Episodic memory: new insights from the study of semantic dementia
Kim S Graham*, Karalyn Patterson and John R Hodges

The study of patients with semantic dementia, the temporal variant of frontotemporal dementia, has provided new insights into the interaction between episodic and semantic memory, and the different roles played by various structures in the temporal lobe. Recent findings indicate that the syndrome of semantic dementia can inform us about the organisation of long-term memory and the relationship between semantic memory and other cognitive systems.

*Correspondence
Kim S Graham, MRC Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge, CB2 2EF, UK
*e-mail: kim.graham@mrc-cbu.cam.ac.uk

Introduction
Neuropsychological investigations in patients with semantic dementia [1,2] have provided a number of theoretical insights into the organisation of a range of cognitive processes in humans. It is not possible to do sufficient justice here to all the topics addressed in recent studies, which include the organisation of semantic memory [2–8,9**,10**,11], the status of implicit conceptual knowledge [12*,13], knowledge of people [14,15*], object knowledge and mechanical problem-solving [16**], numerical ability [17,18], object naming [19,20], and aspects of language and verbal ability other than naming, such as oral word reading [21–25], short-term verbal memory [26,27] and syntax [28,29].

In this review, we will concentrate on research addressing the integrity of episodic memory in semantic dementia. We have divided the content of our review into two main parts: first, a brief summary of the background to the syndrome; and second, a more detailed discussion of recent articles that have investigated remote memory, new learning and repetition priming in patients with semantic dementia.

Variants of frontotemporal dementia
Pick [30,31] was the first to note that patients with neurodegenerative disease could present with focal symptoms such as impaired language function (see also [32]). Following these initial reports, there was a gradual waning of interest until almost a century later when Mesulam [33] described a number of cases with “slowly progressive disease without generalised dementia” (see also [11,34]). Since then, over 100 cases of progressive aphasia have been reported, and it is now evident that there are at least two main subtypes with different underlying cognitive deficits: progressive fluent aphasia and progressive nonfluent aphasia (see [35–37] for more details).

We will focus on progressive fluent aphasia; patients with this syndrome show a deterioration in semantic memory that disrupts their ability to produce words in spontaneous speech and, as the disorder progresses, to comprehend word meaning (see [35,37–40]). As the impairment in semantic memory is also evident in tests of nonverbal knowledge, the term semantic dementia has been adopted by a number of researchers in order to capture the primary deficit in the syndrome [1,2,4,7,41]. Readers should be aware that such patients may also be described clinically as having the temporal variant of frontotemporal dementia (FTD) [42*,43]. The two subtypes of FTD — reflecting the major locus of pathology, predominantly frontal versus temporal — have distinct cognitive profiles in a number of respects, including the status of semantic and episodic memory [44*]. The neuropsychological data described below pertains only to the temporal variant of FTD (i.e. semantic dementia).

Semantic dementia: a disorder of long-term memory
As the name implies, the central deficit in semantic dementia is a progressive deterioration of semantic knowledge about people, objects, facts and words [2,4,7,9**,12*,15*,38,41,45,46,47**]. Patients with semantic dementia perform poorly on tests that require conceptual knowledge, such as picture naming, category fluency (i.e. generating exemplars from semantic categories such as animals, birds, etc.), word–picture matching, sorting pictures or words according to set criteria, defining concepts in response to their names or pictures, selecting the appropriate colour for a black-and-white line drawing of a familiar object with a characteristic colour (e.g. yellow for banana), and drawing animals or objects from memory. By contrast, other cognitive skills, such as visuoperceptual and spatial ability, nonverbal problem-solving, phonology, syntax and working memory can be strikingly preserved, even at relatively late stages of the disease [2,4,7,8,19,35,37,38,41,48,49].

Neuroimaging and neuropathology of semantic dementia
Neuroradiological studies of semantic dementia typically reveal focal atrophy of the inferolateral temporal neocortex on one or both sides, with sparing (at least early in the disease) of the hippocampal complex (i.e. hippocampus...
but much more impaired at retrieving episodes from childhood and early adulthood [47••,50•]. This pattern is the opposite to that typically seen in patients with amnesia and in patients with early-stage Alzheimer’s disease. In a more detailed single-case study of autobiographical memory, Graham and Hodges [50•] demonstrated that the patient was able to produce detailed autobiographical memories only for the two years prior to testing, compared with any time period from the rest of his life. These experiments suggest a dramatic step pattern in the quality of autobiographical memory in semantic dementia, rather than a temporal gradient extending back in time (see Figure 1).

A similar time effect has since been demonstrated on other tests of remote memory for people and public events. Snowden et al. [47••] investigated knowledge of contemporary, past and historical famous names (examples of these three classes in Britain being Paddy Ashdown [a contemporary politician], Winston Churchill and Charles Dickens). Two patients showed better recognition and (to a lesser extent) better semantic knowledge for the contemporary names compared to the past and historic names. Hodges and Graham [15•] also found a significant time effect: a patient in the early stages of semantic dementia was more successful at producing facts about current celebrities (i.e. late 1990s) than about people who had been famous in the 1950s, 1980s and early 1990s. Four other cases at more advanced stages of decline also achieved better performance for current famous personalities, although these patients were profoundly impaired on knowledge of people from all time-periods, including the current one [15•]. Three additional experiments investigating knowledge of people from the patients’ own personal lives have established superior recognition of contemporary, personally relevant individuals compared to personal friends from the past [45,46,60].

Knowledge of people is not the only semantic domain to be modulated by time: the patient described in Hodges and Graham [15•] produced more information about famous events from the three years prior to testing than for all events from the six years preceding 1995 [61]. In an ingenious experiment, Snowden et al. [47••] demonstrated significantly better knowledge of British decimal coins in current usage (e.g. 50 pence) than of pre-decimal coins (e.g. a half crown or shilling), which went out of usage in the early 1970s. In fact, the four patients in this study evinced virtually no familiarity with or knowledge about pre-decimal coins, despite the fact that they had all used these coins for half or more of their lifetimes. Patients with Alzheimer’s disease, though generally poor at recognising coins, were as good if not better on the pre-decimal exemplars.

These experiments indicate that many domains of semantic knowledge (e.g. information about people, public events, money, etc.) are affected early in the course of semantic dementia. As with autobiographical memory, however, personal relevance and repeated exposure seem

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**Remote memory in semantic dementia**

Until recently, there was almost no empirical evidence on the integrity of episodic memory in semantic dementia, despite the fact that one of the five characteristics of the disorder suggested by Hodges et al. [2] was “relatively preserved autobiographical and day-to-day (episodic) memory”. The initial studies of remote memory in patients with semantic dementia partially confirmed this claim: nine patients tested on the Autobiographical Memory Interview [59] were successful in producing autobiographical memories from the most recent time-period

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**Figure 1**

The performance of a patient (AM) with semantic dementia on a modified version of the Galton–Crovitz autobiographical memory test (see [50•] for more details). AM was asked to produce 15 autobiographical memories from each of four different time-periods spanning the whole of his life. Each of these memories was scored from 0–5 for detail and episodic specificity. AM’s ability to produce autobiographical memories was strongly affected by time: virtually all his specific episodes were recalled in the most recent 5 years. Reproduced with permission from [50•].

The performance of a patient (AM) with semantic dementia on a modified version of the Galton–Crovitz autobiographical memory test (see [50•] for more details). AM was asked to produce 15 autobiographical memories from each of four different time-periods spanning the whole of his life. Each of these memories was scored from 0–5 for detail and episodic specificity. AM’s ability to produce autobiographical memories was strongly affected by time: virtually all his specific episodes were recalled in the most recent 5 years. Reproduced with permission from [50•].
to create a degree of resistance to deterioration, as demonstrated by more successful retrieval of semantic knowledge that is personally salient and frequent.

**New learning in semantic dementia**

The evidence for relative preservation of recently acquired episodic and semantic memory suggests that new learning should be possible in patients with semantic dementia. While the results from early studies were equivocal with respect to capacity for new learning (see e.g. [11,62]), recent investigations suggest that nonverbal new learning can be relatively intact. Graham *et al.* [63] have shown that two-alternative forced-choice recognition memory for pictures of real and nonreal (e.g. the head of a dog on the body of a donkey) animals was preserved in a group of patients, even though their ability to identify the same stimulus items as real or nonreal was impaired (see Figure 2).

In a more recent study, eight patients with semantic dementia showed normal recognition memory when the target item (e.g. a coloured picture of a familiar object) in a three-alternative recognition memory test was identical to an item that had been seen at study (KS Graham, JS Simons, KH Pratt, K Patterson, JR Hodges, unpublished data). By contrast, when a perceptual manipulation was introduced between study and test (e.g. a round-dial telephone was replaced by a push-button phone, and the subjects were instructed to select a picture of the same kind of object that they had seen earlier), the patients were significantly impaired relative to control subjects. Furthermore, recognition memory success in the perceptually different condition was related to a semantic measure for the same items, object naming. Another single-case study compared items ‘known’ to the patient with items previously familiar but no longer comprehended: for ‘known’ targets, the patient’s recognition memory was perfect in both the perceptually identical and perceptually different conditions, but for the ‘unknown’ items, recognition memory was significantly better for identical than for perceptually altered targets.

Relearning of vocabulary has also been documented in two cases of semantic dementia. Funnell [64] demonstrated that a patient was able to relearn the names of six vegetables (names that she would easily have produced pre-morbidly but had now forgotten) by practising with their names and some written descriptions. A patient studied by Graham *et al.* [65], when asked to practice ‘forgotten’ words over a two-week period of time, significantly boosted his ability to produce these names as exemplars on a category fluency test. When subsequently instructed to cease his daily practice, however, he showed a striking loss of his recently acquired words over the following 6–10 weeks. It was clear both from this dramatic decline and from the rather rigid manner in which he produced the acquired exemplars after practice, that the significant facilitation in the patient’s vocabulary pro-

**Figure 2**

A comparison of the performance of control subjects, patients with semantic dementia and patients in the early amnesic stage of Alzheimer’s disease on two tests of long-term memory. The semantic memory study task (light grey shading) was object decision for real and nonreal animals. Episodic memory for the same items was tested using a two-alternative forced-choice recognition memory test (dark gray shading). Standard deviations are represented as bars, and the horizontal axis starts at chance (number correct = 16). Ten neurologically normal control subjects, 5 patients with semantic dementia and 4 patients with Alzheimer’s disease were tested. The patients with semantic dementia showed no significant impairment on the recognition memory test compared to control participants, despite poor performance on the study test in which they had to decide whether the stimuli were real or not. By contrast, the patients with early Alzheimer’s disease performed at chance on the test of episodic memory but showed equivalent performance to the controls on the semantic study task. Adapted from [63].

Evidence is accruing, therefore, that patients with semantic dementia can learn and remember both verbal and nonverbal stimuli, even in circumstances where their semantic information about the studied items is degraded. This evidence seems incompatible with a theory suggesting that semantic memory is critical for new episodic learning [66,67]. We propose, instead, that patients with semantic dementia use perceptual information about studied targets to support new learning, a proposal supported by the data documenting normal recognition memory for perceptually identical, but not perceptually different, targets. This hypothesis may also explain why new verbal learning, which provides less perceptual information and presumably is more reliant upon semantic knowledge
about studied items, is typically more impaired than nonverbal new learning.

The capacity for new learning, even for nonverbal material tested with identical target stimuli, gradually becomes compromised as the syndrome advances. Three of the most severe cases tested on our perceptual manipulation experiment showed a mild impairment on the perceptually identical condition (KS Graham, JS Simons, KH Pratt, K Patterson, JR Hodges, unpublished data). The most plausible explanation for this late-stage impairment in nonverbal new learning is the spread of pathology from lateral temporal lobe structures to components of the hippocampal complex critical for the encoding of new episodic memories.

**Repetition priming in semantic dementia**

Virtually all recent investigations of episodic memory in semantic dementia have used explicit assessments of memory that require conscious retrieval on recall or recognition memory tests. Implicit memory tasks that measure priming (i.e. the facilitation in performance on a nonmemory task that results from previous exposure to the same stimuli) can provide another perspective on the integrity of memory.

Srinivas et al. [68••] investigated the status of stored structural descriptions in a patient with semantic dementia who had a typical neuroanatomical picture of bilateral anterolateral and inferior temporal lobe damage. The patient’s normal pattern of priming effects on a series of perceptual tasks suggested an intact system for object representation. The authors concluded that the anterior inferior temporal cortex (at least in humans) “does not play a critical role in the computation, storage, or retrieval of structural descriptions of objects from long-term memory”, but is the area critical for linking stored structural representations to conceptual knowledge about objects. This view explains why patients with semantic dementia may show normal visuoperceptual abilities and perceptually based repetition priming, but significant impairment to the specific perceptual attributes of objects (e.g. colour, typical size, etc.), which are presumably represented within a more anteriorly located conceptual system. Furthermore, the demonstration by Srinivas et al. [68••] of normal perceptual processing/priming in semantic dementia is consistent with the proposal by Graham et al. (KS Graham, JS Simons, KH Pratt, K Patterson, JR Hodges, unpublished data) regarding new learning: given the patients’ degraded conceptual knowledge of familiar objects, their high level of recognition memory for objects is probably based largely on the products of good perceptual processing as input to the episodic memory system.

**Conclusions**

Current research on different forms of learning and memory in semantic dementia provides evidence for, first, better preservation of recent semantic and episodic information compared to more distant memories, second, significant capacity for new learning of nonverbal and, to a lesser extent, verbal information, though in a fashion that is rather intolerant of variation, and third, normal perceptually based repetition priming. The first two points have been interpreted as support for a model of memory consolidation in which the hippocampal complex plays a time-limited role in the acquisition and storage of episodic and semantic memory [15•,47••,50•,53,69–73]. To some extent, therefore, the disorder of semantic dementia can be considered the mirror-image of amnesia: the double dissociations demonstrated on retrograde and anterograde memory tests in semantic dementia and amnesia highlight the differential roles played by structures in the temporal lobe in the acquisition and storage of new memories.

While this review documents a substantial range of empirical evidence relating to memory in semantic dementia, it also establishes that many aspects remain either unexplored or underexplored. For example, the repetition priming technique so elegantly used by Srinivas et al. [68••] will surely have many other potential applications with respect to understanding the relationship between semantic memory and other, closely linked, cognitive domains.

**Acknowledgements**

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**References and recommended reading**

Papers of particular interest, published within the annual period of review, have been highlighted as:

• of special interest

**of outstanding interest**


9. Lauro-Grotto R, Piccini C, Shallice T: Modality-specific operations in semantic dementia. Cortex 1997, 33:593-623. A study of verbal and visual semanitics in a single case of semantic dementia. The patient showed a marked modality-specific semantic deficit, with better performance in experimental tasks designed to investigate the preservation of nonverbal knowledge (and everyday activities) compared to tasks requiring verbal comprehension. The authors provide a detailed discussion of the implications of the results for several models of semantic memory, in particular a new neural network multimodal model of semantic memory.

This is the first study to use functional neuroimaging in patients with semantic dementia. The authors measured PET activation during a semantic decision task in four patients with semantic dementia compared to six control subjects. The patients showed a significant reduction in activity in the left posterior inferior temporal gyrus (BA 37) compared to control subjects. By contrast, voxel-based morphometry revealed significant anterior temporal atrophy (particularly on the left) but no significant structural damage to BA 37. The authors suggest that the reduced regional cerebral blood flow seen in the posterior inferior temporal lobe, which is thought to be involved in lexical retrieval, is consistent with a loss of activation from the more anterior, structurally damaged temporal regions.


Presents a longitudinal investigation of the performance of a patient with semantic dementia on explicit and implicit tests of semantic memory. In the first testing session, the authors found that the patient showed priming for perceptual (e.g. fox-red) and functional (e.g. fox-sly) properties, but not category co-ordinates (e.g. fox-dog) or category labels (e.g. fox-animal). Eleven months later, only functional properties showed a robust priming effect. At the final testing session, none of the conditions primed. One interesting discussion is that the match between the patient's performance on explicit and implicit tests of semantic knowledge (except on tests measuring the relationship between an object concept and its category label). The results are discussed with respect to the structure of conceptual knowledge.


The authors report that knowledge about famous people (as measured using a Famous Names Test) was profoundly impaired in four patients with semantic dementia, suggesting that this domain of semantic memory may be affected early in the disease. A single case study also demonstrated that the integrity of semantic memory is affected by time, with better preservation of knowledge of current celebrities compared to those from other time periods in the past.


Presents a comprehensive study of object use in two patients, one of whom had semantic dementia. The patient with semantic dementia showed virtual normal performance on all tests of single-object use (e.g. demonstrating the appropriate use of an object, such as a pair of scissors) and on more complicated tasks of naturalistic ‘multi-level’ action (e.g. packing a lunch box). The results from the study suggest that the patient had good access to information about object function and could use objects appropriately. The patient made very few errors on the tests that could be attributed to faulty semantic memory, suggesting that intact semantic knowledge is not necessary or sufficient for object use.


[Title translation: On the relationship between senile cerebral atrophy and aphasia.]


[Title translation: Dementia with selective problems of semantic memory: a case study.]


Reports the main clinical and neuropsychiatric features seen in the temporal variant of frontotemporal dementia (FTD) compared with the more frontal presentation of FTD. The authors found that patients with predominantly right-sided temporal damage presented with behavioural disorders, such as irritability, impulsiveness and fixed ideas. By contrast, the predominant clinical symptom in patients with more severe left temporal lobe atrophy was aphasia. The authors discuss these findings with respect to the differential roles of the right and left temporal lobes in mediating behavioural functions and the heterogeneity of frontotemporal dementia.


This experimental study investigated whether patients with the frontal variant of frontotemporal dementia (FTD) show a distinct cognitive profile compared to patients with the temporal lobe variant of FTD and to patients in the presumed early stages of Alzheimer's disease. The authors found strong support for this hypothesis: the predominant impairment in Alzheimer's disease was in episodic memory, whereas patients with semantic dementia showed a profound loss of semantic knowledge. By contrast, patients with the frontal variant of frontotemporal dementia were mildly impaired on episodic memory and verbal fluency.


Throughout the paper, the authors undertake a comprehensive series of experiments aimed at investigating the relationship between semantic and episodic memory. The paper is a useful summary of recent findings from semantic dementia, and the discussion of these results is detailed and thought-provoking.


The authors describe two experiments that investigated the effects of time on autobiographical memory in semantic dementia. On the Autobiographical Memory Interview, a group of patients with semantic dementia were better at producing autobiographical memories from a very recent time-period compared to childhood and early adulthood (the opposite pattern to that seen in a group of patients with a presumed early stage of Alzheimer's disease). A second, more detailed, case-study examined the ability to preserve autobiographical memory for the whole of a patient's life and found that the preservation of autobiographical memories was restricted to the most recent two years.


Describes the longitudinal decline of a patient with semantic dementia and includes neuropsychological findings: spongiform changes of cortical layers (II and III) in temporal, and less severely, in frontal gyrus. The article highlights the fact that, while there are only a few neuropsychological studies in semantic dementia, patients with the disease have Pick's disease, neuronal loss or non-specific spongiform change and gliosis without Alzheimer's or Pick's pathology.


Describes the first detailed investigation of new learning in semantic dementia. Five patients with semantic dementia showed normal recognition memory for real and nonreal animals seen 10 minutes previously, whereas a group of patients in the presumed early stages of Alzheimer's disease were significantly impaired on the test. The authors concluded that the preservation of nonverbal recognition memory in semantic dementia supports the view that new learning depends on the hippocampus and related structures.


Two experiments investigated the retention of 'lost' vocabulary in a case of semantic dementia using category fluency. In both studies, it was found that the patient improved significantly when he practised at home with the names of concepts plus pictures and descriptions of them. When the patient stopped practising, however, his fluency scores on previously improved categories declined. The authors discuss the implications of the results for current views of long-term memory.


An elegant and detailed investigation of the integrity of stored structural descriptions in a single case of semantic dementia. The authors used tests of perceptual priming to determine whether their patient had good access to representations within stored structural descriptions. The normal perceptual priming exhibited by the patient in a number of experiments suggests that he was capable of forming and retaining the structure of objects. The authors propose that the anterior inferior temporal lobe, which was damaged bilaterally in their patient, is not involved in the storage of existing structural descriptions of known objects or the formation of new structural descriptions for novel objects.


