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New learning in semantic dementia: Implications for cognitive and neuroanatomical models of long-term memory

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Abstract

Research involving patients with the syndrome of semantic dementia has provided a number of theoretical insights into the organisation of episodic and semantic memory. Here, we review recent studies which indicate that recognition memory for pictorial stimuli (such as objects, faces, etc.) is typically preserved, in at least the early stages of the disease. This evidence is discussed in the context of theories about the interaction between episodic and semantic memory, and the different contributions made by particular structures in the medial temporal lobe.

Mots clés: Mémoire épisodique, mémoire sémantique, démence frontotemporale, hippocampe, lobe temporal.

Key words: Episodic memory; semantic memory; frontotemporal dementia; hippocampus; temporal lobes.

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INTRODUCTION

In the last few years, attention has focused on the important contribution made by studies of semantic dementia to theoretical debates concerning the cognitive and neural organisation of episodic and semantic memory (Graham, Patterson, & Hodges, 1999a; Hodges, Graham, & Patterson, 1995; Snowden, Griffiths, & Neary, 1996a). In particular, recent investigations of recognition memory in the disease have demonstrated that new episodic learning for pictures of objects and faces can be normal, despite the severe breakdown of semantic knowledge that is the hallmark of the disease (Graham, Becker, & Hodges, 1997a; Graham et al., 1999a; Graham, Simons, Pratt, Patterson, & Hodges, 2000; Simons, Graham, Galton, Patterson, & Hodges, in press; Simons, Graham, & Hodges, 1999). These results have important implications for cognitive theories of the interaction between episodic memory and semantic knowledge (e.g., Tulving, 1995) and for models of the neuroanatomical substrates of new episodic learning (e.g., Aggleton & Brown, 1999; Murray & Bussey, 1999).

SEMANTIC DEMENTIA: DEGRADATION OF CONCEPTUAL KNOWLEDGE

Semantic dementia is the clinical label (Hodges, Patterson, Oxbury, & Funnell, 1992; Snowden, Goulding, & Neary, 1989) given to a syndrome that has been variously termed the temporal variant of frontotemporal dementia (Hodges et al., 1999; Miller et al., 1991; Snowden, Neary, & Mann, 1996b), progressive fluent aphasia (Graham, Becker, Patterson, & Hodges, 1997b; Mesulam, 1982), and a focal temporal lobe form of Pick's disease (Pick, 1892; English translation in Girling & Berrios, 1994). Clinical criteria for the diagnosis of semantic dementia were proposed by Hodges et al. (1992), who documented a selective impairment on any task that required conceptual knowledge about objects, facts, concepts, and the meanings of words. Patients with the syndrome are impaired on tests such as naming pictures of familiar objects or animals, word-picture matching (indicating the correct picture, out of eight, that goes with a given

name), category fluency (generating exemplars from a given category), word or picture sorting, and defining or drawing items given their name. This neuropsychological pattern reflects a progressive breakdown in central semantic knowledge, affecting all input and output modalities (Hodges et al., 1995; Hodges et al., 1992; Hodges, Patterson, & Tyler, 1994).

By contrast, there is relative sparing of other cognitive domains, such as phonological and syntactic aspects of language, visuo-spatial and perceptual abilities, non-verbal problem-solving, and working memory, even at relatively late stages of the disease (Hodges & Patterson, 1996; Hodges et al., 1994). In their description of semantic dementia, Hodges and colleagues (1992) also suggested that autobiographical and day-to day (episodic) memory were relatively preserved. Although this claim was, at the time, based largely on observations that patients were able to remember appointments and keep track of family events, visits to the hospital, etc, experimental studies have confirmed that many aspects of episodic remembering are intact in the disease.

NEUROPATHOLOGY OF SEMANTIC DEMENTIA

Pathological and neuroradiological reports have documented progressive focal atrophy of the inferolateral aspect of the left or right temporal lobes, which usually becomes bilateral by later stages (Breedin, Saffran, & Coslett, 1994; Garrard & Hodges, in press; Graff-Radford et al., 1990; Hodges, Garrard, & Patterson, 1998; Snowden et al., 1996b). The status of medial temporal lobe regions is more equivocal. Some studies describe relative sparing (at least at early stages of the disease) of structures in the hippocampal complex, such as the hippocampus, parahippocampal gyrus, and subiculum (Graham & Hodges, 1997; Harasty, Halliday, Code, & Brooks, 1996; Mummery et al., 1999; Schwarz, De Bleser, Poeck, & Weis, 1998). For example, Mummery, Patterson, Price, Ashburner, Frackowiak, and Hodges (2000) employed an automated voxel-by-voxel morphometric technique to identify changes in grey matter volume in six patients with semantic dementia and found no evidence of significant atrophy to the hippocampus or parahippocampal gyrus. Damage to these structures was, however, reported in a recent investigation that used

volumetric analysis, although there was some variability among the patients (Galton et al., submitted). It is possible that at early stages of semantic dementia, medial temporal lobe regions are largely preserved (on at least one side of the brain), but that as the disease becomes more advanced, the hippocampus and related structures are also implicated in the pathological process (Simons et al., 1999).

REMOTE MEMORY

Many of the studies of episodic memory in semantic dementia have explored memory for past events and experiences. These investigations have indicated that recent autobiographical memories are preserved in semantic dementia, but recollection of those from the more distant past is impaired (Graham & Hodges, 1997; Snowden et al., 1996a). A pattern of better recall of recent compared to distant memories is the reverse of the temporal pattern usually seen in amnesia and Alzheimer's disease, in which medial temporal lobe regions such as the hippocampus and parahippocampal gyrus are affected (Graham & Hodges, 1997; Press, Amaral, & Squire, 1989; Rempelclower, Zola, Squire, & Amaral, 1996; Scoville & Milner, 1957; Simons & Graham, 2000; Zola-Morgan, Squire, & Amaral, 1986). More detailed investigations have demonstrated that autobiographical memory in semantic dementia is characterised by a temporal 'step-function' whereby there is better recall of memories from the two years or so prior to testing (Graham & Hodges, 1997; Graham, Pratt, & Hodges, 1998). The fact that 'memory age' can have such a dramatic effect on memory loss suggests that the hippocampus and related structures may play a time-limited role in encoding and short-term storage of human memories, and that neocortical areas of the temporal lobes may be the location for our enduring stores of autobiographical and semantic memory.

NEW EPISODIC LEARNING

The evidence that recall of recent autobiographical memories is possible in semantic dementia suggests that the encoding of new episodic memories may also be preserved. Early studies documenting performance on tests of recall and recognition memory did not, however, provide a clear picture of the status of these processes. The first reported assessment was conducted by Warrington (1975), whose three patients with semantic dementia showed severe impairment in free recall of ten-word lists. On forced-choice recognition memory for words and faces, the two patients tested performed as poorly as patients with amnesia. Their recognition memory for paintings was, however, in the normal range, even though neither patient could identify any of the items depicted. Diesfeldt (1992) assessed new episodic learning as part of a single case report of semantic dementia. He noted intact recognition memory for five pictures after a ten-minute delay and accurate recollection of where three objects had been hidden more than an hour before, in contrast to the patient's profound loss of semantic memory.

RECOGNITION MEMORY FOR OBJECTS

It was not until some five years later that the first detailed investigations of new episodic learning were reported in semantic dementia. Graham, Becker, and Hodges (1997a) demonstrated preserved forced-choice recognition memory for pictures of real and non-real animals. While there was no significant difference between a group of patients with semantic dementia and a group of normal controls on a test of recognition memory for the pictures, the patients with semantic dementia were significantly impaired when asked to indicate, during the study task, whether the animals were real or not. This was in marked contrast to a group of patients with presumed Alzheimer's disease, who were at chance on the recognition memory test but performed equivalently to controls on the semantic task.

In a more recent study, eight patients with semantic dementia showed preserved forced-choice recognition memory for colour pictures of familiar objects and animals, despite impaired knowledge (as measured by picture naming) about the items depicted (Graham et al., 2000). The patients' recognition memory was impaired relative to controls only when perceptually different exemplars of the test items were used in the study and test phases (e.g., when a red round dial telephone seen at study was replaced by a black touch button telephone at test).

Graham et al. (2000) also reported a single-case study of a patient with semantic dementia (JH) whose conceptual knowledge about familiar objects was assessed. Following this, a yes/no recognition memory test was created both for items she still knew about and items for which she demonstrated severely degraded semantic knowledge. JH showed almost faultless recognition memory performance for perceptually identical items (i.e., the same drawings seen in the study and test phases) even if her conceptual knowledge about them was extremely poor. If perceptually different exemplars were used at study and test, however, then JH's recognition memory was good for items in the 'known' set but impaired for those about which she had degraded semantic knowledge. Graham and colleagues surmised that this manipulation decreased the usefulness of perceptual information available from seeing the item in the study task and made the episodic decision more reliant upon the integrity of conceptual knowledge.

RECOGNITION MEMORY FOR FACES

Although patients with semantic dementia have been shown consistently to have preserved recognition memory for objects and paintings (Graham et al., 1997a; 2000; Simons et al., 1999; Warrington, 1975), Warrington's (1975) two patients were impaired on a test of recognition memory for faces. Similarly, a single-case study of a patient with semantic dementia (VH), who had selective atrophy of the right temporal lobe, also showed markedly poor performance on the faces component of Warrington's (1984) Recognition Memory Test (RMT), even though she was within the normal range on other recognition memory tests (Evans,

Heggs, Antoun, & Hodges, 1995). The issue of recognition memory for faces was investigated in detail in a recent study which examined the influence of different patterns of focal cortical atrophy (Simons et al., in press). Patients in whom pathology affected predominantly the left temporal lobe showed preserved performance on the faces component of the RMT. Those with structural damage to the right temporal lobe were, however, typically impaired. Further analyses indicated that structures such as the parahippocampal gyrus in the right temporal lobe were critical to face recognition memory, suggesting that the poor performance documented in Warrington's (1975) and Evans et al.'s (1995) patients might be attributable to damage to right temporal lobe structures (Simons et al., in press).

The finding of preserved face recognition memory in patients with predominantly left temporal lobe pathology was replicated in two single-case studies. Both patients showed intact recognition memory for photographs of famous faces, even when their semantic knowledge about the celebrities depicted was severely degraded (Simons et al., in press). An effect of semantic knowledge on recognition memory became apparent only when perceptually different photographs of the famous people were used in the study and test phases. The patients performed in the normal range if they possessed semantic knowledge about the famous people, but were markedly impaired on those celebrities about whom they showed no evidence of knowledge.

RELEARNING OF VOCABULARY

There is evidence that, in certain circumstances, learning of verbal stimuli is possible in semantic dementia. Graham and colleagues (1999b) describe a patient, DM, who, before presenting, had already begun recording words he was unable to produce in spontaneous speech in a notebook, from which he practised. Over time, his attempts to maintain his word production became overwhelming, with DM commonly practising for five or six hours a day from books such as the Oxford Picture Dictionary (Parnwell, 1977), and from notebooks of lost items he had created for himself, for example a collection of celebrities' faces assembled from

newspaper photographs.

The effects of this home practice were studied by Graham et al. (1999b) using category fluency (in which the participant must produce as many exemplars from a particular category as possible in a minute). They reported that DM showed significant improvement for semantic categories that were practised as opposed to those not practised, but that his performance for those categories very quickly declined once practice ceased. Together with an analysis of his word-production errors on category fluency, which were mainly phonological in nature, this result suggests that his practice was analogous to rote learning of meaningless stimuli, and that no generalisation or maintenance of semantic knowl edge was taking place. The result does indicate, however, that new learning, even of verbal material, is possible in semantic dementia.

IMPLICATIONS FOR COGNITIVE MODELS OF LONG-TERM MEMORY

From the investigations described above, there is now mounting evidence that recognition memory for pictorial stimuli (and new learning of vocabulary) can be preserved in semantic dementia even when conceptual knowledge about the studied items is severely degraded (Graham et al., 1997a, 1999a, 2000; Simons et al., 1999, in press). These data are problematic for theories of long-term memory in which episodic memory is considered to be solely dependent upon semantic knowledge (Tulving, 1983; 1995; Tulving & Markowitsch, 1998). Instead, they provide support for a view in which perceptual and semantic information typically work together to support new episodic learning. If semantic knowledge is impoverished, however, perceptual information alone can be sufficient for successful recognition memory (Bruce, 1982; Graham et al., 2000; Paivio, 1991).

A hypothesis in which perceptual and semantic information work in concert to support new learning may also explain why patients with semantic dementia typically show poor recognition memory for words (as first noted by Warrington, 1975). Words provide little perceptual information to support the discrimination of particular exemplars in a recog-

nition memory test. New learning of verbal material is presumably much more reliant than pictorial stimuli upon semantic memory and is, therefore, typically more impaired in semantic dementia (unless the patient is permitted as much practice as DM was; Graham et al., 1999b). If a patient has lost semantic knowledge about a chair, s/he will be unlikely to recognise the word 'chair' as having appeared in a studied list of words. S/he may still be able to recognise a picture of a chair as having been in a studied set of pictures, based on perceptual information from having seen the item in the study phase. When perceptually different pictures of chairs are seen at study and test, however, this perceptual information may not be sufficient to allow successful recognition memory and if there is also impoverished input from semantic knowledge, impairment is likely to result (Graham et al., 2000; Simons et al., in press).

THE NEUROANATOMICAL SUBSTRATES OF RECOGNITION MEMORY

The results from studies of recognition memory in semantic dementia have important ramifications for theories which propose that medial temporal lobe regions play a critical role in new learning. Recent formulations (e.g., Aggleton & Brown, 1999) hold that there are two anatomically separate systems contributing to episodic memory: one system consisting of the hippocampus, fornix, mamillary bodies, and anterior nuclei of the thalamus; the other involving the perirhinal cortex and dorso medial thalamic nucleus. According to Aggleton and Brown, these anatomical systems have dissociable functions. The former supports the recollection of stored memories with their associated temporal, spatial, and semantic context, while the latter system underlies familiarity-based recognition of prior occurrence. This hypothesis builds upon the distinction between processes of 'recollection' and 'familiarity' first made by Mandler (1980) and supported by evidence that there are test condition manipulations that affect one process but not the other, and vice versa, producing a double dissociation between the two (Gardiner & Java, 1990; Rajaram, 1993; Yonelinas, 1997; Yonelinas & Jacoby, 1995).

Aggleton and Brown's view that different medial temporal lobe sys-

tems underlie these memory processes (recollection being dependent upon the hippocampal system, and familiarity requiring the perirhinal cortex) is based largely upon studies of non-human primates, which have shown that experimentally induced lesions of the perirhinal cortex lead to severe deficits in recognition memory for stimuli presented visually (Buckley, Gaffan, & Murray, 1997; Meunier, Bachevalier, Mishkin, & Murray, 1993; Murray, 2000; Murray & Bussey, 1999) and in other modalities (Suzuki, Zola-Morgan, Squire, & Amaral, 1993). Monkeys with selective lesions of the hippocampus, fornix, or amygdala, however, can perform normally on tests of recognition memory (Gaffan, Shields, & Harrison, 1984; Murray & Mishkin, 1998; Zola-Morgan, Squire, & Amaral, 1989), suggesting that the hippocampal memory system is not required for tasks that primarily tax familiarity judgements (Aggleton & Brown, 1999).

While caution must be employed in applying conclusions from experiments involving non-human primates to the study of human cognition (Tulving & Markowitsch, 1994), there is also evidence of functionally separate familiarity and recollection memory systems from clinical studies in humans. For example, Aggleton and Shaw (1996) found that amnesic patients with hypoxia resulting in selective hippocampal damage and those with fornix transections performed normally on Warrington's (1984) RMT (although see Reed & Squire, 1997). Similarly, Baxendale (1997) demonstrated that patients with temporal lobe pathology involving both cortical and hippocampal regions performed significantly worse on the RMT than those whose damage selectively involved the hippocampus only (although both were impaired relative to controls). Recently, Vargha-Khadem and colleagues (1997) reported three patients who had suffered isolated hippocampal damage early in life, who showed markedly better recognition memory than recollection-based memory.

As described earlier, patients with semantic dementia consistently demonstrate intact recall of recent autobiographical and semantic memories (Graham & Hodges, 1997; Graham et al., 1998; Snowden et al., 1996a) and preserved performance on various tests of recognition memory (Graham et al., 1997a, 2000; Simons et al., 1999, in press). On the basis of Aggleton and Brown's (1999) model, therefore, it would be expected that

regions such as the hippocampus and the perirhinal cortex should be largely intact in semantic dementia. Although the hippocampus is a well-defined structure, assessment of the status of the perirhinal cortex is complicated by the fact that there is controversy as to its exact location and morphology in man (Galton et al., submitted; Simons et al., 1999). It is currently considered to occupy the banks of the collateral sulcus and extend rostrally onto the medial surface of the temporal pole (Buffalo, Reber, & Squire, 1998; Van Hoesen, 1997). As such, accurate assessment of the status of the perirhinal cortex using current volumetric MRI techniques is problematic.

Although some neuroradiological studies of semantic dementia have reported that pathology largely spares the hippocampus and perirhinal cortex (Mummery et al., 2000), others, in particular a volumetric group study by Galton et al. (submitted) indicate that groups of patients with semantic dementia and with Alzheimer's disease have comparable volume reductions in structures such as the hippocampus and parahippocampal gyrus. The critical fact remains, however, that these subject groups consistently perform qualitatively differently on tests of remote memory and new learning (Graham et al., 1997a, 1999a, 2000; Simons et al., 1999, in press; Warrington, 1975). This contradiction suggests that one needs to be cautious when attempting to correlate simple measures of brain volume, as provided by current MRI assessment techniques, and cognitive performance on episodic memory tests, such as recognition memory. More detailed measures of behaviour and neuroanatomy, and more sophisticated methods for relating these data, are required.

CONCLUSIONS

Although there is still a great deal that is unknown about the cognitive and neural organisation of recognition memory, much has been learned through the study of patients with semantic dementia. It is clear that, contrary to influential theories of episodic and semantic memory (e.g., Tulving, 1983; 1995), normal perceptually-based new learning of pictorial material — presumably carried out primarily by familiarity-based judgements of prior occurrence — can occur in the context of degraded semantic

knowledge about the studied items. There is currently a lack of understanding concerning the precise neuroanatomical pattern of damage in semantic dementia, but evidence suggests that structures such as the hippocampus and the perirhinal cortex — associated with processes of recollection and familiarity, respectively (Aggleton & Brown, 1999) — may be preserved in at least the early stages (Simons et al., 1999). One matter beyond dispute is that semantic dementia is proving to be a particularly valuable disorder for investigating issues relating to the cognitive neuroscience of long-term memory.

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RÉSUMÉ

Les recherches effectuées sur des patients atteints du syndrome de démence sémantique ont permis, d'un point de vue théorique, de mettre en évidence certains principes d'organisation de la mémoire sémantique et de la mémoire épisodique. Dans cet article nous présentons un ensemble d'études récentes qui suggère que la mémoire utilisée lors de la reconnaissance de stimuli picturaux (objets, visages, etc.) est préservée, du moins durant les premiers temps de la maladie. Cette hypothèse est ensuite discutée dans le cadre des théories concernant l'interaction entre la mémoire sémantique et la mémoire épisodique, ainsi que dans le cadre des théories concernant les contributions des différentes structures du lobe médio-temporal.

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