Is the Triple Bottom Line reporting framework flawed or can it be developed to a higher state?

By

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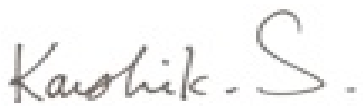
CERTIFICATION

This thesis by publication is submitted in fulfillment of the requirements of the degree of PhD, in the Graduate School of Management, Macquarie University. This represents the original work and contribution of the author, except as acknowledged by general and specific references.

The research presented in this thesis was approved by the Macquarie University Ethics Review Committee (Appendix 12) on the 21st January 2010 (reference number 520093512(D)).

I hereby certify that this has not been submitted for a higher degree to any other university or institution.

Signed:



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Acknowledgement of contribution to the research work and/or authorship

This thesis by publication includes five original papers either published accepted for publication in peer reviewed journals, two of which have been co-authored with Professor Grant Jones. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of the candidate, working within Macquarie Graduate School of Management under the supervision of Professor Grant Jones. The inclusion of a co-author reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.

Confirmation of co-authorship

Paper 1

Name of Publication: A multi-dimensional criticism of the Triple Bottom Line reporting framework

Chapter in thesis- Chapter 2

Journal title: International Journal of Business Governance and Ethics (published- Appendix 7)

Primary author: Kaushik Sridhar

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Abstract

Triple Bottom Line (TBL) reporting has been embedded in corporate practices for the last two decades, without undergoing a great deal of scrutiny in both practical and academic research. This thesis aims to investigate the TBL framework from the perspectives of practitioners who have adopted TBL in the past. The purpose behind this research is to focus on the processes, principles and outcomes of TBL reporting at a corporate level and determine the fundamental limitations within this non-financial reporting framework. The introduction chapter provides a preview of the structural foundation of the thesis, and the research question that will be answered throughout the literature. The thesis comprises of five separate but integrated papers which have been either published in journals, or accepted for publication in journals. Each publication builds on the principles and findings set forth in the previous paper/s and analyzes the limitations within TBL framework based on different academic frameworks. The analysis is primarily based on qualitative data developed through textual analysis of TBL reports; and interviews conducted with the heads of sustainability of forty global corporations considered to have followed TBL reporting as well as being included by major sustainability indexes. The data set includes semi-structured interviews with the executives who are in charge of the sustainability divisions at each of the forty corporations over a one-year period. The methodology chapter provides an overview on different academic theories and theoretical concepts investigated in the thesis. The data analysis draws on stakeholder theory, institutional theory, reputation and legitimacy theory, through which the interviews-data is analyzed; this helped to assess the overall impacts that TBL had in terms of the corporations' non-financial reporting procedures and systems based on their assumptions of what TBL promised to deliver and what it actually delivered, or rather did not.

The results from the interviews signified potential for the corporations to reflect on the current state of affairs with a TBL paradigm, and through further innovation and engagement, create a mind shift towards a more robust and integrated reporting framework that corrects problems faced through a TBL style of reporting. By embedding TBL principles, objectives and indicators into their internal reporting mechanisms, the forty interviewees, or internal stakeholders, were

unable to see the relevance or integration in how TBL reporting processes could feed back into future corporate decisions and strategies related to sustainability as TBL provided minimal opportunities for such reflection. This failure to integrate the past and the present systems with future strategic matters severely undermines the power and potential of TBL reporting to evolve as an integrated and cyclical system that can create change.

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CHAPTER 1

DEMENTIA AND THE CONCEPT OF MILD COGNITIVE IMPAIRMENT

Introduction

The primary aim of this research was to examine the ability of individuals diagnosed with Mild Cognitive Impairment (MCI), a cognitive profile indicating increased risk of developing dementia, to recognise emotional material. The second aim was to explore the real-life impact of emotion recognition difficulties on functional status and caregiver burden.

This chapter commences with an overview of dementia, and in particular the societal and individual costs associated with this neurodegenerative condition. The benefits of early diagnosis and the status of MCI as a diagnostic entity are also described. The evolution of the diagnostic criteria of MCI as well as the emerging importance of markers to predict the presence and aetiology of MCI are presented. The potential for emotion recognition to be used as a marker of progression to dementia is discussed, with details provided regarding its neural substrates.

The concept of dementia and its common forms

Dementia is a common and debilitating neurodegenerative disorder, which typically impacts older individuals. The term dementia encapsulates a diverse range of conditions, with differences in neuropathology and aetiology (Braaten, Parsons, McCue, Sellers, & Burns, 2006). Approximately 50-70% of all dementias cases are attributed to

Alzheimer's disease (AD; Fratiglioni, De Ronchi, & Aguero-Torres, 1999), which is characterised by progressive cognitive decline, typically involving profound memory impairments and anomic aphasia (Hodges, 2006). The symptoms of AD result from cortical degeneration which gradually progresses from medial temporal regions, including the hippocampus, amygdala, parahippocampal gyrus and parietal regions (Brady & Mufson, 1990).

The most common forms of non-Alzheimer dementias are vascular dementia and dementia with Lewy bodies. Vascular dementia (VaD) is caused by cerebrovascular pathology, which encompasses a wide variety of vascular injury such as small vessel disease, severe hypoperfusion, subcortical lacunar lesions and haemorrhagic lesions (Jiwa, Garrard, & Hainsworth, 2010; Rockwood, 2002). Consequently, VaD can be primarily cortical or subcortical, or a combination thereof (Braaten et al., 2006). Accordingly, the pattern of cognitive impairment associated with VaD is variable, due to the diverse syndromes and varying causes underlying VaD, but characteristically includes impaired attention, processing speed and executive dysfunction (O'Brien et al., 2003). It is estimated that VaD accounts for up to 20% of all dementias (Jiwa et al., 2010). Dementia with Lewy bodies (DLB) is characterised by the presence of neuropsychiatric symptoms, Parkinsonism, and sleep and autonomic dysfunction (McKeith et al., 1996). A central feature of DLB is fluctuations in cognition, particularly in attention and alertness (McKeith et al., 1996). However, multiple cognitive domains are detrimentally impacted with disease progression, including language, memory, visuospatial and perceptual

skills (Noe et al., 2004; Tiraboschi et al., 2006). Patients with DLB are estimated to account for between 15-20% of all dementia cases (Weiner, 1999).

Frontotemporal dementia (FTD) encompasses a heterogeneous group of dementias associated with degeneration of the frontal or temporal cortices. It includes a number of clinical subtypes: semantic dementia, progressive non-fluent aphasia and behavioural-variant FTD (Mourik, Rosso, Niermeijer, Duivenvoorden, & Tibben, 2004; Piguet et al., 2011). FTD, and particularly the behavioural variant, is associated with distinct affective and behavioural symptoms including loss of insight, social disinhibition, emotional blunting and selfishness (Knibb, Kipps, & Hodges, 2006; Mourik et al., 2004), often with little initial cognitive decline (Keane, Calder, Hodges, & Young, 2002). It has a prevalence rate of approximately 4% of dementia cases (Brunnström, Gustafson, Passant, & Englund, 2009).

Societal and individual costs of dementia

Dementia is associated with substantial societal costs. In 2009, the worldwide cost of care for 34.4 million dementia patients was estimated to be $422 billion (Wimo, Winblad, & Jönsson, 2010). This includes $142 billion in informal care costs (Wimo, Ljunggren, & Winblad, 1997). Institutionalisation represents the single largest driver of costs, as reflected by a trebling in care costs from the mild to severe disease stages (Leicht et al., 2011). Between 2005 and 2009 the worldwide costs of dementia increased by 34 percent (Wimo, Winblad, & Jönsson, 2010).

As life expectancy increases, the prevalence of dementia is expected to double every 20 years. Without the implementation of effective early diagnosis and preventative strategies, it is estimated that by 2040, 81 million individuals worldwide will have dementia (Ferri et al., 2005). As well as the societal costs, the individual impact associated with dementia is profound and devastating. For the patient, dementia results in a progressive decline in cognition and functional status (Hodges, 2006). Behavioural and psychological symptoms, including aggression, apathy, depression and psychosis, are also frequently associated with dementia, the presence of which increases the risk of institutionalisation (Herrmann et al., 2006). For family members, caring for a dementia patient often leads to high levels of caregiver burden (Brodaty, 1996), depression (Mausbach et al., 2012), diminished quality of life (Shin, Carter, Masterman, Fairbanks, & Cummings, 2005) and greater utilisation of health services (Vitaliano, Zhang, & Scanlan, 2003).

The concept of Mild Cognitive Impairment

Given that dementia is forecast to present an increasingly onerous individual and public health problem for decades to come, a considerable body of literature exists in support of early diagnosis and intervention to arrest subsequent disability, delay institutionalisation and minimise caregiver burden (for a meta-analysis see Brodaty, Green, & Koschera, 2003). There are also significant economic benefits associated with early intervention and diagnosis (Getsios, Blume, Ishak, Maclaine, & Hernández, 2012; Weimer & Sager, 2009).

Research suggests that the pathophysiological process of AD begins years before the clinical diagnosis of dementia (Morris, 2005). Considerable effort has been undertaken, consequently, in mapping the cognitive profile of AD across the span of disease progression. These studies show that a phase of progressive cognitive decline precedes the onset of dementia, which has consequently informed the concept of MCI (Petersen et al., 1999). MCI is widely used as a diagnostic entity to indicate greater risk of dementia, and thus for many people it marks a transitional state between normal ageing and dementia. The syndrome of MCI constitutes cognitive impairment greater than would be expected for an individual's age and education, but not to the severity constituting dementia, in the context of intact basic activities of daily living (Gauthier et al., 2006; Petersen et al., 1999).

The concept of MCI was first associated with two staging measures published in 1982, the Clinical Dementia Rating (CDR; Hughes, Berg, Danziger, Coben, & Martin, 1982) and Global Deterioration Scale (GDS; Reisberg, Ferris, de Leon, & Crook, 1982), in which clinical antecedents of dementia were identified (Reisberg et al., 2008). Subsequent longitudinal studies used the term MCI to identify mildly impaired elderly individuals who, over a specified time period, demonstrated objective cognitive deterioration on psychometric testing but did not meet criteria for mild dementia (Flicker, Ferris, and, & Reisberg, 1991). The initial diagnostic criteria of MCI required the presence of episodic memory impairment (Burns & Zaudig, 2002; Petersen et al., 1999), which is now more commonly referred to as amnestic MCI (aMCI; Petersen, 2004). This

rather narrow perspective, however, failed to take into account the considerable variability demonstrated by cognitively impaired patients and did not delineate the cognitive features found in prodromal forms of non-Alzheimer dementias (Hodges, 2006).

Consequently, modified MCI criteria have been established to enable the identification of other clinical subtypes with more diverse cognitive deficits across non-memory domains such as language, executive function, processing speed and visuospatial skills (Petersen, 2004). The inclusion of this classification, known as the non-amnestic MCI subtype (naMCI), reflects the heterogeneous nature of MCI as a diagnostic entity. A further revision in MCI criteria acknowledged the presence of cognitive deficits across single or multiple cognitive domains in MCI (Petersen, 2004). Throughout the evolution of MCI as a diagnostic entity, neuropsychological testing has remained integral to assess objectively for the presence of cognitive impairment, with evidence of a 1.5 standard deviation decrement on appropriate normative data typically required (Albert et al., 2011).

Prevalence and prognosis of MCI

Community-based studies estimate the prevalence of MCI to be between 3.2% to 19.3% (Ritchie, Artero, and, & Touchon, 2001), however in a sample aged between 70 to 90 years, its prevalence has been reported to be as high 34.8% (Sachdev et al., 2010). The clinical subtypes of MCI are proposed to have diverse aetiologies with differing patterns of neuropathology and, consequently, disease trajectories. The most common

progression from aMCI is to AD, with conversion rates reported from between 10% to 15% per annum (Fisk, Merry, & Rockwood, 2003; Petersen et al., 1999). The trajectory from naMCI is, however, less well understood, but may involve non AD dementias (e.g. FTD, VaD, DLB; Petersen & Morris, 2005). Importantly, some individuals with MCI may never progress to dementia, but remain stable over time (Gauthier et al., 2006) and approximately 28% have been estimated to return to normalcy (Ganguli, Dodge, Shen, & DeKosky, 2004). Indeed, reversible factors following a diagnosis of MCI may include depression, upper airway obstruction, metabolic factors and nutritional impairments (Gauthier & Touchon, 2005).

The importance of markers in MCI

Luppa et al. (2008) found that the direct health costs associated with MCI are no different from those associated with individuals without cognitive deficits. However, this situation clearly changes following conversion to dementia, as outlined above. The high conversion rates associated with progression to dementia from MCI means that it represents an important population who may benefit from the implementation of early interventions to arrest the progression of dementia (Luppa et al., 2008). In this regard, given the importance of early diagnosis, it is critical that any clinical features indicative of the presence of MCI and potential progression to dementia are elucidated. Whilst the diagnostic criteria of MCI are predominantly focused on the presence of cognitive impairment, there is evidence to suggest that the impact of MCI extends beyond purely cognitive factors. Consequently, recommendations have been made

recently by the National Institute on Aging-Alzheimer's Association workgroups to revise the MCI criteria to enhance diagnostic sensitivity (Albert et al., 2011). There is considerable support from research to suggest the presence of increased levels of disability in everyday functioning for MCI patients, as assessed by performance-based (Goldberg et al., 2010), self-report (Wadley et al., 2007) and informant-rated (Teng, Becker, Woo, Cummings, & Lu, 2010) measures. The level of disability is mild, however, with difficulties experienced restricted to independently undertaking higher level abilities (Brown, Devanand, Liu, & Caccappolo, 2011) such as in managing finances, operating household appliances, using transport and communicating about recent events (Kim et al., 2009). Research suggests that impaired daily functioning constitutes a high risk factor for the development of dementia (Luck et al., 2011), with longitudinal studies showing a significantly steeper decline in functioning in MCI patients than in normal controls (Wadley et al., 2007). Consequently, the establishment of core clinical MCI criteria has been recommended, which acknowledges the presence of mild levels of functional difficulties in the MCI diagnostic criteria (Albert et al., 2011).

A further recommended revision of MCI criteria incorporates the use of biomarkers, predictive of dementia progression, to determine the presence and aetiology of MCI (Albert et al., 2011). The presence of an autosomal dominant form of ε4 allele in the apolipoprotein E (*APOE*) gene, which is most frequently associated with aMCI cases (Roberts et al., 2010), has been classified as a likely prodrome to AD dementia (Albert et al., 2011). Additionally, deposits of beta-amyloid protein (Aβ), as detected

in cerebrospinal fluid and plasma, are also proposed to directly reflect AD pathology (Albert et al., 2011). The presence of these biomarkers is recommended to enable a diagnosis of the proposed subtype "MCI due to AD" (Albert et al., 2011). Other proposed biomarkers include those indicative of neuronal injury, such as elevated levels of cerebrospinal fluid tau or phosphorylated tau, and the presence of cerebral or medial temporal atrophy and hippocampal volume loss on structural and functional imaging measures. Finally, the inclusion of markers associated with biochemical change have also been proposed in revised MCI criterion, including the presence of inflammatory biomarkers (i.e., cytokines), and markers of synaptic damage and neurodegeneration such as cell death (Albert et al., 2011).

These revised MCI criteria reflect a concerted effort to ensure that MCI diagnostic criteria more accurately encapsulate the true nature of the disorder. Past research also suggests that there may be other clinical markers which are indicative of the presence of MCI. These include changes in motor/psychomotor domains (Aggarwal, Wilson, Beck, Bienias, & Bennett, 2006) and mild Parkinsonian signs, such as extrapyramidal dysfunction and gait disturbance (Louis et al., 2005), which are more typically reported in individuals with naMCI (Boyle et al., 2005).

The importance of neuropsychiatric symptoms (NPS) in MCI, such as apathy, depression, irritability and agitation (Hwang, Masterman, Ortiz, Fairbanks, & Cummings, 2004; Lyketsos et al., 2002) is also emerging as being highly predictive of progression to dementia (Copeland et al., 2003)

and representative of a non-cognitive prodrome to dementia (Schweitzer, Tuckwell, O'Brien, & Ames, 2002). The presence of NPS correlate with accelerated disease progression (Holtzer et al., 2003) and occur more frequently in MCI patients than in healthy age-matched controls (Hwang et al., 2004).

Emotion recognition as a marker in MCI

It has been theorised that NPS are accompanied by disruptions in the way emotional stimuli are perceived, recognised and evaluated (Leppanen, 2006) - processes conceptually referred to as social perception (Tager-Flusberg & Sullivan, 2000). This term encompasses the processing of emotional stimuli (e.g. recognising and comprehending emotional expressions and emotional prosody) and the evaluation of contextual cues in order to infer the mental state of others and, as a consequence, make sense of the social environment (Beer & Ochsner, 2006). Whilst considerable evidence exists to suggest that emotion recognition is impaired in dementia, particularly AD and FTD (for a review of emotion recognition in AD see McLellan, Johnston, Dalrymple-Alford, & Porter, 2008), there is some evidence that very early deficits may already be present in emotion recognition in MCI (Fujie et al., 2008; Spoletini et al., 2008; Teng, Lu, & Cummings, 2007; Weiss et al., 2008). Research to date, however, is sparse. Hence, further research is required to investigate whether emotion recognition abilities represent a potential biomarker for progression to dementia.

The neurobiological substrates of emotion recognition

Research suggests that multiple interconnected and overlapping brain regions are recruited in emotion recognition. The frontal lobes, and especially the orbitofrontal, ventral and medial prefrontal subdivisions, and cingulate (Craik & Moroz, 1999; Fossati, Hevenor, Graham, & Grady, 2003) are thought to play a central role in the recognition of emotions. Studies also support the involvement of the temporal lobes, particularly the superior temporal sulcus and amygdala (Adolphs & Tranel, 2004; Sato, Bottlender, Schroter, & Moller, 2004). Lesion studies support a role for somatosensory regions and the basal ganglia in emotion recognition (Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000), which may indicate that viewing facial emotional expressions triggers a similar emotional response in the perceiver (Adolphs, 2002). The fusiform gyrus is also implicated in emotion recognition via facial processing (Adolphs, 2001). Neurobehavioural models of emotion posit that the right hemisphere is dominant for emotion processing (for a review see Borod, 1993), although other theories propose that cortical lateralisation may be restricted to the perception and expression of emotion (Davidson, 1984).

There is also evidence to suggest that individual emotions are processed by distinct neural regions. The orbitofrontal cortex, anterior cingulate (Blair, Morris, Frith, Perrett, & Dolan, 1999), medial frontal cortex (Kesler-West et al., 2001), ventral striatum (Calder, Keane, Lawrence, & Manes, 2004), ventrolateral prefrontal cortex (Blair & Curran, 1999), anterior insula (Davidson & Irwin, 1999) and amygdala (Whalen et al., 2001) have been implicated in anger recognition.

Functional imaging studies have implicated the amgydala more generally in the recognition of negative emotions, including fear (Whalen et al., 2001) and sadness (Blair et al., 1999; Whalen et al., 2001). Sadness has also been found to activate the ventral/subgenual anterior cingulate (Liotti et al., 2000). Amydgala activation has been noted, however, for expressions of happiness (Williams, McGlone, Abbott, & Mattingley, 2005) and surprise (Kim et al., 2004). The insula and basal ganglia are thought to engage in the recognition of disgust (Calder, 2003; Sprengelmeyer et al., 1996). The ventral striatum/basal ganglia has also been implicated in recognition of happiness, which may be linked to the role of the dopaminergic system in the reward process (for a meta-analysis see Phan, Wager, Taylor, & Liberzon, 2002).

The following chapter reviews the literature on MCI and emotion recognition.

CHAPTER 2

LITERATURE REVIEW: EMOTION RECOGNITION AND MILD COGNITIVE IMPAIRMENT

Review of emotion recognition in Mild Cognitive Impairment

This paper was accepted for publication in *Dementia and Geriatric Cognitive Disorders* (09/11/2011) following minor revisions and this is the revised manuscript (Reference: McCade, D., Savage, G., & Naismith, S. L. (2011). Review of emotion recognition in mild cognitive impairment. *Dementia and Geriatric Cognitive Disorders*, *32*(4), 257-266.). The paper that follows is in the format required for that publication, with the exception of page numbers and the referencing style, which was revised to be consistent with the thesis as a whole. Some repetition of information and references is unavoidable given the structure of the thesis by paper.

My contribution to this paper was estimated to be 85% including primary responsibility for the design, analysis and manuscript preparation. Associate Professor Sharon Naismith and Associate Professor Greg Savage contributed an estimated 10% and 5% respectively to manuscript preparation.

Review of emotion recognition in Mild Cognitive Impairment

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Abstract

Background: While dysfunction in emotion recognition is sometimes apparent with ageing, and is frequently evident in Alzheimer's disease (AD), it is unclear whether individuals who have a high risk of developing dementia exhibit demonstrable changes. *Method:* A review of the literature pertaining to Mild Cognitive Impairment (MCI) was undertaken to discern the extent to which emotion recognition deficits are evident in this prodromal period. *Results:* A search of Medline, Psycinfo and Psyextra databases using specific keywords identified only six relevant studies. These studies suggest that the ability to accurately identify facial expressions of affect is compromised. *Conclusions:* Research in this area is in its infancy. Suggestions are made for furthering our knowledge about this important ability which affects interpersonal relationships, daily functioning, mental wellbeing and quality of life.

Key words: Dementia; Emotion recognition; Emotion processing; Facial expressions; Social cognition; Mild Cognitive Impairment.

Introduction

Research interest in dementia has predominantly focused on the cognitive deficits associated with disease onset and progression, but there is growing awareness of how dementia influences the processing of emotional stimuli (e.g. recognising and comprehending facial emotional expressions). The neurobiological substrates of emotion recognition include the amygdala and superior temporal sulcus/gyrus (Adolphs, Tranel, Damasio, & Damasio, 1994; Sato, Bottlender, Schroter, & Moller, 2004), as well as fusiform gyri, somatosensory, medial prefrontal and cingulate areas (Adolphs, 2001; Craik & Moroz, 1999). The ability to accurately perceive emotional cues is thought to have evolved in primates to facilitate successful interaction in everyday social life (Brüne & Brüne-Cohrs, 2006). Consequently, impaired emotion recognition can have a devastating impact on social behavioural competence (Mueser et al., 1996) and is associated with increased levels of depression (Carton, Kessler, & Pape, 1999), inappropriate social behavior (Spell & Frank, 2000), interpersonal problems and psycho-behavioural disturbances, all of which are commonly observed in dementia (Chiu, Chen, Yip, Hua, & Tang, 2006; Shimokawa et al., 2001).

For the carers of patients with dementia, psychological and behavioural disturbances are associated with an increase in burden, psychological distress (Brodaty, 1996), and diminished quality of life (Shin, Carter, Masterman, Fairbanks, & Cummings, 2005). For the patient these disturbances also increase the risk of institutionalisation (Brodaty, 1996). Hence, given the significant impact and considerable individual and

societal costs, the early diagnosis of emotion recognition disturbances is important to enable the implementation of appropriate interventions. In this regard, the opportunity for early detection and secondary prevention may lie within the Mild Cognitive Impairment (MCI) population.

The syndrome of MCI is widely used to identify individuals at risk of developing dementia. Clinical research has been predominantly informed by the amnestic MCI (aMCI) subtype, characterised by memory impairment which is subjectively recognised by the self or by others and objectively identified on neuropsychological testing, in the context of intact basic activities of daily living (Petersen et al., 2001; Petersen et al., 1999). Individuals with MCI may present with impairments in either single or multiple cognitive domains (Petersen, 2004). The most common progression from aMCI is to Alzheimer's disease (AD), with conversion rates reported from between 10% to 15% per annum (Fisk, Merry, & Rockwood, 2003; Petersen et al., 1999; Rountree et al., 2007). The non-amnestic MCI subtype (naMCI) is associated with more diverse cognitive deficits across non-memory domains such as language, executive function, processing speed and visuospatial skills (Petersen, 2004). While further longitudinal studies are required for this subtype, conversion from naMCI may involve non-Alzheimer-like conditions such as frontotemporal dementia (FTD), vascular dementia (VaD), and dementia with Lewy bodies (DLB; Petersen & Morris, 2005). Psychological symptoms, including depression, anxiety and apathy, are commonly associated with both aMCI and naMCI subtypes (Apostolova & Cummings, 2008). It is important to note that whilst progression to dementia is elevated for MCI

individuals, some may remain stable over time (Gauthier et al., 2006) and up to 28% have been estimated to return to normalcy (Ganguli, Dodge, Shen, & DeKosky, 2004; Loewenstein, Acevedo, Agron, & Duara, 2007).

The aim of this paper is to review the MCI literature pertaining to emotion recognition. As a backdrop to this focus, an initial review of emotion recognition is outlined, including the profiles associated with both normal aging and the neurodegenerative conditions of AD and FTD. A comprehensive review of literature pertaining to MCI is then presented in order to ascertain whether early changes in the ability to recognise facial expressions of emotion are evident in MCI samples.

What happens to emotion recognition with age?

There is strong support for an age-related decline in emotion recognition. Studies have shown emotion recognition performance improves from childhood through adolescence and early adulthood, but declines in later adulthood (Williams et al., 2009). Older adults are worse than younger adults in recognising some basic emotions, a finding which holds across a range of modalities including faces, voices, bodily contexts and face-voice matching (for a review see Ruffman et al., 2008). The recognition of angry, sad and fearful faces (Calder et al., 2003; Malatesta, Izard, Culver, & Nicolich, 1987; McDowell, Harrison, & Demaree, 1994; Sullivan & Ruffman, 2004) is consistently shown to be problematic for older adults, in the context of relatively preserved recognition of disgust (Suzuki, Hoshino, Shigemasu, & Kawamura, 2007) and happiness (MacPherson, Phillips, & Della Sala, 2002). Indeed some evidence

suggests that the identification of disgust improves with age (Calder et al., 2003), whilst general face recognition remains relatively intact (Silver, Goodman, Knoll, & Isakov, 2004).

Deficits in emotion recognition observed in older adults have been attributed to age-related structural (Jack et al., 1997; Raz & Rodrigue, 2006; Sowell et al., 2003) and functional changes in brain regions, particularly in temporal, limbic and/or prefrontal areas involved in emotion recognition (Adolphs & Tranel, 2003; Bartzokis et al., 2001; Raz et al., 2005) such as the amygdala, orbitofrontal cortex and superior temporal areas (Gunning-Dixon et al., 2003). These age-related changes within distinct neural systems, may underlie emotion recognition difficulties, independent of general cognitive decline (Keightley, Winocur, Burianova, Hongwanishkul, & Grady, 2006; Sullivan & Ruffman, 2004). An alternative account for the emotion-specific effects observed in aging implicates motivational factors. Older adults are thought to prioritise emotion-regulatory goals aimed at minimising negative affect (for a review, see Carstensen and Mikels [2005]), and it has been hypothesised that a tendency to preferentially process material with positive valence (Isaacowitz, Wadlinger, Goren, & Wilson, 2006) results in the selective sparing of positive emotions observed in recognition tasks (Isaacowitz et al., 2007).

Emotion recognition and dementia

Research to date suggests that within samples of patients with dementia, deficits in emotion recognition extend beyond those attributed to normal aging. The conditions most explored are AD and FTD.

Alzheimer's disease

Whilst emotional expression is thought to be largely intact in AD (Magai, Cohen, Gomberg, Malatesta, & Culver, 1996), deficits in the ability of AD patients to comprehend the emotional state of others using facial expressions have been observed when AD patients are compared with age-matched healthy controls (Shimokawa et al., 2000; for a review see McLellan et al. [2008]). Results across studies vary in terms of individual emotions thought to be impaired, such as happiness (Henry et al., 2008; Kohler et al., 2005; Spoletini et al., 2008), sadness (Hargrave, Maddock, & Stone, 2002; Henry et al., 2008; Kohler et al., 2005; Spoletini et al., 2008), surprise (Hargrave et al., 2002; Henry et al., 2008), disgust (Hargrave et al., 2002), fear (Henry et al., 2008; Kohler et al., 2005; Spoletini et al., 2008), and anger (Bediou et al., 2009; Henry et al., 2008; Kohler et al., 2005; Spoletini et al., 2008). Neurodegeneration associated with AD is hypothesised to underlie affect processing deficits, in particular to medial temporal lobe structures (Spoletini et al., 2008). In support of this, one longitudinal study reported that emotion recognition worsened with disease progression (Lavenu & Pasquier, 2005).

Other studies, however, have attributed observed decreases in emotion recognition to general cognitive, linguistic or visuospatial dysfunction

rather than to specific emotional processing deficits (Albert, Cohen, & Koff, 1991; Burnham & Hogervorst, 2004; Cadieux & Greve, 1997; Lavenu, Pasquier, Lebert, Petit, & Van der Linden, 1999; Roudier et al., 1998). Whilst some studies have failed to find any significant emotion processing impairment in AD patients, compared with healthy controls, these studies have had either small sample sizes (i.e., n = 9 [Fernandez-Duque & Black, 2005]; n = 12 [Bucks & Radford, 2004]), mild AD severity samples (i.e., mean Mini-Mental State Examination [MMSE] score of 24.8 [Fernandez-Duque & Black, 2005]), or they have employed emotion identification tasks which were insufficiently sensitive to detect group differences (Ogrocki, Hills, & Strauss, 2000). Overall, studies to date have been characterised by methodological variability in terms of sample size, patient disease severity (e.g. encompassing very mild AD to moderate levels of AD), participant age (e.g. ranging from 70 to 90 years) and inconsistencies in study response formats and stimuli used.

Frontotemporal dementia

FTD encompasses a heterogeneous group of dementias associated with degeneration of the frontal or temporal brain regions. FTD produces a distinct profile of symptoms including loss of insight, social disinhibition, diminished emotions and selfishness (Bathgate, Snowden, Varma, Blackshaw, & Neary, 2001; Bozeat, Gregory, Ralph, & Hodges, 2000; Mourik, Rosso, Niermeijer, Duivenvoorden, & Tibben, 2004), often with little initial cognitive decline (Keane, Calder, Hodges, & Young, 2002). Given the prominent role that behavioural and emotional changes play in FTD patients, it is unsurprising that a number of studies have been

undertaken to explore emotion recognition in this disease group, and empirical evidence strongly suggests an impaired ability to recognise a range of emotional facial expressions. Deficits have been identified in the detection of happiness (Diehl-Schmid et al., 2007; Keane et al., 2002; Rosen et al., 2004); surprise (Diehl-Schmid et al., 2007; Kessels et al., 2007; Lavenu & Pasquier, 2005); sadness (Diehl-Schmid et al., 2007; Fernandez-Duque & Black, 2005; Keane et al., 2002; Lavenu et al., 1999; Rosen et al., 2004; Rosen et al., 2002); disgust (Diehl-Schmid et al., 2007; Fernandez-Duque & Black, 2005; Lavenu & Pasquier, 2005; Lavenu et al., 1999; Lough et al., 2006); fear (Diehl-Schmid et al., 2007; Fernandez-Duque & Black, 2005; Rosen et al., 2004; Rosen et al., 2002); and anger (Diehl-Schmid et al., 2007; Fernandez-Duque & Black, 2005; Keane et al., 2002; Kessels et al., 2007; Lavenu & Pasquier, 2005; Lavenu et al., 1999; Lough et al., 2006; Rosen et al., 2004; Rosen et al., 2002), when compared with healthy controls. There is some support for the finding that the recognition of negative valence emotions (sadness, fear, anger) are more severely impaired than positive valence emotions (happiness; Rosen et al., 2002). Impaired emotion recognition amongst FTD patients has been consistently reported across studies, despite small sample sizes used (i.e., n = 6) (Fernandez-Duque & Black, 2005; Keane et al., 2002), variability in patient MMSE scores (i.e., mean MMSE score = 22.9 in Rosen et al. [2004]; mean MMSE score = 28 in Lough et al. [2006]), differences in disease severity (e.g. encompassing mild to moderate levels of FTD), and stimuli used (e.g. static photographs and video clips). Although the precise pathophysiology of these deficits is not well understood, there is certainly

considerable evidence demonstrating abnormalities in frontal-temporal neural networks. Eslinger et al. (2007) found right hemisphere cortical atrophy in the orbitofrontal, superior temporal, visual association and posterior cingulate, regions implicated in the mediation of emotion recognition. These findings were reinforced in a subsequent meta-analysis by Schroeter, Raczka, Neumann, and von Cramon (2008).

To summarise, strong support exists for specific emotion recognition deficits in FTD patients, demonstrating impairments in the subjective experience of emotion and difficulty accessing the mental states of others, which seems to be independent of general cognitive impairment. In contrast, while there is evidence that emotion recognition is impaired in AD, it is not clear whether this is a primary impairment, or whether it reflects impaired cognition generally.

Method

The literature providing a basis for this review was obtained by searching the Medline, Psycinfo and Psycextra databases for English language articles containing the key terms “Mild Cognitive Impairment” and “MCI”. Other terms entered into the search were “dementia”, “facial emotion recognition”, “face processing”, “emotion processing”, “emotion”, “social cognition” and “social perception”. No restrictions were placed on year, with all articles up until February 2011 included. Relevant papers from the reference lists of identified papers were also reviewed. Given the focus on MCI, only studies with samples from age-associated cognitive impairment were included. Also, only studies which included the diagnostic criteria used to identify MCI cases (e.g. Petersen et

al., 1999), supported by neuropsychological testing to aid diagnosis, were reviewed. Studies with only cognitively normal individuals or that focused solely on psychiatric conditions were excluded. Only studies in which a key research focus was emotion processing were included. One study was excluded because the patient group did not differentiate between individuals with dementia and those with MCI (Washburn & Sands, 2006). A further study was excluded (Modinos, Obiols, Pousa, & Vicens, 2009) due to sample size limitations (i.e., n = 1). Ultimately, only six studies relating to emotion recognition were eligible for inclusion in the present review (table 1).

Results

Participant characteristics and diagnostic criteria

In the six studies reviewed, mean participant age ranged from 71.2 years (Spoletini et al., 2008) to 79.4 years (Teng, Lu, & Cummings, 2007). Whilst not uniformly reported, the mean level of education of MCI participants varied considerably across studies, ranging from 9.8 years (Weiss et al., 2008) to 18.2 years (Teng et al., 2007). Sample size also varied from 9 MCI single domain participants (Teng et al., 2007) to 50 aMCI participants (Spoletini et al., 2008).

Inconsistencies were found in diagnostic criteria used to identify MCI participants across studies. In the majority of studies, diagnoses of MCI were made according to features defined in the early proposal by Petersen et al. (1999); these included Bediou et al. (2009), Fujie et al. (2008), Spoletini et al. (2008), and Teng et al. (2007). Accordingly, individuals

with memory deficits in the context of intact general cognitive functioning (i.e., aMCI) were the primary population sampled. A minority of studies encompassed a more heterogenous view of MCI, in line with the modified criteria of Petersen et al. (2001) including aMCI participants with deficits across multiple cognitive domains (Weiss et al., 2008).

Another study (Henry et al., 2009) did not report a differentiation of MCI subtypes amongst the sample, despite using the modified Petersen (2007) MCI criteria. Hence it is unclear if the sample included both amnestic and non-amnestic MCI subtypes, and also whether participants presented with deficits in single or in multiple-domains. Where disclosed, the level of cognitive impairment was defined by a performance of at least 1.5 standard deviations below either age-adjusted norms (Henry et al., 2009; Teng et al., 2007; Weiss et al., 2008) or a general normative sample (Fujie et al., 2008). Performance was generally assessed by results on neuropsychological testing. In all studies, the MMSE was a key part of neuropsychological evaluation. In two studies, MMSE scores of greater than or equal to 23 (Spoletini et al., 2008) and 24 (Fujie et al., 2008) were required for inclusion in the study.

Neuropsychological testing undertaken generally covered memory, language and executive functioning. However, some studies provided more extensive testing of participants, including visuospatial/constructional ability (Spoletini et al., 2008; Teng et al., 2007; Weiss et al., 2008) and attention/processing speed (Teng et al., 2007). Neuropsychological performance data on cognitive testing are reported for each participant group in four studies (Bediou et al., 2009; Fujie et al.,

2008; Spoletini et al., 2008; Teng et al., 2007). Other studies only partially reported neuropsychological comparison data, most often MMSE scores.

Exclusion criteria reported were generally consistent between studies, excluding participants with disorders known to impact upon cognitive status (e.g. neurological disorders; major medical illnesses) and also emotion processing (e.g. psychiatric disorders; visual acuity). Some studies adopted more stringent strategies (Fujie et al., 2008; Spoletini et al., 2008; Teng et al., 2007), excluding participants based on additional factors such as drug dependence, as well as lesions or abnormalities observed using magnetic resonance imaging. All studies recruited healthy controls as a comparison group. Most control samples were matched demographically with MCI participants; however, sample differences were reported across groups for age and education (Teng et al., 2007).

Emotion recognition measures

All studies adopted a cross-sectional design to assess facial emotion processing. Facial affect recognition tests were used in all studies, whereby participants were required to identify which emotion best accounted for the expression displayed on a photographed face. One study additionally used an emotion discrimination task, in which participants determined whether the expressed emotions on a pair of photographed faces were the same or different, as well as emotion matching and selection tasks, where the participant was required to match the target emotions presented either verbally or visually with a set of photographed faces (Teng et al., 2007).

One study also incorporated neuroimaging in an effort to relate emotion recognition to neural integrity (Fujie et al., 2008). Specifically, the authors used diffusion tensor imaging to calculate the fractional anisotropy of the uncinate fasciculus, a white matter tract connecting the anterior part of the temporal lobe with the orbital and polar frontal cortex, areas which are postulated to contribute to the interaction between cognition and emotion (Barbas, 2000). This in turn was correlated with individual performance on an emotion recognition task.

Stimuli employed

Stimuli used in emotion recognition tasks were typically static photographs of faces. Standardised and validated instruments have chiefly been used, predominantly from the Ekman and Friesen (1976) "Pictures of Facial Affect" series (Fujie et al., 2008; Henry et al., 2009) or the Penn Emotion Recognition Test (Spoletini et al., 2008; Weiss et al., 2008). Studies have varied in the use of either black-and-white (Fujie et al., 2008; Henry et al., 2009) or colour facial photographs (Spoletini et al., 2008; Weiss et al., 2008); all have used stimuli with deliberate, posed facial expressions.

In regard to emotions examined, happiness, anger and fear were examined in all studies. The emotions least explored were surprise and disgust. Two studies incorporated emotional stimuli differing in intensity (Bediou et al., 2009; Spoletini et al., 2008), one of which morphed emotional stimuli with neutral expressions (Bediou et al., 2009).

Task format

Most studies used self-paced, unlimited exposure to stimulus material; however, Bediou et al. (2009) placed time restrictions (e.g. 1 second) on stimuli presentation, potentially increasing working memory demands and presenting a more cognitively difficult exercise. Response formats for tasks were predominantly forced choice, and no studies placed time limits on participant responses. Tasks placed demands on participants not only in regard to their social cognitive skills but also drew on abilities from other cognitive domains. For example, semantic analysis is required to comprehend response options.

Control tasks

The inclusion of tasks to control for perceptual face processing deficits in emotion recognition tasks was noted in four studies. Either an identity discrimination task, in which participants indicated whether photographs of people were the same or different (Fujie et al., 2008; Spoletini et al., 2008; Teng et al., 2007), or gender identification tasks, in which the participant was required to label the gender of presented faces (Bediou et al., 2009), were used.

Synthesis of findings

All of the six identified studies investigated the ability of MCI cases to recognise emotional expressions. Two studies found no significant difference in performance relative to healthy controls: one including aMCI cases specifically (Bediou et al., 2009), with only a small effect size

(Cohen's d = 0.37), and one including MCI cases defined generally (Henry et al., 2009), although the latter study did find a trend towards impairment in MCI cases (p = .062) and a moderate effect size (Cohen's d = 0.59). It is noteworthy that in these studies the MCI participants had either the mildest degree of global cognitive impairment with a mean MMSE of 27.9 (Henry et al., 2009), or a small sample size of only 10 participants (Bediou et al., 2009).

Four studies reported MCI patients to be significantly worse than healthy controls at recognising facial expressions of emotions (Fujie et al., 2008; Spoletini et al., 2008; Teng et al., 2007; Weiss et al., 2008), with effect sizes ranging from moderate (Cohen's d = 0.51 [Spoletini et al., 2008]) to large (Cohen's d = 1.01 [Fujie et al., 2008]; Cohen's d = 1.36 [Weiss et al., 2008]). Interestingly, two of these studies included MCI comparison groups with either single or multiple cognitive domains impaired (Teng et al., 2007; Weiss et al., 2008) but impairment was significant only for those groups with cognitive deficits across multiple-domains. Subsequent analyses in Teng et al. (2007) revealed that in the context of similar MMSE scores, the MCI multiple-domain group had a greater degree of overall cognitive impairment than the MCI single-domain group. Whilst no significant relationship was found to exist between the breadth of cognitive impairments and performance on an emotion discrimination task, performance on neuropsychological tests of executive functioning was reported as the best predictor of emotion discrimination ability within the MCI multiple-domain group.

Emotion-specific deficits were reported in three studies. Diminished ability was reported amongst MCI participants in recognising sad (Fujie et al., 2008; Weiss et al., 2008), fearful (Spoletini et al., 2008; Weiss et al., 2008), angry (Fujie et al., 2008) and neutral (Weiss et al., 2008) faces. Whilst no emotion-specific deficit was found in Teng et al. (2007), MCI multiple-domain cases found happy faces were significantly easier to recognise than sad, angry and fearful faces, and neutral faces were significantly easier to recognise than sad faces.

An effect for emotion intensity was reported by Spoletini et al. (2008). In this study, impaired performance within aMCI participants was found only for low-intensity stimuli, specifically for fearful faces; this finding was attributed to fearful expressions being more subtle and hence more difficult to recognise. This is consistent with findings reported in Bediou et al. (2009), in which the performance of aMCI cases resembled that of mild AD patients when emotional expression was more subtle (e.g. 40% intensity). However, in the latter study, as mentioned above, overall results did not achieve significance.

In terms of other affective biases, depressed individuals have been found to be less accurate in recognising facial affect and to demonstrate a negative bias when interpreting emotional expressions (Leppänen, 2006). Only a small number of studies assessed patient depressive symptoms using either the Geriatric Depression Scale (Teng et al., 2007; Weiss et al., 2008) or the Beck Depression Inventory (Bediou et al., 2009). One study controlled for the potential effect of depressive symptoms on emotion recognition. Weiss et al. (2008) found that whilst depression was

associated with poorer accuracy in emotion recognition, depression did not significantly account for task performance.

Different studies have proposed a variety of factors to account for findings of impaired emotion recognition in MCI. Specific regional pathology proposed includes degeneration of corticolimbic systems, particularly involving the temporal (Spoletini et al., 2008) and frontal lobes (e.g. orbitofrontal regions; Teng et al., 2007) as suggested by performance on specific neuropsychological tests. One study used imaging to correlate white matter pathology with emotion recognition (Fujie et al., 2008). Specifically, aMCI individuals were found to have significantly reduced fractional anisotropy measurements of the left uncinate fasciculus when compared with healthy controls. Within the aMCI group, a significant positive relationship was shown to exist between fractional anisotropy values of the left uncinate fasciculus and accuracy in recognising surprise and fear. The authors concluded that uncinate fasciculus pathology may play either a direct or intervening role in impaired emotion processing, in association with amygdalar or hippocampal pathology. Importantly, in three studies the inclusion of control tasks enabled face processing deficits to be specifically excluded as factors explaining impaired emotion recognition (Fujie et al., 2008; Spoletini et al., 2008; Teng et al., 2007).

Emotion processing deficits were hypothesized to have practical consequence on the non-verbal communication, interpersonal relatedness, and quality of life in MCI cases (Spoletini et al., 2008). However, this

remains speculative as the real-life social functioning and well-being of individuals with MCI was not explored in any of these studies.

Discussion

Although research in emotion recognition in MCI is clearly in its infancy, this review synthesises evidence derived from six studies to date, and suggests that this aspect of social perception is indeed compromised. The underlying aetiology of this decrement, however, is not yet clear. Overall, the majority of the six studies reviewed do report worse facial emotion recognition in MCI cases over and above those associated with normal aging. Furthermore, these deficits appear to occur in the context of intact facial information processing. Although no consistent emotion-specific impairment is reported, there is some evidence to suggest the detection of negative emotions is selectively affected (e.g. anger, fear, sadness). Whilst this may reflect the overrepresentation of negative emotions included in studies, in that of the seven different emotions tested in studies only two (i.e., happiness and surprise) could be regarded as positive emotions, results are consistent with findings in both normal aging and dementia. There is also some limited evidence to suggest that more pervasive neuropsychological impairment (i.e., demonstrated by impairments across multiple cognitive domains) is associated with greater decline in emotion recognition.

Considerable caution must be exercised in drawing any firm conclusions, given the variability in findings within the limited research undertaken to date, as well as inconsistencies in the methodological

approaches taken. For example, studies differed in the type of stimuli used, emotional expressions investigated, and in the difficulty of tasks undertaken by study participants. Furthermore, a number of questions remain unanswered. Critically, does the reported decline in emotion recognition represent subtle changes in otherwise normal performance? In addition, how does diminished accuracy in emotion recognition relate to everyday social functioning, including interpersonal relationships, quality of life, neuropsychiatric symptoms such as depression and anxiety, and caregiver burden?

It is possible that poor performance on emotion recognition tasks reflects the cognitive decline associated with MCI rather than impaired emotion processing, per se. The role played by overall cognitive impairment in negatively influencing emotion recognition has been previously reported within an AD sample (Cadieux & Greve, 1997), in which patients performed poorly due to difficulties comprehending and/or remembering task instructions. Indeed, individuals found to be most impaired in emotion recognition in one study showed greater overall cognitive decline (Teng et al., 2007). However, a more thorough analysis of the impact of cognition on emotion recognition is difficult due to differences across studies in the application of diagnostic criteria employed. In the majority of studies, a broad diagnosis of aMCI or MCI was employed to classify cases. This approach does not differentiate the extent of cognitive decline amongst participants (e.g. single or multiple cognitive domains). Further, some studies undertook only limited neuropsychological testing across a narrow range of cognitive domains.

Nevertheless, the possibility still exists that changes in emotion recognition are indicative of early signs of impaired emotion processing. Support for this may be found in neuroimaging studies of MCI individuals demonstrating atrophy in regions implicated in emotion processing, including the amygdala, fusiform gyrus (Whitwell et al., 2007), superior temporal gyrus, insula (Karas et al., 2004) and anterior cingulate (Chételat et al., 2002). However, only one study to date has correlated emotion recognition results with neuroimaging data (Fujie et al., 2008).

To clarify the aetiology underpinning emotion recognition deficits, future studies should seek to address the limitations evident in current research. Adopting the most recent MCI diagnostic criteria (Petersen, 2004) to classify more precisely MCI cases according to subtypes (e.g. single- or multiple-domains) will help to clarify any specific emotion recognition profiles in an essentially heterogenous patient population. Given its relative recency as a specific subtype of interest, no study has included an naMCI sample. The association of the naMCI single-domain subtype with FTD (Petersen & Morris, 2005), a disease with the most compelling evidence to date of an emotion recognition deficit, strongly suggests that investigation of this subtype is warranted. Similarly, those with prominent frontal-subcortical changes, as often seen in vascular dementia (Rockwood, 2002), warrant investigation since data has linked pathology in this circuitry with early changes in emotion recognition.

Methodological considerations include addressing sample size issues, ensuring uniform matching of patient and control group demographics, and controlling for the potential confounds of facial processing and

visuospatial deficits. The effects of depression or anxiety, known to be prevalent in MCI and to impact detrimentally on emotion processing, must be accounted for.

Future research should aim to explore how changes in emotion recognition affect “real-life” interpersonal behaviour and social functioning in MCI. The reports of significant others represent an important source of information in this regard. Such research would subsequently inform whether early intervention to address emerging behavioural issues would benefit an MCI population (Naismith et al., 2009). Ultimately, longitudinal research will be required to determine the association of emotion recognition with neurodegeneration, and specifically, whether changes in emotion recognition predict clinical diagnosis and functional outcome.

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Table 1. Summary of emotion recognition research in MCI

Author	Number and type of subjects	Subjects' characteristics	Tasks and control tasks	Stimuli	Results
Bediou et al. (2009)	10 = aMCI (Petersen et al. [1999] criteria) 10 = mild dementia (AD; NINCDS-ADRDA criteria)	A = 73.0 ± 9.0; G = 50% male; MMSE = 27.0 ± 2.0 A = 72.0 ± 9.0; G = 50% male; MMSE = 21.0 ± 2.0	Emotion Recognition Task: Name emotion expressed on faces - morphed with neutral expression (happiness, fear, anger, disgust, neutral)	Photographs of faces	MCI = HC: mild AD < HC (anger); FTD < HC (disgust, happiness, fear); FTD < mild AD (disgust)

Table 1. Summary of emotion recognition research in MCI (continued)

Author	Number and type of subjects	Subjects' characteristics	Tasks and control tasks	Stimuli	Results
Bediou et al. (2009) (cont.)	10 = FTD (Neary et al. [1998] criteria)	A = 67.0 ± 7.0; G = 50% male; MMSE = 24.0 ± 4.0	Control Task Facial Gender Task: indicate face gender		HC = MCI = AD = FTD
	10 = HC	A = 70.0 ± 6.0; G = 50% male; MMSE = 30.0			

Table 1. Summary of emotion recognition research in MCI (continued)

Author	Number and type of subjects	Subjects' characteristics	Tasks and control tasks	Stimuli	Results
Fujie et al. (2008)	16 = aMCI (Mayo Clinic Alzheimer's disease Research Centre criteria; Petersen et al. [1999, 2001] criteria)	A = 71.7 ± 7.1; G = 25% male; E = 11.0 ± 2.2; MMSE = 27.2 ± 2.3	Emotion Recognition Task Name emotion expressed (happiness, sadness, fear, anger, disgust, surprise, neutral)	Black-and-white photographs of faces (Pictures of Facial Affect)	aMCI < HC (anger, sadness)

Table 1. Summary of emotion recognition research in MCI (continued)

Author	Number and type of subjects	Subjects' characteristics	Tasks and control tasks	Stimuli	Results
Fujie et al. (2008) (cont.)	14 = HC (Facial Emotion Recognition Task)	A = 74.1 ± 3.2; G = 28% male; E = 12.0 ± 2.2; MMSE = 28.8 ± 1.4	Control Task Benton Facial Recognition Task: identify face from distracters	Benton Facial Recognition Stimulus set	Results not reported
	16 = HC (Diffusion Tensor Imaging)	A = 70.9 ± 4.0; G = 25% male; E = 11.8 ± 2.4; MMSE = 29.2 ± 1.2	Diffusion Tensor Imaging Calculation of FA of the UF		aMCI < HC (FA of left UF)

Table 1. Summary of emotion recognition research in MCI (continued)

Author	Number and type of subjects	Subjects' characteristics	Tasks and control tasks	Stimuli	Results
Henry et al. (2009)	38 = MCI (Petersen [2007] criteria)	A = 78.7 ± 4.5; G = 50% male; E = 11.6 ± 3.6; MMSE = 27.9 ± 1.5	Emotion Recognition Task: Name emotion expressed (happiness, sadness, fear, anger, disgust, surprise)	Black-and-white photographs (Pictures of Facial Affect)	Dementia < HC, MCI; MCI < HC (trend only)
	34 = Dementia (DSM-IV criteria)	A = 79.4 ± 6.1; G = 47% male; E = 11.4 ± 3.6; MMSE = 26.0 ± 3.6			
	34 = HC	A = 77.2 ± 4.3; G = 44% male; E = 11.6 ± 3.6; MMSE = 28.6 ± 1.4			

Table 1. Summary of emotion recognition research in MCI (continued)

Author	Number and type of subjects	Subjects' characteristics	Tasks and control tasks	Stimuli	Results
Spoletini et al. (2008)	50 = aMCI (Petersen et al. [1999] criteria)	A = 71.2 ± 7.5; G = 54% male; E = 9.8 ± 4.6; MMSE = 26.7 ± 2.5	Emotion Recognition Task: Rate the emotional valence expressed in low- and high- intensity faces (happiness, sadness, fear, anger, disgust, neutral)	Colour photographs of faces (Penn Emotion Recognition Test)	Total (high- + low- intensity faces): Mild AD < HC (happiness, sadness, fear, anger, disgust); Mild AD < aMCI (happiness, sadness, fear, anger); HC = aMCI High-intensity faces: Mild AD < HC (happiness, sadness, fear, anger); Mild AD < aMCI (sadness, fear, anger); HC = aMCI
	50 = probable mild AD (NINCDS-ADRDA criteria)	A = 72.7 ± 6.9; G = 50% male; E = 7.9 ± 4.6; MMSE = 22.0 ± 3.3			

Table 1. Summary of emotion recognition research in MCI (continued)

Author	Number and type of subjects	Subjects' characteristics	Tasks and control tasks	Stimuli	Results
Spoletini et al. (2008) (cont.)	50 = HC	A = 71.8 ± 7.4; G = 44% male; E = 9.1 ± 4.2; MMSE = 27.8 ± 1.8			Low-intensity faces: Mild AD < HC (happiness, sadness, disgust, fear); Mild AD < aMCI (happiness, sadness); aMCI < HC (fear)
			Control Task Benton Facial Recognition Task: identify face from distracters	Benton Facial Recognition Stimulus set	HC = aMCI Mild AD < HC, aMCI

Table 1. Summary of emotion recognition research in MCI (continued)

Author	Number and type of subjects	Subjects' characteristics	Tasks and control tasks	Stimuli	Results
Teng et al. (2007)	9 = MCI SD (Petersen et al. [1999] criteria)	A = 79.4 ± 3.8; G = 78% male; E = 18.2 ± 4.5; MMSE = 26.9 ± 2.8	Emotion Recognition Task 4 tasks: discriminate, name, select or match emotion expressed (happiness, sadness, frightened, anger, neutral)	Black-and-white photographs of faces (Florida Affect Battery)	MCI MD < HC, MCI SD (facial affect discrimination) Males < females
	14 = MCI MD (Petersen et al. [1999] criteria)	A = 72.8 ± 7.7; G = 50% male; E = 15.1 ± 2.0; MMSE = 26.4 ± 2.7			
	68 = HC	A = 69.5 ± 9.5; G = 57% male; E = 17.0 ± 2.9; MMSE = 29.2 ± 0.9			

Table 1. Summary of emotion recognition research in MCI (continued)

Author	Number and type of subjects	Subjects' characteristics	Tasks and control tasks	Stimuli	Results
Teng et al. (2007) (cont.)			Control Task Facial Identity Discrimination Task: identify whether faces shown match	Black-and-white photographs of faces (Florida Affect Battery)	MCI-SD = MCI-MD = HC Males < females

Table 1. Summary of emotion recognition research in MCI (continued)

Author	Number and type of subjects	Subjects' characteristics	Tasks and control tasks	Stimuli	Results
Weiss et al. (2008)	21 = aMCI SD (Petersen et al. [2001] criteria; Winblad et al. [2004] criteria)	A = 72.8 ± 6.5; G = 28% male; E = 10.4 ± 3.9; MMSE = 27.0 ± 1.0	Emotion Recognition Task: Recognise emotion expressed (happiness, sadness, fear, anger, neutral)	Colour photographs of faces (Penn Emotion Recognition Test)	aMCI SD = HC aMCI MD < HC (overall emotion, sad, fear, neutral)
	30 = aMCI MD (Petersen et al. [2001] criteria; Winblad et al. [2004] criteria)	A = 74.3 ± 7.0; G = 33% male; E = 9.8 ± 2.7; MMSE = 26.0 ± 1.1			Early AD < HC (overall emotion, sadness, fear, neutral)

Table 1. Summary of emotion recognition research in MCI (continued)

Author	Number and type of subjects	Subjects' characteristics	Tasks and control tasks	Stimuli	Results
Weiss et al. (2008) (cont.)	30 = Early AD (NINCDS-ADRDA criteria)	A = 76.7 ± 8.0; G = 33% male; E = 9.7 ± 2.4; MMSE = 22.5 ± 1.5			Moderate AD < HC (overall emotion, happiness, sad, fear, neutral)
	23 = Moderate AD (NINCDS-ADRDA criteria)	A = 80.1 ± 6.2; G = 30% male; E = 8.7 ± 2.0; MMSE = 16.3 ± 2.7			

Table 1. Summary of emotion recognition research in MCI (continued)

Author	Number and type of subjects	Subjects' characteristics	Tasks and control tasks	Stimuli	Results
Weiss et al. (2008) (cont.)	35 = HC	A = 70.8 ± 7.5; G = 28% male; E = 10.7 ± 3.3; MMSE = 28.9 ± 1.0			

A = Age; E = education; G = gender; HC = healthy controls; MD = multiple domains; SD = single domain; FA = fractional anisotropy; UF = uncinate fasciculus.

CHAPTER 3

MILD COGNITIVE IMPAIRMENT AND EMOTION RECOGNITION: RESEARCH AIMS AND HYPOTHESES

Research findings from literature review

The literature review of the preceding chapter demonstrated that very early deficits in emotion recognition may already be evident in individuals diagnosed with MCI. As previously outlined, however, the research conducted to date is sparse, with a number of methodological issues evident. Of particular note is the omission of the non-amnestic subtype in MCI studies assessing emotion recognition abilities. This omission is surprising given the association between naMCI and FTD, a dementia population with compelling evidence of emotion recognition impairments (Keane, Calder, Hodges, & Young, 2002). As such, the emotion recognition abilities of the naMCI subtype remain unclear. Furthermore, studies to date have only assessed the facial emotion recognition abilities of individuals with aMCI. Whilst there is some evidence to suggest that AD patients have difficulties in decoding emotions from gestures and body movement (Koff, Zaitchik, Montepare, & Albert, 1999), no known research has been undertaken to explore whether early disruptions in the abilities of MCI patients extend beyond facial emotion recognition. Consequently, the first study addresses these issues.

A further limitation of research is that the real-life implications of disrupted emotion recognition in MCI are as yet unknown. However, there

is some evidence to suggest that in AD emotion recognition deficits are associated with decrements in social functioning (Shimokawa et al., 2001) and are predictive of increased caregiver burden (Greve, Cadieux, & Hale, 1995). An understanding of the relationship between emotion recognition difficulties, social functioning and caregiver burden is important as it would inform whether intervention programmes targeted at the emotion recognition abilities of MCI patients are warranted. Hence, the relationship between emotion recognition, caregiver burden and disability is the focus of Study 2.

Aims and hypotheses

The aim of the studies reported in the following chapters was to examine the emotion recognition abilities of patients with MCI. The first study aimed to evaluate the emotion recognition abilities of both aMCI and naMCI subtypes. The second study aimed to examine the emotion recognition abilities and functional disability of MCI patients, as well as the level of burden experienced by caregivers. In addition, the relationship between emotion recognition abilities, and functional disability and caregiver burden was explored.

Study 1: Emotion recognition deficits exist in Mild Cognitive Impairment, but only in the amnestic subtype

The emotion recognition profiles of MCI multiple-domain subtypes were compared with those of healthy age- and education-matched controls. The emotion recognition abilities were examined utilising tasks varying in

(1) the level of cognitive difficulty (i.e., prompted and non-prompted task conditions) and (2) stimuli employed (i.e., facial and body posture/hand gestures). The relationship between emotion recognition abilities and cognition, as measured by performance on neuropsychological tests, and mood was also explored.

Hypotheses

The first hypothesis was that decrements would be evident in the emotion recognition abilities of both naMCI and aMCI subtypes, but not for controls. The second hypothesis was that, consistent with past MCI research, difficulties underlying emotion recognition abilities may be, at least in part, accounted for by cognitive abilities, but not mood.

Study 2: Emotion recognition in Mild Cognitive Impairment: Relationship to disability and caregiver burden

The emotion recognition abilities, level of caregiver burden and functional disability of both naMCI and aMCI multi-domain patient groups were compared with those of healthy age- and education-matched controls. In addition, the relationship between emotion recognition and level of caregiver burden as well as functional disability was explored.

Hypotheses

It was postulated that both naMCI and aMCI subtypes would (1) be less accurate in their emotion recognition ability, (2) have greater functional disability, and (3) have greater levels of burden, as reported by

their caregivers, compared with controls. The second hypothesis was that, consistent with past research within AD patient samples, an association would be evident for both MCI subtypes between impaired emotion recognition, caregiver burden and social dysfunction.

Thesis discussion

A summary of the key research findings from Study 1 and Study 2 is subsequently provided in Chapter 6. In this Discussion section, limitations of both studies, as well as a broad platform of areas for future research, are then presented. In addition, the clinical implications of Study 1 and Study 2 are discussed in detail.

CHAPTER 4

STUDY 1

This paper has been submitted to *Psychology and Aging* and is represented in the format required for that submission, with the exception of page numbers and table numbers which are numbered to be consistent with the thesis as a whole. Some repetition of information and particularly references was unavoidable given the nature of the thesis by papers format.

My contribution to the paper is estimated to be 70%, including the formulation of the research questions, research design, experiment set-up, participant testing, analysis, interpretation and manuscript preparation. Associate Professor Sharon Naismith and Associate Professor Greg Savage contributed an estimated 15% and 5%, respectively, to research design and manuscript preparation. Additional estimated contributions were from Associate Professor Adam Guastella (research design - 5%) and Associate Professor Simon Lewis (neurological input - 5%).

Emotion recognition deficits exist in Mild Cognitive Impairment, but only in the amnestic subtype

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Conflict of Interest: Nil

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ORIGINAL RESEARCH

Abstract

Emotion recognition is impaired in dementia and there is some initial evidence to suggest that milder deficits may be present in Mild Cognitive Impairment (MCI) patients, an "at risk" population for transition to dementia. In this study, we investigated the emotion recognition profile of MCI subgroups. Results show emotion recognition deficits exist for the amnestic subtype with impairment in multiple-domains, with an emotion-specific deficit for anger recognition. Impaired emotion recognition in aMCI was found regardless of task demands, and was independent of patient mood and cognitive deficits. The study is the first to examine the non-amnestic subtype and found no emotion recognition deficits; this finding is surprising given the association between the non-amnestic subtype and frontal systems dysfunction. Impaired emotion recognition could be related to the selective pathophysiology in neural pathways implicated in both aMCI and emotion processing. These findings may have implications for early diagnosis, prognosis and clinical management.

Key words: Dementia; Emotion recognition; Emotion processing; Facial expressions; Social cognition; Mild Cognitive Impairment.

Word Count: 7,272

Introduction

The ability to recognise emotional and contextual information, in order to infer the mental states of others, enables individuals to make sense of their social environment and modify their behaviour accordingly. Emotion recognition, which is typically classified under the rubric of social cognition (Beer & Ochsner, 2006), is critical in facilitating effective communication and interpersonal relationships. Deficits in this ability have been associated with reduced social competence, inappropriate social behaviour and diminished quality of life (Carton, Kessler, & Pape, 1999; Shimokawa et al., 2001).

Research suggests that this critical ability declines with normal ageing, particularly in the recognition of negative emotions (Calder et al. 2003; Isaacowitz et al., 2007). It is thought that this decline may be associated with age-related neurological change (Calder et al. 2003; Phillips, MacLean, & Allen, 2002). Multiple interconnected and overlapping brain regions are thought to be recruited in emotion recognition, including the temporal lobes, particularly the superior temporal sulcus/gyrus and amygdala (Adolphs, Tranel, Damasio, & Damasio, 1994; Sato, Bottlender, Schroter, & Moller, 2004), the fusiform gyri (Adolphs, 2001) and the frontal lobes, especially orbitofrontal, medial prefrontal subdivisions and cingulate areas (Craik & Moroz, 1999; Fossati, Hevenor, Graham, & Grady, 2003).

Neuroimaging studies also show an increased reliance on the medial prefrontal cortex, coupled with reduced amygdala activation, in older

adults compared with young adults during emotion processing (Gunning-Dixon et al., 2003). The temporal and frontal lobes are regions known to be particularly susceptible to age-related change (Bartzokis et al., 2001; Raz et al., 2005).

Degeneration in temporal and frontal cortical regions is also characteristic of many dementing processes and there is evidence to indicate that, over and above age-related cognitive decline, emotion recognition is impaired in some dementias. Deficits in emotion recognition in dementia have been linked with pathological change within the ventromedial frontal cortex and amygdala (Keane, Calder, Hodges, & Young, 2002; Rosen et al., 2002). A specific association with the lateral portion of the right inferior and middle temporal gyri has also been reported for the impaired recognition of negatively valenced emotions in demented patients (Rosen et al., 2006).

Strong empirical support exists for impaired emotion recognition in frontotemporal dementia (FTD) patients (Diehl-Schmid et al., 2007; Lavenu, Pasquier, Lebert, Petit, & Van der Linden, 1999) in the detection of emotional facial expressions including happiness (Keane et al., 2002; Mourik, Rosso, Niermeijer, Duivenvoorden, & Tibben, 2004; Rosen et al., 2004), surprise (Kessels et al., 2007; Lavenu & Pasquier, 2005; Rosen et al., 2004), sadness (Fernandez-Duque & Black, 2005; Keane et al., 2002; Lavenu et al., 1999; Rosen et al., 2004), disgust (Fernandez-Duque & Black, 2005; Lavenu & Pasquier, 2005; Lough et al., 2006; Rosen et al., 2004), fear (Fernandez-Duque & Black, 2005; Keane et al., 2002; Kessels et al., 2007; Rosen et al., 2004) and anger (Fernandez-Duque & Black,

2005; Keane et al., 2002; Lavenu & Pasquier, 2005; Mourik et al., 2004) when compared with healthy controls. These observations confirm the likely clinicopathological correlations between differing aspects of social cognition and focal disease processes.

Individuals with Alzheimer's disease (AD) have been shown to experience difficulties in identifying, labelling, matching and discriminating facial emotions (Allender & Kaszniak, 1989; Hargrave, Maddock, & Stone, 2002; Henry et al., 2008; Phillips, Scott, Henry, Mowat, & Bell, 2010; Spoletini et al., 2008; Weiss et al., 2008) when compared with healthy controls. These abilities have been shown to further decline with disease progression (Lavenu & Pasquier, 2005). A relationship has been reported between emotion recognition abilities and cognitive abilities for AD patients, with specific associations for verbal memory impairment (Spoletini et al., 2008) and executive dysfunction (Phillips et al., 2010). Furthermore, a significant relationship has been found between depression and impaired emotion recognition in AD patients (Weiss et al., 2008), although this has not been universally supported (Phillips et al., 2010). Some studies have, however, failed to detect emotion recognition deficits in AD patients (Fernandez-Duque & Black, 2005) or have attributed observed decreases to general cognitive dysfunction rather than emotion processing impairment per se (Albert, Cohen, & Koff, 1991; Bucks & Radford, 2004; Burnham & Hogervorst, 2004; Cadieux & Greve, 1997; Roudier et al., 1998).

In contrast, little is understood of the profile of emotion recognition in dementias due to cerebrovascular disease or synucleinopathy (i.e., vascular

dementia [VaD] and dementia with Lewy bodies [DLB]). Since degeneration of the frontal and temporal regions are implicated in both diseases, it is plausible to assume that deficits in this function may exist. To the authors' knowledge, only two studies in VaD have been undertaken to date (Shimokawa et al., 2000; Shimokawa et al., 2003), and these suggest that emotion processing impairments are indeed evident. Specifically, VaD patients were found to be significantly worse at recognising emotions from line drawings of a face compared with AD patients and healthy controls (Shimokawa et al., 2000). VaD patients were also impaired in matching the emotional content of line drawings of faces with photographed faces compared with AD patients (Shimokawa et al., 2003).

Despite existing research into the nature and profile of emotion recognition deficits that are evident in dementia, it remains unclear when such deficits actually begin to emerge. Such knowledge may elucidate whether early impairment in emotion recognition is indicative of subsequent disease trajectories, such as progression to Alzheimer's versus vascular dementia. Also, if deficits were evident early, they may form the target of interventions aimed at improving social cognition.

As recently reviewed (McCade, Savage, & Naismith, 2011), a small number of studies have attempted to explore emotion recognition in early neurodegenerative disease by examining these abilities in individuals with Mild Cognitive Impairment (MCI). MCI is widely recognised as an "at risk" state between normal aging and the earliest clinical features of dementia (Petersen et al., 2010). The construct of MCI is used to identify

individuals with either initial memory impairments, referred to as amnestic MCI (aMCI; Petersen et al., 2001), or individuals with initial impairments across cognitive domains other than memory, known as non-amnestic MCI (naMCI; Petersen, 2004). A further sub-classification of MCI patients specifies whether individuals are impaired in single versus multiple cognitive domains (Petersen, 2004). In both aMCI and naMCI groups, cognitive impairment exists within a context of generally preserved activities of daily living.

With regard to prognoses, individuals with aMCI are reported to be at higher risk of progression to AD, with conversion rates of 10% to 18% per annum (Gauthier et al., 2006; Petersen, 2004). In contrast, the disease trajectory of the naMCI subtype is less well understood and is likely to reflect more diverse pathophysiological processes including VaD, FTD and DLB (see review by Gauthier et al., 2006; Mariani et al., 2007). Thus, while individuals with naMCI certainly do have increased conversion rates to AD compared to healthy controls (Busse, Hensel, Guhne, Angermeyer, & Riedel-Heller, 2006), these appear to be much lower than for aMCI (Nordlund et al., 2010). Unsurprisingly, in both aMCI and naMCI subgroups, individuals with multiple-domain MCI have a higher probability of conversion to dementia than those with the single MCI subtype (Rasquin, Lodder, Visser, Lousberg, & Verhey, 2005). Furthermore, cognition in the latter subgroup may even stabilise or return to normal (Diniz, Nunes, Yassuda, & Forlenza, 2009; Forlenza et al., 2009; Ritchie & Tuokko, 2010).

As reviewed elsewhere (McCade et al., 2011), there are some data to suggest that emotion recognition in the amnestic MCI subtype is impaired relative to controls (Fujie et al., 2008; Spoletini et al., 2008; Teng, Lu, & Cummings, 2007; Weiss et al., 2008). Emotion-specific deficits have been found for sad (Fujie et al., 2008; Weiss et al., 2008), fearful (Spoletini et al., 2008; Weiss et al., 2008), angry (Fujie et al., 2008) and neutral (Weiss et al., 2008) faces. Studies which have included both single- and multiple-domain aMCI subtypes have found impaired emotion recognition only in those individuals with deficits across multiple cognitive domains (Teng et al., 2007; Weiss et al., 2008), suggesting that onset of emotion recognition deficits is associated with more advanced and/or diverse neurodegenerative pathology. Indeed, similarities have been found in the emotion processing strategies used by both aMCI and AD patients (Werheid et al., 2010). Specifically, the typical effect of emotional material to enhance episodic memory was found to be diminished in aMCI patients, which is also the case in AD patients (Kensinger, Brierley, Medford, Growdon, & Corkin, 2002). Relationships have also been reported between emotion recognition deficits and cognitive abilities (i.e., executive dysfunction; Teng et al., 2007) and mood (i.e., depression; Weiss et al., 2008). Impaired emotion recognition in MCI patients has not, however, been universally supported, with other studies failing to detect deficits (Bediou et al., 2009; Henry et al., 2009).

To date, emotion recognition studies in MCI have focused specifically on the aMCI subgroup or have used a generic MCI classification. Thus, it remains unclear whether those with non-amnestic forms also exhibit

deficits in this function. Given the proposed association of the naMCI subtype with FTD and VaD (Petersen, 2007), it is plausible to hypothesise that deficits in emotion recognition may also be evident in this MCI subgroup.

Hence, the aim of our study was to determine whether emotion recognition deficits are evident within both aMCI and naMCI subgroups, relative to control subjects. We were also interested in determining the conditions under which deficits in emotion recognition are demonstrated. Whilst emotion recognition is an effortful process with regard to cognitive resources required, some tasks may require a greater cognitive demand than others (Adolphs, 2002). For example, labeling an emotion is arguably less cognitively demanding when the emotion labels are provided (i.e., a forced choice matching task), compared with when the emotion labels are not provided. In the latter case, the independent retrieval of associated knowledge and language about the concept of emotion is required. Consequently this task is more complex, requiring higher order processing which may in turn impact task performance (Adolphs, 2002). In this regard we examined whether task condition influenced emotion recognition. To date, studies in MCI have predominantly used tasks with forced choice formats. We wondered whether recognition accuracy was assisted by the provision of prompts for emotions. Consistent with past research (Teng et al., 2007), it was hypothesised that difficulties underlying emotion recognition abilities may be, at least in part, accounted for by cognitive abilities. Also, previous MCI studies have used facial displays of emotions to assess recognition. We, therefore, explored whether emotional stimuli

type would influence performance by using bodily, as well as facial, displays of emotions. Finally, we examined what factors may underlie deficits in emotion recognition in MCI by exploring the relationship between emotion recognition deficits and both cognition and mood. Given the finding from past studies that emotion recognition deficits were evident only in MCI patients with deficits across multiple, rather than single, cognitive domains (Teng et al., 2007; Weiss et al., 2008), we chose to accordingly focus on the MCI multiple-domain subtype in this study.

Methods

Participants

Thirty-seven patients meeting criteria for Mild Cognitive Impairment (Petersen, 2004) were recruited from a specialist 'Healthy Brain Ageing' Centre at the Brain & Mind Research Institute, Sydney, Australia. This centre receives referrals from local neurologists, psychiatrists and geriatricians and preferentially targets people over the age of 50 who have emerging cognitive and/or mood disorders. The patient sample was restricted to only those with multiple-domain MCI due to the low sensitivity of single-domain MCI as a prognostic test for the development of dementia (Rasquin et al., 2005). In addition, nineteen age- and education-matched healthy volunteers were recruited from the community via local advertisements.

Inclusion criteria for all participants were: age greater than 50 years; English as a first language; and a Mini-Mental State Examination Score (MMSE) $\geq$ 24. Exclusion criteria were: any psychiatric disorder (e.g.

current major depression, schizophrenia) or neurological disorder (e.g. head injury, prior stroke or transient ischaemic attack, epilepsy); established dementia (as determined by comprehensive clinical neuropsychological and psychiatric assessment); intellectual disability; substance abuse; or impaired basic facial processing (as measured by a score of ≤ 41 on the Benton Facial Recognition Test; Benton, Sivan, Hamsher, Varney, & Spreen, 1994). In addition, controls were required to demonstrate intact cognitive functioning with no evidence of impairment defined by performance 1.5 standard deviations (SDs) below age-based norms on a battery of standardised neuropsychological tests.

Measures

Clinical

All participants were assessed by a psychogeriatrician to derive a clinical, medical and psychiatric history, including cognitive complaints, level of functioning and current medications. Current depression severity was ascertained using the 17-item Hamilton Depression Rating Scale (HAM-D; Hamilton, 1960). Each patient was required to have subjective and objective cognitive decline in the context of preserved function, as evidenced by a Global Deterioration Scale score of <3. For patients with MCI, medication details at the time of examination included 13 individuals taking antidepressants regularly (all of whom were taking newer generation serotonergic or noradrenergic agents). Of these patients, six were also taking a benzodiazepine (prn), one was taking a tricylic

antidepressant and two were taking an adjunct atypical antipsychotic (quetiapine, risperidone).

Cognitive

A neuropsychologist administered a standardized test battery to all participants. For descriptive purposes only, the MMSE was used as a broad measure of cognitive functioning and premorbid intellectual ability was estimated using the Wechsler Test of Adult Reading (WTAR; Wechsler, 2001). The test battery was selected for its capacity to examine broad aspects of cognition and, therefore, facilitate accurate clinical diagnoses regarding MCI subtype. To meet criteria for MCI, patients were required to demonstrate objective evidence of cognitive impairment defined by performance 1.5 SDs below age-based norms on a battery of standardised neuropsychological tests. Each patient was required to be impaired in at least two cognitive domains, with aMCI patients required to show impairment on a memory domain. Patients were diagnosed with aMCI if demonstrated memory impairments were of the 'hippocampal-type'. That is, clear evidence of memory storage deficits was required, not merely reflecting poor encoding. Patients were diagnosed with naMCI if deficits were present on tests of other cognitive domains (e.g. processing speed, working memory, language, executive functioning). A standardised test battery, selected for its capacity to examine multiple aspects of cognition in order to facilitate accurate clinical diagnosis regarding MCI and subtype, was administered by a neuropsychologist. Cognitive domains assessed to diagnose MCI were speed of processing, working memory, verbal learning and memory, visual memory, language, visuospatial skills

and executive functioning. Of specific interest was the relationship between emotion recognition and temporal and frontal lobe functioning, as assessed by verbal memory and executive functioning tasks. The Logical Memory subtest of the Wechsler Memory Scale - Third Edition (WMS-III; Wechsler, 1997) was used to assess structured verbal learning and memory. Executive functioning tasks comprised the Controlled Oral Word Association Test (COWAT) to assess letter fluency and the Trail-making Test Part B (Reitan, 1979) to assess mental flexibility.

From these assessments, consensus diagnostic ratings for those cases with MCI were performed by a psychogeriatrician and two neuropsychologists according to established MCI criteria (Petersen, 2004). This included ratings for both amnestic and non-amnestic MCI. As noted above, only those with multi-domain MCI were included in this study.

Facial recognition

To control for perceptually-based face processing deficits, the Short Form Benton Facial Recognition Test (BFRT; Benton et al., 1994), a face matching task, was administered. The Short Form BFRT consists of thirteen still black-and- white photographs of unfamiliar male and female faces. Participants were required to match the frontal view of a target face either with an identical photograph or with three photographs of the target face taken from different angles. No time limit was placed on the stimulus display or on the participant's response.

Emotion recognition

Participants were administered three different tasks assessing emotional recognition:

Emotion recognition with emotion prompts (FEEST)

The Ekman 60 Faces test is a computerised emotion recognition task taken from the Facial Expressions of Emotion: Stimuli and Tests CD-ROM (FEEST; Young et al., 2002). Sixty black-and-white still photographs from the Ekman and Friesen (1976) series of faces portraying six basic emotions (i.e., happiness, sadness, anger, fear, surprise, disgust) were presented one at a time for 5 seconds in a randomised order to participants on a computer screen, with the six basic emotion labels displayed in the bottom half of the screen. Participants were required to select which one of the emotion labels best matched the actor's displayed emotion by clicking a mouse onto the appropriate label. No limit was placed on the participant's time to respond and the next face was not shown until a response was made. A practice trial, which displayed each of the six basic emotions, was provided to familiarise participants with the response process. Participants received one point for each correct answer, with a maximum score of 60 for the overall task and a score out of 10 for each of the six basic emotions.

Emotion recognition without emotion prompts (Emotion Identification task)

In the Emotion Identification task, six photographs of each emotional expression (i.e., disgust, surprise, anger, fear, happiness) as well as six neutral facial presentations were displayed one at a time for 4 seconds each on a computer screen. Participants were asked to identify the actor's emotional display (i.e., "How is this person feeling?"). No prompts were provided and there was no time limit on the participant's response. Subsequent faces were not presented until the participant had provided a response. All photographs were black and white and from the NimStim set of facial expressions (Tottenham et al., 2009). Equal numbers of photographed male and female actors were included in the task and the initial order in which faces were presented was randomised. One point was awarded for each correct answer, with a maximum score of 42 for the overall task and a score out of six for each of the six basic emotions. Participants' responses were judged independently by two trained neuropsychologist assessors using scoring guidelines compiled from dictionary and thesaurus sources, with high inter-rater reliability (k = 0.80). A third trained neuropsychologist assessor was used as an arbiter to determine the final score for participants used in analysis.

Emotion recognition with and without facial cues (Movie Stills Task)

The Movie Stills Task (Losh et al., 2009) measures an individual's ability to use facial and bodily information to determine the emotional content of complex scenes. Sixteen black-and-white photographs, taken

from movie scenes depicting complex situations containing people, were presented individually to participants on a computer screen. Participants were initially shown scenes with the face of the actor(s) digitally erased. Following presentation of all scenes, participants were subsequently shown the same scenes with the faces intact. In addition to facial expressions, scenes contained additional cues such as head and body posture and hand gestures. Participants were asked to select the one emotion from the seven emotion labels displayed on the bottom of screen (i.e., happy, surprised, afraid, angry, disgusted, sad, neutral) which best matched the mood of the scene. No time limit was placed on the stimulus display or on the participant's response. Accuracy of emotion recognition for each participant was assessed for scenes when faces were shown and additionally for scenes without faces cues displayed. Emotions assessed were happiness, surprise, fear, sad, anger and neutral.

The order of tasks was not counterbalanced given prompted conditions were employed before non-prompted conditions. This was done to familiarise subjects to the response process. The order of tasks was FEEST, Emotion Identification task, and finally, Movie Stills Task. Four participants did not undertake the Movie Stills Task due to inability to attend testing sessions and / or subject time constraints.

Statistical analyses

Statistical analyses were performed with PASW Statistics, Release Version 18.0.0 (SPSS, Inc., 2009, Chicago Ill., USA). To test for differences between MCI and control groups, one way Analysis of

Variance (ANOVA) was utilised for normally distributed measures. Kruskal-Wallis non-parametric tests were undertaken to examine group differences for all emotion-specific components of recognition tasks revealed to be significantly non-normal on Kolmogorov-Smirnov tests. Accordingly, subsequent Mann-Whitney analyses were performed on tasks where significant group differences were detected. To control for Type I error, a Bonferroni correction was applied so that all effects are reported at a .0167 level of significance. Spearman's rho correlations were performed to examine the association between emotion recognition measures, clinical symptoms and neuropsychological performance. The alpha level was adjusted to .01 to control for the multiple correlations undertaken.

An ANCOVA was undertaken to control for the impact of executive functioning on one emotion recognition measure (i.e., Movie Stills Task - overall without faces), which had been found to be normally distributed on Kolmogorov-Smirnov testing. To control for the impact of cognition (i.e., executive functioning and working memory) on a further emotion recognition measure (i.e., FEEST - anger), which was found not to be normally distributed, separate analyses were undertaken to partial out the effects of cognitive ability. Separate Kruskal-Wallis non-parametric tests were subsequently undertaken on both saved residuals in order to control for the effects of executive functioning and working memory, respectively.

Results

Table 2 demonstrates the clinical and demographic characteristics of the sample. Of the 37 patients with MCI, nineteen of these patients were

diagnosed with aMCI and 18 with naMCI, according to consensus criteria (Petersen, 2004). The groups were well matched in terms of intellectual functioning (WTAR), age, gender and years of education. The aMCI sample's MMSE scores were significantly lower than both Control subjects and naMCI patients. A trend was evident for naMCI patients to score lower on the MMSE than Control subjects (p = .052). Whilst Control subjects had significantly lower levels of depressive symptoms than patient groups, both Control subjects and aMCI patients were within normal limits, according to a clinician measure (HAM-D) and the naMCI sample had only mild levels of depressive symptoms.

Table 3 displays the neuropsychological performance for each group.

Facial recognition

No significant differences were found between groups in facial recognition, as measured by the Benton Facial Recognition Test (F(2,54) = 1.717, p = .189).

Emotion recognition with emotion prompts (FEEST)

Table 4 shows total scores of each facial emotion assessed using the FEEST in aMCI, naMCI and Control groups. Between-groups analysis of FEEST scores across emotions showed significant group differences in the recognition of anger (Table 4). Subsequent Mann-Whitney between-groups comparisons revealed a significant deficit in the recognition of anger for aMCI patients compared with Control subjects (U = 83.0, z = -2.88, p = .003), which represents a medium effect size (r = -.47). Using the

adjusted alpha level, naMCI patients did not differ significantly from aMCI patients (p = .049) or Control subjects (p = .089) in anger recognition.

Emotion recognition without emotion prompts (Emotion Identification task)

Between-groups analysis of Emotion Identification task scores across emotions (Table 5) showed significant group differences in the overall recognition of emotions, and emotion-specific deficits for anger and neutral. Subsequent Mann-Whitney between-groups comparisons revealed a significant deficit in the identification of total emotions (U = 85.5, z = -2.78, p = .005), which represents a medium effect size (r = -.47), and an emotion-specific deficit for the identification of anger (U = 96.0, z = -2.51, p = .011), a medium effect size (r = -.41), in aMCI patients compared with Controls. Using the adjusted alpha level, aMCI patients did not differ from Controls with regard to neutral faces (U = 108.0, z = -2.15, p = .033). Patients with aMCI were also significantly worse in the identification of anger than naMCI patients (U = 92.5, z = -2.45, p = .013), a medium effect size (r = -.41). Using an adjusted alpha level, there was no difference between patient groups in the identification of total emotions (U = 94.0, z = -2.35, p =.018). Using the adjusted alpha level, naMCI patients did not differ significantly from Control subjects on any measure of emotion recognition without prompts (total emotions: U = 170.0, z = -0.03, p = .982; neutral: U = 103.5, z = -2.08, p = .038; anger: U = 169.0, z = -0.06, p = .951).

Emotion recognition with and without facial cues (Movie Stills Task)

Four participants (two naMCI patients and two Control subjects) did not undertake this task. Between-groups analyses of Movie Stills Task scores across emotions (Table 6) revealed a main effect for overall (i.e., total) emotions with facial cues and an emotion-specific effect for sad scenes, without facial cues. Subsequent Mann-Whitney between-groups comparisons revealed aMCI patients differed significantly from Control subjects for total emotions with facial cues (U = 80.0, z = -2.58; p = .009), a medium effect size (r = -.42). In contrast, naMCI patients did not differ significantly from Control subjects or aMCI patients on any measure. A one-way ANOVA revealed significant between-groups differences for total emotion identification without facial cues. Bonferroni-corrected post hoc tests revealed that aMCI patients were significantly worse than Control subjects in the recognition of total emotions without facial cues (p = .004), a large effect size (Cohen's d = -.81). In contrast, naMCI patients did not differ significantly from Control subjects or from aMCI patients in recognising total emotions without facial cues (p = .092 and p = .857 respectively). No other group differences were detected.

Correlates of emotion recognition

Neuropsychological performance and clinical symptoms were correlated with emotion recognition measures for aMCI patients. Using an adjusted alpha level, there was no significant association between overall cognition (i.e., MMSE) and emotion recognition deficits.

With regard to cognitive functioning, using an adjusted alpha level, worse prompted recognition of anger (i.e., FEEST) and worse recognition of overall emotional scenes without facial cues (i.e., Movie Stills Task) were significantly associated with diminished executive functioning (letter fluency; $r_s = .60$, $p = .006$ and $r = .62$, $p = .005$ respectively).

Worse prompted recognition of anger (i.e., FEEST) was significantly associated with worse working memory (Digit Span; $r_s = .64$, $p = .003$). Surprisingly, worse recognition of overall emotional scenes which included facial cues (i.e., Movie Stills Task) was significantly associated with improved verbal learning and memory performance (Logical Memory I: $r_s = -.77$, $p < .001$, Logical Memory II: $r_s = -.70$, $p = .001$). Using an adjusted alpha level, no association was found between language abilities (i.e., Boston Naming Test; Kaplan, Goodglass, & Weintraub, 1983) and emotion recognition.

Subsequent analyses were undertaken to control for the effects of any variables shown to have a significant relationship with individual emotion recognition measures. Performance on a working memory task (i.e., Digit Span) was used to predict anger recognition (i.e., FEEST). As this measure was not normally distributed, the residuals were then analysed using Kruskal-Wallis non-parametric tests, revealing that, after controlling for the effects of working memory, there continued to be a significant group difference in emotion recognition ($\chi^2 = 8.686$, df = 2, $p = .010$).

Executive functioning (i.e., letter fluency performance) was used to predict anger recognition (i.e., FEEST). The residuals were then analysed

using Kruskal-Wallis non-parametric tests, revealing that, after controlling for the effects of executive functioning, group differences in emotion recognition remained significant ($\chi^2 = 8.325$, df = 2, $p = .013$).

An ANCOVA was undertaken on group differences for overall emotional scenes without faces (i.e., Movie Stills Task), controlling for the effects of executive functioning (i.e., letter fluency performance). The covariate was not significantly related to emotion recognition, $F(1,48) = 2.633$, $p = .111$. After controlling for the effects of executive functioning, however, using an adjusted alpha level emotion recognition was not significant, $F(2,48) = 4.140$, $p = .022$, *partial* $n^2 = .15$.

Using an adjusted alpha level, there was no significant association with depressive symptoms, as measured by the clinician administered HAM-D, and emotion recognition deficits for aMCI patients.

Discussion

This study investigated emotion recognition in MCI to explore whether differences between MCI subgroups exist, when compared with aged-matched healthy controls. Our study is the first to show that whilst there are deficits in emotion recognition in MCI patients, deficits are evident only in individuals with aMCI, in which memory deficits predominate. Furthermore, specific findings of impaired emotion recognition in aMCI patients were found in the three emotion recognition tasks employed in this study. In contrast, deficits in emotion recognition were not evident for naMCI patients, with the performances of this group comparable to those of healthy aged-matched controls across all of the three tasks.

The specific findings of this study are, firstly, when required to identify emotions without the assistance of prompts, aMCI patients were significantly less accurate in their overall recognition of emotions (i.e., in the Emotion Identification task), compared with healthy aged-matched control subjects. An emotion-specific deficit was evident in aMCI patients for the non-prompted recognition of angry faces.

Secondly, the overall and anger-specific emotion recognition deficits were not ameliorated by the provision of prompts (i.e., in the Movie Stills Task and FEEST). It could be argued that the non-prompted task condition (i.e., Emotion Identification task) is a more cognitively challenging task in that the subject is required to generate their responses independently. These results suggest that emotion recognition deficits in aMCI exist independent of task requirements and regardless of the cognitive demands posed by the task. It is noteworthy, however, that no significant difference was found in the performance of groups for overall emotion recognition in one of the prompted task conditions (i.e., FEEST). Why this inconsistency in results was evident across emotion recognition tasks is unclear. It is possible that the FEEST task was not sufficiently sensitive to detect an overall effect of impaired emotion recognition. Whilst the FEEST computerised task has not been previously used in this patient population, other MCI studies (Henry et al., 2009; Fujie et al., 2008) have used the same facial stimuli incorporated into the FEEST (i.e., Ekman and Friesen, 1976). Neither of these studies reported an overall deficit in emotion recognition. However, in line with the current study, Fujie et al. (2008) did find specific recognition deficits for negative emotions (i.e., anger,

sadness). Furthermore, in a study of AD patients which used the FEEST task, the intensity of the stimuli was reduced to render the expressions more subtle (Phillips et al., 2010). This revealed emotion recognition difficulties that were previously not evident when the stimuli were shown at the standard level of intensity. The authors suggest that a failure to find deficits task in some emotions may reflect a ceiling level of performance in the FEEST when intense stimuli are used. Hence, it is possible that this ceiling effect underlies the inconsistency in results across the prompted task condition.

Thirdly, a further new finding was that impaired emotion recognition in aMCI patients extend beyond facial emotion recognition. Using a novel experimental paradigm (i.e., the Movie Stills Task), aMCI patients were less accurate in their ability to use non-facial, peripheral cues (i.e., head and body posture and hand gestures) to recognise the emotional content of scenes, compared with healthy aged-matched controls. Whilst faces are important in conveying emotional information, in real-life social situations individuals also use other sources of affect, such as bodily cues, to understand their social environment (Ruffman, Halberstadt, & Murray, 2009). These results indicate the existence of widespread deficits evident in aMCI patients regardless of the type of visual stimuli used (i.e., whether the source of this information is facial or bodily displays of emotion).

The finding of impaired emotion recognition in aMCI patients in the current study is consistent with past aMCI research (Fuji et al., 2008; Spoletini et al., 2008; Teng et al., 2007; Weiss et al., 2008). Furthermore, an emotion-specific deficit for negatively valenced material has been

reported previously in aMCI patients (Fuji et al., 2008; Spoletini et al., 2008; Weiss et al., 2008). These results, however, are in contrast to studies which have failed to find impaired emotion recognition in MCI patients (Bediou et al., 2009; Henry et al., 2009). One explanation for this discrepancy in results is that the patient sample in the current study was rather stringent in that it only included MCI subjects with demonstrated cognitive impairment across multiple-domains. Studies which reported intact emotion recognition in MCI patients did not classify their patient sample according to the extent of cognitive domain dysfunction (Bediou et al., 2009; Henry et al., 2009). Consequently, it is possible that the patient samples in these prior studies contained at least some single-domain MCI patients. Indeed, as previously reported, past studies have shown that diminished emotion recognition in aMCI is evident only in the multiple-domain subgroup (Teng et al., 2007; Weiss et al., 2007). This is consistent with the association of the multiple-domain subgroup with more advanced or diverse underlying neurodegenerative pathology (Alexopoulos, Grimmer, Perneczky, Domes, & Kurz, 2006), poorer patient outcomes (Hunderfund et al., 2006) and faster progression to dementia (Petersen & Negash, 2008), than the MCI single-domain subgroup.

What factors may underlie these emotion recognition impairments in aMCI patients? Importantly, as performance on the Benton Facial Recognition Task was not impaired, the emotion recognition deficits evident in aMCI patients cannot be accounted for by deficits in facial recognition abilities. Furthermore, no relationship was found between impaired emotion recognition and depressed mood.

It is possible that deficits in this group reflect progressive degeneration in medial temporal lobe brain structures observed in many cases with aMCI. Indeed, the aMCI group performed significantly worse than naMCI patients and Control subjects on memory tasks that have an established association with medial temporal lobe functioning (Apostolova et al., 2010). Patients with aMCI have demonstrated pathologic abnormalities in medial temporal lobe structures (Bell-McGinty et al., 2005; Petersen et al., 2006; Schott, Kennedy, & Fox, 2006) found to play an integral role in emotion recognition (Adolphs & Tranel, 2004; Rosen et al., 2002; Williams, McGlone, Abbot, & Mattingley, 2005). However, although certainly plausible, this hypothesis is difficult to reconcile with our data showing an unexpected inverse correlation between emotion recognition and memory performance, with worse emotion recognition related to better memory ability.

An alternative explanation for impaired emotion recognition is that deficits in semantic language ability, rather than emotion processing per se, account for the poor performance of aMCI patients. This has previously been reported for AD patients (Cadieux et al., 1997). In support of this, aMCI patients performed significantly worse than naMCI patients and Control subjects on the non-prompted task condition. The Emotion Identification task is arguably more reliant on intact language ability than the prompted condition tasks (i.e., FEEST, Movie Stills Task) as the subject is reliant on their own vocabulary to generate a response. However, performance on the Emotion Identification task, or indeed any of the emotion recognition tasks, did not independently correlate with

performance on a neuropsychological test of language functioning (i.e., Boston Naming Test; Kaplan et al., 1983).

A further possibility is that impaired emotion recognition in aMCI patients is an artefact of deficits in executive functioning. Indeed, Teng et al. (2007) found that executive functioning was the single best predictor of impaired emotion recognition in aMCI patients. In the current study, performance on a letter fluency task, thought to be dependent on frontal lobe functioning (Henry & Crawford, 2004), correlated moderately with impaired emotion recognition (i.e., FEEST, Movie Stills Task). Further exploratory analysis, however, revealed that executive functioning alone did not significantly account for impaired emotion recognition.

The possibility remains, therefore, that the poorer performance of the aMCI group in emotion recognition is due to more advanced neurodegeneration extending beyond that of the medial temporal lobes consistent with the diverse neural regions implicated in emotion processing. In support of this, an emotion-specific deficit for anger was found in two of the emotion recognition tasks. Angry faces have been shown to activate multiple brain regions extending beyond temporal lobe structures, such as the amygdala (Davidson & Irwin, 1999; Graham, Devinsky, & LaBar, 2007; Morris, Öhman, & Dolan, 1998; Whalen et al., 2001) and right temporal pole, but also including orbitofrontal (Rosen et al., 2002; Rosen et al., 2006), anterior cingulate (Blair, Morris, Frith, Perrett, & Dolan 1999), medial frontal cortex (Kesler-West et al., 2001; Kilt, Egan, Gideon, & Hoffman, 2003), anterior insula (Davidson & Irwin, 1999), ventral striatum (Calder, Keane, Lawrence, & Manes, 2004;

Lawrence, Calder, McGowan, & Grasby, 2002), and the ventrolateral prefrontal cortex (Blair & Curran, 1999; Sprengelmeyer, Rausch, Eysel, & Przuntek, 1998).

Further support for this notion is derived from the finding that decrements in aMCI patients extended beyond facial emotion recognition. There is evidence to suggest that the recognition of bodily expressions of emotion are also subserved by multiple brain regions including the fusiform cortex (Hadjikhani & de Gelder, 2003; Peelen, Atkinson, Andersson, & Vuilleumier, 2007), cingulate cortex (de Gelder, Snyder, Greve, Gerard, & Hadjikhani, 2004) and orbitofrontal cortex (de Gelder et al., 2004), as well as the amygdala (de Gelder et al., 2004; Hadjikhani et al., 2003; Peelen et al., 2007; Sprengelmeyer et al., 1999).

Neuroimaging studies show extensive regions of cortical volume loss are evident in aMCI multiple-domain patients. Specifically, Whitwell et al. (2007) found significant gray matter volume loss extending bilaterally from the medial and inferior temporal lobes to the posterior cingulate and into the anterior insula and the medial frontal lobe, compared with controls. There is considerable overlap with these regions and those which are important for emotion processing. Hence, it is possible that impaired emotion recognition in aMCI multiple-domain patients is secondary to the extensive and diverse level of neuropathology evident in this patient subgroup. The selective impairment of anger found in the current study may reflect the specific pattern of deficits observed in MCI, such as reduced functional connectivity in the striatum (Han et al., 2012). Functional change in this structure has been hypothesised to indicate

network alterations secondary to AD pathology (Han et al., 2012). Furthermore the striatum is known to project to the orbitofrontal cortex (Kringelbach, 2005), both of which are key structures specifically implicated in anger recognition (Calder, Keane, Lawrence, & Manes, 2004; Rosen et al., 2006).

Why are emotion processing deficits evident only in aMCI, and not in naMCI, patients? Differential emotion recognition in aMCI and naMCI patients may reflect the varied neurobiological underpinnings in the aetiology of these essentially heterogeneous groups. Differences are reported in the rates of cognitive change and progression rates to dementia between MCI subgroups, representative of clinically diverse pathological processes. As previously mentioned, Whitwell et al. (2007) reported widespread and well defined patterns of gray matter loss in aMCI multiple-domain patients, consistent with the concept of aMCI representing prodromal AD. In contrast, only scattered patterns of loss were evident in naMCI multiple-domain patients, with no significant gray matter loss.

Nevertheless, the typical diagnostic conversion for naMCI is to non-Alzheimer dementias including FTD, a condition with clear evidence of impaired emotion recognition. On these grounds, naMCI patients might be at increased risk of emotion recognition difficulties. It is possible that intact emotion recognition in naMCI patients in the current study is an artefact of age. FTD typically occurs in the pre-senium, with a reported age of onset in patients as being less than 60 years (Johnson et al., 2005; Pasquier, Richard, & Lebert, 2004). The mean age of the naMCI sample in

this study, however, was 63.78 years of age, which suggests that this group was relatively older than would be expected for FTD onset and hence not representative of an "at risk" FTD sample.

Patients with naMCI are also proposed to be at risk for conversion to DLB and VaD. These conditions have a considerably later age of onset than FTD, typically after 65 years of age, and in contrast to FTD, their prevalence increases with age (McKeith et al., 1996; Rönnemaa, Zethelius, Lannfelt, & Kilander, 2011). The argument for an age artefact would not, therefore, appear to hold for DLB or VaD. Whilst the profile of DLB patients remains relatively unexplored, there is some evidence to suggest emotion recognition may be impaired in VaD patients. One explanation, therefore, for intact emotion recognition in naMCI patients is that deficits may emerge at a later stage in the clinical progression, potentially upon conversion to dementia, compared with aMCI patients. Ultimately, longitudinal follow-up of this sample may elucidate the longitudinal trajectories of naMCI, and assist in further interpretation of this heterogeneous subgroup.

This is the first study to explore emotion recognition in naMCI patients. It also extends past research with the exploration of emotion processing under different task demands and the inclusion of novel testing paradigm to explore emotion recognition beyond that of facial processing. Despite these strengths, there are a number of limitations. Firstly, the use of static photographs of faces has been argued to be less ecologically relevant than dynamic facial displays (Cadieux & Greve, 1997). It could be argued, however, that scenes from old movies, used in one emotion

recognition task, would be more familiar, age appropriate and motivationally engaging stimuli to an older population than the posed photographs generally used in emotion recognition tasks which have typically garnered such criticism. Indeed, qualitative observations suggest positive participant engagement in this task.

Nevertheless, research suggests that different neural pathways are used to recognise static, relative to dynamic facial displays. Static emotional facial images are reported to require a greater reliance on the motor and premotor cortex, suggesting that the dynamics of the expression influences the mental strategies used to decode emotional displays (Kilt, Egan, Gideon, Ely, & Hoffman, 2003). It is important to note, however, that there remains considerable overlap in the brain regions activated, independent of the expression's dynamics. Future research may seek, however, to utilise more ecologically valid, dynamic stimuli.

Secondly, this study was cross-sectional in nature. Longitudinal studies are required to ascertain the clinical progression of MCI patients and the associated impact on emotion recognition abilities. Future research should seek to address this issue by including a longitudinal follow-up sample.

A plausible conclusion from this study is that very early AD pathology underlies impaired emotion recognition in aMCI. This conclusion remains speculative, given that neuroimaging was not undertaken in this study. Future research, utilising imaging technology, is required to explore the neuroanatomical correlates of emotion processing and how this might compare with naMCI patients. Only one study to date has utilised

neuroimaging data for aMCI patients. Fujie et al (2008) found aMCI patients had reduced fractional anisotropy measurements of the left uncinate fasciculus (UF), white matter tracts connecting the anterior temporal areas with prefrontal and orbitofrontal cortices. A significant positive association was found between fractional anisotropy measurements of the left UF with accuracy in emotion recognition.

Whilst emotion recognition deficits were found in this study in aMCI patients, the "real-life" implications of this finding remain hypothetical. Impaired emotion recognition may be a factor underlying the socio-emotional decline observed in dementia, such as psycho-behavioural disturbances and interpersonal problems (Chiu et al., 2006; Shimokawa et al., 2001). Neuropsychiatric features are commonly observed even in aMCI patients, with apathy, depression, irritability and agitation (Lyketsos et al., 2002) reported at a significantly higher frequency compared with healthy, age-matched controls (Hwang et al., 2004). It is well understood that these problems have significant individual and societal costs including diminished quality of life (Shin et al., 2005), accelerated disease progression (Holtzer et al., 2003), and increased caregiver burden (Brodaty, 1996; Bruce, McQuiggan, Williams, Westervalt, & Tremont, 2008), and are a key determinant of patient institutionalisation (Steele, Rovner, Chase, & Folstein, 1990). The presence of behavioural and psychological symptoms is also thought to be highly predictive of progression to dementia in MCI (Copeland et al., 2003).

Hence, understanding the impact of impaired emotion recognition should be explored in future research, including its association with social

functioning and interpersonal relationships for aMCI patients. In this regard, future research would be enhanced by incorporating an informants' perspective. This research would consequently inform whether early intervention to address emotion recognition disturbances would be beneficial in addressing emerging behavioural issues in an MCI population.

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Table 2. Demographic variables for patients with naMCI, aMCI and control subjects

	naMCI (n = 18)	aMCI (n = 19)	Controls (n = 19)
Gender (Males/Females)	7/11	7/12	9/10
Age, years (SD)	63.78 (8.20)	69.63 (7.25)	64.79 (8.45)
Education, years (SD)	13.61 (3.13)	13.55 (3.72)	12.89 (2.87)
MMSE scores (SD)	28.61 (1.24)^{**b}	26.89 (1.76)	29.32 (0.82)^{***b}
WTAR- Predicted IQ (SD)	105.29 (6.77)	104.32 (7.54)	104.16 (8.02)
Hamilton Depression Rating (SD)	5.22 (4.92)	3.68 (2.79)	1.89 (2.13)^{*a,*b}

Notes: naMCI = non-amnestic Mild Cognitive Impairment multiple-domain; aMCI = amnestic Mild Cognitive Impairment multiple-domain; ^{a} = significant difference compared with naMCI group; ^{b} = significant difference compared with aMCI group; MMSE = Mini-Mental State Examination; WTAR = Wechsler Test of Adult Reading; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 3. Neuropsychological performance for patients with naMCI, aMCI and control subjects

Tests	naMCI	aMCI	Controls
	Mean (SD) N	Mean (SD) N	Mean (SD) N
Working Memory			
Digit Span			
-Age Scale Score	10.28 (3.10) 18	9.79 (3.24) 19	11.53 (3.39) 19
Verbal Learning			
and Memory			
WMS- III LM I			
- Age Scale Score	9.17 (3.50)[*b] 18	6.89 (3.37) 19	12.50 (2.29)[**a,***b] 18
WMS- III LM II			
- Age Scale Score	9.83 (3.20)[**b] 18	6.58 (3.86) 19	12.56 (1.85)[**a,***b] 18
Language			
BNT			
- Age Scale Score	10.29 (3.93) 17	8.47 (4.38) 19	12.44 (3.05)[**b] 18
Visuospatial			
Skills			
RCFT Copy			
- Percentile	2.61 (2.43) 18	2.63 (1.50) 19	4.30 (4.14) 10
Processing Speed			
TMT-A			
- z-score	0.00 (1.02) 18	-0.47 (1.62) 19	0.54 (0.67)[*b] 19

Table 3. Neuropsychological Performance for patients with naMCI, aMCI and control subjects (continued)

Tests	naMCI	aMCI	Controls
	Mean (SD) N	Mean (SD) N	Mean (SD) N
Executive			
Functioning			
COWAT			
- z-score	-0.17 (1.29) 18	-0.16 (0.79) 19	0.56 (1.13)[*a,*b] 19
TMT-B			
- z-score	-0.54 (1.66)[*b] 18	-1.73 (3.21) 19	0.46 (0.71)[*a,**b] 18

Notes: naMCI = non-amnestic Mild Cognitive Impairment multiple-domain; aMCI = amnestic Mild Cognitive Impairment multiple-domain; [a] = significant difference compared with naMCI group; [b] = significant difference compared with aMCI group; WMS-III LM = Wechsler Memory Scale - Third Edition, Logical Memory subtest; BNT = Boston Naming Test; RCFT = Rey Complex Figure Test; TMT = Trail-making Test; COWAT = Controlled Oral Word Association Test; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 4. Emotion recognition with emotion prompts (FEEST)

Emotion	naMCI Mean (SD)	aMCI Mean (SD)	Controls Mean (SD)	χ^2†	df	*p*
Anger	7.72 (1.56)	6.47 (2.06)	8.37 (1.95)	10.04	2	.007
Disgust	8.50 (1.46)	7.58 (2.62)	8.05 (1.78)	0.92	2	.632
Fear	5.44 (2.12)	5.26 (1.91)	6.26 (2.68)	2.13	2	.344
Happy	9.89 (0.32)	9.37 (1.01)	9.68 (0.95)	5.81	2	.055
Sad	7.72 (1.32)	7.00 (1.73)	7.74 (2.21)	2.84	2	.242
Surprise	8.06 (1.39)	8.37 (1.71)	8.53 (1.39)	1.37	2	.504
Total	47.33 (3.95)	44.05 (8.80)	48.53 (6.35)	2.26*	2	.115

Notes: naMCI = non-amnestic Mild Cognitive Impairment multiple-domain; aMCI = amnestic Mild Cognitive Impairment multiple-domain; † Kruskal-Wallis non-parametric test; *one-way ANOVA.

Table 5. Emotion recognition without prompts (Emotion Identification task)

Emotion	naMCI Mean (SD)	aMCI Mean (SD)	Controls Mean (SD)	χ^2†	df	*p*
Anger	4.53 (1.46)	3.11 (1.85)	4.57 (1.34)	8.45	2	.015
Disgust	4.33 (1.71)	3.32 (1.70)	4.37 (1.12)	5.31	2	.070
Fear	1.44 (1.33)	1.16 (1.38)	1.47 (1.58)	0.83	2	.662
Happy	5.83 (0.38)	5.58 (0.84)	5.94 (0.23)	3.33	2	.189
Sad	5.00 (1.41)	4.95 (1.12)	5.53 (0.69)	2.99	2	.225
Surprise	5.39 (1.19)	4.68 (1.20)	5.21 (1.03)	5.41	2	.067
Neutral	2.11 (1.75)	2.21 (1.18)	3.47 (2.04)	6.19	2	.045
Total Emotion	26.50 (4.50)	22.79 (4.93)	27.10 (3.52)	8.95	2	.010

Notes: naMCI = non-amnestic Mild Cognitive Impairment multiple-domain; aMCI = amnestic Mild Cognitive Impairment multiple-domain; † Kruskal-Wallis non-parametric test.

Table 6. Emotion recognition with and without facial cues (Movie Stills Task)

Emotion	naMCI Mean (SD) (n = 16)	aMCI Mean (SD) (n = 19)	Controls Mean (SD) (n = 17)	χ^2†	df	*p*
Anger						
Without Faces	2.64 (0.96)	2.58 (0.88)	3.08 (0.68)	3.46	2	.178
With Faces	3.21 (0.69)	2.65 (1.04)	3.19 (0.74)	3.11	2	.211
Fear						
Without Faces	3.38 (1.04)	3.19 (1.00)	3.78 (0.86)	2.16	2	.340
With Faces	4.08 (1.04)	3.92 (0.89)	4.22 (0.66)	0.94	2	.626
Happy						
Without Faces	1.56 (0.51)	1.58 (0.51)	1.88 (0.33)	4.94	2	.085
With Faces	2.00 (0.00)	1.95 (0.23)	2.00 (0.00)	1.74	2	.420
Sad						
Without Faces	1.58 (0.77)	1.12 (0.98)	1.88 (0.75)	6.36	2	.042
With Faces	1.95 (0.63)	1.76 (0.81)	2.07 (0.76)	1.49	2	.473
Surprise						
Without Faces	0.44 (0.34)	0.52 (0.34)	0.46 (0.29)	1.04	2	.596
With Faces	0.54 (0.35)	0.65 (0.39)	0.68 (0.35)	0.78	2	.676
Neutral						
Without Faces	0.41 (0.33)	0.38 (0.32)	0.35 (0.29)	0.13	2	.937
With Faces	0.55 (0.37)	0.39 (0.34)	0.48 (0.35)	1.86	2	.395

Table 6. Emotion recognition with and without facial cues (Movie Stills Task) (continued)

Emotion	naMCI Mean (SD) (n = 16)	aMCI Mean (SD) (n = 19)	Controls Mean (SD) (n = 17)	χ^2†	df	*p*
Total Emotions						
Without Faces	10.02 (2.14)	9.36 (1.99)	11.42 (1.09)	6.02*	2	.005
With Faces	12.32 (1.44)	11.32 (1.99)	12.65 (1.24)	6.84	2	.030

Notes: naMCI = non-amnestic Mild Cognitive Impairment multiple-domain; aMCI = amnestic Mild Cognitive Impairment multiple-domain; † Kruskal-Wallis non-parametric test; *one-way ANOVA.

CHAPTER 5

STUDY 2

This paper has been submitted to *International Psychogeriatrics* and is represented in the format required for that submission, with the exception of page numbers and table numbers which are numbered to be consistent with the thesis as a whole. Some repetition of information and particularly references was unavoidable given the nature of the thesis by papers format.

My contribution to the paper is estimated to be 70%, including the formulation of the research questions, research design, experiment set-up, data collection, data analysis, interpretation and manuscript preparation. Associate Professor Sharon Naismith and Associate Professor Greg Savage contributed an estimated 15% (analysis assistance, manuscript preparation) and 10% (manuscript preparation) respectively, with. The remaining contributions to manuscript preparation are attributed equally to Associate Professor Adam Guastella, Professor Ian Hickie and Associate Professor Simon Lewis.

Emotion recognition in Mild Cognitive Impairment: Relationship to disability and caregiver burden

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ORIGINAL RESEARCH

Abstract

Background: Previous research suggests that impaired emotion recognition in dementia is associated with increased agitation in patients, caregiver burden and difficulties with behaviour management. Emerging evidence supports the presence of very early emotion recognition difficulties in Mild Cognitive Impairment (MCI) however the relationship between these impairments and functional measures has not yet been explored. *Methods:* Twenty-seven patients with non-amnestic MCI (naMCI), 29 patients with amnestic MCI (aMCI) and 22 age- and education-matched healthy control subjects were assessed with the Ekman 60 Faces emotion recognition test, which assesses the domains of anger, sadness, fear, happiness, surprise and disgust. Self-report measures were used to assess functional disability in patients, whilst informants rated the degree of caregiver burden they experienced. *Results:* An emotion recognition deficit for anger was evident only in those with the amnestic subtype. Whilst both patient groups reported greater disability in aspects of social functioning, compared with control subjects, a relationship between social dysfunction and anger recognition was evident only for naMCI patients. A significant association was also found between caregiver burden and anger recognition for aMCI patients. *Conclusions:* Impaired emotion recognition abilities impact MCI subtypes differentially. Consequently, interventions targeted at both MCI patients and caregivers are warranted.

Key words: Dementia; Emotion recognition; Facial expressions; Caregiver burden; Disability; Mild Cognitive Impairment.

Introduction

The ability to accurately recognise facial emotional expressions is a fundamental prerequisite for successful interaction in everyday social life. Being able to infer what others are feeling enables us to anticipate events, respond appropriately, avoid conflict and regulate our own emotions (Brüne & Brüne-Cohrs, 2006). Accordingly, deficits in emotion recognition can have a devastating impact on social skills and the development and maintenance of key social relationships (Greve, Cadieux, & Hale, 1995).

There is evidence to suggest that emotion recognition is impaired in some forms of dementia. Patients with Alzheimer's disease (AD) have been shown to perform significantly worse than aged-matched control subjects in recognising sad (Spoletini et al., 2008; Weiss et al., 2008), angry (Bediou et al., 2009; Spoletini et al., 2008), fearful (Spoletini et al., 2008; Weiss et al., 2008), surprised (Phillips et al., 2010), happy (Spoletini et al., 2008; Weiss et al., 2008) and disgusted (Spoletini et al., 2008) faces. Imaging studies suggest that the origin of emotion recognition deficits in AD patients may lie within decreased regional cerebral blood flow to posterior frontal lobe regions including the anterior cingulate and medial frontal gyrus (Staff et al., 2011).

The impact of impaired emotion recognition for dementia patients is substantial. Significant associations have been found between deteriorating emotion recognition abilities and indifference to interpersonal relationships and awkward social behaviours in AD patients (Shimokawa

et al., 2001). Greve et al. (1995) found that impaired facial emotion recognition predicted caregiver burden, while Nelis et al. (2011) showed that in early-stage dementia, emotion recognition difficulties were associated with poorer relationship quality, as reported by caregivers. Studies which have explored vocal prosody have reported that emotion processing decrements are associated with poorer marital relationships (Greve et al., 1995). Whilst little is understood about whether emotion recognition impacts the ability of AD patients in everyday functioning, Kipps, Mioshi and Hodges (2009) did not find any association between impaired emotion recognition and activities of daily living, such as self care, and higher level, instrumental activities of daily living (i.e., household management, leisure activities) in patients with frontotemporal dementia (FTD).

Given the apparent psychosocial costs associated with decrements in this important ability, the early identification of emotion recognition difficulties would enable the timely implementation of interventions aimed at addressing these deficits. As such, the opportunity for early detection may lie within the Mild Cognitive Impairment (MCI) population. MCI is a construct widely used to identify individuals at increased risk of developing dementia. Generally MCI is defined by the presence of cognitive impairment in the context of essentially intact activities of daily living (Petersen, 2004). For diagnostic specificity, MCI is divided into subtypes based on either the presence (i.e., amnestic MCI; aMCI) or absence (i.e., non-amnestic MCI; naMCI) of memory deficits, as well as

evidence of impairment across either single or multiple cognitive domains (Petersen, 2004).

Whilst research is in its infancy, there is some evidence to suggest that very early impairments in emotion recognition are already evident in MCI. Individuals with aMCI have been found to be impaired in emotion recognition relative to control subjects (Fujie et al., 2008; Spoletini et al., 2008; Teng, Lu and Cummings, 2007; Weiss et al., 2008), however this finding has not been universally reported (Bediou et al., 2009; Henry et al., 2009). Previous research suggests that negatively valenced emotions are selectively implicated with emotion-specific deficits observed for sad (Fujie et al., 2008; Weiss et al., 2008), fearful (Spoletini et al., 2008; Weiss et al., 2008) and angry (Fujie et al., 2008) faces. Impaired emotion recognition is evident predominantly in individuals with deficits across multiple, and not single, cognitive domains in MCI (Teng et al., 2007; Weiss et al., 2008), which indicates that these deficits are associated with more advanced and/or diverse neurodegenerative pathology.

As previously stated, AD studies have established the association between impaired emotion recognition and functional outcomes. However, in patients with MCI, the role that emotion recognition difficulties may play in mediating functional disability, particularly psychosocial functioning, has not been investigated. The outcome of this will inform whether targeted, evidence-based education and/or intervention programmes are warranted. The aim of the present study was, therefore, to explore: Firstly, do those with MCI experience greater functional disability, particularly in the psychosocial domains of social functioning

and social participation, and caregiver burden than control subjects? This is particularly important as the psychosocial domains have, to the authors' knowledge, not been explored in MCI patients to date. Secondly, does a relationship exist between patient emotion processing abilities and disability and the degree of burden experienced by caregivers?

Methods

Participants

Fifty-six patients meeting criteria for Mild Cognitive Impairment (Petersen, 2004) were recruited from a specialist 'Healthy Brain Ageing' Centre, at the Brain & Mind Research Institute, Sydney, Australia. This centre receives referrals from local neurologists, psychiatrists and geriatricians and targets people over the age of 50 who have emerging cognitive and/or mood disorders. The patient sample was restricted to only those with multiple-domain MCI due to the low sensitivity of single-domain MCI as a prognostic category for the development of dementia (Rasquin, Lodder, Visser, Lousberg, & Verhey, 2005). Twenty-two age- and education-matched healthy volunteers were recruited from the community via local advertisements.

Participants aged between 50 to 85 years were included. Specific inclusion criteria were speaking English as a first language and a Mini-Mental State Examination (MMSE) score ≥ 24. Exclusion criteria were any psychiatric or neurological disorder (e.g. head injury, prior stroke, established dementia, intellectual disability, major depression, schizophrenia, substance abuse). In addition, controls were required to

demonstrate intact cognitive functioning, as defined by no performance placed 1.5 standard deviations (SDs) or more below age-based norms on a battery of standardised neuropsychological tests.

Measures

Clinical

A psychogeriatrician assessed all participants to derive a clinical history, including psychiatric history, medication use and level of functioning. The 17-item Hamilton Depression Rating Scale (HAM-D; Hamilton, 1960) was used as a part of a structured interview to ascertain current depression severity.

For patients with MCI, medication details at the time of examination included 19 individuals (nine naMCI; ten aMCI) taking antidepressants regularly (sixteen of whom were taking newer generation serotonergic or noradrenergic agents and one of whom was taking a tricylic antidepressant). Of these patients, three were also taking a benzodiazepine (prn; two naMCI; one aMCI) and three patients (two naMCI; one aMCI) were taking an adjunctive atypical antipsychotic (quetiapine, risperidone).

Neuropsychological

A neuropsychologist administered a standardized test battery, selected for its capacity to examine multiple aspects of cognition in order to facilitate accurate clinical diagnosis regarding MCI subtype. To meet criteria for MCI, patients were required to demonstrate objective evidence of cognitive impairment defined by performance 1.5 SDs below age-based

norms on a battery of standardised neuropsychological tests. Each patient was required to be impaired in at least two cognitive domains, with aMCI patients required to show impairment on a memory domain. Patients were diagnosed with aMCI if demonstrated memory impairments were of the 'hippocampal-type'. That is, clear evidence of memory storage deficits was required, not merely reflecting poor encoding. Patients were diagnosed with naMCI if deficits were present on tests of other cognitive domains (e.g. processing speed, working memory, language, executive functioning). A standardised test battery, selected for its capacity to examine multiple aspects of cognition in order to facilitate accurate clinical diagnosis regarding MCI and subtype, was administered by a neuropsychologist. For descriptive purposes only, cognitive domains assessed included working memory, verbal learning and memory, language, visuospatial skills, psychomotor processing speed and executive functioning and the MMSE was used as a broad measure of cognitive functioning.

From these assessments, consensus diagnostic ratings for those with MCI were performed by a psychogeriatrician and two neuropsychologists according to established MCI criteria (Petersen, 2004). This included ratings according to MCI subtype. As noted above, only those with multi-domain MCI were included in this study.

Emotion recognition

The Ekman 60 Faces test is a widely used and validated computerised emotion recognition task taken from the Facial Expressions of Emotion:

Stimuli and Tests CD-ROM (FEEST; Young, Perrett, Calder, Sprengelmeyer and Ekman, 2002). Sixty black-and-white photographs portraying six basic emotions (i.e., happiness, sadness, anger, fear, surprise, disgust), were presented one at a time for 5 seconds in a randomised order to participants on a computer screen, with the six basic emotion labels also displayed at the bottom of the screen. Participants were required to select the emotion label which best matched the displayed label. No limit was placed on the participant's time to respond and the next face was not shown until a response was made. Participants received one point for each correct answer, with a maximum score of 60 for the overall task and a score out of 10 for each of the six basic emotions.

Facial recognition

The Short Form Benton Facial Recognition Test (BFRT; Benton, Sivan, Hamsher, Varney, & Spreen, 1983) was administered as a control task to evaluate whether deficits were specific to emotion recognition rather than a general face processing deficits. The Short Form BFRT consists of thirteen black-and-white photographs of unfamiliar male and female faces in which participants match the frontal view of a target face with an identical photograph and with three photographs of the target face taken from different angles.

Disability

The World Health Organization Disability Assessment Schedule II (WHODAS-II; World Health Organisation, 2001) is a 36-item self report measure of functioning indexing six domains, which incorporate basic and

instrumental activities of daily living: understanding and communicating, getting around (i.e., physical mobility), self-care, getting along with others (i.e., interpersonal relationships), life activities and participation in society. The psychosocial domains were of particular interest for the purpose of this study (i.e., understanding and communicating, getting along with others, participation in society). A total score is derived from aggregated domain scores. Higher scores denote greater functional impairment.

Caregiver burden

The Zarit Burden Interview (ZBI: Zarit, Reever, & Bach-Peterson, 1980) is a 22 item self-report inventory which is widely used to assess the burden experienced by caregivers associated with functional and behavioural impairments of dementia patients. The questionnaire is completed by an informant chosen by the participant and it focuses on common areas of concern associated with caring for individuals with dementia (i.e., social life, interpersonal relationships, finances). Caregivers rate their degree of burden on a Likert scale from 0 ('never') to 4 ('nearly always'), with a total score out of 88 calculated. Higher scores denote increased burden.

Statistical analyses

Statistical analyses were performed with PASW Statistics, Release Version 18.0.0 (SPSS, Inc., 2009, Chicago III., USA). To test for differences between MCI and control groups, one way Analysis of Variance (ANOVA) was utilised for normally distributed measures. Where the assumption of normality was violated (via visual inspection and

according to the results of Kolmgorov-Smirnov tests), Kruskal-Wallis non-parametric tests were undertaken, with subsequent Mann-Whitney pair wise comparisons undertaken to explore measures with significant group differences. For comparisons of continuous data, Spearman's rho correlations and Pearson's correlations were applied for non-normally distributed- and normally distributed data, respectively. Due to the exploratory nature of the analyses, multiple correlations were undertaken and consequently an adjusted alpha level of .01 was applied to control for Type I errors.

Results

Demographic and clinical characteristics are presented in Table 7. Twenty-seven patients met diagnostic criteria for non-amnestic MCI (naMCI) and twenty-nine patients were diagnosed with aMCI. One way ANOVAs to compare group performance revealed no differences in regard to age ($F(2,75) = 2.493$, $p = .089$), education ($F(2,75) = 0.841$, $p = .435$), gender ($F(2,75) = 0.169$, $p = .845$) and predicted intellectual functioning ($F(2,74) = 0.004$, $p = .996$). As expected, the patient groups performed significantly worse on a gross measure of cognitive functioning (i.e., MMSE) than Control subjects, and in turn, the aMCI group performed significantly worse than the naMCI group. All groups had depressive symptoms in the normal range (i.e., HAM-D), although the patient groups had higher levels of symptomatology than the Control subjects. No significant group differences were found in facial recognition, as measured by the Benton Facial Recognition Test ($F(2,66) = 2.549$, $p = .068$). Nine

patients (7 aMCI; 2 naMCI) did not undertake the Benton Facial Recognition Test.

Table 8 displays the neuropsychological performance for each group.

Disability

One aMCI patient did not complete the WHODAS-II questionnaire. Means, standard deviations and group differences for WHODAS-II scores for all groups are reported in Table 9. Subsequent Mann-Whitney between-group comparisons revealed that both naMCI and aMCI patients demonstrated significantly more subjective difficulties compared with Control subjects in the domains of understanding and communicating (U = 121.50, z = -3.59, p < .001and U = 85.00, z = -4.40, p < .001 respectively) and participation in society (U = 158.50, z = -2. 80, p = .004 and U = 130.00, z = -3.49, p < .001 respectively), as well as greater overall levels of disability (U = 117.50, z = -2.98, p = .002 and U = 102.00, z = -3.45, p < .001 respectively). The aMCI patient group also reported significantly more difficulty undertaking life activities (U = 170.00, z = -2.82, p = .004) than Control subjects. Patient groups did not significantly differ on these measures.

Caregiver burden

Forty-four caregivers completed the Zarit Burden Interview questionnaire regarding their respective study participant. A one-way ANOVA revealed significant differences in the levels of caregiver burden reported between groups (F(2,41) = 12.164, p < .001). Subsequent post-

hoc pairwise comparisons showed significantly higher levels of caregiver burden reported in the naMCI patients (25.21 ± 12.66; n = 14) compared with Control subjects (7.93 ± 8.38; n = 15; $p < .001$) and aMCI patients (13.73 ± 7.00; n = 15; $p = .002$). There were no significant group differences between and aMCI patients and Control subjects.

Emotion recognition

Kruskal-Wallis between-group analysis of FEEST scores across emotions showed significant group differences in the recognition of anger (Table 10). Subsequent Mann-Whitney between-group comparisons revealed a significant deficit in the recognition of anger for aMCI patients compared with Control subjects ($U = 137.50$, $z = -3.49$, $p < .001$) and naMCI patients ($U = 243.00$, $z = -2.46$, $p = .013$). These results represented moderate effect sizes ($r = -.49$ and $r = -.33$ respectively). Patients with naMCI did not differ significantly from Control subjects ($p = .097$) in anger recognition.

Correlates of emotion recognition

Correlational analyses were performed to examine the possible relationships between emotion recognition and measures in which significant group differences emerged on caregiver burden and disability for patient groups.

Caregiver burden

For aMCI patients, increased caregiver burden was significantly associated with worse recognition of anger ($r_s = -.782$, $p = .001$). The

scatterplot (with regression line included) depicting the relationship between anger recognition and caregiver burden for aMCI patients is presented in Figure 1. There was no significant relationship between emotion recognition and caregiver burden for naMCI patients (r_s= -.420, p = .135).

Disability

There were no significant correlations between disability, as assessed by the WHODAS-II, and emotion recognition for aMCI patients, using the adjusted alpha level. For naMCI patients, poorer anger recognition was significantly associated with increased difficulties in the domain of getting along with others (r_s = -.686, p < .001).

Discussion

The major purpose of this study was to examine the relationship between emotion recognition and key aspects of disability and caregiver burden in MCI. Our results demonstrate that some very early difficulties in emotion recognition are already apparent in MCI however, these are evident only in aMCI patients. This finding is consistent with previous emotion recognition studies (Fujie et al., 2008; Spoletini et al., 2008; Teng et al., 2007; Weiss et al., 2008). The assertion from previous studies that negative emotions are preferentially impacted in MCI is also supported by our findings (Fujie et al., 2008; Spoletini et al., 2008; Weiss et al., 2008), with an emotion-specific deficit found for the recognition of angry faces in aMCI patients.

Importantly, decrements in emotion recognition in aMCI reported in the current study cannot be accounted for by impaired facial perception, with comparable performance demonstrated across all groups on a facial perception task. It is noteworthy that the current study employed stringent inclusion criteria, restricting the patient sample to multi-domain MCI, due to the high sensitivity of the multiple-domain subtype as a prognostic marker for the development of dementia (Rasquin et al., 2005). This may account for the discrepancy in results with those prior studies that reported intact impaired emotion recognition in MCI (Bediou et al., 2009; Henry et al., 2009).

Deficits in emotion recognition in aMCI patients may reflect neurodegeneration in structures also implicated in emotion processing. Neural regions involved in anger recognition include the right orbitofrontal cortex, anterior cingulate, amygdala and ventral striatum (for a review see Hennenlotter & Schroeder, 2006). In a neuroimaging study, Whitwell et al. (2007) assessed aMCI domain patients using voxel-based morphometry, which revealed extensive regions of cortical volume loss, extending bilaterally from the medial and inferior temporal lobes to the posterior cingulate and into the anterior insula and the medial frontal lobe. With this in mind, impaired emotion recognition in aMCI multiple-domain patients may reflect the extensive and diverse level of neuropathology evident in this patient subgroup. In contrast, the finding of intact emotion recognition in naMCI patients may be indicative of its heterogeneity as an MCI subtype, in terms of clinical characteristics, underlying pathophysiology and longitudinal trajectory (Whitwell et al., 2007).

To the authors' knowledge, this is the first study to specifically investigate and report on social disability in MCI patients. Patient groups reported greater difficulties compared with control subjects when participating in society, which includes joining in on community activities, undertaking pleasurable activities, as well as family and social difficulties. Greater difficulties were also reported by patient groups compared with control subjects in the domain of understanding and communicating, which incorporates the critical ability to initiate, maintain and follow conversations, as well as to concentrate, learn new tasks, remember information and solve problems. Patient groups did not, however report significantly elevated difficulties with regard to interpersonal relationships.

To date, MCI studies have typically focused on disability in performing instrumental activities of daily living. Consistent with this prior research (Tabert et al., 2002; Wadley et al., 2007), patient groups in the current study reported significantly greater disability in their overall daily functioning compared with aged-matched controls. Patients with aMCI in the current study reported significantly greater disability in undertaking complex, instrumental tasks, such as managing household activities than control subjects, a finding which is also consistent with research which has used self-rated measures of functioning (Wadley et al., 2007). Unsurprisingly, at this very early stage in the neurodegenerative process, the basic, functional abilities of MCI patients, such as self-care, remain intact. Findings of functional disability in MCI patients are important given that these deficits are associated with a higher conversion rate to dementia (Luck et al., 2011).

We also believe this to be the first study to detail the "real-life" implications of impaired emotion recognition in MCI. A relationship between poorer social functioning and difficulties with anger recognition was found, which has been previously reported in AD patients (Shimokawa et al., 2001). This makes intuitive sense, however, curiously this relationship was found only for naMCI patients. A possible explanation for the failure to find a relationship between social functioning and difficulties with anger recognition may lie in the current study's use of a self-report measure to assess disability. Past studies suggest that MCI patients tend to overestimate their own functional ability (Tabert et al., 2002). Indeed, Nelis et al. (2011) found a loss of awareness of social dysfunction in people with early-stage dementia. Hence, the failure to find a significant relationship with emotion recognition on patient self-report measures may reflect diminished insight in aMCI patients into their level of social and behavioural functioning. Interestingly, the study that reported a relationship between social dysfunction and emotion recognition in AD patients used an informant-rated measure of social functioning (Shimokawa et al., 2001). A further possible explanation is that memory difficulties may be maintaining this decrement in insight, as has found to be the case in AD patients (Agnew & Morris, 1998). Given that patient insight was not measured in this study, future research may seek to include measures assessing patient insight in emotion recognition studies.

It is noteworthy that impaired emotion recognition does not seem to explain difficulties experienced subjectively by aMCI patients, but rather their caregivers. A key finding of this study was the strong association

between difficulties in the recognition of anger and increased caregiver burden for aMCI patients. Whilst this relationship has previously been reported for AD patients (Greve et al., 1995), with impaired facial emotion recognition found to predict caregiver burden, the results from the current study show that this association exists even prior to the onset of dementia. This result is significant given that caregiver burden is an important predictor of cognitive decline and early institutionalisation in MCI patients (Luppa, Luck, Braehler, Koenig, & Riedel-Heller, 2008) and is associated with increased depression and greater lifestyle constraints amongst caregivers (Garand, Dew, Eazor, DeKosky, & Reynolds, 2005). However, emotion recognition did not appear to relate to caregiver burden for naMCI patients. The caregivers of both MCI patient groups reported greater levels of burden than those of control subjects, which suggest that the impact of MCI extends beyond the patient. This difference only reached significance for the naMCI group, with mild levels of burden reported by caregivers. These results corroborate previous findings of elevated burden in MCI caregivers (Garand et al., 2005).

The concept of caregiver burden includes embarrassment, resentment and isolation from society (Zarit et al., 1980).We hypothesize that the perceived burden of caregivers may relate to diminished emotional communication with MCI patients, with the misperception of emotion cues contributing to feelings of frustration in caregivers and exacerbating relationship difficulties. Anger plays an important role in moderating social behaviour whereby expressions of anger can signal the disapproval of violations of socially acceptable behaviour (Averill, 1982). Difficulties

in identifying anger in others may cause aMCI patients to be insensitive to these signals and therefore unable to appropriately respond and modify their behaviour (Kipps et al., 2009). The repeated failure by MCI patients to respond to emotional cues may be perceived by caregivers as intentional acts to annoy or challenge them, engendering frustration, resentment (Savundranayagam, Hummert, & Montgomery, 2005). Caregivers may also perceive poor emotional reactivity as patients' lacking consideration for their concerns (Kipps et al., 2009).

Anger also plays a unique role in social relationships and dispute resolution (van Kleef, van Dijk, Steinel, Harinck, & van Beest, 2008). The ability to attend to and process the anger of others is fundamental to the successful resolution of social conflict. Therefore, impaired anger recognition would be detrimental to the effective resolution of interpersonal conflict and potentially elevate the level of anger experienced by caregivers, leading to increased levels of stress and diminished well-being (Diong & Bishop, 1999).

The relationship between emotion recognition and caregiver burden in this study has important implications. The role of caregiver is crucial for both families and society. Garand et al. (2005) found that even at the early stages of cognitive impairment, spouses of MCI patients assume the role of caregiver. In the current study, caregivers of naMCI patients were already indicating mild levels of burden. Whilst the caregivers of aMCI patients reported sub-threshold levels of burden, the association of emotion recognition deficits and caregiver burden found in this study suggest that interventions targeting the caregiver are certainly warranted.

This research indicates that neuropsychological batteries employed to assess individuals for the presence of MCI should include emotion recognition measures. Relative to the role of cognitive deficits in MCI, relatively little is understood about emotion recognition and its impact on MCI patients. For example, caregivers are likely to anticipate the presence of memory difficulties in aMCI patients. In contrast, a decline in emotion recognition abilities may be unexpected and therefore, is likely to be misunderstood by caregivers as apathy or challenging patient behaviours (Savundranayagam et al., 2005). The current study demonstrates the need to educate caregivers regarding the altered recognition of emotional facial expressions in aMCI and to provide strategies aimed at improving communication to reduce problematic situations and manage the changing nature of the patient/caregiver relationship in this early caregiving stage. Furthermore, the early implementation of appropriate clinical interventions, particularly those relating to caregiver issues may help to reduce long term care costs and carer burden. Whilst the current study found that emotion processing is relatively intact in naMCI patients, evidence of a relationship between social functioning and emotion recognition abilities for this group indicates that the ability to recognise anger may still have functional significance in those with naMCI. Consequently, the inclusion of all MCI subgroups in any caregiver intervention is warranted. In addition, findings of impaired emotion recognition in MCI highlight the need for early intervention targeted at improving the ability of aMCI patients to decode emotional cues.

Despite the strengths of this study, which includes the rather stringent inclusion only of patients with demonstrated multi-domain MCI and the strict statistical controls employed to minimise the potential for Type I error, there are limitations. The current study was cross-sectional in nature and longitudinal studies are required to confirm the clinical trajectory of MCI patients and to track the course and impact of emotion recognition difficulties. Furthermore, the sample size in the current study was relatively small and future studies should seek to replicate using a larger sample size. Finally, self-report measures were used to assess patient disability. Whilst self-report measures are a valuable source of patient information in MCI (Wadley et al., 2007), it is possible that patients have overestimated their levels of functional ability (Tabert et al., 2002), hence future research may benefit from exploring the carer's perspective by the use of informant-rated measures.

In summary, this study is the first to demonstrate the functional significance of emotional recognition deficits in MCI, according to MCI subtype, and the implications for carers. Importantly, the findings show that while differential relationships may exist in those with aMCI and naMCI, reduced anger recognition likely has consequences in terms of interpersonal relationships and caregiver burden. Future studies may focus on early screening and intervention for this deficit and for incorporation of such findings into targeted caregiver education programs.

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Table 7. Demographic variables for patients with naMCI, aMCI and control subjects

	naMCI (n = 27)	aMCI (n = 29)	Controls (n = 22)
Gender (Males/Females)	13/14	12/17	9/13
Age, years (SD)	64.48 (8.53)	68.97 (7.30)	65.18 (8.37)
Education, years (SD)	13.88 (3.65)	13.81 (3.62)	12.73 (2.79)
MMSE scores (SD)	28.59 (1.39)^{**b}	27.21 (1.80)	29.32 (0.84)^{*a,***b}
WTAR- Predicted IQ (SD)	104.96 (10.60)	104.76 (8.62)	104.91 (8.10)
HAM-D (SD)	5.07 (4.42)	3.69 (3.37)	1.95 (2.04)^{**a,*b}

Notes: naMCI = non-amnestic Mild Cognitive Impairment multiple-domain; aMCI = amnestic Mild Cognitive Impairment multiple-domain; ^{a} = significant difference compared with naMCI group; ^{b} = significant difference compared with aMCI group; MMSE = Mini-Mental State Examination; WTAR = Wechsler Test of Adult Reading; Ham-D = Hamilton Depression Rating Scale; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 8. Neuropsychological performance for patients with naMCI, aMCI and control subjects

Neuropsychological Tests	naMCI Mean (SD)	aMCI Mean (SD)	Controls Mean (SD)
Working Memory			
Digit Span			
- Age Scale Score	10.26 (2.78)	9.45 (2.86)	11.55 (3.22)[*b]
Verbal Learning and Memory			
WMS- III LM I			
- Age Scale Score	9.59 (3.60)[*b]	7.48 (3.19)	12.90 (2.43)[**a,***b]
WMS- III LM II			
- Age Scale Score	10.41 (3.35)[***b]	6.90 (3.69)	12.90 (1.95)[**a,***b]
Language			
BNT			
- Age Scale Score	10.46 (4.63)	8.79 (4.06)	12.57 (2.92)[**b]
Visuospatial Skills			
RCFT Copy			
- Percentile	2.52 (2.10)	2.48 (1.50)	4.62 (4.09)†

Table 8. Neuropsychological performance for patients with naMCI, aMCI and control subjects (continued)

Neuropsychological Tests	naMCI Mean (SD)	aMCI Mean (SD)	Controls Mean (SD)
Processing Speed			
TMT-A - z-score	-0.06 (0.95)	-0.21 (1.42)	0.51 (0.67)
Executive Functioning			
COWAT- FAS			
- z-score	-0.60 (1.50)	-1.06 (2.68)	0.71 (1.12)^{**a,**b}
TMT-B - z-score	-0.63 (1.51)	-1.20 (2.74)	0.46 (0.69)^{**a,**b}

Notes: naMCI = non-amnestic Mild Cognitive Impairment multiple-domain; aMCI = amnestic Mild Cognitive Impairment multiple-domain; ^{a} = significant difference compared with naMCI group; ^{b} = significant difference compared with aMCI group; WMS-III LM = Wechsler Memory Scale - Third Edition, Logical Memory subtest; BNT = Boston Naming Test; RCFT = Rey Complex Figure Test; TMT = Trail-making Test; COWAT = Controlled Oral Word Association Test; †n = 13; *$p < .05$; **$p < .01$; ***$p < .001$.

Table 9**.** Disability scores as measured by WHODAS-II for patients with naMCI, aMCI and control subjects

Domain	naMCI Mean (SD)	aMCI Mean (SD)	Controls Mean (SD)	*p**
Understanding and Communicating	24.07 (19.37)	24.91 (18.68)	5.45 (5.75)	.000
Getting Around	18.29 (18.34)	21.43 (24.08)	11.35 (12.74)	.361
Self-care	8.89 (16.17)	11.48 (22.23)	1.82 (6.64)	.056
Getting Along with Others	23.41 (19.49)	14.88 (15.93)	9.83 (12.50)	.045
Life Activities	27.04 (26.43)	29.64 (23.96)	12.27 (23.49)	.009
Participation in Society	25.15 (19.10)	25.15 (17.02)	9.85 (8.09)	.001
Summary Score	21.52 (15.64)	25.92 (23.44)	8.41 (5.59)	.001

Notes: naMCI = non-amnestic Mild Cognitive Impairment multiple-domain; aMCI = amnestic Mild Cognitive Impairment multiple-domain; Higher scores denote greater disability; *Kruskal-Wallis Test.

Table 10. Emotion recognition accuracy (FEEST) for patients with naMCI, aMCI and control subjects

	naMCI	aMCI	Controls			
Emotion	Mean (SD)	Mean (SD)	Mean (SD)	χ^2*	*df*	*p*
Anger	7.70 (1.92)	6.48 (1.96)	8.41 (1.82)	14.111	2	.001
Disgust	8.22 (1.37)	7.76 (2.37)	8.05 (1.68)	0.640	2	.971
Fear	5.70 (2.23)	5.07 (2.09)	6.18 (2.53)	2.966	2	.226
Happy	9.63 (1.04)	9.45 (0.91)	9.73 (0.88)	4.277	2	.113
Sad	7.41 (1.82)	6.86 (1.58)	7.77 (2.20)	4.198	2	.119
Surprise	7.92 (1.49)	8.55 (1.59)	8.59 (1.29)	4.091	2	.128
Total	46.67 (5.53)	44.17 (8.05)	48.64 (6.06)	3.909	2	.145

Notes: naMCI = non-amnestic Mild Cognitive Impairment multiple-domain; aMCI = amnestic Mild Cognitive Impairment multiple-domain; Lower scores denote poorer accuracy; * Kruskal-Wallis Test.

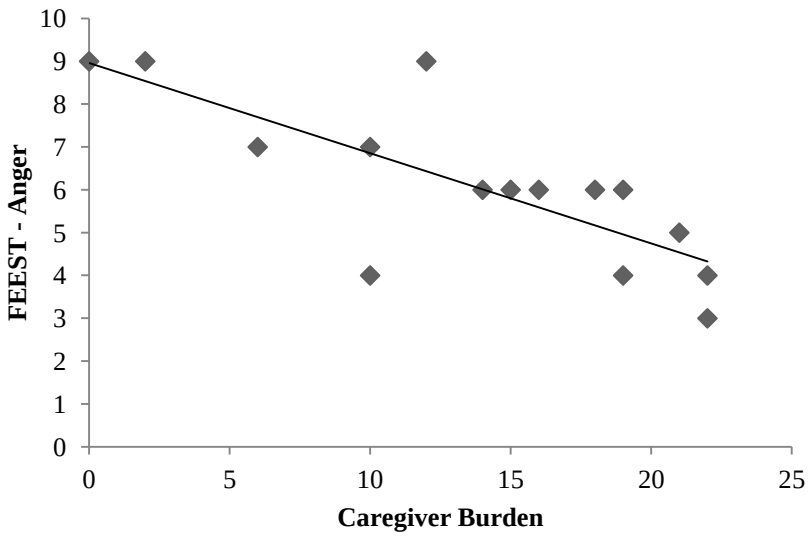

Figure 1. Scatterplot (with regression line) depicting the relationship between emotion recognition for anger (FEEST) and carer burden (as measured by the Zarit Burden Interview) for aMCI patients.

CHAPTER 6

DISCUSSION

This body of work incorporates one published paper which reviewed the existing literature of emotion recognition studies in MCI. Two empirical studies then examined whether deficits in emotion recognition are evident in MCI subtypes, and whether such deficits relate to disability and caregiver burden. The performance of patients with MCI subtypes was compared with age- and education- matched control subjects on a range of emotion recognition tasks in the first study. It was hypothesised that as emotion recognition deficits are evident in dementias including FTD and AD, very early deficits may already be evident in MCI patients. In the second study, the real life implications of emotion recognition deficits were explored, specifically with regard to the functional disability of patients and caregiver burden. Previous research in AD patients had found significant associations between emotion recognition deficits and impaired social functioning as well as caregiver burden. The focus of Study 2 was largely exploratory in nature to investigate for the presence of associations between emotion recognition abilities, functional disability, and caregiver burden for MCI patients. This discussion chapter summarises the key research findings, addresses methodological limitations, future research directions and outlines clinical implications.

Study 1 – Emotion recognition deficits exist in Mild Cognitive Impairment, but only in the amnestic subtype

This study compared the performances of multi-domain amnestic (aMCI) and non-amnestic (naMCI) MCI patients with age- and education-matched control subjects on three tasks assessing emotion recognition ability. These tasks varied in terms of cognitive demands, with a more challenging, non-prompted emotion labelling condition (i.e., Emotion Identification task) and a less challenging condition in which prompts were provided to aid participant recognition (i.e., Movie Stills Task, Losh et al., 2009; Facial Expressions of Emotion: Stimuli and Tests: FEEST, Young et al., 2002). Tasks also varied in terms of the use of facial displays of emotion (i.e., FEEST, Movie Stills Task, Emotion Identification task) and non-facial emotional cues (i.e., bodily gestures and posture; Movie Stills Task). Chapter 4 provides a full discussion of these results, some of which are highlighted below.

In line with our hypothesis, patients with aMCI demonstrated specific decrements in performance in the three task conditions, compared with control subjects. Deficits in emotion recognition were found with each condition, with a decrement in overall emotion found in two task conditions (i.e., Emotion Identification task and Movie Stills Task) and an emotion specific for anger recognition in two conditions (i.e., FEEST and Emotion Identification task). Furthermore, it was found that difficulties in emotion recognition extended beyond facial displays of emotions in that aMCI patients were significantly less accurate when deciphering the

overall emotional content of complex, scenes from peripheral bodily cues. The finding of specific impairments in emotion recognition in aMCI multiple-domain patients is consistent with past research (Fujie et al., 2008; Spoletini et al., 2008; Teng et al., 2007; Weiss et al., 2008). Interestingly, an emotion-specific deficit for anger was found for aMCI patients on two emotion recognition tasks. Impaired anger recognition in aMCI patients is consistent with past research (Fujie et al., 2008) and with the broader finding that negative emotions are preferentially impaired in aMCI patients (Spoletini et al., 2008; Weiss et al., 2008). Importantly, these deficits cannot be attributed to a general impairment in face processing abilities, since there were no significant differences in the performance of aMCI patients on a face matching task, compared with either naMCI patients or control subjects. Moreover, whilst aMCI patients exhibited greater neuropsychological dysfunction compared to controls and naMCI subjects (i.e., Logical Memory I and II subtests, Trail-making Test B), it was found that decrements in emotion recognition exist independent of cognitive functioning. Whilst this finding was contrary to our initial hypothesis, the lack of an association between mood and emotion recognition was anticipated, in line with past research.

This research significantly advances our understanding of the nature of emotion recognition deficits in MCI patients by the inclusion of an naMCI patient group, which had not been the case in previous studies. Unlike aMCI patients, and contrary to our hypothesis, no significant differences were found in the performance of naMCI patients on any emotion recognition task when compared with control subjects. This finding has

promising diagnostic implications for MCI as a clinical entity. A further strength of the current study was the use of multiple means of assessing emotion recognition, including the use of non-facial measures of emotion recognition.

Study 2 – Emotion recognition in Mild Cognitive Impairment: Relationship to disability and caregiver burden

This study investigated the impact of emotion difficulties in MCI in terms of subjective disability and caregiver burden. Chapter 5 provides a full discussion of these results, some of which are highlighted below. Consistent with the results of Study 1 aMCI, but not naMCI, patients were impaired in the recognition of facial expressions of anger, as assessed by the FEEST task. In terms of disability, significantly greater psychosocial disability was reported by both patient groups (WHODAS-II; World Health Organisation, 2001) relative to control subjects, which was in line with our hypothesis. Specifically, one area of heightened disability was in the domain of understanding and communicating, which incorporated the ability to initiate, maintain and understand conversations, as well as to concentrate, and learn new tasks and problem-solve. MCI patients also had greater disability in the domain of participation in society, a domain which assessed the ability to join in on community activities and undertake pleasurable tasks, as well as emotionality, and social and family difficulties. With regard to the correlates of self-reported disability, no association was found between impaired emotion recognition and

psychosocial disability for aMCI patients. However, a significant relationship was revealed for naMCI patients between the ability to recognise anger and the disability domain of getting along with people, which assessed initiating and maintaining social relationships, and sexual activities. The lack of an association between social dysfunction and emotion recognition for aMCI patients was contrary to initial hypothesis.

A further key finding was that whilst the caregivers of naMCI patients reported significantly greater levels of burden, relative to both aMCI patients and control subjects, a significant relationship between caregiver burden and anger recognition existed only for aMCI patients. These findings are only partially consistent with our initial hypotheses.

Overall, the results from Study 2 suggest that decrements in emotion recognition may differentially impact naMCI and aMCI subtypes. For naMCI patients, difficulties in recognising anger may mediate dysfunction in their social relationships. Despite this group having greater caregiver burden, this does not seem to relate, however, to emotion recognition abilities. In contrast, the apparent difficulties in recognising anger in aMCI patients do not appear to relate to self-reported levels of disability, but conversely, appear to mediate a greater level of caregiver burden. It is noteworthy, however, that MCI patients have been found to underestimate their level of functional disability (Tabert et al., 2002). Hence the failure to find a relationship with social dysfunction may be at least in part due to the use of self-report measures of functioning, and may reflect impaired insight of aMCI patients.

This study advances our understanding of the non-cognitive impact of MCI for both patients and caregivers, areas which have been relatively under-explored in research (Springate & Tremont, 2012). To the authors' knowledge, this study was also the first to explore the real-life impact of emotion recognition difficulties, which may have clinical implications for patients and their caregivers. These implications are described in more detail in later sections of this chapter.

Limitations and future directions

The limitations of each study were discussed in Chapter 4 (Study 1) and Chapter 5 (Study 2). Some specific issues and future research implications are explored in more detail below.

The design of both studies was cross-sectional in nature. A plausible conclusion from these studies is that the presence of emotion recognition deficits in MCI patients represents a potential marker, useful in the diagnostic clarification and prognosis of MCI subtype. However, this conclusion is speculative given that the long-term clinical outcome of MCI patients included in the current study has not yet been established. Whilst MCI is viewed clinically as categorising individuals at *increased risk* of progression to dementia, the diagnostic concept of MCI does not necessarily represent a dementia prodrome. As mentioned in previous chapters, a high proportion of MCI patients remain stable or return to normalcy over time. Consequently, a proportion of the individuals diagnosed with MCI in the current study may not progress to dementia. The rather stringent inclusion criteria employed in both studies restricting

the MCI sample to individuals only with deficits across multiple cognitive domains, however, was adopted to maximise the diagnostic sensitivity of MCI, with multi-domain MCI representing the greatest risk for conversion to dementia than single-domain MCI (Rasquin et al., 2005). Nevertheless, future research should incorporate a longitudinal follow-up to ascertain the long-term clinical progression of MCI patients and their performance on emotion recognition measures. Such research would certainly strengthen the current findings regarding the utility of emotion recognition deficits as a biomarker in diagnosis and dementia progression.

The results of both studies must be interpreted with caution because of the small sample size of both patients and controls included in Study 1 and Study 2. Effect sizes for the specific emotion recognition deficits for aMCI patients in both studies ranged from medium to large, which is consistent with previous findings in this field (Fujie et al., 2008; Spoletini et al., 2008; Weiss et al., 2008). To date, most studies exploring emotion recognition in MCI have included modest sample sizes (for a review see McCade et al., 2011). One study included a sample of 50 aMCI patients (Spoletini et al., 2008), larger than that included in Study 1 (n = 19) and Study 2 (n = 29). Upon qualitative inspection, the demographic characteristics of the MCI samples included in Study 1 and Study 2 appear to be generally comparable to those reported in Spoletini et al. (2008). The mean age of aMCI patients in the Spoletini et al. (2008) was 71.2 ± 7.5, which compares favourably with the mean age of aMCI patients in Study 1 (69.6 ± 7.3) and Study 2 (69.0 ± 7.3). Likewise, gross cognitive functioning as assessed by a Mini-Mental State Examination (MMSE) was

similar across aMCI patients (Spoletini et al., 2008: 26.7 ± 2.5; Study 1: 26.9 ± 1.8; Study 2: 27.2 ± 1.8). Whilst the sample in Spoletini et al. (2008) had fewer years of education (Spoletini et al., 2008: 9.8 ± 4.6; Study 1: 13.6 ± 3.7; Study 2: 13.8 ± 3.6), educational attainment has not been found to mediate accuracy in emotion recognition (Sasson et al., 2010). In addition, the proportionate representation of females was greater in Study 1 (63%) and Study 2 (59%) than the 46% of total sample included in Spoletini et al. (2008). Given that females have a noted advantage in emotion recognition accuracy (Calder et al., 2003; Sasson et al., 2010) the inclusion of a greater proportion of women in Studies 1 and 2 may ostensibly have diminished the effect size, and thus our finding could be considered even more remarkable. Spoletini et al. (2008) did not, however, include a naMCI patient group, hence no comparisons can be made for this subtype.

The patient group employed in Studies 1 and 2 also appears to be representative of those MCI patient groups included in larger studies, with regard to demographic characteristics (i.e., age, MMSE scores, sex distribution and years of education). These include a meta-analysis of MCI screening studies (Lonie, Tierney, & Ebmeier, 2009), as well as those determining the clinical characterisation of the MCI profile (Alladi, Arnold, Mitchell, Nestor, & Hodges, 2006) and longitudinal outcome studies (Amieva et al., 2004; Tabert et al., 2006). Variability in the mean age included across MCI studies is apparent, however, with the inclusion of samples with a younger (Nordlund et al., 2010; Visser & Verhey, 2008) or older (Busse, Hensel, Guhne, Angermeyer, & Riedel-Heller, 2006;

Petersen et al., 1999; Unverzagt et al., 2001) mean age than those included in Studies 1 and 2. As the above comparisons are based on qualitative observation only, however, generalisation of the results in Study 1 and 2 will require replication in studies with larger groups.

In Study 1, it was hypothesised that emotion recognition deficits in aMCI patients may be due to advanced neurodegeneration extending beyond the temporal lobes to frontal and limbic cortical regions, such as the ventromedial and orbitofrontal cortices. This hypothesis was based on evidence of overlapping neural regions implicated in both emotion recognition (Blair et al., 1999; Rosen et al., 2002; Rosen et al., 2006) and neuropathology evident in aMCI patients (Whitwell et al., 2007). However, since neuroimaging data were not incorporated in Study 1 or 2, conclusions regarding neural underpinnings cannot be inferred. Future studies incorporating structural and/or functional neuroimaging could thus enhance these findings. Whilst a small number of imaging studies have investigated the neuropathological substrates of emotion recognition in dementia (Keane, Calder, Hodges, & Young, 2002; Rosen et al., 2002; Rosen et al., 2006), this field has been relatively under-explored in MCI, with the inclusion of imaging data in only one study conducted to date (Fujie et al., 2008). In AD, single photon emission computed tomography (SPECT) imaging has shown decreased regional cerebral blood flow (rCBF) in the posterior frontal lobe (which includes the anterior cingulate and medial frontal gyrus) to be associated with facial emotion recognition deficits (Staff et al., 2011). Hence, the use of imaging data in future MCI

studies may enable the neural substrates of emotion recognition deficits to be better understood.

Future studies may also investigate whether alterations in key neurometabolites relate to emotion recognition deficits in aMCI patients, via the use of magnetic resonance spectroscopy (MRS). MRS enables the detection of differences in tissue concentration or resonance frequency of chemical compounds in the brain (Yildiz-Yesiloglu & Ankerst, 2006) and provides measures of neuronal and glial integrity, as well as those pertaining to bioenergetics and excitatory neurometabolites. There is some evidence to suggest that limbic pathways involved in emotion processing are, at least partially, controlled by glutamatergic and dopaminergic neurotransmission (Abel et al., 2003; Brunet-Gouet & Decety, 2006). Since these pathways may be disrupted by disease, it is thus possible that emotion recognition deficits in MCI may be partly mediated by altered in-vivo levels of key metabolites.

A further limitation of both Study 1 and 2 is that participants were required to label and identify emotions using static displays of facial emotional expressions. The Facial Expressions of Emotion: Stimuli and Tests (FEEST; Young et al., 2002) used in Study 1 and Study 2 and the NimStim stimulus set (Tottenham et al., 2009), used in Study 1, consist of photographs of actors with posed expressions which mimic or fake emotional displays. In real life, however, expressions of emotion are highly dynamic signals (Kilts, Egan, Gideon, Ely, & Hoffman, 2003) and a criticism of static emotional facial displays is that they may not capture the complex and dynamic nature of real emotional expressions (McDonald,

2012). Static facial displays may lack the emotional richness of dynamic presentations of facial expressions and vocal prosody, and consequently their ecological validity has been criticised (Cadieux & Greve, 1997). There is some evidence to suggest that dynamic facial displays may enhance both emotion recognition and discrimination (Wehrle, Kaiser, Schmidt, & Scherer, 2000). Dynamic displays of emotion are less reliant on the use of mental strategies to decode cues (Kilts et al., 2003) and may also provide the perceiver with more cues than static displays (McDonald, 2005), compared with static photographic images of facial expressions. Hence, it is possible that difficulties with emotion recognition are inflated by or, at worse an artefact of, stimuli employed. The finding that the performance of individuals with severe chronic brain injuries on emotion recognition tasks utilising static displays of emotional expressions correlated highly with their performance on tasks employing more complex, dynamic, visual and audio emotional cues (McDonald et al., 2006), argues against this claim however. Future studies should seek to maximise the ecological validity of emotion recognition measures by utilising tasks which are more reflective of real-life experiences, incorporating dynamic visual and audio emotional displays (McDonald, 2012).

Furthermore, the emotions explored in both studies were limited to the six basic human emotions (Ekman & Cordano, 2011). Whilst emotions have long thought to be universally shared based on their adaptive, biological role to motivate and regulate behaviour (Darwin, 1998), recently evidence has emerged which challenges this perspective. Culture

may exert powerful influences on the experience and expression of emotions, including the specific facial muscles employed in emotional displays (Jack, Garrod, Yu, Caldara, & Schyns, 2012). Hence future research should examine the role of cross-cultural differences in the emotion processing abilities of MCI patients.

In addition, the six basic emotions explored in both studies reflect relatively simply themed emotional stimuli. Future studies should investigate the recognition of and reactivity to "self-conscious" emotions, such as pride, guilt, shame and embarrassment (Tangney, 1999). These emotions are thought to be more complex, requiring higher-level processing of the self in a social context, with reference to social rules and norms (Sturm, Rosen, Allison, Miller, & Levenson, 2006). Self-conscious emotions require the ability to evaluate one's self and to infer the mental states of others, and are thought to have evolved to regulate approach and inhibition tendencies which may threaten social relations (Baumeister, Stillwell, & Heatherton, 1994; Tangney, Miller, Flicker, & Barlow, 1996). As self-awareness is an integral component, these emotions are important contributors to appropriate social behaviour (Sturm et al., 2006). Future research into these emotions would therefore serve to broaden the understanding of emotion processing in MCI.

The nature of the research undertaken in Studies 1 and 2 was largely exploratory in nature. Across both studies, multiple comparisons were undertaken on emotion recognition variables to explore their relationship with measures of cognition, mood, functional disability and caregiver burden. A consequence of these multiple comparisons, undertaken in

studies with modest sample sizes, is that the potential for Type 1 errors is increased. Consequently, to avoid an inflated Type I error rate and minimise the risk of inadvertently accepting a null effect, a statistically conservative approach was adopted. In Study 1, a Bonferroni correction was applied at the family-wise level and a reduced alpha level of .01 was used for correlational analyses in both studies. Whilst the use of adjusted alpha levels is widely adopted in research it remains controversial and no consensus exists as to how such adjustments should be undertaken (Blakesley et al., 2009). There are, however, a number of limitations associated with this conservative approach, namely the increased potential for Type II errors and consequent loss of statistical power (Field, 2009). As such, it is possible that further genuine effects in these studies have been overlooked.

Clinical implications of research findings

This research highlights the limitations of the current MCI diagnostic criteria, in which the presence of objective cognitive impairment is the core criterion for an MCI diagnosis. This focus on cognition has informed not only the clinical understanding of MCI as an entity, but has also dictated the approach adopted to screen for its presence (Lonie et al., 2009). There are, however, disadvantages with this reliance on cognitive factors to detect MCI. In a review of the literature on cognitive markers used in the detection of pre-clinical AD, Bäckman, Jones, Berger, Laukka, and Small (2004) found a substantial overlap in the distribution of

cognitive scores in those who progress to AD and healthy controls, which suggests that the clinical utility of cognitive markers alone may be limited.

Recently, there has been increased support of the role of non-cognitive factors in the detection of MCI, with recommendations made to include mild difficulties in functional activities in the revised MCI criteria (Albert et al., 2011). It is noteworthy that the proposed concept of functional disability is limited to instrumental activities of daily living, such as shopping, paying bills, and cooking (Albert et al., 2011; Morris, 2012). No suggestion has been made to incorporate social dysfunction. However, the results of Study 2 suggests that initial disability in social functioning is already evident in both naMCI and aMCI multi-domain subtypes, which may warrant the concept of functional disability to be broadened from purely instrumental daily activities. Furthermore, a better understanding of psychosocial dysfunction in MCI patients will facilitate more ecologically valid measures being developed to detect and define functional decline. For example, performance-based measures have been found to be more sensitive tools than questionnaire-based assessments for MCI patients, whilst informant reports may be more accurate in distinguishing levels of functional independence than self-report measures (for a review see Gold, 2012).

Nevertheless, it is an encouraging development that the revised MCI criteria recommendations recognise the validity of non-cognitive factors to enhance MCI diagnostic sensitivity. Changes in motor symptoms (Louis et al., 2005), functional disability (Gold, 2012), as well as the presence of the ε4 allele in the apolipoprotein E (*APOE*) gene (Roberts et al., 2010),

neuronal injury, beta-amyloid protein (Aβ) and tau (Albert et al., 2011) are also emerging as important markers in this regard. So too are the presence of neuropsychiatric symptoms (NPS) in MCI, which are highly predictive of progression to dementia (Copeland et al., 2003). Consistent with this, results from Study 1 and Study 2 demonstrate that difficulties with emotion recognition may also represent an important diagnostic marker for the detection and prognosis of MCI. Measures assessing emotion recognition may be useful in enhancing the diagnostic sensitivity of MCI and should therefore be incorporated into neuropsychological assessment batteries used to screen for MCI. The Awareness of Social Inference Test (TASIT; McDonald et al., 2006), which uses complex, dynamic stimuli to test emotion recognition, as well as the FEEST (Young et al., 2002) and the Social Cognition and Emotional Assessment (Funkiewiez, Bertoux, de Souza, Levy, & Dubois, 2012), both of which incorporate static facial displays of emotion from the Ekman and Friesen (1976) series, have proven clinical utility in this regard.

Given that the clinical understanding of MCI is predominantly based on the presence of cognitive impairment, it is likely that this will shape how patients and their caregivers also view the concept of MCI. Research suggests that there is considerable misperception about the diagnosis of MCI by patients regarding its consequences and prognosis (Lingler et al., 2006). Whilst patients report cognitive symptoms, the presence of which is validated following clinician examination, cognitive difficulties do not solely define their experience of MCI. Loss of skills, changing social and family roles, behavioural disturbances and burden represent the day-to-day

experience of patients and their caregivers (Frank et al., 2006). This suggests the need to better inform patients and their families/caregivers about the non-cognitive aspects of MCI. Study 1 and Study 2 identified the presence of emotion recognition difficulties in aMCI patients and social dysfunction in both patient subgroups. These results highlight the need for educational approaches to help patients and caregivers be aware of and recognise changes in emotion recognition and social functioning, as well as to understand the implication of such changes (Vasterling, Seltzer, Carpenter, & Thompson, 1997). Prior research suggests that both emotion recognition and social functioning are important abilities for the development and maintenance of personal relationships (Kohler et al., 2005; Shimokawa et al., 2001). Whilst insight into abilities was not included in Study 1 or Study 2, past research suggests MCI patients tend to overestimate their functional abilities (Tabert et al., 2002). In addition, poor insight into social and emotion functioning has been demonstrated in AD (Nelis et al., 2011; Vasterling et al., 1997). Awareness of the potential for disrupted social functioning and emotion recognition abilities, as a consequence of MCI, is crucial in enabling patients to recognise potential difficulties in their relationship with their caregiver. Likewise, knowledge of the potential social and emotion deficits could enable caregivers to recognise deficits and understand how these may impact the caregiver/patient relationship, including increasing burden (Nelis et al., 2011). An educational approach must be supplemented with the provision of practical strategies which enable caregivers to effectively manage problematic situations and behaviours which may result from these

deficits. Research suggests that caregivers who are more confident in their ability to find solutions to behavioural problems in dementia are better able to manage the negative effects associated with caregiving and consequently experience lower levels of burden and depression (Papastavrou et al., 2011). Family caregivers represent the cornerstone of support provided to people with dementia (Ferri et al., 2005) and spend considerable amounts of time caring for family members (Fisher et al., 2011), hence the implementation of educational and coping strategies at an early stage in the caregiver journey is critical in minimising the significant individual and societal costs associated with caregiver burden (Springate & Tremont, 2012). Minimising the major burden experienced by caregivers has been shown to improve caregiver quality of life and patient health status, as well as reduce institutional costs (Bell, Araki, & Neumann, 2001; Miller, Rosenheck, & Schneider, 2010).

As well as the need for education and support for caregivers, the results from Study 1 and Study 2 indicate that the implementation of interventions aimed at improving emotion recognition in MCI patients are warranted. Emotion remediation programmes have shown promising results in a variety of clinical populations, including developmental disorders such as autism, where social deficits have long been regarded as intractable (Bölte et al., 2006; Ryan & Charragain, 2010). To date, significant improvements in emotion recognition have been reported following the implementation of remediation programmes for individuals with schizophrenia (Combs et al., 2007; Penn & Combs, 2000; Russell, Chu, & Phillips, 2006), traumatic brain injury (Bornhofen & McDonald,

2008a; Bornhofen & McDonald, 2008b) and intellectual disability (Mcalpine, Singh, Ellis, Kendall, & Hampton, 1992). Evidence of post-treatment gains in emotion recognition abilities have also been reported in remediation studies (Mcalpine et al., 1992; Penn & Combs, 2000; Silver, Goodman, Knoll, & Isakov, 2004). A common focus of remediation programs is training individuals to identify, discriminate and verbalise basic emotions by attending to individual facial features (e.g. mouth and eyes), through hierarchically structured tasks. This involves starting with basic activities (i.e., emotion identification) and graduating to increasingly complex tasks such as integrating emotional cues with social and behavioural contextual information (Frommann, Streit, & Wölwer, 2003). To date, literature on emotion remediation in dementia or MCI is non-existent. Findings of initial deficits in emotion recognition in MCI patients in both studies, however, indicate that further research in developing and trialling an appropriate early intervention programme is warranted.

In addition to emotion remediation, some promising results have been found with the administration of the neuropeptide hormone oxytocin to individuals with impaired emotion recognition. Oxytocin is produced in the hypothalamus and delivered to the pituitary and regions in the central nervous system, including the amygdala and prefrontal cortex (Ross & Young, 2009). Oxytocin is proposed to interact with the dopaminergic connections of the amygdala, a cortical region implicated in emotion recognition (Rosenfeld, Lieberman, & Jarskog, 2011) to mediate social behaviour (Lim & Young, 2006). Animal models have demonstrated that oxytocin plays a role in social interactions that involve emotion

processing, such as social recognition and pair bonding (Hammock & Young, 2006). Human studies have shown that administration of oxytocin may dampen reactions to emotion stimuli, which consequently serves to enhance prosocial behaviours (Baumgartner, Heinrichs, Vonlanthen, Fischbacher, & Fehr, 2008; Domes et al., 2007). In healthy adults, administration of oxytocin has resulted in a significant improvement in the processing of positive expressions (Guastella, Mitchell, & Mathews, 2008) and recognition of negative emotions (Fischer-Shofty, Shamay-Tsoory, Harari, & Levkovitz, 2010). Other studies have shown that oxytocinergic input to the amygdala is modified by the stimuli's social relevance, with resultant reduced activation for fearful and angry expressions (Di Simplicio, Massey-Chase, Cowen, & Harmer, 2009; Kirsch et al., 2005). Given the compelling evidence of emotion recognition deficits in patients with FTD (Diehl-Schmid et al., 2007; Fernandez-Duque & Black, 2005; Keane et al., 2002; Rosen et al., 2004), one study has explored the potential for oxytocin as a symptomatic treatment (Jesso et al., 2011). Twenty FTD patients received a single, intranasal dose of oxytocin. At follow-up testing one week post administration, FTD patients showed no significant treatment effect. Anger recognition was in fact reduced, which potentially may be in part due to oxytocin-induced reductions in amygdala activation for threatening stimuli (Kirsch et al., 2005). There were some small, non-significant improvements in neuropsychiatric symptoms, however. Whilst these results throw some doubt on its potential for dementia patients, it may also reflect that longer duration trials with

repeated oxytocin dosage are required prior to any conclusions being drawn regarding the efficacy of oxytocin.

In summary, emotion recognition abilities are critical for appropriate social behaviour. The relationship of emotion recognition abilities with caregiver burden and with social dysfunction for aMCI and naMCI patients, respectively, demonstrates a need not only to screen for deficits in MCI patients, but to implement targeted educational programmes for caregivers and systematic treatment interventions for patients.

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APPENDICES

Appendix A

Approval letter from Macquarie University Ethics Review Committee

(Human Research)

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19 November 2009

Dr Jenny Batchelor
C3B 421 Psychology Department
Macquarie University

Reference: HE26FEB2010-D00214

Dear Dr Batchelor

Title of project: ***Exploring neuroplasticity with cognitive training; A Healthy Brain Ageing program***

The above application was considered by the Executive of the Ethics Review Committee (Human Research). In accordance with section 5.5 of the *National Statement on Ethical Conduct in Human Research (2007)* the Executive noted the final approval from the University of Sydney and your right to proceed under their authority.

Please do not hesitate to contact the Ethics Secretariat if you have any questions or concerns.

Yours sincerely

Dr Karolyn White
Director of Research Ethics
Chair, Ethics Review Committee (Human Research)

Appendix B

Approval letter from University of Sydney Human Research Ethics Committee

The University of Sydney

Human Research Ethics Committee
Web: http://www.usyd.edu.au/ethics/human

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17 August 2009

Dr. Sharon Naismith
Brain & Mind Research Institute
Mallett Street – M02G
The University of Sydney
Email: snaismith@med.usyd.edu.au

Dear Dr. Naismith,

Thank you for your correspondence dated 31 July 2009 addressing comments made to you by the Human Research Ethics Committee (HREC). After considering the additional information, the Executive Committee at its meeting on **12 August 2009** approved your protocol entitled ***"Exploring neuroplasticity with cognitive training: a healthy brain ageing program"***.

Details of the approval are as follows:

Ref No.:	***08-2009/11962***	
Approval Period:	***August 2009 to August 2010***	
Authorised Personnel:	***Dr. Sharon Naismith***	***Ms. Donna McCade***
	Miss Loren Mowszowksi	***Ms. Keri Diamond***
	Dr. Louise Norrie	***Dr. Daniel Hermens***
	Dr. Adam Guastella	***Dr. Matthew Paradise***
	Dr. Zoe Terpening	***Ms. Phoebe Carter***

The HREC is a fully constituted Ethics Committee in accordance with the *National Statement on Ethical Conduct in Research Involving Humans-March 2007* under *Section 5.1.29*

The approval of this project is **conditional** upon your continuing compliance with the *National Statement on Ethical Conduct in Research Involving Humans.* We draw to your attention the requirement that a report on this research must be submitted every 12 months from the date of the approval or on completion of the project, whichever occurs first. Failure to submit reports will result in withdrawal of consent for the project to proceed.

Chief Investigator / Supervisor's responsibilities to ensure that:

(1) All serious and unexpected adverse events should be reported to the HREC as soon as possible.

(2) All unforeseen events that might affect continued ethical acceptability of the project should be reported to the HREC as soon as possible.

(3) The HREC must be notified as soon as possible of any changes to the protocol. All changes must be approved by the HREC before continuation of the research project. These include:-
- If any of the investigators change or leave the University.
- Any changes to the Participant Information Statement and/or Consent Form.

(4) All research participants are to be provided with a Participant Information Statement and Consent Form, unless otherwise agreed by the Committee. The Participant Information Statement and Consent Form are to be on University of Sydney letterhead and include the full title of the research project and telephone contacts for the researchers, unless otherwise agreed by the Committee and the following statement must appear on the bottom of the Participant Information Statement. *Any person with concerns or complaints about the conduct of a research study can contact the Manager, Ethics Administration, University of Sydney, on (02) 8627 8175 (Telephone); (02) 8627 8180 (Facsimile) or gbriody@usyd.edu.au (Email).*

(5) Copies of all signed Consent Forms must be retained and made available to the HREC on request.

(6) It is your responsibility to provide a copy of this letter to any internal/external granting agencies if requested.

(7) The HREC approval is valid for four (4) years from the Approval Period stated in this letter. Investigators are requested to submit a progress report annually.

(8) A report and a copy of any published material should be provided at the completion of the Project.

Yours sincerely

Professor D I Cook
Chairman
Human Research Ethics Committee

cc: Ms. D. McCade, email: dmccade@med.usyd.edu.au
Miss L. Mowszowski, email: lorenm@med.usyd.edu.au

Encl. Approved Participant Information Sheet
Approved Consent Form
Approved Participant Information Sheet for Family Members / Carers
Approved Consent Form for Family Members / Carers
Approved Participant Self-Report Forms
Approved Significant Other / Carer Self-Report Forms
Approved Participation Satisfaction Questionnaire
Approved Recruitment Flyer

APPENDIX C

Neuropsychological Tests and Normative Data Sources used in Studies 1 and 2 to Diagnose MCI

Cognitive Domain	Test	Normative Data Source
Working Memory	Digit Span subtest of the Wechsler Adult Intelligence Scale -Third Edition (Reference: Wechsler, D. (1997). *Wechsler Adult Intelligence Scale* (3rd ed.). San Antonio: The Psychological Corporation.)	Age-scaled scores from WAIS-III manual.
Verbal learning and memory	The Logical Memory subtest of the Wechsler Memory Scale - Third Edition (Reference: Wechsler, D. (1997). *Wechsler Memory Scale* (3rd ed.). New York: Psychological Corporation: Harcourt Assessment.) The Rey Auditory Verbal Learning Scale was used to assess verbal memory.	Age-scaled scores form WMS-III manual. Age-scaled scores were computed using normative data as well as percentage retention across trials.

Cognitive Domain	Test	Normative Data Source
Visual memory	The Rey Complex Figure Test 3-minute recall (RCFT; (Reference: Meyers, J. E., & Meyers, K. R. (1995). *Rey Complex Figure Test and Recognition Trial: Professional Manual.* Odessa, FL: Psychological Assessment Resources, Inc.) was used to assess visual memory.	Percentile scores were computed using Meyers & Meyers (1995) normative data.
Visuo-spatial skills	Rey Complex Figure Test (Reference: Meyers, J. E., & Meyers, K. R. (1995). *Rey Complex Figure Test and Recognition Trial: Professional Manual.* Odessa, FL: Psychological Assessment Resources, Inc.)	Percentile scores calculated using Meyers & Meyers (1995) normative data.
Psychomotor processing speed	Part A of the Trail-making Test (Reitan, R. (1979). *Trail-making test.* Arizona : Reitan Neuropsychology Laboratory.)	z-scores calculated using normative data: Tombaugh et al. (1996) in Spreen, O., & Strauss, E. (1998). *A Compendium of Neuropsychological Tests: Administration, Norms and Commentary*. New York : Oxford University Press.

Cognitive Domain	Test	Normative Data Source
Language	Boston Naming Test (Kaplan, E., Goodglass, H., & Weintraub, S. (1983). *Boston Naming Test*. Philadelphia: Lea and Febiger.)	Age-scale scores computed using normative data: Ivnik, R. J., Malec, J. F., Smith, G. E., Tangalos, E. G., & Petersen, R. C. (1996). Neuropsychological tests' norms above age 55: COWAT, BNT, MAE token, WRAT-R reading, AMNART, STROOP, TMT, and JLO. *The Clinical Neuropsychologist, 10*(3), 262-278.
	Semantic fluency (animal names; Benton et al., 1983)	Z-scores were computed using normative data (see Tombaugh et al., in Spreen & Strauss, 1998)
Executive functioning	Controlled Oral Word Association Test (COWAT) - verbal fluency	z-scores for verbal fluency and set shifting calculated using normative data: Tombaugh et al. (1996) in Spreen, O., & Strauss, E. (1998). *A Compendium of Neuropsychological Tests: Administration, Norms and Commentary.* New York : Oxford University Press.
	Part B of the Trail-making Test - cognitive flexibility (Reitan, R. (1979). *Trail-making test.* Arizona : Reitan Neuropsychology Laboratory.)	