



# Memory consolidation and the hippocampus: further evidence from studies of autobiographical memory in semantic dementia and frontal variant frontotemporal dementia

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## Abstract

Studies of autobiographical memory in semantic dementia have found relative preservation of memories for recent rather than remote events. As semantic dementia is associated with progressive atrophy to temporal neocortex, with early asymmetric sparing of the hippocampus, this neuropsychological pattern suggests that the hippocampal complex plays a role in the acquisition and retrieval of recent memories, but is not necessary for the recall of older episodic events. In an alternative view of memory consolidation, however, the hippocampus plays a role in the retrieval of all autobiographical memories, regardless of the age of the memory [Curr. Opin. Neurobiol. 7(1997)217]. This 'multiple trace theory' predicts that patients with semantic dementia should show no effects of time in their autobiographical recall. In this article, we ask whether it is possible to reconcile the data from semantic dementia with the multiple trace theory by investigating whether the time-dependent pattern of autobiographical retrieval seen in the disease is due to (i) patients showing this effect being exceptional in their presentation; and/or (ii) patients with semantic dementia exhibiting impaired strategic retrieval from concomitant frontal damage. A series of experiments in patients with semantic dementia, the frontal variant of frontotemporal dementia and Alzheimer's disease clearly demonstrates that neither of these two factors can explain the documented effect of time seen in semantic dementia. Nonetheless, we discuss how damage to semantic knowledge could result in an autobiographical memory deficit and suggest that data from semantic dementia may be consistent with both views of hippocampal involvement in long-term memory. © 2002 Elsevier Science Ltd. All rights reserved.

**Keywords:** Episodic memory; Retrograde amnesia; Semantic memory; Temporal gradients; Strategic retrieval; Frontal lobes

## 1. Introduction

A number of investigations have found that patients with semantic dementia, the temporal lobe variant of frontotemporal dementia, who present with focal atrophy to the neocortex in the context of early sparing of the hippocampal complex, showed effects of time on tests of remote memory, with better preservation of episodic events and semantic facts from very recent life compared with other time-periods [22,24,28,39,84]. It has been proposed that this data offers support for the standard model of memory consolidation in which the

hippocampal complex (i.e. the hippocampus, subiculum, parahippocampal gyrus/entorhinal cortex) plays a critical role in the acquisition and initial retrieval of episodic and semantic memories<sup>1</sup>. The interpretation of these results has been challenged, however, by other researchers, notably Nadel and Moscovitch [65,66,71], who pointed out that other factors, such as strategic

<sup>1</sup> It should be noted that while most researchers argue that medial temporal lobe structures play a key role in the acquisition of new episodic memories, controversy still exists regarding the exact functions of the hippocampus proper (including the dentate gyrus and subiculum) versus the entorhinal and perirhinal cortex [68,87,89]. For the purposes of this article, we will refer to the hippocampal complex (including all aforementioned medial temporal lobe regions) with the caveat that there is accruing evidence for separate learning systems within the medial temporal lobe.

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retrieval deficits due to accompanying frontal lobe pathology, could be resulting in the reverse effect of time. In this article, we addressed empirically two of the issues raised by Moscovitch and Nadel [66], as well as considering in the discussion other possible explanations which have yet to be tested.

## 2. Frontotemporal dementia

Frontotemporal dementia (FTD) is the term currently applied to a number of syndromes in which patients present with degeneration of the frontal and/or temporal lobes (previously referred to as Pick's disease, [41]). The two principle subtypes of FTD—reflecting the major locus of pathology, predominantly frontal versus temporal—have different behavioural and cognitive profiles [44]. In the frontal variant of FTD (fvFTD), frontal lobe pathology predominantly affects the orbitomedial cortex causing changes in behaviour and personality; most notably apathy, loss of empathy or emotional warmth, impulsivity, disinhibition, change in dietary preference and stereotyped or ritualistic behaviours [6,63]. The patients show increasing problems with planning and organising activities, a pattern which has been attributed to impairments in goal-setting and attainment, as well as mental flexibility and set-shifting [31,32]. Rahman et al. [78] found that a group of eight patients with fvFTD showed deficits on the reversal stage of a visual discrimination learning paradigm and increased risk-taking behaviour, a pattern which the authors attributed to dysfunction in orbitomedial frontal cortex. Notably, however, the patients showed little impairment on tests sensitive to damage in dorsolateral prefrontal cortex, such as spatial working memory. Perry and Hodges [77] confirmed that patients with fvFTD could be differentiated from patients with other neurodegenerative conditions by their poorer performance on tests of attention and executive function. Episodic memory was also impaired, although to a lesser degree than the deficit seen in a group with early dementia of the Alzheimer type. Critically, the preservation of semantic memory in the context of impaired executive function in the fvFTD group was the converse to that found in patients with the temporal variant of FTD (also termed semantic dementia, the label we will adopt for the rest of this paper). This result suggests that there are at least two sub-types of frontotemporal dementia and that the patients at the frontal versus temporal ends of the spectrum can be clearly differentiated at a neuropsychological level. It is worth noting, however, that there are cases who present with a more mixed profile of frontal and temporal lobe dysfunction and that over time, all patients eventually show evidence of both frontal and temporal involvement.

Turning to semantic dementia, the predominant cognitive feature is a progressive deterioration of semantic knowledge about people, objects, facts and word meanings. Patients perform poorly on neuropsychological tests dependent upon conceptual information, such as picture naming, category fluency (i.e. generating as many exemplars from a semantic category as possible in one minute), word-picture matching, defining concepts in response to their names or pictures and sorting picture or words according to pre-specified criteria (e.g. electrical versus non-electrical). The deficit is also evident on non-verbal tests of semantic knowledge, such as selecting the correct colour for a black-and-white line drawing (e.g. red for a heart; black or brown for a gorilla), drawing animals or objects from memory [8], sound-picture matching [7], demonstrating the use of objects [36] and selecting which of two pictures (fir tree or palm tree) goes best with a pyramid (Pyramid and Palm Trees Test [46]). By contrast, patients show little impairment, even at relatively late stages of the disease, on tests of phonology and syntax, visuospatial skills and working memory [7,43,76].

Recent neuroradiological studies have found convincing support for the view that anterior and inferior areas of the temporal lobe are affected early in semantic dementia and that this profile is different from other neurodegenerative conditions that affect long-term memory, such as Alzheimer's disease [9,21,34,38,67,83]. With respect to medial temporal lobe regions, there is accruing evidence that the hippocampi and parahippocampal gyri are involved at later stages in the disease [82,9,21].

## 3. Remote memory in semantic dementia

While one of the five characteristics of semantic dementia proposed by Hodges et al. [43] was relatively preserved autobiographical and day-to-day (episodic) memory, more recent studies have revealed a more complex, and theoretically interesting, pattern. Snowden et al. [84] and Graham and Hodges [24] described the performance of patients with semantic dementia on the Autobiographical Memory Interview (AMI [54]). Unlike amnesic patients, who often show better recall of distant memories compared with more recent personal events, patients with semantic dementia showed the opposite pattern: better recall of recent memories compared with those from childhood and early adulthood.

A single case-study, described by Graham and Hodges [24] investigated autobiographical memory in semantic dementia in more detail. The patient, AM, was asked to retrieve autobiographical memories related to the same 15 words in each of four time-periods spanning the whole of his life. AM's memories from the

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