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Insights from semantic dementia on the relationship between episodic and semantic memory

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Abstract

An influential theory of long-term memory, in which new episodic learning is dependent upon the integrity of semantic memory, predicts that a double dissociation between episodic and semantic memory is not possible in new learning. Contrary to this view, we found, in two separate experiments, that patients with impaired semantic memory showed relatively preserved performance on tests of recognition memory if the stimuli were perceptually identical between learning and test. A significant effect of semantic memory was *only* seen when a perceptual manipulation was introduced in the episodic task. To account for these findings, we propose a revision to current models of long-term memory, in which sensory/perceptual information and semantic memory work in concert to support new learning. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Frontotemporal dementia; Alzheimer's disease; Hippocampus; Temporal lobes; New learning; Conceptual knowledge

1. Introduction

1.1. The organisation of long-term memory

Over the last 25 years there has been considerable controversy amongst neuroscientists over the cognitive and neural organisation of long-term memory [38,51,55–58]. In one of the earliest, and most influential, models of long-term memory, Tulving proposed the fractionation of memory into two distinct types, episodic and semantic [55,56]. Episodic memory refers to our repository of personally experienced events, the retrieval of which requires conscious recollection of the specific temporal-spatial setting of an episode from the past. By contrast, semantic memory applies to our store of culturally-shared general knowledge about the world (e.g. the meaning of words, objects, concepts, facts and people). Unlike episodic memory, this type of information does not require recollection of when and where it was initially learnt.

In Tulving's original conception of long-term memory [56], episodic and semantic memory were considered psychologically and neurologically distinct, a dichotomy reflecting the way in which the human brain is supposed to acquire, process and store information. It was initially thought that patients with amnesia, who show impaired new episodic learning but spared semantic knowledge [35,40,61,64], supported the fractionation of long-term memory, although recent studies have challenged this view [8,11,62,65].

To account for the evidence against a simple dissociation between episodic and semantic memory in amnesia, Tulving [38,55,57,58] revised his model, suggesting that episodic memory is a subsystem of semantic memory and is, therefore, dependent upon the integrity of semantic knowledge (see Fig. 6a). The most recent instantiation of his theory (termed SPI, standing for Serial encoding, Parallel storage, and

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Independent retrieval) expands on this hierarchical view. In this model, there are four major categories of cognitive memory system: perceptual representation; semantic; working; and episodic memory. There are three crucial premises to the model: (1) information is *encoded* into systems *serially*, with encoding in one system dependent upon output from the previous stage; (2) information can be *stored* in different systems in *parallel*; and (3) information in different systems can be retrieved independently without any effects on retrieval of information from other systems. This view explains why a patient with a deficit of episodic memory (amnesia) may still be able to retrieve semantic information that was acquired earlier in life [57].

Our study addresses one prediction that has remained constant throughout the revisions to Tulving's model of long-term memory, i.e. that "... a double dissociation between semantic and episodic memory is not possible and only single dissociations (impaired episodic memory and preserved semantic memory) can occur" (p. 844) [57]. This prediction stems from the fact that in the SPI model, encoding of material is serial, that is, the registration of information in episodic memory is contingent upon the output from semantic memory, which in turn is dependent upon input from perceptual systems. Although there is already some neuropsychological evidence that calls into question the strictly serial nature of Tulving's hypothesis [7,9,27], the claim that episodic memory is dependent upon semantic memory, and that one should *never* see patients with normal episodic memory for events and/or stimuli that they fail to comprehend, has never been directly challenged or tested.

In this article, we document precisely this 'impossible' side of the double dissociation in new learning in patients with the disorder of semantic dementia [22,48], and propose an account of the cognitive and neural architecture of long-term memory which reflects the differential contributions of semantic and perceptual inputs to the hippocampal complex.

1.2. Semantic dementia: a specific disorder of long-term semantic memory

Tulving's prediction about the dependence of new learning on semantic memory has never been specifically tested due to the fact that, until recently, there was little evidence (apart from some early reports [45,63]) that patients could present with a selective impairment to semantic memory. This situation has been rectified by a newly described syndrome termed semantic dementia [22,48], also called progressive fluent aphasia [32] or the temporal variant of frontotemporal dementia [4,6,24,33,34], which results in a progressive, relatively selective deterioration of semantic memory. It was Pick [41] (English translation in [10]) who, a century ago, first noted that patients with neurodegenerative disease could exhibit a focal cognitive deficit such as impaired language. Some 90 years after this initial description, Mesulam [32] reported six patients with slowly progressive aphasia, some of whom exhibited fluent and articulate speech which notably contained few content words. This anomic pattern, which is typically present early in semantic dementia, has been shown to reflect a progressive breakdown in the central store of semantic memory affecting both verbal and non-verbal aspects of conceptual knowledge about objects, people, facts, concepts, and the meanings of words.

Patients with semantic dementia perform poorly on any task which requires semantic knowledge, such as picture naming, category fluency (i.e. generating exemplars from semantic categories such as household items), word-picture matching, defining and drawing concepts in relation to their names, selecting an appropriate colour for a black and white line drawing (e.g. red for a tomato) and sorting words or pictures according to a pre-specified criterion (e.g. living or non-living). By contrast, performance on tests measuring other cognitive domains, such as the phonological and syntactic aspects of language, non-verbal problem-solving, working memory and visuo-spatial and perceptual abilities, is relatively unaffected, even at relatively late stages of the disease [19,22,23,48,49].

Neuroradiological investigations in semantic dementia typically reveal focal atrophy of the antero-lateral aspects of one or both temporal lobes, especially the pole and inferior and middle temporal gyri (Brodmann areas (BA) 38/20) [21,36], with sparing (at least at early stages of the disease) of the hippocampal complex (hippocampus proper, parahippocampal gyri and subiculum) [13,16,18]. In a recent functional neuroimaging study, in which regional cerebral blood flow was measured in four patients with semantic dementia while they performed a semantic decision task, the patients showed a significant reduction in activity in the left posterior inferior temporal gyrus compared to control subjects (BA 37) [36]. The imaging results suggest, therefore, a structural and functional disruption to the temporal lobes in semantic dementia. While there has been relatively little neuropathological data collected in the disease (although see [16,28,44,46,50]), a meta-analysis of published and unpublished information for 13 cases revealed that all patients had either classic Pick's disease pathology or non-specific neuronal loss without characteristic Pick or Alzheimer histological markers [17].

The selective nature of the semantic memory impairment in semantic dementia presents cognitive neuropsychologists with a unique opportunity to investigate the cognitive and neural organisation of long-term memory [12,13,19,21–23,48,49]. Recent experiments

Table 1
Summary of the performance of the two patient groups at the time of the experiment and 24 healthy controls [20] on a range of neuropsychological tests

	Controls (n = 24)		Semantic Dementia		Alzheimer's Disease	
Tests	Mean	SD	Mean	SD	Mean	SD
Semantic memory						
Category fluency — 4 categories	55.4	8.6	14.4	17.8	27.9	12.7
Synonym judgement (50)	47.6	2.1	23.8	9.9	44.8	5.4
Word-picture matching[a] (64)	63.7	0.5	39.0	22.5	61.9	1.6
PPT — pictures (52)	51.2	1.4	40.5	6.0	48.6	3.1
Episodic memory						
Rey figure — delayed recall (36)	15.3	7.4	13.8	6.6	3.6	2.7
Visuospatial ability						
Rey figure — copy (36)	34.0	2.9	34.0	2.2	29.4	7.0
Object matching (40)	37.3	3.1	38.4	1.5	38.2	1.3
Working memory						
Digit span — forwards[b]	6.8	0.9	6.3	1.0	7.1	1.1

[a] Control n = 14 for word-picture matching test. Table abbreviations and references: PPT = Pyramids and Palmtrees test [25]; Rey Figure = Rey Complex Figure [39]; Object Matching test [26].
[b] It was not possible to obtain forwards digit span scores for two of the patients with semantic dementia.

that have investigated autobiographical and semantic memory in semantic dementia have found evidence for a reverse temporal gradient (i.e. recent memories were better preserved compared to those from the more distant past) [13,15,18,49]. These studies are important because they hint at the possibility that, at least at an early stage in the disorder, new learning may be normal, a finding which would have fundamental implications for our understanding of the nature of episodic and semantic memory.

In our first experiment, therefore, we investigated episodic and semantic memory in patients with semantic dementia and in amnesic patients with presumed early Alzheimer's disease. In particular, we related the patients' ability to name a picture of a familiar object during a study phase to their subsequent recognition memory for either the identical item or a perceptually different exemplar of the same object. The essence of our hypothesis is that new learning is normally based on a combination of sensory/perceptual information provided by the learning event and semantic information about the content of the event. If the target from the study phase of a recognition memory experiment is replaced at test by a perceptually different exemplar, this manipulation should reduce the usefulness of sensory/perceptual information and place more demands on input from semantic memory. We predicted, therefore, that patients with semantic dementia would show relatively preserved recognition memory in the perceptually identical (PI) condition but that their ability to select the target item in the perceptually different (PD) condition would be reduced relative to control performance as a result of the patients' impaired conceptual knowledge of the items. By contrast, the patients with early Alzheimer's disease should be impaired relative to controls but with equally poor performance on the PI and PD conditions of the episodic task.

2. Experiment one

2.1. Method

2.1.1. Participants

Eight patients with a diagnosis of semantic dementia (mean age 62.6 years, SD = 6.2), eight amnesic patients with presumed early Alzheimer's disease (mean age 73.1 years, SD = 6.5) and 18 elderly healthy control participants (mean age 67.4 years, SD = 5.7) were tested on two specially designed experimental tasks tapping semantic and episodic memory.

All the patients tested in our study presented through the Memory Clinic at Addenbrooke's Hospital, Cambridge, UK and have been tested longitudinally on an extensive neuropsychological battery. The eight patients with semantic dementia have all shown progressive difficulty with word production and both verbal and non-verbal comprehension, as measured by subtests from the Hodges semantic battery [20] such as category fluency, word-picture matching and synonym judgement, and the Pyramids and Palmtrees test [25] (see Table 1). It is worth noting that the word-picture matching task is quite an easy test of semantics, and some of the milder patients performed relatively normally. On a more stringent measure like synonym judgement, however, all the patients with semantic dementia were several standard

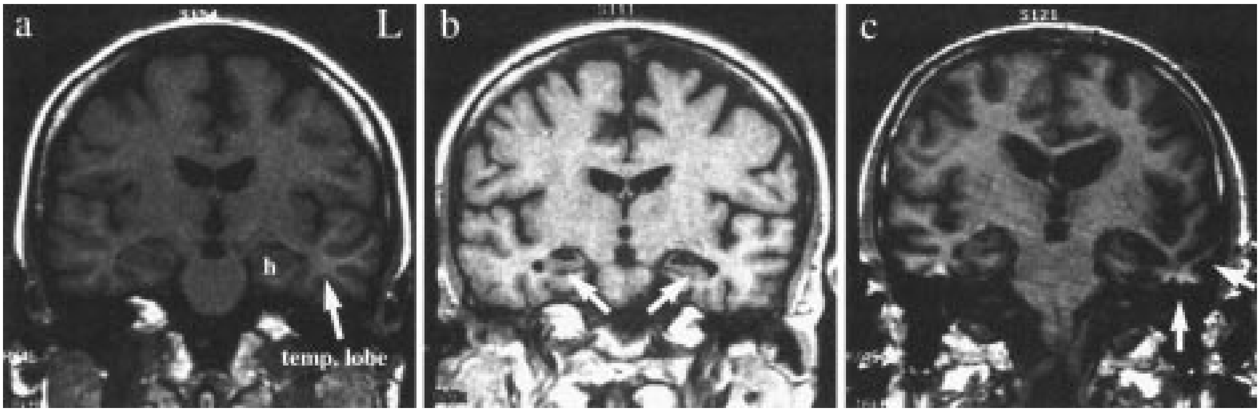

Fig. 1. Coronally oriented MRI scans showing the different patterns of damage due to semantic dementia and Alzheimer's disease. Panel a shows the brain of a healthy control subject, marking the temporal lobe (arrow) and hippocampal complex (h). Panel b shows the scan of an amnesic patient in the early stages of presumed Alzheimer's disease, with bilateral shrinkage of the hippocampal complex (arrows). Panel c displays the brain scan of a patient with semantic dementia, with striking atrophy of inferior and lateral regions of the left temporal lobe (arrows).

deviations outside the control mean. Like other reported cases, the majority of the patients showed no noticeable decline on tests tapping other cognitive domains such as non-verbal episodic memory, working memory, and visuospatial abilities.

The amnesic patients with presumed early Alzheimer's disease presented with a history of progressive decline in new learning of verbal and non-verbal material. Neuropsychological testing (see Table 1) demonstrated that the group performed as well as control participants on most tests of semantic memory (although category fluency was mildly abnormal, possibly reflecting either early frontal or temporal involvement in the disease process). The patients were markedly impaired on tests of episodic memory, such as recall of the Rey Complex Figure [39] (see Table 1) but had working memory and visuo-perceptual skills within the normal range.

2.1.2. Neuroimaging

Coronally oriented MRI scans for the patients with semantic dementia revealed focal atrophy to one or both infero-lateral temporal lobe(s), with relative preservation of the hippocampal complex. CT and/or coronally oriented MRI scans for the amnesic patients with presumed early Alzheimer's disease showed selective hippocampal atrophy, with relatively little involvement of the lateral temporal lobes. Fig. 1 presents sample images from (a) a healthy control subject, (b) an amnesic patient with presumed Alzheimer's disease, and (c) a patient with semantic dementia.

2.1.3. Materials

Forty coloured pictures of familiar objects and animals, scanned from picture books and magazines, were used as stimulus items in the Naming task. In one condition (perceptually identical, PI) of the Recognition Memory task, the same 40 items were used as targets; in the other condition (perceptually different, PD), 40 different pictures constituted the targets. Each PD picture depicted the same stimulus *object* as an original item but displayed either a different orientation (e.g. a side view of an elephant vs a front view) or a different example of the same item (e.g. a touch-button vs a round-dial phone). A further 160 novel items, semantically related to the target items, were used as foils in the recognition memory task.

2.1.4. Procedure

The experimental design consisted of two tests. In the initial semantic test, the participants were asked to name 40 coloured pictures of familiar objects and animals (see Fig. 2a for an example). Thirty minutes later (during which time they engaged in a filler task not involving pictures), recognition memory for the 40 items was tested. Participants were asked to select the item seen earlier from sets of three consisting of either (1) the perceptually identical (PI) target plus two semantic foils, as in Fig. 2b or (2) a perceptually different (PD) exemplar of the same item (e.g. a different type of telephone) plus two semantic foils, as in Fig. 2c. The position of the target amongst the foils was balanced across arrays for each of the three positions on the page. Participants were asked to indicate which of the three items they had seen previously by pointing to their choice.

2.2. Results

As illustrated in Fig. 3a there was a significant effect of group ($F(2,31) = 25.5$, $p < 0.001$) on the picture naming task. Further statistical analyses revealed that the patients with semantic dementia were poorer at naming the pictures of objects compared to the other two groups (controls: $t(7) = 4.2$, $p < 0.005$; patients

Fig. 2. Examples of the stimuli used in (a) the semantic naming task and (b) the perceptually identical (PI) and (c) perceptually different (PD) conditions of the episodic recognition memory test.

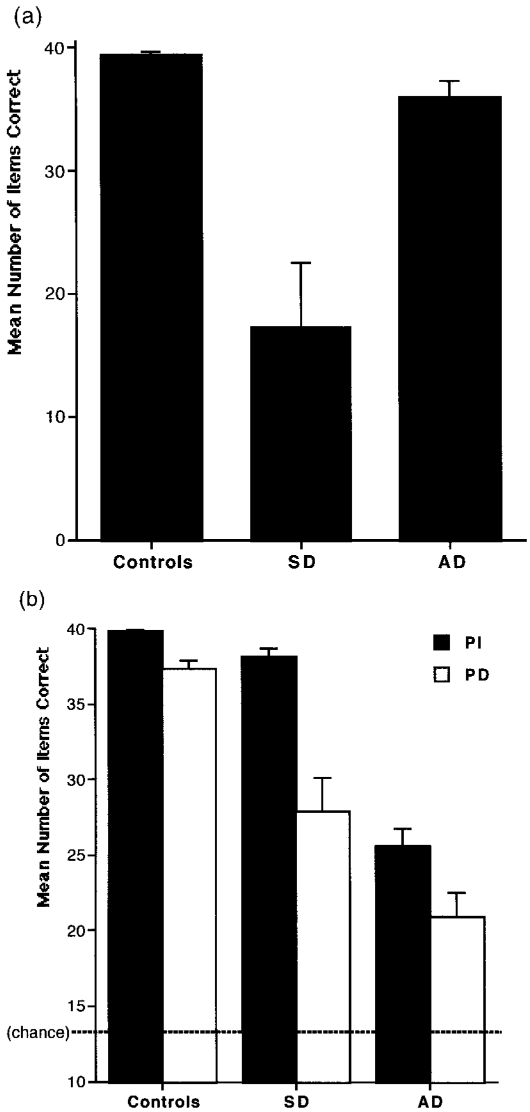

Fig. 3. Performance of the controls, the patients with semantic dementia (SD), and the patients with presumed Alzheimer's disease (AD) on (a) the semantic picture naming task, and (b) the perceptually identical (PI) and perceptually different (PD) conditions of the episodic recognition memory test. Standard errors are represented as bars.

with presumed Alzheimer's disease: $t(8)=3.4$, $p < 0.01$).

Fig. 3b shows the mean scores (and standard errors) for the three groups in both conditions of the episodic task. Statistical analyses revealed main effects of both group ($F(2,31)=128.9$, $p < 0.001$) and condition ($F(1,31)=63.9$, $p < 0.001$), plus a significant interaction between the two factors ($F(2,31)=10.8$, $p < 0.001$). For both the control group and the patients with semantic dementia, there was a significant advantage in recognition memory on the perceptually identical as compared to perceptually different targets (controls: $t(17)=5.6$, $p < 0.001$; patients with

Table 2
Summary of item correspondence between performance of six of the patients with semantic dementia on the semantic picture naming test and the perceptually different (PD) condition of the episodic memory task[a]

		PD recognition	
		✓	x
Picture naming	✓	97	22
	x	59	27

[a] Patients were only credited for consistent correct or incorrect responses across both exposures of the naming test. Two of the patients were excluded from this analysis as their language problems precluded any naming of the items.

semantic dementia: $t(7)=6.1$, $p < 0.001$). The patients with early Alzheimer's disease showed no reliable difference between these two conditions of the episodic memory task ($t(7)=2.2$, ns).

Further statistical analyses revealed significant effects of group for both the perceptually identical ($F(2,31)=211.2$, $p < 0.001$) and perceptually different ($F(2,31)=53.5$, $p < 0.001$) conditions. In the PI condition, there was no significant difference between the control participants and the patients with semantic dementia ($t(7)=3.1$, ns). By contrast, the patients with early Alzheimer's disease performed more poorly on this condition compared to both the control participants ($t(7)=13.1$, $p < 0.001$) and the patients with semantic dementia ($t(14)=10.3$, $p < 0.001$). In the PD condition, there were significant differences between all of the groups (controls vs semantic dementia: $t(8)=4.3$, $p < 0.005$; controls vs Alzheimer's disease: $t(8)=9.9$, $p < 0.001$; semantic dementia vs Alzheimer's disease: $t(14)=2.6$, $p < 0.05$).

In order to assess our hypothesis about the impact of semantic knowledge on new learning, we examined the degree of item-specific correspondence between performance on the picture naming task and in the perceptually different condition of the episodic test. Two patients were excluded from this analysis because they produced no correct picture naming responses. Although object naming in semantic dementia is not a *pure* measure of the integrity of semantic knowledge, because there is evidence that some patients show additional post-semantic naming difficulties [14,29], naming ability is highly sensitive to and correlated with degree of semantic impairment. We found a significant item correspondence between picture naming and episodic memory for the perceptually different stimuli ($\chi^2=4.57$, $p < 0.05$). Table 2 reveals that 55% of the items that failed to result in correct recognition memory choices for patients with semantic dementia were also not named correctly. Furthermore, despite the patients' profound naming difficulties, more than

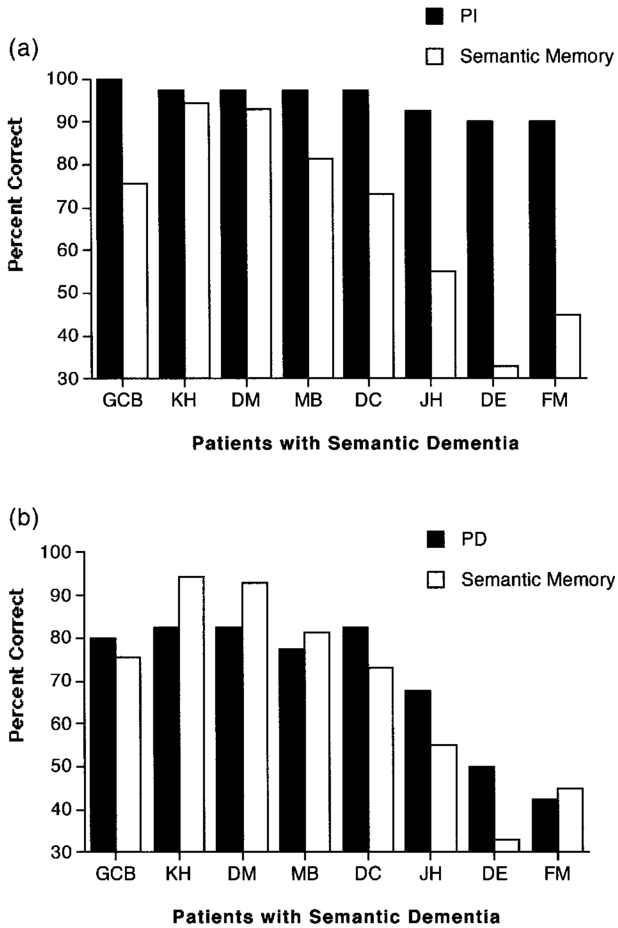

Fig. 4. Performance of each individual patient with semantic dementia on (a) the perceptually identical and (b) the perceptually different conditions of the episodic memory test (dark bars), and a composite semantic memory score (light bars) based on performance on the 3 picture version of the Pyramids and Palmtrees test [25] and a 64-item word-picture matching test (see Table 1 for details).

three-fifths (62%) of the items that were correctly selected in the PD condition of the episodic memory task were 'known' to the patients (as measured by correct naming).

Further confirmation of a direct connection between semantic memory and performance on the PD, but not the PI, condition in semantic dementia is demonstrated in Figs. 4a and b. These graphs show each patient's performance on the two episodic conditions contrasted with an index of semantic memory (a composite score based on the picture version of the Pyramid and Palmtrees Test [25] and a 64-item word-picture matching test). A regression analysis based on these data revealed a significant interaction between the composite semantic memory score and the two versions of the episodic memory test. The slope of the PI condition with respect to semantic memory was significantly less than that for the PD version (b (PI) = 0.15, b (PD) = 0.65; t (12) = 3.7, $p < 0.005$).

2.3. Discussion

In our experiment, patients with semantic dementia showed impaired semantic knowledge, as measured by picture naming, yet relatively preserved episodic memory, as measured by selection of an identical target picture in a recognition memory test; this combination of results is contrary to the predictions of Tulving's SPI model [57,59]. The patients only showed impaired episodic memory when the target item seen at study was replaced with a perceptually different example of the same object at test. As we had predicted, the patients with semantic dementia tended to achieve a high level of success in recognising PD objects as episodically familiar only if they retained some substantial semantic knowledge about the target, as measured directly by the patients' ability to name the items and indirectly by the concordance (shown in Fig. 4b) between performance on the PD items and other tests of semantic memory.

By contrast, the amnesic patients were significantly impaired on both conditions of the episodic memory task, despite demonstrating relatively normal semantic knowledge about the target stimuli in the picture naming test. As mentioned in the Introduction, the evidence for a dissociation in this direction (e.g. impaired episodic memory in combination with normal semantic memory) is well documented in numerous other studies [40,61,64].

The interpretation of this experiment, at least with respect to semantic dementia, must be treated with some caution because the control subjects performed close to ceiling on the PI condition, making it difficult to establish whether PI episodic memory was truly normal in the patient group. This is a pervasive problem in recognition memory experiments, but it is worth noting that normal episodic memory in semantic dementia has been documented on a recognition memory test in which control subjects do *not* perform at ceiling [12].

It is also important to exclude two uninteresting potential explanations for the observed performance in semantic dementia on the PD condition. The first is that the patients might have a high-level perceptual deficit which interferes with their ability to perceive objects from different views. They do not: on an object matching task [26] (see Table 1), in which the participant has to select which two photographs (out of three) represent the same object viewed from different orientations, all patients showed normal performance. Secondly, the impairment of the patients with semantic dementia on the PD condition might, in theory, be due to the PD exemplars being harder to identify than the PI exemplars. It is unlikely, however, that the less 'identifiable' version of each item was consistently assigned to the PD condition, because the exemplar photographs for each target item were distributed randomly between the PI and PD sets. It seems improbable, therefore, that the results obtained here are due to differences in object identification across PI and PD exemplars of the same item.

Our interpretation of the striking results in this experiment is that the manipulation in the PD condition had two effects: (1) it decreased the usefulness of the sensory/perceptual information available from seeing the item earlier in the picture naming task; and (2) it made the episodic decision more reliant upon the conceptual information activated by the original picture. In support of this hypothesis, we found a significant item-specific correspondence between picture naming in the semantic study phase and episodic memory for the perceptually different stimuli (see Table 2).

One of the cases of semantic dementia who participated in Experiment 1, JH, was tested in an additional experiment (Experiment 2) in which it was possible to manipulate more directly the status of her semantic knowledge regarding the material to be remembered. Following an assessment of her knowledge for previously familiar items, an episodic memory test using perceptually identical (PI) and perceptually different (PD) targets was constructed using one set of items still 'known' to the patient, and another set that were now 'unknown' to her. On the basis of the results from Experiment 1, we predicted that JH would have significantly poorer recognition memory in the PD 'unknown' condition compared to the other conditions (i.e. PI and PD 'known' and PI 'unknown'). Note that we always place the terms 'known' and 'unknown' in inverted commas, to signal the important acknowledgement that semantic knowledge about objects and concepts degrades along a continuum and is essentially never all-or-none.

3. Experiment two

3.1. Method

3.1.1. Materials

JH (aged 59 years) was initially given both a picture naming test and a comprehension test (spoken-word-to-picture matching) on all 260 line drawings of familiar objects from the Snodgrass and Vanderwart picture corpus [47]. On the basis of her success on these two tasks, 76 items were selected such that half (38) could be classified as concepts still 'known' by JH (items that she could name and comprehend) while the other half were now 'unknown' (i.e. previously familiar objects that she could no longer name/comprehend). The 'known' and 'unknown' sets were matched as closely as possible for familiarity ('known' set mean 4.16, SD = 0.5; 'unknown' set mean 3.36, SD = 0.5) and for syllable length. For 38 items (19 pairs of 'known' and 'unknown' pictures), another perceptually different black and white line drawing of the same object was selected from other picture naming tests. In the PI condition, the foils were always pictures from the Snodgrass and Vanderwart picture corpus [47], while in the PD condition, the foils were the black and white line drawings from the other picture sets.

3.1.2. Procedure

In the initial semantic naming task, each of the 38 PI target drawings (half 'known' and half 'unknown') was presented singly and JH was asked, without any time pressure, to name the object, and to provide identifying information about it. Fifteen minutes after the study phase (filled with a task not involving pictures), yes/no recognition memory was tested for all 76 items, with the 'known'/'unknown' manipulation applying to both targets and foils, the PI/PD manipulation applying to targets, and the various types of stimulus item occurring in a random order. The line drawings were presented singly and JH was asked to say whether or not she thought each item had been seen in the study phase.

3.2. Results

Fig. 5a confirms that JH possessed substantially more semantic knowledge, as measured by the production of an appropriate name, a superordinate category (e.g. 'fruity one' for *apple*) or a piece of functional semantic knowledge (e.g. 'put on the hand' for *glove*), for items in the pre-selected 'known' set compared with stimuli which were classified as 'unknown' for her ($F(1,36) = 47.42$, $p < 0.001$). Fig. 5b shows how JH's semantic knowledge influenced her ability to respond 'yes' to target objects that had been seen in the study phase (hits) and to reject items which were not seen previously (errors noted as false positives, FP) for each of the four test conditions (PI and PD 'known'; PI and PD 'unknown'). As predicted, JH showed a statistically significant superiority in yes/no recognition memory for items in the PI 'unknown' condition compared to the PD 'unknown' condition ($p < 0.05$), as measured by comparing the d' measures of sensitivity for each of the conditions [30] ($d' = 2.94$ for PI 'unknown' and 1.14 for PD 'unknown'). By contrast, she performed perfectly on both the PI and PD 'known' items ($d' = 3.88$ for PI and PD 'known'). Note that, in the PI 'unknown' condition, JH correctly selected all of the items presented 15 min earlier for naming (hit rate = 1.0) but made three false positive errors to foil pictures.

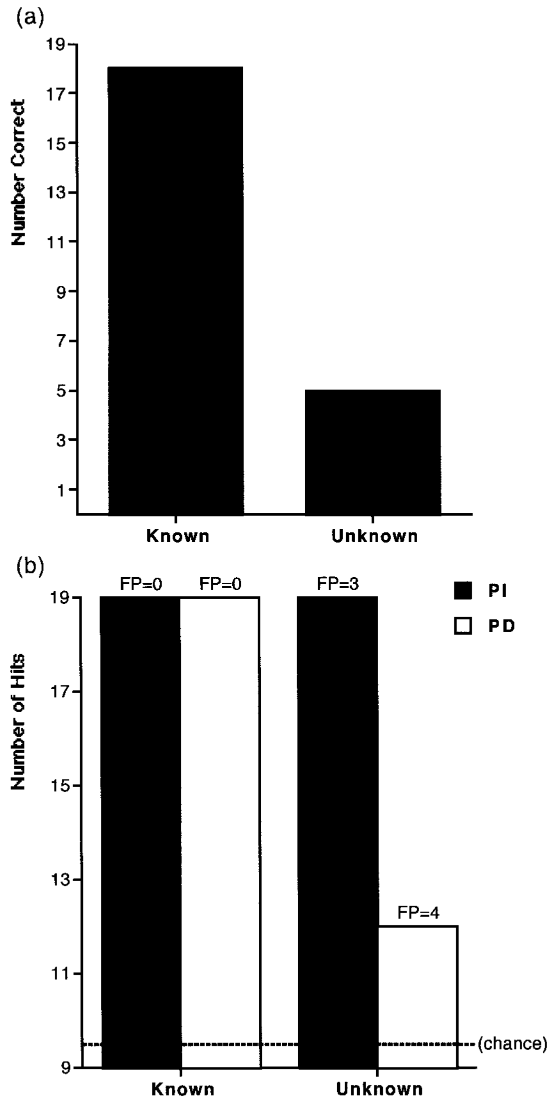

Fig. 5. (a) JH's semantic knowledge of the 'known' and 'unknown' sets of familiar objects. An item was scored as correct if JH produced an appropriate name, a superordinate category (e.g. 'music one' for *piano*) or a piece of functional semantic knowledge (e.g. 'for your timings' for *clock*) about the object. (b) JH's performance on the perceptually identical (PI) and perceptually different (PD) conditions of the 'known' and 'unknown' familiar objects recognition memory test.

3.3. Discussion

This second experiment compared performance on PI and PD recognition memory, in a single case of semantic dementia, for familiar items which could be classified as still 'known' or now 'unknown' to the patient on the basis of prior assessments of comprehension as well as naming. In the circumstances where JH's semantic knowledge about an item was degraded, she was significantly less likely to succeed in recognising the perceptually different item as one seen previously in the study phase of the experiment. These results provide convincing additional evidence that it is degraded semantic knowledge for the materials used in Experiment 1, rather than just the ability to name those pictures, that influenced performance on the PD condition in our group study of semantic dementia.

Interestingly, JH also showed a mild impairment on the 'unknown' PI condition in Experiment 2, by responding 'yes' to three items which were not seen at study. Three of the semantic dementia patients in Experiment 1 (including JH, see Fig. 4a) also made errors in forced choice recognition memory on a very small number of trials in the PI condition. On the basis of existing behavioural and neuroanatomical evidence, we suggest that episodic memory for perceptually identical stimuli can be preserved early in semantic dementia but, as the syndrome progresses, this cognitive ability may be compromised by the encroachment of the disease into medial temporal lobe structures. The data in Fig. 4a, demonstrating that it was the three most severely semantically impaired patients tested in Experiment 1 (including JH) who were mildly impaired on the PI condition, are consistent with this hypothesis.

4. General discussion

In our two experiments, patients with semantic dementia showed impaired semantic knowledge yet relatively preserved episodic memory for perceptually identical items. These results refute Tulving's hypothesis about the hierarchical nature of episodic and semantic memory: it is clearly not the case that the creation of a new episodic memory requires normal functioning of the semantic knowledge system. It was only possible to demonstrate direct effects of impaired semantic knowledge on new episodic learning when the studied target item was replaced by a perceptually different (PD) example of the same object at test.

Our interpretation of these results is that, in neurologically normal subjects, perceptual information and conceptual knowledge about depicted items both support new episodic learning. In the circumstances where there is reduced or impoverished output from the semantic system (as in semantic dementia), episodic memory is only normal if the target picture in the recognition memory test is perceptually similar to the studied item (as was true in the PI condition). The manipulation in the PD condition decreases the usefulness of the sensory/perceptual information available to the subject and, as a result, the episodic decision required in the recognition memory test becomes more contingent upon semantic knowledge. Thus, patients with semantic dementia show an item-specific correspondence between the status of their semantic knowl-

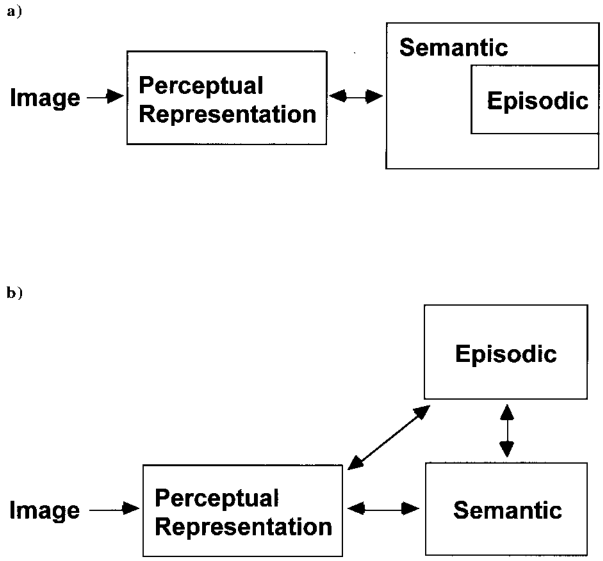

Fig. 6. Diagrams illustrating (a) Tulving's SPI model, demonstrating the dependence of episodic memory upon semantic memory; and (b) our revision, which emphasises the reliance of episodic memory upon perceptual input (e.g. stored structural descriptions) as well as semantic memory. It is also likely that there are links between other sensory modalities (e.g. auditory, tactile, etc.) and episodic memory.

edge about an item and their ability to select it as one seen previously in the PD condition.

4.1. A multiple input account of new learning in humans

This study has advanced our understanding of both cognitive and neural aspects of long-term memory. The results suggest that the relatively 'normal' recognition memory seen in semantic dementia [12], and the ability of normal participants to remember unfamiliar stimuli [3,5,54], is supported by information from perceptual areas in the brain.

At a cognitive level, we are suggesting that the ability to lay down a new memory relies upon a number of different inputs to episodic memory. Tulving's SPI model [57,58] is based on the view that the encoding of information is serial and that perceptual information about a stimulus feeds only into the semantic system, which subsequently transmits information about the meaning of the stimulus to episodic memory (see Fig. 6a). The encoding of information into episodic memory is dependent, therefore, upon the output from the semantic system. Our results suggest that this premise cannot be correct: instead we propose, as illustrated in Fig. 6b, that information from components of the perceptual system can feed directly into episodic memory. Thus perceptual information will — typically in conjunction with, but even in the absence of meaningful input from the semantic system — support new learning.

This revision to Tulving's SPI model also explains why patients with semantic dementia typically perform more poorly on verbal tests of new learning (words) compared to those based on non-verbal stimuli (e.g. pictures) [12,63]. In semantic dementia, when the episodic decision is dependent upon input from the semantic system (as in the perceptually different condition), recognition memory is impaired. New episodic learning of word-based material requires substantial access to semantic information because there is relatively little perceptual information available to aid discrimination in an episodic memory task. By contrast, pictures (in particular, landscapes, coloured drawings, etc.) provide large amounts of useful visual information, reducing the need for input from semantic memory. Face stimuli presumably occupy an intermediate position in the continuum of perceptual and semantic affordance: while faces are perceptually rich in information, they are also more perceptually confusable than objects because faces are inherently visually similar. As there has been no detailed study comparing recognition memory for words, faces and objects in semantic dementia, further studies are required to address this prediction about relative levels of recognition memory for these stimulus classes in semantic dementia.

4.2. The neural basis of long-term memory

The cognitive model proposed here fits with our understanding of the neural basis of long-term memory. It is widely agreed by neuroscientists that the hippocampal complex, which is typically damaged in amnesic patients [2,42], is critically involved in the acquisition of new episodic and semantic memories [13,31,37,43,51,53,66], and that inferolateral areas of the temporal lobes, which are damaged in semantic dementia [36], form the neural substrate for enduring autobiographical and semantic knowledge [13,22,23,31,37,52].

The idea of gradual cortical consolidation is compatible with poor retrieval of recent, and better preserved distant, autobiographical memories in amnesia [42,66], and also with the opposite gradient recently demonstrated for semantic dementia [13,49]. The same idea fits the data presented here: while new learning was impaired in the amnesic patients with presumed early Alzheimer's disease, it was not impaired (except in the perceptually different condition) in the patients with semantic dementia.

To unite the cognitive and neural aspects of this hypothesis, there must be multiple links between different areas in the temporal lobe (and other cortical regions) to the hippocampal complex. For example, while there is obviously a pathway from the neuroanatomical areas subserving semantic memory (in the infero-lateral temporal lobe) to the hippocampal complex, there must also be connections from a higher-order visual system [1], and from perceptual systems dedicated to the analysis of auditory and tactile stimuli [60].

In summary, a model of long-term memory in which episodic memory takes input solely or principally from semantic knowledge cannot explain why patients with semantic dementia can, under certain conditions, show normal new episodic learning. Instead, our results argue that inputs from different neocortical areas in the brain, which subserve perceptual analysis and semantic memory, work in concert to support new learning. This theory provides a more parsimonious explanation than other views (e.g. Tulving's SPI model) for the patterns of results found in both the normal and neuropsychological memory literatures. Furthermore, the research reported here clearly demonstrates that patients with semantic dementia provide cognitive neuropsychologists with an unprecedented opportunity to investigate the architecture of long-term memory, and to advance our understanding of how the human brain acquires, stores and retrieves episodic and semantic information.

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References

[1] Amaral DG, Insausti R, Cowan WM. The entorhinal cortex of the monkey: I. Cytoarchitectonic organization. Journal of Comparative Neurology 1987;264:326–55.
[2] Braak H, Braak E. Neuropathological staging of Alzheimer-related changes. Acta Neuropathologica 1991;82:239–59.
[3] Bruce V. Changing faces: visual and non-visual coding processes in face recognition. British Journal of Psychology 1982;73:105–16.
[4] Brun A, Englund B, Gustafson L, Passant U, Mann DMA, Neary D, Snowden JS. Consensus statement. Clinical and neuropathological criteria for frontotemporal dementia. Lund and Manchester groups. Journal of Neurology, Neurosurgery and Psychiatry 1994;57:416–8.
[5] Cooper LA, Schacter DL, Ballesteros S, Moore C. Priming and recognition of transformed three-dimensional objects: effects of size and reflection. Journal of Experimental Psychology: Learning, Memory, and Cognition 1992;18:43–57.
[6] Edwards-Lee T, Miller BL, Benson DF, Cummings JL, Russell GL, Boone K, Mena I. The temporal variant of frontotemporal dementia. Brain 1997;120:1027–40.
[7] Fleischman DA, Vaidya CJ, Lange KL, Gabrieli JDE. A dissociation between perceptual explicit and implicit memory processes. Brain and Cognition 1997;35:42–57.
[8] Gabrieli JDE, Cohen NJ, Corkin S. The impaired learning of semantic knowledge following bilateral medial temporal-lobe resection. Brain and Cognition 1988;7:157–77.
[9] Gabrieli JDE, Fleischman DA, Keane MM, Reminger SL, Morrell F. Double dissociation between memory systems underlying explicit and implicit memory in the human brain. Psychological Science 1995;6:76–82.
[10] Girling DM, Berrios GE. On the relationship between senile cerebral atrophy and aphasia. History of Psychiatry 1994;5:542–7.
[11] Glisky EL, Schacter DL. Long-term retention of computer learning by patients with memory disorders. Neuropsychologia 1988;26:173–8.
[12] Graham KS, Becker JT, Hodges JR. On the relationship between knowledge and memory for pictures: evidence from the study of patients with semantic dementia and Alzheimer's disease. Journal of the International Neuropsychological Society 1997;3:534–44.
[13] Graham KS, Hodges JR. Differentiating the roles of the hippocampal complex and the neocortex in long-term memory storage: evidence from the study of semantic dementia and Alzheimer's disease. Neuropsychology 1997;11:77–89.
[14] Graham KS, Patterson K, Hodges JR. Progressive pure anomia: insufficient activation of phonology by meaning. Neurocase 1995;1:25–38.
[15] Graham KS, Pratt KH, Hodges JR. A reverse temporal gradient for public events in a single case of semantic dementia. Neurocase 1998;4:461–70.
[16] Harasty JA, Halliday GM, Code C, Brooks WS. Quantification of cortical atrophy in a case of progressive fluent aphasia. Brain 1996;119:181–90.
[17] Hodges JR, Garrard P, Patterson K. Semantic dementia. In: Kertesz A, Munoz DG, editors. Pick's disease and Pick complex. Wiley-Liss, 1998. p. 83–104.
[18] Hodges JR, Graham KS. A reversal of the temporal gradient for famous person knowledge in semantic dementia: implications for the neural organisation of long-term memory. Neuropsychologia 1998;36:803–25.
[19] Hodges JR, Graham N, Patterson K. Charting the progression in semantic dementia: implications for the organisation of semantic memory. Memory 1995;3:463–95.
[20] Hodges JR, Patterson K. Is semantic memory consistently impaired early in the course of Alzheimer's disease? Neuroanatomical and diagnostic implications. Neuropsychologia 1995;33:441–59.
[21] Hodges JR, Patterson K. Nonfluent progressive aphasia and semantic dementia: a comparative neuropsychological study. Journal of the International Neuropsychological Society 1996;2:511–24.
[22] Hodges JR, Patterson K, Oxbury S, Funnell E. Semantic dementia: progressive fluent aphasia with temporal lobe atrophy. Brain 1992;115:1783–806.
[23] Hodges JR, Patterson K, Tyler LK. Loss of semantic memory: implications for the modularity of mind. Cognitive Neuropsychology 1994;11:505–42.
[24] Hodges JR, Patterson K, Ward R, Garrard P, Bak T, Perry R, Gregory CA. The differentiation of semantic dementia and frontal lobe dementia (temporal and frontal variants of frontotemporal dementia) from early Alzheimer's disease: a comparative neuropsychological study. Neuropsychology 1999;13:31–40.
[25] Howard D, Patterson K, editors. Pyramids and palm trees: a test of semantic access from pictures and words. Bury St Edmunds, UK: Thames Valley Test Company, 1992.
[26] Humphreys GW, Riddoch MJ. Routes to object constancy: implications from neurological impairments of object constancy.

Quarterly Journal of Experimental Psychology 1984;36A:385–415.

[27] Keane MM, Gabrieli JDE, Mapstone HC, Johnson KA, Corkin S. Double dissociation of memory capacities after bilateral occipital-lobe or medial temporal-lobe lesions. Brain 1995;118:1129–48.

[28] Kirshner HS, Tanridag O, Thurman L, Whetsell WO. Progressive aphasia without dementia: two cases with focal spongiform degeneration. Annals of Neurology 1987;22:527–32.

[29] Knott RA, Patterson K, Hodges JR. Lexical and semantic binding effects in short-term memory: evidence from semantic dementia. Cognitive Neuropsychology 1997;14:1165–216.

[30] Macmillan NA, Creelman CD. Detection theory: a user's guide. Cambridge: Cambridge University Press, 1991.

[31] McClelland JL, McNaughton BL, O'Reilly RC. Why there are complementary learning systems in the hippocampus and neocortex: insights from the success and failure of connectionist models of learning and memory. Psychological Review 1995;102:419–57.

[32] Mesulam M-M. Slowly progressive aphasia without generalized dementia. Annals of Neurology 1982;11:592–8.

[33] Miller BL, Chang L, Mena I, Boone K, Lesser IM. Progressive right frontotemporal degeneration: clinical, neuropsychological, and SPECT characteristics. Dementia 1993;4:204–13.

[34] Miller BL, Cummings JL, Villanueva-Meyer J, Boone K, Mehringer CM, Lesser IM, Mena I. Frontal lobe degeneration: clinical, neuropsychological, and SPECT characteristics. Neurology 1991;41:1374–82.

[35] Mishkin M, Vargha-Khadem F, Gadian DG. Amnesia and the organization of the hippocampal system. Hippocampus 1998;8:212–6.

[36] Mummery CJ, Patterson K, Wise RJS, Price CJ, Hodges JR, Vandenbergh R. Disrupted temporal lobe connections in semantic dementia. Brain 1999;122:61–73.

[37] Murre JMJ. TraceLink: a model of amnesia and consolidation of memory. Hippocampus 1996;6:675–84.

[38] Nyberg L, Tulving E. Classifying human long-term memory: evidence from converging dissociations. European Journal of Cognitive Psychology 1996;8:163–83.

[39] Osterrieth PA. Le test de copie d'une figure complexe. Archives de Psychologie 1944;30:205–20.

[40] Parkin AJ. Residual learning capability in organic amnesia. Cortex 1982;18:417–40.

[41] Pick A. über die Beziehungen der senilen Hirnatrophie zur Aphasie. Prager Medicinische Wochenschrift 1892;17:165–7.

[42] Press GA, Amaral DG, Squire LR. Hippocampal abnormalities in amnesic patients revealed by high-resolution magnetic resonance imaging. Nature 1989;341:54–7.

[43] Reed JM, Squire LR. Impaired recognition memory in patients with lesions limited to the hippocampal formation. Behavioral Neuroscience 1997;111:667–75.

[44] Scheltens P, Ravid R, Kamphorst W. Pathologic findings in a case of primary progressive aphasia. Neurology 1994;44:279–82.

[45] Schwartz MF, Marin OSM, Saffran EM. Dissociations of language function in dementia: a case study. Brain and Language 1979;7:277–306.

[46] Schwarz M, De Bleser R, Poeck K, Weis J. A case of primary progressive aphasia: a 14-year follow-up study with neuropathological findings. Brain 1998;121:115–26.

[47] Snodgrass JG, Vanderwart M. A standardized set of 260 pictures: norms for name agreement, image agreement, familiarity, and visual complexity. Journal of Experimental Psychology: Human Learning and Memory 1980;6:174–215.

[48] Snowden JS, Goulding PJ, Neary D. Semantic dementia: a form of circumscribed cerebral atrophy. Behavioural Neurology 1989;2:167–82.

[49] Snowden JS, Griffiths HL, Neary D. Semantic-episodic memory interactions in semantic dementia: implications for retrograde memory function. Cognitive Neuropsychology 1996;13:1101–37.

[50] Snowden JS, Neary D, Mann DMA. Fronto-temporal lobar degeneration: fronto-temporal dementia, progressive aphasia, semantic dementia. New York: Churchill Livingstone, 1996.

[51] Squire LR. Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. Psychological Review 1992;99:195–231.

[52] Squire LR, Alvarez P. Retrograde amnesia and memory consolidation: a neurobiological perspective. Current Opinion in Neurobiology 1995;5:169–77.

[53] Squire LR, Zola SM. Episodic memory, semantic memory, and amnesia. Hippocampus 1998;8:205–11.

[54] Srinivas K. Representation of rotated objects in explicit and implicit memory. Journal of Experimental Psychology: Learning, Memory, and Cognition 1995;21:1019–36.

[55] Tulving E. Elements of episodic memory. Oxford: Clarendon Press, 1983.

[56] Tulving E. Episodic and semantic memory. In: Tulving E, Donaldson W, editors. Organisation of memory. New York and London: Academic Press, 1972. p. 381–403.

[57] Tulving E. Organization of memory: quo vadis? In: Gazzaniga MS, editor. The cognitive neurosciences. Cambridge, MA: MIT Press, 1995.

[58] Tulving E, Markowitsch HJ. Episodic and declarative memory: the role of the hippocampus. Hippocampus 1998;8:198–204.

[59] Tulving E, Markowitsch HJ. Memory beyond the hippocampus. Current Opinion in Neurobiology 1997;7:209–16.

[60] Van Hoesen GW. The primate parahippocampal gyrus: new insights regarding its cortical connections. Trends in Neurosciences 1982;5:345–50.

[61] Vargha-Khadem F, Gadian DG, Watkins KE, Connelly A, Van Paesschen W, Mishkin M. Differential effects of early hippocampal pathology on episodic and semantic memory. Science 1997;277:376–80.

[62] Verfaellie M, Croce P, Milberg WP. The role of episodic memory in semantic learning: an examination of vocabulary acquisition in a patient with amnesia due to encephalitis. Neurocase 1995;1:291–304.

[63] Warrington EK. Selective impairment of semantic memory. Quarterly Journal of Experimental Psychology 1975;27:635–57.

[64] Wood F, Ebert V, Kinsbourne M. The episodic-semantic memory distinction in memory and amnesia: clinical and experimental observations. In: Cermak LS, editor. Human memory and amnesia. Hillsdale, NJ: Erlbaum, 1982. p. 167–94.

[65] Zola-Morgan S, Cohen NJ, Squire LR. Recall of remote episodic memory in amnesia. Neuropsychologia 1983;21:487–500.

[66] Zola-Morgan S, Squire LR, Amaral DG. Human amnesia and the medial temporal region: enduring memory impairment following a bilateral lesion limited to field CA1 of the hippocampus. Journal of Neuroscience 1986;6:2950–67.