Neuropsychologia 50 (2012) 592–602

Contents lists available at SciVerse ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Using virtual reality to characterize episodic memory profiles in amnestic mild cognitive impairment and Alzheimer's disease: Influence of active and passive encoding

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ARTICLE INFO

Article history:
Received 9 April 2011
Received in revised form
18 December 2011
Accepted 20 December 2011
Available online 13 January 2012

Keywords:
Episodic memory
Long-term binding
Encoding
Virtual reality
Aging
Dementia
Mild cognitive impairment

ABSTRACT

Most neuropsychological assessments of episodic memory bear little similarity to the events that patients actually experience as memories in daily life. The first aim of this study was to use a virtual environment to characterize episodic memory profiles in an ecological fashion, which includes memory for central and perceptual details, spatiotemporal contextual elements, and binding. This study included subjects from three different populations: healthy older adults, patients with amnestic mild cognitive impairment (aMCI) and patients with early to moderate Alzheimer's disease (AD). Second, we sought to determine whether environmental factors that can affect encoding (active vs. passive exploration) influence memory performance in pathological aging. Third, we benchmarked the results of our virtual reality episodic memory test against a classical memory test and a subjective daily memory complaint scale. Here, the participants were successively immersed in two virtual environments; the first, as the driver of a virtual car (active exploration) and the second, as the passenger of that car (passive exploration). Subjects were instructed to encode all elements of the environment as well as the associated spatiotemporal contexts. Following each immersion, we assessed the patient's recall and recognition of central information (i.e., the elements of the environment), contextual information (i.e., temporal, egocentric and allocentric spatial information) and lastly, the quality of binding. We found that the AD patients' performances were inferior to that of the aMCI and even more to that of the healthy aged groups, in line with the progression of hippocampal atrophy reported in the literature. Spatial allocentric memory assessments were found to be particularly useful for distinguishing aMCI patients from healthy older adults. Active exploration yielded enhanced recall of central and allocentric spatial information, as well as binding in all groups. This led aMCI patients to achieve better performance scores on immediate temporal memory tasks. Finally, the patients' daily memory complaints were more highly correlated with the performances on the virtual test than with their performances on the classical memory test. Taken together, these results highlight specific cognitive differences found between these three populations that may provide additional insight into the early diagnosis and rehabilitation of pathological aging. In particular, neuropsychological studies would benefit to use virtual tests and a multi-component approach to assess episodic memory, and encourage active encoding of information in patients suffering from mild or severe age-related memory impairment. The beneficial effect of active encoding on episodic memory in aMCI and early to moderate AD is discussed in the context of relatively preserved frontal and motor brain functions implicated in self-referential effects and procedural abilities.

1. Introduction

Episodic memory may be described as the conscious recollection of personal events combined with their phenomenological and spatiotemporal encoding contexts (Tulving, 2002). The multiple components of memory (central and contextual information) that together form a complete episodic memory are thought to be linked through a process known as "binding" (Kessels, Hobbel, & Postma, 2007), mainly supported by the hippocampus (Slotnick, 2010). Numerous studies have demonstrated that episodic memory impairment is one of the hallmarks of early clinical manifestations of Alzheimer's disease (AD) (Hodges, 2006) and amnesic mild cognitive impairment (aMCI) (Petersen et al., 2001, 1999). In parallel, some researchers have reported reduced volume in the

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doi:10.1016/j.neuropsychologia.2011.12.013

hippocampus and in other brain regions such as parahippocampal gyrus and cingulate cortex in both AD and aMCI patients (Chételat et al., 2002; De Leon et al., 2006; Dickerson et al., 2001; Fox and Schott, 2004; Gerardin et al., 2009; Risacher et al., 2009). Typically, MCI patients have intermediate brain volumes between AD patients and healthy controls (Evans et al., 2010), with an atrophy of the hippocampus that is less spatially extended compared to AD (Gerardin et al., 2009). In addition, their gray matter density in the posterior association cortex seems preserved compare to AD (Chételat, Villain, Desgranges, Eustache, & Baron, 2009).

Classical neuropsychological tools used to assess episodic memory are far from encompassing the complexity of this kind of memory (for review, Piolino, Desgranges, & Eustache, 2009). Episodic memory is generally assessed with verbal tasks, although much of what people remember in everyday life refers to visual information and to actions that they have performed. The objective of our study was to demonstrate that virtual environments can be used as tools to characterize, in detail, the episodic memory profiles of AD and aMCI patients through tasks that parallel requirements of daily life.

So far, the state of central memory in AD and aMCI, such as memory for items, has been mainly evaluated with words, indicating deficits of free and cued recalls and recognition during AD (Salmon & Bondi, 2009; Spaan, Raaijmakers, & Jonker, 2003, for review), and to a lesser extent, aMCI (Perri, Carlesimo, Serra, & Caltagirone, 2005). Several studies have focused on the retrieval of contextual information in both populations and have observed spatial memory deficits (for review, Iachini, Iavarone, Senese, Ruotolo, & Ruggiero, 2009), including egocentric and allocentric impairments (Hort et al., 2007; Laczó et al., 2009), as well as temporal memory deficits (Putzke, Rickert, Duke, Marson, & Harrell, 2000). However, Delpolyi, Rankin, Mucke, Miller, and Gorno-Tempini (2007) found that after immersion in a real-life contextual environment, aMCI patients recognized landmarks just as effectively as controls but could not find their locations on maps or recall the order in which they had been encountered. In addition, decreases in binding quality have been observed in visuospatial (item with location) and verbal associative learning tasks (placing two words together) (Fowler, Saling, Conway, Semple, & Louis, 2002; Swainson et al., 2001; Troyer et al., 2008). Overall, previous studies have generally led researchers to assume that AD patients suffer from a general episodic memory deficit and aMCI patients from a less profound one corresponding to the progression of the atrophy (Chételat et al., 2009; Evans et al., 2010).

However, various clinical memory tests used in dementia generally measure only one aspect of episodic memory in isolation, rather than offering a complete measure of its components such as memory for what, where, and when, and binding between components. This is in sharp contrast with the requirements of daily life. Moreover, the conditions of these tests are generally far from ecological. Many studies have argued that neuropsychological assessments should bear some degree of similarity to the demands of daily life (Farias, Harrell, Neumann, & Houtz, 2003; Schultheis, Himelstein, & Rizzo, 2002; Wojtasik et al., 2010). Indeed, it has been demonstrated that standard neuropsychological memory assessments are only moderately correlated with behavior-based measures of daily living skills (e.g., dialing a telephone, selecting shopping items with a written list, etc.) (Farias et al., 2003).

To improve the diagnosis and the rehabilitation of aMCI and AD patients, studies can take advantage of new technologies used to develop paradigms that are able to detect functional changes in cognitive abilities and present conditions that resemble daily life. By assessing the various components of an episodic memory (factual, spatial, temporal, and binding) both simultaneously and multimodally, virtual reality (VR) enables the performance of an integrated assessment of episodic memory. To date, only a few neuropsychological studies have used VR to test memory in pathological aging. Previous studies have mainly focused on navigational processes. Some studies with aMCI patients (Cushman, Stein, & Duffy, 2008) have found a close relationship between performance in virtual and real environments. Moreover, other studies with AD patients (Burgess, Trinkler, King, Kennedy, & Cipolotti, 2006; Drzezga et al., 2005; Zakzanis, Quintin, Graham, & Mraz, 2009) have specifically found allocentric spatial impairments. Widmann, Beinhoof and Riepe (2012) immersed AD patients and healthy participants in a virtual environment to assess the learning of verbal material in situations that imitate natural conditions. AD patients were found to be impaired in free memory recall of shop names compared to healthy participants, and the impairment was more marked than that observed with classical list-learning. The study argued that list-learning paradigms wrongly estimated the memory capacities of patients in every day situations. Recently, we developed a virtual reality test that seeks to reflect the definition of episodic memory more closely than other standard neuropsychological tests (for review, Plancher, Nicolas, & Piolino, 2008). Various aspects of episodic memory (what, where, when, and binding) were evaluated in a population of young adults and healthy older adults after they drove a car in a virtual environment representing a city with different, but specific, areas and elements (Plancher, Gyselinck, Nicolas, & Piolino, 2010). We observed a difference between the healthy aged controls and younger participants in memory for spatiotemporal context and binding. Moreover, the virtual test was sensitive to the older subjects' memory complaints, which was contrary to the standard verbal episodic memory test.

One aim of the present study, which follows-up on results obtained by Plancher et al. (2010), was to use this new VR test to determine changes in the various components of episodic memory in pathological aging by comparing aMCI and AD patients with a new population of healthy aged controls. In addition, we aimed to test whether environmental influences on encoding could improve memory performance. Precisely, we sought to determine if active exploration of the virtual environment improves memory compared to passive exploration. It has been previously demonstrated that presenting information in the memory environment can serve as compensatory support for deficient self-initiated processing and can enhance memory performance (Craik, 1983, 1986; Luo & Craik, 2008; Naveh-Benjamin, Craik, & Ben-Shaul, 2002, for review). For example, positive effects of environmental support have been observed when older participants benefited from the provision of more elaborate pictorial information (Park, Puglisi, & Smith, 1986; Schacter, Israel, & Racine, 1999) or context and semantic organizational structure of materials (Park, Smith, Morrell, Puglisi, & Dudley, 1990). An active exploration involves cognitive processes that are different than those engaged during passive exploration. In particular, personal involvement is higher in active exploration, which may potentially result in a self-reference effect that is known to improve memory, even in aging (Gutchess, Kensinger, & Schacter, 2010; Lalanne et al., 2010; Ruby et al., 2009). In addition, encoding information through motion may solicit, even if it is far from real movements, some procedural skills. Self-referential effect and procedural skills mainly depend on medial prefrontal cortex (Craik et al., 1999; Kelley et al., 2002; Martinelli, Sperduti, & Piolino, in press), striatum and motor cortex respectively (Nilsson et al., 2000; Nyberg et al., 2001; Pennartz, Ito, Verschure, Battaglia, & Robbins, 2011; Squire, 2004). These processes and the underlying cortical structures would be partially preserved in mild AD (Chase et al., 1984; Grady et al., 2003). Learning based on implicit procedural skills appears to be one of the best preserved skills found in AD patients (Deweer et al., 1994; Deweer, Pillon, Michon, & Dubois, 1993; Gabrieli, Corkin, Mickel, & Growdon, 1993; Hirono et al., 1997; Lipinska & Backman, 1997; Van Halteren-van Tilborg, Scherder, & Hulstijn, 2007). Further, some studies have previously