

Rapid publication

Medial temporal lobe structures are needed to re-experience remote autobiographical memories: evidence from H.M. and W.R.

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Abstract

The nature and extent of retrograde amnesia in patients with medial temporal lobe (MTL) lesions is currently under debate. While some investigators propose a temporally limited role for the MTL in episodic and semantic memory, others claim that MTL structures are needed for episodic memories of one's entire lifetime, and that only semantic memory becomes independent of the MTL. To address this issue, we tested two amnesic patients, H.M. and W.R., with bilateral MTL lesions on a series of remote memory tests that together distinguished episodic memory from semantic memory performance. Notably, we used a new method to assess autobiographical memory that measured the degree of re-experiencing of personal happenings from the past. Both patients showed relatively spared semantic memory, but severe impairment on measures of autobiographical memory, with no temporal gradient. Our data support the view that MTL structures play a significant role in recalling specific personal episodes, not only from the recent past but from the distant past as well.

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1. Introduction

The importance of medial temporal lobe structures (MTL) in the acquisition of declarative memory has been appreciated for decades (Corkin, 1984; Milner, Corkin, & Teuber, 1968; Scoville & Milner, 1957). Recent theoretical discussions, however, have called into question the role of the MTL in remote memory. A widely held view is that the MTL contribution is temporally circumscribed and becomes unnecessary after consolidation (Squire, 1992; Squire & Alvarez, 1995). According to this model, the Standard Model of Consolidation (SMC), information is established initially as short-lived modifications in the reciprocal connections between neocortex and MTL. The MTL points to and activates sites in the neocortex that contain the attended information. Consolidation occurs when the MTL system re-

peatedly reactivates representations in the cortex, resulting in strong interconnections among cortical sites that can maintain memory independently. The proposed time limited role of the hippocampus and related structures applies to the two types of declarative memory: factual information (semantic memory) and autobiographical,¹ event-specific information (episodic memory) (Squire, 1992). Semantic memory refers to general knowledge that is free of context, including facts about the world as well as oneself. Episodic memory refers to the recollection of contextually bound experiences of happenings that occurred at a specific time and place; it enables the re-experiencing of these past events (Tulving, 1972, 2002).

¹ Autobiographical memory is often considered to be the core of episodic memory, e.g., the memory of an event that happened at a specific time and place. However, autobiographical memory (and autobiographical narratives) also includes information that is semantic in nature, e.g., date and place of birth.

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In contrast to the SMC, the Multiple Trace Theory (MTT) (Moscovitch, Yaschyshyn, Ziegler, & Nadel, 1999; Nadel & Moscovitch, 1997; Nadel, Samsonovich, Ryan, & Moscovitch, 2000) proposes that the MTL is always necessary for the retrieval of episodic memory, but that semantic memory becomes independent from these structures over time. According to the MTT, hippocampal complex neurons provide a substrate in which relevant information represented in neocortical neurons can be bound together to form a coherent memory trace. Each time a memory trace is activated a newly encoded hippocampal trace is formed. Hippocampal traces serve as the basis to reactivate neocortical traces and thereby strengthen neocortical links. Alternatively, they might cause, or facilitate, the creation of a new neocortical node with neocortical links to other neocortical elements contained in the original episodic memory. Thus, semantic memory, but not episodic memory, becomes consolidated and independent from the MTL.

The goal of the present study was to evaluate these alternate models by studying amnesic patients with MTL lesions. Both models make the same predictions for remote semantic memory. Their predictions for remote episodic memory differ. The SMC predicts that MTL lesions should affect episodic and semantic memory equally, and that one should see a temporal gradient, with recent memories more affected than remote ones, due to the consolidation process. The MTT predicts that episodic memory is more affected than semantic memory in retrograde amnesia (RA). It also predicts a temporal gradient for semantic and episodic memory. The MTT assumes a consolidation process for semantic memory, leading to a temporal gradient in RA; it predicts that older episodic memories are more resistant to partial damage of the MTL² than recent episodic memories because older memories are usually associated with a greater number of memory traces. Thus, the critical distinction between the SMC and the MTT rests on whether episodic memory and semantic memory are affected differentially, especially for more remote time periods.

Some previous studies of remote memory found a temporally limited RA in MTL patients that affected episodic and semantic memory equally, thereby supporting the SMC (Fujii, Yamadori, Endo, Suzuki, & Fukatsu, 1999; Kapur & Brooks, 1999; Reed & Squire, 1998; Rempel-Clower, Zola, Squire, & Amaral, 1996; Schnider, Bassetti, Gutbrod, & Ozdoba, 1995). These studies mostly used the Crovitz procedure or the Autobiographical Memory Interview (AMI), which have been criticized on the grounds that they are not sufficiently sensitive in differentiating between memory reports that are rich in detail from those that are just detailed enough to merit the maximum score (Moscovitch et al., 1999; Nadel et al., 2000). Other studies used individually tailored Autobiographical Interviews or recognition tests of autobio-

graphical memory (Fujii et al., 1999; Kapur & Brooks, 1999; Schnider et al., 1995). These tests, however, either examined personal semantic memory rather than episodic memory, or their methods were vaguely described. In further studies, frontal lobe dysfunction or a history of alcohol abuse diminished the usefulness of the cases (Cipolotti et al., 2001; Hirano & Noguchi, 1998; Hirano, Noguchi, & Hosokawa, 1999; Hirano, Noguchi, Hosokawa, & Takayama, 2002; Kartsounis, Rudge, & Stevens, 1995). Thus, previous conclusions about equal deficits in episodic and semantic memory may be erroneous.

A methodological advance was introduced by investigators who scored responses in an autobiographical memory test by simply counting the number of details provided for each memory report (Moscovitch et al., 1999; Nadel et al., 2000). The five amnesic patients tested by these authors demonstrated a loss of details in autobiographical memory reports as well as a flat temporal gradient. These cases, however, cannot adequately address the question of the role of the MTL in remote memory because in three of the five patients, the lesions included not only MTL structures but other areas as well, and in the remaining two cases, MTL structures were spared (Moscovitch et al., 1999).

A recent report describes eight amnesic patients who performed a series of autobiographical memory tests, six with damage limited primarily to the hippocampal region and two with more extensive MTL damage (Bayley, Hopkins, & Squire, 2003). The authors used a modified Crovitz procedure and a refined scoring system to evaluate the number of details contained in each narrative. They categorized only the content of well-formed autobiographical narratives into episodic and semantic details, where episodic details contained information that pertained to an event, and semantic details contained information that did not pertain to the event. The results showed no significant differences in the number of episodic or semantic details between patient and control groups. Although this approach was more rigorous than previous assessments of remote autobiographical memory, the interview did not allow participants to provide details to their full potential: the interviewer gave prompts only "as needed" and subjectively judged when the participant had recalled as many details as possible (Bayley et al., 2003, p. 142). Some investigators have pointed out that the usual level of processing in recalling autobiographical memories is at a level that lacks experience-near details (i.e., highly specific information, such as sounds, sights, tastes, smells, thoughts, and emotions) (Cipolotti et al., 2001; Conway, 2001; Rosch, 1978). By this view, autobiographical memory can be conceptualized along different levels of abstraction, and an adequate understanding of the truly episodic character and the richness of autobiographical memory requires uncovering such experience-near details. A failure in previous studies to ask for this level of information may account for some of the disagreements between proponents of the SMC and MTT. In the present study, we introduced two methodological advances intended to shed light on this debate: (a) an Autobiograph-

² Damage to the entire MTL would produce a flat gradient for episodic memory because it is indexed at the level of and always depends upon the MTL (Nadel & Moscovitch, 1998).

ical Memory Interview and scoring system that was more sensitive than measures used previously in the assessment of remembering specific, experience-near events, and (b) a detailed interview about public events to control for the narrative structure of the autobiographical memory reports and the associated increase in working memory load. We applied these methods to two amnesic patients with MTL lesions, H.M. and W.R. The results indicate that remote autobiographical memory is disproportionately impaired in amnesia relative to remote semantic memory.

2. Participants and methods

2.1. Amnesic patients

W.R. became amnesic in 1982, at age 58, after a left MTL infarct associated with cerebral angiography. Her lesion included the entire left hippocampus, except for the posterior aspect, left fusiform gyrus, and the major part of the left parahippocampal gyrus (Fig. 1). The anterior part of the right hippocampus as well as the right parahippocampal gyrus were atrophic. Both amygdalae were intact. W.R. showed signs of an age-appropriate generalized atrophy; however, the bilateral atrophy (left larger than right) in the inferior parietal lobe may be larger than one would expect with normal aging.

In addition, she had a lesion in the right superior temporal gyrus and a lacunar lesion in the ventrolateral posterior nucleus of the right thalamus. W.R. had 12 years of education and was right-handed. Besides her severe memory deficit, she showed a slight visuospatial deficit on the Rey–Osterreith Complex Figure (copy) but showed no signs of visuospatial neglect (Table 1).

H.M. has been amnesic since 1953 when at age 27 he underwent a bilateral MTL resection as an experimental treatment for medically intractable epilepsy (Scoville & Milner, 1957). Using magnetic resonance imaging, Corkin, Amaral, Gonzalez, Johnson, and Hyman (1997) found that his bilaterally symmetrical lesion included the medial temporal polar cortex, most of the amygdaloid complex, the entorhinal cortex, and approximately half of the rostrocaudal extent of the intraventricular portion of the hippocampal formation (dentate gyrus, hippocampus, and subicular complex) (Fig. 1). The ventral perirhinal cortex on both banks of the collateral sulcus, the parahippocampal complex, and the posterior 2 cm of the hippocampus were spared, but atrophied. The anterior medial temporal cortex was damaged bilaterally, and the subcortical white matter associated with the most anterior portions of the superior, middle, and inferior temporal gyri was compromised. Outside of the temporal lobe, the cerebellum showed pronounced atrophy, and the mammillary nuclei were shrunken. H.M. had 12 years of education and was right-handed. An

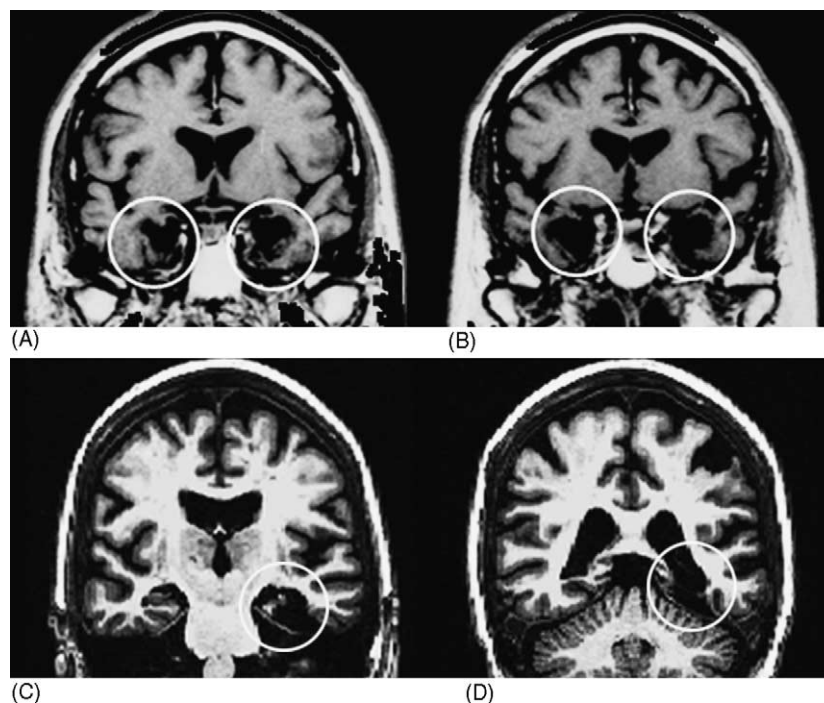


Fig. 1. T1-weighted images showing the locus and extent of bilateral MTL lesions in H.M. and W.R. H.M.'s removal includes approximately half of the rostrocaudal extent of the hippocampal formation (A), and most of the entorhinal cortex (B). W.R.'s lesions include the left parahippocampal gyrus and the hippocampal formation (C), and the left fusiform gyrus (D). Her lesion included the entire left hippocampus, except for the posterior aspect, left fusiform gyrus, and the major part of the left parahippocampal gyrus. The anterior part of the right hippocampus as well as the right parahippocampal gyrus were atrophic. Both amygdalae were intact.

Table 1
Selected standardized test scores for H.M. and W.R.

Test	H.M.	W.R.
Wechsler Adult Intelligence Scale—Revised		
Verbal IQ	104 ^a	119
Performance IQ	124	102
Full-Scale IQ	106	112
Wechsler Memory Scale—Revised		
Verbal memory	74	70
Visual memory	77	90
General memory	72	73
Attention/concentration	87	79
Delayed recall	<65	<65
Rey Auditory–Verbal Learning Test		
Learning list	12/75	20/75
Interference list	10/15	1/15
After interference	0/15	1/15
Delayed recall	0/15	0/15
20-min delayed recognition	4/15	6/15
Rey–Osterreith Complex Figures Test (copy) (z-score)	−7.32 ^b	−3.3
Wisconsin Card Sorting Test		
Categories completed	5	5
Perseverative errors (z-score)	−0.39	1.2
Porteus Mazes	TQ 110	TQ 114
Boston Naming Test	64/85	68/85

Scores indicating impairment are printed in italics.

^a H.M.'s Verbal IQ is relatively lower than his Performance IQ, probably reflecting the low socioeconomic status of his family and his attendance at a technical high-school.

^b H.M.'s poor copy is likely secondary to a sensory neuropathy in his hands following years of medication with Dilantin.

overview of his intelligence and memory scores are given in Table 1.

2.2. Control participants

The control group (CON) consisted of eight healthy volunteers (four women), who were recruited through fliers posted throughout the Boston/Cambridge area and through the Harvard Cooperative on Aging. They were matched to H.M. and W.R. with respect to age, education, and Full-Scale IQ (mean age: 76.8 ± 3 years, mean education: 12.0 ± 0 years, mean Full-Scale IQ: 114 ± 10.9 , mean Memory Quotient: 114 ± 12.4). All were native English speakers and right-handed. Participants were screened to exclude those with a history of alcoholism, major heart disease, cancer, diabetes, and neurological or psychiatric disorders. All participants gave written consent and were compensated for their participation. The study design was approved by the MIT Committee on the Use of Humans as Experimental Subjects and was performed in accordance with the ethical standards of the Declaration of Helsinki.

2.3. Behavioral tasks

The behavioral tasks distinguished between semantic and episodic memory. An impairment was defined as any test

score that was ≥ 2 standard deviations (S.D.) below the mean of the CON group.

2.4. Semantic memory

2.4.1. New Vocabulary Test (Verfaellie, Reiss, & Roth, 1995)

We assessed knowledge of the meaning of 94 words that entered the English language at different time periods. The seven sets of words represented 5-year intervals extending from 1955 to 1990. In addition, 12 low-frequency words that came into common use before 1920 served as control words to provide a baseline measure of performance for low-frequency words. In the recall version of the task, participants defined these words orally. In the recognition version, participants chose their answer from among four choices (one correct answer and three distractors).

2.4.2. Facts about Public Events Test

In this paper and pencil test, participants answered 77 multiple-choice questions about public events that were in the public eye for a circumscribed period of time from 1940 to 2000.³ The questions represented six decades from 1940 on and the year 2000 (1940s: 13 items, 1950s: 11 items, 1960s: 11 items, 1970s: 9 items, 1980s: 14 items, 1990s: 11 items, year 2000: 8 items). A temporal gradient of RA can be accurately measured only when the test performance of, for example, the 1950s represents the knowledge acquired during this time period and not later. To control for the possibility that knowledge of public events acquired after their occurrence was not substantial, we showed in a pilot study that older adults could answer questions for events from the 1940s to the 1980s significantly better than young adults. The difficulty level of the final version was about 72% correct (1940s: 73%, 1950s: 71%, 1960s: 71%, 1970s: 72%, 1980s: 72%, 1990s: 73%, 2000: 74%).

For each item, the correct answer was presented with three distracters. Thus, for the question, "What was the name of the tennis star who was stabbed?" possible answers were (a) Steffi Graf, (b) Monica Seles, (c) Martina Hingis, and (d) Anna Kournikova. The questions related to politics, sport and social events, scandals, natural and man-made catastrophes, aspects of daily living, and technological achievements. This test measured semantic memory because it asked about the gist of a public event, but did not require a recollection of the spatiotemporal context or other details of the event. Items were scored "1" for a correct answer and "0" for an incorrect answer.

2.4.3. WASI Vocabulary subtest (Wechsler, 1999)

CON gave oral definitions for a list of 33 words. H.M. performed the Vocabulary subtest of the Wechsler–Bellevue

³ An important criterion in selecting the events was that they appeared in the media for a restricted time period ranging from several weeks to 12 months.

Scale (42 words) and W.R. the Vocabulary subtest of the WAIS-R (35 words) (Wechsler, 1946, 1981). We used the older test versions for the amnesic patients because these newer versions took into account cultural changes, which these amnesic patients could not be expected to have learned.

2.4.4. WASI Information subtest (Wechsler, 1999)

CON answered 28 questions assessing their general knowledge. H.M. performed the subtest of the Wechsler–Bellevue Scale with 25 questions, and W.R. the subtest of the WAIS-R with 29 questions (Wechsler, 1946, 1981).

2.4.5. Personal semantic memory schedule of the Autobiographical Memory Interview (Kopelman, Wilson, & Baddeley, 1990)

Participants were asked about facts concerning their personal past from three time periods: childhood, early adult life, and recent life. The questions included the names of schools or teachers, colleagues, or similar facts. The maximum score for each time period was 21. Correct responses could earn 2, 1, or 1/2 points as indicated in the scoring manual (Kopelman et al., 1990). We chose not to administer the Autobiographical Incidents Schedule of the AMI because it is a less sensitive measure of memory of personal episodes than Levine et al.'s (2000) Autobiographical Interview.

2.5. Episodic memory

2.5.1. Autobiographical Interview (Levine, Svoboda, Hay, Winocur, & Moscovitch, 2002)

The Autobiographical Interview was developed to assess the degree to which participants were able to re-experience personal happenings from the past. The scoring system assumed that an autobiographical memory report contained episodic and non-episodic information, and that the two were separable. The episodic aspects implicated the re-experiencing of a single event from a specific time and place, including the recollection of contextual details. The major component of the non-episodic aspect was semantic information. Details that did not reflect the recollection of an autobiographical memory, such as metacognitive statements (e.g., “Let me see if I can remember that.”), editorializing (e.g., “That’s amazing.”), and inferences (e.g., “I must have been wearing a coat because it was winter.”) were not included in the analyses.

Participants were asked to recall spontaneously one event specific in time and place, lasting from minutes up to several hours, in which they personally participated, from each of five life periods: childhood (up to age 11), teenage years (ages 12–17), early adulthood (ages 18–35), middle age (ages 36–55), and the year prior to testing. They then provided as many details as possible about that event. If they could not recall an event spontaneously on their own, we presented a list of approximately 100 typical life events (wedding, moving, buying a car) to assist with memory retrieval. We went over the cue list together with the patient and provided ample

time (about 30 min for each time period if necessary) for the participants to recall an event. They needed to describe only one event per lifetime period giving them amnesic patients the maximal opportunity to display their episodic memory. We asked participants to avoid recounting an event they had described frequently since its occurrence. This instruction was intended to preclude participants’ recounting “personal folklore,” a memory told over and over again, such that the teller does not recall so much the original event itself but rather recalls the multiple times he or she told the story. This frequent retelling would be expected to render the memory more semantic than episodic. If possible, relatives of the participants were asked whether they knew about the memory, and whether it was part of their personal folklore.

Two types of retrieval support, general probe and specific probe, elicited supplementary details that were not freely recollected. During free recall, participants talked about the event spontaneously without any interference from the examiner until they reached a natural ending point. After an event was recalled, the examiner gave general probes either to encourage greater recall of details or to clarify instructions. The specific probe condition consisted of a structured interview intended to evoke additional contextual details that were not recalled spontaneously. The interview questions were organized into five categories: event, time, place, perception, and emotion/thought. If free recall and general probing did not elicit a specific event, the experimenter gave the participant the option of selecting a different event that was more likely to lead to effective recall. At the end of the interview, participants rated the vividness of each memory, the emotional change caused by the event, and the personal importance of the event – both at the time of testing as well as at the time of its occurrence – on a scale from 1 to 6, with 1 being the least vivid and 6 being the most vivid. The interviews were tape-recorded and transcribed.

We used standardized procedure for scoring that gave quantitative and qualitative scores (Levine et al., 2002). Each memory narrative, including information from free recall, general probe, and specific probe, was segmented according to the kind of informational details: a unique occurrence, observation, or thought. The details were also classified into two broad categories, internal and external details. Internal details pertained directly to the event, reflecting contextual richness and episodic re-experiencing (episodic memory). External details included factual information or extended events that did not require recollection of a specific time and place, as well as details not pertaining to the main specific autobiographical event that mainly measured semantic memory. Repetitions were not taken into account in either category because it was assumed that amnesic patients would give a higher number of repetitions than CON. Scoring (number of details) was done separately for each retrieval condition. The investigator who scored the transcripts (S.S.) undertook extensive training with one of the developers of the instrument (B.L.). As a further measure of reliability, 12 (24%) of the memories from this study were selected at random by

a research assistant at MIT who was naïve to the purpose of the experiment. These memories were scored again by a research assistant at the University of Toronto who had extensive experience with the scoring system but no knowledge of the experiment. Identifying information about group status (patient versus control) and lifetime period was stripped from the memories. The consistency of the primary scorer vis-à-vis the secondary scorer using the 12 memories was assessed via the intraclass correlation coefficient using a two-way mixed model, consistency type, with scorer treated as a fixed effect. The coefficients for internal and external details following specific probing (which are the main measures reported below) were 0.86 and 0.90, respectively. For reference, the cut-off for “excellent agreement beyond chance” is 0.75 (Fleiss, 1981, p. 218).

2.5.2. *Public Events Interview*

The Public Events Interview was included to control for the narrative structure and the higher working memory load of the Autobiographical Interview compared to the semantic memory tests. This interview qualifies as episodic memory because it asks about the context of events that occurred in particular places at particular times. Participants were asked to recall public events, one from each of five life periods: childhood, teenage years, early adulthood, middle age, and the preceding year. They were instructed to give the contextual details of a public event rather than telling how they learned about the public event, because the latter would reflect an autobiographical memory. We used the same procedure and scoring as for the Autobiographical Interview with two modifications: (a) a different cue list with 16 broad categories of public events was given (e.g., wedding of a famous person, kidnapping), and (b) the events could last more than several hours, but had to be thematically circumscribed. The interviews were tape-recorded, transcribed, and segmented; the details were categorized as internal or external. As with the Autobiographical Interview, internal details were those that pertained directly to the main event, developing the story. External details contained information unrelated to the specific event, including those reflecting personal thoughts and emotions related to the public event. For example, in the public event of the Lindbergh child kidnapping, the information that Charles Lindbergh was a famous pilot would be scored as an external detail, while the information that the cradle was found empty would be scored as an internal detail.

It is important to note that memories of public events do not fall exclusively into the domain of episodic memory because many details that constitute the memory of a public event are part of general knowledge. For example, the description of the public event in which the battleship USS Arizona sunk at Pearl Harbor on December 7, 1941 is based on general knowledge. Thus, internal details may reflect general knowledge as well as episodic memory. Similarly, the external details can include aspects of episodic memory, such as description about how the participant felt when he or she first

learned about the public event. In the Public Events Interview, internal details did not map exclusively onto episodic memory or external details onto semantic memory.

2.6. *Special procedures for amnesic patients*

A short instruction for each test was always within view of W.R. and H.M. to serve as a reminder of the task. For the Autobiographical Interview and the Public Events Interview, a title for the event being recounted was on a sheet of paper in front of the patient. The first 10 words of the cue lists of the Autobiographical Interview and the Public Events Interview were read to the amnesic patients and then offered to them to continue reading through it if desired. The cue list was then kept in the field of view of the patient until a specific event was recalled.

3. Results

3.1. *Semantic memory*

3.1.1. *New Vocabulary Test: free recall and recognition*

The pattern of scores for the free recall and recognition measures did not differ (Fig. 2). W.R. performed well within the range of CON, including for >1980 and >1985 time periods, which fell after the onset of her amnesia. H.M. performed below the range of CON for all time periods starting from 1955 on; all are time periods after he became amnesic. He also showed a deficit for the baseline condition, which consisted of low-frequency words that came into common use before 1920.

3.1.2. *Facts about Public Events*

W.R. performed well within the range of the CON for all time periods, except for the year 2000 (Fig. 2). H.M. was impaired for all time periods during which he was amnesic. He also scored below the CON range for the 1940s.

3.1.3. *Personal semantic memory schedule of the Autobiographical Memory Interview*

W.R. performed within the range of CON for all time periods, including recent life (Fig. 2). H.M. performed well within the range of CON for childhood and early adulthood. He was impaired for the recent time period, when he was amnesic.

3.1.4. *WASI Information and Vocabulary subtests*

W.R. and H.M. showed no impairment, performing within the CON range on both tests (Fig. 2).

3.2. *Episodic memory*

3.2.1. *The Autobiographical Interview*

The number of internal details (episodic memory) and external details (mainly semantic memory) for H.M., W.R., and

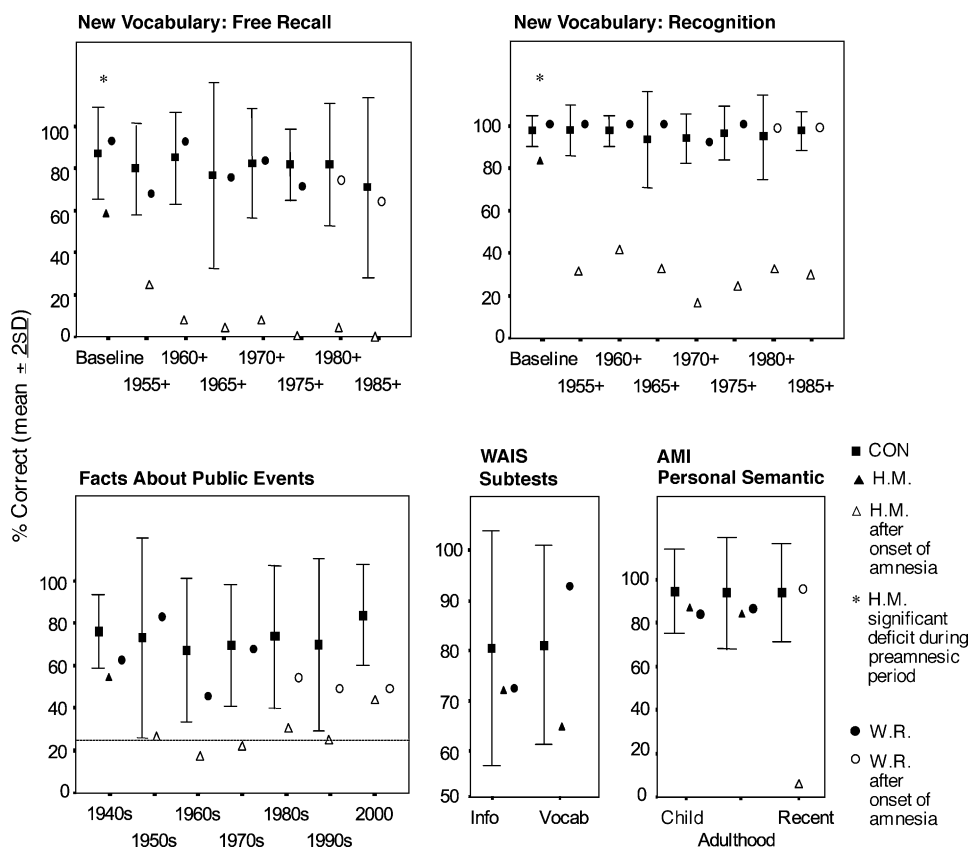


Fig. 2. Semantic memory tasks. Performances at different time periods. Also shown are the results for two WAIS subtests: Information (Info) and Vocabulary (Vocab). Bars indicate ± 2 S.D. *Abbreviations*—child: childhood, recent: recent life.

CON are shown in Figs. 3 and 4. Significant differences between the amnesic patients and the CON were observed after the numbers of details were summed across the different retrieval conditions (Fig. 4). In the following description of the results we refer to the accumulated numbers of details only. W.R. could remember events that were specific to a particular time and place for each time period, even after she had become amnesic, when asked to recall an event from the year prior to testing. She demonstrated a specific deficit for internal details, the episodic aspect of autobiographical memory, for the childhood (up to age 11) and the middle age periods (ages 36–55), and performed at the borderline for the teenage years (ages 12–17). Her scores for external details were well within the CON range. Interestingly, for the time periods after she became amnesic, she was impaired for internal, but not for external, details (middle age, last year). She first recalled a memory from early adulthood that seemed to be part of her personal folklore, so the experimenter asked her to remember another event. For all of her memories reported here, her children confirmed that none of them had been told repeatedly. In five of eight CON, a spouse confirmed that the memories were not from personal folklore. No informant was available for the other three CON.

H.M. provided an autobiographical memory specific in time and place for only one of five time periods. This event occurred when he was 15 years old. He recalled a flight that

he took in a small airplane over his home town. For this event, he was able to provide as many internal and external details as did CON for the same time period. Neither of two researchers who have known H.M. for decades had heard this memory before (Brenda Milner, Suzanne Corkin, personal communications). He also was able to remember another event in detail, the wedding of an uncle, but could not date it to a specific time period. Typically, H.M. gave the gist of events when asked about the time periods after the onset of his amnesia. In some cases, it was obvious that the events occurred before the onset of his amnesia (graduation from high school), and in other cases he could not date them at all.

3.2.2. Ratings for the quality of the autobiographical memories

W.R. rated the vividness of the episodes from her teenage years and early adulthood more than 2 S.D. below the CON mean (Fig. 5). The same was true for the event that stemmed from the year prior to testing, i.e., postmorbidly. She rated the vividness of her childhood and middle age episodes within 2 S.D. of the CON mean. Her ratings of the emotional impact of each event, and its personal importance at time of occurrence and today, were well within 2 S.D. of the CON mean, while her rating of the emotional impact for the middle age period was just within 2 S.D. of the CON mean.

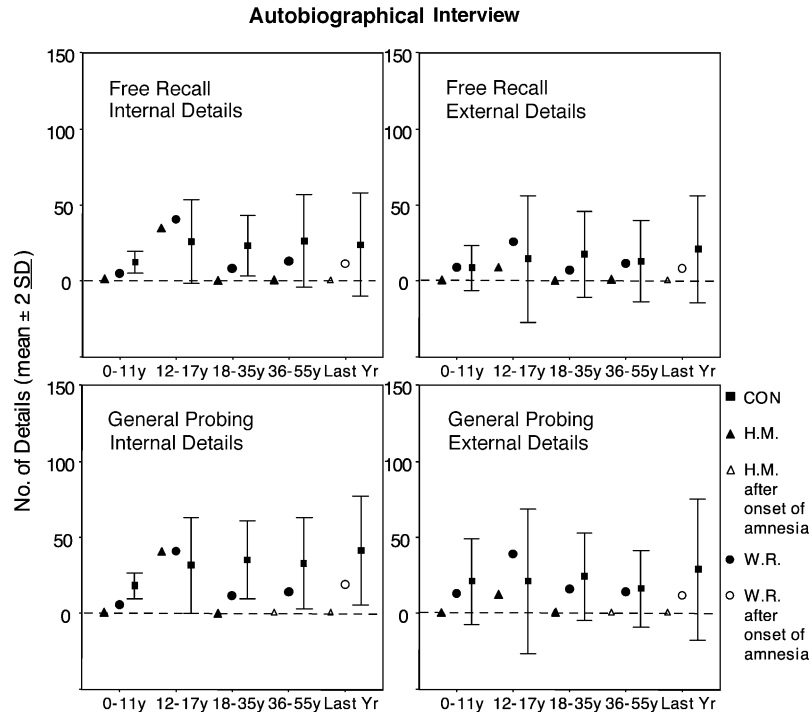


Fig. 3. Autobiographical Interview. Graphs indicate number of details provided for internal and external information at the different time periods of the free recall and the general probing (accumulated) level of retrieval. Bars indicate ± 2 S.D. For each time period, one memory was requested.

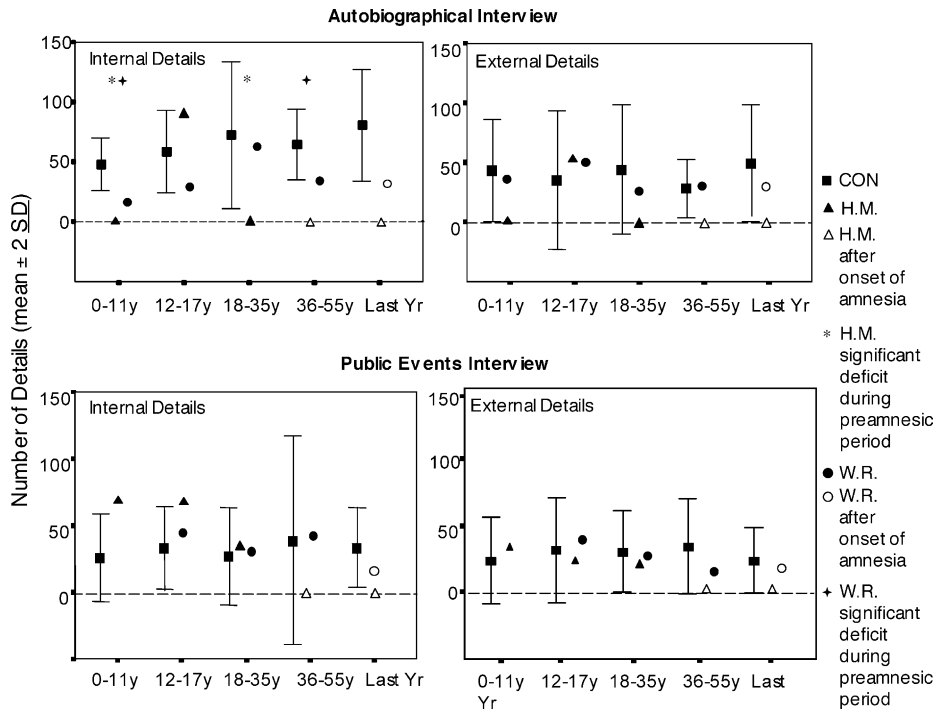


Fig. 4. Episodic memory tasks. Graphs indicate number of details provided for internal and external information at the different time periods sampled in the Autobiographical Interview and the Public Events Interview. Numbers of details are accumulated across all three levels of retrieval. Bars indicate ± 2 S.D. For each time period, one memory was requested.

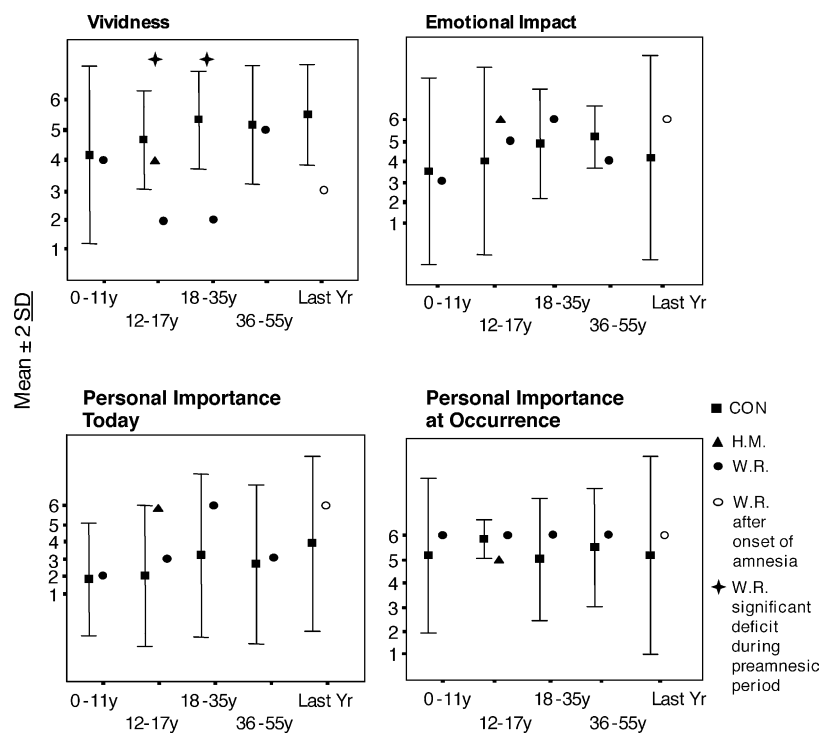


Fig. 5. Autobiographical Interview. Quality ratings for vividness, emotional impact, and personal importance today and at the time the remembered event occurred. A score of 1 indicates the lowest possible rating, while 6 indicates the highest parameter value. Bars indicate ± 2 S.D. For each time period, one memory was requested.

H.M. rated the episode from his teenage years within 2 S.D. of the CON mean for vividness and emotional impact at the time of occurrence (Fig. 5). He rated the personal importance that the episode had for him today approximately 2 S.D. above the CON mean, and the personal importance of the event at the time it occurred more than 2 S.D. below the CON mean.

3.2.3. Public Events Interview

W.R. recalled public events from all time periods questioned, except the childhood period (Fig. 4). She scored well within 2 S.D. of the CON mean for internal and external details, including those from the postmorbid time periods.

H.M. could remember public events for each of the pre-morbid time periods queried (Fig. 4). He provided a public event from the childhood period, which only three of the eight CON did. He scored within or above 2 S.D. of the CON mean for all preamnesic time periods, for internal and external details. He scored more than 2 S.D. above the CON mean for the internal details pertaining to the event from his childhood and teenage year period. He mentioned public events for the time periods when he was amnesic (middle age and last year) – an assassination and a flight into space – but later dated them to the time periods before the onset of his amnesia. Because H.M. questioned the reality of the space flight and said he could not put his “finger on it” this information was not scored.

3.2.4. Ratings for the quality of the memories of public events

Across all time periods, W.R. rated the vividness of the events within 2 S.D. of the CON mean (Fig. 6). She rated the emotional impact of the event more than 2 S.D. above the CON mean for the episode from her teenage years. She rated the importance of the event at occurrence within 2 S.D. of the CON mean for all time periods, except early adulthood, which was greater than 2 S.D. She rated the personal importance of the event today within 2 S.D. for all time periods.

H.M. rated the vividness of all his memories of public events within the CON range. He rated his emotional impact due to the event within 2 S.D. for the teenage and early adulthood years, while his emotionality rating for childhood years was more than 2 S.D. above the CON mean. He rated the personal importance at occurrence of the event from childhood more than 2 S.D. above the CON mean, and within 2 S.D. for the teenage and early adulthood period. He rated the current personal importance within 2 S.D. of the CON mean for all public events.

4. Discussion

The goal of this investigation was to examine remote memory in amnesia, using new methods that gave participants ample opportunity to provide specific details of past events. We administered measures of semantic and episodic memory to

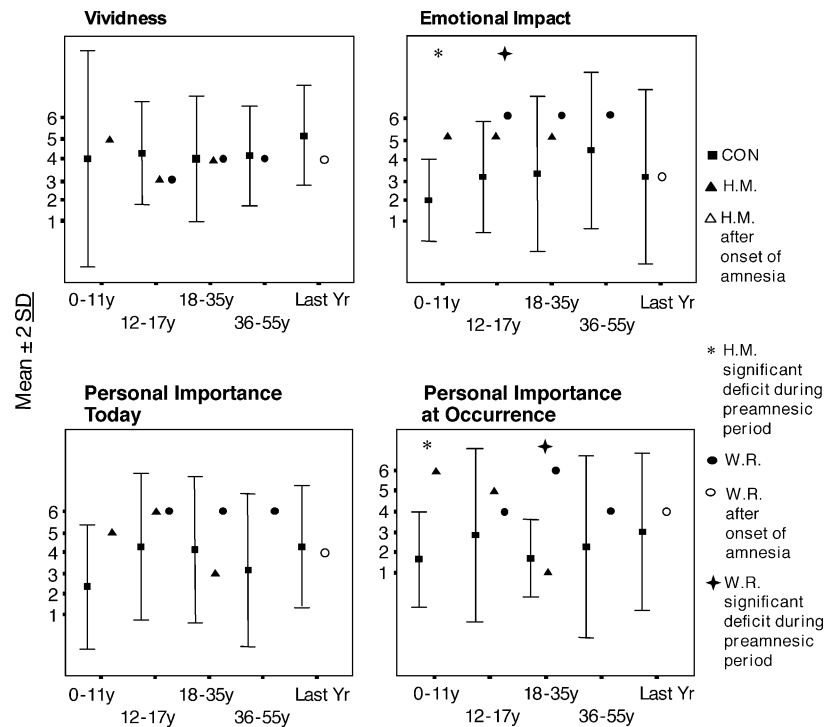


Fig. 6. Public Events Interview. Quality ratings for vividness, emotional impact, and personal importance today and at the time the remembered event occurred. A score of 1 indicates the lowest possible rating, while 6 indicates the highest parameter value. Bars indicate ± 2 S.D. For each time period, one memory was requested.

two amnesic patients with bilateral MTL lesions, H.M. and W.R. We uncovered evidence of severely impaired remote episodic memory and virtually preserved remote semantic memory. Below, we discuss the performance of these patients in these two memory domains, and then consider the extent to which the results support the SMC and the MTT.

4.1. Semantic memory

On five measures of semantic knowledge, W.R. performed normally, indicating that she has no retrograde amnesia in this domain. She also acquired new semantic knowledge during the postmorbid time period, consistent with reports of other amnesic patients (Bayley & Squire, 2002; Kitchener, Hodges, & McCarthy, 1998; O'Kane, Kensinger, & Corkin, 2004; Van der Linden, Meulemans, & Lorrain, 1994; Verfaellie, Koseff, & Alexander, 2000; Westmacott & Moscovitch, 2001). H.M. showed minor deficits on two of five measures for the pre-morbid time period: the New Vocabulary Test and the Facts of Public Events Test. His impairment can be interpreted in two ways. First, it could reflect a true retrograde amnesia, consistent with the SMC and MTT (Nadel & Moscovitch, 1997; Squire, 1992). An alternative explanation relates to the fact that the New Vocabulary Test and the Public Events Test both contain a preponderance of low-frequency items. It is likely that H.M. never acquired knowledge of these difficult word meanings and public events from the pre-morbid period because of his low socioeconomic status, and interrupted schooling due to his long-standing epilepsy (Schmolck,

Stefanacci, & Squire, 2000). As a result, he was impaired on the pre-1950s (baseline) condition of the New Vocabulary Test and on the 1940s items in the Public Events Test. Further evidence of his poor familiarity with low-frequency words comes from a study of his linguistic abilities, based on his solutions to leisure-time crossword puzzles (Skotko et al., 2004). The results showed that, in instances in which his response differed from that of the answer key, he used responses that on average were more common in the English language than those in the key. Further, H.M. consistently performed normally on other measures of semantic memory with high-frequency items. In particular, he achieved normal scores over a period of 47 years on the WAIS Information, Comprehension, Similarities, and Vocabulary subtests, where items were not restricted to low-frequency words (Kensinger, Ullman, & Corkin, 2001). In addition, he performed the Famous Faces Test on nine occasions over a period of 26 years; his scores for the time periods before the onset of his amnesia did not differ from those of CON (Kensinger & Corkin, 2000).

4.2. Episodic memory

4.2.1. Autobiographical memory

Both patients were impaired in remembering particular autobiographical events. W.R.'s deficit was restricted to the episodic aspect (internal details) of autobiographical memory for the period prior to the onset of her amnesia in 1982. She was impaired in the childhood and early adulthood periods

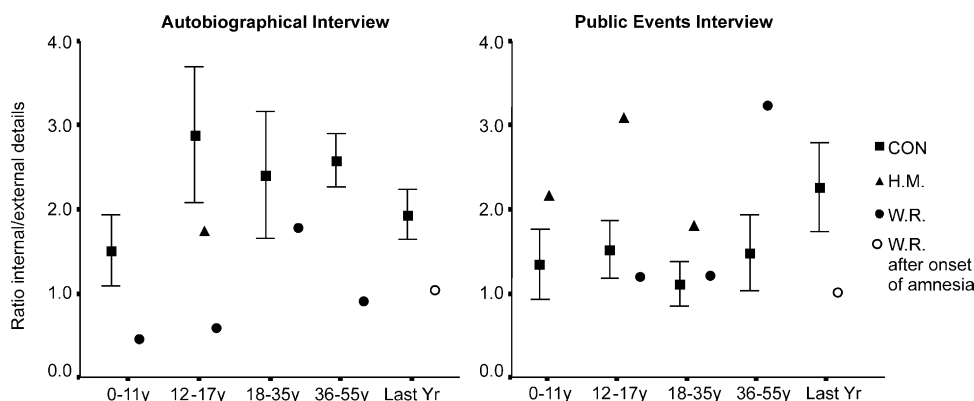


Fig. 7. Mean ratio of internal to external details for the Autobiographical Interview and the Public Events Interview. Error bars indicate standard error of the mean.

and showed borderline performance for the teenage years. She could remember only a few episodic details of specific events, but recalled as many external (mostly semantic) details as did CON. All eight CON provided more internal than external details for each of the five time periods, except for two CON in the childhood period (Fig. 7). W.R. also remembered an autobiographical event for the time period after the onset of her amnesia: she described an emotionally laden event, the premature birth of twin great grandchildren, giving fewer internal, but not fewer external, details than CON. Her deficit in remote episodic memory, despite evidence of new learning after the onset of amnesia, underscores the crucial role of the MTL for this memory domain.

We considered the possibility that W.R.'s subtle spatial deficit might have contributed to her episodic autobiographical memory deficit, such that a deficit in reconstructing the spatial aspects of an event might have limited the number of internal details she could provide. Because the scoring system of the Autobiographical Interview separates internal details into five categories⁴ (time, place, perception, emotion/thought, and event), we could compare the distribution of W.R.'s responses within categories of internal details, summarized across premorbid periods, to those of CON for the identical time periods. If a spatial deficit did contribute to her autobiographical memory deficit, one would expect a more pronounced deficit for spatial details than for the other categories. The results were otherwise (Fig. 8). We also asked whether her left fusiform lesion might have impaired mental imagery, leading to a deficit in remembering details from personal past events (Ishai, Haxby, & Ungerleider, 2002; Ogden, 1993; Rubin & Greenberg, 1998). If this were the case, one would predict an equal decrease in the number of details that included mental imagery pertaining directly to the main event (internal details) and in the number of mental imagery details

that were not part of the main story (external details). Two categories of details, perception and event, record mental imagery. W.R. showed a decrease only for internal perceptual and internal event details, but not for external perceptual and external event details (Fig. 8). It, therefore, seems unlikely that a mental imagery problem, related to the fusiform lesion, was fundamental to W.R.'s autobiographical memory deficit. Further, her lesion in the ventrolateral posterior nucleus of the right thalamus is unlikely to have contributed to her autobiographical memory deficit because this nucleus is believed to support somatosensory and motor capacities, but not memory functions (Schmahmann, 2003) (Fig. 9).

Evidence that H.M. had a severe autobiographical memory deficit is his failure to recount an event specific in time and place from his childhood, early adult, and middle adult years (i.e., prior to age 27 when he had the operation that rendered him amnesic). For these time periods, he could give only a script-like description of 'taking a test at school,' 'falling in love' (childhood), or 'examination before surgery' and 'operation upstairs' (early adulthood) (for details, see Appendix A). When interviewed about the early adulthood period, he

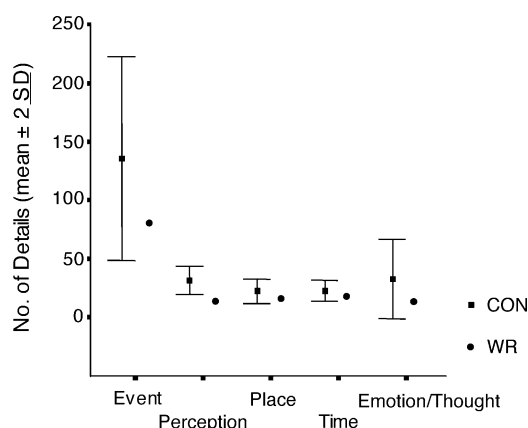


Fig. 8. Autobiographical Interview. Scores for CON (mean \pm 2 S.D.) and W.R. showing number of internal details categorized for the event, place, time, perception, and emotion/thought summarized for the time periods before the onset of W.R.'s amnesia.

⁴ We defined place details as information in space, except one's own orientation in space; time details as information regarding dating and time, except time duration; perceptual details as sensory and spatial-temporal information; and emotion/thought details as information that pertained to the mental state of the participant at the time of the event. Event details included information that revealed the story and did not belong in any other category.

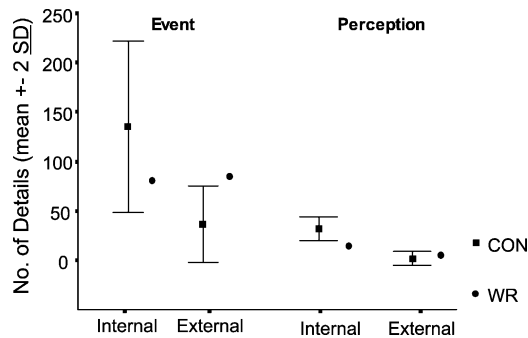


Fig. 9. Autobiographical Interview. Scores for CON (mean \pm 2 S.D.) and W.R. showing number of details for the internal event, external event, internal perception, and external perception collapsed across the time periods before the onset of W.R.'s amnesia.

talked about a wedding of an uncle, but dated the event inconsistently, at ages 12 and 7. Also, his narrative included inconsistencies, so that it was unclear whether he was talking about one or several events. Importantly, we cued him extensively for at least 30 min for each of the time periods tested to assist him in recounting a detailed event, specific in time and place. Despite this persistent cueing, he could recount the details of only one event, which was from the teenage period: a ride in a small airplane. For this event, he could provide as many details as CON. Further, in interviews conducted with H.M. in 1992 and 1998, he could not describe a single detailed event specific in time and place. On two other occasions, after this interview, when asked to recollect any personal event, he could not describe even one specific event in detail, despite extensive cueing. The dearth of autobiographical recollections cannot be attributed to a general inability to produce complex narratives because, when interviewed about public events, he started recounting promptly and fluently; no elaborative cueing was necessary. Further, the paucity of autobiographical memories produced by H.M. and W.R. cannot be explained by language impairment or slow speech. Neither patient was dysphasic, and although H.M.'s speech is characteristically slow, he was given extensive probing and ample time to respond. We also want to point out that H.M.'s life before his operation, while certainly severely affected by his epilepsy, did not spare him the life experiences that most of us encounter.⁵

One cannot conclude from this single narrative that H.M.'s remote memory for his teenage years is preserved. Thus, in search of further evidence, we asked him to recall a personal event from any time period. He did not choose an event from his teenage years, but instead reported an event from his childhood (age 7 or 8) when he milked a cow in Canada. He

could not provide details for this event, nor could he recount any other specific event, despite extensive cueing for about 30 min.

We considered the possibility that H.M.'s frequent seizure activity during his early life contributed to his autobiographical memory deficit. Specifically, the onset of petit mal attacks might have interfered with the perception, encoding, and storage of new information. While we cannot fully exclude this possibility, one would expect that if his autobiographical memory deficit reflects an anterograde memory deficit rather than a retrograde memory deficit, he should have been able to remember specific events from all time periods before the onset of his minor seizures (at age 9). H.M., however, could not remember a specific event from his childhood, despite undergoing repeated interviews and probing lasting about 30 min for each time period. While he could remember more general events that occurred repeatedly, as well as the gist of events, he had severe difficulty recalling details of specific events that only lasted several hours (see also, *Corkin, 2002*). This deficit can be classified at the level of unique events consisting of "highly event specific, sensory details" (*Conway, 2001, p. 1375*).

4.2.2. Earlier evaluations of H.M.'s remote memory functions

It is noteworthy that H.M.'s severe autobiographical memory deficit was not detected earlier. We believe that methodological differences explain the divergence between our current and earlier results. An advanced appreciation of how autobiographical memory differs from semantic memory has led to the development of instruments that capture self-aware recollection of specific episodes (*Levine, 2004; Moscovitch et al., 1999; Nadel et al., 2000*). Early studies used non-standardized clinical interviews to assess autobiographical memory (*Corkin, 1984; Kensinger & Corkin, 2000; Marslen-Wilson & Teuber, 1975; Milner et al., 1968; Ogden & Corkin, 1991; Sagar, Cohen, Corkin, & Growdon, 1985; Scoville & Milner, 1957*). A more detailed examination in the 1980s showed that his RA encompassed the 11 years prior to his operation (*Corkin, 1984; Sagar et al., 1985*). These studies, however, did not explicitly differentiate episodic from semantic memory. A closer inspection of the previous results, however, shows more severely impaired remote episodic than remote semantic memory (*Corkin, 1984; Sagar et al., 1985*). Specifically, on the *Crovitz* test, H.M. demonstrated an episodic memory deficit, but on measures of semantic memory, a *Public Events Test* and a recall and recognition test of famous scenes, he was unimpaired. Nevertheless, the magnitude of the autobiographical memory deficit was not explored. Because we used advanced methods in the present study, we were able to detect the severity of H.M.'s (and W.R.'s) autobiographical memory impairment.

In our view, the *Crovitz* procedure is not sensitive enough to measure alterations in autobiographical memory in amnesic patients. In the *Crovitz* procedure, a common word is presented to elicit a personal memory associated with this

⁵ H.M. graduated from high school and held several jobs, including one in a department store, electric motor store, movie theatre, and typewriter plant. He reported having two girl friends and going on several summer trips with his family. He went to church regularly and had first communion and confirmation. He moved twice. In his leisure-time, he went hunting, swimming, and skating, played cards, and listened to favorite radio shows.

word. This task can evoke memories of several similar events, and it facilitates superimposing details of different events onto one memory narrative. In contrast, the Autobiographical Interview used here not only minimized the possibility of interference, but it also allowed participants to provide more vivid and specific details through a structured interview.

4.2.3. Memories of public events

In the Public Events Interview, we asked participants to remember and describe public events in detail, focusing on the public event itself rather than on their personal experience when they learned about the event. This task was used to control for the narrative structure and memory load of autobiographical narratives. H.M. and W.R. performed this task as well as CON. Because CON showed high variability in their results, it was unfeasible to score more than 2 S.D. below the mean. Both patients, however, scored either above or near the CON mean for each premorbid time period on internal and external details. Only W.R. scored below the CON mean in the middle age time period on external details, but her score was within 1S.D. of the CON mean. Thus, the conclusion that both amnesic patients are unimpaired is supported by the data. H.M. and W.R.'s preserved memories of public events provide compelling evidence that their autobiographical memory deficit cannot be attributed to a deficit in retrieving, recalling, or describing a detailed narrative structure, as Reed and Squire (1998) have suggested.

To be fair, an amnesic deficit might have emerged if we had required subjects to recall more public events (Fig. 2). H.M., after all, was impaired in recognizing facts about public events. No such deficit, however, was found for W.R. Thus, the point remains that memory performance was far better for public than for autobiographical events in both H.M. and W.R.

It is of interest that even though H.M.'s three public events all stemmed from his childhood, he dated two of them to other lifetime periods. If misdating reflects a RA for public events, then we should have seen less misdating of public events in CON. We found misdating in 16 of 35 episodes from CON and in 1 episode from W.R., indicating that misdating was not specific to H.M. and not a signpost for RA (Table 2).

Table 2
Relation between the actual date of a public event and the date assigned by participants

Actual date	Date given by participants				
	0–11 years	12–17 years	18–35 years	36–55 years	Last year
Before birth	2				
0–11 years	1 (H.M.)	4 (H.M.)	2 (H.M.)		
12–17 years		4	1	1 (W.R.)	
18–35 years			5	2	
36–55 years			2	6	2
Last year					7

Bold numbers indicate correct dating. Patient's initials indicate his or her inclusion in the adjacent numbers of participants.

4.2.4. Quality ratings

The question arose as to whether the amnesic patients rated the quality of remembered events differently from CON. While some of the patients' ratings were outside the range of CON (above and below), most were within the CON range (Figs. 5 and 6). Further, there was no strong relation between the quality ratings and the number of details recalled by the amnesic patients. W.R. rated two of her premorbid autobiographical memories as less vivid than CON, but the time period of these events did not correspond to the time periods for which she demonstrated a deficit in episodic memory. H.M. rated his one premorbid autobiographical episode as being personally less important at the time of occurrence than CON, but rated the personal importance of the same event slightly higher at the time of testing. Further, both amnesic patients rated the emotional impact and personal importance at occurrence for one of their premorbid public events higher than did CON, which may have facilitated their later recollection.

4.3. Differences between H.M. and W.R.

H.M. had a global deficit in recalling autobiographical events, while W.R. demonstrated a deficit that was specific to the internal aspect of autobiographical memory, which is characterized by contextual richness and re-experiencing. This discrepancy may stem from differences in the locus and extent of their lesions: H.M.'s lesion included bilaterally most of the MTL and only spared portions of the ventral perirhinal cortex and the parahippocampal cortex. In W.R., the posterior part of the right hippocampus, parahippocampal gyrus and the right entorhinal cortex spared as were parts of the left entorhinal cortex and the anterior hippocampus. Lesion studies in monkeys indicate that bilateral lesions of the entorhinal and/or perirhinal cortices, structures excised in H.M., may be necessary to cause a severe amnesia (Meunier, Bachevalier, Mishkin, & Murray, 1993; Zola-Morgan, Squire, Clower, & Rempel, 1993).

4.4. Evaluation of the SMC and MTT

A critical question in weighing the SMC against the MTT is whether episodic memory and semantic memory are affected differentially in amnesia. The SMC predicts that both forms of declarative memory should be affected equally by MTL damage (Bayley et al., 2003; Squire, 1992; Squire & Alvarez, 1995). In contrast, the MTT predicts that episodic memory should be more severely impaired than semantic memory because the theory assumes that episodic memory always relies on the MTL, whereas semantic memory becomes independent from it (Moscovitch et al., 1999; Nadel & Moscovitch, 1997; Nadel et al., 2000). Our results, demonstrate a more severe impairment in episodic than semantic memory as is evident from the ratio of internal to external details from the Autobiographical Interview and the Public Events Interview, respectively (Fig. 7). Thus, our results

support the MTT and are inconsistent with the SMC. A recent review of 147 cases of hippocampal amnesia concluded that a greater impairment of episodic than semantic memory is characteristic of amnesic patients with MTL lesions (Spiers, Maguire, & Burgess, 2001). Although this tabulation included some cases with complex pathologies, the results clearly showed that semantic retrograde memory loss was typically less severe than autobiographical episodic memory loss.

Several previous studies concluded that the role of the MTL in semantic and episodic memory is temporally limited, thus favoring the SMC (Bayley et al., 2003; Milner, Squire, & Kandel, 1998). A recent behavioral investigation by Bayley et al. (2003) did not find impairment in remote autobiographical recollection in eight MTL amnesic patients. Six of the eight amnesic patients had damage limited primarily to the hippocampal region. The remaining two had more extensive damage to the medial temporal lobe, more similar to H.M. and W.R.

Methodological differences may explain the discrepancy between these results and ours. We used the Autobiographical Interview to sample events from five life periods (Levine et al., 2002), whereas Bayley et al. (2003) used the Crovitz technique to query participants about events only from the first third of their lives. The Crovitz technique, though useful in cueing memories, may not elicit many detailed ones, particularly from so long ago. The absence of autobiographical recollections in very early childhood, called childhood amnesia, reduced the likelihood of detecting differences in episodic details between patients and controls, given the more semantic than episodic character of those earlier memories. Autobiographical recollection is understood to emerge at about age 4, ranging from 2 to 7 years (Bruce, Dolan, & Phillips-Grant, 2000; Levine, 2004; Wetzler & Sweeney, 1986). Accordingly, our own results showed a relatively smaller number of internal autobiographical details in CON for the childhood period (ages 0–11) than for the other time periods.

Further, Bayley et al. (2003) did not use a standardized prompting method; prompts “were given as needed” and “continued until the interviewer judged that the participant had recalled as many details as possible.” We believe that standardized, structured probing is necessary, in addition to unspecified prompting, because the preferred level of processing in autobiographical memory is at a more general level, and does not place emphasis on experience-near details (Conway, 2001; Rosch, 1978). Typically, the participant and the interviewer both process autobiographical memories at that level, so that an incomplete picture of the participant’s abilities may emerge if no further guidance is provided. In our study, we detected differences between amnesic patients and CON only after combining the scores across all three levels of recall (free recall, general probing, and specific probing). While the average number of details per narrative in the Bayley et al. study was below 20 (18.8 for patients and 17.9 for control participants), our study and others (Levine et al., 2002) that have used the Autobiographical Interview

recorded about 50 details per narrative. These differences suggest that the memories sampled by Bayley et al. were impoverished and likely semanticized, which accounts for their not being sensitive to MTL damage. Bayley et al. suggested that autobiographical memory loss in other patients may be due to damage to the lateral temporal, frontal and occipital cortices. This explanation is untenable for H.M. and W.R. Although W.R.’s lesion in the right superior temporal gyrus cannot be ruled out as contributing to her autobiographical memory deficit, this area has also been implicated in semantic memory, possibly to a larger degree than in episodic memory (Dalla Barba, Parlato, Jobert, Samson, & Pappata, 1999; Wiggs, Weisberg, & Martin, 1999). W.R., however, did not show a semantic memory deficit and even experienced semantic learning after the onset of her amnesia (Fig. 2). This evidence makes it unlikely that her right temporal lesion was a factor in her autobiographical memory deficit.

Conway’s autobiographical memory model offers a framework into which results from our study and others can be structured and explained (Conway, 1993; Conway & Fthenaki, 2000). He proposed three levels of abstraction at which autobiographical memory can be conceptualized. At the most abstract and temporally extended level are “lifetime periods,” which contain knowledge about others, activities, locations, feelings, and evaluations common to a period as a whole, e.g., “at high school.” At the next lower level are “general events,” representing repeated events, e.g., “going hunting,” or extended events, e.g., “holiday in Canada.” At the lowest level are, what Conway called, “episodic memories,”⁶ which contain experience-near, highly specific, sensory-perceptual details of events that lasted comparatively short periods of time (minutes–hours) (Conway, 2001). By this view, recollective experience, the sense of the self in the past, is introduced at the level of experience-near “episodic memories.” This level is where we observed the autobiographical memory deficit in H.M. and W.R. It is possible that earlier studies of autobiographical memory, including the Bayley et al. study, accessed primarily the level of “general events” and, therefore, did not detect a deficit in MTL amnesic patients. Without a structured interview that systematically asks about phenomenal characteristics of the remembered event, the investigator may not access and extract the particulars of the level of experience-near “episodic memories.”

Several neuroimaging investigations have contributed to the debate between the SMC and MTT. In a recent fMRI study, participants recalled particular events from their recent and remote past. The results showed no significant increase in neural activation specific to remote autobiographical memory (Piefke, Weiss, Zilles, Markowitsch, & Fink, 2003). Stimuli were tailored individually using interviews with the participants conducted several weeks before scanning. Because each time one retrieves an episodic memory

⁶ Note that Conway used a different definition of ‘episodic memory’ than Tulving, whose definition of episodic memory was used in our study.

one encodes the retrieved information anew, it is impossible to ascertain whether the activation observed in this study was exclusive to remote autobiographical memory or whether it was caused by new encoding of the old memories (Buckner, Wheeler, & Sheridan, 2001). Further, this study contrasted a remote autobiographical memory condition and a recent autobiographical memory condition to assess activation specific to remote autobiographical memory. If MTL activation is associated with remote autobiographical memory retrieval but is smaller than MTL activation for recent autobiographical memory, then the comparison chosen in the study would not detect this increase in activation. The authors did not report a comparison of the remote autobiographical memory condition versus baseline nor did they use a semantic memory condition as an additional control condition that would have allowed them to uncover a relatively smaller activation for remote autobiographical memory. The contribution of this study to uncovering the role of the MTL in remote memory is, therefore, limited.

Support for the MTT comes from several other neuroimaging studies that observed MTL activation, particularly in the hippocampus, even for very remote autobiographical memories (Addis, Moscovitch, Crawley, & McAndrews, 2004; Fink et al., 1996; Maguire, 2001; Maguire & Frith, 2003; Maguire, Henson, Mummery, & Frith, 2001; Ryan et al., 2001). Again, the significance of these studies is compromised because the individually tailored stimuli were based on interviews conducted several weeks or even immediately before scanning. As argued above, this confound makes it impossible to determine whether the brain activity was specific to remote autobiographical memory (Buckner et al., 2001). A study that avoided this confound used photographs of past personal events that participant had not seen in many years (Gilboa, Winocur, Grady, Hevenor, & Moscovitch, 2004). They found no differences in a region of interest analysis (ROI) within the MTL, especially the hippocampus, between remote and recent autobiographical events that were vividly re-experienced. The ROI, however, did not include the entire MTL so that this experiment was not a rigorous test of the MTT (Moscovitch & Nadel, 1998).

The dispute between proponents of the SMC and MTT is also addressed in the semantic dementia literature. The neuropathological changes in semantic dementia are believed to be complementary to those seen in MTL amnesia: semantic dementia patients are reported to show degenerative changes in the polar and inferolateral temporal neocortex with relative sparing, at least in the early stages, of the MTL. Behaviorally, they show a progressive deterioration in their semantic knowledge about people, facts, and word meanings, and relatively preserved episodic memory (Murre, Graham, & Hodges, 2001). Recent autobiographical memory is reported to be relatively preserved compared to remote memory (Hodges & Graham, 2001; Murre et al., 2001; Nestor, Graham, Bozeat, Simons, & Hodges, 2002). This finding can be interpreted in two ways. First, as support for the SMC because neocortical pathology results in progressive loss of

remote semantic and episodic long-term memory, but sparing of the MTL allows the encoding and subsequent retrieval of recently experienced autobiographical events (Hodges & Graham, 2001; Murre et al., 2001). A different interpretation is that autobiographical memory depends on the normal functioning of semantic memory, so that the loss of remote autobiographical memory in semantic dementia is not a direct result of neocortical degeneration, but a secondary effect of semantic memory impairment (O’Kane et al., 2004; Greenberg & Rubin, 2003; Hodges & Graham, 2001; Murre et al., 2001; Piolino et al., 2003). Because most instruments used in these studies to assess autobiographical memory did not distinguish between the episodic and non-episodic aspect of autobiographical memory, a confounding of episodic and semantic memory could have occurred. Two case studies that used either family photographs as cues or provided increasingly detailed cues inquiring about specific events suggest that when appropriate techniques are used patients with semantic dementia can retrieve remote autobiographical memories (Moss, Kopelman, Cappelletti, de Mornay Davies, & Jaldow, 2003; Westmacott, Leach, Freedman, & Moscovitch, 2001). This finding lends support to the view that MTL structures support remote autobiographical memory.

5. Conclusions

Our investigation uncovered a severe deficit in remote memory in two MTL amnesic patients, H.M. and W.R. This impairment was specific for remote autobiographical memory, while remote semantic memory was far better preserved. These results support the MTT and not the SMC. It is possible that the autobiographical memory impairment appears only at the level of, what Conway called, “experience-near episodic memories” and that autobiographical memory at the level of “general events” and knowledge of “lifetime periods” undergoes consolidation and becomes independent of the MTL. As demonstrated here, however, MTL structures are necessary for recollective experiences of specific remote events no matter how long ago they occurred.

Acknowledgements

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Appendix A

H.M.

Falling in love

E: Did you once fall in love with somebody?

H.M.: Yes.

E: O.k. Tell me about it.

H.M.: **Well, just how you felt and everything and the ways it could be. And they would fall for you. And you still don't know.**

E: Can you tell me about when you first felt that you were falling in love with somebody? . . . One specific event?

H.M.: No.

E: No, you can't think of that? . . . Can you think of one specific event lasting for several hours from your early childhood? . . . Can you come up with anything like that?

H.M.: No, I can't.

W.R.

First day at a new school

W.R.: As I said, **I was then very, very, shy, and meeting new people was a big thing for me. I remember walking in, there was a, one of the students used to do the janitorial chores around the school, so he was sweeping the school when I walked in. And physically you sat in those old desks, where you had two people to a desk, uh there were two rooms there, and this was nine grades in two rooms, the small room just for certain subjects that the assistant taught, otherwise everything was down in front of the whole school. What else, . . .**

CON

A trip to New York

CON: **Okay, that was that was when I was still single, and I went to New York, I went down, how I did go down . . ., I went down by bus, yeah, I did, I went down by bus. I remember it was quite a long walk, it was through a very, the area was a little bit seedy, where that bus terminal landed. And I was a little nervous as there were homeless people and questionable characters, you know, along the way. I walked down to the XY, where I checked in, and uh, then I went roaming around and bumped into the model that I recognized, and I stopped her, she was very nice, and I talked with her, and she asked where I was from, and I told her, . . .**

Italic font represents 'episodic'; bold font represents 'mainly semantic'; normal font represents 'other'.

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