Differential Effects of Early Hippocampal Pathology on Episodic and Semantic Memory

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Differential Effects of Early Hippocampal Pathology on Episodic and Semantic Memory

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Global anterograde amnesia is described in three patients with brain injuries that occurred in one case at birth, in another by age 4, and in the third at age 9. Magnetic resonance techniques revealed bilateral hippocampal pathology in all three cases. Remarkably, despite their pronounced amnesia for the episodes of everyday life, all three patients attended mainstream schools and attained levels of speech and language competence, literacy, and factual knowledge that are within the low average to average range. The findings provide support for the view that the episodic and semantic components of cognitive memory are partly dissociable, with only the episodic component being fully dependent on the hippocampus.

One influential view of memory organization (*1*) pictures the cognitive or declarative form, comprising both fact and event memory, as a unitary process that is dependent on the hippocampal system, a set of heavily interconnected medial temporal-lobe structures consisting of the hippocampus and underlying entorhinal, perirhinal, and parahippocampal cortices. According to this notion, both fact (or semantic) memory and event (or episodic) memory are impaired together in a graded manner depending on the extent of damage to the hippocampal system as a whole. An earlier view (*2*), which still has its adherents (*3*), proposed instead that the core defect in temporal-lobe amnesia is a loss of context-rich episodic memory, in that in some amnesic cases, semantic memory, which is free of context, appears to have been relatively preserved. An opportunity to assess these different views has been provided by our study of patients with amnesia due to hippocampal pathology sustained, in two of our patients, very early in life, before they had acquired the knowledge base that characterizes semantic memory. The results suggest a possible reconciliation of the two views, namely that episodic memory depends primarily on the hippocampal component of the larger system, whereas semantic memory depends primarily on the underlying cortices.

Previously, in the absence of any reported cases of amnesia due to very early bilateral injury to the medial temporal lobe (*4*), it had seemed that such early damage might so impede cognitive development that the resulting syndrome would take the form, not of amnesia, but of severe mental retardation (*5*). The findings described here show instead that early bilateral pathology that is limited largely to the hippocampus produces a severe loss of episodic memory but leaves general cognitive development, based mainly on semantic memory functions, relatively intact.

The first of our three patients (*6*), Beth, now aged 14, was born after a difficult delivery, and she remained without a heartbeat for 7 to 8 min before being resuscitated. She also sustained injury to the right brachial plexus. Two hours after resuscitation, she had a generalized seizure, and such attacks recurred sporadically for 2 to 3 days despite treatment with anticonvulsant medication. Within 2 weeks, however, Beth had made a good recovery, although the brachial plexus injury resulted in permanent impairment of the right arm and hand due to partial loss of the nerve function deriving from the fifth and sixth cervical nerve roots. No other neurological problems were evident until she reached age 5 when memory difficulties were first noted on her entrance into a mainstream school. The second patient, Jon, now aged 19, was delivered prematurely at 26 weeks of gestation. Weighing just under 1 kg and suffering from breathing problems, he was kept in an incubator for 2 months, during which time he was tube-fed and placed on a ventilator. Thereafter, he improved steadily and developed normally. At the age of 4, he suffered two, protracted (1.5 to 2 hours), afebrile convulsions. His memory impairment was first noted by his parents about a year and a half after the two long-lasting attacks. The third patient, Kate, now aged 22, was an average student until the age of 9, when she accidentally received a toxic dose (400 mg for 3 days) of theophylline, a drug with which she was being treated for asthma. An acute episode of seizures, unconsciousness, and respiratory arrest ensued, from which she showed good physical recovery but which left her profoundly amnesic. Subsequently, at age 17, she developed temporal lobe epilepsy, which has been well controlled with anticonvulsant medication.

Neuropsychological examination showed

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that Jon and Kate have memory quotients (*7*) (MQs) (which are largely a measure of verbal memory) that fall 16 to 20 points below their verbal intelligence quotients (VIQs), a discrepancy that is characteristic of amnesia in adults; Beth, on the other hand, has no such VIQ-MQ discrepancy (Table 1). Because the relation between VIQ and MQ in normal children of varying levels of ability was unknown [the Wechsler Memory Scale (WMS) (*7*) having been standardized only on individuals aged 18 and above], we examined this relation in a group of normal children ($n = 59$) ranging in age from 11 to 14. We found that normal adolescents with the same VIQs as Beth (75 to 84; $n = 6$) have MQs that are, on average, 20 points higher than their VIQs (as VIQs increase, this difference gradually lessens until, at VIQs of 105 and above, the difference disappears). The results suggest that, like Jon and Kate, Beth too has an MQ that is about 20 points lower than her VIQ would predict. The lack of a VIQ-MQ discrepancy in her case is a reflection not of preserved memory (see below) but, presumably, of mildly impaired verbal intellectual development [a VIQ of 82 compared with her parents' scores of more than 100, although there is a more serious retardation in the development of performance intelligence quotient (PIQ)]. A possible explanation for such an intellectual impairment is suggested by the magnetic resonance findings that are described later.

Confirmation that Beth's memory is impaired no less than that of the other two patients is provided by the extremely low scores that all three obtained when a 90-min delay was interposed between their initial and subsequent recall of the WMS stories (Fig. 1A) and a 40-min delay was interposed between their initial and subsequent reproduction of the WMS designs (Fig. 1B). In both cases, all three patients performed close to the lowest possible level. The same result was obtained on other standard memory tests, including delayed recall of the word list contained in the Children's Auditory Verbal Learning Test (*8*) (Fig. 1C) and delayed reproduction of the Rey-Osterreith Figure (*9*) (Fig. 1D). By contrast, on immediate memory for the word list (Fig. 1C), as well as on both digit span and a spatial analog of digit span (Corsi blocks) (Table 1), all three patients performed within normal limits (*10*), a finding that is also characteristic of adult-onset amnesia.

The symptoms that brought these patients to our attention were the reports by the parents of their children's failure to remember the events of daily life. The incidence and severity of these everyday memory difficulties were then ascertained from a parental questionnaire (*11*). The situations posing the most pronounced problems for the three patients can be broadly divided into three categories. (i) Spatial: None of the three patients can reliably find their way in familiar surroundings, remember where objects and belongings are usually located, or remember where they have placed them. (ii) Temporal: None is well oriented in date and time, and they must frequently be reminded of regularly scheduled appointments and events, such as particular classes or extracurricular activities. (iii) Episodic: None can provide a reliable account of the day's activities or reliably remember telephone conversations or messages, stories, television programs, visitors, holidays, and so on. According to all three sets of parents, these everyday memory losses are so disabling that none of the patients can be left alone, much less lead lives commensurate with their age, circumstances, and aspirations.

The parental ratings were confirmed by results obtained from the Rivermead Behavioural Memory Test (*12*), which was specifically designed as an objective measure of the ability to store and retrieve within a testing session the types of items that appear in the parental questionnaire (*11*). The test items include remembering a route, where a belonging was placed, an appointment, the date, a message to be delivered, a name for a pictured individual, a story, pictures, and so forth. Out of a possible score of 12 and with a cutoff for impairment of nine correct items or less, Beth, Jon, and Kate obtained scores of 2, 3, and 4, respectively, which are indicative of severe impairment in each of them.

To assess neuropathology in the patients, we used three different quantitative magnetic resonance techniques, namely, volumetric measurements and T2 relaxometry for the detection of hippocampal abnormalities and proton magnetic resonance spectroscopy (^{1}H MRS) for the detection of more diffuse temporal-lobe abnormality (*13*). These techniques were selected because of their known sensitivity to temporal-lobe pathology (*14*–

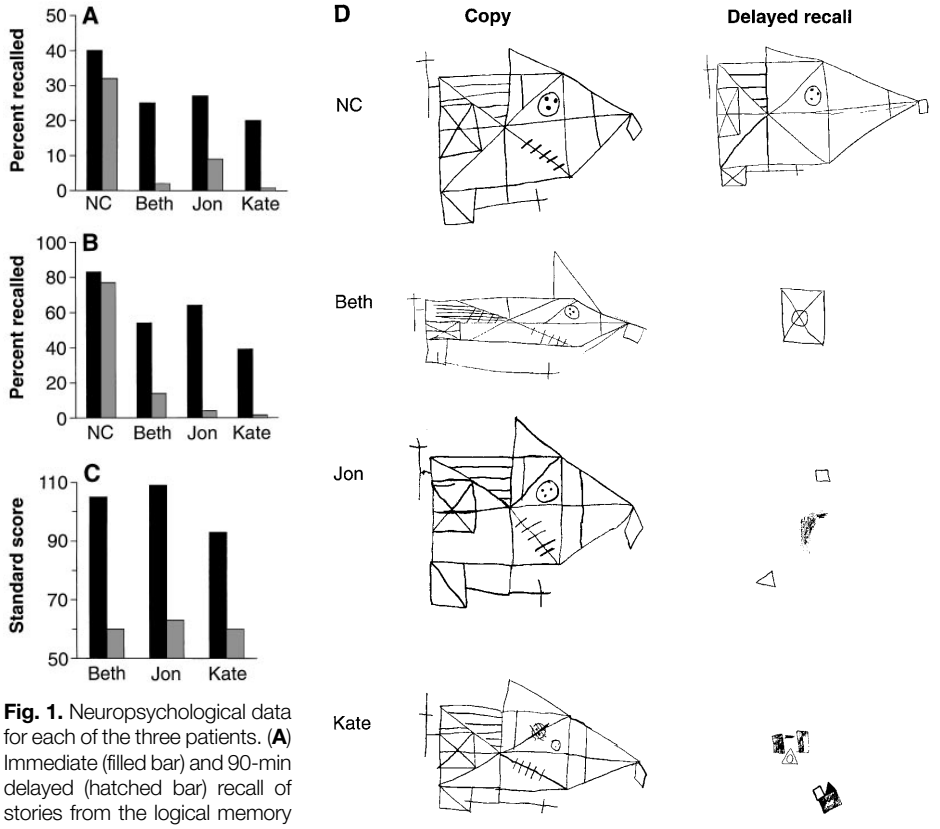


Fig. 1. Neuropsychological data for each of the three patients. (**A**) Immediate (filled bar) and 90-min delayed (hatched bar) recall of stories from the logical memory subtest of the WMS. NC, a group of 47 normal control individuals ranging in age from 12 to 42. The SE of the mean in the NC group is 1% for both immediate and delayed recall. (**B**) Immediate (filled bar) and 40-min delayed (hatched bar) reproduction of geometric designs from the visual memory subtest of the WMS. NC is as in (A). SE in the NC group is 2% for immediate recall and 3% for delayed recall. (**C**) Standard scores for immediate memory span (filled bar, the sum of the recall scores for two 16-word lists immediately after their first presentation) and delayed recall (hatched bar, 20 min after completion of five learning trials of the first 16-word list; the presentation and recall of the second, or interference, list; and immediate recall of the first list) from the Children's Auditory Verbal Learning Test. The normal mean score ± SD is 100 ± 15; the lowest possible score is 60. (**D**) Copy (for at least 3 min and no longer than 5 min) of the Rey-Osterreith Complex Figure and 40-min delayed reproduction of it. NC, copy and delayed reproduction by a typical 13-year-old.

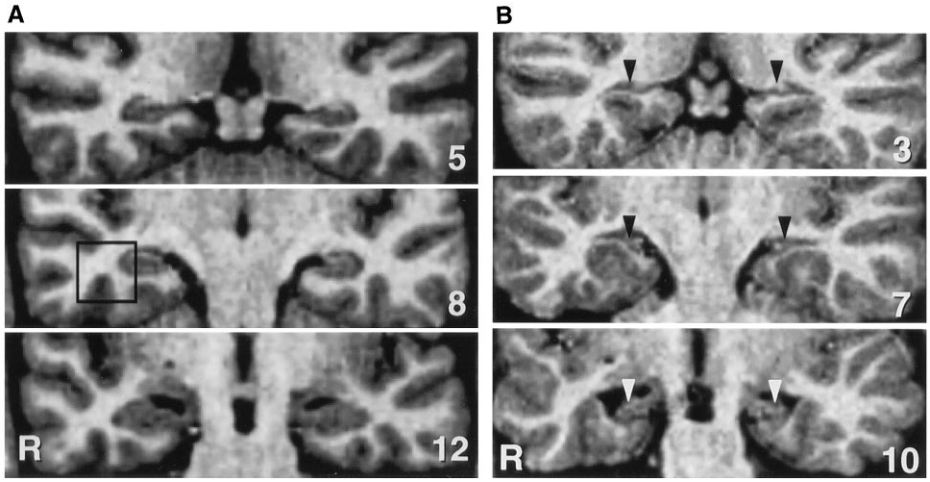
17). Volumetric measurements derived from three-dimensional (3D) data sets showed that in each of the three patients, the hippocampi are abnormally small bilaterally, with volumes ranging from 43 to 61% of the mean value of normal individuals (Figs. 2 and 3A). Furthermore, T2 relaxometry revealed that the hippocampal water T2 values are elevated bilaterally in all three patients (Fig. 3B), which indicates that even the hippocampal tissue that remains is severely compromised in each case. In contrast, the ^{1}H spectra of the relatively large (2 by 2 by 2 cm) temporal lobe region illustrated in Fig. 2A showed signal intensity ratios that are within the normal range for Beth bilaterally and for Jon and Kate on the left; only on the right are the ratios for Jon and Kate below normal and then only marginally so (Fig. 3C) (*18*).

Given their pronounced amnesia for everyday events and the logical possibility that a memory disorder of such magnitude sustained so early in life would seriously interfere with their subsequent cognitive development, it is noteworthy how well all three patients, and Beth and Jon in particular, have fared in mainstream education. As indicated by their scores on the Wechsler Objective Reading Dimensions (WORD) Test (*19*), all three patients are not only competent in speech and language but have learned to read, write, and spell (with the exception of Jon's spelling) at levels that are commensurate with their VIQs (Table 2). Although the motor routines and behavioral skills needed to first learn to read and write must depend largely on noncognitive procedural or habit learning, the requisite symbolic knowledge, as well as the ability to comprehend and express ideas through reading and writing, can only come from the semantic component of cognitive memory. With regard to the acquisition of factual knowledge, which is another hallmark of semantic memory, the vocabulary, information, and comprehension subtests of the VIQ scale are among the best indices available,

Table 1. Results of neuropsychological tests in the three patients and in normal control individuals (NC). The measures are of VIQ, PIQ, MQ, digit span, and block span.

	Beth	Jon	Kate	NC (n = 47) [mean (SD)]
Age at testing	12 years, 10 months	16 years, 4 months	19 years, 2 months	12 to 42 years
VIQ	82	109	86	101.5 (15.1)
PIQ	61	109	79	102.6 (13.8)
MQ	83	93	66	108.6 (15.1)
Digit span				
Forward	6	8	7	6.6 (1.3)
Backward	5	6	4	4.6 (1.7)
Block span				
Forward	4	7	5	5.6 (0.9)*
Backward	6	8	5	5.5 (1.0)*

*See (*10*).



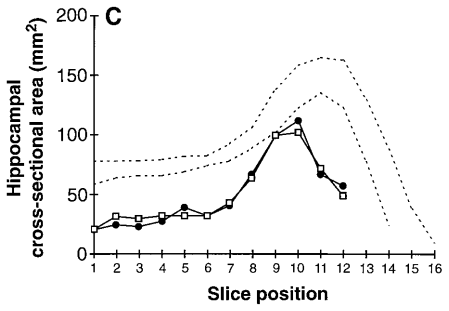


Fig. 2. (**A** and **B**) Selected slices of the reformatted 3D images, showing the temporal lobes and hippocampi in a control individual (A) and in one of the amnesic patients (Beth) (B). R refers to the right side of the brain. The black square in (A) illustrates the position of the 2 by 2 by 2 cm region selected for ^{1}H MRS of the right temporal lobe; the homologous position was used to acquire data from the left temporal lobe. The numbers refer to the slice positions, as represented in (C). The patient shows diffuse hippocampal atrophy [black arrows on slices 3 and 7 and white arrows on slice 10 in (B)]. (**C**) Hippocampal cross-sectional area as a function of slice position. The dashed lines are 2 SD above and below the mean for normal hemispheres. The open squares and filled circles represent the areas of Beth's left and right hippocampi, respectively.

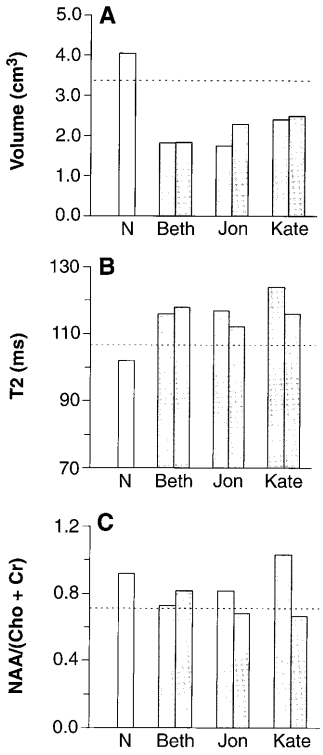


Fig. 3. Magnetic resonance data for each of the three patients and the mean values for normal individuals (N). Data for left and right hippocampi and for left and right temporal lobes of the three patients are shown as left and right bars, respectively. (**A**) Hippocampal volumes. The hippocampal volume for 22 normal individuals was 4.048 ± 0.325 cm^3 (mean ± SD; n = 44), and the dashed line (2 SD below the mean) represents the lower limit of normal. (**B**) Hippocampal T2 values. The hippocampal T2 value of 39 normal individuals was 102.4 ± 2.8 ms (mean ± SD; n = 78), and the dashed line (2 SD above the mean) represents the upper limit of normal (*14*). (**C**) MRS signal intensity ratios. The dashed line [NAA/(Cho + Cr) = 0.72] represents the lower limit of normal [see (*13*)].

and here, too, all three patients obtained scores within the normal range (Table 2).

A remarkable feature of Beth's and Jon's stores of semantic memories is that they were accumulated after these patients had incurred the damage to their hippocampi. How sensory information can enter a semantic memory store in the face of an early-onset amnesia characterized by a disabling loss of episodic memory is unknown. One possibility, predicated on the notion that the only gateway to semantic memory is through episodic memory, is that episodic memory, even though degraded in the patients, is sufficiently preserved to have allowed the acquisition, through repetition in different contexts, of context-free linguistic and factual knowledge. The implication of this proposal is that, despite the putative difference in the sparing of episodic and semantic memory, they have in fact been spared to the same degree. This interpretation is consistent with the view that the two components of cognitive memory constitute a unitary process mediated by the hippocampal system as a whole (*1*). The other possibility is that the apparent inequality of sparing is real (*2, 3*) and that it results from the fact that semantic memories can be stored partly independently of episodic memory. One way in which this partly independent storage could have been achieved is suggested by the following observations.

Table 2. Academic attainments (normal mean scores, 100 ± 15) and selected VIQ subtest scores (normal mean, 10 ± 3) in the three patients. Ages at testing are as in Table 1. WISC-III, Wechsler Intelligence Scale for Children–Third Edition, United Kingdom; WAIS-R, Wechsler Adult Intelligence Scale–Revised.

	Beth	Jon	Kate
Literacy (*WORD*) subtests			
Basic reading			
Actual score	85	102	102
IQ predicted score	83	106	89
Spelling			
Actual score	77	84*	99
IQ predicted score	85	105	89
Reading comprehension†			
Actual score	84	97	88
IQ predicted score	81	107	87
WISC-III and WAIS-R subtests			
Information‡	9	10	6
Vocabulary§	7	14	8
Comprehension‖	7	11	7

*Actual score is significantly ($P < 0.01$) lower than the score predicted from the IQ. †The patient read a passage (shown here in quotes) and was asked a question (Q) about it; the passage remained in view until the patient answered. Examples include the following: "Most of our clothes are made from huge bolts of cloth knitted or woven from long strings called yarn. Yarn is spun from short strands of plant or animal fibers or, in the case of nylon and other synthetics, from fibers made from petroleum." Q: According to the passage, what happens before cloth is made? Beth: Yarn is spun from short strands of plant or animal fibers. "The evidence, though circumstantial and, at that, only inconsistently corroborated, seemed in the eyes of the jurors to be incontrovertible; only when the accused was subsequently vindicated by the unforeseen occurrence of the true perpetrator's confession did they, upon reflection, consider that their verdict had sought reprisal more than justice." Q: How was the innocence of the accused established? Jon: By the confession of the true perpetrator. "According to statistics, heart disease, cancer, and Jellinek's disease are receiving more consideration as the consequences of drinking and driving are becoming manifest. Jellinek was a famous researcher who studied substance abuse." Q: Why is Jellinek's disease receiving more attention? Kate: Consequences of drinking and driving are becoming manifest. ‡For example: Q: Which country in the world has the largest population? Beth: China. Q: Who was Martin Luther King? Jon: An American; fought for black rights; black rights leader in the 1970s; got assassinated. Q: What is the Koran? Jon: Holy Book of Moslems. Q: What is the capital of Italy? Kate: Rome. §For example: Q: What does "boast" mean? Beth: If someone has done something, they boast about it; they show off. Q: What is a "sanctuary"? Jon: Safe haven; place of safety everyone can go to. Q: What does "encumber" mean? Jon: When you try and burden them with lots of things. Q: What does "obstruct" mean? Kate: To get in the way of something. ‖For example: Q: Why is it important for the government to make sure that meat is inspected before it is sold? Beth: Because it could be not clean and people could get a disease and die. Q: What does this saying mean? "One swallow does not make a summer." Jon: Just because you see a little bit of evidence toward something, unless you've got more evidence it's not really proof that you're right. Q: Why do some people prefer to borrow money from a bank rather than from a friend? Kate: Because they can pay back the money in their own time; a friend may pester them.

Besides the tests described earlier, 12 computerized, two-choice, recognition memory tasks modeled after those used with nonhuman primates (*20*) were administered to the 3 amnesic patients and 11 normal individuals. The tasks included one-trial recognition for lists of words, nonwords, familiar faces, and unfamiliar faces (each tested with five lists of 12 items each); one-trial associative recognition for lists of paired items involving each of the same four types of material as above (10 six-pair lists for each); and multitrial associative recognition for lists of nonword pairs, face pairs, voice-face pairs, and object-place pairs (one 20-pair list for each). Among these 12 tasks, the only ones that yielded significant group differences (evaluated by unrelated *t* tests with Bonferroni corrections) were voice-face (*21*) and object-place associations (*22*). These findings in the amnesic patients are strikingly similar to those reported previously in monkeys with hippocampal lesions. After sustaining such lesions, monkeys too are severely impaired in learning object-place associations (*23*) and yet are unimpaired on other two-choice recognition tasks, such as those requiring one-trial object recognition (*24*) and object-reward association (*25*), as well as multitrial visual-visual (*26*) and tactile-visual associations (*27*). The absence of impairment in hippocampectomized monkeys on the nonspatial recognition tasks is not due to their insensitivity to medial temporal damage, because performance on all of them is severely disrupted by ablation of the perirhinal and entorhinal cortices located below the hippocampus (*18, 26*). The patients' pattern of performance on the computerized tasks, combined with the evidence in monkeys, suggests that the basic sensory memory functions of the cortex subjacent to the hippocampus are substantially spared in the amnesic patients just as they are in hippocampectomized monkeys.

The above considerations, together with the evidence suggesting differential preservation of semantic memory in our amnesic patients, lead us to propose that the basic sensory memory functions of the perirhinal and entorhinal cortices may be largely sufficient to support the formation of context-free semantic memories but not of context-rich episodic memories, which must therefore require the additional processing provided by the hippocampal circuit (*28*). Such a proposal is consistent not only with the behavioral results but also with the anatomical evidence that the higher order cortical sensory areas and the hippocampus communicate with each other only indirectly through the perirhinal and entorhinal cortices (*29*). Because of this hierarchical arrangement, the latter cortices are in a position to mediate the acquisition of some forms of memory independently of the hippocampus.

From postmortem analyses of the brains of several individuals who became amnesic after hypoxic or ischemic accidents in adulthood, Zola-Morgan and colleagues (*30*) concluded that the syndrome of global anterograde amnesia can result from bilateral pathology to the hippocampus alone. The evidence presented here is consistent with that conclusion but further suggests that the amnesic syndrome produced by such damage takes the form of a severe loss of episodic memory with relative sparing of semantic memory owing to the fact that the latter can be largely supported by the underlying cortices. According to this proposal, perhaps only when the hippocampus and underlying cortices are damaged together, as in the famous case of H.M. (*31*), does the anterograde amnesia affect both components of cognitive memory equally.

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13. Magnetic resonance imaging (MRI) and MRS studies were carried out on a 1.5 T Siemens system with a standard quadrature head coil. Structural MRI investigations included 3D data acquisition with the T1-weighted magnetization prepared rapid acquisition gradient echo sequence [J. P. Mugler and J. R. Brookeman, *Magn. Reson. Med.* **15**, 152 (1990)], with the following parameters: repetition time, 10 ms; echo time, 4 ms; inversion time, 200 ms; flip angle, 12°; matrix size, 256 by 256; field of view, 250 mm; partition thickness, 1.25 mm; 128 sagittal partitions in the third dimension; acquisition time, 8.3 min. For the measurements of hippocampal volumes, the data sets were reformatted into 1-mm-thick contiguous slices in a tilted coronal plane that was perpendicular to the long axis of the hippocampus. We measured hippocampal cross-sectional areas along the entire length of the hippocampi, using every third slice as described previously (*14*). We calculated the volumes by summing the cross-sectional areas and then multiplying them by the distance between the measured slices (that is, 3 mm). A correction was then made for intracranial volume, and the hippocampal volumes are presented here in this corrected form. Hippocampal water T2 values were obtained from T2 maps constructed from a 16-echo sequence, as previously described (*14, 15*). The cross section from which the hippocampal T2 values were taken was oriented in a tilted coronal plane along the anterior border of the brain stem perpendicular to and at the level of the body of the hippocampus. We measured T2 values by placing a region of interest in the largest possible circular area within the hippocampus while avoiding boundaries at which partial volume effects with cerebrospinal fluid may occur. For the assessment of more diffuse or widespread pathology, we obtained ^{1}H MRS data from 2 by 2 by 2 cm cubes centered on the medial portions of the right and left temporal lobes, using a 90°-180°-180° spin-echo technique (TR, 1600 ms; TE, 135 ms) as described previously (*16*). Signal intensities at 2.0 parts per million (ppm) [primarily N-acetylaspartate (NAA)], 3.0 ppm [creatine + phosphocreatine (Cr)], and 3.2 ppm [choline-containing compounds (Cho)] were measured from the peak areas by integration and corrected for differences in radio-frequency coil loading among the different individuals. The data are presented in the form of the signal-intensity ratio NAA/(Cho + Cr), which provides a simple index of spectral abnormality, with values below 0.72 (the lower limit of the 95% reference range) being indicative of neuronal loss or damage or astrocytosis, or both (*16*); J. H. Cross *et al*., *Ann. Neurol.* **39**, 107 (1996); D. G. Gadian *et al*., *Neurology* **46**, 974 (1996)]. The positioning and volume of the selected regions are such that the hippocampi in the amnesic subjects make only a minor contribution to the observed signal intensities.
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18. Although our MRS findings suggest that the bilateral temporal-lobe pathology is focal rather than widespread, the low spatial resolution of the technique does not preclude the possibility that the pathology extended into the underlying perirhinal and entorhinal cortices, an area known to be critical for many types of memory formation in monkeys [M. Meunier, J. Bachevalier, M. Mishkin, E. A. Murray, *J. Neurosci.* **13**, 5418 (1993); B. J. Spiegler and M. Mishkin, *Soc. Neurosci. Abstr.* **5**, 323 (1979); E. A. Murray and D. Gaffan, *ibid.* **19**, 438 (1993); S. Goulet and E. A. Murray, *ibid.* **21**, 1446 (1995)]. We therefore carefully examined the MRI 3D data sets for any evidence of structural abnormality in this specific region as well as in other regions throughout the brain. Although the possibility of undetected damage in the perirhinal and entorhinal regions or elsewhere in the three patients cannot be excluded, the only visible abnormalities noted outside the hippocampal formation were in Beth's scans, in which there was an increase in T2-weighted signal intensity in the periventricular and particularly peritrigonal white matter, accompanied by a marked loss of white matter bulk and thinning of the corpus callosum. These extrahippocampal abnormalities could well be the cause of Beth's impaired intellectual development, described earlier. No extrahippocampal abnormalities were detectable in the other two patients. Thus, as far as we could determine from the magnetic resonance findings, the only abnormality common to all three patients was bilateral pathology of the hippocampal formation.
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20. Like the tests used in monkeys (*18*), the tests for humans were designed with memory loads (that is, number of items and length of delays) that exceeded online working memory capacity so as to tap memory storage ability. It should be emphasized that these tests are not considered to be selective measures of either episodic or semantic learning [see (*28*)].
21. Photos of 20 different female faces were presented in succession on the computer monitor, with each one paired with a recording of that person's voice uttering the phrase "I am sorry I am not able to meet you, but I hope you will remember me." After presentation of the 20 face-voice pairs, one of the recorded voices uttering the same phrase was repeated while two faces were presented on the monitor: the correct face for that particular voice, together with an incorrect one associated with a different voice. The individual responded by touching one of the faces, which produced an indication of "correct" or "incorrect" on the screen, depending on the choice. Such choice tests for all 20 face-voice pairs completed a trial, and the trials were repeated until the individual achieved at least 18 correct responses in one trial or had received a maximum of 10 trials. Each of the normal control individuals learned these associations rapidly (mean, 1.8 trials; range, 1 to 5 trials) and accumulated very few errors (mean, 5.8 errors; range, 1 to 23 errors). By contrast, among the amnesic patients, only Jon performed as well as the poorest control individual, requiring five trials to learn and making 20 errors; Kate learned the associations in six trials (31 errors), and Beth was unable to reach the criterion in the 10-trial limit, making 57 errors. The group difference was significant at $P < 0.05$ for both trials and errors.
22. Pictures of 20 different objects were presented in succession on the right side of the computer monitor, with each object paired with a different circle in an irregular array of 40 circles located in the center of the monitor; the paired circle was illuminated and the object then appeared within it. After presentation of the 20 object-place pairs, one of the previously lit circles was relit, while two objects were presented on the right: the correct object for that particular circle in the array, together with an incorrect one associated with a different circle. The individual responded by touching one of the objects, which produced a voice-recorded "correct" or "incorrect," depending on the choice. Such choice tests for all 20 object-place pairs completed a trial, and the trials were repeated until the individual achieved at least 18 correct responses in one trial or had received a maximum of 10 trials. Each of the normal individuals learned these object-place associations rapidly (mean, 1.7 trials; range, 1 to 5 trials) and accumulated very few errors (mean, 4.2 errors; range, 0 to 19 errors). By contrast, none of the amnesic patients learned within the 10-trial limit, each one barely exceeding chance performance (Beth, 86 errors in 200 responses; Jon, 75 errors; Kate, 95 errors). The group differences in trials and errors were each significant at $P < 0.01$.
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28. This proposal does not imply that the computerized recognition tasks are tests of semantic learning; however, neither are they tests of episodic learning. The distinction between the two forms of cognitive memory applies not to the moment that memories are first acquired but rather to their long-term content. At the moment that attended sensory information is encoded for initial storage, the information is necessarily in the form of an unfolding event or episode replete with context, including time, place, surroundings, and persons; how much of the information in that episode is retained in long-term memory is what determines whether the memory is properly classified as episodic or semantic.
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