ELSEVIER

Neuropsychologia 46 (2008) 1965–1978

NEUROPSYCHOLOGIA

www.elsevier.com/locate/neuropsychologia

Recollection and familiarity in amnestic mild cognitive impairment: A global decline in recognition memory

David A. Wolk [a,b,*], Eric D. Signoff [a,b], Steven T. DeKosky [a,b]

[a] *Alzheimer's Disease Research Center, University of Pittsburgh, Pittsburgh, PA, United States*
[b] *Department of Neurology, University of Pittsburgh, Pittsburgh, PA, United States*

Received 20 September 2007; received in revised form 19 January 2008; accepted 25 January 2008
Available online 2 February 2008

Abstract

Despite memory failures being a central feature of amnestic mild cognitive impairment (a-MCI), there is limited research into the nature of the memory impairment associated with this condition. A further understanding could lead to refinement of criteria needed to qualify for this designation and aid in prediction of who will progress to development of clinical Alzheimer's disease. Dual process models posit that recognition memory is supported by the dissociable processes of recollection and familiarity. The present study sought to evaluate recognition memory in a-MCI in the framework of the dual process model. Patients with a-MCI and age- and education-matched controls were tested on three memory paradigms. Two paradigms were modifications of the process-dissociation procedure in which recollection required either memory of word-pair associations (associative) or the font color of words at study (featural). A final paradigm utilized the task-dissociation methodology comparing performance for item and visual spatial source memory. All three tasks revealed that familiarity was impaired to at least the same extent as recollection. As familiarity is thought to be spared in normal aging, its measurement may provide a relatively specific marker for the early pathological changes of Alzheimer's disease.

Keywords: Alzheimer's disease; Memory; Dual process; Process-dissociation procedure; Task dissociation

1. Introduction

Mild cognitive impairment (MCI) has been conceptualized as a transitional state from normal aging to clinical Alzheimer's disease (AD) or other forms of dementia. Consistent with this notion a number of studies have found that people with MCI develop AD at a rate much higher than age-matched controls without cognitive impairment [10–15%/year versus 1–2%/year, respectively; (Gauthier et al., 2006; Petersen, 2004)]. Further, pathological studies support that a significant percentage of patients classified with MCI have AD pathology (Guillozet, Weintraub, Mash, & Mesulam, 2003; Kordower et al., 2001; Mitchell et al., 2002; Petersen et al., 2006). However, notwithstanding the controversy as to whether MCI should be classified as 'early AD' (Morris, 2006; Morris et al., 2001), not all cases using current criteria appear to develop clinical AD. This is most evident in community-based studies in which there is a much lower rate of conversion to dementia and even a proportion of patients reverting back to a non-impaired designation over time (Ganguli, Dodge, Shen, & DeKosky, 2004; Larrieu et al., 2002). Additionally, there is not complete consensus on what specific criteria to use with regard to psychometrics and other factors. Thus, MCI represents a heterogeneous population which is, in part, driven by the manner in which the criteria are applied and the population studied.

In the last several years, MCI has been divided into subgroups; amnestic and non-amnestic types. These groups have been further divided based on whether there is the presence of a single or multiple domains of cognitive impairment (Petersen, 2004). Although recent work has suggested that a proportion of all classes of MCI will develop AD (Busse, Hensel, Guhne, Angermeyer, & Riedel-Heller, 2006), the majority of work on this diagnostic construct has focused on amnestic-MCI (a-MCI) presuming that this entity represents the transitional state to clinical AD. Despite this large body of work and the pre-eminent position of memory impairment in its classification,

* Corresponding author at: Alzheimer's Disease Research Center, UPMC Montefiore, 4 West 200 Lothrop Street, Pittsburgh, PA 15213-2582, United States. Tel.: +1 412 692 4644; fax: +1 412 692 2710.
E-mail address: wolkda2@upmc.edu (D.A. Wolk).

0028-3932/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.neuropsychologia.2008.01.017

there remains somewhat limited investigation into the nature of the memory impairment beyond standard clinical psychometrics. A more detailed understanding of the phenotype of early AD memory impairment may be useful in further refining the criteria for MCI to reduce heterogeneity and aid in distinguishing those with true AD pathology. An approach informed by novel memory measures developed in the cognitive neuroscience literature may be of particular utility for this endeavor.

One major theory in the memory literature is that of the dual process model of recognition memory. While accounts vary in detail, the general notion is that recognition judgments are subserved by the functionally distinct processes of recollection and familiarity (Curran, Tepe, & Piatt, 2006; Eichenbaum, Yonelinas, & Ranganath, 2007; Jacoby, 1991; Mandler, 1980; Yonelinas, 2002). Recollection is defined as a conscious retrieval of associations and context while familiarity is an acontextual sense of prior exposure. Familiarity is usually conceived of as varying in strength and may be best described by signal detection or global matching models while recollection involves a qualitative, high threshold recovery of associates. While this model is not without disagreement (Donaldson, 1996; Slotnick & Dodson, 2005; Squire, Wixted, & Clark, 2007; Wixted, 2007), converging data from a variety of different modalities of enquiry are supportive, including studies of rodents and primates (Brown & Aggleton, 2001; Eichenbaum, 2004), healthy young and elderly subjects (Davidson & Glisky, 2002; Howard, Bessette-Symons, Zhang, & Hoyer, 2006; Yonelinas, 2002), patients with amnesia (Holdstock et al., 2002; Yonelinas et al., 2002b), functional MRI (fMRI; see Eichenbaum et al., 2007, for review), and event-related potentials (ERPs; see Rugg & Curran, 2007, for review). Much of this work has supported an anatomic dissociation within the medial temporal lobes in support of these processes. Recollection has been linked to hippocampal function while familiarity appears related to perirhinal activity, as well as possibly that of the lateral entorhinal cortex (Brown & Aggleton, 2001; Eichenbaum et al., 2007). However, not all work has supported this anatomic dissociation with some suggesting that these regions differentially support weak and strong memories, orthogonal to recollection and familiarity (Wais, Wixted, Hopkins, & Squire, 2006; Wixted & Squire, 2004; see Squire et al., 2007 for review).

In addition to the hippocampus, recollection, considered a more controlled process, appears dependent on neocortical structures, including prefrontal cortex. For example, patients with frontal lobe injury appear to have a relatively selective impairment of associative or source-based memories (thought to be dependent on recollection) (Johnson, O'Connor, & Cantor, 1997; Wheeler, Stuss, & Tulving, 1995; Yonelinas, 2002). Relative sparing of item memory (thought to be dependent on familiarity) in these patients suggests that the prefrontal cortex plays a less critical role for familiarity and that it is a more automatic memory process than recollection (Jacoby, 1991).

A number of studies have examined the impact of aging on recollection and familiarity. Using a variety of different methodologies, the majority of these studies support a general decline in recollection with little or no impairment in familiarity relative to younger subjects (Davidson & Glisky, 2002; Howard et al., 2006; Jennings & Jacoby, 1997; Light, Patterson, Chung, & Healy, 2004; Parkin & Walter, 1992; Yonelinas, 2002). Recent work has suggested that the sparing of familiarity is associated with intact and, perhaps, compensatory increases in perirhinal activity (Cabeza et al., 2004; Daselaar, Fleck, Dobbins, Madden, & Cabeza, 2006). On the other hand, recollection decline appears related to measures of frontal lobe function (Davidson & Glisky, 2002; Parkin & Walter, 1992). The relationship of prefrontal dysfunction with age-associated memory impairment is consistent with fMRI studies demonstrating aberrant recruitment during the encoding and retrieval of older participants relative to their younger counterparts (Cabeza, Anderson, Locantore, & McIntosh, 2002; Grady et al., 1995; Logan, Sanders, Snyder, Morris, & Buckner, 2002; Rosen et al., 2002). It is also consistent with imaging findings that the largest age-related changes involve prefrontal-striatal structures (for review, see Buckner, 2004; Raz & Rodrigue, 2006). The direct role of the hippocampus in decline of recollection with healthy aging is less clear (Van Petten, 2004), but likely is, in part, related to disruption of prefrontal-hippocampal communication, if not intrinsic hippocampal dysfunction (Albert, 2002; Buckner, 2004).

Studies of recollection and familiarity in patients with AD have been limited; however, most work suggests an impairment of memories supported by both recollection and familiarity (Budson, Desikan, Daffner, & Schacter, 2000; Gallo, Sullivan, Daffner, Schacter, & Budson, 2004; Smith & Knight, 2002). This finding is consistent with the significant neurofibrillary tangle (NFT) pathology in the medial temporal lobes, involving both hippocampal and extra-hippocampal structures, by the time of clinical AD diagnosis (Braak & Braak, 1991; Delacourte et al., 1999).

There have been no studies which directly estimate recollection and familiarity in a-MCI. Some have reported failures of item recognition in addition to associative memory which would be suggestive of an impairment in both memory processes (Bennett, Golob, Parker, & Starr, 2006; Dudas, Clague, Thompson, Graham, & Hodges, 2005; Hudon et al., 2006). Alternatively, one study suggested a sparing of familiarity based on control-level performance on a forced-choice memory task using highly similar foils (Westerberg et al., 2006).

The present study sought to determine the degree to which recollection and familiarity are impaired in a-MCI relative to healthy controls. Although a heterogeneous population, it is expected that a significant percentage of our a-MCI patients have early AD pathology and will eventually develop clinical AD (as in other memory disorders clinics, our conversion rate is approximately 15%/year). In this context, we predicted that both recollection and familiarity would be lower than that of our control group. The rationale for this hypothesis comes from the fact that, at least for those destined to develop AD, there is expected to be early pathological changes of the disease. Interestingly, the earliest areas of NFT involvement in AD are the transentorhinal and entorhinal cortices (Braak & Braak, 1991; Delacourte et al., 1999). The transentorhinal cortex may be considered part of the medial aspect of the perirhinal cortex although exact boundaries remain controversial (Suzuki & Amaral, 2003). Regardless, perirhinal pathology is likely an early feature of