon, or why someone might find it funny. Responses for the physical cartoons were deemed correct if the humour of the scenario was adequately conveyed. For the ToM scenarios, correct responses required appropriate attribution of mental states to the characters (e.g., 'he doesn't realise', 'unbeknownst to them'). No time limit was imposed, however, if correct responses were not provided on the first attempt, participants were given a single, generic prompt (e.g., 'Is there anything else you can tell me about why someone might find this funny?'). A maximum score of 10 was possible for both physical and ToM cartoons.

The same bvFTD patient excluded from the Level 2 VPT task was also unable to complete the ToM task due to cognitive impairment, leaving a final sample of 14 bvFTD and 15 healthy Controls completing the ToM task.

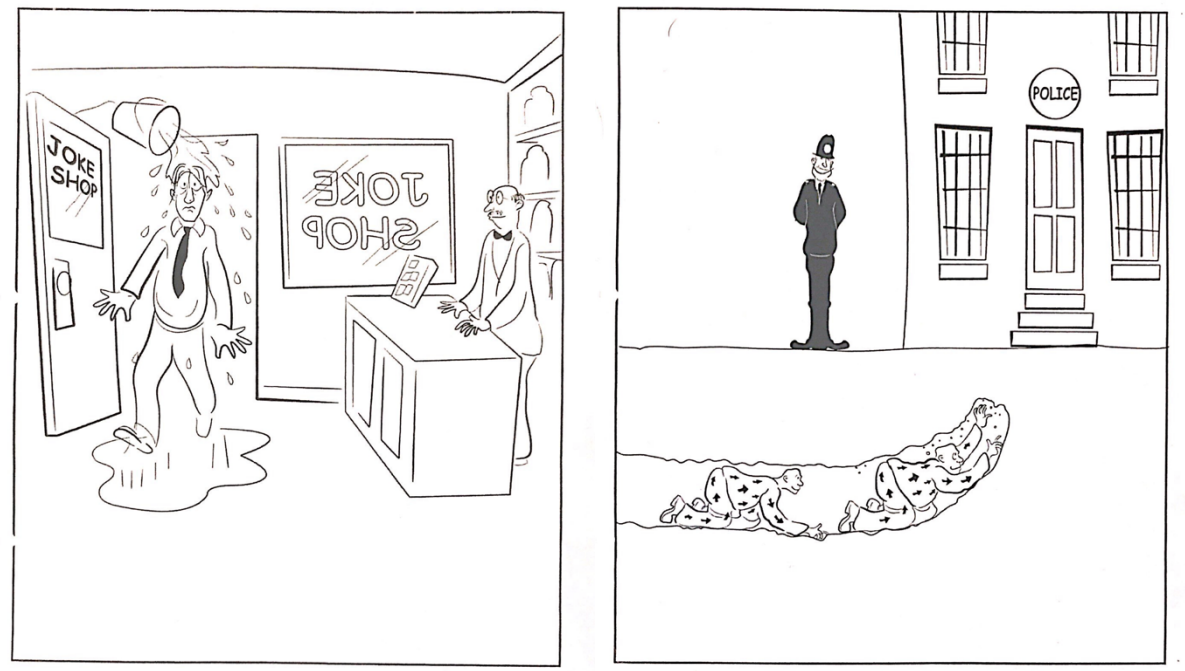



*Figure 6.3.* Example trials for the Physical (left) and Theory of Mind (right) cartoons. Stimuli adapted from Lough et al. (2006).

***Mental rotation task***

A computerised mental rotation task was completed to assess the potential effect of mental rotation abilities on performance on the Level 2 VPT task. The task was administered using the PsyToolkit online software program (Stoet, 2010, 2016). Participants were presented with three 2-dimensional shapes, and were required to choose which of the bottom two shapes represented a rotated version of the top one, via a mouse click (Figure 6.4.). Participants completed 5 practice trials and 10 test trials and had unlimited time to complete the items. Accuracy was recorded as the primary measure of interest.

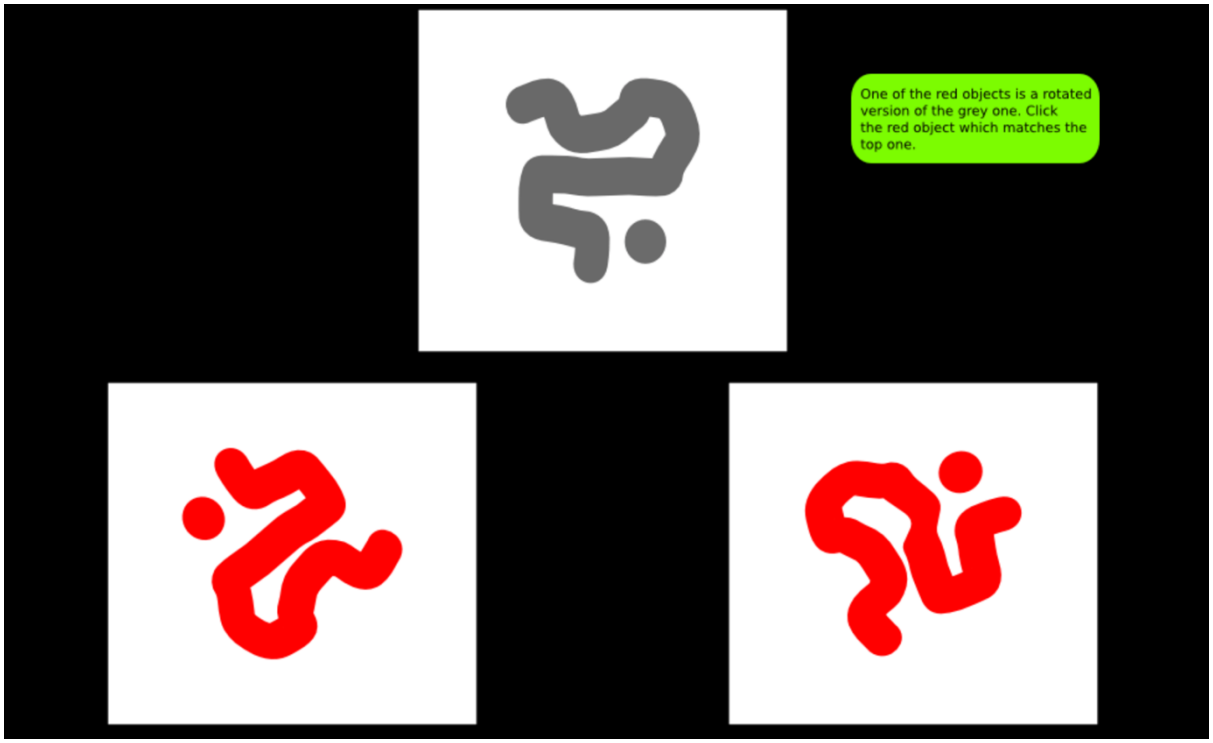



*Figure 6.4.* Example trial for the mental rotation task, adapted from the PsyToolkit online software program (Stoet, 2010, 2016). The correct answer is the left object.

***Interpersonal Reactivity Index (IRI)***

The Interpersonal Reactivity Index (IRI; Davis, 1983) was completed as a measure of perspective taking in daily life. Given the well-documented lack of insight in bvFTD, carers completed the questionnaire with reference to patients with bvFTD, whereas Control participants completed the self-report version. The IRI comprises 28 statements about thoughts and feelings, and requires the respondent to rate the degree to which each of these describe oneself/the patient. Responses are made on a five-point Likert scale (ranging from 'Does not describe me/him/her well' to 'Describes me/him/her very well'). The IRI contains four 7-item subscales, though the primary measure of interest for the present study was the Perspective Taking (PT) subscale, indexing the ability to imagine the perspective of another in daily life (e.g., 'He/she sometimes tries to understand their friends better by imagining how things look from their perspective'). A higher score on this subscale reflects greater reported perspective taking (maximum = 35). For the bvFTD patients, carers were required to rate the patient on the statement both before the onset of dementia, and at the present time. IRI data

was missing for one Control, and ratings for prior to disease onset were missing for one bvFTD patient.

***Egocentric Behaviour questionnaire (EBQ)***

The Egocentric Behaviour Questionnaire (EBQ) (Bon, Belliard, Eustache, & Desgranges, 2009) is a carer report measure of egocentric behaviour in daily life. The original questionnaire was translated from French into English for the present study. Thirty-six behaviours are listed, with carers rating the extent to which they agree with each of the statements in relation to the patient, on a 4-point Likert scale (Strongly Agree, Somewhat Agree, Somewhat Disagree, Strongly Disagree). Four 9-item subscales are produced, namely Egocentric Speech (e.g., 'He/she talks about himself/herself a lot'), Impaired Empathy (e.g., 'He/she is sensitive to your feelings'), Imposing Preferences (e.g., 'He/she always wants to have the last word') and Failure to Consider Others ('e.g., 'He/she sometimes says or does things that irritate or offend others'), along with a Total score. Higher values represent increased egocentric behaviour. EBQ data was missing for 1 bvFTD patient.

### 6.2.3. Statistical analyses

Independent samples t-tests were employed to assess group differences on demographic measures and neuropsychological tasks. The frequencies of dichotomous variables (i.e., sex) were compared using chi-squared tests ($\chi^2$). Between-group differences on experimental variables were examined using parametric analyses, namely independent samples t-tests, where possible (i.e., when the raw variables were normally distributed in the patient group, or logarithmic transformation of the variable restored normality in the patient group). Otherwise, non-parametric tests were employed (i.e., Mann Whitney U). These analyses were chosen over repeated-measures tests given the primary interest in examining between-group differences on the tasks, rather than within-subject differences between different task components. Relationships between the experimental variables were explored using the robust Spearman's correlation coefficient, given non-normality in some of the experimental variables. The significance level was set at $p < .05$ for all analyses (including the correlation analyses, given these were exploratory in nature), and effect sizes were calculated using Cohen's d (for parametric analyses) and $\eta^2$ (for nonparametric analyses).

### 6.2.4. Neuroimaging analysis

Twenty-five participants (12 bvFTD, 13 Controls) were included in the voxel-based morphometry (VBM) analysis. Full details of MRI acquisition and pre-processing are outlined in Chapter 2.

For analyses of grey matter intensity, permutation-based non-parametric testing was employed using unbiased whole-brain General Linear Models (GLM) in FSL, with 5000 permutations per contrast (Nichols & Holmes, 2002). Differences in grey matter intensity between bvFTD and Controls were assessed using *t*-tests. Age was included as a covariate of no interest in these atrophy analyses. Significant clusters were extracted using the threshold-free cluster enhancement (TFCE) method at a threshold of $p < .001$ uncorrected, with a cluster extent cut-off of 200 contiguous voxels. This statistical approach takes into consideration the small sample size and balances the risk of Type I versus Type II errors (Lieberman & Cunningham, 2009). Significant results were overlaid on the MNI standard brain, with maximum co-ordinates provided in MNI stereotaxic space. Anatomical labels were determined with reference to the Harvard-Oxford probabilistic cortical and subcortical atlases.

Next, a region of interest approach was employed to explore associations between grey matter intensity and perspective-taking task/questionnaire performance, irrespective of group membership (i.e., bvFTD patients and Controls combined). Four brain areas were selected based on meta-analyses of studies on VPT and ToM, namely the mPFC, TPJ, precuneus, and IFG (Molenberghs, Johnson, Henry, & Mattingley, 2016; Schurz et al., 2013; Schurz et al., 2014; Van Overwalle, 2009), and bilateral masks of these regions were extracted using the Harvard-Oxford probabilistic atlas. One-tailed Spearman's correlations (with an alpha of $p < .05$, given the exploratory nature of these analyses) were employed to explore associations between the extracted grey matter intensities and perspective taking performance, such that higher grey matter intensity was associated with better task performance.

## 6.3. Results

### 6.3.1. Demographics and neuropsychological performance

Participant demographics and neuropsychological performance are presented in Table 6.1. Groups did not significantly differ in age ($p$ = .08), sex ($p$ = .07), or years of education ($p$ = .07).

In keeping with their characteristic clinical profile, bvFTD patients showed impairments in behaviour (CBI Total), global cognitive functioning (ACE-III Total), processing speed (Trails A) and executive function (Hayling and Trails B-A). By contrast, visuospatial function was relatively preserved (ACE-III Visuospatial and RCF Copy).

**Table 6.1.** Demographics and clinical characteristics of the study cohort

| Variable | bvFTD | Control | *t* value | *p* value |
|---|---|---|---|---|
| N | 15 | 15 | | |
| Age | 61.27 (8.75) | 66.07 (5.59) | -1.79 | ns |
| Sex (M/F) | 11/4 | 6/9 | $X^2$ = 3.39 | ns |
| Education (Years) | 11.92 (2.99) | 13.93 2.76) | -1.92 | ns |
| Disease duration (Months) | 99.08 (64.82) | n/a | n/a | n/a |
| CBI Total Frequency (180) | 68.33 (32.63) | 6.38 (4.81) | 6.77 | < .001 |
| ACE-III Visuospatial (16) | 14.67 (1.35) | 15.47 (.92) | -1.90 | ns |
| ACE-III Total (100) | 81.93 (11.61) | 93.93 (2.94) | -3.88 | .002 |
| RCF Copy (36) | 28.97 (5.30) | 31.37 (3.23) | -1.50 | ns |
| Hayling Total AB score | 10.00 (9.87) | 3.47 (3.56) | 2.40 | .03 |

| | | | | |
|---|---|---|---|---|
| Trail Making Test Part A | 43.47 (16.13) | 31.27 (10.62) | 2.45 | .02 |
| Trail Making Test Part B-A | 98.50 (70.66) | 50.87 (26.25) | 2.44 | .03 |

*Notes:* ACE-III: Addenbrooke's Cognitive Examination-III; CBI: Cambridge Behavioural Inventory (CBI); ns = nonsignificant; RCF: Rey Complex Figure.

Disease duration missing for 1 bvFTD patient, CBI missing for 2 Controls, Hayling missing for 1 bvFTD patient, Trail Making Test Part B missing for 1 bvFTD patient.

### 6.3.2. Level 1 VPT task performance

On the Level 1 VPT task, bvFTD patients made significantly more egocentric errors compared with Controls (i.e., errors on Inconsistent Other perspective trials, which involved projecting one's own visual perspective onto the avatar) (Mann Whitney U = 64.00, exact two-sided $p$ = .03, $\eta^2$ = .17). By contrast, no significant difference between the groups emerged for altercentric errors (i.e., errors on Inconsistent Self perspective trials, which involved adopting the avatar's visual perspective as one's own) (Mann Whitney U = 105.50, exact two-sided $p$ = .78, $\eta^2$ = .003) (Figure 6.5.)[21]. Furthermore, groups did not significantly differ on errors for the Consistent Self perspective trials (Mann Whitney U = 97.50, exact two-sided $p$ = .48, $\eta^2$ = .07), though bvFTD patients did make more errors on the Consistent Other perspective trials, compared with Controls (Mann Whitney U = 75.00, exact two-sided $p$ = .04, $\eta^2$ = .20)[22].

[21] Outlying error rates (i.e., > 3 SD from the group mean) were observed for 1 bvFTD and 1 Control participant on Inconsistent Other errors. The significant difference between the groups was, however, maintained when the outlying participants were removed (Mann Whitney U = 50.00, $p$ = .02, $\eta^2$ = 0.22). For the Inconsistent Self condition, no participants made error rates > 3 SD from the group mean.

[22] The same bvFTD patient described above also displayed outlying error rates for Consistent Self and Consistent Other conditions. Removal of this participant, however, did not change the patterns of results (Consistent self: Mann Whitney U = 97.50, $p$ = .48, $\eta^2$ = .04; Consistent Other: Mann Whitney U = 75.00, $p$ = .04, $\eta^2$ = .17).

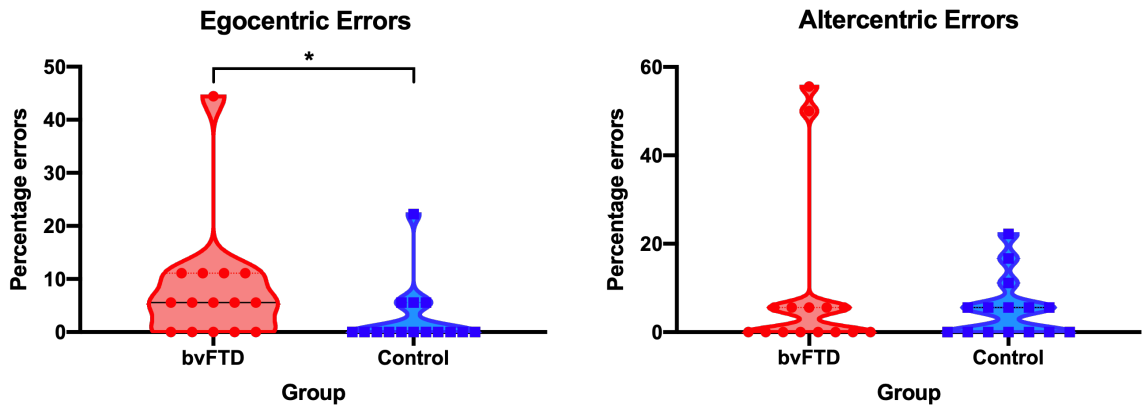



*Figure 6.5.* Egocentric (left) and altercentric (right) error rates for the two groups on the Level 1 Visual Perspective Taking (VPT) task. bvFTD = behavioural variant frontotemporal dementia. Asterisk denotes significant between-group difference at *$p < .05$.

In terms of the reaction time analysis, no significant difference was apparent between the groups for egocentric interference scores (i.e., the difference in reaction time between Inconsistent and Consistent Other perspective trials) ($t(28) = -.02$, $p = .98$, d = .008) or altercentric interference scores (i.e., the difference in reaction time between Inconsistent and Consistent Self perspective trials) ($t(28) = 1.64$, $p = .11$, d = .60).

### 6.3.3. Level 2 VPT task performance

On the Level 2 VPT task, the variances in egocentric error rates significantly differed between the groups, as revealed by a significant Levene's test (F = 25.17, $p < .001$). As such, the degrees of freedom were modified to account for unequal variances. Relative to Controls, bvFTD patients made significantly more egocentric errors ($t(13.73) = 3.56$, $p = .003$, d = 1.34) (Figure 6.6.). No significant differences were apparent for spatial errors ($t(27) = 1.52$, $p = .14$, d = 0.56) or reaction time (t(27) = .25, $p = .81$, d = .09).

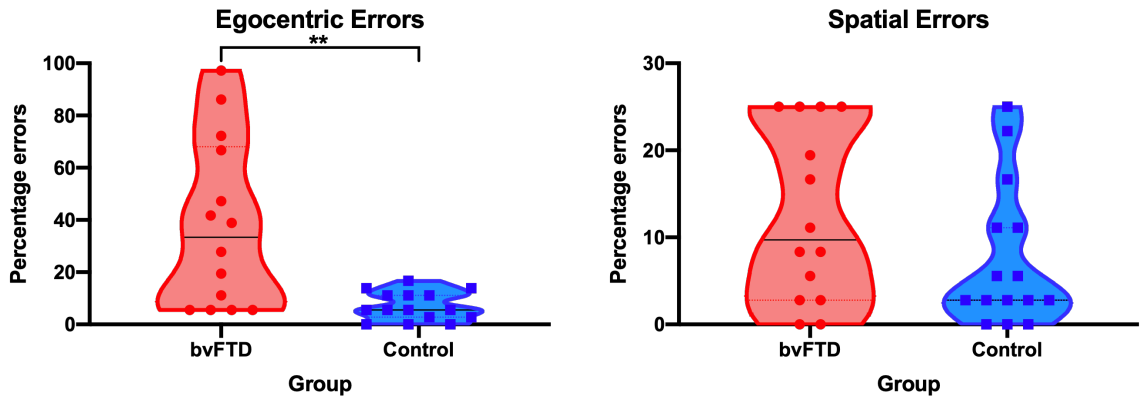



*Figure 6.6.* Egocentric (left) and spatial (right) error rates for the two groups on the Level 2 Visual Perspective Taking (VPT) task. bvFTD = behavioural variant frontotemporal dementia. Asterisk denotes significant between-group difference at $^{**}p < .01$.

### 6.3.4. Theory of mind task performance

On the ToM task, the variances in accuracy on the ToM and physical cartoons significantly differed between the groups, as revealed by a significant Levene's test (ToM: $F = 21.93$, $p < .001$; Physical: $F = 4.48$, $p = .04$), with the degrees of freedom modified accordingly. bvFTD patients performed worse than Controls on the theory of mind cartoons ($t(15.36) = -4.64$, $p < .001$, d = 1.75) (Figure 6.7.). bvFTD patients were also impaired relative to Controls on the physical cartoons ($t(20.178) = -3.79$, $p = .001$, d = 1.42). When controlling for performance on the physical cartoons, however, the ToM impairments in bvFTD remained apparent, with patients performing significantly worse than Controls on the ToM cartoons ($F(1, 26) = 9.33$, $p = .005$, partial $\eta^2 = .26$). This suggests the findings reflect a ToM deficit in bvFTD, over and above any impairment in detecting humour in general.

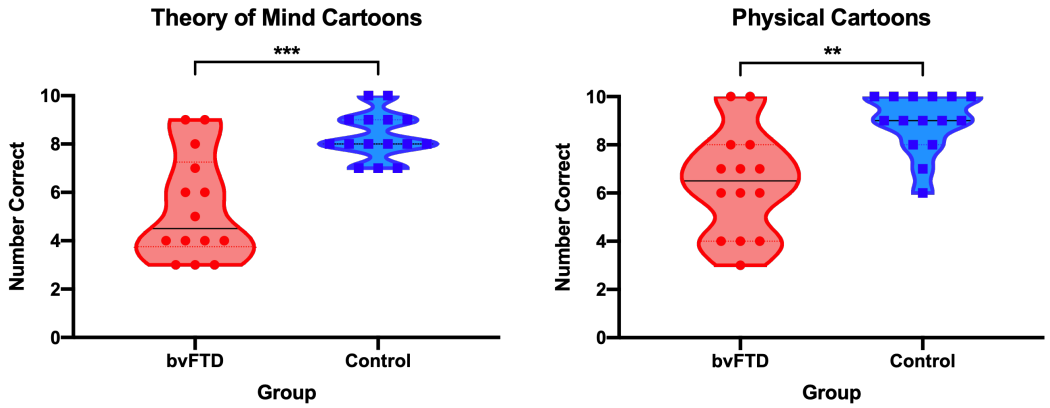



*Figure 6.7.* Performance on Theory of Mind (left) and Physical (right) cartoons in each group. bvFTD = behavioural variant frontotemporal dementia. Asterisks denote significant between-group difference at ***$p < .001$; **$p < .01$.

### 6.3.5. Mental rotation task performance

No significant difference emerged between bvFTD and Control participants on mental rotation accuracy ($t(28) = -1.53$, $p = .14$, d = .56).

### 6.3.6. Interpersonal reactivity index (IRI)

No significant difference emerged for Perspective Taking ($t(26) = -.71$, $p = .49$, d = .27) between Controls (self-rated) at the present time and bvFTD patients prior to their disease onset (informant-rated). This suggests that before the onset of bvFTD, these patients displayed normal perspective taking behaviour. At the present time, however, bvFTD patients were rated as displaying significantly worse Perspective Taking ($t(27) = -6.08$, $p < .001$, d = 2.26) than Controls.

### 6.3.7. Egocentric behaviour questionnaire (EBQ)

bvFTD patients were rated as displaying high degrees of Overall Egocentric Behaviour (EBQ Total: M = 66.64, SD = 14.87), Egocentric Speech (M = 17.64, SD = 4.57), Impaired Empathy (M = 15.21, SD = 5.01), Imposing Preferences (M = 16.14, SD = 4.38) and Failure to Consider Others (M = 17.64, SD = 4.31). This measure was not completed in Controls given its specificity to symptoms of FTD.

### 6.3.8. Correlations between the measures

Two-tailed Spearman's correlations were conducted to examine the relationship between the various perspective taking measures and questionnaires in the patient group, using the primary measure of interest for each task (Table 6.2.). Furthermore, correlations were examined between Level 2 perspective taking and mental rotation performance. Given the limited range of participant scores on the Level 1 VPT task (i.e., the majority of participants making between 0-2 errors), correlations with performance on this measure were unable to be performed.

Interestingly, a significant negative correlation was observed between Egocentric errors on the Level 2 VPT task and Total Score on the EBQ, such that *more* egocentric errors were associated with carer ratings of *less* egocentric behaviour in bvFTD. The EBQ was also negatively correlated with the IRI PT scale, such that greater egocentric behaviour was related to poorer perspective taking in daily life. Finally, a significant negative correlation emerged between Egocentric errors on the Level 2 VPT task and Mental Rotation performance, with worse mental rotation associated with more egocentric errors. No other significant correlations were apparent between any of the measures of perspective taking.

**Table 6.2.** Correlations between perspective taking and questionnaire variables in the behavioural variant of frontotemporal dementia (bvFTD)

| Test | ToM cartoons | IRI PT | EBQ | Mental Rotation |
|---|---|---|---|---|
| Level 2 VPT egocentric errors | -.05 | .24 | **-.58*** | **-.55*** |
| ToM cartoons | | .03 | .22 | |
| IRI PT | | | **-.65*** | |

*Notes:* Mental rotation and IRI available for 15 patients, Level 2 VPT available for 14 patients, ToM available for 14 patients, EBQ available for 13 patients. bvFTD = behavioural variant frontotemporal dementia, EBQ = Egocentric Behaviour Questionnaire, IRI = Interpersonal

Reactivity Index, PT = Perspective Taking, ToM = Theory of Mind, VPT = Visual Perspective Taking. Asterisks represent significant correlation at * $p < .05$.

### 6.3.9. Voxel-based morphometry analyses

***Group differences in grey matter intensity***

Briefly, compared with Controls, bvFTD patients displayed reduced grey matter intensity in bilateral frontal and temporal lobes, including frontal pole, orbitofrontal and medial prefrontal cortex, superior, middle, and inferior frontal gyri, precentral gyrus, insula, and temporal pole (Figure 6.8.). Atrophy extended into the right caudate, left cerebellum, and posterior cortical regions including bilateral posterior cingulate cortex, precuneus, and lateral parietal and occipital areas on the left. Atrophy in posterior regions is commonly reported in bvFTD patients with the *C9orf72* genetic mutation (Whitwell et al., 2012), consistent with the high proportion of such patients in this study (4/12 included in imaging).

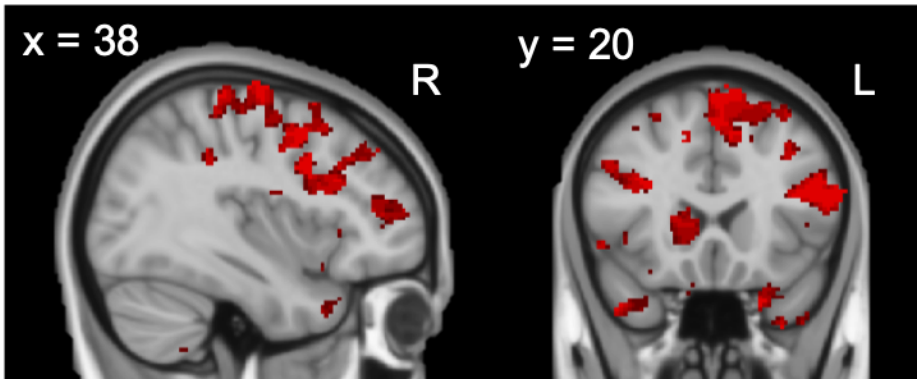
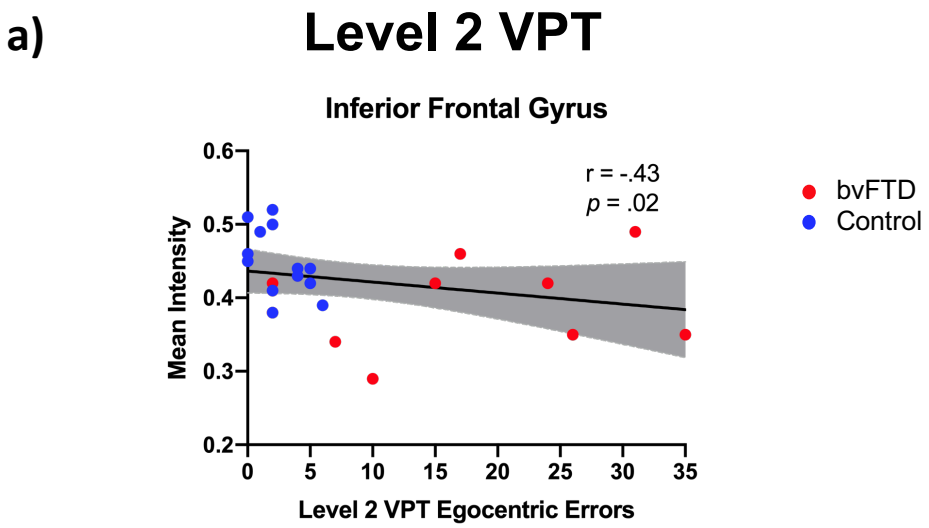


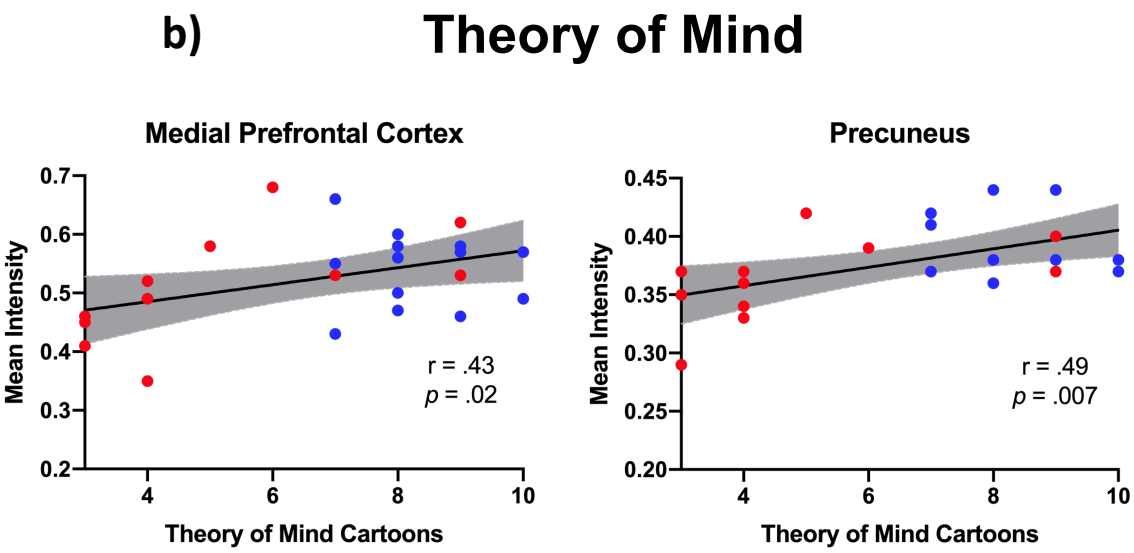

*Figure 6.8.* Voxel-based morphometry (VBM) analyses showing brain areas with decreased grey matter intensity in behavioural variant frontotemporal dementia (bvFTD) compared with Controls. Coloured voxels emerged as significant in a threshold-free cluster enhancement (TFCE) analysis at $p < .001$ uncorrected, with a cluster extent threshold of 200 contiguous voxels. Clusters are overlaid on the Montreal Neurological Institute (MNI) standard brain. L = Left; R = Right.

***Region of interest analyses***

Given the wide range of variability in the regional grey matter intensities within both bvFTD and Control groups, correlation analyses between grey matter integrity and perspective taking performance were performed for all participants combined. This increased the

statistical power to detect meaningful brain-behaviour relationships. One-tailed Spearman's correlations between the perspective taking performance (on the Level 2 VPT task, theory of mind, and IRI PT) and regional grey matter intensity across all participants are displayed in Figure 6.9. Significant correlations represent regions where worse perspective taking was associated with less grey matter intensity. Egocentric errors on the Level 2 VPT task were significantly associated with reduced integrity of the IFG (r = -.43, $p$ = .02) (Figure 6.9.a). Poorer performance on the ToM cartoon task correlated with reduced integrity of the mPFC (r = .43, $p$ = .02) and precuneus (r = .49, $p$ = .007) (Figure 6.9.b). Finally, poorer reported perspective taking on the IRI was significantly associated with reduced integrity of TPJ (r = .42, $p$ = .02), precuneus (r = .69, $p$ < .001), and IFG (r = .46, $p$ = .01) (Figure 6.8c). No other significant correlations emerged (all $p$ values > .06). Figure 6.10. collectively depicts the brain regions associated with the different aspects of perspective taking in this study.


a)
Level 2 VPT
Inferior Frontal Gyrus
r = -.43
p = .02
bvFTD
Control
Mean Intensity
0.6
0.5
0.4
0.3
0.2
0
5
10
15
20
25
30
35
Level 2 VPT Egocentric Errors


b)
Theory of Mind
Medial Prefrontal Cortex
r = .43
p = .02
Mean Intensity
0.7
0.6
0.5
0.4
0.3
0.2
4
6
8
10
Theory of Mind Cartoons
Precuneus
r = .49
p = .007
Mean Intensity
0.45
0.40
0.35
0.30
0.25
0.20
4
6
8
10
Theory of Mind Cartoons

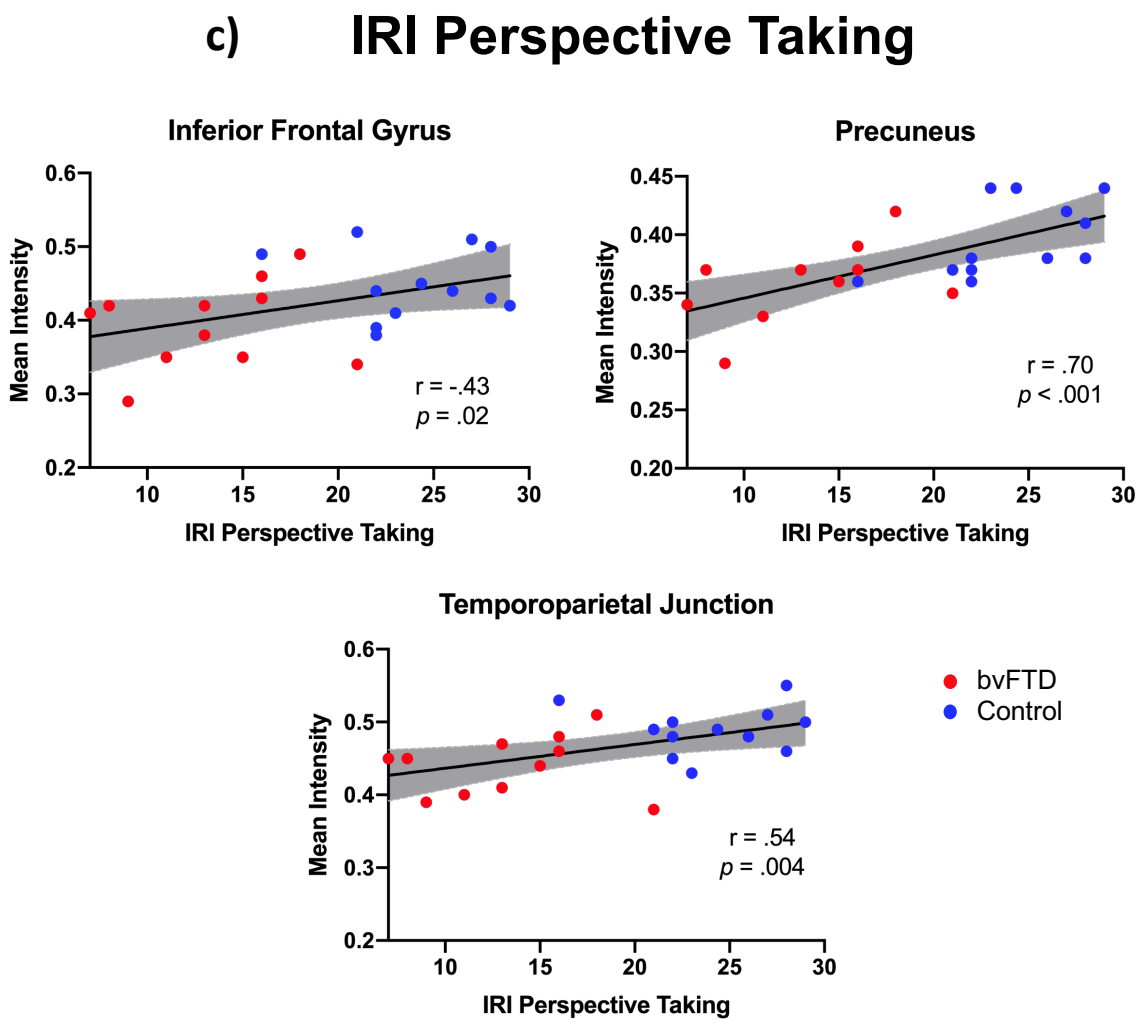



*Figure 6.9.* Significant correlations between perspective taking task performance and grey matter intensity within the selected regions-of-interest, for all participants combined. bvFTD = behavioural variant of frontotemporal dementia, IRI = Interpersonal Reactivity Index, VPT = Visual Perspective Taking.

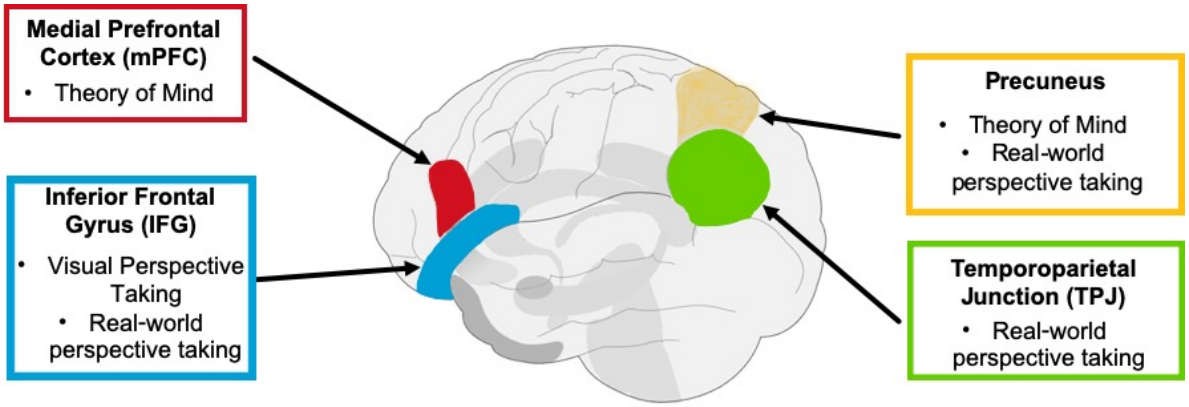



*Figure 6.10.* Brain regions-of-interest that were significantly correlated with different forms of perceptive taking in this study. Real world perspective taking refers to the Perspective Taking subscale on the Interpersonal Reactivity Index (i.e., IRI PT).

## 6.4. Discussion

This study aimed to examine VPT and ToM concurrently in patients with bvFTD, in order to clarify the neurocognitive mechanisms of, and relationship between, these forms of perspective taking, and how they manifest in daily life. Compared with healthy Controls, bvFTD patients were impaired on all aspects of perspective taking, including Level 1 and Level 2 VPT, ToM, and carer ratings of everyday perspective taking. Despite intact mental rotation performance in bvFTD at an overall group level, poorer performance on this task in the patient group correlated with deficits in Level 2 VPT. Furthermore, impairments in Level 2 VPT in bvFTD were associated with carer ratings of *less* egocentric behaviour in daily life. Finally, distinct neural correlates emerged for Level 2 VPT versus ToM, which partially overlapped with those implicated in perspective taking in daily life. Overall, despite deficits in these functions co-occurring in bvFTD, the current findings support a distinction between VPT and ToM.

In relation to Controls, bvFTD patients provided an elevated amount of egocentric errors on the Level 1 VPT task. In other words, they had difficulty imagining what another person sees, instead projecting their own visual perspective onto the character in the task. Increased errors rates, however, were also observed in bvFTD on trials on which the participant and

avatar shared the same visual perspective, and a response about the avatar's perspective was required (Consistent Other trials). Together, these findings hint at a generalised deficit in adopting the visual perspective of another in bvFTD, regardless of one's own visual perspective. Caution should be taken, though, when interpreting these results, given the majority of participants (both bvFTDs and Controls) made very low error rates on the Level 1 VPT task (i.e., between 0-2 errors in each condition). This reduced range of responses also precluded any correlational analyses between Level 1 VPT and the other behavioural or neuroanatomical measures. Furthermore, unlike in studies of other populations using the original Samson et al. (2010) task (Drayton et al., 2018; Schwarzkopf et al., 2014), no differences between patients and Controls emerged on reaction time measures on the Level 1 VPT task, purported to capture implicit VPT. As such, the modifications made to the task for the current study, while ensuring suitability for the cognitive abilities of bvFTD, may have rendered the task too simple to reliably detect between-group differences in Level 1 VPT. Future studies focused on developing sensitive, though cognitively appropriate, measures of Level 1 VPT in bvFTD are clearly warranted in order to clarify the nature and extent of VPT deficits in this syndrome. This would also aid in better establishing the brain regions essential for Level 1 VPT, and how this ability relates to Level 2 VPT, ToM, and real-world behaviour.

By contrast, robust impairments in Level 2 VPT emerged in bvFTD (Cohen's d = 1.34), with patients making significantly more egocentric errors on the task, involving a projection of their own perspective onto the virtual character. These impairments were specific to perspective taking, with patients and Controls making a similar number of spatial errors on the task. Surprisingly, despite no difference between bvFTD and Controls in visuospatial function, including performance on a mental rotation task, increased egocentric errors on Level 2 VPT were significantly correlated with worse mental rotation performance in the patient group. As discussed in Chapter 1, the involvement of spatial abilities in Level 2 VPT is well-established (Zacks & Tversky, 2005), however, the mental rotation required by these tasks, of rotating oneself to adopt the viewpoint of another, is often considered distinct from the capacity to mentally rotate an object relative to the self, as measured by classic mental rotation tasks (Inagaki et al., 2002; Wraga et al., 2000; Zacks, 2008). Nonetheless, the current findings, albeit correlational, tentatively suggest that object-based mental rotation may be

involved in Level 2 VPT. Exploring the potential causal link between these mental rotation and Level 2 VPT abilities will be an important avenue for future inquiry.

In line with the established socioemotional deficits in this syndrome (see Section 6.1.), ToM was impaired in bvFTD on the cartoon task. Carer reports of behavioural change in bvFTD revealed the difficulties in perspective taking extend to the real world (on the IRI questionnaire), along with high levels of egocentric behaviour (EBQ questionnaire). No significant correlations, however, emerged between ToM and Level 2 VPT in bvFTD, suggesting these two forms of perspective taking may in fact involve divergent mechanisms. While no associations were found between ToM and the carer-reported measures, a strong negative correlation ($r = -.58$) emerged between egocentric errors on the Level 2 VPT task and carer reports of egocentric behaviour in bvFTD, such that poorer visual perspective taking was related to *less* self-centred behaviour in daily life. This suggests that Level 2 VPT as captured on the laboratory task forms a distinct, even inversely related, ability from the egocentricity occurring in the real-world in these patients. Adopting another's visual perspective, therefore, may not necessarily be required for the social behaviours that are captured by the questionnaire, such as considering the preferences, interests, or feelings of the other person.

Further supporting their potential dissociation, region-of-interest neuroimaging analyses revealed distinct grey matter correlates of Level 2 VPT versus ToM, irrespective of group membership. Namely, increased egocentric errors on the Level 2 VPT task related to reduced grey matter integrity of the IFG. This finding meshes well with the established role of the IFG in inhibiting one's own perspective (Ramsey et al., 2013), a process heavily relied upon for successful performance on the Level 2 VPT task. Furthermore, a specific deficit in inhibiting one's own perspective has also been found in bvFTD on ToM tasks, which also correlated with metabolism of the ventrolateral frontal lobe in these patients (Le Bouc et al., 2012). On the other hand, integrity of the mPFC and precuneus were associated with performance on the ToM task in the current study. As outlined in Chapter 1 and Section 6.1., the mPFC is typically viewed as the central brain region implicated in ToM, purported to play a role in decoupling from current perceptions to imagine alternative circumstances, as well as processing emotional and socially relevant information about others: key processes required by the cartoons task. This socioemotional component supported by the mPFC likely represents a

source of divergence between ToM and Level 2 VPT processes. Despite the inclusion of a virtual character, the situations represented in the Level 2 VPT tasks (pictures of rooms) did not involve any social interaction. This is in contrast to the ToM cartoons, which were inherently interpersonal in nature and embedded in a broader social context (e.g., a woman unknowingly sticking her umbrella into the back of a man, who believes he is being held up). Compared with the mPFC, the role of the precuneus in ToM is less well-defined, though is believed to represent internal states, and/or lend visual imagery to enable the representation of another person's perspective (Cavanna & Trimble, 2006). Given this latter proposed function, it is interesting that this region emerged exclusively for the ToM, and not the VPT task, with the latter predicted to draw upon visual imagery to simulate the alternative visual perspective. As such, it is tentatively proposed that ToM and Level 2 VPT may draw upon dissociable forms of visual imagery with distinct neural underpinnings (e.g., object versus spatial; Kozhevnikov, Kosslyn, & Shephard, 2005), though further studies incorporating manipulations of the visual requirements of the tasks are required to confirm this.

Finally, poorer carer-reported perspective taking on the IRI questionnaire correlated with reduced grey matter integrity in IFG, precuneus, and TPJ. That is, the neural correlates of perspective taking in daily life incorporated regions also implicated in Level 2 VPT and ToM, implying perspective taking in everyday life may involve a combination of visual and ToM elements. Closer inspection of the IRI questionnaire supports this proposal, with the perspective taking subscale incorporating items that capture VPT (e.g., 'seeing things from the other guy's point of view', as well as ToM ('imagining how I would feel in their place'). This is in contrast to the divergence between Level 2 VPT performance and carer-reports of egocentric behaviour in daily life found in bvFTD, with the latter scale focusing more on empathic concern (i.e., the consideration of others, which involves additional emotional processing) rather than perspective taking *per se*. While no significant relationships between TPJ integrity and performance on Level 2 VPT and ToM tasks emerged in the current study, this region has previously been associated with both of these processes, attributable to its involvement in the representation of differing perspectives, regardless of task demands (McCleery et al., 2011; Perner et al., 2006). Taken together, these findings suggest that the fundamental processes of ToM and Level 2 VPT as measured in the laboratory, while potentially distinct from one another, may both be involved in perspective taking in the real-

world: a process underpinned by a distributed brain network. Level 2 VPT, however, at least in bvFTD, is proposed to be distinct from the behavioural manifestations of empathy, with the ability to visually simulate another perspective perhaps not necessarily required for the consideration of others in everyday social interactions.

Overall, by integrating theoretically driven, objective measures of perspective taking in the laboratory with ecologically valid insights into everyday behaviour, the findings of this study suggest that VPT and ToM form distinct abilities, with different cognitive and neural underpinnings. While Level 2 VPT was associated with mental rotation and brain regions associated with the inhibition of one's own perspective, and inversely linked with egocentric behaviour (i.e., the empathic consideration of others), the neural correlates of ToM included areas implicated in socioemotional processing and visual imagery. Despite their dissociation in the laboratory, however, it is tentatively proposed that VPT and ToM may jointly occur in perspective taking in daily life, potentially drawing upon a distributed network of brain regions. As such, attempting to parcellate complex aspects of social interactions into discrete elements may overlook the ways in which they inherently intertwine in the real-world, and the importance of the broader social context. These findings have important implications for refining the understanding the interpersonal self. While the ability to adopt other's perspectives has long been recognised as crucial for successful social relationships (Mead, 1934), this study aids in characterising the distinct forms of perspective taking, which seem to both be important for interpersonal function. As was raised in Chapter 5, the severity of the impairment in social functioning in bvFTD may stem from the *combined* deficits in multiple dissociable components of the interpersonal self (in this case, both VPT and ToM). These ideas will be developed further in Chapter 7.

# Chapter 7

# General discussion

## 7.1. Introduction

The objective of this thesis was to leverage modern theory and methods from cognitive neuroscience, combined with neurodegenerative lesion models, to improve characterisation of the neurocognitive mechanisms underlying the extended and interpersonal aspects of the 'self'. Employing a novel experimental method (the 'NExt' taxonomy), Part 1 of this thesis (Chapters 3 and 4) illustrates the complex interplay of episodic and semantic memory in supporting the extended self. Moreover, Part 2 (Chapters 5 and 6) reveals how the complex social interactions that comprise the interpersonal self can be deconstructed into several distinct, yet interacting, neurocognitive components. How these findings integrate with one another, and the broader literature on the self, will be considered in the following sections. Clinical implications will also be discussed, along with reflections on methodological limitations and potential future directions.

## 7.2. Part 1: The extended self

As outlined in Chapter 1, existing work on the extended self has predominantly focused on the contribution of episodic memory to the autonoetic, subjective component of self-continuity. By contrast, the contribution of different forms of memory to one's life story, i.e., narrative continuity of the self, remains poorly understood. Drawing upon contemporary theoretical frameworks proposing a continuum between episodic and semantic memory, the new scoring taxonomy employed in Chapters 3 and 4 ('NExt') reveals important insights into the mechanisms underlying narrative self-continuity. Distinct profiles of external details were uncovered for each patient group (AD and SD) compared with Controls, which varied across remote, recent, and future epochs. These details arguably represent relevant contextual background information for one's life story, and as such, provide a proxy for narrative continuity of the self. In Chapter 1, it was hypothesised that episodic and semantic memory may differentially contribute to narrative continuity, contingent upon the time period (Figure 1.4.). The fine-grained NExt method, however, exposes how a full spectrum of episodic to

semantic details may be used to support narrative continuity across all lifetime periods. Importantly, the novel findings from Part 1 of this thesis highlight how, in neurodegenerative disorders, episodic and semantic representations may be preferentially drawn upon to provide a sense of narrative self-continuity, in the face of impairment to their counterpart. Indeed, this observation aligns well with recent theoretical models (e.g., Irish, 2020; Renoult et al., 2019; Sekeres, Winocur, & Moscovitch, 2018), which propose that memories may be recalled in many different ways, dependent upon the accessibility of the representations, and the demands of the situation or task. The current findings suggest that this flexibility in memory retrieval may also be applied when narrating one's life story, with the available episodic or semantic content harnessed by AD and SD patients in order to maintain continuity of the extended self. Interestingly, such a shift toward the most preserved memory representations to support one's life story has also been documented with the normal ageing process (Acevedo-Molina, Matijevic, & Grilli, 2019; Craik & Bialystok, 2006; Levine et al., 2002; Spreng et al., 2018), corresponding to the harnessing of intact brain regions (Spreng et al., 2018). Whether this relative dependence on a 'preferred' memory type to provide narrative self-continuity also occurs in other clinical populations, however, or indeed, young, healthy individuals, remains to be determined. The individual differences in episodic and semantic autobiographical memory abilities and preferences, which map on to distinct neural fingerprints (Hodgetts et al., 2017; Sheldon et al., 2016; Spreng et al., 2018), do hint at this possibility. Nonetheless, as observed in the AD and SD patients in Chapters 3 and 4, this preference is expected to shift contingent upon the particular context, conditions under which autobiographies are narrated, as well as the current goals of the self (Conway & Pleydell-Pearce, 2000). Future studies exploring the relationship between autobiographical memory and narrative self-continuity across an array of ages, clinical groups, and task conditions will be of utmost interest in further characterising how episodic and semantic memory give rise to a sense of self across time.

Findings from Chapter 3 and 4 also unveil the temporal shift in the extended self that may occur in response to memory impairment. Namely, patients with AD, experiencing deficits in episodic memory and subjective continuity, retain a degree of narrative continuity for the remote past, supported by semantic memory. For the first time, however, this thesis reveals that some semblance of narrative continuity for recent time periods may also persist in AD.

Despite the specific profiles of external details in AD diverging between Chapters 3 and 4, these patients nonetheless provided an abundance of semantic information, compared with Controls, during autobiographical narration of the recent past in both studies. Typically, a temporal gradient exists for semantic ABM in AD, such that remote facts about the self remain preserved, in the context of impaired recall of personal semantic information for recent epochs (reviewed in Chapter 1). Accordingly, as proposed in Chapter 3, it is possible that the semantic details provided during recent ABM narration in AD are drawn from these patients' early life, with their sense of self for the recent past experienced as markedly similar to their remote self. Unlike previous studies, however, this thesis suggests that the temporal gap between current reality and the preserved, remote self in AD may reflect a continuous form of self-narrative, albeit lacking in growth or change over time. Such observations provide a poignant reflection of the innate human tendency to maintain continuity in one's sense of self, despite the disruptions produced by memory impairment (see also Conway, 2005; Medved & Brockmeier, 2008; Rathbone et al., 2009). On the other hand, the somewhat outdated or 'petrified' nature of the personal narrative in AD may lead to an unawareness of their disease (Mograbi, Brown, & Morris, 2009; Morris & Mograbi, 2013). This 'anosognosia' can negatively impact upon the quality of life of carers of AD patients (Conde-Sala et al., 2016), who find the poor insight challenging to deal with. By contrast, it may have a somewhat protective effect for the mental wellbeing of patients themselves, with increased anosognosia associated with *better* quality of life in AD (Conde-Sala et al., 2016). These findings further highlight the complexity of the relationship between memory and the extended self, and its subsequent manifestation in daily life.

This 'static' self-narrative for the past also appears to also persist into the future in both AD and SD. In Chapter 4, applying the NExt taxonomy, both patient groups were observed to project self-relevant information from their past, into their future life story. The composition of the details comprising these future narratives, however, varied for each patient group compared with Controls. The nature of the external detail profiles, combined with their neurocognitive correlates, suggested AD patients drew upon semantic information to populate their narrative, whereas SD patients harnessed episodic content. As such, the qualitative flavour of the future self likely diverges between these two patient groups. For example, a future self-narrative based upon episodic details from one's recent past, as is the

case in SD, is likely to be more specific and rigid, than the more vague, general future life story drawn from semantic elements in AD. In fact, these contentions are borne out at the behavioural level, in the characteristic inflexibility observed in SD (Kamminga et al., 2014) and vagueness seen in AD (Klimova, Maresova, Valis, Hort, & Kuca, 2015). It is interesting to note, then, that marked anguish in relation to the static future self has been documented in SD (Hsiao et al., 2013). By contrast, a recent meta-analysis revealed associations between a *less* specific future self and higher levels of both major and subclinical depression (Gamble, Moreau, Tippett, & Addis, 2019). Further research is clearly required to clarify how the relative contributions of episodic and semantic memory to future self-narratives affects mental health and wellbeing.

## 7.3. Part 2: The interpersonal self

An individual's moral traits, along with their ability to adopt other's perspectives, enable the adaptive social interactions that give rise to the interpersonal self. The component mechanisms underlying these complex human processes, however, have remained incompletely characterised. Chapters 5 and 6 help to refine our understanding of the interpersonal self, by deconstructing the cognitive and neural underpinnings of morality and perspective taking. While typically considered an exclusively emotional process, Chapter 5 unveils the additional importance of conceptual knowledge for highly conflictual personal moral reasoning, supported by a frontotemporal brain network. Findings from Chapter 6 support a distinction between visual and conceptual (ToM) perspective taking, at both the cognitive and neural level. Despite their dissociation, however, these two forms of perspective taking appear to interact during social interactions in daily life. Taken together, findings from Part 2 of this thesis suggest that the interpersonal self hinges upon a synergy of emotional, conceptual, and visuospatial functions, underpinned by a widespread brain network incorporating DMN, as well as extra-DMN regions, namely medial and lateral prefrontal, parietal, and temporal cortices.

Based on principles from lesion network neuroscience (Boes et al., 2015), impairment to one or more of the brain regions within the neural network uncovered in Part 2 of this thesis is expected to be sufficient to produce a disruption to the interpersonal self. Moreover, as

proposed in Chapters 5 and 6, the level of interpersonal dysfunction is expected to scale with the number of neurocognitive components affected. Indeed, observations in clinical populations support these proposals. For example, individuals with acquired, circumscribed lesions to bilateral amygdalae, despite primary deficits in emotion processing, do not display obvious impairments in social behaviour (Ortega-Escobar, Alcázar-Córcoles, Puente-Rodríguez, & Peñaranda-Ramos, 2017). On the other hand, the developmental disorder of psychopathy is associated with structural and functional abnormalities of the amygdala, but involves additional disruptions to orbitofrontal and ventromedial prefrontal cortex (Blair, 2013). These patients display marked social dysfunction, including disproportionate rates of criminality (Kiehl & Hoffman, 2011). Nonetheless, in some cases, individuals with psychopathy may function somewhat effectively in society (Patrick, Cuthbert, & Lang, 1994). This may be attributable to their preserved social conceptual knowledge (Cima, Tonnaer, & Hauser, 2010), and *ability* to adopt alternative visual perspectives (Drayton et al., 2018), despite a reduced propensity to do so. By contrast, bvFTD patients experience degradation to all of the component processes of the interpersonal self characterised in this thesis, resulting in pervasive impairments in social functioning. The relative contribution and level of importance of each of the fundamental cognitive and neural mechanisms in producing the interpersonal self, however, remains to be uncovered. In fact, it is possible that specific neurobiological processes may be disproportionately implicated. For example, early deposition of pathology in bvFTD is thought to selectively target von Economo neurons, which reside exclusively in the salience network (i.e., ACC and insula) (Seeley, 2008). These neurons are hypothesised to be evolutionarily specialised to allow rapid responses to social situations, including those crucial for the interpersonal self, such as adopting others' perspectives, and making decisions in situations of high conflict/ambiguity (Allman, Watson, Tetreault, & Hakeem, 2005). Studies comparing distinct clinical groups, with varying degrees of socio-cognitive and neural impairment, on a combination of experimental tasks, real-world behavioural measures, and neuroimaging, will be of pivotal importance in exploring these claims.

Further intriguing insights about the nature of the interpersonal self stem from the experimental findings in bvFTD in this thesis. These patients reflect somewhat of a paradox, by which they become increasingly self-centered with the onset of disease, and have difficulty shifting from their own perspective, though in turn, this egocentricity leads to the dysfunction

in social interactions and the subsequent breakdown of the interpersonal self described in Chapter 1. Interpersonal relationships are particularly affected by the egocentricity in bvFTD (Takeda et al., 2019), given this behaviour represents a stark contrast from the individuals' premorbid personality, which is difficult for close others to adjust to (Strohminger & Nichols, 2015; see further in Section 7.4.). According to Neisser's (1988) model of the five selves, the 'ecological self' represents the self as perceived with respect to the physical environment, that is, one's egocentric perspective of the world. As such, the ecological self appears to be heightened in bvFTD (egocentric navigation is also intact, Tu, Spiers, Hodges, Piguet, & Hornberger, 2017), but this comes at the expense of a disrupted interpersonal self. The extent of the difficulties in everyday functioning that occur in bvFTD, however, suggest that the interpersonal, compared with the ecological, aspect of the self may be more important for adaptive functioning in daily life. In fact, the disintegration in the ecological self that occurs during certain psychological states (e.g., meditation, under the influence of psychedelic drugs) often results in an increased feeling of connection to others (i.e., a heightened interpersonal self) (Letheby & Gerrans, 2017; Millière, Carhart-Harris, Roseman, Trautwein, & Berkovich-Ohana, 2018; Nour, Evans, Nutt, & Carhart-Harris, 2016). This perception corresponds to increased whole-brain functional connectivity with the TPJ and insula (Tagliazucchi et al., 2016), key regions implicated in the interpersonal self (Chapters 5 and 6). Most importantly, the extent of dissolution of the ecological self under the psychedelic state strongly correlates with subjective ratings of subsequent improvements in well-being (Nour et al., 2016). As such, it is proposed that a precise balance may need to be struck between the different aspects of the self in order to ensure optimal functioning. While this thesis exclusively focused on extended and interpersonal aspects of the self, further cognitive neuroscientific examination of the other 'selves' proposed by Neisser (1988), and their interactions, is clearly required.

## 7.4. The self

Collectively, this thesis uncovers the multiple distinct cognitive and neural mechanisms that underlie interpersonal and extended aspects of the self. By further breaking down the self into its constituent elements, the current body of work extends our understanding of the building blocks that lay beneath the elusive construct of the self. Despite this demonstrated

ability to deconstruct the self, however, in reality the self is experienced as a coherent and continuous whole. Extensive philosophical debate has ensued regarding how the separate components of the self are perceived as a unified entity. The 'pattern theory' of self holds that a number of discrete features together give rise to the self, though on their own do not constitute a self (S. Gallagher, 2013). This theory is likened to the underpinnings of emotion, whereby distinct components such as autonomic processes, expressions, cognitions, and situational aspects are not themselves sufficient, but in combination produce an emotion (S. Gallagher, 2013). Extending this theory, in this thesis the patterns underlying the self, and their cognitive and neural nature, are further characterised. What is it then, that holds these disparate elements together? Clues may be drawn from the field of etymology, with the word 'self' stemming from the Old Gothic word for 'I' and the Anglo-Saxon word for 'same' (Levin, 1992). In other words, it is the *same* I who remembers the past and imagines the future, and behaves a certain way across social situations, with this consistency across time and place proposed to represent the glue that binds the self (see also Conway, Singer, & Tagini, 2004). If this consistency is able to be maintained, even in the face of impairment to its neurocognitive underpinnings, some persistence of the self is expected. For example, in AD and SD, despite the alterations to the component processes underlying the extended self revealed in Chapters 3 and 4, these patients nonetheless seem to retain relative consistency in their self-narrative across time. By contrast, as documented in Chapters 5 and 6, the interpersonal self in bvFTD undergoes marked changes when compared with previous social behaviour in these individuals. It is precisely this departure from the patients' premorbid personality that leads to such profound distress in close others and results in the deterioration of interpersonal relationships (Strohminger & Nichols, 2015). The lack of consistency in the self in bvFTD therefore seems to result in much more severe disruptions to daily functioning, compared with the other syndromes.

While considered separately in this thesis, the extended and interpersonal aspects of the self are inherently intertwined. For example, ABM has an important social function, enabling the building of intimacy and trust within relationships, and the display of empathy (Alea & Bluck, 2003). Indeed, memories of personal experiences and facts about the self contribute to moral decision making (Casebeer & Churchland, 2003), inference of others' mental states (Duclos, Desgranges, Eustache, & Laisney, 2018), empathic responding (Ciaramelli, Bernardi, &

Moscovitch, 2013), and prosocial behaviour (Gaesser & Schacter, 2014). Furthermore, patients with episodic amnesia display alterations in moral reasoning (McCormick et al., 2016) (but see Craver et al., 2016), empathy (Beadle, Tranel, Cohen, & Duff, 2013), and social judgment (Staniloiu, Borsutzky, Woermann, & Markowitsch, 2013), along with difficulty establishing and maintaining social relationships (Davidson, Drouin, Kwan, Moscovitch, & Rosenbaum, 2012). Finally, a relationship between impairments in ABM and ToM have also been uncovered in individuals with schizophrenia (Corcoran & Frith, 2003) and autism (Adler, Nadler, Eviatar, & Shamay-Tsoory, 2010). The relationship between the extended and interpersonal selves, however, is not unidirectional, with social processes also affecting memory. In particular, moral traits and memories of moral actions are central to the construction of one's autobiographical narrative (Stanley, Henne, & De Brigard, 2019; Stanley, Henne, Iyengar, Sinnott-Armstrong, & De Brigard, 2017). Remembering the past and imagining the future also often involves VPT, with approximately one-third of episodic ABMs spontaneously recalled from a third-person (i.e., observer) rather than first-person (i.e., field) perspective (Nigro & Neisser, 1983). These egocentric and allocentric reference frames employed during recollection and imagination overlap with those applied to social situations, when representing the perspective of self and others (Arzy & Schacter, 2019). Perspective-taking is further involved in establishing a self-narrative, with accurate representation of one's personality traits requiring the 'seeing' of one's own social behaviour through the eyes of others (Ruby et al., 2009; Ruby et al., 2007). Despite this established overlap between extended and interpersonal aspects of the self, few studies have comprehensively examined these functions, and their interactions, within the same sample of participants: which represents an essential direction for future research. Experimental paradigms combining these two aspects, such as generating (past/future) personal events involving moral transgressions (e.g., Stanley et al., 2017), or relating to other people versus oneself (e.g., Bertossi, Tesini, Cappelli, & Ciaramelli, 2016), may also be of interest in this regard.

Nonetheless, considering the syndromes of AD, SD, and bvFTD provides preliminary insights into the relationship between the interpersonal and extended selves. First, observations in AD and SD hint at a role for personal semantic memory in supporting interpersonal functions. Namely, patients with AD, in which the extended self appears to be largely supported by semantic processes (see Chapters 3 and 4), are widely reported to maintain appropriate social

functioning, at least in the mild-to-moderate stages of the disease. In particular, social graces, interpersonal warmth, and the ability to form and maintain interpersonal relationships remain intact in AD (Rankin, Kramer, Mychack, & Miller, 2003; Sabat & Gladstone, 2010; Sabat & Lee, 2011), along with empathic concern and behaviour (Dermody et al., 2016). In fact, preliminary evidence suggests that socio-emotional sensitivity and empathy may even be *enhanced* with the onset of AD (Sturm et al., 2013; Zhou et al., 2010). By contrast, in SD, where the extended self relies upon recent episodic experiences, patients can exhibit similar social behavioural disturbances to those seen bvFTD (Hodges & Patterson, 2007), albeit to a milder degree, corresponding to the encroachment of atrophy into right frontotemporal regions (Irish, Hodges, et al., 2014). This includes deficits in ToM (Duval, Bejanin, et al., 2012; Irish, Hodges, et al., 2014) and empathy (Rankin et al., 2006; Rankin, Kramer, & Miller, 2005), along with increased egocentric behaviour manifesting in a failure to consider others' perspectives (Bon et al., 2009). Few studies, however, have directly examined the contribution of personal semantic memory to the interpersonal self. On the other hand, patients with bvFTD, presenting with severe disruptions to multiple components of the interpersonal self (characterised in Chapters 5 and 6), additionally appear to experience pervasive impairments in both subjective (Bastin et al., 2011; Irish, Hodges, & Piguet, 2013; Irish, Hornberger, et al., 2011) and narrative (Irish et al., 2013; Thomas-Anterion, Jacquin, & Laurent, 2000) aspects of self-continuity. Such alterations to the extended self in bvFTD, though, are attributed as *secondary* to the social dysfunction and alterations in personality and behaviour that define the interpersonal self (Irish, Piguet, & Hodges, 2012; Wong et al., 2017). Empirical studies examining the directionality of the association between extended and interpersonal aspects of the self will therefore be of critical interest. Given neurodegenerative populations may also experience alterations to the other 'selves' defined by Neisser (i.e., the ecological, private, and conceptual self) (see Seeley & Miller, 2005), exploring these additional aspects of the self, and their interactions, represents another important future research direction.

As outlined in Chapter 1, at a neural level, the experience of the 'self' has primarily been attributed to the DMN. This spatially-distributed brain network is anchored on cortical midline regions (i.e., mPFC and PCC), believed particularly crucial for self-referential processing (Northoff & Bermpohl, 2004), though also incorporates medial and lateral temporal and parietal structures. It is interesting to note, therefore, that the mPFC emerged as the sole

common neural correlate of the extended and interpersonal self across all studies in this thesis (Chapters 4-6). In addition, however, a widespread neural network beyond the mPFC was also implicated, which included regions both common and unique to the extended and interpersonal self (Figure 7.1.). Namely, components of the DMN including medial and lateral parietal cortices were associated with both aspects of the self (Chapters 4 and 6), with medial and lateral temporal regions correlating exclusively with moral reasoning performance (Chapter 5). Surprisingly, though, regions beyond the DMN were implicated in both the extended and interpersonal self, including lateral prefrontal cortices typically considered part of the frontoparietal or 'executive control' network (Menon, 2011). As such, evidence from this thesis suggests that the self is not necessarily specific to the mPFC or DMN. It is interestingly to note that the DMN and frontoparietal networks represent the most phylogenetically recent regions within the human brain (Hill et al., 2010; Vendetti & Bunge, 2014). This is of particular relevance given the uniquely human nature of the self, specifically its extended and interpersonal components (MacLean, 2016; Suddendorf & Busby, 2003) (but see Fabbro, Aglioti, Bergamasco, Clarici, & Panksepp, 2015; Hills & Butterfill, 2015). Further studies of comparative psychology and neurobiology will help to clarify whether the emergence of a sense of self in human evolution may have been the product of the concurrent development of the multiple, higher-level neurocognitive processes characterised in this thesis.

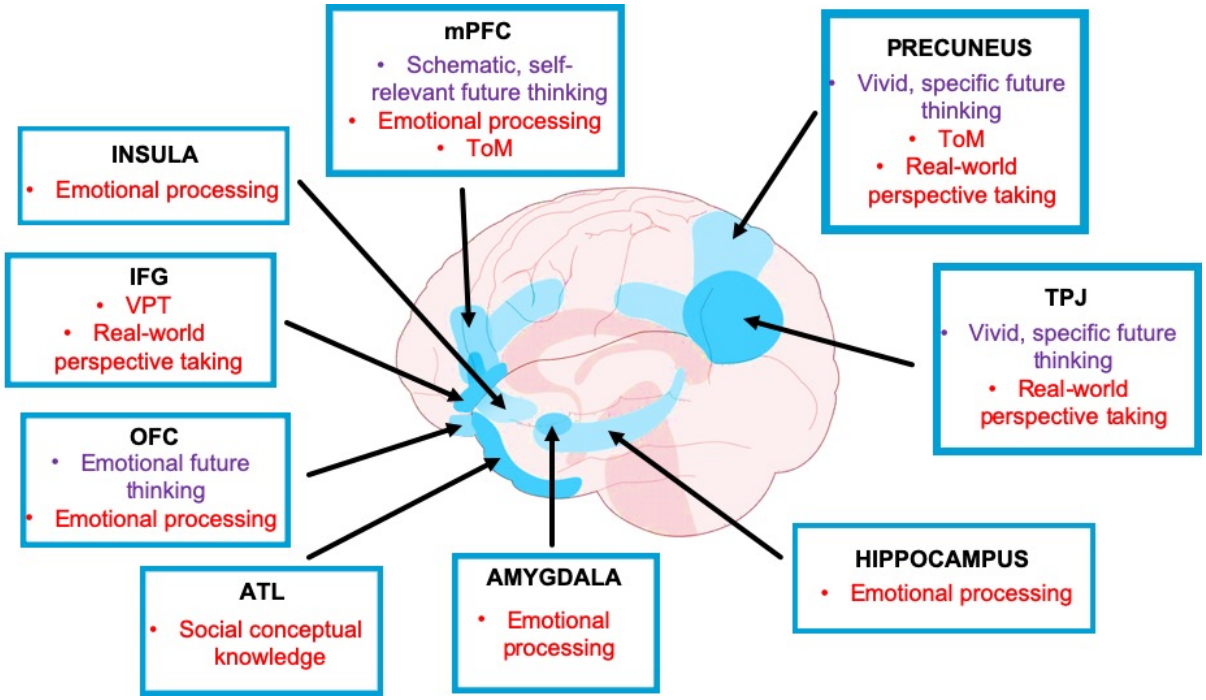



*Figure 7.1.* Brain regions associated with the extended (purple) and interpersonal (red) aspects of the self in this thesis. This is not intended to represent an exhaustive neurocognitive model of the self, rather, it encompasses those aspects that were examined in this thesis (i.e., moral reasoning, perspective taking, and future narrative self-continuity). ATL = anterior temporal lobe; IFG = inferior frontal gyrus; mPFC = medial prefrontal cortex; OFC = orbitofrontal cortex; ToM = theory of mind; TPJ = temporoparietal junction; VPT = visual perspective taking.

## 7.5. Clinical implications

In addition to extending the theoretical characterisation of the self, this thesis has a number of significant clinical implications. By highlighting the dynamic and multifaceted nature in which the self may change with the onset of different forms of dementia, these findings have important ramifications for person-centered care. Notably, in contrast to a prevailing view in the field (as noted by Feast et al., 2016), this thesis reveals how the self is not entirely lost in dementia. Rather, by leveraging those cognitive and neural functions which remain relatively preserved, patients with AD and SD may maintain some sense of self-continuity, albeit temporally shifted. Understanding the self-experience of these patients can inform personalised management strategies. For example, environments may be modified and

communication tailored to support the individual's current sense of self, such as encouraging the enacting of roles from remote lifetime periods in AD (e.g., a previous nurse helping out in the nursing home, interactions with young children), and the provision of regular routines in SD (e.g., allowing repetition of recently performed activities for which they have preserved recollection). Furthermore, as outlined in Section 7.3., despite demonstrating impairments across all constituent elements of the interpersonal self, bvFTD patients nonetheless appear to retain some ecological sense of self, manifesting as a heightened representation of their own egocentric perspective of the world. This observation, combined with the established impairments in mentally-projecting oneself beyond the here-and-now in bvFTD (see Section 7.4. and O'Callaghan, Shine, Hodges, Andrews-Hanna, & Irish, 2019), suggests that interactions with these patients may be most successful if focused on the immediately perceived environment. While such a reorienting of attention towards preserved, rather than impaired, function in neurological patients is not new (Caddell & Clare, 2011; Clark & Maguire, 2016; Midorikawa et al., 2016; B. L. Miller & Hou, 2004), this thesis is the first to offer a comprehensive breakdown of the specific elements of the extended and interpersonal self that are affected versus intact in different dementia syndromes, with the aim to improve functioning and quality of life in these individuals.

## 7.6. Methodological considerations

Collectively, this thesis emphasises the utility of cognitive neuroscience in refining the understanding of philosophical constructs. Several methodological issues regarding this approach, however, warrant consideration.

In Chapters 3 and 4, external details on the Autobiographical Interview (AI) and Past-Future task are employed as a measure of narrative continuity. These details are held to represent the contextual, background information that is integral to one's life story. The AI and Past-Future task are extremely popular tools for examining ABM and episodic future thinking, though unfortunately a large portion of the data collected with these measures (i.e., the external details) is often discarded or inaccurately interpreted (see Chapter 3). As such, the NExt taxonomy provides a resourceful means of harnessing existing data in order to provide relevant insights into narrative self-continuity. As mentioned in Chapter 4, however, the

differential methodology (i.e., cues, probing, and number of events) of the AI and Past-Future task may affect the composition of information within the narratives provided, limiting comparability between the tasks. Furthermore, it should be noted that these tasks directly probe for an account of a specific episode, rather than requesting a description of one's life story, which has the potential to bias the nature of the subsequent details elicited. Interestingly, however, in healthy older adults the nature of the information provided within descriptions of unique events on the AI is largely similar to that provided when participants are explicitly asked to narrate their life story (Acevedo-Molina et al., 2019). Further studies comparing the full spectrum of episodic to semantic information provided during these two types of autobiographical narration (using the NExt taxonomy), across various populations, will aid in confirming the utility of AI external details as a measure of narrative continuity.

Like the majority of psychological research, existing studies of the extended and interpersonal self, including the current thesis, have predominantly been conducted in Western, educated, industrialised, rich, and democratic (i.e., WEIRD) societies, who only represent approximately 12% of the world's population (Henrich, Heine, & Norenzayan, 2010). Such findings regarding the cognitive and neurobiological underpinnings of the self, therefore, are not necessarily generalisable to humankind as a whole. For example, the importance of specific episodic memories for supporting the extended self appears to be unique to Western cultures, with such detailed remembering of one's own experiences seen as incongruent with Asian societal norms that emphasise a collective, rather than unique, identity (Markus & Kitayama, 1991). In fact, highly specific, episodic remembering has been associated with *negative* mental health and wellbeing in Chinese individuals (Wang, Hou, Koh, Song, & Yang, 2018). In this culture, personal semantic facts including general events, that convey social routines and schemas, may be more important for supporting the extended self (Wang et al., 2018). Similar cultural differences are also evident in the mechanisms underlying the interpersonal self. While morality is often assumed to represent an innate and universal human capacity (Fleischacker, 1997), emerging evidence points to significant variation in the cognitive processes employed, and even brain regions involved, in moral decision making across cultures (reviewed in Sachdeva, Singh, & Medin, 2011). The crucial role of social norms in moral reasoning revealed in Chapter 5 further supports this notion, in that moral decisions are likely largely influenced by the behaviours considered socially acceptable in one's own

society. Intriguingly, distinct neural correlates of perspective taking have also emerged across cultures, with distinct recruitment of IFG and TPJ during ToM in American versus Japanese individuals (Kobayashi, Glover, & Temple, 2007). Evidently, cross-cultural studies will be vital for accurately characterising the nature of the self across our entire species.

As a final remark, consistent with the majority of studies in cognitive neuroscience, the psychological tests employed in this thesis relied upon self-reports, via either detailed descriptions or simple multiple-choice responses. Accordingly, these measures inherently require some access to one's subjective consciousness (Caddell & Clare, 2013). Directly testing whether patients with dementia indeed retain the ability to reliably report their personal mental experience, however, is an extremely difficult endeavour (Caddell & Clare, 2013). As discussed in Chapter 1, therefore, it is important to draw upon observable manifestations of the self (i.e., patient behaviour) as convergent evidence for the findings from cognitive neuroscience measures. In addition to anecdotal reports and carer questionnaires, though, borrowing tools from the fields of evolutionary, comparative, and developmental psychology may also prove useful in capturing behavioural expressions of the self. For example, the classic 'mirror mark test' is often used in children and animals to ascertain the presence of a 'self' (Gallup Jr, Anderson, & Shillito, 2002). In this test, unbeknownst to the participant, a mark is placed on the individual's forehead. The participant is then presented with a mirror, with touching of the mark interpreted as reflecting an intact sense of self. Such self-recognition, however, only represents the presence of an 'ecological' or 'physical' self (Neisser, 1988). By contrast, a lesser-used extension of this task, involving delayed video feedback, provides a behavioural measure of the extended self (Povinelli, Landau, & Perilloux, 1996). This time, the placing of the mark on the forehead is filmed, with participants later watching the footage. Touching of the mark during viewing of the video is therefore interpreted as recognition of one's past self, reflecting preserved self-continuity. As such, the video mark test may be employed to objectively characterise the extended self in cognitively impaired populations, in which self-report measures are not appropriate. Such cross-disciplinary collaborations represent an exciting opportunity to bring us closer to an exhaustive model of how a sense of self is produced.

## 7.7. Conclusions

By integrating philosophy, cognitive neuroscience, and clinical lesion populations, this thesis offers novel insights into the cognitive and neural mechanisms underlying the extended and interpersonal aspects of the self. These findings highlight the importance of both episodic and semantic memory for supporting a sense of self-continuity. Indeed, the relative contribution of these forms of memory to the extended self may scale dependent upon the integrity of its counterpart, the lifetime period in question, as well as the task demands and current goals of the self. Further, multiple neurocognitive processes underpinning the interpersonal self are uncovered, including emotional, conceptual, and visuospatial functions, supported by frontal, parietal, and temporal brain regions. Finally, at a clinical level, distinct profiles of the self across AD, SD, and bvFTD reveal how 'all is not lost' in neurodegeneration. Together, this thesis highlights the complex and multifaced nature of the self, ultimately advancing our understanding of what it means to be human.

# References


Acevedo-Molina, M. C., Matijevic, S., & Grilli, M. D. (2019). Beyond episodic remembering: elaborative retrieval of lifetime periods in young and older adults. *Memory*, 1-11. doi:10.1080/09658211.2019.1686152

Addis, D. R., McIntosh, A. R., Moscovitch, M., Crawley, A. P., & McAndrews, M. P. (2004). Characterizing spatial and temporal features of autobiographical memory retrieval networks: a partial least squares approach. *Neuroimage, 23*(4), 1460-1471. doi:10.1016/j.neuroimage.2004.08.007

Addis, D. R., Moscovitch, M., Crawley, A. P., & McAndrews, M. P. (2004). Recollective qualities modulate hippocampal activation during autobiographical memory retrieval. *Hippocampus, 14*(6), 752-762. doi:10.1002/hipo.10215

Addis, D. R., Moscovitch, M., & McAndrews, M. P. (2007). Consequences of hippocampal damage across the autobiographical memory network in left temporal lobe epilepsy. *Brain, 130*(Pt 9), 2327-2342. doi:10.1093/brain/awm166

Addis, D. R., Sacchetti, D. C., Ally, B. A., Budson, A. E., & Schacter, D. L. (2009). Episodic simulation of future events is impaired in mild Alzheimer's disease. *Neuropsychologia, 47*(12), 2660-2671. doi:10.1016/j.neuropsychologia.2009.05.018

Addis, D. R., & Schacter, D. L. (2008). Constructive episodic simulation: temporal distance and detail of past and future events modulate hippocampal engagement. *Hippocampus, 18*(2), 227-237. doi:10.1002/hipo.20405

Addis, D. R., & Tippett, L. (2004). Memory of myself: Autobiographical memory and identity in Alzheimer's disease. *Memory, 12*(1), 56-74. doi:10.1080/09658210244000423

Addis, D. R., & Tippett, L. J. (2008). The contributions of autobiographical memory to the content and continuity of identity: A social-cognitive neuroscience approach *Self continuity: Individual and collective perspectives.* (pp. 71-84). New York, NY, US: Psychology Press.

Addis, D. R., Wong, A. T., & Schacter, D. L. (2007). Remembering the past and imagining the future: Common and distinct neural substrates during event construction and elaboration. *Neuropsychologia, 45*(7), 1363-1377. doi:10.1016/j.neuropsychologia.2006.10.016

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. doi:10.1111/j.1467-9280.2008.02043.x

Adenzato, M., Cavallo, M., & Enrici, I. (2010). Theory of mind ability in the behavioural variant of frontotemporal dementia: an analysis of the neural, cognitive, and social levels. *Neuropsychologia, 48*(1), 2-12. doi:10.1016/j.neuropsychologia.2009.08.001

Adler, N., Nadler, B., Eviatar, Z., & Shamay-Tsoory, S. G. (2010). The relationship between theory of mind and autobiographical memory in high-functioning autism and Asperger syndrome. *Psychiatry Research, 178*(1), 214-216. doi:10.1016/j.psychres.2009.11.015

Adnan, A., Barnett, A., Moayedi, M., McCormick, C., Cohn, M., & McAndrews, M. P. (2016). Distinct hippocampal functional networks revealed by tractography-based parcellation. *Brain Structure and Function, 221*(6), 2999-3012. doi: 10.1007/s00429-015-1084-x

Adolphs, R. (1999). Social cognition and the human brain. *Trends in Cognitive Sciences, 3*(12), 469-479. doi:10.1016/S1364-6613(99)01399-6

Ahmed, R. M., Irish, M., Kam, J., van Keizerswaard, J., Bartley, L., Samaras, K., . . . Piguet, O. (2014). Quantifying the eating abnormalities in frontotemporal dementia. *JAMA Neurol, 71*(12), 1540-1546. doi:10.1001/jamaneurol.2014.1931

Aichhorn, M., Perner, J., Kronbichler, M., Staffen, W., & Ladurner, G. (2006). Do visual perspective tasks need theory of mind? *Neuroimage, 30*(3), 1059-1068. doi:10.1016/j.neuroimage.2005.10.026

Aizpurua, A., & Koutstaal, W. (2010). Autobiographical Memory and Flexible Remembering-Gender-Differences. *International Journal of Social, Behavioral, Educational, Economic, Business and Industrial Engineering, 4*(6), 1534-1540.

Aizpurua, A., & Koutstaal, W. (2015). A matter of focus: Detailed memory in the intentional autobiographical recall of older and younger adults. *Consciousness and Cognition, 33*, 145-155. doi:10.1016/j.concog.2014.12.006

Alea, N., & Bluck, S. (2003). Why are you telling me that? A conceptual model of the social function of autobiographical memory. *Memory, 11*(2), 165-178. doi:10.1080/741938207

Allison, T., Puce, A., & McCarthy, G. (2000). Social perception from visual cues: role of the STS region. *Trends in Cognitive Sciences, 4*(7), 267-278. doi:10.1016/S1364-6613(00)01501-1

Allman, J. M., Watson, K. K., Tetreault, N. A., & Hakeem, A. Y. (2005). Intuition and autism: a possible role for Von Economo neurons. *Trends in Cognitive Sciences, 9*(8), 367-373. doi:10.1016/j.tics.2005.06.008

Ally, B. A., Hussey, E. P., & Donahue, M. J. (2013). A case of hyperthymesia: rethinking the role of the amygdala in autobiographical memory. *Neurocase, 19*(2), 166-181. doi:10.1080/13554794.2011.654225

Andersson, J. L. R., Jenkinson, M., & Smith, S. (2007). Non-linear registration aka Spatial normalisation FMRIB Technial Report TR07JA2. *FMRIB Analysis Group of the University of Oxford*.

Andrews-Hanna, J. R. (2012). The brain's default network and its adaptive role in internal mentation. *Neuroscientist, 18*(3), 251-270. doi:10.1177/1073858411403316

Andrews-Hanna, J. R., Reidler, J. S., Huang, C., & Buckner, R. L. (2010). Evidence for the default network's role in spontaneous cognition. *J Neurophysiol, 104*(1), 322-335. doi:10.1152/jn.00830.2009

Andrews-Hanna, J. R., Reidler, J. S., Sepulcre, J., Poulin, R., & Buckner, R. L. (2010). Functional-anatomic fractionation of the brain's default network. *Neuron, 65*(4), 550-562. doi:10.1016/j.neuron.2010.02.005

Arzy, S., & Schacter, D. L. (2019). Self-Agency and Self-Ownership in Cognitive Mapping. *Trends in Cognitive Sciences, 23*(6), 476-487. doi:10.1016/j.tics.2019.04.003

Ashburner, J., & Friston, K. J. (2000). Voxel-based morphometry - the methods. *Neuroimage, 11*(6), 805-821. doi:10.1006/nimg.2000.0582

Barnabe, A., Whitehead, V., Pilon, R., Arsenault-Lapierre, G., & Chertkow, H. (2012). Autobiographical memory in mild cognitive impairment and Alzheimer's disease: A comparison between the Levine and Kopelman interview methodologies. *Hippocampus, 22*(9), 1809-1825. doi:10.1002/hipo.22015

Barnier, A. J., Priddis, A. C., Broekhuijse, J. M., Harris, C. B., Cox, R. E., Addis, D. R., . . . Congleton, A. R. (2014). Reaping what they sow: Benefits of remembering together in intimate couples. *Journal of Applied Research in Memory and Cognition, 3*(4), 261-265. doi:10.1016/j.jarmac.2014.06.003

Baron, J. M., & Bluck, S. (2009). Autobiographical memory sharing in everyday life: Characteristics of a good story. *International Journal of Behavioral Development, 33*(2), 105-117. doi:10.1177/0165025408098039

Baron-Cohen, S. (1995). *Mindblindness: An essay on autism and theory of mind.* Cambridge: MIT Press.

Barsalou, L. W. (1988). The content and organisation of autobiographical memories. In U. Neisser & E. Winograd (Eds.), *Remembering reconsidered: Ecological and traditional approaches to the study of memory.* (pp. 193-243). New York: Cambridge University Press.

Barsuglia, J. P., Nedjat-Haiem, F. R., Shapira, J. S., Velasco, C., Jimenez, E. E., Mather, M. J., & Mendez, M. F. (2014). Observational themes of social behavioral disturbances in frontotemporal dementia. *International psychogeriatrics, 26*(9), 1475-1481. doi:10.1017/S104161021400091X

Bastin, C., Feyers, D., Jedidi, H., Bahri, M. A., Degueldre, C., Lemaire, C., . . . Salmon, E. (2013). Episodic autobiographical memory in amnestic mild cognitive impairment: what are the neural correlates? *Human Brain Mapping, 34*(8), 1811-1825. doi:10.1002/hbm.22032

Bastin, C., Feyers, D., Souchay, C., Guillaume, B., Pepin, J. L., Lemaire, C., . . . Salmon, E. (2011). Frontal and posterior cingulate metabolic impairment in the behavioral variant of frontotemporal dementia with impaired autonoetic consciousness. *Human Brain Mapping*. doi:10.1002/hbm.21282

Bayley, P. J., Hopkins, R. O., & Squire, L. R. (2003). Successful Recollection of Remote Autobiographical Memories by Amnesic Patients with Medial Temporal Lobe Lesions. *Neuron, 38*, 135-144.

Beadle, J., Tranel, D., Cohen, N., & Duff, M. (2013). Empathy in Hippocampal Amnesia. *Frontiers in Psychology, 4*(69). doi:10.3389/fpsyg.2013.00069

Belfi, A. M., Karlan, B., & Tranel, D. (2016). Music evokes vivid autobiographical memories. *Memory, 24*(7), 979-989. doi:10.1080/09658211.2015.1061012

Benjamin, M. J., Cifelli, A., Garrard, P., Caine, D., & Jones, F. W. (2015). The role of working memory and verbal fluency in autobiographical memory in early Alzheimer's disease and matched controls. *Neuropsychologia, 78*, 115-121. doi:10.1016/j.neuropsychologia.2015.10.006

Berntsen, D., & Bohn, A. (2010). Remembering and forecasting: The relation between autobiographical memory and episodic future thinking. *Mem Cognit, 38*(3), 265.

Berryhill, M. E., Phuong, L., Picasso, L., Cabeza, R., & Olson, I. R. (2007). Parietal lobe and episodic memory: bilateral damage causes impaired free recall of autobiographical memory. *Journal of Neuroscience, 27*(52), 14415-14423. doi:10.1523/JNEUROSCI.4163-07.2007

Bertossi, E., Tesini, C., Cappelli, A., & Ciaramelli, E. (2016). Ventromedial prefrontal damage causes a pervasive impairment of episodic memory and future thinking. *Neuropsychologia*. doi:10.1016/j.neuropsychologia.2016.01.034

Bertoux, M., O'Callaghan, C., Dubois, B., & Hornberger, M. (2015). In two minds: executive functioning versus theory of mind in behavioural variant frontotemporal dementia. *Journal of Neurology, Neurosurgery, and Psychiatry*. doi:10.1136/jnnp-2015-311643

Binder, J. R., Desai, R. H., Graves, W. W., & Conant, L. L. (2009). Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies. *Cerebral Cortex, 19*(12), 2767-2796. doi:10.1093/cercor/bhp055

Binetti, G., Locascio, J. J., Corkin, S., Vonsattel, J. P., & Growdon, J. H. (2000). Differences Between Pick Disease and Alzheimer Disease in Clinical Appearance and Rate of Cognitive Decline. *JAMA Neurol, 57*(2), 225-232. doi:10.1001/archneur.57.2.225

Biringer, F., & Anderson, J. R. (1992). Self-recognition in Alzheimer's Disease: A Mirror and Video Study. *Journal of Gerontology, 47*(6), P385-P388. doi:10.1093/geronj/47.6.P385

Blair, R. J. R. (2013). Psychopathy: cognitive and neural dysfunction. *Dialogues in clinical neuroscience, 15*(2), 181-190.

Boes, A. D., Prasad, S., Liu, H., Liu, Q., Pascual-Leone, A., Caviness, V. S., Jr, & Fox, M. D. (2015). Network localization of neurological symptoms from focal brain lesions. *Brain, 138*(10), 3061-3075. doi:10.1093/brain/awv228

Bon, L., Belliard, S., Eustache, F., & Desgranges, B. (2009). Behavioural egocentrism in semantic dementia: Effect of deficits in theory of mind or cognitive egocentrism? *Revue de Neuropsychologie, 1*, 133-149. doi:10.1684/nrp.2009.0020

Bond, T. G., & Fox, C. M. (2007). *Applying the Rasch model: Fundamental measurement in the human sciences (2 ed.)*. Mahwah, NJ, US: Lawrence Erlbaum Associates Publishers.

Borke, H. (1975). Piaget's mountains revisited: Changes in the egocentric landscape. *Developmental Psychology, 11*(2), 240. doi:10.1037/h0076459

Braak, H., & Braak, E. (1991). Neuropathological stageing of Alzheimer-related changes. *Acta Neuropathol, 82*, 239-249. doi:10.1007/bf00308809

Bressler, S. L., & Menon, V. (2010). Large-scale brain networks in cognition: emerging methods and principles. *Trends in Cognitive Sciences, 14*(6), 277-290. doi:10.1016/j.tics.2010.04.004

Bright, P., & Kopelman, M. (2004). Remote memory in Alzheimer's disease. *Cognitive neuropsychology of Alzheimer's disease, 2*, 141-151.

Brioschi Guevara, A., Knutson, K. M., Wassermann, E. M., Pulaski, S., Grafman, J., & Krueger, F. (2015). Theory of mind impairment in patients with behavioural variant fronto-temporal dementia (bv-FTD) increases caregiver burden. *Age Ageing, 44*(5), 891-895. doi:10.1093/ageing/afv059

Brown, L., Hansnata, E., & La, H. A. (2016). Economic cost of dementia in Australia 2016–2056. *NATSEM at the Institute for Governance and Policy Analysis, University of Canberra, and Alzheimer's Australia*.

Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain's default network: anatomy, function, and relevance to disease. *Annals of the New York Academy of Science, 1124*, 1-38. doi:10.1196/annals.1440.011

Buckner, R. L., & Carroll, D. C. (2007). Self-projection and the brain. *Trends in Cognitive Sciences, 11*(2), 49-57. doi:10.1016/j.tics.2006.11.004

Buckner, R. L., & DiNicola, L. M. (2019). The brain's default network: updated anatomy, physiology and evolving insights. *Nature Reviews Neuroscience*. doi:10.1038/s41583-019-0212-7

Buckner, R. L., Snyder, A. Z., Shannon, B. J., LaRossa, G., Sachs, R., Fotenos, A. F., . . . Mintun, M. A. (2005). Molecular, structural, and functional characterization of Alzheimer's disease: evidence for a relationship between default activity, amyloid, and memory. *Journal of Neuroscience, 25*(34), 7709-7717. doi:10.1523/JNEUROSCI.2177-05.2005

Burgess, P. W., & Shallice, T. (1997). *The Hayling and Brixton Tests*. Thurston Suffolk: Thames Valley Test Company.

Burianová, H., & Grady, C. L. (2007). Common and unique neural activations in autobiographical, episodic, and semantic retrieval. *Journal of Cognitive Neuroscience, 19*(9), 1520-1534. doi:10.1162/jocn.2007.19.9.1520

Cabeza, R., Ciaramelli, E., Olson, I. R., & Moscovitch, M. (2008). The parietal cortex and episodic memory: an attentional account. *Nature Reviews Neuroscience, 9*(8), 613-625. doi:10.1038/nrn2459

Caddell, L. S., & Clare, L. (2010). The impact of dementia on self and identity: A systematic review. *Clinical Psychology Review, 30*(1), 113-126. doi:10.1016/j.cpr.2009.10.003

Caddell, L. S., & Clare, L. (2011). Interventions supporting self and identity in people with dementia: A systematic review. *Aging & Mental Health, 15*(7), 797-810. doi:10.1080/13607863.2011.575352

Caddell, L. S., & Clare, L. (2013). Studying the self in people with dementia: How might we proceed? *Dementia, 12*(2), 192-209. doi:10.1177/1471301211418486

Caminiti, S. P., Canessa, N., Cerami, C., Dodich, A., Crespi, C., Iannaccone, S., . . . Cappa, S. F. (2015). Affective mentalizing and brain activity at rest in the behavioral variant of frontotemporal dementia. *Neuroimage Clinical, 9*, 484-497. doi:10.1016/j.nicl.2015.08.012

Campbell, J., Nadel, L., Duke, D., & Ryan, L. (2011). Remembering all that and then some: recollection of autobiographical memories after a 1-year delay. *Memory, 19*(4), 406-415. doi:10.1080/09658211.2011.578073

Carr, A. R., Paholpak, P., Daianu, M., Fong, S. S., Mather, M., Jimenez, E. E., . . . Mendez, M. F. (2015). An investigation of care-based vs. rule-based morality in frontotemporal dementia, Alzheimer's disease, and healthy controls. *Neuropsychologia, 78*, 73-79. doi:10.1016/j.neuropsychologia.2015.09.033

Casebeer, W. D., & Churchland, P. S. (2003). The Neural Mechanisms of Moral Cognition: A Multiple-Aspect Approach to Moral Judgment and Decision-Making. *Biology and Philosophy, 18*(1), 169-194. doi:10.1023/a:1023380907603

Cavanna, A. E., & Trimble, M. R. (2006). The precuneus: a review of its functional anatomy and behavioural correlates. *Brain, 129*(Pt 3), 564-583. doi:10.1093/brain/awl004

Cerami, C., Dodich, A., Canessa, N., Crespi, C., Marcone, A., Cortese, F., . . . Cappa, S. F. (2014). Neural correlates of empathic impairment in the behavioral variant of frontotemporal dementia. *Alzheimers Dementia, 10*(6), 827-834. doi:10.1016/j.jalz.2014.01.005

Chandler, M. J., Lalonde, C. E., Sokol, B. W., & Hallett, D. (2003). Personal persistence, identity development, and suicide: A study of Native and Non-native North American adolescents. *Monographs of the Society for Research in Child Development, 68*(2), vii-viii. doi:10.1111/j.1540-5834.2003.00246.x

Chapleau, M., Aldebert, J., Montembeault, M., & Brambati, S. M. (2016). Atrophy in Alzheimer's disease and semantic dementia: an ALE meta-analysis of voxel-based morphometry studies. *Journal of Alzheimer's disease, 54*(3), 941-955. doi:10.3233/JAD-160382

Chare, L., Hodges, J. R., Leyton, C. E., McGinley, C., Tan, R. H., Kril, J. J., & Halliday, G. M. (2014). New criteria for frontotemporal dementia syndromes: clinical and pathological diagnostic implications. *Journal of Neurology, Neurosurgery and Psychiatry, 85*(8), 865-870. doi:10.1136/jnnp-2013-306948

Chessell, Z. J., Rathbone, C. J., Souchay, C., Charlesworth, L., & Moulin, C. J. A. (2014). Autobiographical Memory, Past and Future Events, and Self-images in Younger and Older Adults. *Self and Identity, 13*(4), 380-397. doi:10.1080/15298868.2013.836132

Chiong, W., Wilson, S. M., D'Esposito, M., Kayser, A. S., Grossman, S. N., Poorzand, P., . . . Rankin, K. P. (2013). The salience network causally influences default mode network activity during moral reasoning. *Brain, 136*(Pt 6), 1929-1941. doi:10.1093/brain/awt066

Christensen, J. F., & Gomila, A. (2012). Moral dilemmas in cognitive neuroscience of moral decision-making: A principled review. *Neuroscience & Biobehavioral Reviews, 36*(4), 1249-1264. doi:10.1016/j.neubiorev.2012.02.008

Ciaramelli, E., Bernardi, F., & Moscovitch, M. (2013). Individualized Theory of Mind (iToM): When Memory Modulates Empathy. *Frontiers in Psychology, 4*, 4. doi:10.3389/fpsyg.2013.00004

Ciaramelli, E., Muccioli, M., Làdavas, E., & di Pellegrino, G. (2007). Selective deficit in personal moral judgment following damage to ventromedial prefrontal cortex. *Social Cognitive and Affective Neuroscience, 2*(2), 84-92. doi:10.1093/scan/nsm001

Cima, M., Tonnaer, F., & Hauser, M. D. (2010). Psychopaths know right from wrong but don't care. *Social Cognitive and Affective Neuroscience, 5*(1), 59-67. doi:10.1093/scan/nsp051

Clare, L., Whitaker, C. J., Nelis, S. M., Martyr, A., Markova, I. S., Roth, I., . . . Morris, R. G. (2013). Self-concept in early stage dementia: profile, course, correlates, predictors and implications for quality of life. *International Journal of Geriatric Psychiatry, 28*(5), 494-503. doi:10.1002/gps.3852

Clark, I. A., & Maguire, E. A. (2016). Remembering Preservation in Hippocampal Amnesia. *Annual Review of Psychology, 67*, 51-82. doi:10.1146/annurev-psych-122414-033739

Cohen, J. D., Perlstein, W. M., Braver, T. S., Nystrom, L. E., Noll, D. C., Jonides, J., & Smith, E. E. (1997). Temporal dynamics of brain activation during a working memory task. *Nature, 386*(6625), 604. doi:10.1038/386604a0

Conde-Sala, J. L., Turró-Garriga, O., Piñán-Hernández, S., Portellano-Ortiz, C., Viñas-Diez, V., Gascón-Bayarri, J., & Reñé-Ramírez, R. (2016). Effects of anosognosia and neuropsychiatric symptoms on the quality of life of patients with Alzheimer's disease: a 24-month follow-up study. *International Journal of Geriatric Psychiatry, 31*(2), 109-119. doi:10.1002/gps.4298

Conway, M. A. (1996). Autobiographical memories and autobiographical knowledge. *Remembering our past: Studies in autobiographical memory, 67*, 93. doi:10.1017/CBO9780511527913.003

Conway, M. A. (2005). Memory and the self. *Journal of Memory and Language, 53*, 594-628. doi:10.1016/j.jml.2005.08.005

Conway, M. A., & Pleydell-Pearce, C. W. (2000). The construction of autobiographical memories in the self-memory system. *Psychol Rev, 107*(2), 261-288. doi:10.1037/0033-295x.107.2.261

Conway, M. A., & Rubin, D. C. (1993). The structure of autobiographical memory *Theories of memory.* (pp. 103-137). Hillsdale, NJ, US: Lawrence Erlbaum Associates, Inc.

Conway, M. A., Singer, J. A., & Tagini, A. (2004). The self and autobiographical memory: Correspondence and coherence. *Social Cognition, 22*(5), 491-529. doi:10.1521/soco.22.5.491.50768

Corcoran, R., & Frith, C. D. (2003). Autobiographical memory and theory of mind: evidence of a relationship in schizophrenia. *Psychological medicine, 33*(5), 897-905. doi:10.1017/s0033291703007529

Cotelli, M., Adenzato, M., Cantoni, V., Manenti, R., Alberici, A., Enrici, I., . . . Borroni, B. (2018). Enhancing theory of mind in behavioural variant frontotemporal dementia with transcranial direct current stimulation. *Cognitive, Affective, & Behavioural Neuroscience*. doi:10.3758/s13415-018-0622-4

Craik, F. I., & Bialystok, E. (2006). Cognition through the lifespan: mechanisms of change. *Trends in Cognitive Sciences, 10*(3), 131-138. doi:10.1016/j.tics.2006.01.007

Craver, C. F., Keven, N., Kwan, D., Kurczek, J., Duff, M. C., & Rosenbaum, R. S. (2016). Moral judgment in episodic amnesia. *Hippocampus, 26*(8), 975-979. doi:10.1002/hipo.22593

Crete-Nishihata, M., Baecker, R. M., Massimi, M., Ptak, D., Campigotto, R., Kaufman, L. D., . . . Black, S. E. (2012). Reconstructing the Past- Personal Memory Technologies Are Not Just Personal and Not Just for Memory. *Human-Computer Interaction, 27*(1-2), 92-123. doi:10.1080/07370024.2012.656062

D'Argembeau, A., Lardi, C., & Van der Linden, M. (2012). Self-defining future projections: exploring the identity function of thinking about the future. *Memory, 20*(2), 110-120. doi:10.1080/09658211.2011.647697 [doi]

David, N., Aumann, C., Santos, N. S., Bewernick, B. H., Eickhoff, S. B., Newen, A., . . . Vogeley, K. (2008). Differential involvement of the posterior temporal cortex in mentalizing but not perspective taking. *Social Cognitive and Affective Neuroscience, 3*(3), 279-289. doi:10.1093/scan/nsn023

Davidson, P. S., Anaki, D., Ciaramelli, E., Cohn, M., Kim, A. S., Murphy, K. J., . . . Levine, B. (2008). Does lateral parietal cortex support episodic memory? Evidence from focal lesion patients. *Neuropsychologia, 46*(7), 1743-1755. doi:10.1016/j.neuropsychologia.2008.01.011

Davidson, P. S., Drouin, H., Kwan, D., Moscovitch, M., & Rosenbaum, R. S. (2012). Memory as social glue: close interpersonal relationships in amnesic patients. *Frontiers in Psychology, 3*, 531. doi:10.3389/fpsyg.2012.00531

Davis, M. H. (1983). Measuring individual differences in empathy: Evidence for a multidimensional approach. *J Pers Soc Psychol, 44*, 113-126. doi:10.1037/0022-3514.44.1.113

Day, G. S., Farb, N. A. S., Tang-Wai, D. F., Masellis, M., Black, S. E., Freedman, M., . . . Chow, T. W. (2013). Salience Network Resting-State Activity: Prediction of Frontotemporal Dementia Progression. *JAMA Neurol, 70*(10), 1249-1253. doi:10.1001/jamaneurol.2013.3258

De Simone, M. S., Fadda, L., Perri, R., Aloisi, M., Caltagirone, C., & Carlesimo, G. A. (2016). Does retrieval frequency account for the pattern of autobiographical memory loss in early Alzheimer's disease patients? *Neuropsychologia, 80*, 194-200. doi:10.1016/j.neuropsychologia.2015.11.024

Decety, J., & Jackson, P. L. (2004). The functional architecture of human empathy. *Behavioural and Cognitive Neuroscience Reviews, 3*(2), 71-100. doi:10.1177/1534582304267187

Dermody, N., Wong, S., Ahmed, R., Piguet, O., Hodges, J. R., & Irish, M. (2016). Uncovering the Neural Bases of Cognitive and Affective Empathy Deficits in Alzheimer's Disease

and the Behavioral-Variant of Frontotemporal Dementia. *Journal of Alzheimers Disease, 53*(3), 801-816. doi:10.3233/jad-160175

Downing, P. E., Jiang, Y., Shuman, M., & Kanwisher, N. (2001). A cortical area selective for visual processing of the human body. *Science, 293*(5539), 2470-2473. doi:10.1126/science.1063414

Drayton, L. A., Santos, L. R., & Baskin-Sommers, A. (2018). Psychopaths fail to automatically take the perspective of others. *Proceedings of the National Academy of Sciences, 115*(13), 3302-3307. doi:10.1073/pnas.1721903115

Dritschel, B. H., Williams, J. M. G., Baddeley, A. D., & Nimmo-Smith, I. (1992). Autobiographical fluency: A method for the study of personal memory. *Mem Cognit, 20*(2), 133-140. doi:10.3758/bf03197162

Duclos, H., Desgranges, B., Eustache, F., & Laisney, M. (2018). Impairment of social cognition in neurological diseases. *Revue Neurologique, 174*(4), 190-198. doi:10.1016/j.neurol.2018.03.003

Dunbar, R. I. (2012). The social brain meets neuroimaging. *Trends in Cognitive Sciences, 16*(2), 101-102. doi:10.1016/j.tics.2011.11.013

Duval, C., Bejanin, A., Piolino, P., Laisney, M., de La Sayette, V., Belliard, S., . . . Desgranges, B. (2012). Theory of mind impairments in patients with semantic dementia. *Brain, 135*(Pt 1), 228-241. doi:10.1093/brain/awr309

Duval, C., Desgranges, B., de La Sayette, V., Belliard, S., Eustache, F., & Piolino, P. (2012). What happens to personal identity when semantic knowledge degrades? A study of the self and autobiographical memory in semantic dementia. *Neuropsychologia, 50*(2), 254-265. doi:10.1016/j.neuropsychologia.2011.11.019

Eack, S. M., Wojtalik, J. A., Keshavan, M. S., & Minshew, N. J. (2017). Social-cognitive brain function and connectivity during visual perspective-taking in autism and schizophrenia. *Schizophrenia research, 183*, 102-109. doi:10.1016/j.schres.2017.03.009

Ernst, A., Botzung, A., Gounot, D., Sellal, F., Blanc, F., de Seze, J., & Manning, L. (2012). Induced brain plasticity after a facilitation programme for autobiographical memory in multiple sclerosis: a preliminary study. *Multiple Sclerosis International, 2012*, 820240. doi:10.1155/2012/820240

Ernst, A., Noblet, V., Denkova, E., Blanc, F., de Seze, J., Gounot, D., & Manning, L. (2015). Functional cerebral changes in multiple sclerosis patients during an autobiographical memory test. *Memory, 23*(8), 1123-1139. doi:10.1080/09658211.2014.955805

Ernst, A., Sourty, M., Roquet, D., Noblet, V., Gounot, D., Blanc, F., . . . Manning, L. (2016). Functional and structural cerebral changes in key brain regions after a facilitation programme for episodic future thought in relapsing-remitting multiple sclerosis patients. *Brain Cogn, 105*, 34-45. doi:10.1016/j.bandc.2016.03.007

Eslinger, P. J., Moore, P., Troiani, V., Antani, S., Cross, K., Kwok, S., & Grossman, M. (2007). Oops! Resolving social dilemmas in frontotemporal dementia. *Journal of Neurology, Neurosurgery, and Psychiatry, 78*(5), 457-460. doi:10.1136/jnnp.2006.098228

Esopenko, C., & Levine, B. (2017). Autobiographical memory and structural brain changes in chronic phase TBI. *Cortex, 89*, 1-10. doi:10.1016/j.cortex.2017.01.007

Eustache, F., Piolino, P., Giffard, B., Viader, F., De La Sayette, V., Baron, J. C., & Desgranges, B. (2004). 'In the course of time': a PET study of the cerebral substrates of autobiographical amnesia in Alzheimer's disease. *Brain, 127*(Pt 7), 1549-1560. doi:10.1093/brain/awh166 [doi]

Eustache, M. L., Laisney, M., Juskenaite, A., Letortu, O., Platel, H., Eustache, F., & Desgranges, B. (2013). Sense of identity in advanced Alzheimer's dementia: A cognitive dissociation between sameness and selfhood? *Consciousness and Cognition, 22*(4), 1456-1467. doi:10.1016/j.concog.2013.09.009

Fabbro, F., Aglioti, S. M., Bergamasco, M., Clarici, A., & Panksepp, J. (2015). Evolutionary aspects of self- and world consciousness in vertebrates. *Front Hum Neurosci, 9*(157). doi:10.3389/fnhum.2015.00157

Farrant, B. M., Fletcher, J., & Maybery, M. T. (2006). Specific Language Impairment, Theory of Mind, and Visual Perspective Taking: Evidence for Simulation Theory and the Developmental Role of Language. *Child Development, 77*(6), 1842-1853. doi:10.1111/j.1467-8624.2006.00977.x

Feast, A., Orrell, M., Charlesworth, G., Melunsky, N., Poland, F., & Moniz-Cook, E. (2016). Behavioural and psychological symptoms in dementia and the challenges for family carers: Systematic review. *British Journal of Psychiatry, 208*(5), 429-434. doi:10.1192/bjp.bp.114.153684

Flavell, J. H. (1977). *The development of knowledge about visual perception.* Paper presented at the Nebraska symposium on motivation.

Flavell, J. H. (1992). Cognitive development: Past, present, and future. *Developmental Psychology, 28*(6), 998-1005. doi:10.1037/0012-1649.28.6.998

Flavell, J. H., Everett, B. A., Croft, K., & Flavell, E. R. (1981). Young children's knowledge about visual perception: Further evidence for the Level 1–Level 2 distinction. *Developmental Psychology, 17*(1), 99. doi:10.1037/0012-1649.17.1.99

Flavell, J. H., Flavell, E. F., Green, F. L., & Wilcox, S. A. (1980). Young children's knowledge about visual perception: Effect of observer's distance from target on perceptual clarity of target. *Developmental Psychology, 16*(1), 10-12. doi:10.1037/0012-1649.16.1.10

Fleischacker, S. (1997). The Ethics of Culture. *Philosophy and Phenomenological Research, 57*(1), 233-235. doi:10.2307/2953794

Fletcher, P. C., Frith, C. D., Baker, S. C., Shallice, T., Frackowiak, R. S., & Dolan, R. J. (1995). The mind's eye--precuneus activation in memory-related imagery. *Neuroimage, 2*(3), 195-200. doi:10.1006/nimg.1995.1025

Fong, S. S., Navarrete, C. D., Perfecto, S. E., Carr, A. R., Jimenez, E. E., & Mendez, M. F. (2017). Behavioral and autonomic reactivity to moral dilemmas in frontotemporal dementia versus Alzheimer's disease. *Soc Neurosci, 12*(4), 409-418. doi:10.1080/17470919.2016.1186111

Foot, P. (1967). The problem of abortion and the doctrine of double effectVirtues and Vices: and other essays in moral philosophy. https://www.oxfordscholarship.com/view/10.1093/0199252866.001.0001/acprof-9780199252862-chapter-2.: Oxford University Press.

Ford, J. H., Rubin, D. C., & Giovanello, K. S. (2014). Effects of task instruction on autobiographical memory specificity in young and older adults. *Memory, 22*(6), 722-736. doi:10.1080/09658211.2013.820325

Friesdorf, R., Conway, P., & Gawronski, B. (2015). Gender Differences in Responses to Moral Dilemmas. *Personality and Social Psychology Bulletin, 41*(5), 696-713. doi:10.1177/0146167215575731

Frith, C. D., & Frith, U. (2006). The neural basis of mentalizing. *Neuron, 50*(4), 531-534. doi:10.1016/j.neuron.2006.05.001

Frith, C. D., & Frith, U. (2007). Social cognition in humans. *Current Biology, 17*(16), R724-R732. doi:10.1016/j.cub.2007.05.068

Fuentes, A., & Desrocher, M. (2011). Autobiographical Memory in Emerging Adulthood: Relationship with Self-Concept Clarity. *Journal of Adult Development, 19*(1), 28-39. doi:10.1007/s10804-011-9131-1

Fuentes, A., & Desrocher, M. (2013). The effects of gender on the retrieval of episodic and semantic components of autobiographical memory. *Memory, 21*(6), 619-632. doi:0.1080/09658211.2012.744423

Gaesser, B., & Schacter, D. L. (2014). Episodic simulation and episodic memory can increase intentions to help others. *Proc Natl Acad Sci U S A, 111*(12), 4415-4420. doi:10.1073/pnas.1402461111

Gallagher, H., & Frith, C. (2003). Functional imaging of "theory of mind'. *Trends in Cognitive Sciences, 7*(2), 77-83. doi:10.1016/s1364-6613(02)00025-6

Gallagher, H., Jack, A. I., Roepstorff, A., & Frith, C. D. (2002). Imaging the intentional stance in a competitive game. *Neuroimage, 16*(3), 814-821. doi:10.1006/nimg.2002.1117

Gallagher, S. (2000). Philosophical conceptions of the self: implications for cognitive science. *Trends in Cognitive Sciences, 4*(1), 14-21. doi:10.1016/S1364-6613(99)01417-5

Gallagher, S. (2013). A Pattern Theory of Self. *Front Hum Neurosci, 7*. doi:10.3389/fnhum.2013.00443

Gallup Jr, G. G., Anderson, J. R., & Shillito, D. J. (2002). The mirror test. *The cognitive animal: Empirical and theoretical perspectives on animal cognition*, 325-333.

Galton, C., Patterson, K., Graham, K., Lambon-Ralph, M., Williams, G., Antoun, N., . . . Hodges, J. (2001). Differing patterns of temporal atrophy in Alzheimer's disease and semantic dementia. *Neurology, 57*(2), 216-225. doi:10.1212/WNL.57.2.216

Gamble, B., Moreau, D., Tippett, L. J., & Addis, D. R. (2019). Specificity of Future Thinking in Depression: A Meta-Analysis. *Perspectives on Psychological Science, 14*(5), 816-834. doi:10.1177/1745691619851784

Gamboz, N., De Vito, S., Brandimonte, M. A., Pappalardo, S., Galeone, F., Iavarone, A., & Della Sala, S. (2010). Episodic future thinking in amnesic mild cognitive impairment. *Neuropsychologia, 48*(7), 2091-2097. doi:10.1016/j.neuropsychologia.2010.03.030

Gardini, S., Cornoldi, C., De Beni, R., & Venneri, A. (2006). Left mediotemporal structures mediate the retrieval of episodic autobiographical mental images. *Neuroimage, 30*(2), 645-655. doi:10.1016/j.neuroimage.2005.10.012

Gascoigne, M. B., Barton, B., Webster, R., Gill, D., & Lah, S. (2015). Autobiographical memory in children with Idiopathic Generalised Epilepsy. *Neuropsychologia, 66*, 10-17. doi:10.1016/j.neuropsychologia.2014.11.010

Gascoigne, M. B., Smith, M. L., Webster, R., Barton, B., Gill, D., & Lah, S. (2013). Autobiographical memory in children with temporal lobe epilepsy. *Journal of the International Neuropsychological Society, 19*(10), 1076-1086. doi:10.1017/S1355617713000970

Gilboa, A., & Marlatte, H. (2017). Neurobiology of Schemas and Schema-Mediated Memory. *Trends in Cognitive Sciences, 21*(8), 618-631. doi:10.1016/j.tics.2017.04.013

Gilboa, A., Ramirez, J., Kohler, S., Westmacott, R., Black, S. E., & Moscovitch, M. (2005). Retrieval of autobiographical memory in Alzheimer's disease: relation to volumes of

medial temporal lobe and other structures. *Hippocampus, 15*(4), 535-550. doi:10.1002/hipo.20090 [doi]

Gilboa, A., Winocur, G., Rosenbaum, R. S., Poreh, A., Gao, F., Black, S. E., . . . Moscovitch, M. (2006). Hippocampal contributions to recollection in retrograde and anterograde amnesia. *Hippocampus, 16*(11), 966-980. doi:10.1002/hipo.20226

Gleichgerrcht, E., Ibanez, A., Roca, M., Torralva, T., & Manes, F. (2010). Decision-making cognition in neurodegenerative diseases. *Nature Reviews Neurology, 6*(11), 611-623. doi:10.1038/nrneurol.2010.148

Gorno-Tempini, M. L., Hillis, A. E., Weintraub, S., Kertesz, A., Mendez, M., Cappa, S. F., . . . Grossman, M. (2011). Classification of primary progressive aphasia and its variants. *Neurology, 76*(11), 1006-1014. doi:10.1212/WNL.0b013e31821103e6

Graham, K. S., & Hodges, J. R. (1997). Differentiating the roles of the hippocampal complex and the neocortex in long-term memory storage: evidence from the study of semantic dementia and Alzheimer's disease. *Neuropsychology, 11*(1), 77-89. doi:10.1037//0894-4105.11.1.77

Graham, K. S., Lambon Ralph, M. A., & Hodges, J. R. (1997). Determining the Impact of Autobiographical Experience on "Meaning": New Insights from Investigating Sports-related Vocabulary and Knowledge in Two Cases with Semantic Dementia. *Cogn Neuropsychol, 14*(6), 801-837. doi:10.1080/026432997381367

Greaves, C. V., & Rohrer, J. D. (2019). An update on genetic frontotemporal dementia. *Journal of neurology, 266*(8), 2075-2086. doi:10.1007/s00415-019-09363-4

Greenberg, D. L., & Verfaellie, M. (2010). Interdependence of episodic and semantic memory: evidence from neuropsychology. *Journal of the International Neuropsychological Society, 16*(5), 748-753. doi:10.1017/S1355617710000676

Greene, J. D. (2014). *Moral tribes: Emotion, reason, and the gap between us and them*: Penguin.

Greene, J. D., Nystrom, L. E., Engell, A. D., Darley, J. M., & Cohen, J. D. (2004). The neural bases of cognitive conflict and control in moral judgment. *Neuron, 44*(2), 389-400. doi:10.1016/j.neuron.2004.09.027

Greene, J. D., Sommerville, R. B., Nystrom, L. E., Darley, J. M., & Cohen, J. D. (2001). An fMRI investigation of emotional engagement in moral judgment. *Science, 293*(5537), 2105-2108. doi:10.1126/science.1062872

Greene, J. W. D., Hodges, J. R., & Baddeley, A. D. (1995). Autobiographical memory and executive function in early dementia of Alzheimer type. *Neuropsychologia, 33*(12), 1647-1670. doi:10.1016/0028-3932(95)00046-1

Gregory, C., Lough, S., Stone, V., Erzinclioglu, S., Martin, L., Baron-Cohen, S., & Hodges, J. R. (2002). Theory of mind in patients with frontal variant frontotemporal dementia and Alzheimer's disease: theoretical and practical implications. *Brain, 125*(Pt 4), 752-764. doi:10.1093/brain/awf079

Gregory, C., Serra-Mestres, J., & Hodges, J. R. (1999). Early diagnosis of frontal variant of frontotemporal dementia: How sensitive are standard neuroimaging and neuropsychologic tests? *Neuropsychiatry, Neuropsychology, & Behavioral Neurology*.

Greicius, M. D., Krasnow, B., Reiss, A. L., & Menon, V. (2003). Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. *Proceedings of the National Academy of Science USA, 100*(1), 253-258. doi:10.1073/pnas.0135058100

Grilli, M. D., & Verfaellie, M. (2014). Personal semantic memory: insights from neuropsychological research on amnesia. *Neuropsychologia, 61*, 56-64. doi: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. doi:10.1093/scan/nsv056

Grilli, M. D., & Verfaellie, M. (2016). Experience-near but not experience-far autobiographical facts depend on the medial temporal lobe for retrieval: Evidence from amnesia. *Neuropsychologia, 81*, 180-185. doi:10.1016/j.neuropsychologia.2015.12.023

Grysman, A. (2017). Gender Differences in Episodic Encoding of Autobiographical Memory. *Journal of Applied Research in Memory and Cognition, 6*(1), 51-59. doi:10.1016/j.jarmac.2016.07.012

Hamilton, A. F. d. C., Brindley, R., & Frith, U. (2009). Visual perspective taking impairment in children with autistic spectrum disorder. *Cognition, 113*(1), 37-44. doi:10.1016/j.cognition.2009.07.007

Harré, R. (1991). The Discursive Production of Selves. *Theory & Psychology, 1*(1), 51-63. doi:10.1177/0959354391011004

Harrison, B. E., Therrien, B. A., & Giordani, B. J. (2005). Alzheimer's disease behaviors from past self-identities: An exploration of the memory and cognitive features. *American Journal of Alzheimer's Disease & Other Dementias, 20*(4), 248-254. doi:10.1177/153331750502000405

Harrison, B. J., Pujol, J., López-Solà, M., Hernández-Ribas, R., Deus, J., Ortiz, H., . . . Cardoner, N. (2008). Consistency and functional specialization in the default mode brain network. *Proceedings of the National Academy of Sciences, 105*(28), 9781-9786. doi:10.1073/pnas.0711791105

Haslam, C., Jetten, J., Haslam, S. A., Pugliese, C., & Tonks, J. (2011). 'I remember therefore I am, and I am therefore I remember': Exploring the contributions of episodic and semantic self-knowledge to strength of identity. *102*(2), 184-203. doi:10.1348/000712610x508091

Hassabis, D., Kumaran, D., Vann, S. D., & Maguire, E. A. (2007). Patients with hippocampal amnesia cannot imagine new experiences. *Proceedings of the National Academy of Sciences U S A, 104*(5), 1726-1731. doi:10.1073/pnas.0610561104

Hassabis, D., & Maguire, E. A. (2007). Deconstructing episodic memory with construction. *Trends in Cognitive Sciences, 11*(7), 299-306. doi:10.1016/j.tics.2007.05.001

Hauser, M., Cushman, F., Young, L., Kang-Xing Jin, R., & Mikhail, J. (2007). A Dissociation Between Moral Judgments and Justifications. *Mind & Language, 22*(1), 1-21. doi:10.1111/j.1468-0017.2006.00297.x

Hehman, J. A., German, T. P., & Klein, S. B. (2005). Impaired Self–Recognition from Recent Photographs in a Case of Late–Stage Alzheimer's Disease. *Social Cognition, 23*(1), 118-124. doi:10.1521/soco.23.1.118.59197

Henrich, J., Heine, S. J., & Norenzayan, A. (2010). Most people are not WEIRD. *Nature, 466*(7302), 29. doi:10.1038/466029a

Hershfield, H. E. (2011). Future self-continuity: how conceptions of the future self transform intertemporal choice. *Annals of the New York Academy of Sciences, 1235*(1), 30-43. doi:10.1111/j.1749-6632.2011.06201.x

Hill, J., Inder, T., Neil, J., Dierker, D., Harwell, J., & Van Essen, D. (2010). Similar patterns of cortical expansion during human development and evolution. *Proceedings of the National Academy of Sciences of the United States of America, 107*(29), 13135-13140. doi:10.1073/pnas.1001229107

Hills, T. T., & Butterfill, S. (2015). From foraging to autonoetic consciousness: The primal self as a consequence of embodied prospective foraging. *Current Zoology, 61*(2), 368-381. doi:10.1093/czoolo/61.2.368

Hodges, J. R., Davies, R. R., Xuereb, J. H., Casey, B., Broe, M., Bak, T. H., . . . Halliday, G. M. (2004). Clinicopathological correlates in frontotemporal dementia. *Ann Neurol, 56*(3), 399-406. doi:10.1002/ana.20203

Hodges, J. R., Mitchell, J., Dawson, K., Spillantini, M. G., Xuereb, J. H., McMonagle, P., . . . Patterson, K. (2009). Semantic dementia: demography, familial factors and survival in a consecutive series of 100 cases. *Brain, 133*(1), 300-306. doi:10.1093/brain/awp248

Hodges, J. R., & Patterson, K. (2007). Semantic dementia: a unique clinicopathological syndrome. *The Lancet Neurology, 6*(11), 1004-1014. doi:10.1016/S1474-4422(07)70266-1

Hodgetts, C. J., Postans, M., Warne, N., Varnava, A., Lawrence, A. D., & Graham, K. S. (2017). Distinct contributions of the fornix and inferior longitudinal fasciculus to episodic and semantic autobiographical memory. *Cortex, 94*, 1-14. doi:10.1016/j.cortex.2017.05.010

Hohman, T. J., Peynircioglu, Z. F., & Beason-Held, L. L. (2013). Flexibility of event boundaries in autobiographical memory. *Memory, 21*(2), 249-260. doi:10.1080/09658211.2012.725737

Holland, A. C., Addis, D. R., & Kensinger, E. A. (2011). The neural correlates of specific versus general autobiographical memory construction and elaboration. *Neuropsychologia, 49*(12), 3164-3177. doi:10.1016/j.neuropsychologia.2011.07.015

Hornberger, M., Mohamed, A., Miller, L., Watson, J., Thayer, Z., & Hodges, J. R. (2010). Focal retrograde amnesia: Extending the clinical syndrome of transient epileptic amnesia. *Journal of Clinical Neuroscience, 17*(10), 1319-1321. doi:10.1016/j.jocn.2010.03.005

Hornberger, M., & Piguet, O. (2012). Episodic memory in frontotemporal dementia: a critical review. *Brain, 135*(Pt 3), 678-692. doi:10.1093/brain/aws011

Hornberger, M., Piguet, O., Graham, A. J., Nestor, P. J., & Hodges, J. R. (2010). How preserved is episodic memory in behavioral variant frontotemporal dementia? *Neurology, 74*(6), 472-479. doi:10.1212/Wnl.0b013e3181cef85d

Hou, C., Miller, B., & Kramer, J. (2005). Patterns of autobiographical memory loss in dementia. *International Journal of Geriatric Psychiatry, 20*(9), 809-815. doi: 10.1002/gps.1361

Hsiao, J. J., Kaiser, N., Fong, S. S., & Mendez, M. F. (2013). Suicidal behavior and loss of the future self in semantic dementia. *Cognitive and Behavioral Neurology, 26*(2), 85-92. doi:10.1097/WNN.0b013e31829c671d

Hsieh, S., Irish, M., Daveson, N., Hodges, J. R., & Piguet, O. (2013). When One Loses Empathy: Its Effect on Carers of Patients With Dementia. *J Geriatr Psychiatry Neurol*. doi:10.1177/0891988713495448

Hsieh, S., Irish, M., Foxe, D., Caga, J., Devenney, E., Ahmed, R., . . . Kiernan, M. C. (2016). My memories are important to me: Changes in autobiographical memory in

amyotrophic lateral sclerosis. *Neuropsychology, 30*(8), 920-930. doi:10.1037/neu0000291

Hsieh, S., Schubert, S., Hoon, C., Mioshi, E., & Hodges, J. R. (2013). Validation of the Addenbrooke's Cognitive Examination III in Frontotemporal Dementia and Alzheimer's Disease. *Dement Geriatr Cogn Disord, 36*(3-4), 242-250. doi:10.1159/000351671

Hume, D. (1739). *A Tretise on Human Nature*: Clarendon Press.

Hume, D. (1751). *An Enquiry Concerning the Principles of Morals*: A. Millar.

Hurley, N. C., Maguire, E. A., & Vargha-Khadem, F. (2011). Patient HC with developmental amnesia can construct future scenarios. *Neuropsychologia, 49*(13), 3620-3628. doi:10.1016/j.neuropsychologia.2011.09.015

Inagaki, H., Meguro, K., Shimada, M., Ishizaki, J., Okuzumi, H., & Yamadori, A. (2002). Discrepancy between mental rotation and perspective-taking abilities in normal aging assessed by Piaget's three-mountain task. *Journal of Clinical and Experimental Psychology, 24*(1), 18-25. doi:10.1076/jcen.24.1.18.969

Irish, M. (2016). Semantic memory as the essential scaffold for future oriented mental time travel. In K. Michaelian, S. B. Klein, & K. Szpunar (Eds.), *Seeing the Future: Theoretical Perspectives on Future-Oriented Mental Time Travel* (pp. 388-408). New York: Oxford University Press.

Irish, M. (2020). On the interaction between episodic and semantic representations - Constructing a unified account of imagination. In A. Abraham (Ed.), *The Cambridge Handbook of Imagination*.

Irish, M., Addis, D. R., Hodges, J. R., & Piguet, O. (2012a). Considering the role of semantic memory in episodic future thinking: evidence from semantic dementia. *Brain, 135*(Pt 7), 2178-2191. doi:10.1093/brain/aws119

Irish, M., Addis, D. R., Hodges, J. R., & Piguet, O. (2012b). Exploring the content and quality of episodic future simulations in semantic dementia. *Neuropsychologia, 50*(14), 3488-3495. doi:10.1016/j.neuropsychologia.2012.09.012

Irish, M., Bunk, S., Tu, S., Kamminga, J., Hodges, J. R., Hornberger, M., & Piguet, O. (2016). Preservation of episodic memory in semantic dementia: The importance of regions beyond the medial temporal lobes. *Neuropsychologia, 81*, 50-60. doi:10.1016/j.neuropsychologia.2015.12.005

Irish, M., Cunningham, C. J., Walsh, J. B., Coakley, D., Lawlor, B. A., Robertson, I. H., & Coen, R. F. (2006). Investigating the enhancing effect of music on autobiographical memory in mild Alzheimer's disease. *Dement Geriatr Cogn Disord, 22*(1), 108-120. doi:10.1159/000093487

Irish, M., Hodges, J. R., & Piguet, O. (2013). Episodic future thinking is impaired in the behavioural variant of frontotemporal dementia. *Cortex, 49*(9), 2377-2388. doi:10.1016/j.cortex.2013.03.002

Irish, M., Hodges, J. R., & Piguet, O. (2014). Right anterior temporal lobe dysfunction underlies theory of mind impairments in semantic dementia. *Brain, 137*(4), 1241-1253. doi:10.1093/brain/awu003

Irish, M., Hornberger, M., El Wahsh, S., Lam, B. Y., Lah, S., Miller, L., . . . Piguet, O. (2014). Grey and White Matter Correlates of Recent and Remote Autobiographical Memory Retrieval - Insights from the Dementias. *PLoS One, 9*(11), e113081. doi:10.1371/journal.pone.0113081

Irish, M., Hornberger, M., Lah, S., Miller, L., Pengas, G., Nestor, P. J., . . . Piguet, O. (2011). Profiles of recent autobiographical memory retrieval in semantic dementia, behavioural-variant frontotemporal dementia, and Alzheimer's disease. *Neuropsychologia, 49*(9), 2694-2702. doi:10.1016/j.neuropsychologia.2011.05.017

Irish, M., Kamminga, J., Addis, D. R., Crain, S., Thornton, R., Hodges, J. R., & Piguet, O. (2016). 'Language of the past' - Exploring past tense disruption during autobiographical narration in neurodegenerative disorders. *Journal of Neuropsychology, 10*(2), 295-316. doi:10.1111/jnp.12073

Irish, M., Landin-Romero, R., Mothakunnel, A., Ramanan, S., Hsieh, S., Hodges, J. R., & Piguet, O. (2018). Evolution of autobiographical memory impairments in Alzheimer's disease and frontotemporal dementia - A longitudinal neuroimaging study. *Neuropsychologia, 110*, 14-25. doi:10.1016/j.neuropsychologia.2017.03.014

Irish, M., Lawlor, B. A., O'Mara, S. M., & Coen, R. F. (2008). Assessment of behavioural markers of autonoetic consciousness during episodic autobiographical memory retrieval: a preliminary analysis. *Behav Neurol, 19*(1-2), 3-6. doi:10.1155/2008/691925

Irish, M., Lawlor, B. A., O'Mara, S. M., & Coen, R. F. (2011). Impaired capacity for autonoetic reliving during autobiographical event recall in mild Alzheimer's disease. *Cortex, 47*(2), 236-249. doi:10.1016/j.cortex.2010.01.002

Irish, M., & Piguet, O. (2013). The pivotal role of semantic memory in remembering the past and imagining the future. *Frontiers in Behavioural Neuroscience, 7*, 27. doi:10.3389/fnbeh.2013.00027

Irish, M., Piguet, O., & Hodges, J. R. (2012). Self-projection and the default network in frontotemporal dementia. *Nature Reviews Neurology, 8*(3), 152-161. doi:10.1038/nrneurol.2012.11

James, W., Burkhardt, F., Bowers, F., & Skrupskelis, I. K. (1890). *The principles of psychology* (Vol. 1): Macmillan London.

Johnen, A., & Bertoux, M. (2019). Psychological and Cognitive Markers of Behavioral Variant Frontotemporal Dementia-A Clinical Neuropsychologist's View on Diagnostic Criteria and Beyond. *Frontiers in neurology, 10*, 594-594. doi:10.3389/fneur.2019.00594

Jones, D. T., Knopman, D. S., Gunter, J. L., Graff-Radford, J., Vemuri, P., Boeve, B. F., . . . Alzheimer's Disease Neuroimaging, I. (2016). Cascading network failure across the Alzheimer's disease spectrum. *Brain : a journal of neurology, 139*(Pt 2), 547-562. doi:10.1093/brain/awv338

Kamminga, J., O'Callaghan, C., Hodges, J. R., & Irish, M. (2014). Differential prospective memory profiles in frontotemporal dementia syndromes. *Journal of Alzheimer's disease, 38*(3), 669-679. doi: 10.3233/JAD-131118

Kant, I., Schneewind, J. B., Baron, M., & Kagan, S. (2002). *Groundwork for the Metaphysics of Morals*: Yale University Press.

Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: a module in human extrastriate cortex specialized for face perception. *Journal of Neuroscience, 17*(11), 4302-4311. doi:10.1523/JNEUROSCI.17-11-04302.1997

Karas, G. B., Scheltens, P., Rombouts, S. A., Visser, P. J., van Schijndel, R. A., Fox, N. C., & Barkhof, F. (2004). Global and local gray matter loss in mild cognitive impairment and Alzheimer's disease. *Neuroimage, 23*(2), 708-716. doi:10.1016/j.neuroimage.2004.07.006

Kazui, H., Hashimoto, M., Hirono, N., Imamura, T., Tanimukai, S., Hanihara, T., . . . Mori, E. (2000). A Study of Remote Memory Impairment in Alzheimer's Disease by Using the Family Line Test. *Dement Geriatr Cogn Disord, 11*(1), 53-58. doi:10.1159/000017214

Kessler, K., & Thomson, L. A. (2010). The embodied nature of spatial perspective taking: embodied transformation versus sensorimotor interference. *Cognition, 114*(1), 72-88. doi:10.1016/j.cognition.2009.08.015

Keysers, C., & Gazzola, V. (2007). Integrating simulation and theory of mind: from self to social cognition. *Trends in Cognitive Sciences, 11*(5), 194-196. doi:10.1016/j.tics.2007.02.002

Kiehl, K. A., & Hoffman, M. B. (2011). The criminal psychopath: History, neuroscience, treatment, and economics. *Jurimetrics, 51*, 355.

King, M. J., MacDougall, A. G., Ferris, S., Herdman, K. A., Bielak, T., Smith, J. R., . . . McKinnon, M. C. (2013). Impaired episodic memory for events encoded during mania in patients with bipolar disorder. *Psychiatry Research, 205*(3), 213-219. doi:10.1016/j.psychres.2012.08.005

Kirk, M., & Berntsen, D. (2018). The life span distribution of autobiographical memory in Alzheimer's disease. *Neuropsychology, 32*(8), 906-919. doi:10.1037/neu0000486

Kirwan, C. B., Bayley, P. J., Galvan, V. V., & Squire, L. R. (2008). Detailed recollection of remote autobiographical memory after damage to the medial temporal lobe. *Proceedings of the National Academy of Sciences of the United States of America, 105*(7), 2676-2680. doi:10.1073/pnas.0712155105

Klein, S. B. (2013). The complex act of projecting oneself into the future. *WIREs Cogn Sci, 4*, 63-79. doi:10.1002/wcs.1210

Klein, S. B., Cosmides, L., & Costabile, K. A. (2003). Preserved Knowledge of Self in a Case of Alzheimer's Dementia. *Social Cognition, 21*(2), 157-165. doi:10.1521/soco.21.2.157.21317

Klein, S. B., Loftus, J., & Kihlstrom, J. F. (2002). Memory and temporal experience: the effects of episodic memory loss on an amnesic patient's ability to remember the past and imagine the future. *Social Cognition, 20*(5), 353-379. doi:10.1521/soco.20.5.353.21125

Klimova, B., Maresova, P., Valis, M., Hort, J., & Kuca, K. (2015). Alzheimer's disease and language impairments: social intervention and medical treatment. *Clinical interventions in aging, 10*, 1401-1407. doi:10.2147/CIA.S89714

Kobayashi, C., Glover, G. H., & Temple, E. (2007). Cultural and linguistic effects on neural bases of 'Theory of Mind' in American and Japanese children. *Brain research, 1164*, 95-107. doi:10.1016/j.brainres.2007.06.022

Koenigs, M., Young, L., Adolphs, R., Tranel, D., Cushman, F., Hauser, M., & Damasio, A. (2007). Damage to the prefrontal cortex increases utilitarian moral judgements. *Nature, 446*(7138), 908-911. doi:10.1038/nature05631

Kohlberg, L. (1963). The development of children's orientations toward a moral order: I. Sequence in the development of moral thought. *Vita Humana, 6*(1-2), 11-33.

Kopelman, M. D., Wilson, B. A., & Baddeley, A. D. (1989). The autobiographical memory interview: a new assessment of autobiographical and personal semantic memory in amnesic patients. *J Clin Exp Neuropsychol, 11*(5), 724-744. doi:10.1080/01688638908400928

Kosslyn, S. M., Shin, L. M., Thompson, W. L., McNally, R. J., Rauch, S. L., Pitman, R. K., & Alpert, N. M. (1996). Neural effects of visualizing and perceiving aversive stimuli: a

PET investigation. *Neuroreport, 7*(10), 1569-1576. doi:10.1097/00001756-199607080-00007

Kozhevnikov, M., Kosslyn, S., & Shephard, J. (2005). Spatial versus object visualizers: A new characterization of visual cognitive style. *Mem Cognit, 33*(4), 710-726. doi:10.3758/bf03195337

Krebs, D., & Rosenwald, A. (1977). Moral reasoning and moral behavior in conventional adults. *Merrill-Palmer Quarterly of Behavior and Development, 23*(2), 77-87.

Kumfor, F., Irish, M., Hodges, J. R., & Piguet, O. (2013). The orbitofrontal cortex is involved in emotional enhancement of memory: evidence from the dementias. *Brain, 136*(Pt 10), 2992-3003. doi:10.1093/brain/awt185

Kumfor, F., Landin-Romero, R., Devenney, E., Hutchings, R., Grasso, R., Hodges, J. R., & Piguet, O. (2016). On the right side? A longitudinal study of left- versus right-lateralized semantic dementia. *Brain, 139*(3), 986-998. doi:10.1093/brain/awv387

Kumfor, F., Teo, D., Miller, L., Lah, S., Mioshi, E., Hodges, J. R., . . . Irish, M. (2016). Examining the Relationship Between Autobiographical Memory Impairment and Carer Burden in Dementia Syndromes. *Journal of Alzheimers Disease, 51*(1), 237-248. doi:10.3233/JAD-150740

Lam, B. Y. K., Halliday, G., Irish, M., Hodges, J. R., & Piguet, O. (2014). Longitudinal white matter changes in frontotemporal dementia subtypes. *Human Brain Mapping, 35*(7), 3547-3557. doi:10.1002/hbm.22420

Langdon, R., & Coltheart, M. (2001). Visual perspective-taking and schizotypy: evidence for a simulation-based account of mentalizing in normal adults. *Cognition, 82*(1), 1-26. doi:10.1016/s0010-0277(01)00139-1

Langdon, R., Coltheart, M., Ward, P. B., & Catts, S. V. (2001). Visual and cognitive perspective-taking impairments in schizophrenia: A failure of allocentric simulation? *Cogn Neuropsychiatry, 6*(4), 241-269. doi:10.1080/13546800143000005

Latif, D. A. (2000). The Link between Moral Reasoning Scores, Social Desirability, and Patient Care Performance Scores: Empirical Evidence from the Retail Pharmacy Setting. *Journal of Business Ethics, 25*(3), 255-269. doi:10.1023/A:1006049605298

Le Bouc, R., Lenfant, P., Delbeuck, X., Ravasi, L., Lebert, F., Semah, F., & Pasquier, F. (2012). My belief or yours? Differential theory of mind deficits in frontotemporal dementia and Alzheimer's disease. *Brain, 135*(Pt 10), 3026-3038. doi:10.1093/brain/aws237

LePort, A. K., Stark, S. M., McGaugh, J. L., & Stark, C. E. (2015). Highly Superior Autobiographical Memory: Quality and Quantity of Retention Over Time. *Frontiers in Psychology, 6*, 2017. doi:10.3389/fpsyg.2015.02017

Leslie, A. M. (1987). Pretense and representation: The origins of “theory of mind". *Psychol Rev, 94*(4), 412. doi:10.1037/0033-295X.94.4.412

Letheby, C., & Gerrans, P. (2017). Self unbound: ego dissolution in psychedelic experience. *Neuroscience of Consciousness, 2017*(1). doi:10.1093/nc/nix016

Levin, J. D. (1992). *Theories of the self*. Washington, DC, US: Hemisphere Publishing Corp.

Levine, B. (2019). Autobiographical Interview Bibliography. Retrieved from http://levinelab.weebly.com/ai-testing.html

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), 677-689. doi:10.1037//0882-7974.17.4.677

Levine, B., Svoboda, E., Turner, G. R., Mandic, M., & Mackey, A. (2009). Behavioral and functional neuroanatomical correlates of anterograde autobiographical memory in

isolated retrograde amnesic patient M.L. *Neuropsychologia, 47*(11), 2188-2196. doi:10.1016/j.neuropsychologia.2008.12.026

Levine, B., Turner, G. R., Tisserand, D., Hevenor, S. J., Graham, S. J., & McIntosh, A. R. (2004). The Functional Neuroanatomy of Episodic and Semantic Autobiographical Remembering: A Prospective Functional MRI Study. *Journal of Cognitive Neuroscience, 16*(9), 1633-1646. doi:10.1162/0898929042568587

Leyhe, T., Muller, S., Milian, M., Eschweiler, G. W., & Saur, R. (2009). Impairment of episodic and semantic autobiographical memory in patients with mild cognitive impairment and early Alzheimer's disease. *Neuropsychologia, 47*(12), 2464-2469. doi:10.1016/j.neuropsychologia.2009.04.018

Lieberman, M. D., & Cunningham, W. A. (2009). Type I and Type II error concerns in fMRI research: re-balancing the scale. *Social Cognitive and Affective Neuroscience, 4*(4), 423-428. doi:10.1093/scan/nsp052

Liljegren, M., Naasan, G., Temlett, J., Perry, D. C., Rankin, K. P., Merrilees, J., . . . Miller, B. L. (2015). Criminal behavior in frontotemporal dementia and Alzheimer disease. *JAMA Neurol, 72*(3), 295-300. doi:10.1001/jamaneurol.2014.3781

Lin, W.-J., Horner, A. J., & Burgess, N. (2016). Ventromedial prefrontal cortex, adding value to autobiographical memories. *Scientific Reports, 6*, 28630. doi:10.1038/srep28630

Locke, J. (1690). *An Essay Concerning Human Understanding* (Vol. 3): Oxford University Press.

Lough, S., Kipps, C., Treise, C., Watson, P., Blair, J., & Hodges, J. (2006). Social reasoning, emotion and empathy in frontotemporal dementia. *Neuropsychologia, 44*(6), 950-958. doi:10.1016/j.neuropsychologia.2005.08.009

MacDougall, A. G., McKinnon, M. C., Herdman, K. A., King, M. J., & Kiang, M. (2015). The relationship between insight and autobiographical memory for emotional events in schizophrenia. *Psychiatry Research, 226*(1), 392-395. doi:10.1016/j.psychres.2014.12.058

Mack, M. L., Love, B. C., & Preston, A. R. (2016). Dynamic updating of hippocampal object representations reflects new conceptual knowledge. *Proceedings of the National Academy of Sciences, 113*(46), 13203-13208. doi:10.1073/pnas.1614048113

MacLean, E. L. (2016). Unraveling the evolution of uniquely human cognition. *Proceedings of the National Academy of Sciences, 113*(23), 6348-6354. doi:10.1073/pnas.1521270113

Maddock, R. J. (1999). The retrosplenial cortex and emotion: new insights from functional neuroimaging of the human brain. *Trends in neurosciences, 22*(7), 310-316. doi:10.1016/s0166-2236(98)01374-5

Maguire, E. A. (2001). Neuroimaging studies of autobiographical event memory. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 356*(1413), 1441-1451. doi:10.1098/rstb.2001.0944

Maguire, E. A., & Frith, C. D. (2003). Aging affects the engagement of the hippocampus during autobiographical memory retrieval. *Brain, 126*(Pt 7), 1511-1523. doi:10.1093/brain/awg157

Maguire, E. A., Kumaran, D., Hassabis, D., & Kopelman, M. D. (2010). Autobiographical memory in semantic dementia: A longitudinal fMRI study. *Neuropsychologia, 48*(1), 123-136. doi:10.1016/j.neuropsychologia.2009.08.020

Maguire, E. A., & Mummery, C. J. (1999). Differential modulation of a common memory retrieval network revealed by positron emission tomography. *Hippocampus, 9*(1), 54-61. doi:10.1002/(sici)1098-1063(1999)9:1<54::Aid-hipo6>3.0.Co;2-o

Maguire, E. A., Vargha-Khadem, F., & Hassabis, D. (2010). Imagining fictitious and future experiences: Evidence from developmental amnesia. *Neuropsychologia, 48*(11), 3187-3192. doi:10.1016/j.neuropsychologia.2010.06.037

Mair, A., Poirier, M., & Conway, M. A. (2017). Supporting older and younger adults' memory for recent everyday events: A prospective sampling study using SenseCam. *Consciousness and Cognition, 49*, 190-202. doi:10.1016/j.concog.2017.02.008

Markus, H. R., & Kitayama, S. (1991). Culture and the self: Implications for cognition, emotion, and motivation. *Psychol Rev, 98*(2), 224. doi:10.1037/0033-295X.98.2.224

Masangkay, Z. S., McCluskey, K. A., McIntyre, C. W., Sims-Knight, J., Vaughn, B. E., & Flavell, J. H. (1974). The early development of inferences about the visual percepts of others. *Child Development*, 357-366. doi:10.2307/1127956

Mason, M. F., Norton, M. I., Van Horn, J. D., Wegner, D. M., Grafton, S. T., & Macrae, C. N. (2007). Wandering minds: the default network and stimulus-independent thought. *Science, 315*(5810), 393-395. doi:10.1126/science.1131295

Mauss, M. (1985). A category of the human mind. In M. Carrithers, S. Collins, & S. Lukes (Eds.), *The Category of the Person: Anthropology, Philosophy, History* (pp. 1--25): Cambridge University Press.

Mbiti, J. S. (1969). *African religions & philosophy*: Heinemann.

McAdams, D. P. (2001). The Psychology of Life Stories. *Review of General Psychology, 5*(2), 100-122. doi:10.1037/1089-2680.5.2.100

McCabe, K., Houser, D., Ryan, L., Smith, V., & Trouard, T. (2001). A functional imaging study of cooperation in two-person reciprocal exchange. *Proceedings of the National Academy of Sciences, 98*(20), 11832-11835. doi:10.1073/pnas.211415698

McCleery, J. P., Surtees, A. D. R., Graham, K. A., Richards, J. E., & Apperly, I. A. (2011). The Neural and Cognitive Time Course of Theory of Mind. *The Journal of Neuroscience, 31*(36), 12849-12854. doi:10.1523/jneurosci.1392-11.2011

McCormick, C., Rosenthal, C. R., Miller, T. D., & Maguire, E. A. (2016). Hippocampal Damage Increases Deontological Responses during Moral Decision Making. *Journal of Neuroscience, 36*(48), 12157-12167. doi:10.1523/jneurosci.0707-16.2016

McCormick, C., St-Laurent, M., Ty, A., Valiante, T. A., & McAndrews, M. P. (2013). Functional and Effective Hippocampal–Neocortical Connectivity During Construction and Elaboration of Autobiographical Memory Retrieval. *Cerebral Cortex, 25*(5), 1297-1305. doi:10.1093/cercor/bht324

McDonald, S., Flanagan, S., Rollins, J., & Kinch, J. (2003). TASIT: A new clinical tool for assessing social perception after traumatic brain injury. *Journal of Head Trauma and Rehabilitation, 18*(3), 219-238. doi:10.1097/00001199-200305000-00001

McKhann, G. M., Knopman, D. S., Chertkow, H., Hyman, B. T., Jack, C. R., Jr., Kawas, C. H., . . . Phelps, C. H. (2011). The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers & Dementia, 7*(3), 263-269. doi:10.1016/j.jalz.2011.03.005

McKinnon, M. C., Black, S. E., Miller, B. L., Moscovitch, D. A., & Levine, B. (2006). Autobiographical memory in semantic dementia- implications for theories of limbic-

neocortical interaction in remote memory. *Neuropsychologia, 44*(12), 2421-2429. doi:10.1016/j.neuropsychologia.2006.04.010

McKinnon, M. C., Nica, E. I., Sengdy, P., Kovacevic, N., Moscovitch, M., Freedman, M., . . . Levine, B. (2008). Autobiographical memory and patterns of brain atrophy in frontotemporal lobar degeneration. *Journal of Cognitive Neuroscience, 20*(10), 1839-1853. doi:10.1162/jocn.2008.20126

McKinnon, M. C., Palombo, D. J., Nazarov, A., Kumar, N., Khuu, W., & Levine, B. (2015). Threat of death and autobiographical memory: a study of passengers from Flight AT236. *Clinical Psychological Science, 3*(4), 487-502. doi:10.1177/2167702614542280

Mead, G. H. (1934). *Mind, self and society* (Vol. 111): Chicago University of Chicago Press.

Medved, M. I., & Brockmeier, J. (2008). Continuity Amid Chaos: Neurotrauma, Loss of Memory, and Sense of Self. *Qualitative Health Research, 18*(4), 469-479. doi:10.1177/1049732308315731

Mendez, M. F., Anderson, E., & Shapira, J. S. (2005). An Investigation of Moral Judgement in Frontotemporal Dementia. *Cognitive and Behavioral Neurology, 18*(4), 193-197. doi:10.1097/01.wnn.0000191292.17964.bb

Mendez, M. F., Chen, A. K., Shapira, J. S., & Miller, B. L. (2005). Acquired Sociopathy and Frontotemporal Dementia. *Dement Geriatr Cogn Disord, 20*(2-3), 99-104. doi:10.1159/000086474

Mendez, M. F., Fong, S. S., Shapira, J. S., Jimenez, E. E., Kaiser, N. C., Kremen, S. A., & Tsai, P.-H. (2014). Observation of Social Behavior in Frontotemporal Dementia. *American Journal of Alzheimer's Disease & Other Dementias®, 29*(3), 215-221. doi:10.1177/1533317513517035

Mendez, M. F., & Shapira, J. S. (2009). Altered emotional morality in frontotemporal dementia. *Cogn Neuropsychiatry, 14*(3), 165-179. doi:10.1080/13546800902924122

Menon, V. (2011). Large-scale brain networks and psychopathology: a unifying triple network model. *Trends in Cognitive Sciences, 15*(10), 483-506. doi:10.1016/j.tics.2011.08.003

Metcalfe, J., Snellenberg, J. X. V., DeRosse, P., Balsam, P., & Malhotra, A. K. (2012). Judgements of agency in schizophrenia: an impairment in autonoetic metacognition. *Philosophical Transactions of the Royal Society B: Biological Sciences, 367*(1594), 1391-1400. doi:doi:10.1098/rstb.2012.0006

Meulenbroek, O., Rijpkema, M., Kessels, R. P., Rikkert, M. G., & Fernandez, G. (2010). Autobiographical memory retrieval in patients with Alzheimer's disease. *Neuroimage, 53*(1), 331-340. doi:10.1016/j.neuroimage.2010.05.082

Midorikawa, A., Leyton, C. E., Foxe, D., Landin-Romero, R., Hodges, J. R., & Piguet, O. (2016). All is not lost: positive behaviors in Alzheimer's disease and behavioral-variant frontotemporal dementia with disease severity. *Journal of Alzheimer's disease, 54*(2), 549-558. doi:10.3233/JAD-160440

Miles, A. N., Fischer-Mogensen, L., Nielsen, N. H., Hermansen, S., & Berntsen, D. (2013). Turning back the hands of time: autobiographical memories in dementia cued by a museum setting. *Consciousness and Cognition, 22*(3), 1074-1081. doi:10.1016/j.concog.2013.07.008

Miller, B. L., & Hou, C. E. (2004). Portraits of artists: emergence of visual creativity in dementia. *Arch Neurol, 61*(6), 842-844. doi:10.1001/archneur.61.6.842

Miller, B. L., Seeley, W. W., Mychack, P., Rosen, H. J., Mena, I., & Boone, K. (2001). Neuroanatomy of the self: evidence from patients with frontotemporal dementia. *Neurology, 57*(5), 817-821. doi:10.1212/wnl.57.5.817

Miller, T. D., Chong, T. T., Aimola Davies, A. M., Ng, T. W., Johnson, M. R., Irani, S. R., . . . Rosenthal, C. R. (2017). Focal CA3 hippocampal subfield atrophy following LGI1 VGKC-complex antibody limbic encephalitis. *Brain, 140*, 1212-1219. doi:10.1093/brain/awx070

Millière, R., Carhart-Harris, R. L., Roseman, L., Trautwein, F.-M., & Berkovich-Ohana, A. (2018). Psychedelics, Meditation, and Self-Consciousness. *Frontiers in Psychology, 9*, 1475-1475. doi:10.3389/fpsyg.2018.01475

Milton, F., Butler, C. R., & Zeman, A. Z. (2011). Transient epileptic amnesia: deja vu heralding recovery of lost memories. *Journal of Neurology, Neurosurgery, and Psychiatry, 82*(10), 1178-1179. doi:10.1136/jnnp.2009.200147

Milton, F., Muhlert, N., Pindus, D. M., Butler, C. R., Kapur, N., Graham, K. S., & Zeman, A. Z. (2010). Remote memory deficits in transient epileptic amnesia. *Brain, 133*(Pt 5), 1368-1379. doi:10.1093/brain/awq055

Mioshi, E., Dawson, K., Mitchell, J., Arnold, R., & Hodges, J. R. (2006). The Addenbrooke's Cognitive Examination Revised (ACE R): a brief cognitive test battery for dementia screening. *International Journal of Geriatric Psychiatry, 21*(11), 1078-1085. doi:10.1002/gps.1610

Mioshi, E., Hsieh, S., Savage, S., Hornberger, M., & Hodges, J. R. (2010). Clinical staging and disease progression in frontotemporal dementia. *Neurology, 74*(20), 1591-1597. doi:10.1212/WNL.0b013e3181e04070

Mioshi, E., Kipps, C. M., Dawson, K., Mitchell, J., Graham, A., & Hodges, J. R. (2007). Activities of daily living in frontotemporal dementia and Alzheimer disease. *Neurology, 68*(24), 2077-2084. doi:10.1212/01.wnl.0000264897.13722.53

Mograbi, D. C., Brown, R. G., & Morris, R. G. (2009). Anosognosia in Alzheimer's disease – The petrified self. *Consciousness and Cognition, 18*(4), 989-1003. doi:10.1016/j.concog.2009.07.005

Molenberghs, P., Johnson, H., Henry, J. D., & Mattingley, J. B. (2016). Understanding the minds of others: A neuroimaging meta-analysis. *Neuroscience & Biobehavioral Reviews, 65*, 276-291. doi:10.1016/j.neubiorev.2016.03.020

Moll, H., Meltzoff, A. N., Merzsch, K., & Tomasello, M. (2013). Taking versus confronting visual perspectives in preschool children. *Developmental Psychology, 49*(4), 646-654. doi:10.1037/a0028633

Moll, J., Zahn, R., de Oliveira-Souza, R., Krueger, F., & Grafman, J. (2005). Opinion: the neural basis of human moral cognition. *Nature Reviews Neuroscience, 6*(10), 799-809. doi:10.1038/nrn1768

Moller, C., Hafkemeijer, A., Pijnenburg, Y. A. L., Rombouts, S., van der Grond, J., Dopper, E., . . . van der Flier, W. M. (2016). Different patterns of cortical gray matter loss over time in behavioral variant frontotemporal dementia and Alzheimer's disease. *Neurobiology of Aging, 38*, 21-31. doi:10.1016/j.neurobiolaging.2015.10.020

Morin, A. (2006). Levels of consciousness and self-awareness: A comparison and integration of various neurocognitive views. *Consciousness and Cognition, 15*(2), 358-371. doi:10.1016/j.concog.2005.09.006

Morris, R. G., & Mograbi, D. C. (2013). Anosognosia, autobiographical memory and self knowledge in Alzheimer's disease. *Cortex, 49*(6), 1553-1565. doi:10.1016/j.cortex.2012.09.006

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. doi:10.1016/j.conb.2006.03.013

Müller, S., Saur, R., Greve, B., Melms, A., Hautzinger, M., Fallgatter, A., & Leyhe, T. (2013). Similar autobiographical memory impairment in long-term secondary progressive multiple sclerosis and Alzheimer's disease. *Multiple Sclerosis Journal, 19*(2), 225-232. doi:10.1177/1352458512450352

Munera, C. P., Lomlomdjian, C., Gori, B., Terpiluk, V., Medel, N., Solis, P., & Kochen, S. (2014). Episodic and semantic autobiographical memory in temporal lobe epilepsy. *Epilepsy Research and Treatment, 2014*, 157452. doi:10.1155/2014/157452

Murphy, K. J., Troyer, A. K., Levine, B., & Moscovitch, M. (2008). Episodic, but not semantic, autobiographical memory is reduced in amnestic mild cognitive impairment. *Neuropsychologia, 46*(13), 3116-3123. doi:10.1016/j.neuropsychologia.2008.07.004

Nadel, L., Campbell, J., & Ryan, L. (2007). Autobiographical memory retrieval and hippocampal activation as a function of repetition and the passage of time. *Neural Plasticity, 2007*, 90472. doi:10.1155/2007/90472

Nadel, L., & Moscovitch, M. (1997). Memory consolidation, retrograde amnesia and the hippocampal complex. *Current Opinion in Neurobiology, 7*(2), 217-227.

Naylor, E., & Clare, L. (2008). Awareness of memory functioning, autobiographical memory and identity in early-stage dementia. *Neuropsychol Rehabil, 18*(5-6), 590-606. doi:10.1080/09602010701608681

Neary, D., Snowden, J. S., Northen, B., & Goulding, P. (1988). Dementia of frontal lobe type. *Journal of Neurology, Neurosurgery and Psychiatry, 51*(3), 353-361.

Neisser, U. (1981). John Dean's memory: A case study. *Cognition, 9*, 1-22. doi:10.1016/0010-0277(81)90011-1

Neisser, U. (1988). Five kinds of self-knowledge. *Philosophical Psychology, 1*(1), 35-59. doi:10.1080/09515088808572924

Nelson, K. (1986). *Event knowledge : structure and function in development* Hillsdale, N.J: Erlbaum.

Nestor, P. J., Graham, K. S., Bozeat, S., Simons, J. S., & Hodges, J. R. (2002). Memory consolidation and the hippocampus: further evidence from studies of autobiographical memory in semantic dementia and frontal variant frontotemporal dementia. *Neuropsychologia, 40*(6), 633-654. doi:10.1016/s0028-3932(01)00155-5

Newen, A., & Vogeley, K. (2003). Self-representation: Searching for a neural signature of self-consciousness. *Consciousness and Cognition, 12*(4), 529-543. doi:10.1016/S1053-8100(03)00080-1

Nichols, T. E., & Holmes, A. P. (2002). Nonparametric permutation tests for functional neuroimaging: a primer with examples. *Human Brain Mapping, 15*(1), 1-25. doi:10.1002/hbm.1058

Nigro, G., & Neisser, U. (1983). Point of view in personal memories. *Cognitive Psychology, 15*(4), 467-482. doi:10.1016/0010-0285(83)90016-6

Northoff, G., & Bermpohl, F. (2004). Cortical midline structures and the self. *Trends in Cognitive Sciences, 8*(3), 102-107. doi:10.1016/j.tics.2004.01.004

Northoff, G., Heinzel, A., de Greck, M., Bermpohl, F., Dobrowolny, H., & Panksepp, J. (2006). Self-referential processing in our brain—A meta-analysis of imaging studies on the self. *Neuroimage, 31*(1), 440-457. doi:10.1016/j.neuroimage.2005.12.002

Nour, M. M., Evans, L., Nutt, D., & Carhart-Harris, R. L. (2016). Ego-Dissolution and Psychedelics: Validation of the Ego-Dissolution Inventory (EDI). *Front Hum Neurosci, 10*(269). doi:10.3389/fnhum.2016.00269

O'Brien, R. G., & Kaiser, M. K. (1985). MANOVA method for analyzing repeated measures designs: An extensive primer. *Psychological Bulletin, 97*(2), 316-333. doi:10.1037/0033-2909.97.2.316

O'Callaghan, C., Shine, J. M., Hodges, J. R., Andrews-Hanna, J. R., & Irish, M. (2019). Hippocampal atrophy and intrinsic brain network dysfunction relate to alterations in mind wandering in neurodegeneration. *Proceedings of the National Academy of Sciences, 116*(8), 3316-3321. doi:10.1073/pnas.1818523116

Ogden, J. A., & Corkin, S. (1991). Memories of H. M *Memory mechanisms: A tribute to G. V. Goddard.* (pp. 195-215). Hillsdale, NJ, US: Lawrence Erlbaum Associates, Inc.

Olson, I. R., McCoy, D., Klobusicky, E., & Ross, L. A. (2013). Social cognition and the anterior temporal lobes: a review and theoretical framework. *Social Cognitive and Affective Neuroscience, 8*(2), 123-133. doi:10.1093/scan/nss119

Ortega-Escobar, J., Alcázar-Córcoles, M. Á., Puente-Rodríguez, L., & Peñaranda-Ramos, E. (2017). Psychopathy: Legal and neuroscientific aspects. *Anuario de Psicología Jurídica, 27*(1), 57-66. doi:10.1016/j.apj.2017.01.003

Palmer, E. J. (2003). An overview of the relationship between moral reasoning and offending. *Australian Psychologist, 38*(3), 165-174. doi:10.1080/00050060310001707177

Palmer, E. J. (2005). The relationship between moral reasoning and aggression, and the implications for practice. *Psychology, Crime & Law, 11*(4), 353-361. doi:10.1080/10683160500255190

Palombo, D. J., Alain, C., Soderlund, H., Khuu, W., & Levine, B. (2015). Severely deficient autobiographical memory (SDAM) in healthy adults: A new mnemonic syndrome. *Neuropsychologia, 72*, 105-118. doi:10.1016/j.neuropsychologia.2015.04.012

Palombo, D. J., Kapson, H. S., Lafleche, G., Vasterling, J. J., Marx, B. P., Franz, M., & Verfaellie, M. (2015). Alterations in autobiographical memory for a blast event in Operation Enduring Freedom and Operation Iraqi Freedom veterans with mild traumatic brain injury. *Neuropsychology, 29*(4), 543-549. doi:10.1037/neu0000198

Palombo, D. J., McKinnon, M. C., McIntosh, A. R., Anderson, A. K., Todd, R. M., & Levine, B. (2016). The neural correlates of memory for a life-threatening event: An fMRI study of passengers from flight AT236. *Clinical psychological science, 4*(2), 312-319. doi:10.1177/2167702615589308

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. doi:10.1016/j.cortex.2012.08.023

Panchal, H., Paholpak, P., Lee, G., Carr, A., Barsuglia, J. P., Mather, M., . . . Mendez, M. F. (2016). Neuropsychological and Neuroanatomical Correlates of the Social Norms Questionnaire in Frontotemporal Dementia Versus Alzheimer's Disease. *American Journal of Alzheimer's Disease & Other Dementias®, 31*(4), 326-332. doi:10.1177/1533317515617722

Parlar, M., Densmore, M., Hall, G. B. C., Lanius, R., & McKinnon, M. C. (2017). Neural and behavioural correlates of autobiographical memory retrieval in patients with major depressive disorder and a history of trauma exposure. *Neuropsychologia*. doi:10.1016/j.neuropsychologia.2017.07.004

Pascual, L., Rodrigues, P., & Gallardo-Pujol, D. (2013). How does morality work in the brain? A functional and structural perspective of moral behavior. *Frontiers in integrative neuroscience, 7*, 65-65. doi:10.3389/fnint.2013.00065

Patrick, C. J., Cuthbert, B. N., & Lang, P. J. (1994). Emotion in the criminal psychopath: fear image processing. *Journal of Abnormal Psychology, 103*(3), 523. doi:10.1037//0021-843x.103.3.523

Pearson, A., Ropar, D., & Hamilton, A. F. d. (2013). A review of visual perspective taking in autism spectrum disorder. *Front Hum Neurosci, 7*, 652. doi:10.3389/fnhum.2013.00652

Peng, W., & Huashan, L. (2014). Association between Moral Reasoning and Moral Behavior: A Systematic Review and Meta-Analysis. *Acta Psychologica Sinica, 46*(8), 1192-1207. doi:10.3724/sp.J.1041.2014.01202

Perner, J., Aichhorn, M., Kronbichler, M., Staffen, W., & Ladurner, G. (2006). Thinking of mental and other representations: The roles of left and right temporo-parietal junction. *Soc Neurosci, 1*(3-4), 245-258. doi:10.1080/17470910600989896

Perner, J., & Leekam, S. (2008). The curious incident of the photo that was accused of being false: Issues of domain specificity in development, autism, and brain imaging. *The Quarterly Journal of Experimental Psychology, 61*(1), 76-89. doi:10.1080/17470210701508756

Perry, R. J., Rosen, H. R., Kramer, J. H., Beer, J. S., Levenson, R. L., & Miller, B. L. (2001). Hemispheric dominance for emotions, empathy and social behaviour: evidence from right and left handers with frontotemporal dementia. *Neurocase, 7*(2), 145-160. doi:10.1093/neucas/7.2.145

Philippi, N., Noblet, V., Botzung, A., Despres, O., Renard, F., Sfikas, G., . . . Blanc, F. (2012). MRI-based volumetry correlates of autobiographical memory in Alzheimer's disease. *PLoS One, 7*(10), e46200. doi:10.1371/journal.pone.0046200

Philippi, N., Rousseau, F., Noblet, V., Botzung, A., Despres, O., Cretin, B., . . . Manning, L. (2015). Different Temporal Patterns of Specific and General Autobiographical Memories across the Lifespan in Alzheimer's Disease. *Behav Neurol, 2015*, 14. doi:10.1155/2015/963460

Piaget, J. (1924). *Le jugement et le raisonnement chez l'enfant.* Neuchatel: Delachaux et Niestle.

Piaget, J. (1932). *The moral judgment of the child*. Oxford, England: Harcourt, Brace.

Piaget, J., & Inhelder, B. (1956). *The child's conception of space*: Routledge & K. Paul.

Piguet, O., Hornberger, M., Mioshi, E., & Hodges, J. R. (2011). Behavioural-variant frontotemporal dementia: diagnosis, clinical staging, and management. *The Lancet. Neurology, 10*(2), 162-172. doi:S1474-4422(10)70299-4

Piguet, O., Kumfor, F., & Hodges, J. (2017). Diagnosing, monitoring and managing behavioural variant frontotemporal dementia. *Medical Journal of Australia, 207*(7), 303-308. doi:10.5694/mja16.01458

Piolino, P., Belliard, S., Desgranges, B., Perron, M., & Eustache, F. (2003). Autobiographical Memory and Autoneotic Consciousness in a case of Semantic Dementia. *Cogn Neuropsychol, 20*(7), 619-639. doi:10.1080/02643290242000899

Piolino, P., Desgranges, B., Belliard, S., Matuszewski, V., Lalevée, C., De La Sayette, V., & Eustache, F. (2003). Autobiographical memory and autonoetic consciousness: Triple dissociation in neurodegenerative diseases. *Brain, 126*(10), 2203-2219. doi:10.1093/brain/awg222

Piolino, P., Desgranges, B., & Eustache, F. (2000). *La mémoire autobiographique: théorie et pratique*: Solal Marseille.

Pizarro, D. (2007). Encyclopedia of Social Psychology. In R. F. Baumeister & K. D. Vohs (Eds.), (Vol. 1, pp. 591-592). Thousand Oaks

Thousand Oaks, California: SAGE Publications, Inc. Retrieved from http://sk.sagepub.com/reference/socialpsychology. doi:10.4135/9781412956253

Poletti, M., Enrici, I., & Adenzato, M. (2012). Cognitive and affective Theory of Mind in neurodegenerative diseases: neuropsychological, neuroanatomical and neurochemical levels. *Neuroscience and Biobehavioral Reviews, 36*(9), 2147-2164. doi:10.1016/j.neubiorev.2012.07.004

Poppenk, J., Evensmoen, H. R., Moscovitch, M., & Nadel, L. (2013). Long-axis specialization of the human hippocampus. *Trends in Cognitive Sciences, 17*(5), 230-240. doi:10.1016/j.tics.2013.03.005

Possin, K. L., Feigenbaum, D., Rankin, K. P., Smith, G. E., Boxer, A. L., Wood, K., . . . Kramer, J. H. (2013). Dissociable executive functions in behavioral variant frontotemporal and Alzheimer dementias. *Neurology, 80*(24), 2180. doi:10.1212/WNL.0b013e318296e940

Povinelli, D. J., Landau, K. R., & Perilloux, H. K. (1996). Self-Recognition in Young Children Using Delayed versus Live Feedback: Evidence of a Developmental Asynchrony. *Child Development, 67*(4), 1540-1554. doi:10.2307/1131717

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

Premack, D., & Woodruff, G. (1978). Does the chimpanzee have a theory of mind? *Behavioral and Brain Sciences, 1*(4), 515-526. doi:10.1017/S0140525X00076512

Rabin, J. S., & Rosenbaum, R. S. (2012). Familiarity modulates the functional relationship between theory of mind and autobiographical memory. *Neuroimage, 62*(1), 520-529. doi:10.1016/j.neuroimage.2012.05.002

Rabinovici, G. D., Seeley, W. W., Kim, E. J., Gorno-Tempini, M. L., Rascovsky, K., Pagliaro, T. A., . . . Rosen, H. J. (2007). Distinct MRI atrophy patterns in autopsy-proven Alzheimer's disease and frontotemporal lobar degeneration. *American Journal of Alzheimers Disease and Other Dementias, 22*(6), 474-488. doi:10.1177/1533317507308779

Race, E., Keane, M. M., & Verfaellie, M. (2011). Medial temporal lobe damage causes deficits in episodic memory and episodic future thinking not attributable to deficits in narrative construction. *Journal of Neuroscience, 31*(28), 10262-10269. doi:10.1523/JNEUROSCI.1145-11.2011

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Science United States of America, 98*(2), 676-682. doi:10.1073/pnas.98.2.676

Ramanan, S., Piguet, O., & Irish, M. (2018). Rethinking the Role of the Angular Gyrus in Remembering the Past and Imagining the Future: The Contextual Integration Model. *The Neuroscientist, 24*(4), 342-352. doi:10.1177/1073858417735514

Ramsey, R., Hansen, P., Apperly, I., & Samson, D. (2013). Seeing it my way or your way: frontoparietal brain areas sustain viewpoint-independent perspective selection processes. *Journal of Cognitive Neuroscience, 25*(5), 670-684. doi:10.1162/jocn_a_00345

Ranasinghe, K. G., Rankin, K. P., Lobach, I. V., Kramer, J. H., Sturm, V. E., Bettcher, B. M., . . . Miller, B. L. (2016). Cognition and neuropsychiatry in behavioral variant frontotemporal dementia by disease stage. *Neurology, 86*(7), 600-610. doi:10.1212/WNL.0000000000002373

Ranganath, C., & Ritchey, M. (2012). Two cortical systems for memory-guided behaviour. *Nature Reviews Neuroscience, 13*(10), 713-726. doi:10.1038/nrn3338

Rankin, K. P., Baldwin, E., Pace-Savitsky, C., Kramer, J. H., & Miller, B. L. (2005). Self awareness and personality change in dementia. *Journal of Neurology, Neurosurgery and Psychiatry, 76*(5), 632-639. doi:10.1136/jnnp.2004.042879

Rankin, K. P., Gorno-Tempini, M. L., Allison, S. C., Stanley, C. M., Glenn, S., Weiner, M. W., & Miller, B. L. (2006). Structural anatomy of empathy in neurodegenerative disease. *Brain, 129*(Pt 11), 2945-2956. doi:10.1093/brain/awl254

Rankin, K. P., Kramer, J. H., & Miller, B. L. (2005). Patterns of cognitive and emotional empathy in frontotemporal lobar degeneration. *Cognitive Behavioral Neurology, 18*(1), 28-36. doi:00146965-200503000-00004

Rankin, K. P., Kramer, J. H., Mychack, P., & Miller, B. L. (2003). Double dissociation of social functioning in frontotemporal dementia. *Neurology, 60*(2), 266-271. doi:10.1212/01.wnl.0000041497.07694.d2

Rascovsky, K., Hodges, J. R., Knopman, D., Mendez, M. F., Kramer, J. H., Neuhaus, J., . . . Miller, B. L. (2011). Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain, 134*(Pt 9), 2456-2477. doi:10.1093/brain/awr179

Rathbone, C. J., Conway, M. A., & Moulin, C. J. A. (2011). Remembering and imagining: The role of the self. *Consciousness and Cognition, 20*(4), 1175-1182. doi:10.1016/j.concog.2011.02.013

Rathbone, C. J., Ellis, J. A., Ahmed, S., Moulin, C. J. A., Ernst, A., & Butler, C. R. (2019). Using memories to support the self in Alzheimer's disease. *Cortex*. doi:10.1016/j.cortex.2019.09.007

Rathbone, C. J., Holmes, E. A., Murphy, S. E., & Ellis, J. A. (2015). Autobiographical memory and well-being in aging: The central role of semantic self-images. *Consciousness and Cognition, 33*, 422-431. doi:10.1016/j.concog.2015.02.017

Rathbone, C. J., Moulin, C. J. A., & Conway, M. A. (2009). Autobiographical memory and amnesia: Using conceptual knowledge to ground the self. *Neurocase, 15*(5), 405-418. doi:10.1080/13554790902849164

Reiman, E. M. (1997). The application of positron emission tomography to the study of normal and pathologic emotions. *Journal of Clinical Psychiatry, 58*, 4-12.

Reiman, E. M., Lane, R. D., Ahern, G. L., Schwartz, G. E., Davidson, R. J., Friston, K. J., . . . Chen, K. (1997). Neuroanatomical correlates of externally and internally generated human emotion. *American Journal of Psychiatry, 154*(7), 918-925. doi:10.1176/ajp.154.7.918

Reitan, R. M. (1958). Validity of the Trail Making Test as an indicator of organic brain damage. *Perceptual and motor skills, 8*(3), 271-276. doi:10.2466/pms.1958.8.3.271

Reniers, R. L. E. P., Corcoran, R., Völlm, B. A., Mashru, A., Howard, R., & Liddle, P. F. (2012). Moral decision-making, ToM, empathy and the default mode network. *Biological Psychology, 90*(3), 202-210. doi:10.1016/j.biopsycho.2012.03.009

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), 550-558. doi: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*. doi:10.1016/j.tics.2019.09.008

Renoult, L., & Rugg, M. D. (2019). An historical perspective on Endel Tulving's episodic-semantic dichotomy. *psyarxiv*. doi:10.31234/osf.io/uzdpf

Renoult, L., Tanguay, A., Beaudry, M., Tavakoli, P., Rabipour, S., Campbell, K., . . . Davidson, P. S. (2016). Personal semantics: Is it distinct from episodic and semantic memory? An electrophysiological study of memory for autobiographical facts and repeated events in honor of Shlomo Bentin. *Neuropsychologia, 83*, 242-256. doi:10.1016/j.neuropsychologia.2015.08.013

Rensen, Y. C. M., Kessels, R. P. C., Migo, E. M., Wester, A. J., Eling, P., & Kopelman, M. D. (2017). Personal semantic and episodic autobiographical memories in Korsakoff syndrome: A comparison of interview methods. *J Clin Exp Neuropsychol, 39*(6), 534-546. doi:10.1080/13803395.2016.1248811

Rey, A. (1941). L'examen psychologique dans les cas d'encéphalopathie traumatique. *Archives de Psychologie, 28*, 215-285.

Ribot, T. (1881). *Les maladies de la mémoire*. Paris: Germer Baillière.

Ricoeur, P. (2010). *Time and narrative* (Vol. 3): University of Chicago Press.

Roberts, S., Henry, J. D., & Molenberghs, P. (2019). Immoral behaviour following brain damage: A review. *Journal of Neuropsychology, 13*(3), 564-588. doi:10.1111/jnp.12155

Robin, J., & Moscovitch, M. (2017). Details, gist and schema: Hippocampal–neocortical interactions underlying recent and remote episodic and spatial memory. *Current Opinion in Behavioral Sciences, 17*, 114-123. doi:10.1016/j.cobeha.2017.07.016

Rosen, H. J., Allison, S. C., Ogar, J. M., Amici, S., Rose, K., Dronkers, N., . . . Gorno-Tempini, M. L. (2006). Behavioral features in semantic dementia vs other forms of progressive aphasias. *Neurology, 67*(10), 1752-1756. doi:10.1212/01.wnl.0000247630.29222.34

Rosen, H. J., Gorno-Tempini, M. L., Goldman, W. P., Perry, R. J., Schuff, N., Weiner, M., . . . Miller, B. L. (2002). Patterns of brain atrophy in frontotemporal dementia and semantic dementia. *Neurology, 58*(2), 198-208. doi:10.1212/wnl.58.2.198

Rosenbaum, R. S., McKinnon, M. C., Levine, B., & Moscovitch, M. (2004). Visual imagery deficits, impaired strategic retrieval, or memory loss: disentangling the nature of an amnesic person's autobiographical memory deficit. *Neuropsychologia, 42*(12), 1619-1635. doi:10.1016/j.neuropsychologia.2004.04.010

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. doi:10.1162/jocn.2008.20105

Ruby, P., Collette, F., D'Argembeau, A., Péters, F., Degueldre, C., Balteau, E., . . . Salmon, E. (2009). Perspective taking to assess self-personality: What's modified in Alzheimer's

disease? *Neurobiology of Aging, 30*(10), 1637-1651. doi:10.1016/j.neurobiolaging.2007.12.014

Ruby, P., Schmidt, C., Hogge, M., D'Argembeau, A., Collette, F., & Salmon, E. (2007). Social Mind Representation: Where Does It Fail in Frontotemporal Dementia? *Journal of Cognitive Neuroscience, 19*(4), 671-683. doi:10.1162/jocn.2007.19.4.671

Rudoy, J. D., Weintraub, S., & Paller, K. A. (2009). Recall of remote episodic memories can appear deficient because of a gist-based retrieval orientation. *Neuropsychologia, 47*(3), 938-941. doi:10.1016/j.neuropsychologia.2008.12.006

Rueckert, D., Sonoda, L. I., Hayes, C., Hill, D. L., Leach, M. O., & Hawkes, D. J. (1999). Nonrigid registration using free-form deformations: application to breast MR images. *IEEE Transactions on Medical Imaging, 18*(8), 712-721. doi:10.1109/42.796284

Rugg, M. D., & King, D. R. (2018). Ventral lateral parietal cortex and episodic memory retrieval. *Cortex, 107*, 238-250. doi:10.1016/j.cortex.2017.07.012

Rugg, M. D., & Vilberg, K. L. (2013). Brain networks underlying episodic memory retrieval. *Current Opinion in Neurobiology, 23*(2), 255-260. doi:10.1016/j.conb.2012.11.005

Sabat, S. R., & Gladstone, C. M. (2010). What intact social cognition and social behavior reveal about cognition in the moderate stage of Alzheimer's disease: A case study. *Dementia, 9*(1), 61-78. doi:10.1177/1471301210364450

Sabat, S. R., & Lee, J. M. (2011). Relatedness among people diagnosed with dementia: Social cognition and the possibility of friendship. *Dementia, 11*(3), 315-327. doi:10.1177/1471301211421069

Sachdeva, S., Singh, P., & Medin, D. (2011). Culture and the quest for universal principles in moral reasoning. *International Journal of Psychology, 46*(3), 161-176. doi:10.1080/00207594.2011.568486

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. doi:10.1016/j.dadm.2017.10.004

Salmon, D. P., & Bondi, M. W. (2009). Neuropsychological assessment of dementia. *Annual Review of Psychology, 60*, 257-282. doi:10.1146/annurev.psych.57.102904.190024

Samson, D., Apperly, I. A., Braithwaite, J. J., Andrews, B. J., & Bodley Scott, S. E. (2010). Seeing it their way: Evidence for rapid and involuntary computation of what other people see. *Journal of Experimental Psychology: Human Perception and Performance, 36*(5), 1255-1266. doi:10.1037/a0018729

Savage, S. A., Hsieh, S., Leslie, F., Foxe, D., Piguet, O., & Hodges, J. R. (2013). Distinguishing Subtypes in Primary Progressive Aphasia: Application of the Sydney Language Battery. *Dement Geriatr Cogn Disord, 35*(3-4), 208-218. doi:10.1159/000346389

Saxe, R., & Powell, L. J. (2006). It's the thought that counts: specific brain regions for one component of theory of mind. *Psychological Science, 17*(8), 692-699. doi:10.1111/j.1467-9280.2006.01768.x

Schacter, D. L., & Addis, D. R. (2007a). The cognitive neuroscience of constructive memory: Remembering the past and imagining the future. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 362*(1481), 773-786. doi:10.1098/rstb.2007.2087

Schacter, D. L., & Addis, D. R. (2007b). On the constructive episodic simulation of past and future events. *Behavioral and Brain Sciences, 30*(03), 331-332. doi:10.1017/S0140525X07002178

Schmidt, M. (1996). *Rey Auditory and Verbal Learning Test: A handbook*. Los Angeles: Western Psychological Services.

Schroeter, M. L., Ettrich, B., Menz, M., & Zysset, S. (2010). Traumatic brain injury affects the frontomedian cortex—An event-related fMRI study on evaluative judgments. *Neuropsychologia, 48*(1), 185-193. doi:10.1016/j.neuropsychologia.2009.09.004

Schroeter, M. L., Stein, T., Maslowski, N., & Neumann, J. (2009). Neural correlates of Alzheimer's disease and mild cognitive impairment: a systematic and quantitative meta-analysis involving 1351 patients. *Neuroimage, 47*(4), 1196-1206. doi:10.1016/j.neuroimage.2009.05.037

Schurz, M., Aichhorn, M., Martin, A., & Perner, J. (2013). Common brain areas engaged in false belief reasoning and visual perspective taking: a meta-analysis of functional brain imaging studies. *Front Hum Neurosci, 7*, 712-712. doi:10.3389/fnhum.2013.00712

Schurz, M., Radua, J., Aichhorn, M., Richlan, F., & Perner, J. (2014). Fractionating theory of mind: A meta-analysis of functional brain imaging studies. *Neuroscience & Biobehavioral Reviews, 42*, 9-34. doi:10.1016/j.neubiorev.2014.01.009

Schwarzkopf, S., Schilbach, L., Vogeley, K., & Timmermans, B. (2014). “Making it explicit” makes a difference: Evidence for a dissociation of spontaneous and intentional level 1 perspective taking in high-functioning autism. *Cognition, 131*(3), 345-354. doi:10.1016/j.cognition.2014.02.003

Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery & Psychiatry, 20*(1), 11-21. doi:10.1136/jnnp.20.1.11

Seeley, W. W. (2008). Selective functional, regional, and neuronal vulnerability in frontotemporal dementia. *Current opinion in neurology, 21*(6), 701-707. doi:10.1097/WCO.0b013e3283168e2d

Seeley, W. W., Crawford, R. K., Zhou, J., Miller, B. L., & Greicius, M. D. (2009). Neurodegenerative diseases target large-scale human brain networks. *Neuron, 62*(1), 42-52. doi:10.1016/j.neuron.2009.03.024

Seeley, W. W., & Miller, B. L. (2005). Disorders of the self in dementia. In T. E. Feinberg & J. P. Keenan (Eds.), *The Lost Self: Pathologies of the Brain and Identity* (pp. 147--165): Oxford University Press.

Seeley, W. W., Zhou, J., & Kim, E.-J. (2012). Frontotemporal Dementia:What Can the Behavioral Variant Teach Us about Human Brain Organization? *The Neuroscientist, 18*(4), 373-385. doi:10.1177/1073858411410354

Seidl, U., Lueken, U., Thomann, P. A., Geider, J., & Schroder, J. (2011). Autobiographical memory deficits in Alzheimer's disease. *Journal of Alzheimers Disease, 27*(3), 567-574. doi:10.3233/JAD-2011-110014

Seixas Lima, B., Levine, B., Graham, N., Leonard, C., Tang-Wai, D., Black, S., & Rochon, E. (2019). Impaired Coherence for Semantic but not Episodic Autobiographical Memory in Semantic Variant Primary Progressive Aphasia. *Cortex*. doi:10.1016/j.cortex.2019.10.008

Sekeres, M. J., Winocur, G., & Moscovitch, M. (2018). The hippocampus and related neocortical structures in memory transformation. *Neuroscience letters, 680*, 39-53. doi:10.1016/j.neulet.2018.05.006

Sheldon, S., & Chu, S. (2017). What versus where: Investigating how autobiographical memory retrieval differs when accessed with thematic versus spatial information. *Quarterly Journal of Experimental Psychology, 70*(9), 1909-1921. doi:10.1080/17470218.2016.1215478

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. doi:https://doi.org/10.1016/j.cortex.2015.11.005

Sheldon, S., & Levine, B. (2016). The role of the hippocampus in memory and mental construction. *Annals of the New York Academy of Sciences, 1369*(1), 76-92. doi:10.1111/nyas.13006

Simons, J. S., Graham, K. S., & Hodges, J. R. (2002). Perceptual and semantic contributions to episodic memory: evidence from semantic dementia and Alzheimer's disease. *Journal of Memory and Language, 47*(2), 197-213. doi:10.1016/S0749-596X(02)00003-7

Singer, N., Kreuzpointner, L., Sommer, M., Wüst, S., & Kudielka, B. M. (2019). Decision-making in everyday moral conflict situations: Development and validation of a new measure. *PLoS One, 14*(4), e0214747. doi:10.1371/journal.pone.0214747

Smith, E. E., & Jonides, J. (1997). Working memory: A view from neuroimaging. *Cognitive Psychology, 33*(1), 5-42. doi:10.1006/cogp.1997.0658

Smith, S. (2002). Fast robust automated brain extraction. *Human Brain Mapping, 17*(3), 143-155. doi:10.1002/hbm.10062

Smith, S., Jenkinson, M., Johansen-Berg, H., Rueckert, D., Nichols, T. E., Mackay, C. E., . . . Behrens, T. E. (2006). Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. *Neuroimage, 31*(4), 1487-1505. doi:10.1016/j.neuroimage.2006.02.024

Smith, S., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E. J., Johansen-Berg, H., . . . Flitney, D. E. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *Neuroimage, 23*, S208-S219. doi:10.1016/j.neuroimage.2004.07.051

Snowden, J. S., Bathgate, D., Varma, A., Blackshaw, A., Gibbons, Z. C., & Neary, D. (2001). Distinct behavioural profiles in frontotemporal dementia and semantic dementia. *Journal of Neurology, Neurosurgery and Psychiatry, 70*(3), 323-332. doi:10.1136/jnnp.70.3.323

Snowden, J. S., Griffiths, H., & Neary, D. (1994). Semantic dementia: Autobiographical contribution to preservation of meaning. *Cogn Neuropsychol, 11*(3), 265-288. doi:10.1080/02643299408251976

So, M., Foxe, D., Kumfor, F., Murray, C., Hsieh, S., Savage, G., . . . Piguet, O. (2018). Addenbrooke's Cognitive Examination III: Psychometric Characteristics and Relations to Functional Ability in Dementia. *Journal of the International Neuropsychological Society, 24*(8), 854-863. doi:10.1017/s1355617718000541

Soderlund, H., Moscovitch, M., Kumar, N., Daskalakis, Z. J., Flint, A., Herrmann, N., & Levine, B. (2014). Autobiographical episodic memory in major depressive disorder. *Journal of Abnormal Psychology, 122*(1), 51-60. doi:0.1037/a0035610

Sodian, B., Thoermer, C., & Metz, U. (2007). Now I see it but you don't: 14-month-olds can represent another person's visual perspective. *Developmental Science, 10*(2), 199-204. doi:10.1111/j.1467-7687.2007.00580.x

Sollberger, M., Stanley, C. M., Wilson, S. M., Gyurak, A., Beckman, V., Growdon, M., . . . Rankin, K. P. (2009). Neural basis of interpersonal traits in neurodegenerative diseases. *Neuropsychologia, 47*(13), 2812-2827. doi:10.1016/j.neuropsychologia.2009.06.006

Sommer, M., Rothmayr, C., Dohnel, K., Meinhardt, J., Schwerdtner, J., Sodian, B., & Hajak, G. (2010). How should I decide? The neural correlates of everyday moral reasoning. *Neuropsychologia, 48*(7), 2018-2026. doi:10.1016/j.neuropsychologia.2010.03.023

Spreng, R. N., Lockrow, A. W., DuPre, E., Setton, R., Spreng, K. A. P., & Turner, G. R. (2018). Semanticized autobiographical memory and the default - executive coupling hypothesis of aging. *Neuropsychologia, 110*, 37-43. doi:10.1016/j.neuropsychologia.2017.06.009

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. doi:10.1162/jocn.2008.21029

Squire, L. R., Cohen, N. J., & Nadel, L. (1984). The Medial Temporal Region and Memory Consolidation: A New Hypothesis *Memory consolidation* (pp. 197-222): Psychology Press.

Squire, L. R., & Kandel, E. R. (2009). *Memory: From Mind to Molecules*: Roberts & Company.

St-Laurent, M., Moscovitch, M., Levine, B., & McAndrews, M. P. (2009). Determinants of autobiographical memory in patients with unilateral temporal lobe epilepsy or excisions. *Neuropsychologia, 47*(11), 2211-2221. doi:10.1016/j.neuropsychologia.2009.01.032

St-Laurent, M., Moscovitch, M., Tau, M., & McAndrews, M. P. (2011). The temporal unraveling of autobiographical memory narratives in patients with temporal lobe epilepsy or excisions. *Hippocampus, 21*(4), 409-421. doi:10.1002/hipo.20757

St. Jacques, P. L., & Levine, B. (2007). Ageing and autobiographical memory for emotional and neutral events. *Memory, 15*(2), 129-144. doi:10.1080/09658210601119762

St. Jacques, P. L., Rubin, D. C., & Cabeza, R. (2012). Age-related effects on the neural correlates of autobiographical memory retrieval. *Neurobiology of Aging, 33*(7), 1298-1310. doi:10.1016/j.neurobiolaging.2010.11.007

Staniloiu, A., Borsutzky, S., Woermann, F. G., & Markowitsch, H. J. (2013). Social cognition in a case of amnesia with neurodevelopmental mechanisms. *Frontiers in Psychology, 4*, 342-342. doi:10.3389/fpsyg.2013.00342

Stanley, M. L., Henne, P., & De Brigard, F. (2019). Remembering moral and immoral actions in constructing the self. *Mem Cognit, 47*(3), 441-454. doi:10.3758/s13421-018-0880-y

Stanley, M. L., Henne, P., Iyengar, V., Sinnott-Armstrong, W., & De Brigard, F. (2017). I'm not the person I used to be: The self and autobiographical memories of immoral actions. *Journal of Experimental Psychology: General, 146*(6), 884-895. doi:10.1037/xge0000317

Steinvorth, S., Levine, B., & Corkin, S. (2005). Medial temporal lobe structures are needed to re-experience remote autobiographical memories: evidence from H.M. and W.R. *Neuropsychologia, 43*(4), 479-496. doi:10.1016/j.neuropsychologia.2005.01.001

Stevens, J. (1992). *Applied multivariate statistics for the social sciences, 2nd ed*. Hillsdale, NJ, US: Lawrence Erlbaum Associates, Inc.

Stoet, G. (2010). PsyToolkit: A software package for programming psychological experiments using Linux. *Behavior Research Methods, 42*(4), 1096-1104. doi:10.3758/brm.42.4.1096

Stoet, G. (2016). PsyToolkit: A Novel Web-Based Method for Running Online Questionnaires and Reaction-Time Experiments. *Teaching of Psychology, 44*(1), 24-31. doi:10.1177/0098628316677643

Strohminger, N., & Nichols, S. (2014). The essential moral self. *Cognition, 131*(1), 159-171. doi:10.1016/j.cognition.2013.12.005

Strohminger, N., & Nichols, S. (2015). Neurodegeneration and Identity. *Psychological Science, 26*(9), 1469-1479. doi:10.1177/0956797615592381

Sturm, V. E., Yokoyama, J. S., Seeley, W. W., Kramer, J. H., Miller, B. L., & Rankin, K. P. (2013). Heightened emotional contagion in mild cognitive impairment and Alzheimer's disease is associated with temporal lobe degeneration. *Proceedings of the National Academy of Sciences, 110*(24), 9944-9949. doi:10.1073/pnas.1301119110

Stuss, D. T., Gallup, G. G., Jr., & Alexander, M. P. (2001). The frontal lobes are necessary for 'theory of mind'. *Brain, 124*(Pt 2), 279-286. doi:10.1093/brain/124.2.279

Suddendorf, T., Addis, D. R., & Corballis, M. C. (2009). Mental time travel and the shaping of the human mind. *Philosophical Transactions of the Royal Society B: Biological Sciences, 364*(1521), 1317-1324. doi:10.1098/rstb.2008.0301

Suddendorf, T., & Busby, J. (2003). Mental time travel in animals? *Trends in Cognitive Sciences, 7*(9), 391-396. doi:10.1016/S1364-6613(03)00187-6

Syed, M., & Nelson, S. C. (2015). Guidelines for Establishing Reliability When Coding Narrative Data. *Emerging Adulthood, 3*(6), 375-387. doi:10.1177/2167696815587648

Synn, A., Mothakunnel, A., Kumfor, F., Chen, Y., Piguet, O., Hodges, J. R., & Irish, M. (2018). Mental States in Moving Shapes: Distinct Cortical and Subcortical Contributions to Theory of Mind Impairments in Dementia. *J Alzheimers Dis, 61*(2), 521-535. doi:10.3233/JAD-170809

Szpunar, K. (2010). Episodic Future Thought. *Perspectives on Psychological Science, 5*(2), 142-162. doi:10.1177/1745691610362350

Szpunar, K., Watson, J., & McDermott, K. B. (2007). Neural substrates of envisioning the future. *Proceedings of the National Academy of Sciences, 104*(2), 642-647. doi:10.1073/pnas.0610082104

Taber-Thomas, B. C., Asp, E. W., Koenigs, M., Sutterer, M., Anderson, S. W., & Tranel, D. (2014). Arrested development: early prefrontal lesions impair the maturation of moral judgement. *Brain : a journal of neurology, 137*(Pt 4), 1254-1261. doi:10.1093/brain/awt377

Tagliazucchi, E., Roseman, L., Kaelen, M., Orban, C., Muthukumaraswamy, S. D., Murphy, K., . . . Crossley, N. (2016). Increased global functional connectivity correlates with LSD-induced ego dissolution. *Current Biology, 26*(8), 1043-1050. doi:10.1016/j.cub.2016.02.010

Takeda, A., Sturm, V. E., Rankin, K. P., Ketelle, R., Miller, B. L., & Perry, D. C. (2019). Relationship Turmoil and Emotional Empathy in Frontotemporal Dementia. *Alzheimer Disease & Associated Disorders, 33*(3), 260-265. doi:10.1097/wad.0000000000000317

Thomas, B. C., Croft, K. E., & Tranel, D. (2011). Harming kin to save strangers: further evidence for abnormally utilitarian moral judgments after ventromedial prefrontal

damage. *Journal of Cognitive Neuroscience, 23*(9), 2186-2196. doi:10.1162/jocn.2010.21591

Thomas-Anterion, C., Jacquin, K., & Laurent, B. (2000). Differential mechanisms of impairment of remote memory in Alzheimer's and frontotemporal dementia. *Dement Geriatr Cogn Disord, 11*(2), 100-106. doi:10.1159/000017221

Thompson, P. M., Hayashi, K. M., Dutton, R. A., Chiang, M.-C., Leow, A. D., Sowell, E. R., . . . Toga, A. W. (2007). Tracking Alzheimer's disease. *Annals of the New York Academy of Sciences, 1097*, 183-214. doi:10.1196/annals.1379.017

Thomsen, D. K. (2009). There is more to life stories than memories. *Memory, 17*(4), 445-457. doi:10.1080/09658210902740878

Thomson, J. J. (1976). Killing, letting die, and the trolley problem. *The Monist, 59*(2), 204-217.

Tippett, L. J., Prebble, S. C., & Addis, D. R. (2018). The Persistence of the Self over Time in Mild Cognitive Impairment and Alzheimer's Disease. *Frontiers in Psychology, 9*(94). doi:10.3389/fpsyg.2018.00094

Todd, C. M., & Perlmutter, M. (1980). Reality recalled by preschool children. *New Directions for Child and Adolescent Development, 1980*(10), 69-85. doi:10.1002/cd.23219801007

Tombaugh, T. N. (2004). Trail Making Test A and B: normative data stratified by age and education. *Archives of Clinical Neuropsychology, 19*(2), 203-214. doi:10.1016/S0887-6177(03)00039-8

Torralva, T., Gleichgerrcht, E., Torres Ardila, M. J., Roca, M., & Manes, F. F. (2015). Differential Cognitive and Affective Theory of Mind Abilities at Mild and Moderate Stages of Behavioral Variant Frontotemporal Dementia. *Cognitive and Behavioral Neurology, 28*(2), 63-70. doi:10.1097/WNN.0000000000000053

Trevarthen, C. (1984). Emotions in infancy: Regulators of contact and relationships with persons. *Approaches to emotion*, 129-157.

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. doi:10.3233/JAD-160592

Tulving, E. (1972). Episodic and semantic memory. In E. Tulving & W. Donaldson (Eds.), *Organization of memory.* (pp. 381-403). New York: Academic Press.

Uddin, L. Q. (2015). Salience processing and insular cortical function and dysfunction. *Nature Reviews Neuroscience, 16*(1), 55. doi:10.1038/nrn3857

Valdesolo, P., & DeSteno, D. (2006). Manipulations of Emotional Context Shape Moral Judgment. *Psychological Science, 17*(6), 476-477. doi:10.1111/j.1467-9280.2006.01731.x

van den Berg, E., Kant, N., & Postma, A. (2012). Remember to buy milk on the way home! A meta-analytic review of prospective memory in mild cognitive impairment and dementia. *Journal of the International Neuropsychological Society, 18*(4), 706-716. doi:10.1017/S1355617712000331

Van den Stock, J., Stam, D., De Winter, F. L., Mantini, D., Szmrecsanyi, B., Van Laere, K., . . . Vandenbulcke, M. (2017). Moral processing deficit in behavioral variant frontotemporal dementia is associated with facial emotion recognition and brain changes in default mode and salience network areas. *Brain and Behaviour, 7*(12), e00843. doi:10.1002/brb3.843

Van Overwalle, F. (2009). Social cognition and the brain: A meta-analysis. *Human Brain Mapping, 30*(3), 829-858. doi:10.1002/hbm.20547

Vanderveren, E., Bijttebier, P., & Hermans, D. (2017). The Importance of Memory Specificity and Memory Coherence for the Self: Linking Two Characteristics of Autobiographical Memory. *Frontiers in Psychology, 8*. doi:10.3389/fpsyg.2017.02250

Vemuri, P., Gunter, J. L., Senjem, M. L., Whitwell, J. L., Kantarci, K., Knopman, D. S., . . . Jack, C. R., Jr. (2008). Alzheimer's disease diagnosis in individual subjects using structural MR images: validation studies. *Neuroimage, 39*(3), 1186-1197. doi:10.1016/j.neuroimage.2007.09.073

Vendetti, M. S., & Bunge, S. A. (2014). Evolutionary and developmental changes in the lateral frontoparietal network: a little goes a long way for higher-level cognition. *Neuron, 84*(5), 906-917. doi:10.1016/j.neuron.2014.09.035

Viard, A., Piolino, P., Belliard, S., de La Sayette, V., Desgranges, B., & Eustache, F. (2014). Episodic future thinking in semantic dementia: a cognitive and FMRI study. *PLoS One, 9*(10), e111046. doi:10.1371/journal.pone.0111046

Von Der Heide, R. J., Skipper, L. M., Klobusicky, E., & Olson, I. R. (2013). Dissecting the uncinate fasciculus: disorders, controversies and a hypothesis. *Brain : a journal of neurology, 136*(Pt 6), 1692-1707. doi:10.1093/brain/awt094

Wammes, J. D., Good, T. J., & Fernandes, M. A. (2017). Autobiographical and episodic memory deficits in mild traumatic brain injury. *Brain Cogn, 111*, 112-126. doi:10.1016/j.bandc.2016.11.004

Wang, Q., Hou, Y., Koh, J. B. K., Song, Q., & Yang, Y. (2018). Culturally Motivated Remembering: The Moderating Role of Culture for the Relation of Episodic Memory to Well-Being. *Clinical psychological science, 6*(6), 860-871. doi:10.1177/2167702618784012

Wechsler, D. (1997). *Wechsler Memory Scale - Third edition: Administration and Scoring Manual.* San Antonio, TX: Psychological Corporation.

Wedderburn, C., Wear, H., Brown, J., Mason, S. J., Barker, R. A., Hodges, J. R., & Williams-Gray, C. (2008). The utility of the Cambridge Behavioural Inventory in neurodegenerative disease. *Journal of Neurology, Neurosurgery and Psychiatry, 79*(5), 500-503. doi:10.1136/jnnp.2007.122028

Westmacott, R., Leach, L., Freedman, M., & Moscovitch, M. (2001). Different patterns of autobiographical memory loss in semantic dementia and medial temporal lobe amnesia: A challenge to consolidation theory. *Neurocase, 7*(1), 37-55. doi:10.1093/neucas/7.1.37

Westmacott, R., & Moscovitch, M. (2003). The contribution of autobiographical significance to semantic memory. *Neuropsychologia, 31*(5), 761-774. doi:10.1016/s0028-3932(03)00147-7

Wheatley, T., & Haidt, J. (2005). Hypnotic Disgust Makes Moral Judgments More Severe. *Psychological Science, 16*(10), 780-784. doi:10.1111/j.1467-9280.2005.01614.x

Wheeler, M. A., Stuss, D. T., & Tulving, E. T. (1997). Toward a theory of episodic memory: The frontal lobes and autonoetic consciousness. *Psychological Bulletin, 121*, 331-354. doi:10.1037/0033-2909.121.3.331

Whitwell, J. L., Boeve, B. F., Weigand, S. D., Senjem, M. L., Gunter, J. L., Baker, M. C., . . . Josephs, K. A. (2015). Brain atrophy over time in genetic and sporadic

frontotemporal dementia: a study of 198 serial magnetic resonance images. *European Journal of Neurology, 22*(5), 745-752. doi:10.1111/ene.12675

Whitwell, J. L., Weigand, S. D., Boeve, B. F., Senjem, M. L., Gunter, J. L., DeJesus-Hernandez, M., . . . Josephs, K. A. (2012). Neuroimaging signatures of frontotemporal dementia genetics: C9ORF72, tau, progranulin and sporadics. *Brain, 135*(Pt 3), 794-806. doi:10.1093/brain/aws001

Wiggins, J. S. (1995). *Interpersonal Adjective Scales*: Psychological Assessment Resources.

Willoughby, K. A., Desrocher, M., Levine, B., & Rovet, J. F. (2012). Episodic and Semantic Autobiographical Memory and Everyday Memory during Late Childhood and Early Adolescence. *Frontiers in Psychology, 3*, 53. doi:10.3389/fpsyg.2012.00053

Willoughby, K. A., McAndrews, M. P., & Rovet, J. (2013). Effects of early thyroid hormone deficiency on children's autobiographical memory performance. *Journal of the International Neuropsychological Society, 19*(4), 419-429. doi:10.1017/S1355617712001488

Wimmer, H., & Perner, J. (1983). Beliefs about beliefs: Representation and constraining function of wrong beliefs in young children's understanding of deception. *Cognition, 13*(1), 103-128. doi:10.1016/0010-0277(83)90004-5

Wong, S., Irish, M., & Hornberger, M. (2018). Behavioural-variant frontotemporal dementia: A unique window into the disrupted self: Reply to Genon & Salmon. *Cortex, 104*, 130-132. doi:10.1016/j.cortex.2018.02.010

Wong, S., Irish, M., Leshikar, E. D., Duarte, A., Bertoux, M., Savage, G., . . . Hornberger, M. (2017). The self-reference effect in dementia: Differential involvement of cortical midline structures in Alzheimer's disease and behavioural-variant frontotemporal dementia. *Cortex, 91*, 169-185. doi:10.1016/j.cortex.2016.09.013

Wraga, M., Creem, S. H., & Proffitt, D. R. (2000). Updating displays after imagined object and viewer rotations. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 26*(1), 151. doi:10.1037/0278-7393.26.1.151

Yirmiya, N., Sigman, M., & Zacks, D. (1994). Perceptual perspective-taking and seriation abilities in high-functioning children with autism. *Development and psychopathology, 6*(2), 263-272. doi:10.1017/S0954579400004570

Young, L., Cushman, F., Hauser, M., & Saxe, R. (2007). The neural basis of the interaction between theory of mind and moral judgment. *Proceedings of the National Academy of Sciences, 104*(20), 8235-8240. doi:10.1073/pnas.0701408104

Young, L., Dodell-Feder, D., & Saxe, R. (2010). What gets the attention of the temporo-parietal junction? An fMRI investigation of attention and theory of mind. *Neuropsychologia, 48*(9), 2658-2664. doi:10.1016/j.neuropsychologia.2010.05.012

Zacks, J. M. (2008). Neuroimaging studies of mental rotation: a meta-analysis and review. *Journal of Cognitive Neuroscience, 20*(1), 1-19. doi:10.1162/jocn.2008.20013

Zacks, J. M., & Tversky, B. (2005). Multiple systems for spatial imagery: Transformations of objects and bodies. *Spatial Cognition and Computation, 5*(4), 271-306. doi:10.1207/s15427633scc0504_1

Zeman, A., Byruck, M., Tallis, P., Vossel, K., & Tranel, D. (2017). Touching the void – first and third person perspectives in two cases of autobiographical amnesia linked to temporal lobe epilepsy. *Neuropsychologia*. doi:0.1016/j.neuropsychologia.2017.07.007

Zeman, A., Hoefeijzers, S., Milton, F., Dewar, M., Carr, M., & Streatfield, C. (2016). The GABAB receptor agonist, baclofen, contributes to three distinct varieties of amnesia

in the human brain - A detailed case report. *Cortex, 74*, 9-19. doi:10.1016/j.cortex.2015.10.005

Zhang, F., Ho, Y. W., & Fung, H. H. (2015). Learning from Normal Aging: Preserved Emotional Functioning Facilitates Adaptation among Early Alzheimer's Disease Patients. *Aging and disease, 6*(3), 208-215. doi:10.14336/AD.2014.0620

Zhang, Y., Brady, M., & Smith, S. (2001). Segmentation of brain MR images through a hidden Markov random field model and the expectation-maximization algorithm. *IEEE Transactions on Medical Imaging, 20*(1), 45-57. doi:10.1109/42.906424

Zhou, J., Greicius, M. D., Gennatas, E. D., Growdon, M. E., Jang, J. Y., Rabinovici, G. D., . . . Seeley, W. W. (2010). Divergent network connectivity changes in behavioural variant frontotemporal dementia and Alzheimer's disease. *Brain, 133*(Pt 5), 1352-1367. doi:10.1093/brain/awq075

Zysset, S., Huber, O., Samson, A., Ferstl, E. C., & von Cramon, D. Y. (2003). Functional specialization within the anterior medial prefrontal cortex: a functional magnetic resonance imaging study with human subjects. *Neuroscience letters, 335*(3), 183-186. doi:10.1016/S0304-3940(02)01196-5

# Appendix A

## Chapter 2

**Table A2.1.** Summarised international consensus criteria for Alzheimer's disease (AD)

| **Dementia** |
|---|
| Presence of cognitive or behavioural symptoms that: |
| Interfere with functioning |
| Represent a decline from previous levels of functioning |
| Are not explained by delirium or major psychiatric disorder |
| Are detected and diagnosed through a combination of history-taking and objective assessment |
| Involve a minimum of two of the following domains: |
| Memory |
| Executive function |
| Visuospatial function |
| Language |
| Personality or behaviour |
| **Probable AD** |
| Meets criteria for dementia, AND |
| Insidious onset |
| Clear deterioration in cognition |
| Initial and most prominent deficits are evidence in one of the following categories: |
| Amnestic presentation: deficits include impairment in learning and recall of recently learned information, along with cognitive dysfunction in one other cognitive domain |
| Non-amnestic presentations: |
| Language presentation: most prominent deficits are in word-finding, but deficits in other cognitive domains are also present |

| | |
|---|---|
| | Visuospatial presentation: most prominent deficits are in spatial cognition, but deficits in other cognitive domains are also present |
| | Executive dysfunction: most prominent deficits are impaired reasoning, judgment, and problem-solving, but deficits in other cognitive domains are also present |

*Notes:* Taken from McKhann et al. (2011).

**Table A2.2.** Summarised international consensus criteria for semantic dementia (SD)

| |
|---|
| **Primary progressive aphasia (PPA)** |
| Most prominent clinical feature is difficulty with language |
| These deficits are the principal cause of impaired daily living activities |
| Aphasia should be the most prominent deficit at symptom onset and for the initial phases of the disease |
| **Semantic dementia (SD)** |
| Meets criteria for PPA |
| Both of the following core features must be present: |
| Impaired confrontation naming |
| Impaired single word comprehension |
| At least three of the following other diagnostic features must be present: |
| Impaired object knowledge |
| Surface dyslexia or dysgraphia |
| Spared repetition |
| Spared speech production (grammar and motor speech) |
| **Imaging supported diagnosis of SD** |
| Clinical diagnosis of SD, AND |
| Neuroimaging results consistent with SD (i.e., predominant anterior temporal lobe atrophy on MRI and/or predominant anterior temporal lobe hypometabolism/hypoperfusion on PET or SPECT) |
| **SD with definite pathology** |
| Clinical diagnosis of SD, AND |
| Histopathological evidence of a specific neurodegenerative pathology, OR |

| | |
|---|---|
| | Presence of a known pathogenic mutation |

*Notes:* Taken from Gorno-Tempini et al. (2011). MRI = magnetic resonance imaging; PET = positron emission tomography; SPECT = single-photon emission computed tomography.

**Table A2.3** Summarised international consensus criteria for the behavioural variant of frontotemporal dementia (bvFTD)

| **Possible bvFTD** |
|---|
| Three of the following symptoms must be present, persistent, and/or recurrent: |
| Disinhibition |
| Apathy |
| Loss of empathy |
| Perseverative/stereotyped behaviour |
| Hyperorality/dietary changes |
| Executive function deficits with relative sparing of memory & visuospatial function |
| **Probable bvFTD** |
| Meets criteria for possible bvFTD |
| Exhibits significant functional decline |
| Neuroimaging results consistent with bvFTD (i.e., frontal and/or temporal atrophy on MRI/CT; frontal and/or temporal hypometabolism/hypoperfusion on PET or SPECT) |
| **Definite bvFTD** |
| Meets criteria for possible or probable bvFTD, AND |
| Histopathological evidence of FTLD on biopsy or post-mortem, OR |
| Presence of a known pathogenic mutation |

*Notes:* Taken from Rascovsky et al. (2011). CT = computed tomography; FTLD = frontotemporal lobar degeneration; MRI = magnetic resonance imaging; PET = positron emission tomography; SPECT = single-photon emission computed tomography.

# Appendix B

## Chapter 3

*A3.1. Excerpt from a Control participant's memory with external details (Specific Episodes [SE], Extended Episodes [EE], Personal Semantics [PS] and General Semantics [GS]) separated according to the NExt taxonomy, and internal (INT) details delineated based on the original Levine et al. (2002) scoring protocol*

"My 2 children… both travelled from England [GS] for my 70th birthday (INT)… my son said to me 'Did you have an inkling that I was coming?' [SE]…And we all went out (INT)… they took me to a beautiful restaurant (INT)… and it was just superb (INT)… It was a restaurant that I'd always wanted to go to [PS]. It was a very exclusive restaurant [GS]… always, when I drove past, used to look at it and think, 'Oh, one day I'd like to go there' [EE]."

*A3.2. Overall performance on the AI*

Figure A3.1. displays the Total Content details summed across all time points for each group. Total content did not significantly differ between the groups ($F(2, 47 = 1.74$, $p = .19$).

*A3.3. Internal detail performance*

Across all time periods combined, a significant between-group effect was apparent ($F(2, 47) = 9.94$, $p < .001$), such that patient groups provided significantly less Internal details than Controls ($ps = .003$ and .001 for SD and AD, respectively), with no significant differences between AD and SD ($p = 1.00$) (Figure A3.2.). This was also the case for the Remote period ($F(2, 47) = 7.36$, $p = .002$), with patients providing less Internal details than Controls ($ps = .01$ & .003 for SD and AD), and no significant between-patient group differences ($p = 1.00$). However, in the Recent period ($F(2, 47) = 6.85$, $p = .002$), while ADs gave significantly less Internal details than Controls ($p = .002$), SDs performed at Control level ($p = .11$). No significant differences were found between SD and AD ($p = .68$).

*A3.4. Overall external detail performance*

No between-group differences emerged for External details provided across all time periods combined ($F(2, 47) = .24$, $p = .79$), nor for the Remote ($F(2, 47) = .66$, $p = .52$) or Recent periods ($F\ 2, 47) = .49$, $p = .61$) (Figure A3.3.).

*A3.5. Effect of dementia onset during Middle Adulthood on AI performance*

No significant differences in the number of Total Content, Internal details, or any of the NExt external detail categories (Specific Episodes, Extended Episodes, Personal Semantic or General Semantics) for the Middle Adulthood period were apparent between patients with disease onset during this period (i.e., between age 35 and 55 years) and those with onset post-age 55 in either SD *(Total Content:* U = 15, $p = .63$; *Internal:* U = 16, $p = .75$; *SE:* U = 17.5, $p = .94$; *EE:* 12.5, $p = .37$; *PS*: *U* = 13.5, $p = .46$, *GS:* U = 16.5, $p = .81$) or AD patients (*Total Content:* U = 27, $p = .92$; *Internal:* U = 25, $p = .75$; *SE:* U = 25, $p = .75$; *EE:* U = 24, $p = .67$; *PS:* U = 24.5, $p = .71$, GS: U = 26.5, $p = .87$). This suggests that dementia onset in the Middle Adulthood period did not impact upon the profile of details provided for this epoch.

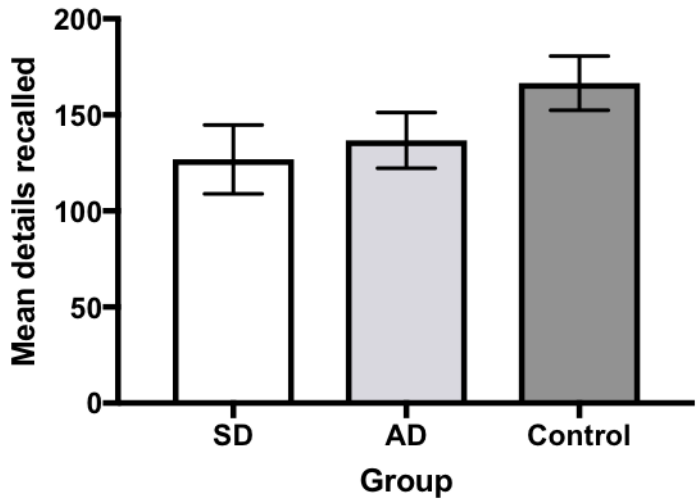



*Figure A3.1.* Total Content details summed across all time periods for each group (estimated marginal means controlling for age; error bars represent SEM). SD: semantic dementia; AD: Alzheimer's disease.

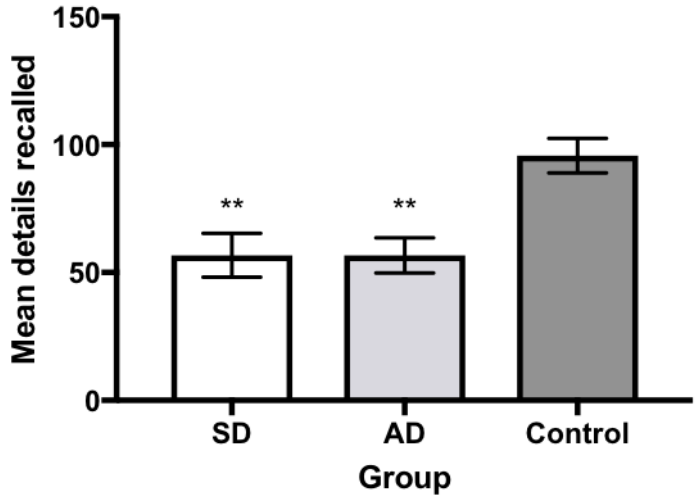



*Figure A3.2.* Total Internal details summed across all time periods for each group (estimated marginal means controlling for age; error bars represent SEM). SD: semantic dementia; AD: Alzheimer's disease. Significant difference from Control performance at ** $p < .01$.

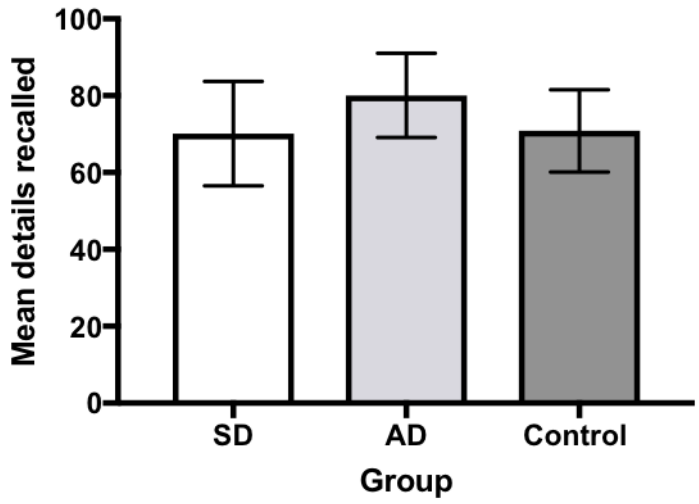



*Figure A3.3.* Total External details summed across all time periods for each group (estimated marginal means controlling for age; error bars represent SEM). SD: semantic dementia; AD: Alzheimer's disease.

# Appendix C

**Chapter 4**

*A4.1. Excerpt from a Control participant's future event with external details (Specific Episodes [SE], Extended Episodes [EE], Personal Semantics [PS] and General Semantics [GS]) separated according to the NExt taxonomy, and internal (INT) details delineated based on the original Levine et al. (2002) scoring protocol*

"I love driving cars [PS]… I'm thinking of changing (INT) to a twin cab (INT) with similar power (INT). That means I can put the boat trailer [EE] and the motor [EE] and everything in the back [EE] and still put the dogs [EE] in the backseat [EE] and still go [EE]... We may even upgrade the caravan [SE]. It will happen in Melbourne (INT)… knowing Melbourne it could be one of three seasons [GS]."

*A4.2. Overall performance on the Past-Future thinking task*

Figure A4.1. displays the Total Content details provided by each group, for Past and Future events. For the Past period, a significant between-group effect emerged ($F(2, 35) = 6.99$, $p = .003$, partial $\eta^2 = .29$), such that AD patients provided significantly less Total Content than Controls ($p = .002$). No significant differences emerged between SD and Control ($p = .45$) or SD and AD patients ($p = .07$). A similar pattern was apparent for Future events ($F(2, 35) = 4.23$, $p = .02$, partial $\eta^2 = .20$), with less Total Content details provided by AD compared with Controls ($p = .02$), with no significant differences between SD and Control ($p = .23$) or AD ($p = .62$) groups.

*A4.3. Internal detail performance*

For Past events, a significant between-group effect emerged for Internal details ($F(2, 35) = 15.94$, $p < .001$, partial $\eta^2 = .48$, such that AD patients produced significantly less Internal details compared with Controls ($p < .001$) and SDs ($p = .01$), while SD patients performed in line with Controls ($p = .05$) (Figure A4.2.). For Future events, a significant effect of group was also found ($F(2, 35) = 23.77$, $p < .001$, partial $\eta^2 = .58$, with both SD and AD groups providing reduced Internal details compared with Controls (*p*s both < .001). No significant differences emerged between SD and AD groups ($p = .98$).

*A4.5. Overall external detail performance*

No between-group differences emerged for the External details provided for Past ($F(2, 35) = .97$, $p = .39$, partial $\eta^2 = .05$) or Future ($F(2, 35) = 2.56$, $p = .09$, partial $\eta^2 = .13$) events (Figure A4.3.).

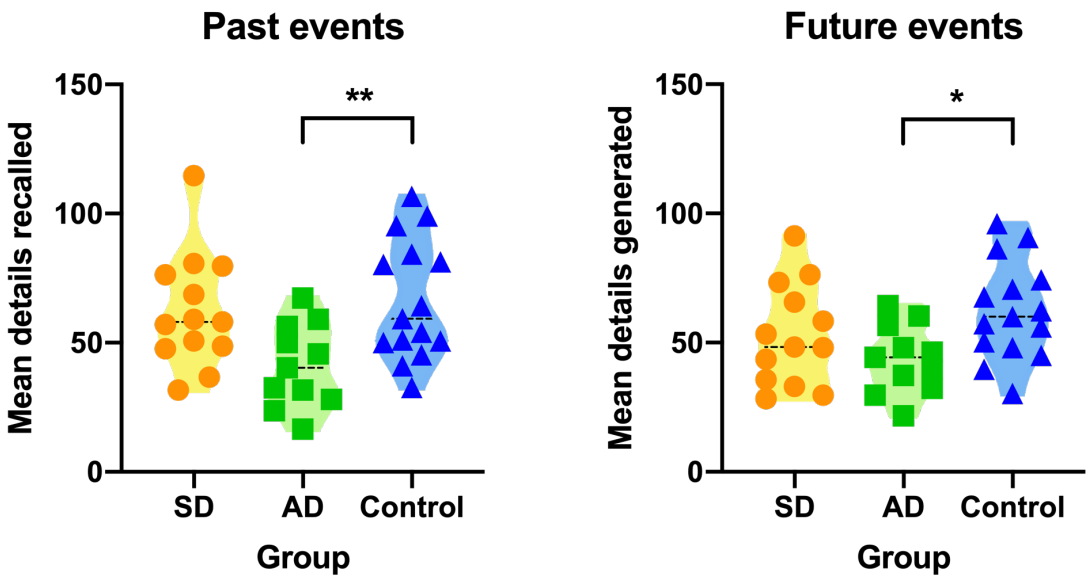



*Figure A4.1.* Violin plots representing the mean Total Content details provided by each group, for Past (left) and Future (right) events. AD = Alzheimer's disease; SD = semantic dementia. Asterisks denote significant difference between groups at *$p < .05$ and **$p < .01$.

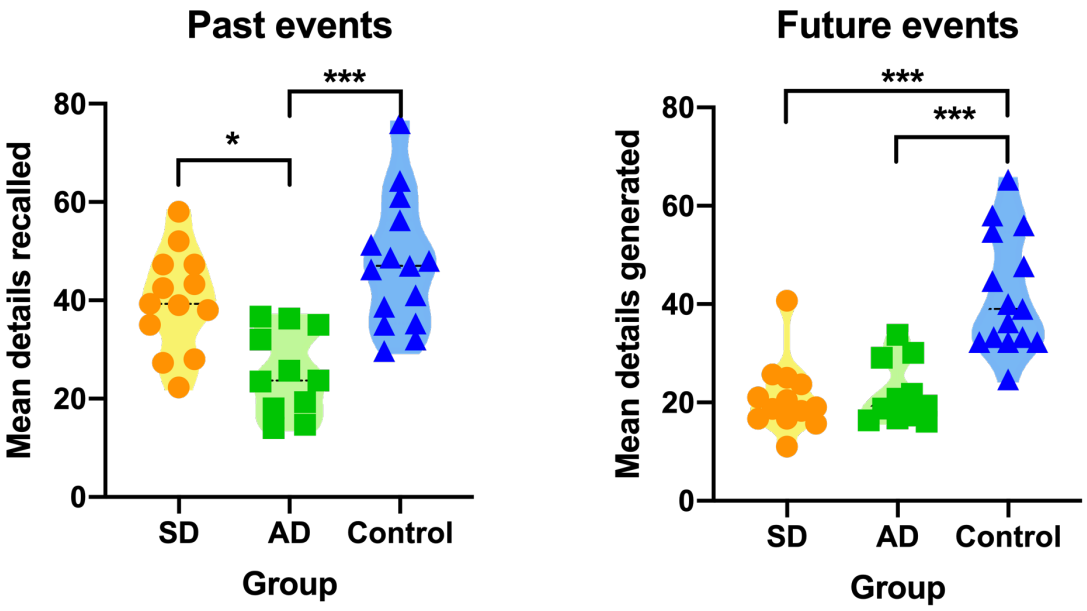



*Figure A4.2.* Violin plots representing the mean Internal details provided by each group, for Past (left) and Future (right) events. AD = Alzheimer's disease; SD = semantic dementia. Asterisks denote significant difference between groups at *$p$ < .05 and ***$p$ < .001.

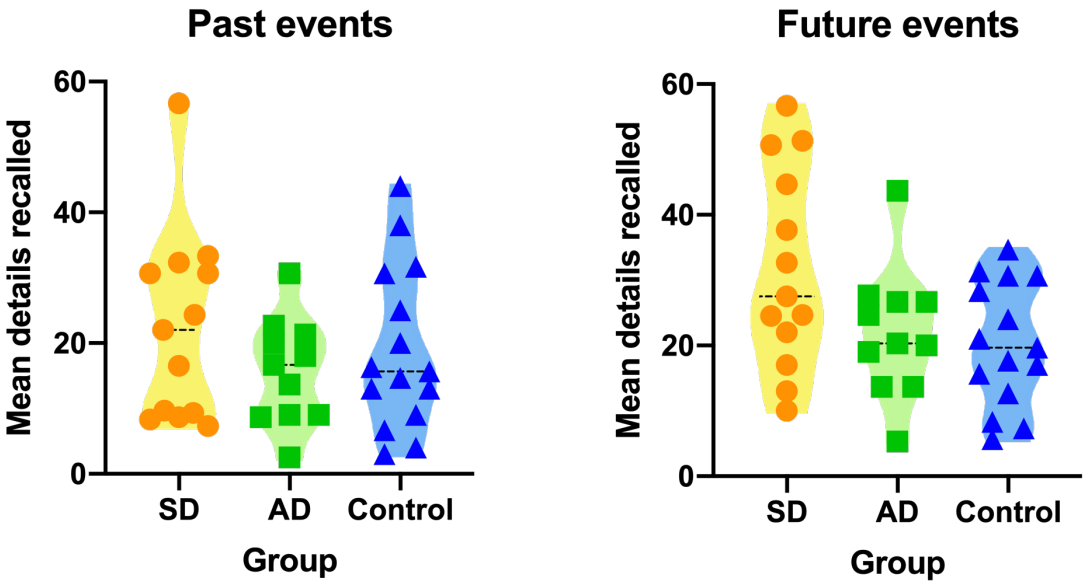



*Figure A4.3.* Violin plots representing the mean External details provided by each group, for Past (left) and Future (right) events. AD = Alzheimer's disease; SD = semantic dementia.

# Appendix D

**Chapter 5**

*A5.1. Neutral scenarios*

You have brought your broken DVD player to the local repair shop. The woman working at the shop tells you that it will cost you about $100 to have it fixed. You notice that the electronics shop next door is selling a new DVD player, which is slightly better than your old one, for $100. Would you have your old DVD player fixed in order to avoid spending money on a new one?

You are a farmer on a tractor that is approaching two different paths. By choosing the path on the left you can pick 30 tonnes of apples. By choosing the path on the right you can pick 15 tonnes of apples. If you do nothing your tractor will turn to the left. Would you turn your tractor to the right in order to harvest 15 tonnes of apples instead of 30?

You want to buy a new computer. At the moment the computer that you want costs $1000. A friend who knows a lot about computers has told you that this computer's price will drop to $500 next month. If you wait until next month to buy your new computer you will have to use your old computer for a few weeks longer than you would like to. Nevertheless you will be able to do everything you need to do using your old computer during that time. Would you use your old computer for a few more weeks in order to save $500 on the purchase of a new computer?

An old friend has invited you to spend the weekend with him at his holiday home down the coast. You plan to travel there by car, and there are two routes that you can take: the highway and the coastal road. The highway will get you to your friend's house in about three hours, but the scenery along the highway is very boring. The coastal road will get you to your friend's house in about three hours and fifteen minutes, and the scenery along the coastal road is breathtakingly beautiful. Would you take the coastal road in order to look at the beautiful scenery as you drive?

*A5.2. Impersonal moral dilemmas*

You are at the wheel of a runaway train quickly approaching a fork in the tracks. On the track to the left is a group of five railway workmen. On the track to the right there is one railway workman. If you do nothing the train will continue to the left, causing the deaths of the five workmen. The only way to avoid the deaths of these workmen is to hit a switch on your dashboard that will cause the train to go to the right, causing the death of one workman. Would you hit the switch in order to avoid the deaths of the five workmen?

You are a hospital security guard. Due to an accident in the building next door, there are deadly fumes rising up through the hospital's ventilation system. In a certain room of the hospital are three patients. In another room there is one patient. If you do nothing the fumes will rise up into the room containing the three patients and cause their deaths.
The only way to avoid the deaths of these patients is to hit a switch, which will cause the fumes to bypass the room containing the three patients. As a result of doing this the fumes will enter the room containing the single patient, causing his death. Would you hit the switch in order to avoid the deaths of the three patients?

You are walking down the street when you find a wallet lying on the ground. You open the wallet and find that it contains several hundred dollars in cash as well the owner's driver's licence. From the credit cards and other items in the wallet it's very clear that the wallet's owner is wealthy. You, on the other hand, have been hit by hard times recently and could really use some extra money. You consider sending the wallet back to the owner without the cash, keeping the cash for yourself. Would you keep the money you found in the wallet in order to have more money for yourself?

You are the owner of a small business trying to make ends meet. You realise that you could lower your taxes by pretending that some of your personal expenses are business expenses. For example, you could pretend that the stereo in your bedroom is being used in the lounge at the office, or that your dinners out with your wife are dinners with clients. Would you pretend that certain personal expenses are business expenses in order to lower your taxes?

*A5.3. Personal low-conflict moral dilemmas*

You are a doctor. You have five patients, each of whom is about to die due to a failing organ of some kind. You have another patient who is a healthy young man. The only way that you can save the lives of the first five patients is to transplant five of this healthy young man's organs (against his will) into the bodies of the other five patients. If you do this, the young man will die, but the other five patients will live. Would you perform this transplant in order to save five of your patients?

Your plane has crashed in the mountains. The only survivors are yourself, another man, and a young boy. The three of you travel for days, battling extreme cold and wind. Your only chance at survival is to find your way to a small village on the other side of the mountain, several days away. The boy has a broken leg and cannot move very quickly. He basically has zero chance of surviving the journey. Without food, you and the other man will probably die as well. The other man suggests that you kill the boy and eat his remains over the next few days. Would you kill this boy so that you and the other man might survive your journey to safety?

*A5.4. Personal high-conflict moral dilemmas*

You are the leader of a small group of soldiers. You are deep in enemy territory when one of your men steps in a trap that has been set by the enemy and is badly injured. The trap is connected to a radio device that by now has alerted the enemy to your presence. They will soon be on their way. If the enemy finds your injured man they will torture him and kill him. He begs you not to leave him behind, but if you try to take him with you your entire group will be captured. The only way to prevent this injured soldier from being tortured is to shoot him yourself. Would you shoot this soldier in order to prevent him from being tortured by the enemy?

You are part of a group of ecologists who live in a remote stretch of jungle. The entire group, which includes eight children, has been taken hostage by a group of terrorists. One of the terrorists takes a liking to you. He tells you that his leader plans to kill you and the rest of the hostages the next morning. He is willing to help you and the children escape, but as an act of good faith he wants you to kill one of your fellow hostages whom he does not like. If you

refuse his offer all the hostages including the children and yourself will die. If you accept his offer then the others will die in the morning but you and the eight children will escape. Would you kill one of your fellow hostages in order to escape from the terrorists and save the lives of the eight children?

You are on a cruise ship when there is a fire on board, and the ship has to be abandoned. The lifeboats are carrying many more people than they were designed to carry. The lifeboat you're in is sitting dangerously low in the water—a few inches lower and it will sink. The seas start to get rough, and the boat begins to fill with water. If nothing is done it will sink before the rescue boats arrive and everyone on board will die. However, there is an injured person who will not survive in any case. If you throw that person overboard the boat will stay afloat and the remaining passengers will be saved. Would you throw this person overboard in order to save the lives of the remaining passengers?

You are negotiating with a powerful and determined terrorist who is about to set off a bomb in a crowded area. However, you have his teen-age son in your custody. There is only one thing that you can do to stop him from detonating his bomb, which will kill thousands of people. To stop him, you must contact him over the satellite hook-up and, in front of the camera, break one of his son's arms and then threaten to break the other one if he does not give himself up. Would you break the terrorist's son's arm in order to prevent the terrorist from killing thousands of people with his bomb?