HIPPOCAMPUS 9:247–254 (1999)

Temporally-Specific Retrograde Amnesia in Two Cases of Discrete Bilateral Hippocampal Pathology

Narinder Kapur[1,2*] and David J. Brooks[3]

[1]*Wessex Neurological Centre, Southampton General Hospital, Southampton, England*
[2]*Department of Psychology, University of Southampton, Southampton, England*
[3]*MRC Cyclotron Unit, Hammersmith Hospital, London, England*

ABSTRACT: The role of the hippocampus in retrograde amnesia remains controversial and poorly understood. Two cases are reported of discrete bilateral hippocampal damage, one of which was a rare case of limbic encephalitis secondary to the human herpes virus 6. Detailed memory testing showed marked anterograde memory impairment, but only mild, temporally-limited retrograde amnesia that covered a period of several years in both autobiographical and factual knowledge domains. The absence of extensive retrograde amnesia in these two cases points to a time-limited role for the hippocampus in the retrieval of retrograde memories, and suggests that entorhinal, perirhinal, parahippocampal, or neocortical areas of the temporal lobe may be more critical than the hippocampus proper for long-term retrograde memory functioning. Our findings offer general support to theories of memory consolidation that propose a gradual transfer of memory from hippocampal to neocortical dependency. *Hippocampus 1999; 9:247–254.* © 1999 Wiley-Liss, Inc.

KEY WORDS: human herpes 6 virus; limbic encephalitis; remote memory

The role of the hippocampus and related structures in retrograde memory functioning has only recently become the focus of research in cognitive neuroscience. The status of retrograde amnesia in the human amnesic syndrome and its neural basis is more uncertain and controversial than the status of anterograde amnesia. As noted by Hodges (1995, p 101) in a recent review, "Much has been learnt, but uncertainty remains in many areas." While the hippocampus has always been strongly implicated in memory formation, there has been a greater emphasis on neocortical or hippocampal-neocortical interaction in the case of retrieval of stored memories (Eichenbaum, 1997). In his classic paper, Squire (1992, p 222–223) concluded on the basis of evidence up to that point, "The facts of retrograde amnesia can be summarized as follows: 1. When damage is limited to the CA1 region of human hippocampus, retrograde amnesia is limited to a period of a year or two at the most. 2. In patients with more complete damage to the hippocampal formation, retrograde amnesia can be extensive and temporally graded across a decade or more, with sparing of very old memories. 3. Hippocampal damage causes retrograde amnesia for both factual information and autobiographical, event-specific information." As Squire and Alvarez (1995, p 173) have pointed out, data relating to the severity and pattern of retrograde amnesia have implications for theories of memory consolidation. They concluded that "the facts of temporally-graded retrograde amnesia, and virtually all accounts of this phenomenon that involve the concept of memory consolidation, suggest that memory storage and retrieval come eventually to be supported by neocortex as the result of gradual changes in connectivity within neocortex."

Human lesion studies have offered some clues as to the role of the hippocampus in retrograde memory, although many of the published studies suffer from some limitations. Investigations relating to the patient HM have variously reported a mild retrograde amnesia of 1–2 years to a retrograde amnesia of up to 13 years. As has been pointed out elsewhere (e.g., Ogden and Corkin, 1991; Kapur et al., 1994a), there are some difficulties in interpreting HM's retrograde memory performance. In addition, his lesion is not restricted to the hippocampus (Corkin et al., 1997), and so his case study has a limited amount to offer with regard to our understanding of the role of the hippocampus in retrograde memory functioning.

Schnider et al. (1994) reported dense anterograde and retrograde amnesia in their patient who suffered bilateral infarction of the hippocampi, with extension of the infarct on the left side to more lateral structures, including the parahippocampal gyri and neocortex of the posterior temporal/anterior occipital lobe. Although formal retrograde memory test data were not reported, the memory loss for pre-illness information appeared to equally affect autobiographical and semantic memories, and to extend back to the patient's childhood with little in the way of a temporal gradient. The patient also had a significant naming deficit, and there may have been some contribution of this deficit to part of his retrograde amnesia. Lee et al. (1992) reported a 4-month period of autobiographical retrograde amnesia in their patient who suffered an amnesic attack associated with a tempo-

Grant sponsor: Wellcome Trust; Grant number: 045045.
*Correspondence to: Professor N. Kapur, Wessex Neurological Centre, Southampton General Hospital, Southampton, SO16 6YD England.
E-mail: n.kapur@soton.ac.uk
Accepted for publication 3 March 1999

ral lobe seizure. The anterograde memory impairment in this patient was more variable than in a classical amnesic syndrome. It is of note that an MR scan carried out several days after the apparent resolution of the retrograde amnesia showed bilateral hippocampal lesions, with no visible extension into more lateral structures.

In a later study, Schnider et al. (1995) found that their patient, a 55-year-old farmer with bilateral hippocampal lesions who was different from the case reported by Schnider et al. (1994), was unaware of personal events over the previous 10–15 years. He recognized the photographs of cattle that he owned more than 15 years ago, but not more recent ones. He was also reported to have a temporally-graded retrograde amnesia for politicians who had become prominent over the previous 10–15 years. The lesions appeared to be restricted to swelling of both hippocampi, though it is difficult to be certain that there was no swelling of adjacent hippocampal formation structures. The aetiology of the lesion is uncertain, though the primary medical condition of the patient was systemic lupus erythematosus (SLE). The relatively sudden onset of the amnesia suggests a vascular aetiology, though the authors themselves suggested a pathology related to an autoimmune process. Reported cerebral complications of SLE tend to be more diffuse than selective hippocampal pathology of the type reported here, and there remains the possibility of additional lesions in this case that were not detected on MRI. A further note of caution is that the patient was a farmer, and it is not clear the extent to which he was interested in public events of the type that were used as part of the retrograde amnesia assessment; no formal test scores or control data were reported in this respect.

Reed and Squire (1998) found extensive episodic and factual retrograde amnesia following hippocampal pathology only when that pathology was accompanied by lesions in additional temporal lobe neocortex and not when it was confined to the hippocampus alone. These patients with extensive retrograde amnesia had lesions associated with herpes simplex encephalitis. Mattioli et al. (1996) reported FDG (fluorodeoxyglucose) PET scan data in a case of focal retrograde amnesia, and found evidence of bilateral hippocampal and anterior cingulate glucose metabolic values. The resolution of their scan did not permit the more detailed anatomical fractionation of the lesion.

In one of the few post-mortem studies of amnesic patients (Rempel-Clower et al., 1996, p 5252), the authors concluded that "temporally-graded retrograde amnesia covering 15 years or more can occur after relatively circumscribed damage to the hippocampal formation." A further post-mortem study involved the case RB (Zola-Morgan et al., 1986) who showed a moderate anterograde amnesia and minimal retrograde amnesia in association with a discrete lesion of the hippocampal formation that was restricted to the CA1 region.

Recently, a case was reported (Kartsounis et al., 1995) that postulated similar underlying lesions to those in the patient RB, although the damage in this new case appeared to extend to CA2 fields. The authors reported the presence of severe, ungraded retrograde amnesia in addition to a marked anterograde memory loss. Kartsounis et al. offered a note of caution, suggesting that, although detailed MRI scanning indicated only circumscribed structural damage in their patient, it was not possible to exclude subtle histological changes in other areas or remote hypoactivation effects of the hippocampal infarcts, particularly with regard to adjacent cortical areas and the mammillo-thalamic system. A more recent PET study of this patient (Kapur et al., 1999) showed additional pathology in the right thalamus, and so the role of the hippocampal damage in this patient's retrograde amnesia remains uncertain.

In light of the above studies, it is clear that further evidence needs to be gathered from well-documented cases of discrete hippocampal lesions in order to clarify the role of the hippocampus in retrograde memory function. Although such patients are rare, we were able to study two such cases whose hippocampal lesions could be verified using advanced brain imaging procedures. One of these cases was an instance of paraneoplastic encephalitis induced by the human herpes virus 6 in a patient who was immune-compromised due to a bone marrow transplant procedure (Drobyski et al., 1994).

CASE 1

BE (dob March 24, 1946) is a right-handed man who worked as a college lecturer. His past medical history was unremarkable except for mild symptoms in the early 1980s related to a possible diagnosis of rheumatoid arthritis. These symptoms resolved with a change in dietary regime, and he only took medication for a short period of time. He developed a viral encephalitis in May 1991, which was accompanied by acute memory loss for recent events, an odd sense of smell, and episodes of déjà vu. In the days following admission, he had two grand mal seizures. There were no positive findings to suggest a herpes simplex virus, though antiviral treatment was given. A CT scan on the day of admission was reported as normal, as was a routine MRI scan carried out 11 days after admission. EEG investigations around this time showed bilateral temporal lobe abnormalities.

In May 1992, a further MRI scan was carried out using a specially designed protocol (described in Kapur et al., 1994b) that gave detailed views of memory-related brain structures. The scans were independently reviewed by two neuroradiologists, who were blind to the neuropsychological test data. The scans were interpreted as showing discrete bilateral lesions (Fig. 1) that were restricted to the hippocampus (due to some degree of artefact on axial slices, only coronal images are shown here). An FDG PET scan confirmed the presence of a focal area of bilateral hypometabolism in the medial temporal region.

Neuropsychological Investigations

These investigations were carried out in 1992. On the basis of six subtests of the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981), BE had a Verbal IQ of 120, a Performance IQ of 133, and a Full Scale IQ of 128. On the National Adult Reading Test-NART (Nelson, 1982), BE had a predicted Full Scale IQ of 112. He performed normally on tests of naming (24/30) (McKenna and Warrington, 1983) and problem-solving ability (Nelson, 1976).

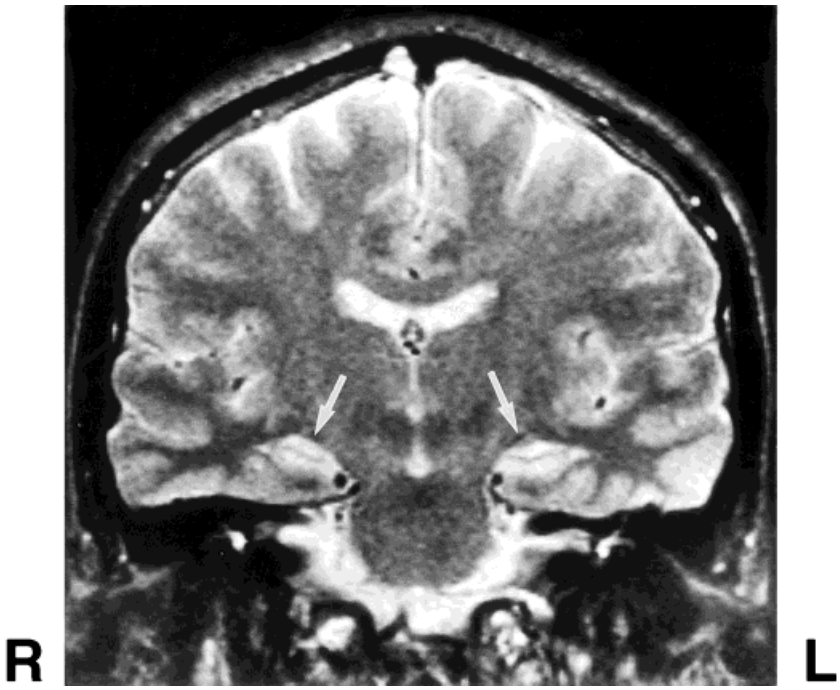

FIGURE 1. Coronal MR scan of patient BE, showing bilateral hippocampal lesions (arrowed). Right and left sides are reversed, i.e., reader's right refers to the left side of the brain.

On the Wechsler Memory Scale-Revised (Wechsler, 1987), BE had a General Memory Quotient of 82 and a Delayed Recall Quotient of 59. On the List Learning and Design Learning subtests of the Adult Memory and Information Processing Battery (Coughlan and Hollows, 1985), BE scored at less than the tenth percentile on the delayed recall trials. On the words and faces subtests of the Recognition Memory Test (Warrington, 1984) his performance was moderately impaired for words (raw score = 39, age-scaled score = 5) but normal for faces (raw score = 42, age-scaled score = 12).

On the Autobiographical Memory Interview (Kopelman et al., 1990), given in December 1993, BE's recall of personal semantic events from childhood, early adult life, and recent adult life was normal, as was his recall of specific incidents from early childhood and early adult life. There was a marked impairment in his recall for specific incidents from his recent life, this covering periods that related to post-illness events. In some patients, the Autobiographical Memory Interview can appear to be a relatively crude instrument, and may not do justice to specific experiences that are unique to an individual. We therefore carried out a detailed, but more informal, interview separately with BE and with his wife about recent events, such as holidays, which they had taken part in together. These sets of interviews provided consistent evidence of a pre-illness autobiographical amnesia of 2 years duration.

Most autobiographical memory tests suffer from a general limitation relating to the verification of responses. BE was also administered a specially designed test of autobiographical memory that includes an element of verification within the design of the test. This test, the Shared Experiences Test, provides the subject with a list of towns and also several events (e.g., funeral, wedding), with the items displayed in two columns on an A4 sheet of paper. These are presented as a recognition test. The subject has to circle those towns he has visited with his spouse. Towns in the test mainly refer to major cities in the United Kingdom, together with local towns. The test is given twice, once with instructions to cover the whole of the person's life, and a second time to cover the period of time since the onset of the patient's amnesia. If the subject indicates that he has been to towns A, B, C, D, and E throughout his life, and on the second testing indicates that he has been to towns D and E in the time since his illness, then the visits to the towns A, B, and C are considered to reflect pre-illness (retrograde) memories. To provide a means of verifying responses, the test is also given to the patient's spouse, with identical instructions. In the case of BE, he had been together with his wife for about 20 years, and the time of testing was 1993, 2 years after the onset of his amnesia. Using this procedure, BE accurately referred to 15 of the 17 places that his wife indicated they had visited together prior to his amnesia, omitting only two places. He did make a number of false-positive responses, i.e., he indicated that he had been to places with his wife that she had not marked. There were in all ten such responses; it is possible that he genuinely confused places that he had visited alone, either during or before his married life, with places he and his wife had visited together.

On the Dead-or-Alive Test (Kapur et al., 1989), where he had to indicate whether a famous personality was dead or alive, how the person died, and when they died, BE had significantly impaired performance ($t = 6.92$, $P < 0.05$) for items from the 1980s, but he performed within normal limits for earlier items. He had a mild impairment for indicating whether current personalities were still alive, presumably reflecting in part his anterograde amnesia. His performance, along with that of four

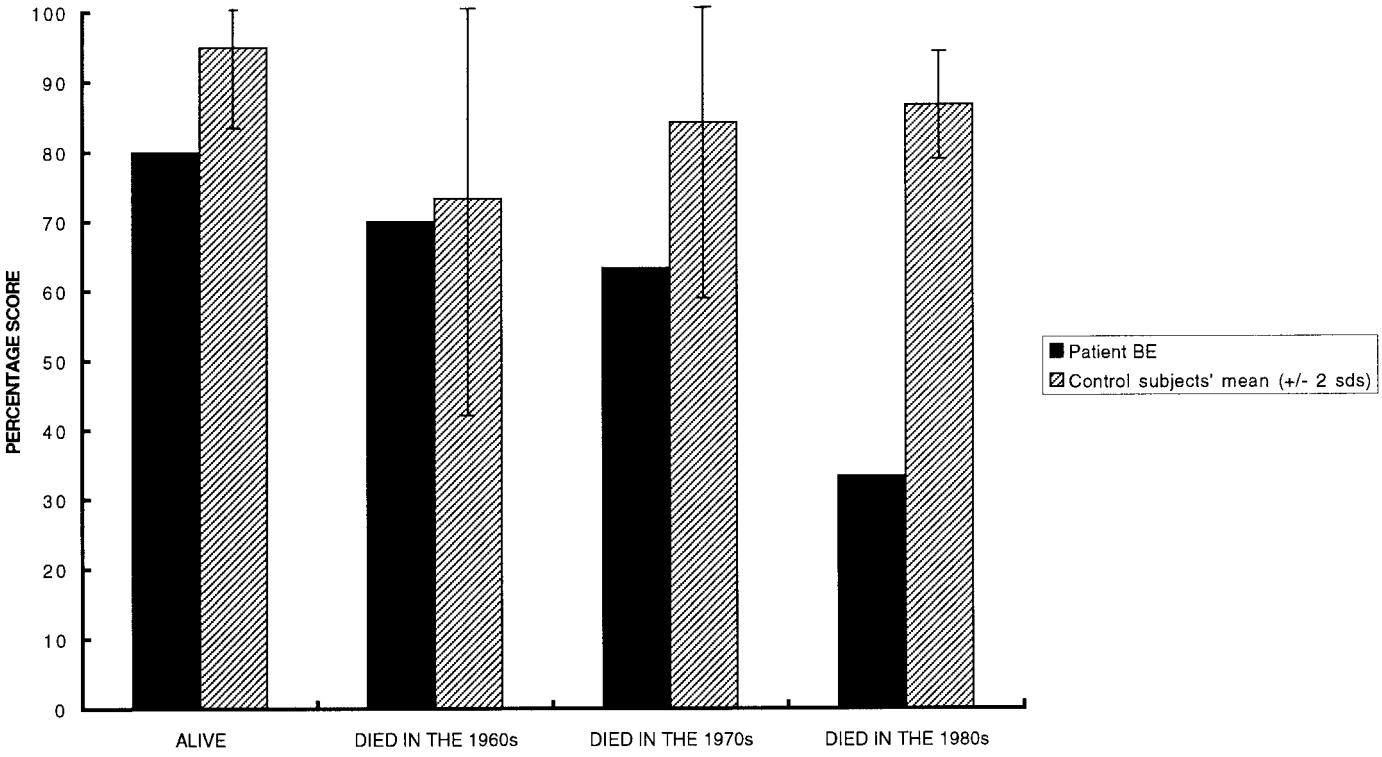

FIGURE 2. BE's performance on the Dead-or-Alive Test.

matched control subjects is shown in Figure 2 (mean age of control subjects = 51 years, range = 50–54 years, mean NART IQ = 115, range = 105–123).

CASE 2

LC (dob July 5, 1961) was a right-handed man who had worked as a lawyer. In 1996, he developed chronic myelocytic leukaemia, and in July 1997 he underwent a bone-marrow transplant procedure. This was a technical success, but in late August 1997 he developed encephalitis, which was traced to the herpes virus 6. His symptoms included a marked impairment of recent memory that initially had some elements of confabulation.

Magnetic resonance imaging (Fig. 3) showed discrete bilateral lesions in the area of the medial temporal lobes. The scans were independently reviewed by two neuroradiologists who were blind to the neuropsychological test data. Using the rating procedures referred to above, they noted abnormal, high signals to be present in the hippocampus bilaterally and also to a more limited extent in the left uncus/entorhinal cortex.

His condition deteriorated, and he died in late September 1997. Although a post-mortem was carried out, the brain pathology had by then advanced to such a stage that precise and meaningful brain-behavior correlations could not be made. As found on subsequent MR scans and at post-mortem, these changes included dilatation of the lateral ventricles, involvement of the basal ganglia, and softening of the white matter throughout the brain.

It should be borne in mind that his condition progressed at a fairly rapid rate after the onset of his amnesia. His MR scan was carried out on September 3, 1997 and most of the neuropsychological testing was carried out on September 9, 1997, with further testing on September 15, 1997. It is quite possible that lesions additional to those in the hippocampus were present at the time of the neuropsychological assessment, though the fact that his retrograde amnesia remained relatively discrete around this time is all the more remarkable in the context of his general medical condition, the severity of his anterograde amnesia, and the presence of some confabulation.

Neuropsychological Investigations

These investigations were limited by his general medical condition and extreme tiredness.

LC was disoriented for time, and he gave his age as 5 years younger than he was. On the Wechsler Memory Scale-Revised (Wechsler, 1987), LC was markedly impaired on immediate and 30-minute delayed recall of stories (4%le and 1%le, respectively). He did not even recall having been told the stories. His immediate recall of designs was also impaired (2%le), and he was unable to recall any of the designs after a delay.

Assessment of his autobiographical memory was limited by his naming difficulties and occasional confabulation. LC's wife estimated that his memory loss for personal events stretched back for one year. Semi-structured interviews showed a patchy memory loss for a few events in the previous few years, but when given cues

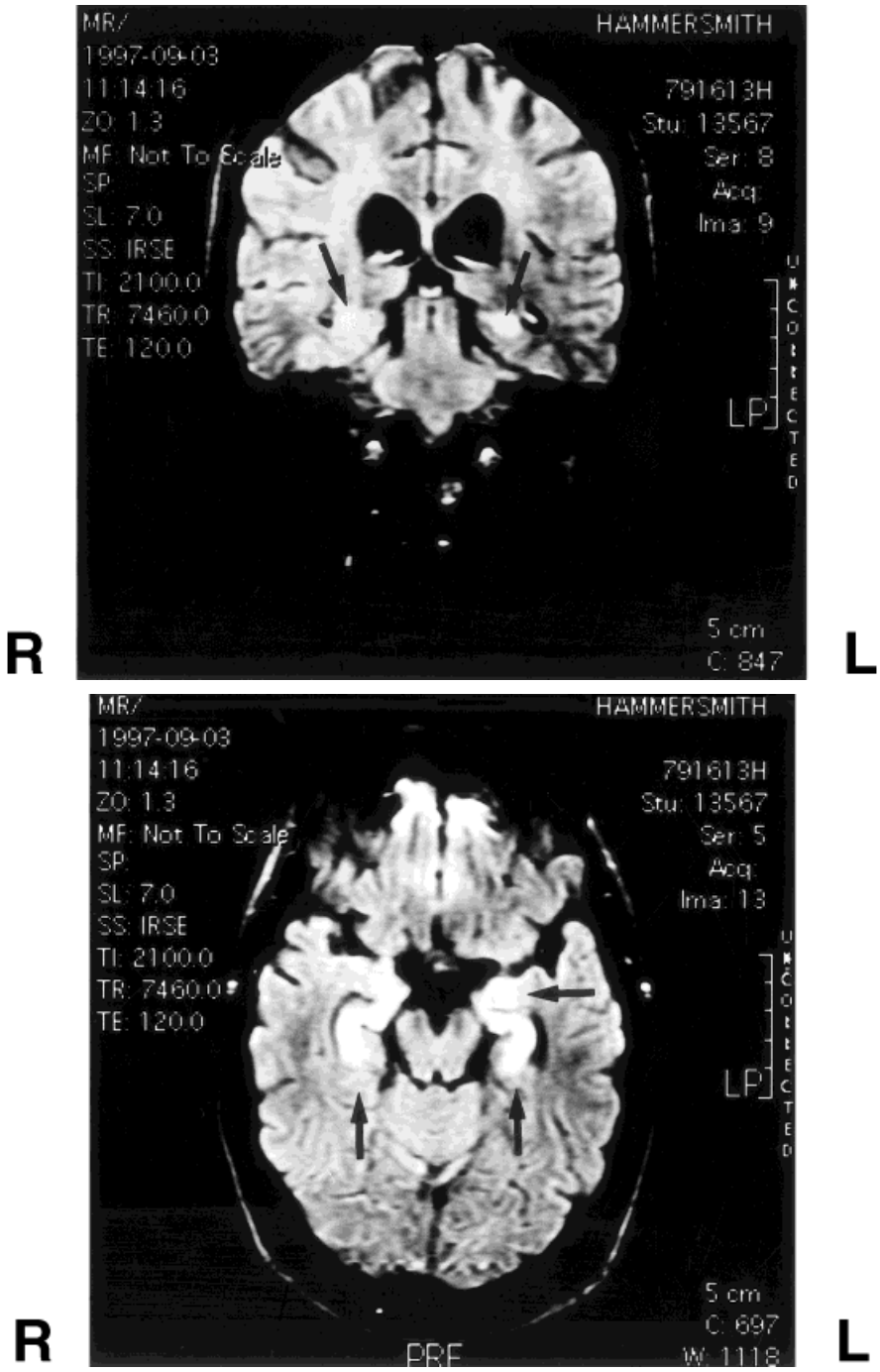

FIGURE 3. Coronal and axial MR scans of patient LC, showing hippocampal lesions and left uncal/entorhinal lesion (arrowed). Right and left sides are reversed, i.e., reader's right refers to the left side of the brain.

he was usually able to provide some information relating to the events. He would give a fairly accurate account of the jobs he had held in the previous 10 years.

Using a short form of the Dead-or-Alive Test (Kapur et al., 1989), he was presented with a list of names of personalities who had become famous during the last 40 years, and he had to indicate which ones had died. For personalities who had died, he performed rather lower than a group of five matched control subjects (mean age = 33 years, range = 30–38 years, mean NART = 116, range = 112–120) for items from the 1980s and 1990s, though his scores remained within two standard deviations of those of the control subjects (LC's score for the 1980s = 58.82% and LC's score for the 1990s = 38.89%; control subjects' mean score for items from the 1980s = 75.29%, standard deviation = 12.75, control subjects' mean score for items from the 1990s = 60.22%, standard deviation = 12.76).

LC was administered a short form of the Verbal News Events Test (Kapur et al., 1996) where he had to indicate which of three

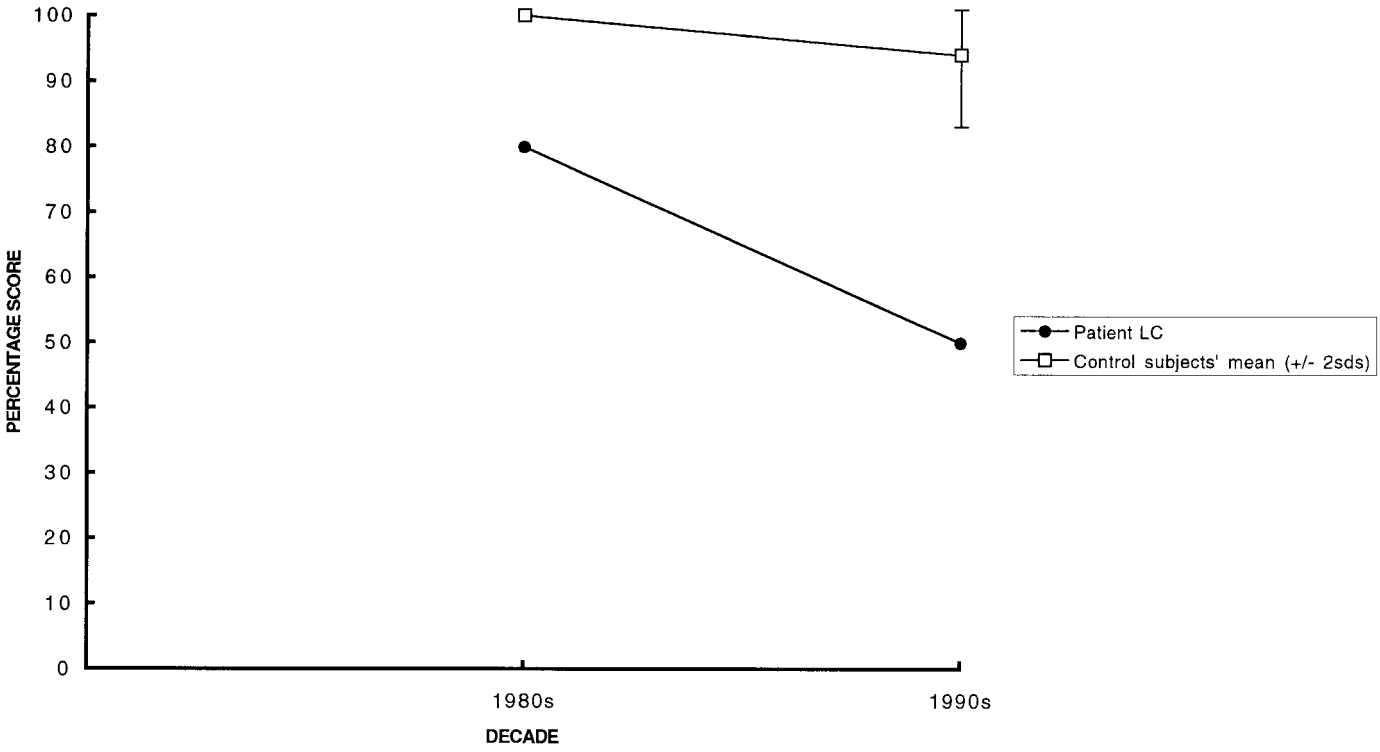

FIGURE 4. LC's performance on the Verbal News Events Test.

events (one real event, two fictitious events) had occurred. He showed (Fig. 4) a significant impairment for items from the 1990s ($t = 3.59$, $P < 0.05$). He performed much better for items from the 1980s, performing closer to a group of five matched control subjects (mean age = 33, range = 30–38, mean NART = 116, range = 112–120), though a ceiling effect may have masked a mild impairment; the presence of a temporal gradient in this data, therefore, needs to be treated with caution

Only a limited amount of more general cognitive testing could be given. On the basis of an adult reading test (Nelson, 1982), his score was equivalent to an IQ of 117. On the Information subtest of the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981), LC had an age-scaled score of 10. He had a moderate impairment on a picture naming test (McKenna and Warrington, 1983), scoring 14/30, and on the modified card sorting test (Nelson, 1976) he was only able to achieve two categories, with a 33.3% rate of perseverative responses.

DISCUSSION

Our two cases of discrete, bilateral hippocampal damage showed a limited degree of retrograde amnesia, in the context of quite marked anterograde memory impairment. The retrograde amnesia that was present was mild and limited to a few years prior to the onset of amnesia. It did not differentially affect episodic rather than semantic retrograde memory functions.

Our findings support the observations of Reed and Squire (1998) that the hippocampus proper has a limited role during the performance of retrograde memory tasks, and that it is adjacent cortical and white matter structures in the temporal lobe, which may be more critical to retrograde memory functioning. One component of these structures includes the rhinal cortices (entorhinal and perirhinal cortex). Thornton et al. (1997) trained monkeys on two sets of object discrimination learning tasks, one at 16 weeks prior to lesioning and the other at 1 week prior to lesioning. Following bilateral rhinal lesions, the monkeys showed memory loss for both sets of tasks, with no evidence of a temporal gradient in the memory loss (although it should be noted that the period of 16 weeks is within the period of retrograde amnesia suffered by our two patients). Of significant interest was the further observation that the monkeys could now normally learn a new set of object discriminations. This apparently critical role of the rhinal cortex for retrograde memory functions finds parallel in a study by Yoneda et al. (1994). In patients with amnesia following herpes simplex encephalitis, Yoneda et al. reported that the degree of retrograde amnesia correlated with the extent of parahippocampal atrophy (which included the entorhinal area in their measurements). In this study, retrograde amnesia appeared to be a composite of autobiographical and public events memories.

Our observations of limited retrograde amnesia following bilateral hippocampal damage are supported by two post-mortem studies, an earlier study by Penfield, and a more recent study by Oxbury et al. (1997). Penfield and Mathieson (1974) reported detailed post-mortem findings on a case of marked anterograde amnesia, and mild retrograde amnesia, in a patient where there was bilateral pathology in the hippocampus, and also additional pathology in lateral temporal lobe structures. They also briefly

reported a second similar case, but this case did not come to post-mortem. (Although their two cases are of interest in view of the detailed anatomical lesion information, it should be cautioned that no formal retrograde memory test data were reported in the paper.) Their primary case was of an engineer, who had suffered temporal lobe seizures since 1940 (further details of this case are reported by Penfield and Milner, 1958). In 1946, he underwent removal of the anterior part of the lateral left temporal lobe, but his seizures continued. Five years later in 1951, he underwent removal of the anterior left hippocampus as well as the uncus. He was left with a severe anterograde amnesia, and a retrograde amnesia that was described as initially covering "recent years," but shrinking to a period of several months. Post-mortem findings showed that the lesion on the left side was restricted to the left anterior hippocampus, the amygdala, and the other left temporal areas removed at the time of surgery. The parahippocampal gyrus was reported as intact. The left entorhinal cortex is not specifically mentioned; its close proximity to the uncus (which was removed at surgery) suggests that it may have been compromised, but it is of note that the left parahippocampal gyrus is reported as normal. White matter gliosis was reported to be present in remaining parts of the left temporal lobe, but the neocortex in this region was considered to be intact. On the right side, the right hippocampus was shrunken; there was substantial neuronal loss in the pyramidal cell layer, the dentate gyrus was involved, and the alveus was gliosed. There was diffuse gliosis of gyral white matter in the parahippocampal, occipito-temporal and inferior temporal gyri on the right, but no abnormality was reported from the associated areas of the right temporal lobe neocortex. It is of note that the patient continued to work as an engineer after his amnesia, though he had to make extensive use of memory aids, and that his Wechsler Memory Quotient was 94. This suggests a moderate rather than severe amnesia. Both his anterograde amnesia, and the hippocampal pathology, would appear to be similar to the case RB (Zola-Morgan et al., 1986), but the Penfield and Mathieson patient had more extensive left lateral temporal lobe damage, and also more white matter gliosis in the temporal lobes.

Oxbury et al. (1997) noted an unusual case of dense anterograde amnesia, and much milder retrograde amnesia, in a patient who had several distinct pathologies. When 18 years of age, he underwent a left temporal lobectomy for long-standing temporal lobe epilepsy. This entailed removal of the medial and lateral left temporal lobe, including the hippocampus and sparing the superior temporal gyrus. He recovered well from this procedure, apart from being left with a mild verbal memory impairment. Eight years later, in 1991, he sustained a minor head injury, and this was followed by a major convulsion. Over the next few years, he had further seizures. In 1992, he had a major convulsion, associated with a probable episode of hypoxia. MRI scanning did not show any abnormality, other than that associated with the left temporal lobe lesion. After this, he was left with a dense anterograde amnesia. MRI scanning later showed significant right hippocampal atrophy. Retrograde memory testing showed a definite autobiographical memory loss for a 16-month period prior to onset of amnesia (though it should be borne in mind that he did have some seizure activity in this period). There was evidence of a patchy retrograde amnesia for earlier years, mainly with regard to sequencing and detail of events. No tests of public events knowledge were given. The patient subsequently died 2 years after the onset of his amnesia. Post-mortem examination revealed, in addition to the old left temporal lobe abnormality, a pathological right hippocampus. There was sparing of the right entorhinal cortex, right parahippocampal gyrus, and the remaining lateral structures in the right temporal lobe.

It would appear likely that the neural basis of retrograde memory functioning entails a matrix of distributed neural networks that is responsible for the laying down, storage, and retrieval of episodic memories. This view is similar to that espoused by Fuster (1997) for memory processes in general, and is consistent with recent functional imaging data relating to experiential recall (Andreasen et al., 1995; Fink et al., 1996). Implicit in this proposal is a multi-stage model of memory consolidation that critically involves the hippocampal complex in the early stages, and involvement of entorhinal, perirhinal, and parahippocampal cortices, together with the neocortex, in later stages. It is worth noting that recent animal studies of retrograde amnesia have pointed to a sequential role for such structures in long-term memory consolidation (e.g., Cho and Kesner, 1996; Izquierdo et al., 1997; Izquierdo and Medina, 1997).

In summary, absence of major retrograde amnesia in our two cases points to a temporally-specific role for the hippocampus in retrieval of retrograde memories, and suggests that rhinal/parahippocampal or neocortical areas of the temporal lobe may be more critical than more medial structures for long-term retrograde memory functioning. Our findings offer general support to theories of memory consolidation (Squire and Alvarez, 1995) that propose a gradual transfer of memory from hippocampal to neocortical dependency.

Acknowledgments

We thank Pat Abbott for her assistance with this study. We are grateful for the comments of two anonymous referees.

REFERENCES

Andreasen NC, O'Leary DS, Cizadlo T, Arndt S, Rezai K, Watkins L, Boles Ponto LL, Hichwa R. 1995. Remembering the past: two facets of episodic memory explored with positron emission tomography. Am J Psychiatry 52:1576–1585.

Cho YH, Kesner RP. 1996. Involvement of entorhinal cortex or parietal cortex in long-term spatial discrimination memory in rats: retrograde amnesia. Behav Neurosci 110:436–442.

Corkin S, Amaral D, Gonzalez R, Johnson K, Hyman B. 1997. HM's medial temporal lobe lesion: Findings from magnetic resonance imaging. J Neurosci 17:3964–3979.

Coughlan AK, Hollows SE. 1985. The adult memory and information processing test battery. Leeds: St James' University Hospital.

Drobyski WR, Knox K, Majewski D, Carrigan D. 1994. Brief report: Fatal encephalitis due to variant B human herpes virus-6 infection in a bone marrow-transplant recipient. N Engl J Med 330:1356–1360.

Eichenbaum H. 1997. To cortex: thanks for the memories. Neuron 19:481–484.

Fink G, Markowitsch H, Reinkemeier M, Bruckbauer T, Kessler J, Heiss W-D. 1996. Cerebral representation of one's own past: neural networks involved in autobiographical memory. J Neurosci 16:4275–4282.

Fuster J. 1997. Network memory. Trends Neurosci 20:451–459.

Hodges J. 1995. Retrograde amnesia. In: Baddeley AD, Wilson B, Watts F, editors. Handbook of memory disorders. Chichester: J Wiley & Sons. p 81–107.

Izquierdo I, Medina JH. 1997. Memory formation: the sequence of biochemical events in the hippocampus and its connection to activity in other brain structures. Neurobiol Learn Mem 68:285–316.

Izquierdo I, Quillfeldt JA, Zanatta M, Quevedo J, Schaeffer E, Schmitz P, Medina J. 1997. Sequential role of hippocampus and amygdala, entorhinal cortex and parietal cortex in formation and retrieval of memory for inhibitory avoidance in rats. Eur J Neurosci 9:786–793.

Kapur N, Young A, Bateman D, Kennedy P. 1989. Focal retrograde amnesia: A long-term clinical and neuropsychological follow-up. Cortex 25:387–402.

Kapur N, Ellison D, Parkin AJ, Hunkin N, Burrows EH, Sampson SA, Morrison EA. 1994a. Bilateral temporal lobe pathology with sparing of medial temporal lobe structures: Lesion profile and pattern of memory disorder. Neuropsychologia 32:23–38.

Kapur N, Barker S, Burrows EH, Ellison D, Brice J, Illis LS, Scholey K, Colbourn C, Wilson B, Loates M. 1994b. Herpes simplex encephalitis: long-term magnetic resonance imaging and neuropsychological profile. J Neurol Neurosurg Psychiatry 57:1334–1342.

Kapur N, Scholey K, Moore E, Barker S, Brice J, Thompson S, Shiel A, Carn R, Abbott P, Fleming J. 1996. Long-term retention deficits in two cases of disproportionate retrograde amnesia. J Cog Neurosci 8:416–434.

Kapur N, Thompson P, Kartsounis LD, Abbott P. 1999. Retrograde amnesia: clinical and methodological caveats. Neuropsychologia 37:27–30.

Kartsounis LD, Rudge P, Stevens JM. 1995. Bilateral lesions of CA1 and CA2 fields of the hippocampus are sufficient to cause a severe amnesic syndrome in humans. J Neurol Neurosurg Psychiatry 59:95–98.

Kopelman MD, Wilson B, Baddeley AD. 1990. The autobiographical memory interview. Bury St Edmunds: Thames Valley Test Company.

Lee BI, Lee BC, Hwang YM, Sohn YH, Jung JW, Park SC, Han MH. 1992. Prolonged ictal amnesia with transient focal abnormalities on magnetic resonance imaging. Epilepsia 33:1042–1046.

Mattioli F, Grassi F, Perani D, Cappa SF, Miozzo A, Fazio F. 1996. Persistent post-traumatic retrograde amnesia: A neuropsychological and (18F) FDG PET study. Cortex 32:121–129.

McKenna P, Warrington EK. 1983. The graded naming test. Windsor, Berkshire: NFER-Nelson.

Nelson HE. 1976. A modified card sorting test sensitive to frontal lobe defects. Cortex 12:313–324.

Nelson HE. 1982. The national adult reading test. Windsor, Berkshire: NFER-Nelson.

Ogden, J. Corkin, S. 1991. Memories of H.M. In: Abraham WC, Corbassis M, White K, editors. Memory mechanisms. Hillsdale, NJ: Lawrence Erlbaum Associates. p 200–205.

Oxbury S, Oxbury J, Renowden S, Squier W, Carpenter K. 1997. Severe amnesia: an unusual late complication after temporal lobectomy. Neuropsychologia 35:975–988.

Penfield W, Milner B. 1958. Memory deficit produced by bilateral lesions in the hippocampal zone. Arch Neurol Psychiatry 79:475–497.

Penfield W, Mathieson G. 1974. Memory: autopsy findings and comments on the role of hippocampus in experiential recall. Arch Neurol 31:145–154.

Reed J, Squire L. 1998. Retrograde amnesia for facts and events: findings from four new cases. J Neurosci 18:3943–3954.

Rempel-Clower N, Zola SM, Squire LR, Amaral DG. 1996. Three cases of enduring memory impairment following bilateral damage limited to the hippocampal formation. J Neurosci 16:5233–5255.

Schnider A, Regard M, Landis T. 1994. Anterograde and retrograde amnesia following bitemporal infarction. Behav Neurol 7:87–92.

Schnider A, Bassetti C, Gutbrod K, Ozdoba C. 1995. Very severe amnesia with acute onset after isolated hippocampal damage due to systemic lupus erythematosis. J Neurol Neurosurg Psychiatry 59:644–645.

Squire LR. 1992. Memory and the hippocampus: A synthesis from findings with rats, monkeys and humans. Psychol Rev 99:195–231.

Squire LR, Alvarez P. 1995. Retrograde amnesia and memory consolidation: a neurobiological perspective. Curr Opin Neurobiol 5:169–177.

Thornton J, Rothblat L, Murray E. 1997. Rhinal cortex removal produces amnesia for preoperatively learned discrimination problems but fails to disrupt postoperative acquisition and retention in rhesus monkeys. J Neurosci 17:8536–8549.

Warrington EK. 1981. Recognition memory test. Windsor, Berkshire: NFER-Nelson.

Wechsler D. 1981. Wechsler Adult Intelligence Scale-Revised. San Antonio: Psychological Corporation.

Wechsler D. 1987. Wechsler Memory Scale-Revised. San Antonio: Psychological Corporation.

Yoneda Y, Mori E, Yamashita H, Yamadori A. 1994. MRI volumetry of medial temporal lobe structures in amnesia following herpes simplex encephalitis. Eur Neurol 34:243–252.

Zola-Morgan S, Squire LR, Amaral DG. 1986. Human amnesia and the medial temporal region: Enduring memory impairment following a bilateral lesion limited to field CA1 of the hippocampus. J Neurosci 6:2950–2967.