
Different Patterns of Autobiographical Memory Loss in Semantic Dementia and Medial Temporal Lobe Amnesia: a Challenge to Consolidation Theory

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Abstract

Temporally graded retrograde memory loss, with a disproportionate impairment of recent relative to remote memories, is considered a hallmark of medial temporal lobe amnesia. According to consolidation theory, the hippocampal complex, which includes the hippocampal formation, parahippocampal gyrus, the entorhinal and perirhinal cortex, plays a time-limited role in memory, needed only until consolidation in the neocortex is complete (Squire, *Psychological Review* 1992; 99: 195–231). Recent support for this theory comes from findings of a reverse gradient in people with semantic dementia with neocortical degeneration but a relatively preserved hippocampal complex (Hodges and Graham, *Neuropsychologia* 1998; 36: 803–25). Consolidation theory is challenged by evidence that remote autobiographical memory is not always spared in amnesia (Nadel and Moscovitch, *Current Opinion in Neurobiology* 1997; 7: 217–27) and that semantic memory becomes highly personalized in semantic dementia (Snowden *et al.*, *Memory* 1995; 3: 225–46). According to Nadel and Moscovitch, the hippocampal complex is needed to retain and retrieve detailed memories of autobiographical episodes no matter how old they are. To test consolidation theory against the opposing view, we investigated the role of the hippocampal complex in recent and remote autobiographical and personal semantic memory by contrasting the memory of a semantic dementia patient, EL, with that of an amnesic patient, KC, using family photographs as recall cues. KC demonstrated a complete loss of autobiographical episodes with a sparing of autobiographical facts; EL demonstrated well-preserved memory for episodes with a reverse gradient for personally relevant names. The influence of autobiographical significance on memory for names of public figures was examined further by comparing the effect that familiarity and recollection had on recognition of names of famous people and famous places. EL's memory was influenced by autobiographical significance, whereas KC's was not. We propose that the hippocampal complex plays a permanent role in the storage and retrieval of autobiographical episodes and that autobiographical significance may affect semantic representations.

Introduction

Research on the neuropsychology of retrograde amnesia has important implications for understanding the organizational structure of long-term memory and the neural mechanisms mediating memory storage and retrieval. Whereas anterograde amnesia involves an impaired ability to learn new information and to store new memories, retrograde amnesia refers to the loss of memories acquired prior to the onset of brain damage or disease. The types of memories that are selectively preserved or impaired are not consistent across all patients with retrograde memory loss. Rather, patterns of spared ability and deficit have been found to vary systematically between distinct patient populations, depending on the specific lesion site and the extent of brain damage (Warrington

and McCarthy, 1988; Hodges and McCarthy, 1995; Kapur, 1999). By comparing the patterns of memory loss observed among patient populations, researchers hope to uncover the cognitive principles that govern the categorization of long-term memories and that determine the nature of their inter-relationships. Furthermore, this comparative approach is useful in developing a functional-anatomical model of the brain mechanisms mediating long-term memory storage. In keeping with this approach, the purpose of the present study was to investigate episodic and semantic memory in a person with semantic dementia and to compare them with those of a person with amnesia who has bilateral medial temporal lobe lesions.

One particularly influential model that has emerged from extensive clinical and experimental research proposes that the hippocampus and adjacent structures in the medial temporal lobe, which include the entorhinal, perirhinal, and parahippocampal cortex, form a distinct system or module, the hippocampal complex, responsible for the acquisition of new memories and their consolidation into a permanent store (e.g. Damasio, 1989; Squire, 1992; Squire *et al.*, 1992; Alvarez and Squire, 1994; McClelland *et al.*, 1995). Consolidation is thought to be a gradual process necessary for the integration of newly acquired information with previously stored memories in the neocortex. The hippocampal complex receives input from the regions of polymodal and association neocortex that are involved in the initial perceptual processing of the incoming information. This system is thought to play a time-limited role in memory consolidation either by binding together these novel perceptual experiences into coherent memories (e.g. Moscovitch, 1992, 1995; Murre, 1997) or, alternatively, by temporarily storing condensed versions of these newly acquired memories (e.g. Alvarez and Squire, 1994; McClelland *et al.*, 1995). With time, recently acquired long-term memories become less and less dependent upon this hippocampal module as they are consolidated within the neocortex (e.g. Squire, 1992; Alvarez and Squire, 1994). Thus, according to the standard consolidation theory, the recall of post-consolidation memories—in either semantic or episodic format—is solely dependent upon the temporal neocortex, and does not involve the hippocampal complex at all.

Consolidation theory predicts that damage to the hippocampal complex will result in a greater loss of memories that remain dependent upon it than those which do not. Thus, patients diagnosed with medial temporal lobe amnesia are expected to demonstrate a temporally graded retrograde memory loss characterized by a disproportionate impairment of recently acquired memories relative to remote memories (e.g. Squire, 1992; Alvarez and Squire, 1994). In contrast, consolidation theory makes opposite predictions regarding temporally graded patterns of memory loss in patients with semantic dementia, a neurodegenerative disorder characterized by neocortical atrophy centered in the anterior and inferior surface of the temporal lobe, and by hippocampal sparing. Because the hippocampal tissue preserves recently acquired information, and the neocortex mediates already consolidated memories, semantic dementia patients are predicted to demonstrate a disproportionate impairment of remote relative to recent memories (e.g. Graham and Hodges, 1997; Hodges and Graham, 1998). The prediction received apparent confirmation from recent findings of reverse temporally graded memory loss in semantic dementia with a disproportionate impairment of remote relative to recent memory for famous names, faces and events, as well as for some types of autobiographical information (e.g. Graham and Hodges, 1997; Graham *et al.*, 1997; Hodges and Graham, 1998; Hodges *et al.*, 1999). Although reversed, the memory loss was not graded but rather showed a step function with

equally severe loss of all remote memories, except for the ones acquired most recently which were relatively spared.

Despite some evidence to suggest that semantic memory for famous names, public events and personal facts undergoes consolidation, eventually becoming hippocampally independent (but see Fujii *et al.*, 2001), the status of this model as it applies to autobiographical episodes is under debate (see Van der Linden *et al.*, 1992; Nadel and Moscovitch, 1997; Moscovitch and Nadel, 1998). In reviewing the evidence, Nadel, Moscovitch and Fujii noted that retrograde amnesia can extend back decades and sometimes shows no temporal gradient (for earlier retrieval deficit explanations of retrograde amnesia see Sanders and Warrington, 1971; Warrington, 1982, 1996; Shallice, 1988). Furthermore, the consolidation theory is unable to account for observations that semantic knowledge tends to become highly personal and idiosyncratic in semantic dementia. The latter finding is important in that it suggests that recency may not be the only critical factor insulating memories from disruption following neocortical degeneration in semantic dementia (Snowden *et al.*, 1994, 1995, 1996).

To account for the evidence, Moscovitch and Nadel proposed a multiple trace theory of memory, arguing that the hippocampal complex is needed to recover detailed memories of autobiographical episodes no matter what their age (Moscovitch and Nadel, 1998). In this view, the memory trace for an autobiographical event consists of a hippocampal-neocortical ensemble, and it is the entire ensemble that needs to be reactivated at the time of recall. Moreover, when an old memory is retrieved, new, distributed, hippocampally mediated memory traces are created. As a result, older memories are represented by multiple traces, making them less vulnerable to hippocampal damage than newer ones. According to the model, the extent and severity of retrograde amnesia depends on the age of the memory and the extent of hippocampal complex damage. The authors argue further that reports of patients who do demonstrate temporally graded memory loss for autobiographical episodes can be explained in terms of the accumulation of 'multiple traces' associated with memories that have been recalled over and over again. Amnesic patients who demonstrate temporally graded autobiographical episodic memory loss typically have partial hippocampal damage (Nadel and Moscovitch, 1997; Moscovitch and Nadel, 1998); thus, it is suggested that the severity of the temporal gradient increases (i.e. the further into the past that the amnesic period extends) depending upon the amount of hippocampal complex tissue that is damaged.

The present study focused on patterns of memory loss for autobiographical episodes and personal semantics because that evidence is pivotal for distinguishing between the consolidation and multiple trace theories. Specifically, we compared the performance of a medial temporal lobe amnesic patient with that of an advanced-stage semantic dementia patient in an autobiographical memory interview using as cues family photographs taken at different periods in the person's life

and the names of people who became famous in different 5-year periods extending back to the 1940s. The present study had two goals: first, to determine whether or not the hippocampal complex plays a time-limited role in the storage and retrieval of autobiographical episodic memory by looking at the patterns of memory loss in amnesia and semantic dementia (experiment one); and second, to explore the possibility, first raised by Snowden *et al.* (1994, 1995, 1996), that autobiographical significance, in addition to memory recency, influences the likelihood that a given 'semantic' memory will be preserved (at least partially) following damage to the temporal neocortex (experiment two). These observations do not directly contradict or confirm either theory but they do suggest that memory recency is not the only factor that influences which memories are impaired or preserved in semantic dementia, and will have to be taken into account in theory development.

Experiment one: autobiographical episodic recall

The goal of experiment one was to evaluate the consolidation (e.g. Squire, 1992) and multiple trace (e.g. Nadel and Moscovitch, 1997) theories of long-term memory storage by exploring temporal patterns of memory loss for autobiographical episodes in medial temporal lobe amnesia and semantic dementia. Specifically, we sought to determine whether the hippocampal complex plays a temporary role in the retrieval of autobiographical episodes, as has been shown with most semantic information, or whether autobiographical episodic recall always requires the hippocampal complex.

Graham and colleagues (e.g. Graham and Hodges, 1997; Graham *et al.*, 1998; Hodges and Graham, 1998; Graham, 1999) cite demonstrations of a reversed temporal pattern of memory loss in semantic dementia as crucial evidence in favor of the time-limited role of the hippocampus in all types of semantic and episodic memory, and against the notion of multiple trace accumulation. There is substantial evidence to suggest that semantic dementia is associated with a preferential sparing of recent memory for famous names, public events, and personally significant names. The studies exploring memory loss for autobiographical information in semantic dementia, however, have focused upon personal semantics to the relative exclusion of personal episodes.

The only techniques that have been used to investigate autobiographical memory, such as the Autobiographical Memory Interview (Kopelman *et al.*, 1996) and the Crovitz cue-word test (Crovitz and Schiffman, 1974), rely heavily on verbal reception and production abilities, and explicit strategies for search and recall (Snowden *et al.*, 1996; Graham and Hodges, 1997; Hodges and Graham, 1998). This is particularly problematic because a severe decline in verbal ability is inherent in the diagnostic criteria of semantic dementia (Warrington, 1996). In addition, although patients showed more frequent and/or more detailed recall of recent relative to remote events, it is unclear whether this pattern is qualitatively different than the performance pattern typical

of normal control participants who also show better recall of recent life events (e.g. Crovitz and Schiffman, 1974; Bahrack *et al.*, 1975; Squire and Slater, 1975). Moreover, it is possible that any discrepancies observed between episodic recall of remote and recent life events are reflective of the disproportionate deficit in remote personal semantics; that is, the patients' recall of recent experiences may be judged to be superior than the recall of remote experiences due to the relative ease with which names of people and places of recent personal significance can be remembered.

Rather than asking patients to recount, in detail, specific life experiences from a particular time period (e.g. early childhood) with no supportive cues to provide a frame of reference, autobiographical episodic recall was examined by using family photographs as prompts. These photographs varied along the recent-remote continuum and each was accompanied by a corresponding description provided by the subject's family. Episodic recall was assessed by asking the patients to identify the people in the picture (if not by proper name, then by description; e.g. 'my friend from high school') and to provide as much detail—through words, gestures or drawings—about the temporal-spatial context in which the photograph was taken. This method has been used in studies of autobiographical memory with medial temporal lobe amnesics (e.g. Tulving *et al.*, 1988). However, no study to date has used family photographs to examine autobiographical episodic memory in semantic dementia patients, a population who, perhaps, has the most to gain from this technique.

As Graham and Hodges (1997) note, it is critical to compare patterns of memory loss for autobiographical episodes in semantic dementia and amnesia because predictions regarding this type of memory are what distinguish between consolidation and multiple trace theories (Graham and Hodges, 1997). Consolidation theory predicts the loss of recent, but not remote, autobiographical memories in amnesia and the reverse in semantic dementia. Multiple trace theory predicts the retention of recent and remote autobiographical memories in semantic dementia, as long as the hippocampal complex is preserved and neocortical loss is not so severe that it cannot support some traces. In contrast, multiple trace theory predicts the loss of recent and remote autobiographical memory in medial temporal lobe amnesia, even when remote semantic memory is spared.

Materials and methods

Participants. The present study focused on the autobiographical memory abilities of two memory-impaired individuals: an advanced-stage semantic dementia patient, EL, and a medial temporal lobe amnesic patient, KC.

EL is a 66-year-old, right-handed man. He received 10 years of formal education in England and worked as a graphics designer/illustrator for a media corporation. He was forced to stop work in 1996, after a 2-year period of progressive memory and verbal communication difficulties accompanied by severe depression. The results of a neuro-

Table 1. Neuropsychological test scores for EL and KC

Test	Patient and date of test	
	EL (1996)	KC (1996)
Dementia rating scale—total	100/144	N/A
WAIS-R scores		
Full-scale IQ	88	88
Verbal IQ	75	96
Performance IQ	110	79
Vocabulary ^a	5	9
Information ^a	4	9
Digit span ^a	13	12
Block design ^a	15	6
WMS-R scores		
Verbal memory index	61	67
Visual memory index	108	67
Logical memory I	5th %	5th %
Logical memory II	8th %	1st %
Visual reproduction I	88th %	13th %
Visual reproduction II	74th %	1st %
Boston Naming	7/60	57/60
COWAT ^b	15	N/A
Animal naming	4	N/A
Rey–Osterrieth Figure—copy	36/36	36/36
Rey–Osterrieth Figure—delay	23	0
Judgment of line orientation ^a	N/A	23/30
Warrington Recognition—words	N/A	26/50
Warrington Recognition—faces	N/A	26/50

^aAge-corrected scaled score.

^bBased on the total of three 1-min trials.

COWAT, Controlled Oral Word Association Test; CVLT, California Verbal Learning Test; WAIS-R, Wechsler Adult Intelligence Scale-Revised; WMS-R, Wechsler Memory Scale-Revised.

psychological assessment performed in 1996 are summarized in Table 1. EL's verbal abilities were severely compromised yet his non-verbal skills in terms of constructional tasks, drawing and non-verbal memory were well preserved. His scores on verbal memory tests were extremely impaired but he retained 91% of the details of the Rey–Osterrieth after 45 min. Phonetic and semantic verbal fluency were both severely impaired. Naming was severely impaired and phonetic cueing did not facilitate word retrieval. Despite having difficulty naming items, EL clearly indicated that he recognized the items and often used the words that comprised the correct response. For example, when attempting to name a toothbrush he responded '... brush your teeth with (it)' or for a coat hanger he stated '... what I hang my coat on'. In addition, he exhibited evidence of semantic memory impairment. His performance on the vocabulary subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) revealed a severe semantic memory loss. His score on the latter subtest was rated at the fifth percentile but more telling were his responses to items that revealed a loss of word meaning. For example, when asked to define the word 'fabric', he responded; 'I forget what the word is — I'm sorry'. When asked to define the word 'domestic', he stated; 'I used to know what that is but I've forgotten'. He also exhibited difficulty retrieving factual knowledge on the WAIS-R information subtest. For example, when asked how many weeks constitute a year, he responded; 'Four weeks in

a month – 12 months in a year – so 48 or 50'. Despite these problems with retrieval of certain types of knowledge, he exhibited evidence of knowledge of relatively recent events. For example, when attempting to name the most recent presidents of the USA (which he was unable to do) he identified one as 'a movie star – now has Alzheimer's disease and can't remember anymore'.

Behaviorally EL appeared nervous and agitated, but nevertheless cooperated with the testing. He was clearly aware of his difficulties, stating from the outset of the assessment that he was '... losing my memory in the last few years'. He reported that he often forgot words and people's names and had difficulty reading because he was constantly looking up the meaning of words in the dictionary. Despite his apparent loss of word knowledge, his speech was fluent and grammatical.

EL was reassessed in 1999. He continued to exhibit severe word-finding problems and subjectively he appeared to have greater difficulty comprehending. From a behavioral standpoint, he continued to exhibit awareness of his deficits and had developed a stereotypic response when introducing himself 'Hello, my name is _____, I've lost my brain'. He also appeared very anxious. His wife reported that he was capable of the basic activities of daily living, although she found it necessary to select his clothing for him. He exhibited less initiation and had stopped performing routine chores around the house that he used to do, such as mowing the lawn and vacuuming. He also required meals to be fixed. His intake at meals had diminished, although he had begun to exhibit a penchant for chocolate. Nevertheless, he still took daily, unsupervised walks without becoming lost and he took it upon himself to go to his bank to ensure that his pension income had been deposited and his account updated. His wife also reported that he appeared to remember recent events; he did not repeat tasks or repeatedly ask questions.

His assessment in 1999 was shortened by his refusal to do many of the non-verbal tasks that he was willing and able to complete in 1996. Although his verbal abilities had deteriorated, his non-verbal skills remained surprisingly intact. His score on the block design subtest of the WAIS-R remained unchanged (95th percentile) over a 3-year period. In the autumn of 1999, shortly after we completed our study, he scored near perfect on tests of line orientation, and average on face recognition. Although we did not administer all the items, he made no errors on the difficult items of a view shifts test and on the colored progressive matrices. At the same time, he scored zero on the Pyramids and Palm Trees Test and was unable to name or sort any of the Snodgrass pictures. EL's remote medical history included a closed-head injury at the age of 21 years without apparent cognitive deficits. He received speech therapy as an adult for developmental stuttering. At the time of the assessment he was still receiving clomipramine for depression.

Magnetic resonance imaging (MRI) performed in January 1997 and April 2000 (Fig. 1) revealed radiological findings consistent with cortical degeneration characteristics of

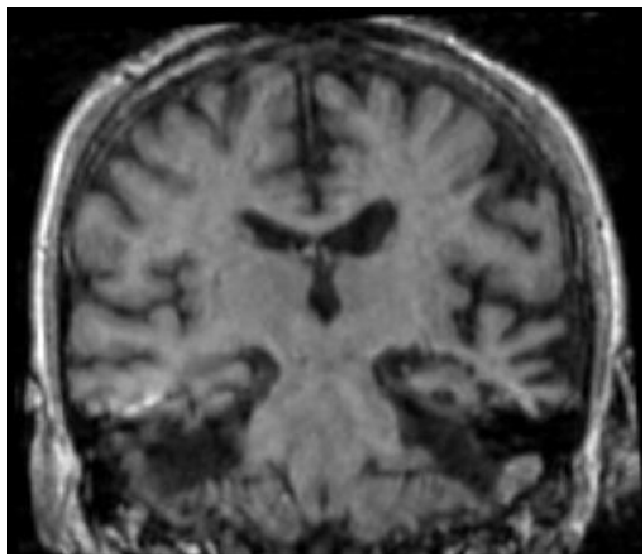


Fig. 1. E.L.'s MRI scan from April 2000 (coronal slice presented) shows evidence of cerebral atrophy that is most pronounced in the left anterior temporal region. In addition, the hippocampus appears slightly smaller on the left side.

semantic dementia. The profile was similar in the two instances, perhaps with some evidence of increased atrophy. Cerebral atrophy was most noticeable in the anterior temporal region, particularly on the left side; the hippocampus appeared to be well preserved relative to KC (see below), although it may be slightly smaller on the left. There was evidence of encephalomalacia in the subcortical white matter of the left anterior temporal lobe, possibly resulting from the closed-head injury suffered by EL as a young adult. The MRI scan also revealed an arachnoid cyst located in the medial left middle cranial fossa. A SPECT scan conducted in February 1997 indicated a mild perfusion deficit involving the left cerebral hemisphere, most noticeably in the frontotemporal region. An electroencephalogram (EEG) conducted in July 1999 was within normal limits and showed no evidence of lateralized or generalized abnormality.

In contrast to patient EL, KC has amnesia with preserved semantic memory. KC is 47 years old and has completed 15 years of formal education. He has been tested extensively over the course of the nearly 20 years since becoming amnesic after a motorcycle accident in October 1981. A summary of his neuropsychological status is presented in Table 1. Magnetic resonance and computerized tomography scans illustrating the specific loci of brain damage suffered by KC have been documented elsewhere (e.g. Tulving *et al.*, 1988; Tulving, 1989; Rosenbaum *et al.*, 2000). KC suffered almost complete bilateral destruction of the hippocampus in addition to a right occipital lesion and a left fronto-parietal lesion. In a 1996 neuropsychological assessment, KC received a full-scale IQ score of 88, and scores of 96 and 79 on the verbal and performance scales, respectively. He scored poorly on the Wechsler Memory Scale-Revised (WMS-R): his general memory score was 61; his verbal scale score was 67 and his visual scale score was 69. On the WMS-R subscales,

KC's performance was at the fifth percentile for logical memory I; the 13th percentile for visual reproduction I; and he received a score of zero on both logical memory II and visual reproduction II. He also performed poorly on the Warrington Recognition Memory Test, scoring 26 out of 50 on both the words and faces subscales.

KC's performance on the Token Test and the Benton Visual Naming Test was well within the range of normal, indicating that his language comprehension and production abilities remain intact. However, he was impaired on the Benton Word Fluency (FAS) Test and scored within the fourth percentile. Perceptual abilities also remain intact in KC. He performed perfectly on the Rey copy, and within the normal range on the Hooper Visual Organization Test, the Wisconsin Card Sorting Task, the Benton Visual Discrimination Test and judgments of line orientation. However, KC's performance on the Benton Face Recognition Task was extremely poor; he received a score of 31 out of 54, placing him in the first percentile, caused either by poor vision related to his glaucoma or by a higher order visual loss related to damage in the medial occipital lobe.

The data obtained in KC's 1996 neuropsychological assessment were generally stable, with only a few small declines in performance on the WAIS-R performance scales in comparison with earlier assessments (e.g. Tulving *et al.*, 1988); this change is most likely due to the increasing difficulties that the patient has with glaucoma and muscular weakness. KC also demonstrated a slight decline in verbal IQ between the 1988 and 1996 assessments; however, because there were no similar declines in performance on tests of vocabulary and verbal fluency, we do not think that this reflects a significant deterioration in verbal ability. There is not sufficient reason to believe that KC's psychometric profile would have changed significantly between the 1996 assessment and the spring of 1999 when we tested him.

Because our autobiographical memory task relies heavily upon visual memory, KC's medial occipital lesion may be at the root of his impaired remote autobiographical memory. Although it is possible that his occipital lesion may contribute to some of his autobiographical memory problems, it is unlikely that it accounts for most of it, as it does in some patients with visual agnosia and loss of imagery (Ogden, 1993; Rubin and Greenberg, 1998). Although he scored poorly on the Benton-Van Allen Face Recognition Test, KC is not prosopagnosic or visually object agnosic. He had no difficulty identifying known people, places and objects presented in photographs. He has good visual imagery of salient landmarks and excellent cognitive maps of his area, except for a deficit in recognizing less salient houses (Rosenbaum *et al.*, 2000). Finally, although KC exhibited somewhat flat affect, he showed no signs of depressed mood or dysphoria that would have a negative impact on his autobiographical memory performance.

Procedure. EL's autobiographical episodic memory was assessed using a set of 50 family photographs that were

approximately evenly distributed along the recent–remote continuum; these photographs and their corresponding descriptions were provided by EL’s family. Similarly, KC’s autobiographical episodic memory was assessed using a comparable set of 45 family photographs with accompanying descriptions provided by family members. It was assured that the patients had not reviewed these photographs recently¹, thereby permitting the examination of memory for autobiographical experiences associated with particular times from each one’s life. Moreover, there were no obvious differences in emotional salience or autobiographical significance between the family photographs of KC and EL. Upon the presentation of each photograph, the patient was asked to identify the people in the picture (either by proper name or through a description of his relationship with the individual) and to provide as much detail (through words, demonstrations or drawings) about the temporal–spatial context in which the photograph was taken (e.g. ‘where was this picture taken?’, ‘when was this picture taken?’, ‘what is going on in this picture?’) and any personal experiences that related to the photograph. The patients were asked whether or not the photograph triggered a sense of familiarity or remembering, or an emotional response. The patients were encouraged to provide as much information through prompting by the examiners.

For each photograph, the patient’s description was transcribed manually by the examiners; in addition, the examiners noted the patient’s tone of voice, gestures, emotional expressions and other salient behaviors. Subsequently, each description was assessed according to seven criteria: (1) familiarity recognition of people in the photograph; (2) identification of people by name; (3) sense of recognition (signaled by phrases such as ‘I remember..’; ‘I know this..’; ‘Oh yes, this was when..’); (4) knowledge of temporal context (e.g. year; season; own age at time of photograph); (5) knowledge of spatial/situational context (e.g. location; country; ongoing event or activity); (6) expression of emotion in response to the presentation of the photograph (e.g. smiling; laughing; emotional tone of voice; verbal description of emotion); and (7) narrative structure (e.g. describes sequence of events; relates photograph to other life experiences). The examiners were not blind to the patient’s diagnosis; however, two examiners were present throughout the testing sessions in order to maximize the reliability of the coding; the examiners made notes independently during testing and final coding was achieved through collaboration after the end of the session.

The evaluation of performance in this autobiographical episodic memory task did not depend on accurate, fluent verbal descriptions, nor did it depend on the ability to provide specific names of people and places. Rather, responses were evaluated according to the degree to which they suggested the existence of an intact experiential representation or a sense of ‘remembering’ (Tulving, 1989). This assessment technique was judged to be more appropriate than previously used methodologies (e.g. Snowden *et al.*, 1996; Graham and Hodges, 1997; Hodges and Graham, 1998) for use with

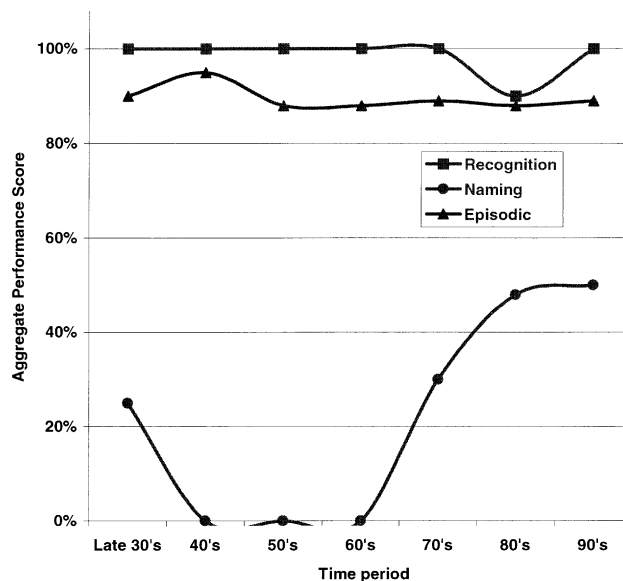


Fig. 2. EL’s performance scores in percentage for successive 5-year periods on the recognition, naming and episodic variables in the photograph description task.

lexically impaired individuals, such as EL, for the reasons discussed earlier. Family photographs have been used in the assessment of autobiographical episodic memory in several studies involving amnesic patients (e.g. Dall’Ora *et al.*, 1989; Hodges and McCarthy, 1993); however, this technique has not been used with semantic dementia patients.

Results and comment

For each family photograph, the patient’s verbal description, gestures, tone of voice and emotional response were recorded by the experimenters, as was the approximate year during which the photograph was taken. Each description of each photograph was assessed according to the seven aforementioned criteria. In addition, performance scores were calculated for each patient in each of the time periods by calculating a percentage by dividing the number of points received by the total number of points possible and multiplying by 100 (i.e. a maximum of seven points could be obtained for each photograph, thus the total number of points possible for each time period varied with the number of photographs). Criteria that were not applicable for a given photograph were taken into consideration, and were not included in the total number of possible points (e.g. ability to name individuals was not included in the criteria if there were no people in the photograph). Three performance scores were calculated for EL in each time period: two individual semantic scores—recognition and naming; and one episodic score that included the latter five criteria (Fig. 2). Two performance scores were calculated for KC in each time period: the recognition and naming criteria were collapsed into a single semantic score as performance was identical in both; and the latter five criteria were collapsed into a single episodic score (Fig. 3).

There were several dramatic differences between the

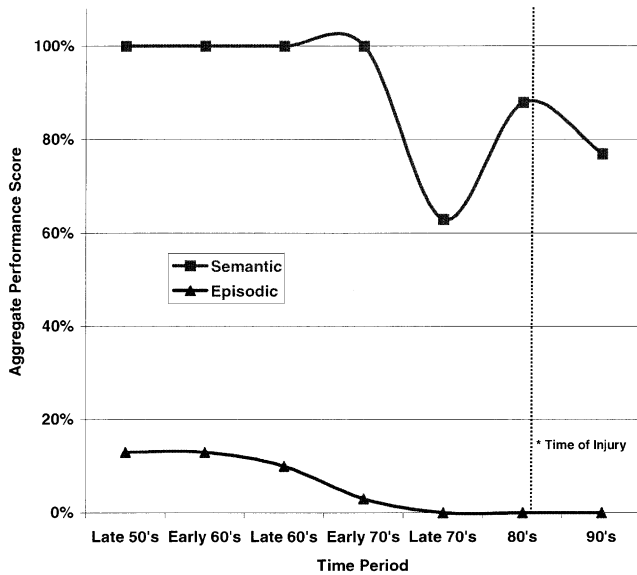


Fig. 3. KC's performance scores in percentage for successive 5-year periods on the semantic and episodic variables in the photograph description task. The dotted vertical line indicates the onset of KC's amnesia.

descriptions provided by these two patients. First, whereas KC was able to name correctly the individuals in all of the photographs from across the temporal continuum, EL was severely impaired at naming and could only provide the correct names for his wife and three children. Indeed, prior to the 1980s time period, the only points that he received for naming were from photographs of himself. EL clearly recognized all the individuals in photographs across all time periods; however, he was unable to name people from his childhood and early adulthood, including extremely salient individuals such as his brothers, parents and co-workers. Although EL showed a slightly reversed gradient in naming ability such that he could name only those individuals currently in his day-to-day life, KC demonstrated the opposite gradient. KC had an excellent memory for names of individuals whom he had encountered prior to his 1981 accident, but was less certain with respect to the names of individuals whom he encountered just recently. For instance, the names of childhood friends and neighbors, siblings' girlfriends and school teachers, were recalled immediately. In contrast, the names of recently born nephews and nieces were slower to be recalled and were recalled with less confidence than names encountered prior to his accident. Even when he knew the names of these recently encountered individuals, and their relationships to him, he was unable to recall a single encounter with them. It was as if KC was not quite sure how he came to know this information. Moreover, he was unable to describe the personalities or appearances of these recently encountered individuals and could not form an image of them in his head². He seemed to possess very little knowledge regarding these individuals, including their present ages and occupations.

Other striking contrasts between the two patients were reflected in their abilities to re-experience events, to provide

details regarding the temporal and spatial context in which the pictures were taken, and in the expression of emotional responses to the photographs. Despite his poor verbal abilities, EL was able to demonstrate quite specific knowledge regarding the ongoing events in the photograph and was able to place those events in an accurate temporal-spatial context. The experimenters agreed that EL demonstrated a clear sense of re-experiencing the autobiographical events portrayed in virtually every photograph shown to him, regardless of recency. Moreover, he expressed a range of emotional reactions to the photographs.

For example, as discussed by Moscovitch and Nadel, EL could describe in detail his early childhood memories of hiding in his family's cellar in London, UK, while they were being bombed by the Germans (Moscovitch and Nadel, 1999). Similarly, he could recall in detail his experiences of traveling around the world as a young man; his immigration to Canada at the age of 23 years; the church at which he was married 17 years ago and many details about his wedding day; the births of each of his three children; his work experiences; the annual driving trips to Florida with his wife and children; and a recent visit to a restaurant with his family.

Furthermore, EL's descriptions of the photographs often followed a narrative structure in the sense that he outlined the ongoing sequence of events and related the episode depicted in the photograph to other episodes that had occurred previously and to events that took place subsequently (e.g. upon viewing an old photograph of his father-in-law from several decades ago, EL described how the man now lived next door and was in good health despite his old age). Finally, EL demonstrated a tendency to talk about his own, and his family's, future; he frequently expressed concern about his own state of health and his financial status and demonstrated awareness of ongoing and upcoming events in his life. Thus, EL appeared to show a clear sense of temporal continuity and an understanding of himself as a continuous entity with a past, a present and a future.

In contrast, despite the fact that KC was much more proficient in verbal comprehension and production than EL, he could provide very little information regarding his family photographs outside of naming the individuals portrayed. In general, KC's descriptions of his family photographs were matter-of-fact, brief, unelaborated and unemotional. Indeed, except for names, KC was not able to provide any information in addition to that which was evident to the experimenters, upon seeing the photographs for the first time. Consistent with the observations of Tulving *et al.* (1988), KC relied on his intact personal semantics, general semantics, and logical reasoning abilities to construct plausible explanations of what might be going on in the photographs. For instance, upon presentation of a photograph in which all of his family members were dressed up, KC responded, 'I guess we must have been going somewhere special. It might have been a family portrait that we had done for the house. I don't know'. In fact, the photograph was an official portrait of his brother's wedding in 1979, at which KC was part of the wedding

party. The performance of KC in the photograph description task was generally consistent with previously published reports of his autobiographical episodic and autobiographical semantic recall (Tulving *et al.*, 1988; Tulving, 1989).

Discussion

There were two major findings: (1) memory for autobiographical events was severely impaired across the life-span in amnesia associated with medial temporal damage, but relatively well preserved in semantic dementia; (2) memory for personal names and facts showed the reverse pattern. Overall, the findings from experiment one were more consistent with the predictions of multiple trace theory than with those of consolidation theory. Amnesia due to medial temporal lobe damage was associated with almost complete loss of personal episodes with a sparing of personal semantics prior to the onset of amnesia. In contrast, semantic dementia characterized by neocortical atrophy with a sparing of medial temporal structures was associated with good preservation of autobiographical episodic memory across the life-span. The multiple trace theory accounts for these findings by suggesting that the hippocampal complex is crucial in the storage and retrieval of all episodic memories, regardless of age. In the case of extensive bilateral hippocampal complex destruction, as in the patient KC, the multiple trace theory predicts a virtually complete loss of all autobiographical episodes encompassing the entire lifetime.

In a previous qualitative assessment of autobiographical memory involving an open-ended interview based on information, photographs and specific experiential accounts provided by KC's family, Tulving *et al.* (1988) determined that KC was unable to recall any autobiographical episodes from any time in his life. In contrast, KC showed a remarkable ability to recall personal semantics from all time periods prior to his accident; he was able to recall the names of friends, family members, schools, addresses and obscure personal facts about significant people in his life. KC demonstrated a great deal of 'semantic' self-knowledge regarding his pre-amnesic years, as well as a substantial amount of information regarding his post-amnesic life; however, he was unable to re-experience or recount a single autobiographical event from any point in his life. In the present study, we found that, despite his ability to recite the names and addresses of friends, family, schools and places of work from his life prior to becoming amnesic, KC could not remember attending his elementary or high school graduations, going on his first date, attending Expo'67, standing up at his brother's wedding, or the death of his youngest brother in a boating accident.

Memory for personal episodes that occurred just prior, and subsequent, to his accident was even more severely impaired than his remote episodic memory; photographs or questions about post-amnesic events did not trigger even a hint of familiarity, nor did he even know that they had taken place. Finally, none of KC's photograph descriptions was

narrative in structure or emotional in content, and he seemed unable to contemplate or hypothesize about future events, and to link disparate life events occurring at different points in time.

Tulving *et al.* (1988) note that such a striking dissociation between intact personal semantics and impaired personal episodes is unique to KC; however, several other patients have been found to demonstrate similar dissociations, such that a very few isolated, early life episodes were preserved along with personal semantic information (e.g. Kinsbourne and Wood, 1975; Cermak and O'Connor, 1983; Damasio *et al.*, 1985; De Renzi *et al.*, 1987; Hodges and McCarthy, 1993; Kapur *et al.*, 1996). Thus, the present findings are consistent with the interpretation of Tulving *et al.* (1988) that KC has preserved personal semantics accompanied by a virtually complete loss of personal episodic memory (see also Kinsbourne and Wood, 1975). The multiple trace theory can account for previously documented findings that partial destruction of the hippocampal complex typically results in graded loss in autobiographical episodes related to the size of the lesion (see Nadel and Moscovitch, 1997 for a review). Our data on KC indicate that the phenomenon of temporally graded retrograde memory loss and the standard notion of consolidation does not apply to all types of memory. Rather, our findings suggest that autobiographical episodic memory remains hippocampally dependent on a permanent basis, whereas remote memory related to personal semantics or facts remains hippocampally dependent temporarily, becoming independent of these structures once consolidation is complete.

Because KC's lesions are not restricted to the hippocampal complex, it is not possible to attribute his autobiographical memory impairment to damage to that region alone without also taking other evidence into account. Thus, EL, who like KC also has extensive neocortical damage but relatively preserved medial temporal lobes, does not show an extensive autobiographical memory deficit, suggesting that this type of memory is supported, at least partially, by the medial temporal lobe. Moreover, if damage to consolidated memory traces in the neocortex was the source of KC's severe autobiographical memory deficit, then one would expect to find an equally severe deficit for personal and general semantic knowledge extending across KC's entire lifetime; however, we found this not to be the case (Westmacott and Moscovitch, in preparation, 2001a). His general semantic knowledge, like his knowledge of personal facts, was impaired only for the period just prior to his trauma and subsequent to it. Unlike autobiographical memory, remote semantic knowledge was relatively well preserved. Thus, one would have to argue that KC's neocortical lesions selectively affect autobiographical memory, an unlikely hypothesis based on what we know of neocortical function. Nor is the loss of autobiographical memory related primarily to KC's medial occipital damage as he does not show the severe visual object agnosia and prosopagnosia that characterize those patients who also have an extensive retrograde amnesia for autobiographical events

(Ogden, 1993; Rubin and Greenberg, 1998). For these reasons, we attribute the differences between EL's and KC's autobiographical episodic memory performance primarily to the fact that the medial temporal lobe is intact in the former and damaged in the latter. Indeed, it may be that in addition to being damaged, the medial temporal lobe is also partially disconnected from the neocortex as a result of white matter shearing that typically accompanies closed-head injuries. Such damage would destroy the neocortical–medial temporal lobe connections which are needed to form and maintain cohesive, autobiographical memory traces, as the multiple trace theory predicts, and exacerbate the amnesia for autobiographical events.

With regard to semantic dementia, our results are consistent with multiple trace theory in that even very remote memory of autobiographical episodes is relatively preserved in relation to semantic memory and naming as long as the medial temporal lobes are viable and there is sufficient neocortical tissue left to support and express those memories. Because we relied as much on non-verbal as verbal measures to score autobiographical recall, it was not possible to compare EL's performance on these tasks with that of a normal control who could use language to provide extensive details about the event in question. Our point, however, is not to argue that EL's remote and recent verbal episodic memory is normal; we believe it probably is not. Rather, we wish to demonstrate that he retains a great deal of autobiographical memories of his remote past and, insofar as our assessment techniques permit us to judge, they are not abnormally less detailed than his recent memories.

Experiment two: effect of autobiographical significance on remote semantic memory

The goal of the second experiment was to test the hypothesis that autobiographical significance influences the susceptibility of remote semantic memory to disruption after brain damage. Following Snowden *et al.*'s lead, it is proposed that semantic information is less likely to become completely independent of the hippocampal complex if it is somehow significant to one's personal autobiography (Snowden *et al.*, 1996). Moreover, we predict that such personally significant semantic information is more likely to remain partially preserved in semantic dementia due to the continued hippocampal dependence of the memory representation.

To assess the episodic significance of person-related semantic information, such as may be involved in the recognition of famous names, we asked a large group of normal, control participants, to make 'remember/know' judgments about them, just as they would about words or pictures on tests of episodic memory. We instructed participants to give a 'remember' response if they could conjure up a particular episode associated with the name, and a 'know' response if the person was merely familiar, even if they knew many facts about him/her. For example, someone would give a 'remember' response to the name 'Marilyn Monroe' if she/

he could remember watching her in a movie or if she/he could remember being affected by the news of her death, and a 'know' response if they only knew factual information about her (e.g. she was a famous actress who died of an overdose). Based on the data we collected, we ranked the names according to the proportion of people giving 'remember' responses. Although this 'remember/know' paradigm is relatively new in the psychological literature, it is viewed as a valid measure for assessing whether a piece of information evokes a memory of the autobiographical event at retrieval (Tulving, 1985; Gardiner, 1988; Levine *et al.*, 1998).

The underlying assumption of this task is that famous names receiving a high proportion of 'remember' responses are likely to evoke personal memories and, thereby, be more personally relevant or emotionally significant to most people than those names receiving a 'know' response. Thus, if autobiographical significance does influence the susceptibility of memory to brain damage and if autobiographically significant semantic information remains partially dependent upon the hippocampal complex even after consolidation is complete, then we would expect to see a relationship between the control subjects' performance on the 'remember/know' task and the patients' ability to recognize the famous names. Specifically, EL was expected to demonstrate superior recognition of famous names of individuals whom he had met in person, or who were judged by others within his age cohort to have had an impact on their lives in some personal manner (as indicated by response patterns in a 'remember/know' paradigm). In contrast, KC was not expected to show any effect of autobiographical significance in his recognition of famous names; rather, his performance was predicted to be influenced by the overall familiarity of the name and the time period during which fame was first achieved.

We also assessed the possible influence that autobiographical significance might have on the preservation of place-related semantic information by contrasting EL's recognition memory and speed of reading for names of places that he had visited with names of places that he had not visited. If autobiographically significant semantic information is preferentially spared—at least partially—in semantic dementia, then EL should demonstrate more accurate and faster reading times and better recognition for the names of places that he had visited as compared with unvisited and fictitious places.

Materials and methods

Participants. Experiment two involved the same two patients, EL and KC, who participated in experiment one. Each patient's performance was contrasted with that of a control group consisting of 45 neurologically intact subjects—29 male and 16 female—matched with EL with respect to age (mean = 63.8 years); education (mean = 11.7 years); handedness (right); and ethnic background (Anglo-Saxon).

Procedure. The effect of autobiographical experience upon remote semantic memory was examined with respect to

person-related and place-related information. Person-related semantic memory was assessed using a stimulus set of 139 famous names representing the entire 20th century. Names were not chosen in order to obtain an equal distribution across all time periods, nor were the candidates for inclusion in the task restricted to those whose fame was confined to a short time period. Rather, famous individuals were chosen based on their stature, their significance in 20th-century Western history and, most importantly, on the likelihood that they would have had some personal impact upon individual citizens. As a result, the fame of many of the people spanned many years.

Each of the 45 subjects in the control group was presented with the set of 139 famous names and was asked to make a 'remember/know' judgment for each name. The control subjects were instructed to read each famous name and to give a 'remember' response if they could re-experience a particular episode in which they watched, listened to, or heard about the famous individual. If the subject knew the identity of the famous individual but could not recall a specific episode in which this person was encountered, then she/he was instructed to provide a 'know' response. In addition, the subjects were asked to rate the familiarity of each famous name on a seven-point scale.

The person with amnesia, KC, was presented with the same list of 139 names; for each famous name, he was asked to decide if he 'remembered' the famous person, if he simply 'knew' the identity of the person, or if he did not know the identity of the person at all. KC was given the same instructions as the control group for determining whether to give a 'remember' response or a 'know' response. KC was also asked to rate the familiarity of each name. In contrast to the task given to KC and the control subjects, EL was instructed to read each famous name aloud and to indicate whether or not he recognized the name as belonging to a famous individual. If he had difficulty reading a name, it was pronounced correctly for him. Due to the extensive verbal impairment suffered by the patient, different scoring criteria were applied. A recognition response was recorded if any of the following conditions was met: the individual was identified according to occupation or activity description (e.g. 'he was an author'); the individual's name triggered some sense of familiarity ('I think I know that name; now who is that?'); the name was repeated several times aloud or followed by a long pause, indicating that some memory was triggered by the name. This method of scoring was possible because EL had difficulty reading most of the names and, even when they were pronounced correctly for him, he continued without hesitation to the next name on the list.

EL's memory for place-related semantic information was assessed using a stimulus set of 70 names of cities, countries and geographical regions, and 58 names of landmarks and tourist attractions. As confirmed by his wife, EL had visited 34 of these cities, countries and geographical regions; he had not visited the remaining 36 places. With respect to the set of landmark and tourist attraction names, 24 had been visited

by EL while the remaining 34 had not. EL's knowledge of these place names was contrasted with that of six control subjects matched with respect to age (mean = 67.2 years); education (mean = 10.8 years); handedness (right); and ethnic background (white Anglo-Saxon).

In the recognition task, the subjects were asked to read the place or landmark name aloud and to indicate whether or not it was familiar; the subjects were asked to indicate the approximate location of each recognized place on an unlabeled world map and to provide a brief description of each recognized landmark. An accurate location or description was required in order for a control subject's response to be recorded as correct. Similar criteria to those discussed above were used to determine the recording of recognition responses for EL. In addition, we asked him to locate these names on a map, map reading being a skill which was remarkably well preserved (also see Snowden *et al.*, 1996).

In the reading times task, the subjects were asked to read aloud six 14-item lists as quickly and accurately as possible. The lists represented the following experimental conditions: visited place names, unvisited place names, fictitious place names, visited landmarks, unvisited landmarks, and fictitious landmarks. The reading time, in hundredths of seconds, was measured for each list using a stopwatch and then recorded by the experimenter. In addition, pronunciation errors were recorded.

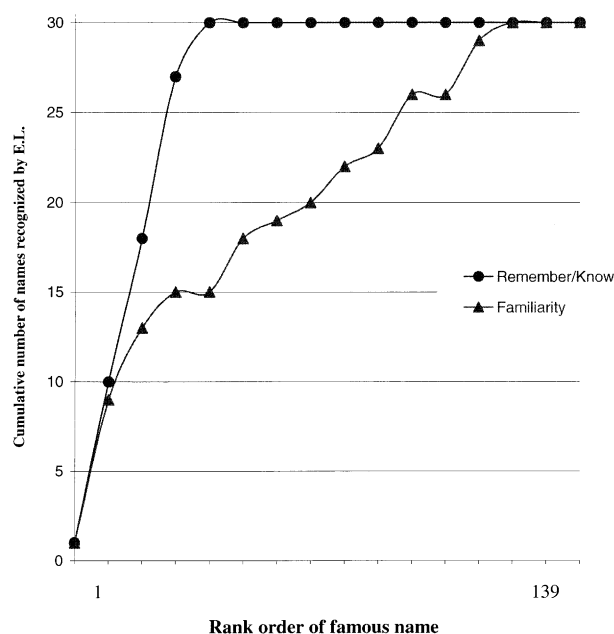
Results and comment

EL demonstrated some evidence that he recognized 30 of the 139 famous names included in the stimulus set; these names are listed in Table 2. Specifically, seven names were identified according to occupation or activity; 12 names triggered a sense of familiarity as indicated by comments such as 'I think I used to know who that is'; and the remaining 11 names were repeated aloud more than three times. All 30 of the recognized names were pronounced correctly in contrast to only 28 (25.7%) of the unrecognized names. Several of the names that were recognized by EL cannot be pronounced phonetically (e.g. Joe DiMaggio, Slobodan Milosevic). Similar to most individuals with semantic dementia, EL's reading is marked by a surface dyslexia; that is, he pronounces words according to the grapheme-phoneme conversion rules of the English language. The fact that he was able to pronounce correctly names that do not correspond to these phonemic rules provides strong evidence to suggest that, to some degree, these names are still represented within his semantic system.

With respect to the control subjects' data, average familiarity ratings and the number of 'remember' (as opposed to 'know') judgments were calculated for each of the 139 famous names. Twenty-two of the famous names that triggered a sense of familiarity in EL were given a 'remember' response by greater than 90% of the control subjects; the remaining eight names that were familiar to EL were given a 'remember' response by greater than 80% of the control subjects. All 30

Table 2. The 30 famous names recognized by EL in the 'remember/know' task from experiment two

1. Adolf Hitler
2. Bette Davis
3. Bill Clinton
4. Christopher Reeve
5. Duke Ellington
6. Elvis Presley
7. Elvis Stojko
8. Frank Sinatra
9. Fred Astaire
10. Humphrey Bogart
11. Jack Kavorkian
12. Joe DiMaggio
13. John F. Kennedy
14. John Lennon
15. Joseph Stalin
16. Judy Garland
17. Lee Harvey Oswald
18. Lucille Ball
19. Marilyn Monroe
20. Martin Luther King
21. Neil Armstrong
22. Nelson Mandela
23. O. J. Simpson
24. Paul Bernardo
25. Richard Nixon
26. Ronald Reagan
27. Slobodan Milosevic
28. Terry Fox
29. Tiger Woods
30. Walter Cronkite

**Fig. 4.** Famous names recognized by EL (plotted as cumulative recognition scores) and their rankings by control subjects with respect to remember/know and familiarity.

famous names recognized by EL ranked within the top 45 in terms of the percentage of 'remember' responses.

Conversely, with respect to familiarity ratings, only 16 of the names recognized by EL ranked within the top 45. Figure 4 contrasts the rank order of famous names according to

both familiarity and percentage of 'remember' responses from controls with the cumulative recognition score of EL. The figure illustrates the fact that the names recognized by EL are all very high in the 'remember/know' rank order; however, these recognized names are much more dispersed throughout the familiarity ratings rank order. This suggests that the percentage of 'remember' responses was a better predictor of EL's recognition ability than mean familiarity rating.

KC showed a strikingly different pattern of performance as compared with EL. KC recognized and identified 67 of the 139 famous names; however, his performance did not seem to be influenced by the 'remember/know' rank ordering obtained from the control subjects. Unlike EL, who showed superior recognition of names receiving many 'remember' responses, only 25 of the famous names recognized by KC ranked with the top 45. The remaining 42 names were scattered throughout the 'remember/know' rank order, with many of the recognized names falling near the bottom. KC pronounced correctly all 67 of the recognized names and 55 (76.4%) of the unrecognized names.

With respect to familiarity ratings, 30 of the famous names recognized by KC ranked within the top 45; the remaining 37 names were scattered throughout the rank order. Familiarity did not seem to have any more of an influence upon KC's recognition ability than did the 'remember/know' rankings; rather, his performance appeared to depend exclusively on the time period during which the individual became famous. KC was able to recognize and identify every individual who had achieved fame prior to the late 1970s; in contrast, he was unable to identify virtually all of the famous individuals from the years just prior to his accident to the present. The failure to find an effect of familiarity may be due to the fact that all of the famous names were ranked quite highly on the familiarity scale by the control subjects. Perhaps an effect of familiarity would have been found to exist had the task included some relatively unfamiliar famous names. We should note that the results suggest that he has a temporally graded retrograde amnesia for these names that extends for about 5–10 years prior to his accident. This is confirmed in another study (Westmacott and Moscovitch, in preparation, 2001b) on semantic memory.

Figure 5 contrasts the rank order of famous names according to both familiarity and percentage of 'remember' responses from controls with the cumulative recognition score of KC. The figure illustrates the fact that the names recognized by KC were not influenced by either familiarity or 'remember/know' rank order; the number of names recognized increased steadily and gradually as the number of names presented increased. The time at which the individual became famous was a better predictor of KC's recognition performance than either familiarity or the 'remember/know' ranking.

With respect to place-related semantic information, the control subjects recognized easily all of the names of cities, countries, geographical regions, and landmarks; each subject

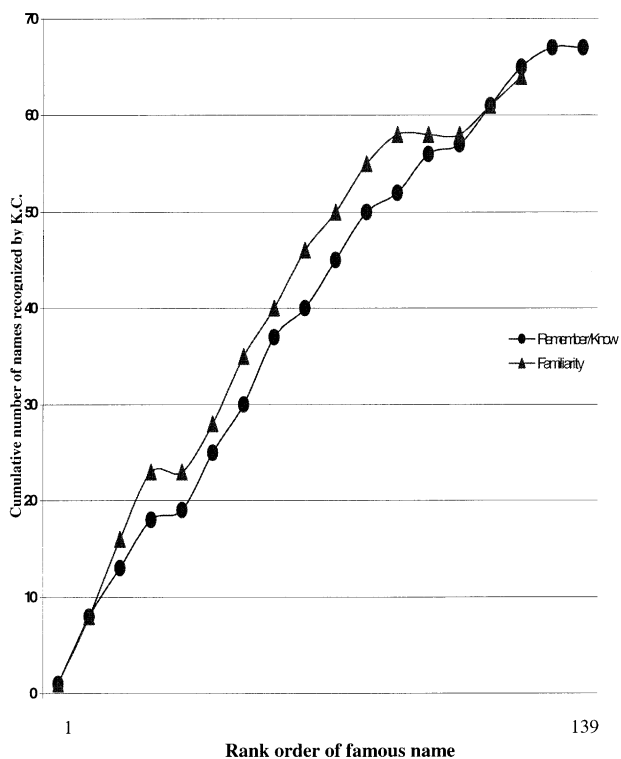


Fig. 5. Famous names recognized by KC (plotted as cumulative recognition scores) and their rankings by control subjects with respect to remember/know and familiarity.

received perfect scores in recognizing names from both the visited and unvisited lists. In contrast, EL demonstrated a clear difference in his ability to recognize place names from the visited and unvisited lists: he was able to recognize and locate correctly almost 50% of the names from the list of places that he had visited and 21% of the visited landmarks. However, EL did not indicate even a hint of familiarity with any of the unvisited landmark names and was able to recognize only one name from the list of unvisited places. Interestingly, he recognized the name ‘Kosovo’ and was able to indicate its location on the unlabeled map. Furthermore, he indicated some knowledge of the recent war in Kosovo by stating that, ‘It’s a sad place ... lots of hurting and people going down... and lots of this (makes shooting gestures with his hands) and it’s a very sad place’. The fact that this was the only item on the unvisited list that was recognized by EL is significant, as it is consistent with the hypothesis that recently learned general semantic knowledge is more likely to be intact (at least partially) in semantic dementia as compared with more remotely learned information. Moreover, it is consistent with the hypothesis that information carrying emotional significance is more likely to remain intact than equally familiar, non-emotional information. Finally, the error data from the recognition task are further consistent with the hypothesis that personally significant place names would be more likely to remain intact than place names that were not significant. Of the visited places, 25 (73.5%) were pronounced correctly; of the visited landmarks, 17 (70.8%); of the

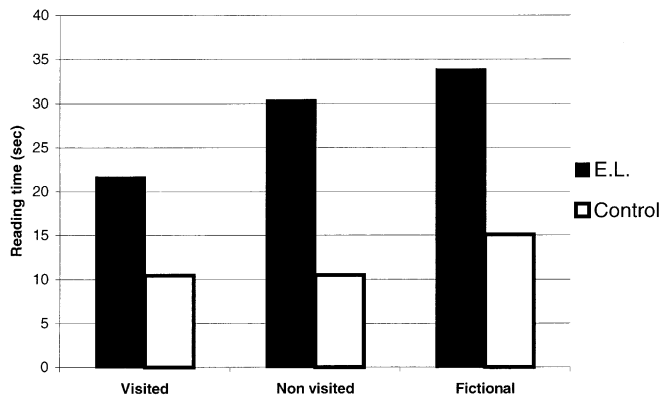


Fig. 6. Reading times, in s, for EL and matched controls for names of places that were visited by EL, equally familiar places not visited by him, and fictitious places.

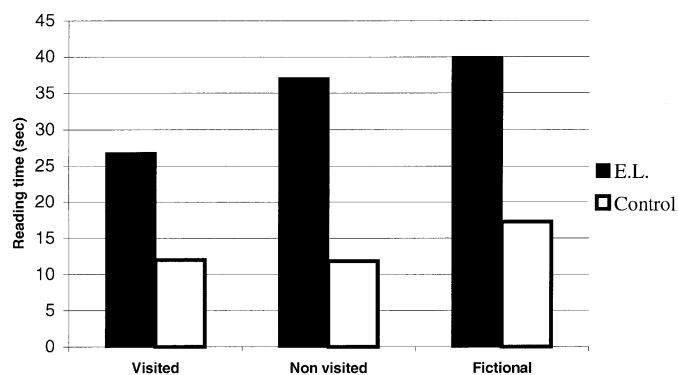


Fig. 7. Reading times, in s, for EL and matched controls for names of landmarks that were visited by EL, equally familiar landmarks not visited by him, and fictitious landmarks.

unvisited places, eight (22.2%); and four (11.8%) of the unvisited landmarks. Control subjects did not make any pronunciation errors in the place recognition task.

Analogous to the performance in the place recognition task, the control subjects’ reading times did not differ between the lists of visited and unvisited places and landmarks; however, the control subjects were faster at reading real place and landmark names (regardless of whether they were from the visited or unvisited list) as compared with fictitious names (Figs 6 and 7). Conversely, EL read more quickly the names of places and landmarks that he had visited as compared with both unvisited real place/landmark names and fictitious place/landmark names. In fact, with respect to both places and landmarks, EL’s reading time for the unvisited list was closer to that for the fictitious list than it was to that for the visited list. This suggests that EL treats real, unvisited place names and fictitious place names more similarly than he treats the visited and unvisited real place names. Furthermore, EL was more likely to pronounce correctly the names of visited places (92.9%) and visited landmarks (78.6%) as compared with unvisited places (35.7%) and unvisited landmarks (14.3%). The control subjects made no pronunciation errors in the reading times task.

Discussion

It was proposed that autobiographical significance serves to help preserve 'semantic' memory in patients with semantic dementia because memories high in personal relevance remain partially dependent upon the hippocampal complex, even after consolidation is complete. This hypothesis was supported by the observation that EL demonstrated superior memory for famous names that carried some personal, emotional or autobiographical significance for individuals of his age cohort, and presumably for him as well. Specifically, EL displayed superior recognition of famous names that received many 'remember' responses from the control subjects relative to names that received few 'remember' responses. Furthermore, EL demonstrated faster reading times and superior recognition for the names of places that he had visited as compared with both unvisited and fictitious place names.

Although these findings are not necessarily inconsistent with consolidation theory, they cannot be explained by this theory either. The possibility that autobiographically significant, post-consolidation semantic information may retain some hippocampal representation is more consistent with multiple trace theory and, perhaps, this proposition can be viewed as an extension of the Nadel and Moscovitch (Nadel and Moscovitch, 1997) model. The time-limited, hippocampally dependent process of consolidation as it has been described by Squire and colleagues (e.g. Squire, 1992; Squire and Alvarez, 1995) may be applicable to the majority of long-term semantic memories; however, there is an increasing body of evidence to suggest that autobiographical episodic memories and, perhaps, even some types of semantic information remain partially dependent upon the hippocampal complex (Snowden *et al.*, 1996).

The findings from experiment two extend the ideas of Snowden regarding the interaction between episodic and semantic information and provide further suggestion for a necessary revision to the classification of different types of autobiographical and non-autobiographical memory (Snowden *et al.* 1995, 1996, 1999). The category of autobiographical memory is divided into personal semantics and personal episodes; non-autobiographical memory is broken down into general semantics and person- and event-related semantics (i.e. information regarding famous individuals, events and places). The present data suggest that there may exist a unique type of memory that spans the autobiographical and non-autobiographical categories: *personalized semantics*. This type of semantic information may be distinguished from personal semantics in that it does not pertain to the self directly. Rather personalized semantics represent general information, non-specific to the self, that is somehow colored or shaped by personal experience. This type of semantic information, whether recent or remote, may remain dependent upon the hippocampal complex and may provide a wealth of information over and above that which is common across individuals. Furthermore, this personalized semantic information may exist independently of more general

semantic knowledge in patients, such as EL, with profound neocortical atrophy.

In support of this hypothesis, KC, who has bilateral hippocampal damage and virtually non-existent autobiographical memory, showed no effect of personalized semantics in his reading and recognition of famous names. Instead, his performance was influenced strongly by the time at which the name became known. In this regard, he shows the typical temporally graded retrograde amnesia predicted by traditional consolidation theory. This was confirmed in a more detailed investigation of semantic memory for famous names and vocabulary (Westmacott and Moscovitch, in preparation, 2001a). These results suggest that, in contrast to autobiographical memory, semantic memory can become independent of the hippocampal complex once consolidation is complete.

General discussion

Two major findings are reported in our study. The first is that EL, a person with semantic dementia, demonstrates episodic memory for very remote autobiographical events if testing does not place undue demands on his impaired, verbal and semantic abilities. His performance contrasts with that of KC, a person with amnesia following extensive bilateral, medial temporal damage whose semantic memory is relatively spared but whose autobiographical memory for recent and remote events is virtually absent. The second finding is the demonstration that EL's relatively spared episodic memory contributes to the maintenance of whatever semantic memory is preserved for people and places. We discuss each of these findings in turn, and relate both to models of memory and consolidation.

Autobiographical memory

The finding of relatively preserved autobiographical episodic memory extending across EL's entire lifetime is significant in light of the current theoretical debate regarding the neurological mechanisms of long-term memory storage and retrieval. Hodges, Graham and colleagues (e.g. Graham and Hodges, 1997; Graham *et al.*, 1998; Hodges and Graham, 1998) observed a small number of semantic dementia patients and concluded that the disease is characterized by a reverse temporally graded memory loss with respect to both semantics and episodes. The authors went on to argue that this finding, in combination with well-established demonstrations of the Ribot gradient in medial temporal lobe amnesia (see Squire, 1992 for a review), supported the standard model of consolidation.

The present findings on semantic dementia and on amnesia question these conclusions. By encouraging EL, a person with semantic dementia, to express his memory for autobiographical events depicted in family photographs in verbal and non-verbal ways, we were able to reveal a preservation of both recent and remote autobiographical episodes with no

obviously reversed gradient, in a patient with advanced-stage semantic dementia.

Currently, there are no other documented cases of people, like EL, with semantic dementia and relatively preserved memory for remote autobiographical episodes. Although ours is the first report of evidence of preserved remote episodic memory in semantic dementia, it is important to note that De Renzi reported the case of a patient who demonstrated a virtually complete loss of general and non-personal semantics with a sparing of autobiographical semantics and episodes following a bout of herpes encephalitis (De Renzi *et al.*, 1987). This patient's profile provides support for the arguments proposed in the present study in two ways: first, it demonstrates the dissociation between autobiographical and non-autobiographical information; autobiographical information was largely spared whilst non-autobiographical knowledge was severely impaired. Second, it supports the proposed distinction between two components of semantic memory: that which is semanticized and bereft of episodic relevance, and that which is personalized and relies on some autobiographical information. Memory for public events and personalities was virtually non-existent with one interesting exception; memory representations were intact for world events and famous people that had somehow affected her personally. This finding seems analogous to the present finding of preserved memory representations in EL for famous people that were particularly memorable from a personal standpoint.

Research on episodic memory in semantic dementia, however, is still in its early stages, effectively having begun with the seminal observations of Warrington, Snowden *et al.* and Graham and Hodges (Warrington, 1975; Snowden *et al.*, 1996; Graham and Hodges, 1997). Furthermore, the present study is the first to attempt to circumvent the verbal impairments in semantic dementia by utilizing family photographs as prompts and by adopting a different set of evaluation criteria in testing autobiographical memory. More investigations, using appropriate measures, are needed to corroborate our evidence and determine whether the sparing of remote, episodic memory is typical of this disorder. At this stage, it is unclear whether the pattern of performance demonstrated by EL applies to all semantic dementia patients or only to a subset of them.

Given the nature of our test, it may be difficult to demonstrate a temporal gradient in the integrity of autobiographical episodic memory. Our point, however, is not that there is no gradient, but rather that, given the proper testing conditions, it is possible to demonstrate that remote autobiographical memories are not invariably lost; even in the advanced stages of semantic dementia, they can be rich and evocative. Viewed in the light of the present study, the 'reversed' temporal pattern observed in the studies of Graham and Hodges (Graham and Hodges, 1997) may be the result of the testing method they used and an exaggeration of the normal forgetting curve seen in controls when tests challenge their memory (Crovitz and Schiffman, 1974; Rubin and

Schulkind, 1997; Moscovitch and Nadel, 1999). Memory for recent events is best and, except for a 'reminiscence bump' in one's late teens and early twenties, tails off as more remote periods are sampled.

Like Snowden *et al.* and Graham and Hodges, we attribute the relative sparing of episodic memory to the preservation of the medial temporal lobe in semantic dementia, although we believe it applies as much to remote as to recent memory. It is important to note, however, that according to multiple trace theory, the autobiographical memory trace does not depend on the medial temporal lobes alone, but on an ensemble of medial temporal lobe–neocortical neurons that represents the conscious experience of a particular event. Degeneration or lesions of the neocortical component should also affect autobiographical memory. That autobiographical memory remains well preserved in EL suggests that some neocortical component is still viable. EL's performance on psychometric tests shows that visuo-spatial functions and syntax are maintained in comparison with verbal, semantic functions. Extrapolating from reports of other similar cases in the literature, one can surmise that the degeneration associated with dementia affected primarily the posterior and superior aspects of the temporal lobe in the left hemisphere. One possibility is that the neocortical component of the memory trace depends on the remaining healthy tissue in the left hemisphere, or the relatively preserved tissue on the right, or both. As the insidious, degenerative process of the disease encroaches on these areas, both recent and remote episodic memory will suffer, even if the medial temporal lobe is untouched. Exactly what the course of this disorder is, with respect to episodic memory, is not yet known, but the step function in autobiographical memory loss observed by Graham and Hodges, suggests that the loss, when it occurs, may be catastrophic (Graham, 1999).

In contrast to the unique aspects of our evidence with regard to EL, the severe loss of remote autobiographical episodes demonstrated by patient KC is closer to being the norm than the exception in people with extensive medial temporal lobe lesions. Although KC may be unusual in that he cannot recall a single personal experience from his entire lifetime, he is not unique. There is substantial evidence to suggest that significant damage to the medial temporal lobes typically results in severe retrograde amnesia for episodes that extend back 20 years or longer. Several studies have documented amnesic patients showing a loss of autobiographical episodes extending across the entire lifetime without a temporal gradient (reviewed in Fujii *et al.*, 2001). It should be noted, however, that such far-reaching loss of memory for autobiographical episodes is associated with damage that extends beyond the hippocampus proper to include the adjacent regions of the medial temporal lobe that form the hippocampal complex. This is as true of KC as it is of the other patients. Moreover, because KC's damage extends to other regions of the neocortex, we cannot attribute his autobiographical memory loss to hippocampal complex damage alone. Evidence from other studies points in that

direction (Viskontas *et al.*, 2000; Fuji *et al.*, 2001), although extensive loss of autobiographical memory with sparing of semantic memory can occur following damage to other regions (Hodges and McCarthy, 1993; Levine *et al.*, 1998; Kapur, 1999).

Neuroimaging studies in normal people provide further support for the idea that the retrieval of recent and remote memories depends on the hippocampal complex. Fink *et al.* used positron emission tomography in order to image the brains of subjects while they recalled autobiographical episodes from across their lifetime as well as non-personal episodes describing life events of other individuals (Fink *et al.*, 1996). When these two conditions were contrasted using the subtraction method, a host of brain regions—largely concentrated in the right hemisphere—were preferentially activated in the autobiographical episodic recall condition. These regions included the right pre-frontal cortex, the right hippocampus, parahippocampus and amygdala, and interconnecting regions, such as the right insula and right posterior cingulate. The non-autobiographical event recall condition was not associated with an increase in hippocampal activation (see also Conway *et al.*, 1999).

More recently, Ryan *et al.* (as cited in Nadel *et al.*, 2000) conducted a functional magnetic resonance imaging (fMRI) study in which seven participants recollected 10 recent autobiographical memories from the last 2 years, or 10 remote memories older than 20 years while being scanned. During each 20-s scan, the subjects were asked to re-experience a particular personal event in as much detail as possible. Activation during the autobiographical memory condition was compared with two control conditions: a resting baseline and a non-autobiographical semantic memory condition in which participants had to complete five sentences with the most appropriate word that came to mind. They found equivalent, significant levels of hippocampal activation in recent and remote memory as compared with the two control conditions in all seven participants. In five of the participants, hippocampal activation was bilateral, whereas in the other two it was unilateral, with one greater on the right, and the other on the left.

The episodic preservation observed in EL combined with the loss of virtually all autobiographical episodes in KC, along with the neuroimaging evidence, provide strong support for the claim that the hippocampal complex plays a permanent role in the storage and retrieval of autobiographical episodic memories, as predicted by multiple trace theory, rather than a time-limited role that ends upon completion of the consolidation process, as predicted by traditional consolidation theory.

Autobiographical contribution to semantic memory: personalized semantics

We found that EL read the names of places he visited more quickly and correctly than the names of those he did not, and read and recognized the names of famous people if they

were high on personal relevance rather than mere familiarity to most people in his cohort, and presumably to him. By contrast, personal relevance had no influence on KC's name recognition. EL also read more accurately and quickly, and was more likely to recognize, the names of places and landmarks he had visited as compared with the names of unvisited places and landmarks and fictitious names. His reading accuracy extended even to low frequency, exception words (which many of the places and names are). These results suggest that autobiographically significant information, which is likely to be hippocampally dependent, contributes to semantic memory and the orthographic lexicon, and is relatively preserved following extensive neocortical damage.

Our evidence provides additional support for the argument, first advanced by Snowden *et al.*, that autobiographical significance influences the degree to which semantic information remains 'personalized', retaining aspects of episodic information which is likely to be dependent upon the hippocampal complex (Snowden *et al.*, 1994, 1995, 1996). Their observations suggested that the knowledge of names and the semantic concepts that they denote, such as those related to objects, people, animals, and places, become restricted and highly personalized in semantic dementia. For example, patients only retain bits of information about how objects relate to their personal lives, such as their own vase or furniture or utensils, while losing general knowledge about the same objects if they are unfamiliar and have no personal relevance. Thus, shown their own vase and chair, they demonstrate that they understand what it is and can produce the correct name while failing to do so for unfamiliar objects of the same kind. Snowden *et al.* account for this phenomenon by arguing that personally relevant information about a concept is more likely to remain intact in semantic dementia because it is this part of the conceptual representation that remains hippocampally dependent. Non-personal pieces of information are more likely to have become semanticized, thereby losing their hippocampal representation.

Graham *et al.* (1977a,b, 1999) challenged this notion that autobiographical significance contributes to the representation of semantic information and preferentially insulates some information in cases of severe neocortical atrophy by showing that vocabulary knowledge and place knowledge pertaining to a favorite sport was not spared in two semantic dementia patients (Graham *et al.*, 1997a,b). The authors argued that if autobiographical relevance served to insulate semantic information from damage in semantic dementia, then their patients should have demonstrated intact vocabulary knowledge for terms related to a sport in which they participated regularly as compared with unplayed sports. Moreover, they argued that, if Snowden *et al.*'s hypothesis is correct, then a patient who is an avid golfer should be better able to locate golf courses on a map as compared with cities. Such preservation was not found; the patients were equally poor on all sports-related vocabulary terms regardless of the sport to which they referred, and golf courses were not more easily

located than cities by the golfing patient. Based on these findings, Graham *et al.* argued that autobiographical significance does not affect semantic integrity in semantic dementia; rather, they suggested that the recency of acquisition is the critical factor in determining which semantic information remains intact. Furthermore, they argued that the concept knowledge shown by Snowden *et al.*'s patients is not truly semantic, but merely rather 'semantic-like', existing solely at an implicit or procedural level (Snowden *et al.*, 1994, 1995, 1996).

In their reply, Snowden *et al.* (1999) argued that the Graham *et al.* findings do not challenge their original hypothesis because they do not predict that autobiographical significance will have a generalized insulating effect such that personally relevant semantics are preserved in their entirety. According to Snowden *et al.*, autobiographically significant semantic information is not expected to be normal in individuals with semantic dementia; rather, this information is expected to be only partially spared such that its conceptual representation becomes highly constrained by personal experience. Thus, semantic dementia patients would not be expected to show normal vocabulary knowledge for terms related to a favorite sport or hobby unless those words were somehow critical to the patients' direct experience. Similarly, Graham *et al.*'s golfing patient would not be expected to show spared knowledge of golf courses unless he had direct personal experience with the golf course, perhaps by having played there himself.

The tasks pertaining to place and landmark knowledge in experiment two provided a direct test of this hypothesis. Our findings suggest that personally relevant semantic information pertaining to places is preferentially spared—at least partially—in an advanced-stage semantic dementia patient. Not only was EL faster and more accurate at reading and recognizing autobiographically significant names, he was also able to locate many of these places on an unmarked map. This provides strong evidence to suggest that this preserved knowledge is not merely procedural or implicit; rather, EL seems to have some explicit semantic knowledge of these places and landmarks. The profound verbal impairment experienced by our patient prevented us from exploring the degree to which his knowledge for these personally relevant places is richly elaborated. However, in line with the views of Snowden *et al.* (1999), we would not expect that EL's conceptual representations of place and landmark names would be completely intact and comparable to those of control subjects. If, as we have argued, personally relevant information remains partially dependent upon the hippocampal complex, then autobiographically significant concepts should be more likely than non-personal concepts to retain some sort of semantic representation in patients with semantic dementia; however, these partially preserved concepts should by no means be 'normal' in terms of content and structure. Rather, the patient's understanding of these concepts should be fragmented and highly constrained by personal experience. We have called this type of knowledge *personalized*

semantics. We are currently conducting studies designed to explore the characteristics of personalized semantics, and to determine how this knowledge differs from, and interacts with, general semantic information.

As with studies of autobiographical memory, neuroimaging studies could address the specific suggestion that autobiographical significance influences the way in which semantic information is stored and retrieved. Different patterns of activation should be associated with personally relevant and impersonal semantic knowledge, with the former relying more on hippocampal complex activation than the latter under appropriate conditions.

Conclusion

We draw two main conclusions from our study. The first is that the hippocampal complex is needed to retain and retrieve memories of autobiographical episodes dating to early childhood. If the hippocampal complex is relatively preserved, those memories can be retrieved even by a person with advanced semantic dementia given the proper cues and an opportunity to respond that does not depend only on language, provided that enough viable neocortical tissue remains to support those memories. By contrast, extensive damage to the hippocampal complex leads to a severe retrograde amnesia for autobiographical episodes even if the semantic memory system and language is relatively preserved. These findings favor multiple trace theory over consolidation theory. The present findings from patient EL raise the possibility that episodic memory may exist in the absence of semantic memory, calling into question, but not refuting, Tulving's hypothesis (Tulving, 1989) that episodic memory is dependent upon an intact semantic system (but not vice versa). More work is needed to explore this hypothesis because our study also shows that semantic and episodic systems interact in ways that were not anticipated when Tulving advanced it.

The second conclusion is that episodic memory contributes to semantic memory as it is traditionally understood. EL was able to recognize better and read more quickly and accurately the names of people and places with which he had some personal experience as compared with those that were equally familiar but with which he had no personal experience. We refer to this knowledge as personalized semantics, and extend this notion, first introduced by Snowden (Snowden *et al.*, 1996), to cover not just recent experiences but remote ones as well. It remains to be determined whether personalized semantics are also dependent on the hippocampal complex as long as they are used, or whether they require the hippocampal complex only for acquisition and until consolidation is complete.

Notes

¹KC had not reviewed these photographs in the last 5–10 years. EL had not reviewed his childhood and early adult

photographs in decades, and had not reviewed any recent photographs in the last 3 or 4 years.

²Some of the information regarding KC's knowledge of recently born family members and recently encountered friends was gathered in an open-ended interview; he was not shown photographs of all these individuals.

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References

- Alvarez P, Squire LR. Memory consolidation and the medial temporal lobe: A simple neural network model. *Proceedings of the National Academy of Sciences* 1994; 91: 7401–5.
- Bahrick HP, Bahrick PO, Wittlinger RP. Fifty years of memory for names and faces: A cross-sectional approach. *Journal of Experimental Psychology: General* 1975; 104: 54–75.
- Cermak LS, O'Connor M. The anterograde and retrograde retrieval ability of a patient with amnesia due to encephalitis. *Neuropsychologia* 1983; 2: 213–34.
- Conway MA, Turk DJ, Miller SL, Logan J, Nebes RD, Meltzer CC *et al.* A positron emission tomography (PET) study of autobiographical memory retrieval. *Memory* 1999; 5–6: 679–702.
- Crovitz HF, Schiffman H. Frequency of episodic memories as a function of their age. *Bulletin of the Psychonomic Society* 1974; 4: 519–21.
- Dall' Ora P, della Sala S, Spinnler H. Autobiographical memory: Its impairment in amnesia syndromes. *Cortex* 1989; 25: 197–217.
- Damasio AR. Time-locked multiregional retroactivation: A systems-level proposal for the neural substrates of recall and recognition. *Cognition* 1989; 33: 25–62.
- Damasio AR, Eslinger PJ, Damasio H, Van Hoesen GW. Multimodal amnesic syndrome following bilateral temporal and basal forebrain damage. *Archives of Neurology* 1985; 42: 252–9.
- De Renzi E, Liotti M, Nichelli P. Semantic amnesia with preservation of autobiographical memory: A case report. *Cortex* 1987; 23: 575–97.
- Fink GR, Markowitsch HJ, Reinkemeier M, Bruckbauer T, Kessler J, Heiss WD. Cerebral representations of one's own past: Neural networks involved in autobiographical memory. *Journal of Neuroscience* 1996; 16: 4275–82.
- Fujii T, Moscovitch M, Nadel L. Consolidation, retrograde amnesia, and the temporal lobe. In: Boller F, Grafman J, editors. *The handbook of neuropsychology*, Vol. 4. Amsterdam: Elsevier, 2001; in press.
- Gardiner JM. Functional aspects of recollective experience. *Memory and Cognition* 1988; 16: 309–13.
- Graham KS. Semantic dementia: A challenge to the multiple-trace theory? *Trends in Cognitive Sciences* 1999; 3: 85–7.
- Graham KS, Hodges JR. Differentiating the roles of the hippocampal system and the neocortex in long-term memory storage. *Neuropsychology* 1997; 11: 77–89.
- 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* 1997a; 3: 534–44.
- Graham KS, Lambon Ralph MA, Hodges JR. Determining the impact of autobiographical experience on 'meaning': New insights from investigating sports-related vocabulary and knowledge in two cases with semantic dementia. *Cognitive Neuropsychology* 1997b; 14: 801–37.
- 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.
- Graham KS, Lambon Ralph MA, Hodges JR. A questionable semantics: The interaction between semantic knowledge and autobiographical experience in semantic dementia. *Cognitive Neuropsychology* 1999; 16: 689–98.
- 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.
- Hodges JR, McCarthy RA. Autobiographical amnesia resulting from bilateral paramedian thalamic infarction. *Brain* 1993; 116: 921–40.
- Hodges JR, McCarthy RA. Loss of remote memory: A cognitive neuropsychological perspective. *Current Opinion in Neurobiology* 1995; 5: 178–83.
- Hodges JR, Patterson K, Ward R, Garrard P, Bak T, Perry R, Gregory E. 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.
- Kapur N. Syndromes of retrograde amnesia: A conceptual and empirical synthesis. *Psychological Bulletin* 1999; 6: 800–25.
- Kapur N, Scholey K, Moore E, Barker S, Brice J, Thompson S *et al.* Long-term retention in two cases of disproportional retrograde amnesia. *Journal of Cognitive Neuroscience* 1996; 8: 416–34.
- Kinsbourne M, Wood F. Short-term memory processes and the amnesic syndrome. In: Deutsch D, Deutsch JA, editors. *Short-term memory processes*. New York: Academic Press, 1975: 258–91.
- Kopelman MD, Wilson BA, Baddeley AD. *The Autobiographical Memory Interview*. Bury St. Edmunds: Thames Valley Test Company, 1996.
- Levine B, Black SE, Cabeza R, Sinden M, McIntosh AR, Toth JP *et al.* Episodic memory and the self in a case of isolated retrograde amnesia. *Brain* 1998; 121: 1951–73.
- McClelland JL, McNaughton BL, O'Reilly RC. Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. *Psychological Review* 1995; 102: 419–57.
- Moscovitch M. Memory and working with memory: A component process model based on modules and central systems. *Journal of Cognitive Neuroscience* 1992; 4: 257–67.
- Moscovitch M. Recovered consciousness: A hypothesis concerning modularity and episodic memory. *Journal of Clinical and Experimental Neuropsychology* 1995; 17: 276–90.
- Moscovitch M, Nadel L. Consolidation and the hippocampal complex revisited: In defense of the multiple-trace model. *Current Opinion in Neurobiology* 1998; 8: 297–300.
- Moscovitch M, Nadel L. Multiple-trace theory and semantic dementia: Response to K. S. Graham (1999). *Trends in Cognitive Sciences* 1999; 3: 87–9.
- Murre JMJ. Implicit and explicit memory in amnesia: Some explanations and predictions by the Trace Link model. *Memory* 1997; 6: 675–84.
- Nadel L, Moscovitch M. Memory consolidation, retrograde amnesia and the hippocampal complex. *Current Opinion in Neurobiology* 1997; 7: 217–27.
- Nadel L, Samsonovich A, Ryan L, Moscovitch M. Multiple trace theory of human memory: Computational, neuroimaging, and neuropsychological results. *Hippocampus* 2000; 10: 1044–8.
- Ogden JA. Visual object agnosia, prosopagnosia, achromatopsia, loss of visual imagery, recovery from cortical blindness: Case M.H. *Neuropsychologia* 1993; 31: 571–89.
- Rosenbaum RS, Priselac S, Kohler S, Black SE, Gao F, Nadel L, Moscovitch M. Remote spatial memory in an amnesic person with extensive bilateral hippocampal lesions. *Nature Neuroscience* 2000; 10: 1044–8.

- Rubin DC, Greenberg DL. Visual memory-deficit amnesia: A distinct amnesic presentation and etiology. *Proceedings of the National Academy of Sciences USA* 1998; 95: 5413–6.
- Rubin DC, Schulkind MD. Distribution of important and word-cued autobiographical memories in 10-, 35-, and 70-year-old adults. *Psychology and Aging* 1997; 12: 524–35.
- Sanders HI, Warrington EK. Memory for remote events in amnesic patients. *Brain* 1971; 94: 661–8.
- Shallice T. *From neuropsychology to mental structure*. New York: Cambridge University Press, 1988.
- Snowden JS, Griffiths HL, Neary D. Semantic dementia: Autobiographical contribution to preservation of meaning. *Cognitive Neuropsychology* 1994; 11: 265–88.
- Snowden JS, Griffiths HL, Neary D. Autobiographical experience and word meaning. *Memory* 1995; 3: 225–46.
- Snowden JS, Griffiths HL, Neary D. Semantic–episodic memory interactions in semantic dementia: Implications for retrograde memory function. *Cognitive Neuropsychology* 1996; 13: 1101–37.
- Snowden JS, Griffiths HL, Neary D. The impact of autobiographical experience on meaning: Reply to Graham, Lambon Ralph and Hodges. *Cognitive Neuropsychology* 1999; 16: 673–87.
- Squire LR. Memory and the hippocampus: A synthesis from findings with rats, monkeys and humans. *Psychological Review* 1992; 99: 195–231.
- Squire LR, Alvarez P. Retrograde amnesia and memory consolidation: A neurobiological perspective. *Current Opinion in Neurobiology* 1995; 5: 169–77.
- Squire LR, Slater PC. Forgetting in very long-term memory as assessed by an improved questionnaire technique. *Journal of Experimental Psychology: Human Learning and Memory* 1975; 104: 50–4.
- Squire LR, Ojemann JG, Miesin FM, Peterson SE, Videen TO, Raichle FM. Activation of the hippocampus in normal humans: A functional anatomical study of memory. *Proceedings of the National Academy of Sciences USA* 1992; 89: 1837–41.
- Tulving E. Memory and consciousness. *Canadian Psychologist* 1985; 25: 1–12.
- Tulving E. Remembering and knowing the past. *American Scientist* 1989; 77: 361–7.
- Tulving E, Schacter DL, McLachlan DR, Moscovitch M. Priming of semantic autobiographical memory: A case study of retrograde amnesia. *Brain and Cognition* 1988; 8: 3–20.
- Van der Linden M, de Partz M, Schils J, Seron X. Semantic and autobiographical memory: Neuropsychological dissociations? In: Conway MA, Rubin DC, Spinnler H, editors. *Theoretical perspectives on autobiographical memory*. Boston: Kluwer, 1992: 473–94.
- Viskontas IV, McAndrews MP, Moscovitch M. Remote episodic memory deficits in patients with unilateral temporal lobe epilepsy and excisions. *Journal of Neuroscience* 2000; 20: 5853–7.
- Warrington EK. The selective impairment of semantic memory. *Quarterly Journal of Experimental Psychology* 1975; 27: 635–57.
- Warrington EK. Neuropsychological studies of object recognition. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences* 1982; 298: 15–33.
- Warrington EK. Studies of retrograde memory: A long-term view. *Proceedings of the National Academy of Sciences USA* 1996; 93: 13523–6.
- Warrington EK, McCarthy R. The fractionation of retrograde amnesia. *Brain and Cognition* 1988; 7: 184–200.

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Different patterns of autobiographical memory loss in semantic dementia and medial temporal lobe amnesia: a challenge to the consolidation theory

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Abstract

Temporally graded retrograde memory loss, with a disproportionate impairment of recent relative to remote memories, is considered a hallmark of medial temporal lobe amnesia. According to consolidation theory, the hippocampal complex, which includes the hippocampal formation, parahippocampal gyrus, the entorhinal and perirhinal cortex, plays a time-limited role in memory, needed only until consolidation in the neocortex is complete (Squire, *Psychological Review* 1992; 99: 195–231). Recent support for this theory comes from findings of a reverse gradient in people with semantic dementia with neocortical degeneration but a relatively preserved hippocampal complex (Hodges and Graham, *Neuropsychologia* 1998; 36: 803–25). Consolidation theory is challenged by evidence that remote autobiographical memory is not always spared in amnesia (Nadel and Moscovitch, *Current Opinion in Neurobiology* 1997; 7: 217–27) and that semantic memory becomes highly personalized in semantic dementia (Snowden *et al.*, *Memory* 1995; 3: 225–46). According to Nadel and Moscovitch, the hippocampal complex is needed to retain and retrieve detailed memories of autobiographical episodes no matter how old they are. To test consolidation theory against the opposing view, we investigated the role of the hippocampal complex in recent and remote autobiographical and personal semantic memory by contrasting the memory of a semantic dementia patient, EL, with that of an amnesic patient, KC, using family photographs as recall cues. KC demonstrated a complete loss of autobiographical episodes with a sparing of autobiographical facts; EL demonstrated well-preserved memory for episodes with a reverse gradient for personally relevant names. The influence of autobiographical significance on memory for names of public figures was examined further by comparing the effect that familiarity and recollection had on recognition of names of famous people and famous places. EL's memory was influenced by autobiographical significance, whereas KC's was not. We propose that the hippocampal complex plays a permanent role in the storage and retrieval of autobiographical episodes and that autobiographical significance may affect semantic representations.

Journal

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Primary diagnosis of interest

Semantic dementia

Author's designation of case

EL and KC

Key theoretical issue

- Does the hippocampal complex play a temporary or permanent role in autobiographical episodic memory?

Key words: semantic dementia; amnesia; consolidation; autobiographical memory; episodic memory; temporally graded retrograde memory loss

Scan, EEG and related measures

MRI, SPECT, EEG for EL; MRI, PET for KC

Standardized assessment

WAIS-R, WMS-R, Controlled Oral Word Association Test, Dementia Rating Scale, California Verbal Learning Test, Boston Naming Test, Rey–Osterrieth Figure, Warrington Recognition Test, Benton Face Discrimination Test, Judgment of Line Orientation

Other assessment

Autobiographical episodic memory, semantic memory for famous names and places

Lesion location

- EL: global, mild–moderate cerebral atrophy, noticeable especially in the anterior temporal lobe, and more pronounced on the left than on the right. The hippocampus may be slightly smaller on the left
- KC: bilateral hippocampus and perhippocampal tissue, right occipital, left fronto-parietal

Lesion type

EL: progressive atrophy possibly due to Pick's disease
KC: multiple infarct lesion due to closed-head injury

Language

English