Brain and Cognition 69 (2009) 504–513

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

An evaluation of recollection and familiarity in Alzheimer's disease and mild cognitive impairment using receiver operating characteristics

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ARTICLE INFO

Article history:
Accepted 6 November 2008
Available online 19 December 2008

Keywords:
Alzheimer's disease
Recognition memory
Familiarity
Recollection
Receiver operating characteristics
ROC
Dual process

ABSTRACT

There is a need to investigate exactly how memory breaks down in the course of Alzheimer's disease (AD). Examining what aspects of memorial processing remain relatively intact early in the disease process will allow us to develop behavioral interventions and possible drug therapies focused on these intact processes. Several recent studies have worked to understand the processes of recollection and familiarity in patients with mild cognitive impairment (MCI) and very mild AD. Although there is general agreement that these patient groups are relatively unable to use recollection to support veridical recognition decisions, there has been some question as to how well these patients can use familiarity. The current study used receiver operating characteristic (ROC) curves and a depth of processing manipulation to understand the effect of MCI and AD on the estimates of recollection and familiarity. Results showed that patients with MCI and AD were impaired in both recollection and familiarity, regardless of the depth of encoding. These results are discussed in relation to disease pathology and in the context of recent conflicting evidence as to whether familiarity remains intact in patients with MCI. The authors highlight differences in stimuli type and task difficulty as possibly modulating the ability of these patients to successfully use familiarity in support of memorial decisions.

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1. Introduction

Dual-process models of recognition memory theorize that accurate recognition decisions rely on two independent neural processes: *recollection* and *familiarity* (Jacoby & Dallas, 1981; Mandler, 1980; Yonelinas, 1994). Recollection refers to the retrieval of specific context-bound information about an item or event, while familiarity is defined as a more general, acontextual sense that an item or event has been previously encountered. These two constructs are often vividly experienced in daily life. For example, the unexpected sight of a particular man on a crowded city street may elicit an immediate feeling of knowing him without being able to produce any specific details about who he is or how he is known. After a moment of thought, these details may come into mind and the man's identity – say, the waiter at a restaurant you had visited one week earlier – becomes apparent. Familiarity describes the initial feeling of knowing the man without being able to place him, while recollection captures the subsequent remembering of the specific details of his identity.

Several behavioral paradigms have been devised to empirically quantify familiarity and recollection for individual recognition decisions in the laboratory (for review see Yonelinas, 2002). These process-estimation methods include process-dissociation (Jacoby, 1991), remember/know (Tulving, 1985), and confidence-based ROC procedures (Yonelinas, 1994) – the latter being the focus of the current investigation. In a prototypical recognition memory experiment, the participant is exposed to a series of items during a "study" phase. These items are then re-presented along with some number of novel items during a "test" phase. The participant must indicate at test whether each item is "old" (previously studied) or "new" (not previously studied). In the confidence-based ROC paradigm, this binary old/new decision is expanded to reflect how confident the participant is that each test item has or has not been previously encountered. For each test item, the participant provides a response ranging from certainty that the item was previously studied (i.e., "certain the item is old") to certainty that the item was not previously studied (i.e., "certain the item is new") with several intermediate options (e.g., "sort of certain the item is old", "not at all certain the item is old", "not at all certain the item is new", "sort of certain the item is new").

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0278-2626/$ - see front matter Published by Elsevier Inc.
doi:10.1016/j.bandc.2008.11.003

Analysis using ROC curves has been used since the 1950s to describe recognition memory decisions (e.g., Egan, 1958), and Yonelinas (1994) devised a dual-process model of confidence-based ROC data that could estimate the separate contributions of recollection and familiarity. The Yonelinas high threshold model assumes that recognition memory decisions are made based on either recollection or familiarity (Yonelinas, 1994). In recent years, these ROC analyses have been used to estimate recollection and familiarity in healthy older adults (Howard, Bessette-Symons, Zhang, & Hoyer, 2006; Prull, Dawes, Martin, Rosenberg, & Light, 2006), individuals with thalamic lesions (Kishiyama et al., 2005), and individuals with selective hippocampal or more diffuse medial temporal lobe lesions (Aggleton et al., 2005; Cipolotti et al., 2006; Wais, Wixted, Hopkins, & Squire, 2006; Yonelinas, Kroll, Dobbins, Lazzara, & Knight, 1998; Yonelinas et al., 2002). These investigations, in addition to numerous functional neuroimaging studies, have provided an understanding of the neuroanatomical basis of recognition memory decisions. Though far from settled, research has argued that the hippocampus (Cansino, Maquet, Dolan, & Rugg, 2002; Dobbins, Rice, Wagner, & Schacter, 2003; Eldridge, Knowlton, Furmanski, Bookheimer, & Engel, 2000; Yonelinas, Otten, Shaw, & Rugg, 2005), prefrontal regions (Burgess & Shallice, 1996; Dobbins, Foley, Schacter, & Wagner, 2002; Simons, Owen, Fletcher, & Burgess, 2005), and parietal regions (Ally, Simons, McKeever, Peers, & Budson, 2008; Skinner & Fernandes, 2007; Wagner, Shannon, Kahn, & Buckner, 2005) are critical to recollection, whereas more anterior medial temporal and parahippocampal regions are critical to familiarity (Brown & Xiang, 1998; Cansino et al., 2002; Eichenbaum, Yonelinas, & Ranganath, 2007; Henson, Cansino, Herron, Robb, & Rugg, 2003).

Understanding the neural and cognitive correlates of recollection and familiarity is critically important in determining the nature of memory impairment in clinical populations (Aggleton et al., 2005; Cipolotti et al., 2006; Wais et al., 2006; Yonelinas et al.,1998, 2002). Along with the understanding of the nature of memory impairment of AD, we hope that the current study can help to elucidate how memory breaks down in the earliest stages of the disease. This understanding may in turn allow new drug therapies and early behavioral interventions to be developed. The processes of recollection and familiarity have only recently begun to be systematically investigated in patients with mild cognitive impairment (MCI) and Alzheimer's disease (AD). Two such studies have examined recollection and familiarity in patients with MCI (Westerberg et al., 2006; Wolk, Signoff, & DeKosky, 2008), but neither study used ROC procedures that have proven particularly informative in other clinical populations. Based largely on the methodology of Yonelinas et al. (1998), the goal of the present study is to use the Yonelinas high threshold model to estimate recollection and familiarity for word stimuli in healthy older adults, patients with MCI-amnestic type (a-MCI), and patients with mild AD.

Evidence in healthy older adults using ROC and other process-estimation methods has suggested that compared to young adults, recollection is differentially impaired for certain groups of healthy older adults (Cabeza, Anderson, Locantore, & McIntosh, 2002; Davidson & Glisky, 2002; Duarte, Ranganath, Winward, Hayward, & Knight, 2004) or for certain types of stimuli (Ally et al., 2008), while familiarity generally is spared (Daselaar, Fleck, Dobbins, Madden, & Cabeza, 2006; Howard et al., 2006; Jacoby, 1999; Jennings & Jacoby, 1993; Jennings & Jacoby, 1997; Rybash & Hoyer, 1996; Spencer & Raz, 1995; Titov & Knight, 1997; Yonelinas, 2001). It has been suggested that a decline in the attentional resources allocated at encoding and retrieval, perhaps due to frontal lobe changes associated with normal aging, may be responsible for a decrease in recollection in this group (Anderson, Craik, & Naveh-Benjamin, 1998; Buckner, 2004; Park, Smith, Dudley, & Lafronza, 1989; Salthouse, 1994; Whiting & Smith, 1997).

In addition to the cognitive changes that may occur with normal aging, Alzheimer's disease damages key brain structures involved in language, executive functioning, and memory. The earliest and most prominent of these cognitive abilities to be affected is episodic memory. Studies have shown that when memory loss is clinically apparent, significant AD pathology is evident in medial temporal structures including perirhinal cortex, entorhinal regions, hippocampus, amygdala, and nucleus basalis (Arriagada, Growdon, Hedley-Whyte, & Hyman, 1992; Braak & Braak, 1991; Gomez-Isla et al., 1996; Mesulam, 2000; Van Hoesen, Hyman, & Damasio, 1991). Many researchers and clinicians believe that MCI may be the transitional state between normal aging and mild AD (Bell-McGinty et al., 2005; Petersen et al., 2001), and note that the amnestic variant of MCI has the highest rate of conversion to AD (Petersen, 2004). Patients with amnestic-type MCI have significant memory loss for their age, but do not have impaired activities of daily living needed to meet the clinical diagnosis of AD (Petersen, 2004; Petersen et al., 2001). Neuropathology and structural imaging studies lend support to the supposition that MCI may be the earliest stage of AD, showing a significant link between structures affected by the two groups (Grundman et al., 2004; Killiany et al., 2002; McKee et al., 2006; Mitchell et al., 2002; Petersen, 2004). By the time memory loss is clinically evident, warranting a diagnosis of MCI, significant AD neurofibrillary pathology is seen in limbic regions, including transentorhinal regions, perirhinal cortex, amygdala, nucleus basalis (Arriagada et al., 1992; Braak & Braak, 1991; Mesulam, 2000; Van Hoesen et al., 1991), and most prominently in hippocampus and entorhinal cortex (Gomez-Isla et al., 1996). These regions continue to be affected as AD progresses (Mesulam, 1999), with pathology spreading to neocortical areas such as temporal, parietal, occipital association, and frontal cortex in clinical AD (Braak & Braak, 1991; Delacourte et al., 1999; Grady et al, 1988; Ibanez et al., 1998; McKee et al. 2006).

Numerous studies have reported impaired recollection in patients with AD (Budson, Daffner, Desikan, & Schacter, 2000; Christensen, Kopelman, Stanhope, Lorentz, & Owen, 1998; Dalla Barba, 1997; Gallo, Sullivan, Daffner, Schacter, & Budson, 2004; Knight, 1998; Koivisto, Portin, Seinela, & Rinne, 1998; Smith & Knight, 2002). In fact, recollection appears to be severely impaired even in the earliest stages of the disease, resulting in an increased reliance on familiarity-based memory (Balota, Burgess, Cortese, & Adams, 2002; Budson et al., 2000; Lekeu et al., 2003; Wolk et al., 2005). Although patients with AD may be more reliant on familiarity (Budson et al., 2000; Smith & Knight, 2002), it remains unclear whether this type of memory is impaired in MCI or mild AD (see Westerberg et al., 2006; Wolk et al., 2008). Given the early pathological changes to areas critical to the processes of recognition in patients with MCI and AD, we would expect both groups to be impaired in recollection *and* familiarity compared to healthy older adults on a standard old/new recognition test.

The goal of the current study is to use a depth of encoding manipulation and ROC procedures similar to Yonelinas et al. (1998) to investigate how MCI and mild AD affect the memorial processes of recollection and familiarity. A possible concern using ROC methodology in patients with MCI or AD may be the ability of these patients to assess confidence for memory decisions. However, research investigating the ability to retrieve and monitor stored general knowledge in patients with AD has shown that these patients can successfully make confidence ratings regarding the certainty of their answers (Backman & Lipinska, 1993). Given evidence that AD pathology affects brain structures critical to both recollection and familiarity in MCI and the earliest stages of AD (Csernansky et al., 2004; Gomez-Isla et al., 1996; Jack et al., 2004; Kantarci et al., 2005; Karas et al., 2004), we hypothesized that both patient groups would show impairment in recollection *and* familiarity compared to healthy older adults.

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