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# Perceptual and semantic contributions to episodic memory: evidence from semantic dementia and Alzheimer's disease

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**Abstract**

Previous group studies involving patients with semantic dementia, who have impaired semantic memory associated with temporal lobe atrophy, have documented the preservation of pictorial recognition memory, in contrast to patients with early Alzheimer's disease, who characteristically exhibit amnesia. The present study replicated this general pattern, although four of the semantic dementia patients with the most severe semantic deficit additionally had impaired recognition memory. Three factors that might contribute to this pattern of memory performance were examined: atrophic damage to medial temporal lobe regions, degradation of semantic representations, and disruption to visuoperceptual processes. Assessment of MRI scans revealed that atrophy affecting the perirhinal cortex region accurately predicted the recognition memory deficit seen at advanced stages of semantic dementia, but there was no evidence that it could be attributed directly either to degraded semantic knowledge or disrupted perceptual processing. In Alzheimer's disease, evidence suggested that visuoperceptual impairment might be involved in the poor recognition memory typically seen in the disorder. These results have implications for the differential diagnosis of semantic dementia and Alzheimer's disease and for cognitive and neural theories of human long-term memory. 

*Keywords:* Recognition memory; Semantic memory; Frontotemporal dementia; Temporal lobe; Hippocampus; Perirhinal cortex

It was some 30 years ago that Tulving (1972) first suggested the fractionation of long-term memory into two psychologically and neurologically distinct systems: episodic and semantic memory. Episodic memory allows the "reliving" of events that an individual has personally experienced in past life. It is responsible for memorial phenomena as diverse as, for example, recalling seeing an elephant on safari last year or recognizing a picture of an elephant as having been present in a previous set of drawings. By contrast, semantic memory can be thought of as our store of knowledge about the world, including vocabulary, concepts, and facts—information that is retrieved without recalling when and where it was

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initially learned (such as the fact that an elephant has a trunk, for example). Although this distinction has endured (Tulving, 1995; Tulving & Markowitsch, 1998) and has undoubted relevance to the clinical diagnosis of patients with memory disorders (Garrard, Perry, & Hodges, 1997; Patterson & Hodges, 2000), there remains considerable debate among psychologists and neuroscientists over the nature of the cognitive and neural relationship between these two types of memory (e.g., Hintzman, 1984; McKoon, Ratcliff, & Dell, 1986; Squire & Zola, 1998; Vargha-Khadem et al., 1997).

Semantic dementia is a particularly useful disorder in which to investigate the relationship between semantic and episodic memory because patients with the disease show poor performance on a range of tests of semantic memory, including those measuring semantic knowledge about words, pictures, and sounds. For example, patients typically exhibit impairment at naming pictures of familiar objects and animals, word to picture matching, sorting words or pictures into categories, and demonstrating the use of everyday objects (Hodges, Patterson, Oxbury, & Funnell, 1992; Hodges, Patterson, & Tyler, 1994; Hodges, Bozeat, Ralph, Patterson, & Spatt, 2000). It is important to stress that this impairment does not simply reflect a naming problem: deficits are also seen on tasks for which the name of a test item is less critical, such as the Pyramid and Palmtrees test (Howard & Patterson, 1992), in which participants judge which of two pictures is associated with a target picture (see Fig. 1a for an example), and on tests requiring matching environmental sounds to pictures (Bozeat, Lambon Ralph, Garrard, Patterson, & Hodges, 2000). Language remains fluent and naming errors are semantic rather than phonological in type. It has been argued that the consistent neuropsychological pattern of deficits in semantic dementia indicates a progressive degradation of central semantic knowledge (Bozeat et al., 2000; Hodges et al., 1994; Patterson & Hodges, 2000).

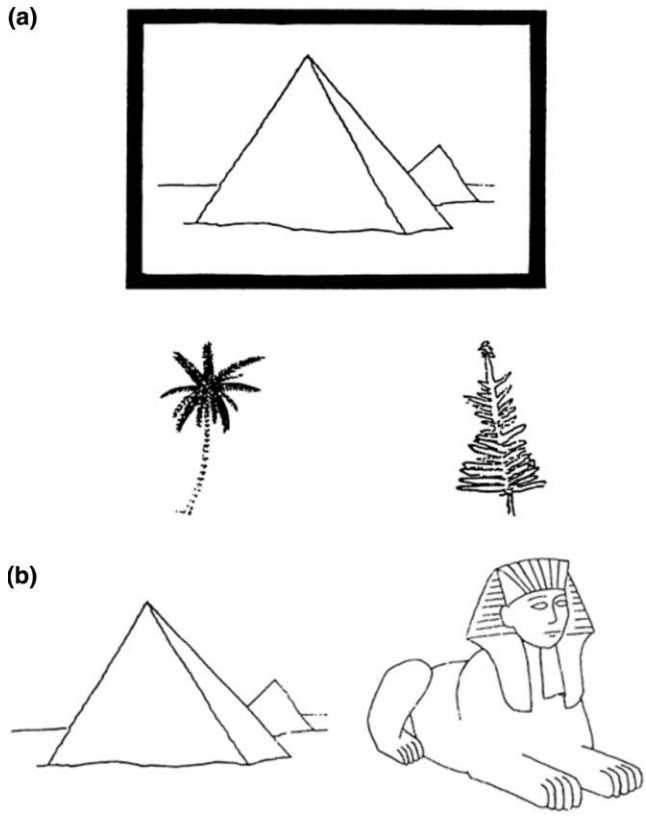


Fig. 1. Examples from (a) the Pyramid and Palmtrees test (Howard & Patterson, 1992) and (b) the Pyramid and Palmtrees recognition memory test.

By contrast, other cognitive abilities, such as nonverbal problem-solving, basic perceptual and visuospatial abilities, and working memory are typically unaffected, even at relatively advanced stages of the disease (Breedin, Saffran, & Coslett, 1994; Hodges et al., 1992, 1994; Snowden, Goulding, & Neary, 1989; Snowden, Griffiths, & Neary, 1994). It is possible, therefore, to investigate the impact of conceptual knowledge disruption on episodic memory directly in this disease, without the additional cognitive deficits that accompany other disorders affecting semantic memory, such as Alzheimer's disease or herpes simplex virus encephalitis.

## Episodic memory in semantic dementia

Anecdotal reports suggest that patients with semantic dementia are well oriented in time and place, remember appointments, and do not show the everyday memory problems typically seen in amnesia (Hodges et al., 1992; Warrington, 1975). Experimental studies have confirmed that patients can recall (albeit anomically) autobiographical events, showing a temporal step-function, with relative preservation of recent memories compared to those from the more distant past (Graham & Hodges, 1997; Nestor, Graham, Bozeat, Simons, & Hodges, 2002; Snowden, Griffiths, & Neary, 1996; although see Nadel & Moscovitch, 1997; Westmacott, Leach, Freedman, & Moscovitch, 2001).

The preservation of recent autobiographical memories in semantic dementia suggests that new episodic learning may be normal in at least the early stages of the disease. This contention was supported by evidence of preserved recognition memory for pictures of real and nonreal animals in a group of patients with semantic dementia (Graham, Becker, & Hodges, 1997). The patients were significantly impaired at the semantic study task of indicating whether the animals were real or not, in marked contrast to a group of patients with presumed Alzheimer's disease, who were at chance at recognition memory but performed equivalently to controls on the test of semantic memory. In a more recent study, a group of eight patients with semantic dementia showed highly accurate forced-choice recognition memory for color pictures of familiar objects and animals, despite impaired knowledge (as measured by picture naming) about the items depicted (Experiment 1 in Graham, Simons, Pratt, Patterson, & Hodges, 2000). Again, patients with early Alzheimer's disease showed the opposite pattern: preserved semantic knowledge but impaired episodic memory, raising the possibility that in the early stages, patients with semantic dementia and Alzheimer's disease might be distinguished from one another by their performance on tests of semantic and episodic memory (Hodges et al., 1999; Perry & Hodges, 2000).

The evidence that patients with semantic dementia can typically perform highly accurately at recognition memory despite degraded semantic knowledge was interpreted as suggesting that episodic memory usually relies upon multiple inputs from perceptual and semantic systems (for related approaches, see Bruce, 1982; Paivio & Csapo, 1973). Drawing upon the findings from studies of normal individuals' recognition memory for familiar and unfamiliar items (e.g., Bruce, 1982; Cooper, Schacter, Ballesteros, & Moore, 1992; Srinivas, 1995), it was hypothesized that in the absence of meaningful semantic input, recognition memory can be sustained on the basis of perceptual information encoded when stimuli were seen at study (Graham et al., 2000; Simons & Graham, 2000; Simons, Graham, Galton, Patterson, & Hodges, 2001a; Warrington, 1975). This multiple input hypothesis was supported by evidence from three single cases of semantic dementia whose recognition memory abilities were studied in circumstances where both perceptual and semantic contributions to memory were manipulated as experimental variables. Varying either contribution individually had little effect on recognition memory; the only situation in which memory impairment was observed was when the availability of both perceptual *and* semantic information was reduced (see Graham et al., 2000; Simons et al., 2001a, for details).

Returning to Graham et al.'s (2000) group study, an additional point that was noted by the authors was that although, as a group, there was no significant difference in recognition memory between the patients with semantic dementia and the control participants, inspection of the patients' individual scores revealed that the three whose semantic impairment was most severe showed a mild, three- to four-point, recognition memory deficit (see Fig. 4a in Graham et al., 2000). Assuming this result can be replicated, there are obvious implications for the use of recognition memory tests in distinguishing between patients with semantic dementia and those with Alzheimer's disease. This is important in terms of

the early clinical differentiation between the two disorders, which is a critical issue given the current development of drug therapies and treatment regimens. Furthermore, the profiles of recognition memory ability in Alzheimer's disease and semantic dementia have theoretical implications concerning the role played by medial temporal lobe structures in long-term memory.

Recognition memory is thought to draw upon two kinds of memory processes, building on the distinction between "recollection" and "familiarity" first made by Mandler (1980). There is much evidence to support the separation of recollection- and familiarity-based memory on cognitive grounds (e.g., Gardiner & Java, 1990; Jacoby, 1991; Jacoby, Toth, & Yonelinas, 1993; Rajaram, 1993), and recent proposals have suggested that anatomically separate systems might underlie these memory processes (Aggleton & Brown, 1999; Brown & Aggleton, 2001; although see Zola et al., 2000). One system (which includes the hippocampus) supports the recollection of stored memories with their associated temporal and spatial context ("remembering"), while the second system (involving the perirhinal cortex) underlies familiarity-based recognition of prior occurrence ("knowing"). This is consistent with the traditional view of Alzheimer's disease, where pathology is thought to originate in the transentorhinal region before spreading into the hippocampal formation proper (Braak & Braak, 1991; Van Hoesen, Hyman, & Damasio, 1991) and where recognition memory is typically impaired. Following this view, the successful recognition memory seen in most patients with semantic dementia suggests that the hippocampus and/or perirhinal cortex may be functioning adequately in at least the early stages of the disease.

The present article sought replication of the pattern of recognition memory performance observed in Graham et al.'s (2000) experiment and examined three possible contributory factors. At a neural level, the deficit at late stages of semantic dementia might reflect the progression of atrophy into regions of the medial temporal lobe known to be important for recognition memory function (Aggleton & Brown, 1999; Squire, 1992). Alternatively, or additionally, it is possible that recognition memory may be failing because of disruption to the processes responsible for contributing perceptual and/or semantic information about stimuli to the memory decision.

## Medial temporal lobe damage and recognition memory

In a study investigating recognition memory for faces in semantic dementia (Simons et al., 2001a), measures of medial temporal lobe atrophy (obtained using a visual rating technique; Galton et al., 2001) were compared with recognition memory performance. The authors documented a significant correlation between atrophy affecting the right parahippocampal gyrus (a measure that included the perirhinal cortex) and recognition memory impairment. This correspondence was significantly greater than that between hippocampal atrophy and face recognition memory deficit, consistent with Aggleton and Brown's (1999) model of long-term memory, according to which the perirhinal cortex plays a more important role in recognition memory. A prediction from Simons et al.'s result, therefore, is that it may be possible to explain the pattern of recognition memory performance observed by Graham et al. (2000) in terms of atrophy to the medial temporal lobe. Perhaps regions such as the perirhinal cortex are preserved sufficiently at early stages of the disease to support recognition memory but, as the disease progresses, become affected to such an extent by the advance of pathology that recognition memory can no longer be sustained (Simons, Graham, & Hodges, 1999). If this is the case, it may be possible to replicate the result of Simons et al. (2001a) in a less strongly lateralized task (such as recognition memory for objects) and observe a difference in medial temporal lobe atrophy between patients with semantic dementia who perform well at recognition memory and those who exhibit impairment.

## Degradation of semantic representations and recognition memory

A cognitive explanation for the pattern of recognition memory observed by Graham et al. (2000) is that semantic knowledge may be required for successful recognition memory (as maintained by Tulving's model of memory; Tulving, 1995; Tulving & Markowitsch, 1998). By this account, the patients with semantic dementia who showed preserved recognition memory in Graham et al.'s experiment may still have possessed sufficiently intact semantic representations about a large enough number of target items to support a good score on the recognition memory

test. The semantic knowledge store of the three patients with impaired recognition memory may, however, have degraded to such an extent that recognition memory was less successful.

Two investigations of episodic and semantic memory in patients with Alzheimer's disease and aphasia suggested that impaired semantic knowledge can affect recognition memory. Dalla Barba and colleagues reported that, when analyzed as a group, patients' performance on a test of associative semantics similar to Howard and Patterson's (1992) Pyramid and Palmtrees test correlated positively with performance on a subsequent yes/no recognition memory test (Dalla Barba, Frasson, Mantovan, Gallo, & Denes, 1996; Dalla Barba & Goldblum, 1996). Based on this evidence, they concluded that "episodic memory is dependent upon the integrity of semantic memory" (Dalla Barba & Goldblum, 1996, p. 1185). The authors did not undertake item-by-item analyses of episodic and semantic memory, however, which meant they were unable to provide evidence on the crucial point as to whether, at an item-specific level, poor semantic knowledge precluded subsequent recognition memory. In the absence of such evidence, all that can be justifiably concluded is that an impairment in one form of memory can occur concurrently with an impairment in another form of memory; it is not possible to adjudicate on whether one is dependent upon the other. Evidence of a significant item-specific correspondence between episodic and semantic memory is required, therefore, before definitive conclusions can be drawn about a putative association between the two.

As noted earlier, recognition memory has been studied in three single cases of semantic dementia in the light of prior assessments of each patient's conceptual knowledge about familiar objects and famous faces (Graham et al., 2000; Simons et al., 2001a). There was no significant difference in recognition memory between items that were still "known" to the patients and previously familiar items that were now "unknown," so long as the items were perceptually identical at study and test. This evidence suggests that, at an item-specific level, semantic information about the target items, although undoubtedly contributing to the decision about an item's prior occurrence (e.g., Craik & Tulving, 1975), is not a prerequisite for success (cf. Tulving, 1995; Tulving & Markowitsch, 1998). It should be noted, however, that the single-case studies assessed semantic knowledge about test items using picture naming, word-to-picture matching, and definition generation tasks. In contrast, Dalla Barba and colleagues utilized a variant of the Pyramid and Palmtrees test, which gauges associative semantic knowledge. It is important, therefore, to examine the item-specific relationship between conceptual knowledge and recognition memory in semantic dementia using a similar semantic task to that employed by Dalla Barba et al. If Tulving's (1995) model is correct, impairment to semantic knowledge should, at an item-by-item level, result in failure at recognition memory.

## Disruption to perceptual processes and recognition memory

As noted earlier, the multiple input hypothesis asserts that recognition memory typically draws upon input from perceptual and semantic processes (Graham et al., 2000; Simons & Graham, 2000; Simons et al., 2001a). A further prediction from this hypothesis, therefore, is that atrophy affecting visuoperceptual processing systems could be at least part of the explanation for the pattern of recognition memory performance seen in Graham et al.'s (2000) experiment. There is evidence that the episodic memory deficits seen in early Alzheimer's disease may, to some extent, be the result of visuoperceptual impairment (Morrison, Hof, & Bouras, 1991; Rizzo, Anderson, Dawson, & Nawrot, 2000). Similarly, studies involving nonhuman primates have suggested that some previously reported recognition memory impairments could be attributable to deficits in the perceptual processing of visual information (Eacott, Gaffan, & Murray, 1994; Murray & Bussey, 1999). For example, Eacott et al. (1994) found that monkeys with rhinal cortex lesions were impaired not only at a delayed matching-to-sample recognition memory task, but also at simultaneously matching the sample and test items. On the basis of such findings, Murray and Bussey (1999) recently proposed that the perirhinal cortex participates in both perception and memory and that damage to this region should result in impairment to both processes. In the visual domain, this would mean deficits being apparent on tasks assessing both visuoperceptual abilities and recognition memory.

Previous studies of semantic dementia have not found evidence of perceptual deficits in the disorder (e.g., Bozeat et al., 2000; Graham et al., 1997; Graham et al., 2000; Hodges et al., 1999; Perry & Hodges, 2000; Simons et al., 2001a; Srinivas, Breedin, Coslett, & Saffran, 1997). Similarly, two

studies of recognition memory in human amnesia demonstrated that patients who failed at recognition memory tasks involving several seconds' delay between study and test nevertheless performed normally when the same task was conducted with 0- or 2-s delays (Buffalo, Reber, & Squire, 1998; Holdstock, Gutnikov, Gaffan, & Mayes, 2000). It is possible, however, that such tasks are not sufficiently sensitive for significant perceptual deficits to be observed, but that subtle variations in performance on perceptual tests might be uncovered when patients who perform well at recognition memory are directly compared with those who show recognition memory impairment. It would accord with the multiple input hypothesis that disruption to perceptual function would result in impoverished perceptual information reaching memory systems and, as a result, impairment to recognition memory.

## Rationale for the current study

To summarize, this experiment sought to identify the bases of the poor recognition memory reported at advanced stages of semantic dementia by Graham et al. (2000). It was first determined whether the pattern of successful recognition memory in most patients with semantic dementia, and impairment in some patients with the most severe semantic deficit, could be replicated using a different task to the one employed by Graham and colleagues (recognition memory for items from the Pyramid and Palmtrees test). Patients with early Alzheimer's disease were administered the same recognition memory task in order to confirm that, even in the mildest stages, such patients would show characteristic amnesia that would distinguish them from most patients with semantic dementia. Assuming these patterns of performance could be replicated, three possible explanations for the deficit at advanced stages of semantic dementia were investigated. Analyses were undertaken to examine whether the recognition memory impairment could be attributed to atrophy affecting regions of the medial temporal lobe, as reported by Simons et al. (2001a) in a recognition memory task involving faces. Evidence was further sought to determine whether this recognition memory deficit might reflect degradation of semantic representations, as predicted by Tulving (1995), and/or disruption to visuoperceptual abilities, as predicted by Murray and Bussey (1999). It should be noted that these possible explanations (one neural and two cognitive in nature) are not necessarily mutually exclusive.

## Participants

A total of 32 participants were involved in the experiment: 12 with semantic dementia (5 men and 7 women), 10 in the early amnesic stage of presumed Alzheimer's disease (7 men and 3 women), and 10 control participants (7 men and 3 women), matched by age to the semantic dementia patients. Mean (and standard deviation) ages for the groups tested were semantic dementia, 61.1 (7.6), Alzheimer's disease, 73.4 (4.8), and controls, 64.6 (4.9).

The patients with semantic dementia presented to the Memory Clinic at Addenbrooke's Hospital, Cambridge, complaining of difficulties with word production (especially for the names of people, places, and words that were previously familiar to them). Spouses confirmed the anomia and also noted difficulties with comprehension of word meaning. A summary of the patients' performance on a battery of neuropsychological tests is shown in Table 1. All 12 patients showed significant impairment on subtests from the Hodges and Patterson semantic battery (Hodges & Patterson, 1995), such as naming familiar pictures, word to picture matching (pointing to the picture, in an array, that goes with a given name), and category fluency (generating as many exemplars as possible from a particular category). Similarly, all of the patients with semantic dementia were impaired on the pictures version of the Pyramid and Palmtrees test (Howard & Patterson, 1992) and on a test of synonym judgement. Like most other reported cases of semantic dementia, none of the patients showed noticeable impairment on tests tapping cognitive domains other than semantic memory. For example, they performed well on tests of perceptual and visuospatial abilities (Osterrieth, 1944; Warrington & James, 1991) and working memory (digit span) (Wechsler, 1981). Six of the patients (KH, GCB, JH, DC, FM, and DE) also participated in the experiments reported by Graham et al. (2000).

The amnesic patients also presented to the Memory Clinic in Cambridge with an informant confirmed history of a progressive anterograde memory disorder affecting both verbal and nonverbal material, which was interfering with their everyday functioning. They showed no other obvious cognitive difficulties, but over time have

Table 1
Performance of the two patient groups on a range of neuropsychological tests

| Tests | Semantic dementia | | Alzheimer's disease | | Controls ($N = 24$) | |
|---|---|---|---|---|---|---|
| | *M* | *SD* | *M* | *SD* | *M* | *SD* |
| Semantic memory | | | | | | |
| Picture naming (64) | 20.8 | 20.0 | 55.3 | 10.0 | 62.3 | 1.6 |
| Word–picture matching (64) | 34.2 | 22.9 | 60.7 | 3.0 | 63.7 | 0.5 |
| Category fluency | 23.5 | 21.5 | 44.8 | 15.4 | 113.9 | 12.3 |
| PPT—pictures (52) | 38.9 | 8.6 | 47.9 | 2.8 | 51.2 | 1.4 |
| Synonym judgment (50) | 26.3 | 10.2 | 42.2 | 6.5 | 47.6 | 2.1 |
| Episodic memory | | | | | | |
| Rey figure—recall (36) | 12.1 | 7.3 | 1.1 | 1.9 | 15.25 | 7.4 |
| RMT—faces (25) | 19.3 | 2.7 | 18.3 | 3.9 | 24.4 | 0.6 |
| RMT—words (25) | 20.1 | 3.3 | 14.4 | 2.6 | 24.5 | 1.0 |
| Logical memory | 4.6 | 6.8 | 0.3 | 0.7 | 8.5 | 3.4 |
| Visuoperceptual ability | | | | | | |
| Rey figure—copy (36) | | | | | | |
| VOSP | 32.0 | 4.3 | 27.3 | 7.3 | 34.0 | 2.9 |
| Screening test (20) | 19.4 | 1.1 | 19.3 | 0.8 | 19.3 | 0.9 |
| Dot counting (10) | 10.0 | 0.0 | 9.4 | 1.0 | 9.9 | 0.3 |
| Position discrimination (20) | 19.2 | 1.6 | 18.7 | 2.1 | 19.8 | 0.6 |
| Working memory | | | | | | |
| Digit span—forward | 5.0 | 2.8 | 7.0 | 0.9 | 6.8 | 0.9 |
| Digit Span—backward | 3.4 | 2.5 | 4.3 | 1.2 | 4.7 | 1.2 |

*Note*. PPT, Pyramid and Palmtrees test; RMT, Recognition Memory test; VOSP, Visual Object and Space Perception battery; *M*, mean; *SD*, standard deviation. See text for test references.

developed mild semantic memory impairment (as measured by category fluency or stringent picture naming tests) and/or visuospatial deficits (Osterrieth, 1944; Warrington & James, 1991), as shown in Table 1. Studies of similar patients have suggested that such an isolated amnesic prodrome may present for as much as a decade prior to the development of a full-blown dementia syndrome (Caffarra & Venneri, 1996; Hodges, 1998). A full battery of investigations, including CT and/or MRI failed to reveal any alternative cause of their memory loss. Six of the patients involved in this experiment (PL, VJ, VA, RB, HM, and ATy) were members of the Alzheimer's disease group in Experiment 1 of Graham et al.'s (2000) study; the remaining amnesic patients showed a similar neuropsychological profile to these six.

## Method

### *Behavioral tasks*

Each participant completed a semantic study task and a subsequent recognition memory test. The same 49 items were used as targets in both tests, selected from the Pyramid and Palmtrees test (PPT) designed by Howard and Patterson (1992).[1] In the associative semantic task, a target picture was presented with two further pictures below (see Fig. 1a for an example) and participants were asked to indicate, by pointing, which item (e.g., *palm tree* or *fir tree*) went with the target picture in the box (e.g., *pyramid*). No feedback was provided during the semantic memory task. Following a 15-min delay, during which a filler task not involving pictures was used, participants were presented with 49 pairs of black and white line drawings. One of the line drawings in every pair was an "old" item which had been a target picture in the previous semantic association test (e.g., *pyramid*). The other member of the pair was a "new" semantically related black and white line drawing (e.g., *sphinx*) that had not seen earlier (see Fig. 1b for an example). Participants were asked to indicate, by

[1] The standard version of the PPT contains 52 target items, but a number of the items are seen more than once throughout the test, either as target or foil items (e.g., eskimo, mouse, etc.). Only items that appeared once were selected for use in the present experiment.

pointing, which picture in the pair they had seen in the previous study phase.

As part of their longitudinal assessment test battery, the patients with semantic dementia and Alzheimer's disease were also administered several standard tests of visual perception. These included subtests from the Visual Object and Space Perception battery (VOSP; Warrington & James, 1991) such as picking out an "X" shape from a masking pattern, counting the number of dots in an array, discriminating the accurate position of a dot, locating a number in an array, and counting the number of cubes in a three-dimensional arrangement. The patients were also asked to undertake a copy of the Rey complex figure (Osterrieth, 1944) to assess visuospatial discrimination and perceptual organization.

### *Assessment of medial temporal lobe atrophy*

The degree of atrophy affecting the left and right hippocampus and parahippocampal gyrus (principally involving the perirhinal cortex) in 11 of the 12 patients with semantic dementia and 9 of the 10 patients with Alzheimer's disease was assessed by a single rater, Dr. Clare Galton, using the same MRI visual rating technique as described and volumetrically validated by Galton et al. (2001) and used by Simons et al. (2001a). Due to technical difficulties, atrophy ratings could not be obtained for 1 of the patients with semantic dementia (AT) and 1 of those with Alzheimer's disease (ATy). To reiterate the details of the two measures used, the hippocampal atrophy measure (ranging from zero to four) involves visual assessment of the width of the choroidal fissure, the width of the temporal horn, and the height of the hippocampal formation using the best coronal slice that depicts both hippocampal formations (usually at the level of the anterior pons). The parahippocampal gyrus atrophy measure (ranging from zero to three) involves visual assessment of the depth of the collateral sulcus (on the banks of which the perirhinal cortex is located) on the same coronal slice as that on which the hippocampus is assessed. As such, this measure is primarily an estimate of atrophy affecting the perirhinal cortex rather than, for example, the nearby entorhinal cortex (Galton et al., 2001).

In the literature, amnesia has typically been associated with damage to the medial temporal lobes bilaterally (for a review, see Aggleton & Brown, 1999). Furthermore, there is functional imaging evidence that recognition memory for nameable objects typically involves bilateral brain regions, both in prefrontal and medial temporal cortices (e.g., Kelley et al., 1998; Simons, Graham, Owen, Patterson, & Hodges, 2001b). For this reason, measures of bilateral atrophy in the hippocampus and parahippocampal gyrus were calculated by taking the mean of the left and right atrophy ratings.

## Results

### *Semantic and episodic memory tasks*

The results from the semantic and episodic components (shown in Fig. 2) were analyzed separately with one-way ANOVAs. Examination of performance on the semantic task revealed a significant main effect of group [$F(2, 29) = 19.8$, $p < .001$]; post-hoc Fisher PLSD pairwise comparisons disclosed that the patients with semantic dementia were significantly worse on the PPT than both the control participants and the patients with presumed early Alzheimer's disease (both $p$ values $< .001$). There was no significant difference between the control participants and the patients with Alzheimer's disease. On the recognition memory task, in which the participants had to select which item (of two) they had seen previously, there was a significant main effect of group

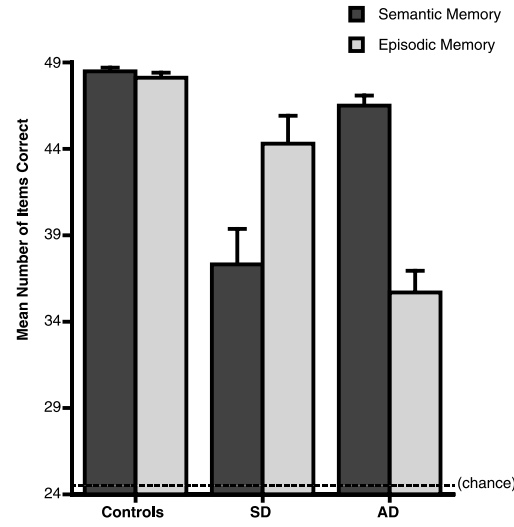


Fig. 2. The performance of the control participants, the patients with semantic dementia, and those with presumed Alzheimer's disease on the semantic memory and the episodic memory tasks.

[$F(2, 29) = 24.8$, $p < .001$]. By contrast to the previous analysis, post hoc tests revealed that the amnesic patients with early Alzheimer's disease showed a significant impairment on the test compared with the control participants and the semantic dementia patients (both $p$ values $< .001$). There was also a significant difference between the group of patients with semantic dementia and the control participants ($p < .05$).

To allow a comparison between the patients with semantic dementia and the amnesic patients with presumed early Alzheimer's disease, $z$-score conversions were performed for both the semantic and episodic memory tests. Patients were rank ordered according to their performance on the semantic memory task. It can be seen from Figs. 3a and b that while all the patients with semantic dementia were at least 2 *SD* outside the control mean on the PPT, only three of the patients with Alzheimer's disease were significantly impaired on the test (RB, HM, and ATy). Furthermore, as would be expected, the degree of impairment on the test of associative semantic knowledge was strikingly greater for the patients with semantic dementia.

The opposite pattern was seen on the test of episodic memory: all 10 patients with presumed early Alzheimer's disease were impaired on this task, while only 4 of the patients with semantic dementia scored outside the control range (IF,

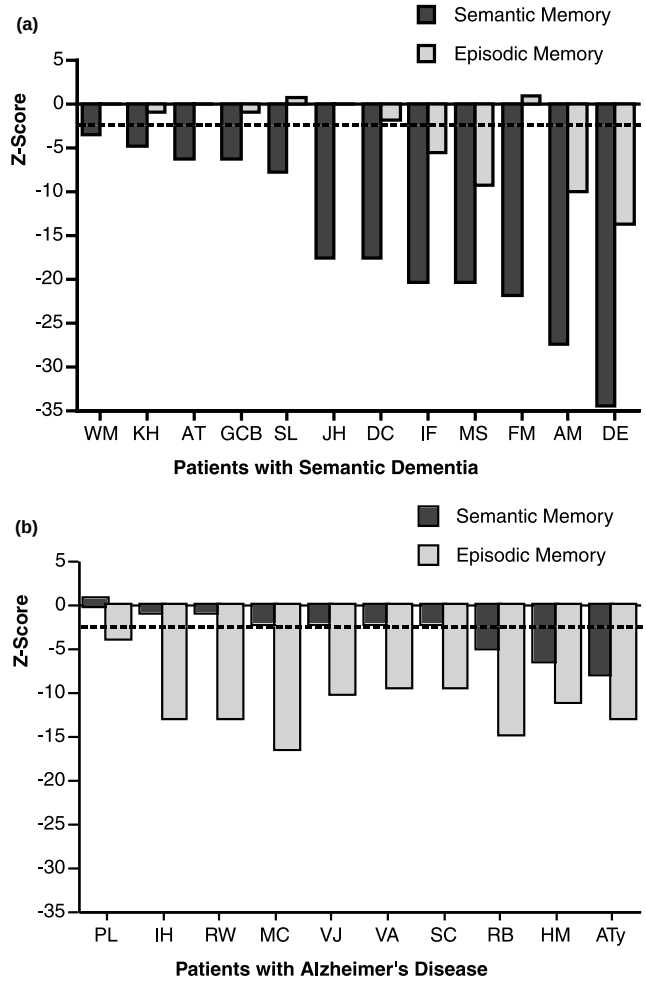


Fig. 3. The performance of each patient with (a) semantic dementia and (b) Alzheimer's disease on the semantic and episodic memory tasks (measured using $z$ scores). The dashed line at $z = -2$ indicates performance that is 2 *SD* below the control mean. Patients are ordered by performance on the semantic task.

Table 2
Ratings of atrophy affecting the bilateral medial temporal lobes in 11 of the patients with semantic dementia and 10 of the patients with Alzheimer's disease

| | Semantic dementia | | Alzheimer's disease | |
|---|---|---|---|---|
| | *M* | *SD* | *M* | *SD* |
| Hippocampus | 2.23 | 0.9 | 2.06 | 0.2 |
| Parahippocampal gyrus (including perirhinal cortex) | 2.09 | 0.7 | 1.06 | 0.7 |

*Note*. Hippocampus—range 0 (no atrophy)–4 (severe); parahippocampal gyrus (including perirhinal cortex)—range 0–3. *M*, mean; *SD*, standard deviation.

MS, AM, and DE). The deficits in these 4 patients, relative to the control group, were confirmed using Crawford and Howell's (1998) modified $t$ test, which is a more accurate method of comparison than $z$ scores given the size of the control group [IF, $t(9) = 5.3$; MS, $t(9) = 8.8$; AM, $t(9) = 9.6$; DE, $t(9) = 13.1$; all $p$ values $< .001$]. The other 8 patients scored within 2 *SD* of the control participants and as a group their performance was not statistically different from that of the controls [$F(1, 16) = 0.47, p = .50$].

The $z$-score plots are revealing with regard to the integrity of episodic memory in semantic dementia, as they suggest that most patients with the disorder show little impairment on the type of task used in this experiment, but that those later in the disease course may show a deficit in recognition memory. The group profile in this study is similar to that observed in Experiment 1 of Graham et al. (2000); specifically, four of five of the patients with semantic dementia who had the greatest semantic impairment showed a significant deficit on the recognition memory task. The data from this study further indicate that there is no consistent relationship between loss of episodic and semantic memory in Alzheimer's disease: typically all patients were profoundly impaired on the recognition memory task regardless of their level of performance on the semantic memory test.

### *Comparison between recognition memory and medial temporal lobe atrophy*

As described above, bilateral atrophy rating measures of the parahippocampal gyrus (perirhinal cortex) and the hippocampus were derived for 11 of the 12 patients with semantic dementia and 9 of the 10 patients with Alzheimer's disease (see Table 2). Using these ratings, it was possible to assess whether atrophy affecting medial temporal lobe regions was related to recognition memory impairment for items from the PPT. The 11 patients with semantic dementia were divided into two groups: a "good recognition memory" group, containing the 7 patients (excluding AT) who performed within control limits on the recognition memory task, and a "poor recognition memory" group, containing the four patients (IF, MS, AM, and DE) who showed a deficit on the recognition memory task.

An independent samples $t$ test revealed that significantly less parahippocampal gyrus atrophy affected the "good recognition memory" group (mean atrophy rating, 1.79, $SD = 0.76$) than the "poor recognition memory" group (mean rating, 2.63, $SD = 0.25$) [$t(9) = 2.69$, $p < .05$]. Comparison of hippocampal atrophy ratings revealed a numerical difference between the "good recognition memory" group (mean rating, 2.0, $SD = 0.96$) and the "poor recognition memory" group (mean rating, 2.63, $SD = 0.63$), although this did not reach significance [$t(9) = 1.3$, n.s.]. These results were mirrored in correlations between atrophy ratings and recognition memory performance.[2] Parahippocampal gyrus atrophy and recognition memory score correlated significantly with one another [$r = -.63$, $p < .05$], whereas the correlation between hippocampal atrophy and recognition memory performance did not reach significance [$r = -.41$, n.s.]. Taken together, these analyses suggest that the pattern of recognition memory performance observed in semantic dementia can be largely explained neuroanatomically by the extent of atrophy affecting the perirhinal cortex region.

Matters are not so clear when attempting to examine the relationship between medial temporal lobe atrophy and recognition memory impairment in Alzheimer's disease. As described above, all of the patients with Alzheimer's disease involved in the present study were profoundly impaired at

[2] Since these comparisons are between extent of atrophy and recognition memory score, we would expect correlations to be negative.

Table 3
Item-specific correspondences between performance on the Pyramid and Palmtrees associative semantic test and the forced choice recognition memory test for three (of the four) patients who showed significantly impaired new learning compared to the control participants

| | | Recognition memory | | | | | |
|---|---|---|---|---|---|---|---|
| | | IF | | MS | | AM | |
| | | √ | × | √ | × | √ | × |
| Semantic | √ | 28 | 5 | 27 | 7 | 22 | 7 |
| Knowledge | × | 13 | 2 | 11 | 4 | 15 | 5 |

recognition memory for items from the PPT, precluding comparison of atrophy in patients with preserved and impaired memory. Correlations between medial temporal lobe atrophy and recognition memory performance were not significant either for the parahippocampal gyrus [$r = .14$, n.s.] or the hippocampus [$r = -.34$, n.s.]. These results suggest that, although atrophy in Alzheimer's disease may originate in transentorhinal regions (Braak & Braak, 1991; Van Hoesen et al., 1991), the recognition memory deficit typically observed in the disease may be due to damage in other regions such as, perhaps, posterior cortical areas (Morrison et al., 1991; Rizzo et al., 2000) or the basal forebrain (Coyle, Price, & DeLong, 1983; Lawrence & Sahakian, 1998).

*Item-specific comparison between semantic and episodic memory*

The performance of three of the patients with semantic dementia, IF, MS, and AM, was sufficiently poor on both the semantic and episodic memory tests that it was possible to determine whether there was an item-specific correspondence between the two components of long-term memory.[3] DE, the other patient with semantic dementia who showed poor performance on the recognition memory task, performed at chance on the PPT (24/49), making a direct comparison between semantic and episodic memory invalid. By analyzing the data from IF, MS, and AM in an item-by-item manner, it was possible to address the crucial question of whether degraded conceptual knowledge about an item (e.g., pyramid) had a direct impact on the ability of a patient to select that item in the recognition memory test.

Two-by-two comparison tables for each patient are shown in Table 3. Analyses of these data using Fisher Exact probability tests (because some of the expected cell frequencies did not exceed five) revealed that none of the patients showed a significant item correspondence between the semantic and episodic memory tests (IF, $p = .62$; MS, $p = .45$; AM, $p = .6$). It is important to note, however, that both of the tests used in the analyses were forced-choice with a single distractor. It is possible, therefore, that no correspondence was observed in this analysis because a number of items may have been correctly selected by chance (on both tests). In an attempt to circumvent this problem, further analysis was undertaken of the data from one of the patients with semantic dementia, AM.

*Additional item-specific analysis for semantic dementia patient AM*

On a subsequent occasion, AM was asked to define all the target items from the PPT. This definition data was combined with that from the standard forced-choice administration of the PPT (described above), and the 49 items were divided into three categories: *Preserved semantic knowledge* ($n = 11$)—correct on the PPT and evidence of some semantic knowledge in the definition to the picture (excluding information about the physical form of the item); *Partial semantic knowledge* ($n = 24$)—incorrect on the PPT and evidence of some semantic knowledge in the definition to the picture *or* correct on the PPT and a poor or incorrect definition to the target picture; *Degraded semantic knowledge* ($n = 14$)—incorrect on the PPT and a poor *or* incorrect definition to the picture. A $3 \times 2$ $\chi^2$ analysis revealed no direct

[3] To avoid the possibility of misleading results because of skewing in the data (for discussion, see Poldrack, 1996), the criterion of performance greater than 20% and less than 80% correct on both semantic and episodic tasks was adopted. None of the patients with Alzheimer's disease fell within these boundaries, so item-specific analysis was not possible in that patient group.

correspondence between the amount of semantic knowledge AM possessed about an item and his ability to remember that item in the recognition memory test [$\chi^2(2) = 1.99$, $p = .4$]. It is possible that items in the "partial semantic knowledge" category were obscuring the $3 \times 2$ analysis; when comparison was restricted to items about which AM showed strong evidence of preserved or degraded knowledge (i.e., items in the first and third categories), a Fisher Exact test confirmed that there was no evidence of association with recognition memory ($p = .41$).

*Performance on tests of visual perception*

As before, the 12 patients with semantic dementia were divided into two groups: a "good recognition memory" group, containing the eight patients who performed within control limits on the recognition memory task, and a "poor recognition memory" group, containing the four patients (IF, MS, AM, and DE) who were impaired at recognition memory. The patients with semantic dementia and those with Alzheimer's disease were administered a battery of tests of visual perception in order to determine whether the recognition memory impairment in the "poor recognition memory" semantic dementia group and the patients with Alzheimer's disease could be attributed to disrupted visuoperceptual abilities. The performance of the groups on subtests of the VOSP and at copying the Rey complex figure are shown in Table 4, as are the results of one-way ANOVA comparisons.

It can be seen from the table that there was no significant difference between the semantic dementia patient groups on any of the perceptual tests undertaken. A slight numerical difference between the good recognition memory and poor recognition memory groups was evident on copy of the Rey figure, but this did not reach statistical significance [$F(1, 10) = 3.1$, n.s.]. The patients with Alzheimer's disease, however, did perform significantly worse than the good recognition memory semantic dementia group on this task [$F(1, 16) = 5.2$, $p < .05$]. These results suggest that impairment of visuoperceptual function may be playing a role in the recognition memory deficit typically seen in Alzheimer's disease, but is unlikely to be the explanation for the poor recognition memory exhibited by four of the patients with semantic dementia.

## Discussion

The main aim of this experiment was to investigate the possible causes for the impairment to recognition memory seen at late stages of semantic dementia in Experiment 1 of Graham et al.'s (2000) study. In a similar pattern to that observed previously, 8 of the 12 patients with semantic dementia tested in the present experiment showed preserved performance on a recognition memory task, despite varying impairments in semantic knowledge for the same target items. All of the 10 patients with early Alzheimer's disease exhibited profoundly impaired recognition memory, suggesting that performance on such tasks may still provide a useful clinical method of distinguishing between the two disorders, in at least their early stages. Four of the 12 patients with semantic dementia, who had reached a more advanced stage of the disease, showed deficits on both the episodic and semantic memory tests,

Table 4
Summary of the performance of the patient groups on tests of visual perception

| Tests | Semantic dementia | | | | Alzheimer's disease | |
|---|---|---|---|---|---|---|
| | Good RM | | Poor RM | | *M* | *SD* |
| | *M* | *SD* | *M* | *SD* | | |
| VOSP | | | | | | |
| Screening test (20) | 19.4 | 1.2 | 19.5 | 1.0 | 19.3 | 0.8 |
| Dot counting (10) | 10.0 | 0.0 | 10.0 | 0.0 | 9.4 | 1.0 |
| Position discrimination (20) | 19.0 | 2.0 | 19.7 | 0.6 | 18.7 | 2.1 |
| Number location (10) | 8.5 | 2.4 | 7.7 | 0.6 | 7.8 | 2.7 |
| Cube analysis (10) | 9.3 | 1.9 | 9.3 | 1.2 | 7.7 | 2.5 |
| Rey figure copy (36) | 33.4 | 2.0 | 29.1 | 6.6 | 27.3* | 7.3 |

*Note*. VOSP, Visual Object and Space Perception battery; RM, recognition memory; *M*, mean; *SD*, standard deviation.

* Significant impairment relative to the "good RM" semantic dementia group. See text for test references.

consistent with the observation from Graham et al. (2000). The recognition memory impairment in these 4 patients was similar in extent (5–10 *SD* below the control mean) to that seen in the patients with Alzheimer's disease.

Comparison of 11 of the patients with semantic dementia on measures of medial temporal lobe atrophy revealed that the status of the perirhinal cortex region bilaterally was significantly related to performance on the recognition memory test. Critically, there was no evidence from item-by-item correspondence analyses that degraded semantic knowledge about a particular item necessarily resulted in poor recognition memory for that item. As expected, the majority of the patients in the early stages of Alzheimer's disease were *not* impaired on the PPT, but showed deficits on the recognition memory task. There was no evidence from *z*-score plots (Fig. 3b) that loss of semantic knowledge was related to degree of impairment to recognition memory in this patient group. Finally, no evidence could be found that the poor recognition memory at late stages of semantic dementia was attributable to perceptual deficits. Direct comparison between patients with good recognition memory and those with recognition memory impairment revealed no significant differences on any of the tests of visual perception undertaken. There was some evidence of a perceptual deficit in the patients with Alzheimer's disease, however, suggesting that their characteristically poor recognition memory may, in part, be due to disrupted perceptual function.

Ratings of atrophy in medial temporal lobe structures such as the hippocampus and parahippocampal gyrus indicated that the patients with semantic dementia whose recognition memory was preserved had significantly less atrophy in the parahippocampal gyrus bilaterally, but that there was no significant difference in hippocampal atrophy. This result is consistent with that found by Simons et al. (2001a) when atrophy ratings were compared with recognition memory for faces. In both experiments, parahippocampal gyrus atrophy predicted recognition memory more accurately than did atrophy in the hippocampus. As noted earlier, the parahippocampal gyrus measure is derived by assessing the depth of the collateral sulcus; as a result, it represents a satisfactory measure of the status of the perirhinal cortex, which in humans lies on the banks of the collateral sulcus (Buffalo et al., 1998). The two sets of findings, therefore, are consistent with Aggleton and Brown's (1999) hypothesis that recognition memory relies, to a large extent, on a familiarity-based memory system that includes the perirhinal cortex. Moreover, the results of this experiment support the hypothesis that the pattern of recognition memory performance seen in semantic dementia cross-sectionally—both in this experiment and in that reported by Graham et al. (2000)—can be attributed to atrophy progressing to affect this medial temporal lobe region (Simons et al., 1999).

Ratings of medial temporal lobe atrophy were not significantly related to recognition memory impairment in the patients with early Alzheimer's disease. This could be due to the relatively little parahippocampal gyrus atrophy in the present cohort (less than in the patients with semantic dementia; see Table 2), a surprisingly small amount given the evidence that atrophy originates in nearby transentorhinal structures (Braak & Braak, 1991; Van Hoesen et al., 1991). It is possible that the visual rating technique used in the present study may be insensitive to the kinds of histological changes characteristic of Alzheimer's disease, such as the buildup of amyloid plaques and neurofibrillary tangles. Perhaps these neuropathological deposits do not reduce the perceived volume of a structure like the parahippocampal gyrus in the same way as the neuronal degeneration associated with semantic dementia. A further point is that there is evidence that pathology in Alzheimer's disease may additionally affect other regions, including posterior cortical regions responsible for visuoperceptual function (Morrison et al., 1991; Rizzo et al., 2000) and basal forebrain cholinergic systems that innervate the medial temporal lobe (Coyle et al., 1983; Lawrence & Sahakian, 1998). It may be damage to these areas that results in the profound anterograde memory impairment observed in the early stages of Alzheimer's disease (Weintraub & Mesulam, 1993), which serves to differentiate the disorder from semantic dementia.

We now turn to the first of the possible cognitive explanations for the recognition memory deficit seen at late stages of semantic dementia. The striking lack of item-specific correspondence between episodic and semantic memory seen in the present study is evidence against the view that the recognition memory impairment is directly caused by degraded semantic representations (as predicted by Tulving's model of memory; Tulving, 1995; Tulving & Markowitsch, 1998). Although there is much evidence that semantic knowledge can contribute toward normal episodic memory (e.g., Craik & Tulving, 1975), the fact that there was no direct correspondence between items a

patient possessed semantic knowledge about and items recognized as seen previously suggests that conceptual knowledge need not be a prerequisite for successful recognition memory, at least for pictorial stimuli. This result is entirely consistent with the evidence from previous studies of semantic dementia, which manipulated the state of semantic knowledge about previously familiar items as an experimental variable (Graham et al., 2000; Simons et al., 2001a). Patients were quite capable of recognizing a picture of an item as having been seen earlier, regardless of whether the items were still "known" to them or were now "unknown."

As described earlier, Dalla Barba and colleagues reported in their patients that total score on a test of semantic knowledge correlated with recognition memory performance (Dalla Barba et al., 1996; Dalla Barba & Goldblum, 1996). From the results of the present experiment, it is possible to speculate that if Dalla Barba et al. had undertaken similar item-specific analyses in their patients with Alzheimer's disease to those conducted in this experiment in patients with semantic dementia, they might also have found no item-by-item correspondence between semantic and episodic memory. It is important, at this stage, to acknowledge the point that recognition memory is only one example of episodic memory and may not capture the full-blown recollective experience of "remembering" an event along with its associated contextual information (Tulving, 2001). Although the present data appear to be problematic for Tulving's (1995) model, therefore, replication is required using tests that tap more recollective aspects of episodic memory (such as source memory, associative recognition, etc.) before definitive conclusions can be drawn. Data from an experiment assessing source memory in patients with semantic dementia would appear to provide such replication: none of the patients tested showed a significant correspondence between semantic knowledge about items and ability to attribute those items to the correct source in an episodic memory test (Simons et al., in press).

Moving on to the third possible explanation for the pattern of recognition memory performance in semantic dementia, no evidence could be found that disruption of visuoperceptual function might be contributing to the recognition memory deficit seen in some of the patients. The hypothesis that perceptual deficits might underlie the recognition memory impairment was prompted by evidence from previous studies of Alzheimer's disease (Morrison et al., 1991; Rizzo et al., 2000) and from experiments involving nonhuman primates (Eacott et al., 1994; Murray, 2000). The lack of evidence of perceptual impairment in semantic dementia is consistent with the findings in many previous studies of the disorder, all of which have documented unimpaired performance on standard perceptual tests (Bozeat et al., 2000; Graham et al., 1997; Graham et al., 2000; Hodges et al., 1999; Perry & Hodges, 2000; Simons et al., 2001a; Srinivas et al., 1997). It is important to note, however, that this failure to find impairment on standard perceptual tasks does not necessarily mean that visual perception is entirely normal in semantic dementia. There was some variation in performance on copying the Rey complex figure, although this did not reach statistical significance, unlike in the patients with Alzheimer's disease who were significantly impaired on this task. It is possible that patients with semantic dementia may have subtle perceptual deficits that might emerge with more stringent testing, although it seems unlikely that perceptual impairments that are so modest as to be virtually undetectable on standard tests could be sufficient to explain the substantial deficits in recognition memory observed in four of the patients with semantic dementia.

The evidence points toward the likely explanation, therefore, that the recognition memory deficit seen at late stages of semantic dementia is primarily related to the progression of pathology into medial temporal lobe structures, such as the perirhinal cortex. This may not hold true for other forms of dementia, such as Alzheimer's disease, which, as seen in the present study, can be associated with similar perceived levels of medial temporal lobe atrophy as in semantic dementia (Chan et al., 2001; Galton et al., 2001) but a strikingly different pattern of recognition memory performance. At a cognitive level, it appears that in most patients with semantic dementia, both the perceptual analysis of stimuli and the encoding, storage, and retrieval of mnemonic information are functioning adequately to sustain accurate recognition memory. In late stages of the disorder, however, the data suggest that while perceptual analysis remains functional, the processes responsible for memorizing the occurrence of perceived stimuli can become deficient. It is, of course, difficult when examining a patient's memory impairment to specify whether the deficit may be occurring at encoding, storage, or retrieval. All that can be concluded from the present data is that the recognition memory failure seen at

late stages of semantic dementia appears to be attributable to difficulty in utilizing available perceptual (and perhaps semantic) information about an item as a long-term memory trace.

Importantly, the proposed explanation for the pattern of recognition memory performance seen in semantic dementia is consistent with the multiple input hypothesis of long-term memory (Graham et al., 2000; Simons & Graham, 2000; Simons et al., 2001a). According to this view, the successful recognition memory seen in most patients with semantic dementia (even those with quite severe semantic deficits) is based on perceptual information from seeing target items during the study phase. As already discussed, the recognition memory deficit seen at late stages of semantic dementia appears not directly to reflect degraded semantic representations or disrupted perceptual processes. Instead, it is likely that atrophy affecting medial temporal lobe structures such as the perirhinal cortex results in impairment in the utilization of perceptual and semantic information in a lasting mnemonic trace. The evidence presented in the present study confirms the existence of qualitatively different patterns of cognitive performance in the early stages of semantic dementia and Alzheimer's disease. While it may be difficult to differentiate the two disorders in their later stages, therefore, there is good evidence that a progressive impairment to semantic knowledge in the context of preserved recognition memory is likely to be diagnostic of a patient with semantic dementia rather than Alzheimer's disease.

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