Detailed recollection of remote autobiographical memory after damage to the medial temporal lobe

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Contributed by Larry R. Squire, December 22, 2007 (sent for review November 27, 2007)

Previous findings of intact remote autobiographical memory in patients with medial temporal lobe damage have been questioned on the grounds that the narrative recollections were impoverished and fact-like and that the methods were not sufficiently sensitive to detect an impairment. We adopted a newer method, the Autobiographical Interview [Levine B, Svoboda E, Hay JF, Winocur G, Moscovitch M (2002) *Psychol Aging* 17:677–689], which uses extensive probing to elicit an average of 50 or more details per memory (in contrast to the ≈20 details per memory elicited with previous methods). We found that autobiographical recollection was impaired in patients with medial temporal lobe damage when memories were drawn from the recent past but fully intact when memories were drawn from the remote past. Impaired remote autobiographical memory, which has sometimes been reported with this and other tests, is likely caused by significant damage outside the medial temporal lobe.

amnesia | consolidation | hippocampus | retrograde

In humans and experimental animals, damage to the hippocampus and related medial temporal lobe structures impairs new learning (anterograde amnesia) and memory for information acquired before the damage occurred (retrograde amnesia; ref. 1). When retrograde amnesia occurs, recently acquired memories are typically more impaired than remote memories (2). For example, memory-impaired patients with hippocampal damage were impaired at remembering famous faces (3, 4), famous names (3), and public events (4–7) that had been in the news only recently, but they exhibited intact memory for the same material when it would have been learned remotely. Similarly, >20 studies of experimental animals have found recent memory to be impaired and remote memory to be intact after hippocampal lesions (8).

There is less agreement about the status of recent and remote autobiographical memory in memory-impaired patients. The study of autobiographical memory presents a number of challenges. One approach has been to use a simple, standardized test like the Autobiographical Memory Interview (9), which asks three questions about each of three different past time periods. Using this test, or a modified version of it, a number of studies have found remote memory to be intact after damage limited to the medial temporal lobe (7, 10–12). Yet, a few single-case studies have found remote memory to be impaired (refs. 13 and 14 and see ref. 7 for comment). There is also a concern that this particular test may not always be sensitive enough to reliably detect impairment (2, 15).

A different approach has been to obtain tape-recorded narratives of extended recollections and determine the number of details produced about events from early life. In one study, 6 patients with limited hippocampal lesions, 2 patients with large medial temporal lobe lesions, and 25 controls attempted to recall up to 24 different episodes from their early lives (16). The recollections of the patients and the recollections of the controls contained the same number of details (±5%) and were also similar on several other measures. An alternate method for obtaining autobiographical narratives (The Autobiographical Interview; ref. 17) elicits one memory from each of five time periods and uses extensive, structured probing to obtain as many details as possible.

These two methods have yielded different results. First, the narratives obtained from the Autobiographical Interview contained more details than in the study by Bayley *et al.* (16). Thus, the Autobiographical Interview elicited ≈50 details per episode (17, 18), and the study that obtained up to 24 different recollections (16) elicited ≈20 details per episode. This difference might reflect the extended probing that is part of the Autobiographical Interview, or perhaps it is simply easier to recall a large number of details about one prominent autobiographical episode than to recall a large number of details from ≈24 different episodes. Second, in contrast to the finding that 8 patients and 25 controls recalled the same number of remote autobiographical details (16), a recent study of two patients using the Autobiographical Interview found remote memory to be impaired (18). This finding raised the suggestion that, when only 20 details are obtained for an episode (as in ref. 16), the memories may be impoverished and fact-like (18). It has been further suggested that only when an interview is structured to probe for and elicit maximal remembered detail will the test be adequate to elicit specific episodic memories and be sufficiently sensitive to detect impaired autobiographical memory (18, 19).

We have reexplored the status of remote autobiographical memory in memory-impaired patients with medial temporal lobe damage. Specifically, we asked whether the Autobiographical Interview (and its ability to elicit 50 details per memory) might reveal an impairment that was missed by a test that elicited only 20 details per memory. We administered the Autobiographical Interview to three patients with limited hippocampal damage, two patients with large medial temporal lobe lesions, and five controls. In the Autobiographical Interview, participants are asked to provide one memory from each of five time periods: childhood (up to age 11), teenage years (12–17 years old), early adulthood (18–35 years old), middle age (36–55 years old), and the year before testing. We attempted in every respect to replicate both the testing methods and the scoring methods used in earlier studies with this test (17, 18).

Results

The Autobiographical Interview provides participants with three levels of retrieval support: free recall, general probing, and specific probing. Following the procedures from earlier work with this method (17, 18), we first collapsed the counts of internal details across the three levels of retrieval support (free

Author contributions: P.J.B. and L.R.S. designed research; C.B.K., P.J.B., and V.V.G. analyzed data; and C.B.K., P.J.B., and L.R.S. wrote the paper.

The authors declare no conflict of interest.

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This article contains supporting information online at www.pnas.org/cgi/content/full/0712155105/DC1.

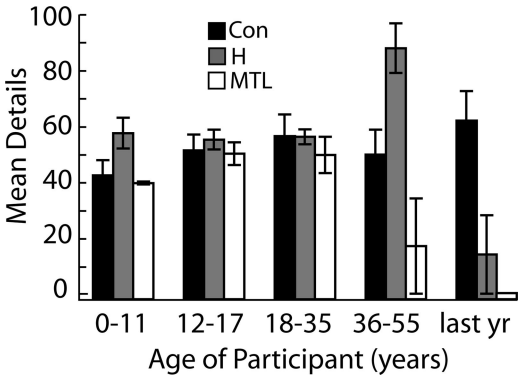

Fig. 1. Total number of internal (episodic) details across time periods. Patients with damage thought to be limited to the hippocampus (H group), patients with larger medial temporal lobe lesions (MTL group), and controls (Con) were asked to retrieve one autobiographical memory from each of five time periods. Error bars indicate SEM.

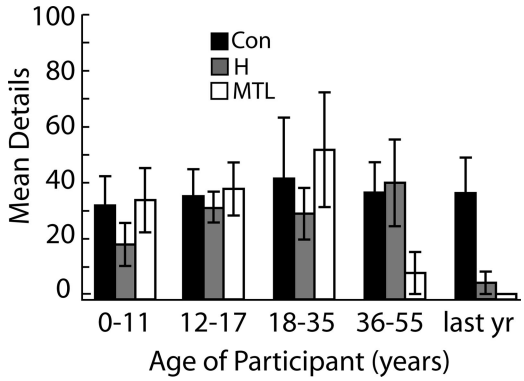

Fig. 2. Total number of external (semantic) details across time periods for the H group, MTL group, and controls (Con). Error bars indicate SEM.

recall, general probe, and specific probe) to obtain the total number of internal details recalled as the result of all probing. Fig. 1 shows the number of internal (episodic) details accumulated for the three groups [controls, patients with damage limited to the hippocampus (H group), and patients with larger MTL lesions (MTL group)] at each of the five time periods. The three patients in the H group were able to provide unique autobiographical memories from the four remote time periods of the Autobiographical Interview. One of the three patients in this group was able to provide a memory from the most recent time period as well. The two patients in the MTL group (E.P. and G.P.) were similarly able to provide autobiographical memories but had particular difficulty providing memories from the most recent two time periods. Patient E.P. was unable to provide a memory from the most recent time period (last year), and G.P. was unable to provide a memory from either this time period or the time period 36–55 years of age. The controls were able to provide autobiographical memories from all five time periods.

A two-way ANOVA (three groups, five time periods) revealed an effect of time period [$F(4) = 9.23$, $P < 0.001$] but no effect of group [$F(2) = 2.54$, $P = 0.15$]. There was also a group $\times$ time period interaction [$F(8) = 9.93$, $P < 0.001$], reflecting the fact that the patients but not controls had difficulty recalling postmorbid events and recent premorbid events. Post hoc t tests revealed for the most recent time period (last year) that the control group provided more episodic details (61.8) than either the H group (14.0) or the MTL group (0) ($P < 0.05$). For the 36- to 55-year time period, the H group provided more episodic details (87.7) than either the control group (49.6) or the MTL group (17) ($P < 0.05$).

Fig. 2 shows the total number of external (semantic) details, again collapsed across the three levels of retrieval support, which were accumulated by each group at each of the five time periods. An ANOVA yielded no effect of group or time period and no interaction ($P > 0.1$). As in the case of internal (episodic) details (Fig. 1), both patient groups performed poorly in the most recent time period. The H group recalled 4.0 details and the MTL group recalled no details (controls, 36.0 details). The MTL group also performed poorly in the 36- to 55-year time period (7.5 details vs. 36.4 and 39.7 details for the control group and the H group, respectively).

Fig. 3 shows the vividness ratings given for episodic memories for each group at each of the time periods. An ANOVA yielded no effect of group or time period and no interaction ($P > 0.1$). Note that the MTL patients have no vividness ratings for the last-year period because they recalled no memories from that time period. In addition, only patient E.P. contributed a vividness rating to the 36- to 55-year time period, because only E.P. could recall a memory for that time period.

Discussion and Conclusions

We administered the Autobiographical Interview (17) to five memory-impaired patients (three with limited hippocampal damage and two with large MTL lesions) and five control participants. All of the patients successfully retrieved memories from the three most remote time periods covered by the test (early childhood, adolescence, and early adulthood). In those time periods, the memories produced by the patients contained as many episodic details and semantic details as the memories produced by the controls. In addition, the memories of the patients and the controls were similar in their rated vividness.

For the two most recent time periods, the patients produced fewer episodic and semantic details than the controls. Both patient groups performed poorly in the most recent time period, and the MTL group also performed poorly in the next most recent time period (36–55 years). In contrast, in the next most recent time period, the H group recalled even more memories than controls. These findings conform to what has been reported previously in patients with limited hippocampal damage and patients with large MTL lesions. First, retrograde amnesia is

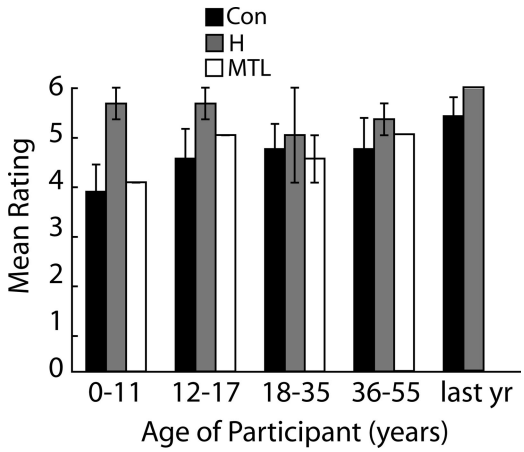

Fig. 3. Mean vividness ratings for episodes recalled for each of five time periods. No vividness ratings were collected for time periods in which participants [H group, MTL group, and controls (Con)] did not provide autobiographical memories (last year for the MTL group and L.J. and G.W. from the H group, and the 36- to 55-year time period for G.P. in the MTL group). Error bars indicate SEM.

Table 1. Characteristics of amnesic patients

Patient	Age at test, years	Age at onset of amnesia, years	Education, years	WAIS-III IQ score	WMS-R scores				
					Attention	Verbal	Visual	General	Delay
K.E.	65	63	13.5	108	114	64	84	72	55
L.J.	70	51	12	101	105	83	60	69	<50
E.P.	84	70	12	98	94	59	92	68	56
G.P.	60	41	16	98	102	79	62	66	50
G.W.	48	42	12	108	105	67	86	70	<50

The Wechsler Adult Intelligence Scale-III (WAIS-III) and the Wechsler Memory Scale-Revised (WMS-R) yield mean scores of 100 in the normal population, with a SD of 15. The WMS-R does not provide numerical scores for individuals who score <50.

more extensive after large MTL lesions than after lesions limited to the hippocampus itself (7). Second, very remote memory is intact after both kinds of lesions (16, 20).

The main finding was that each of the amnesic patients was able to provide detailed autobiographical memories from the three most remote time periods that were sampled. In an earlier study using the Autobiographical Interview (18), the noted patient H.M. was able to provide a memory only for the adolescent time period (12–17 years) and provided no memories from any other time period. Specifically, his single memory for the adolescent time period contained nearly 100 details (above the control mean), but he was unable to describe any other specific events even when cued persistently on multiple other occasions. A second patient (W.R.) was also deficient at producing detailed episodic memories from early life. The authors proposed that the impairment in H.M. and W.R. was detected because their test had improved sensitivity, i.e., the test successfully elicited a large number of details in controls (≈50 per memory). Further, the authors proposed that earlier reports of intact remote autobiographical memory in memory-impaired patients (7, 16, 20) depended on an insufficiently sensitive test, specifically, a test that could elicit only 20 details per memory.

One can now rule out this explanation of the different findings, because the present study using the Autobiographical Interview yielded about the same number of details as in previous work with this test. In the study by Steinvorth *et al.* (18), control subjects provided a mean of ≈59 episodic details across the three most remote time periods of the test (estimated from their figure 4). In the present study, control subjects provided a mean of 49.9 details across the same three time periods. We propose that our earlier studies (16, 20) elicited only ≈20 details per memory because it is difficult to produce a large number of details when the task is to produce 24 different episodes from a given time period. In any case, we have found remote autobiographical memory to be intact after medial temporal lobe damage, regardless of whether patients produce narrative recollections composed of ≈20 details (16, 20) or recollections composed of ≈50 details (the present study).

If methodological differences in testing methods cannot account for why some memory-impaired patients are impaired and others are intact at recollecting remote autobiographical memories, it seems likely that the explanation lies in the locus and extent of damage in the patients being studied. The two patients studied by Steinvorth *et al.* (18), H.M. and W.R., deserve particular comment. With respect to H.M., a recent neuroimaging study (21) documented significant alterations in his brain during the period 1998 to 2002–2003 that were thought to be of recent origin and that were far worse than what had been found in an earlier imaging study (22). Specifically, there was widespread cortical thinning, cortical and subcortical atrophy, large amounts of abnormal white matter, and infarcts in subcortical gray matter, notably in the putamen and thalamus. Inasmuch as H.M.'s autobiographical memory was tested (and found to be impaired) during the time period that these alterations appear to have occurred, it is difficult to interpret his impairment as caused specifically by medial temporal lobe damage. Similar concerns can be raised about patient W.R., who has bilateral medial temporal lobe damage, but who also has a lesion in the right superior temporal gyrus, a lacunar lesion of the ventrolateral posterior nucleus of the right thalamus, and apparent bilateral atrophy in the inferior parietal parietal lobe.

Other single-case reports of remote autobiographical memory impairment are also tempered, in almost all instances, by the presence of documented damage outside of the medial temporal lobe (for review, see ref. 2). Further, the available group studies, which come from three different laboratories (11, 12, 20), have found that remote autobiographical memory is intact when damage is limited to the medial temporal lobe and that impaired autobiographical memory is associated with lateral temporal or frontal lobe pathology.

In summary, we used the Autobiographical Interview to assess the status of remote autobiographical memory in memory-impaired patients with damage to the medial temporal lobe. This test has the advantage of being more sensitive than other standardized tests such as the Autobiographical Memory Interview (9). Even using this more sensitive method, we found remote autobiographical memory to be intact for three patients with limited hippocampal damage and two other patients with large medial temporal lesions. We suggest that findings of impaired remote autobiographical memory in memory-impaired patients are caused by significant damage outside of the medial temporal lobe.

Materials and Methods

Participants. Five memory-impaired patients participated (four males) (Table 1). Of these, three patients (H group: K.E., L.J., G.W.) have bilateral lesions thought to be limited to the hippocampal region (CA fields, dentate gyrus, and subicular complex). Two patients (MTL group: E.P., G.P.) have damage to the hippocampal region and adjacent medial temporal lobe cortex.

K.E. became amnesic in 2004 after an episode of ischemia associated with kidney failure and toxic shock syndrome. L.J. became amnesic in 1988 during a 6-month period with no known precipitating event. Her memory impairment has been stable since that time. Patient G.W. became amnesic in 2001 after a drug overdose and associated respiratory failure. Patients E.P. and G.P. became amnesic in 1992 and 1987, respectively, after contracting viral encephalitis.

Estimates of the patients' medial temporal lobe damage were based on quantitative analysis of magnetic resonance images compared with data for 19 controls (for K.E., G.W., E.P. and G.P.) or 11 controls (for L.J.). Nine coronal MR images from each of the five patients and a control, together with detailed descriptions of the lesions, are available in supporting information (SI) Fig. 4. The volume of the full anterior-posterior length of the hippocampus and the parahippocampal gyrus were measured following published procedures (23–25). For each patient, the volumes of the hippocampus and parahippocampal gyrus were divided by the intracranial volume to correct for brain size (25). In the H group, K.E., L.J., and G.W. have an average bilateral reduction in hippocampal volume of 49, 46, and 48%, respectively (all values >3 SDs below the control mean). On the basis of two patients (L.M. and W.H.) with similar bilateral volume loss in the hippocampus for whom detailed postmortem

neurohistological information was obtained (4), this degree of volume loss likely reflects nearly complete loss of hippocampal neurons (25). In comparison, the volume of the parahippocampal gyrus is reduced by 17%, −8%, and 12%, respectively (all values within 2 SDs of the control mean).

In the MTL group, patients E.P. and G.P. have an average bilateral reduction in hippocampal volume of 97% and 96%, respectively (all values >9 SDs below the control mean). In addition, the volume of the parahippocampal gyrus was reduced by 94% and 93%, respectively (all values >10 SDs below the control mean). In both patients, there is complete loss of perirhinal and entorhinal cortex and significant damage to parahippocampal cortex (73% bilaterally for E.P. and 71% bilaterally for G.P.).

Additional measurements, based on four controls for each patient, were carried out for the frontal lobes, lateral temporal lobes, parietal lobes, occipital lobes, insular cortex, and fusiform gyrus (20). For the H group, the volumes of each of these regions are within 16% of control volumes and none of the patients has volume reductions >2 SDs below the control mean. For E.P. and G.P., the volumes of each of the major lobes are all within 9% and 13% of control volumes, respectively, and within 2 SDs of the control mean. However, E.P.'s lesion also includes the rostral portion of the fusiform gyrus, which is reduced in volume compared with controls by 39% on the left and 68% on the right. In addition, the insula is reduced in size compared with controls by 32% on the left and 30% on the right. G.P.'s lesion also includes the fusiform gyrus, which is reduced in volume compared with controls by 41% on the left and 56% on the right. The insula is reduced in volume by 80% on the left and 49% on the right.

Five healthy participants (four male) served as a control group. The control group was matched to the patients with respect to age (M = 65.4 and 68.8 for patients and controls, respectively) and education (M = 12.2 and 13.4, respectively).

Test of Autobiographical Memory. Autobiographical memories were collected and scored by using the Autobiographical Interview (17). In accordance with published procedures (17), participants were asked to recall one autobiographical event from each of five time periods: childhood (up to age 11), teenage years (12–17 years old), early adulthood (18–35 years old), middle age (36–55 years old), and the year before testing. The events that were recalled had to be specific to a particular time and place. If participants were unable to recall an event, they were shown a list of ≈100 typical life events to assist with memory retrieval. Participants were asked not to provide memories for events that they talked about frequently. This instruction was intended to avoid memories that had become part of ''personal folklore'' and that may have become more semantic than episodic in quality. Interviews were recorded and transcribed for later scoring.

Participants were asked to provide an autobiographical memory from each time period, starting with the earliest time period (childhood) and continuing to the most recent time period. Two levels of retrieval support were provided initially: free recall and general probing. During free recall, participants spontaneously described an event from the time period in question without interruption from the examiner. The narrative continued until a natural ending point was reached. At this juncture, the examiner began general probing by using nonspecific cues that encouraged a fuller description of the event (e.g., ''Can you tell me more about that?'' or ''Can you describe a specific incident related to that event?''). After general probing, the examiner asked the participant to provide an autobiographical memory from the next time period, first using free recall and then general probing. The test continued in this manner until all five time periods had been covered.

At this point, the examiner provided specific probing for each of the events that had been recalled by the participant. This third level of retrieval support involved a structured interview and was intended to evoke additional contextual details that were not likely to be recalled spontaneously. The probes were organized into five separate categories: event, time, place, sensory information, and emotion/thought. As in an earlier analysis of data collected with these methods (18), we report here the results for the Autobiographical Interview that were accumulated across the three levels of probing and across the five categories used for specific probing.

At the end of the interview, participants used a six-point rating scale to rate the vividness of each memory. Participants also rated on the same six-point scale how often they think or talk about the recalled event (1 = ''once every few years'' to 6 = ''once per week''). Following the analysis of Steinvorth *et al.* (18), we excluded memories from further analysis that received a 6 on this rating scale to avoid semanticized versions of personal events. This resulted in the exclusion of the memory that had been provided for the most recent time period (last year) for three patients (G.W., L.J., and G.P.).

Scoring. Standard procedures were used for scoring (17). Each narrative was segmented into ''details,'' which were defined as a piece of information, observation, statement, or thought. A detail usually corresponded to a grammatical clause, a sentence or part of a sentence that independently conveyed information. Each detail was then categorized as ''internal'' or ''external.'' Internal details were episodic information relating directly to the autobiographical event being recalled. External details included mostly semantic information (factual information that formed background to the narrative) and other details (i.e., metacognitive statements, editorializing, or inferences). In addition, external details included episodic information that was not part of the autobiographical event being recalled. Repetitions were also tabulated, but did not contribute to the total number of internal or external details.

Verification of Narratives. A potential problem with the Autobiographical Interview is that no method is provided to determine the validity of the autobiographical memories. To assess the validity of each memory from the five time periods, we adopted a method used previously (16). Specifically, at a substantial interval after the original interview (median = 9 months; range = 3–22 months), participants were interviewed again. The rationale was that participants would have more difficulty answering questions about a fabricated memory than about a true memory. For each autobiographical memory that had been previously reported (maximum = 5), participants were given two cues from their original narrative. They were then asked four specific questions about the narrative. The two groups performed similarly. Across all of the recollections, the patients answered 3.4 questions of four in a manner consistent with their earlier narratives, and the controls answered 3.8 questions in a consistent manner [$t(4) = 1.6$, $P > 0.1$].

Reliability of Scoring. The narratives from all 12 participants were scored for detail by one rater (V.V.G.). To determine the reliability of the scoring method, a second, independent rater (P.J.B.) also scored narratives from four participants selected at random (two patients and two controls). The two raters counted a similar number of details (mean difference = 15.2%). An interrater correlation was calculated based on the number of internal and external details counted for each participant by the two raters across the three levels of retrieval support (free recall, general probe, and specific probe) (r = 0.93).

ACKNOWLEDGMENTS. We thank Jennifer Frascino for research assistance. This work was supported by the Medical Research Service of the Department of Veterans Affairs, National Institute of Mental Health Grant 24600, the Metropolitan Life Foundation, and National Institute of Mental Health Training Grant T32-MH2002.

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