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Does retrieval frequency account for the pattern of autobiographical memory loss in early Alzheimer's disease patients?

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ABSTRACT

Episodic autobiographical memory (ABM) has been found to be impaired from the early stage of Alzheimer's disease (AD). Previous works have focused on how ABM decreases over the lifespan, but no study has deeply investigated whether the extent of episodic autobiographical amnesia is mediated by the retrieval frequency of the episodic trace itself. The aim of the present study was to determine whether the frequency of trace retrieval has an effect on the quality of autobiographical incidents recall and whether the extent of this contribution changes over time. For this purpose, the episodic component of ABM was assessed in patients in the early stage of AD through a questionnaire which allowed evaluating memory of past personal incidents as a function of both their age of acquisition and retrieval frequency. We found that both AD patients and healthy controls took advantage of greater retrieval frequency across all time segments, because of their better memory performance on frequently retrieved episodes than less frequently retrieved ones. Although in the AD group the retrieval frequency effect (i.e., higher scores on the episodes rated as more frequently retrieved) was found in all time segments, the extent of its beneficial effect on memory performance was temporally-graded and inversely related to the time course. Our findings provide new evidence that the combined action of both age of memory and retrieval frequency could provide a valuable framework for predicting patterns of ABM loss, at least in early AD patients. In line with the Multiple Trace Theory, we speculated that retrieval frequency protects episodic trace recall against hippocampal damage by reinforcing the neural representation of personal context-rich memories, which consequently are easier to access and recall. Furthermore, the age of memory should change the amplitude of this beneficial effect as a function of the remoteness of the trace.

1. Introduction

Autobiographical memory (ABM) is commonly defined as memory for the events and facts of one's own life and has a fundamental role in the self, emotions and experience of personhood over time (Conway and Pleydell-Pearce, 2000). In the literature, ABM has been conceptualized as involving two main components: personal episodic and semantic autobiographical memory (Kopelman, 1989). The former contains information about personal incidents that happened to an individual in a specific space and time of his own past; they critically involve a sense of autonoetic consciousness that allows re-experiencing or reliving the past (Levine, 2004). Conversely, personal semantic memory includes general information or facts about one's life such as addresses, friends' names or anniversaries, which can be retrieved in the absence of any recollection, e.g., from a "database" (Tulving, 1999). In a neurobiological perspective, two predominant theoretical positions are adopted to explain how these types of autobiographical memory are stored and retrieved. The Cortical Reallocation Theory, also known as the Standard Consolidation Model (SCM) (Alvarez and Squire, 1994; Squire, 2004), suggests a time-limited involvement of the medial temporal lobe (MTL) structures, i.e., the hippocampus and parahippocampal cortices, in the storage and recovery of both episodic and semantic traces; hence, over time the consolidation process leads to the formation of a permanent memory stored in the neocortex that is capable of sustaining the memory trace alone and mediating its retrieval (Alvarez and Squire, 1994).

By contrast, the most recent Multiple Trace Theory (MTT)

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(Nadel and Moscovitch, 1997; Moscovitch et al., 2005) makes a distinction between episodic and semantic autobiographical memories regarding the neural mechanisms involved in trace retrieval. Overall, this model postulates that once the memory trace has been consolidated only semantic information, fixed in cortical networks, is recalled independently of the hippocampal formation. Conversely, autobiographical episodes remain strictly dependent on the cortical-hippocampal system throughout a person's life because these structures are always necessary for recalling the spatial and temporal contextual information that characterizes an episodic trace (Schacter, 1987; Nadel and Moscovitch, 1997). Consequently, these two models make distinct predictions about how remote memory is affected by the physical location and extent of brain damage (Bright et al., 2006). According to the SCM model, in the presence of a hippocampal lesion both episodic and semantic past memories should be subject to temporally graded retrograde amnesia, following Ribot's law (Ribot, 1881). In other words, memories will be spared as long as they have been consolidated into cortical networks, while more recent, not yet consolidated hippocampal-dependent memories will be lost (Alvarez and Squire, 1994; Shimamura, 2002). Otherwise, according to the MTT, the severity of the decline in recalling personal memories depends on both the type of autobiographical memory under investigation-indeed, only remote personal semantic memories should survive MTL damage as they have become independent of the hippocampus over time-and the severity of the MTL or hippocampal damage (Nadel and Moscovitch, 1997; Nadel et al., 2007). More specifically, according to the MTT, memories are continuously updated and re-encoded after each retrieval, leading to the formation of multiple memory traces. In this way, frequently retrieved remote memories are represented by more and stronger hippocampal–neocortical traces than less frequent memories, making them less susceptible to disruption by brain damage. Since memory traces are sparse and distributed, even minimal damage at any location of the hippocampal formation can affect acquisition, retention and recovery of any of them. Older memories are associated with a greater number of traces and retrieval become easier as the number of traces and the number of access routes to them proliferate. This implies that newly acquired traces should be particularly vulnerable in the case of mild hippocampal damage; but older memories, which are multiply represented, should be able to withstand the loss of more hippocampal complex tissue (Nadel and Moscovitch, 1997). In any case, severe hippocampal pathology should lead to a flat gradient for autobiographical episodic information that extends throughout life.

In the early stages of Alzheimer's disease (AD), cerebral atrophy is concentrated in the MTL, particularly in the hippocampus and entorhinal cortex (Deweer et al., 2001; Du et al., 2001; Devanand et al., 2007). Therefore, early AD patients might be an excellent model for investigating the role of these regions in memory and thus for testing the two above mentioned theoretical models. Although deficits in anterograde memory are the hallmark of AD, this is not the only kind of memory that is affected. In patients with AD, retrograde amnesia is present from the early stage of dementia, as indicated by the loss of autobiographical memories (Kopelman et al., 1989; Piolino et al., 2003; Leyhe et al., 2009; Irish et al., 2011a, 2011b; Müller et al., 2012), famous public events' information (Dorrego et al., 1999; Starkstein et al., 2005; Leyhe et al., 2010; Müller et al., 2014), and the inability to recognize famous faces or famous names (Hodges et al., 1993; Greene and Hodges, 1996a, 1996b; Thompson et al., 2002; Clague et al., 2011). Although interest in studying past memories has grown exponentially in the past few decades, behavioral studies in AD patients have produced ambiguous results and many of the critical issues are still being widely debated (Kopelman, 2002, 2008). Specifically, while there have been consistent reports of ABM impairment in AD patients (Greene et al., 1995; Greene and Hodges, 1996b; Graham and Hodges, 1997; Dorrego et al., 1999; Addis and Tippett, 2004; Hou et al., 2005; Ivanoiu et al., 2006; Meeter et al., 2006; Leyhe et al., 2009; Irish et al., 2011a, 2011b; Barnabe et al., 2012; Müller et al., 2012 for a review also see El Haj et al., 2015a), there is still disagreement about the specific pattern of retrograde amnesia. This is an important factor as it could serve to distinguish between the two models of memory consolidation. Overall, whereas the personal episodic component of autobiographical memory has been consistently found to be affected in AD (Greene et al., 1995; Greene and Hodges, 1996b; Addis and Tippett, 2004; Hou et al., 2005; Ivanoiu et al., 2006; Meeter et al., 2006; Leyhe et al., 2009; Irish et al., 2011a, 2011b; Müller et al., 2012), the semantic component has been found to be either impaired (Addis and Tippett, 2004; Leyhe et al., 2009; Müller et al., 2012) or preserved (Murphy et al., 2008; Irish et al. 2011a; Martinelli et al., 2013) in patients at different clinical stages of AD. Moreover, controversial results have been reported about the presence or absence of a Ribot temporal gradient in assessing episodic autobiographical memory in AD. In particular, many studies found evidence of a Ribot gradient (Kopelman, 1989; Greene et al., 1995; Graham and Hodges, 1997; Leyhe et al., 2009; Irish et al., 2011b; Müller et al., 2012), whereas others reported no significant differences in memory accuracy between remote and recent incidents (Addis and Tippett, 2004; Gilboa et al., 2005; Hou et al., 2005; Ivanoiu et al., 2006; Meeter et al., 2006; Addis et al., 2009). Results obtained from assessing the semantic component of ABM are also controversial: some authors found a significant graded-like Ribot's amnesia in AD patients (Kopelman, 1989; Addis and Tippett, 2004; Ivanoiu et al., 2006; Leyhe et al., 2009; Müller et al., 2012) and others found a flat gradient in the same type of patient (Greene et al., 1995; Graham and Hodges, 1997; Gilboa et al., 2005; Hou et al., 2005; Meeter et al., 2006; Addis et al., 2009).

Overall, previous studies focused on what we can define as "memory trace aging", i.e., how ABM decreases over the course of life, and reported inconsistent results. As yet, the MTT assumption regarding the retrieval frequency effect, which postulates that frequently retrieved, and thus multiply represented, remote memories are less susceptible to destruction than seldom retrieved ones in the case of mild hippocampal damage, has not been explored deeply. To the best of our knowledge, only one study considered retrieval frequency in assessing retrograde memory (Müller et al., 2014). In this study, the authors assessed the recall of famous public events in early AD patients using a novel approach that allows evaluating how memory accuracy changes as a function of the events' age (remote vs recent events) and the trace retrieval frequency (more frequently- vs less frequently retrieved events) separately. They found that in all three tasks administered (subjective memory rating task, dating accuracy task and contextual memory task) both early AD patients and normal controls derived similar benefits from greater retrieval frequency in terms of higher memory performance, independently of the age of the public events to recall. They concluded that the frequency of retrieval, rather than the age of memory acquisition, affects the severity of retrograde amnesia.

In light of these findings, we aimed to extend the results of Muller and al.'s study (2014) by investigating the impact of retrieval frequency on the episodic component of ABM. Comparing ABM recall in an education- and gender-matched sample of healthy controls and patients with early AD, we aimed to assess whether, in the case of mild hippocampal atrophy, the extent and severity of episodic ABM would be mediated by: i) retrieval frequency, i.e., better preservation of more frequently recalled memories than less frequently recalled ones regardless of the remoteness of the traces; ii) the age of memory acquisition, i.e.,