



Right medial thalamic lesion causes isolated retrograde amnesia

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Abstract

Pervasive retrograde amnesia without anterograde memory impairment has rarely been described as a consequence of circumscribed brain damage. We report this phenomenon in a 33 yr-old, right-handed man (JG) in association with the extension in the right thalamus of a previously small, bilateral thalamic lesion. JG presented with a dense amnesia for autobiographical material more than a few years old, with some sparing of recent memories. Furthermore, he was completely unable to recognise famous people or world events. Many other aspects of semantic knowledge were intact and there was no evidence of general intellectual impairment, executive dysfunction or loss of visual imagery. Magnetic resonance imaging revealed an acute lesion in the right thalamus and two small, symmetrical, bilateral non-acute thalamic lesions. Follow-up neuropsychological assessment indicated a stable pattern of impaired retrograde and spared anterograde memory over 18 months and psychiatric assessments yielded no evidence of confabulation, malingering or other symptoms to suggest psychogenic amnesia. JG's profile indicates that the division of declarative memory into just two categories – episodic and semantic – is inadequate. Rather, his case adds to the growing body evidence to suggest that world knowledge pertaining to people and events is stored or accessed similarly to autobiographical information and differently from other types of more general factual knowledge. We hypothesize that the right mediodorsal thalamic nucleus and immediately surrounding regions comprise the central processing mechanism referred to by McClelland (*Revue Neurologique*, 150 (1994) 570) and Markowitsch (*Brain Research Review*, 21 (1995) 117) as responsible for inducing and co-ordinating the recall of these sorts of cortically stored memory engrams. © 2001 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Retrograde amnesia occurring together with anterograde amnesia has been noted after thalamic injury [88], infarction [4,16,31,36,42,71,90,97], in Wernicke–Korsakoff syndrome, which involves the thalamus [11,38,59,96], and in transient global amnesia, where right thalamic hypometabolism has been noted on PET scanning [5]. Because, in previously reported cases, the

loss of past memories has always occurred together with an anterograde memory deficit, a precise role for the thalamus in retrograde memory has yet to be defined. Here we present, for the first time, a case of isolated retrograde amnesia associated with a well-defined thalamic lesion. This case has significant implications both for the organisation of memory and for the neural circuitry involved in mnemonic function.

Significant and persistent retrograde amnesia without an anterograde memory impairment has been reported in a small number of patients with circumscribed damage, either to the frontal lobes [19,21] or to the posterior cingulate gyrus and/or retrosplenial region [30,44,57,73]. In other cases where this phenomenon

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has been observed, there has been more diffuse damage resulting from trauma or encephalitis [12,14,20,48,55,62,89,91,100]. In most of these cases, there has been additional cognitive compromise resulting in attribution of the retrograde memory disorder to the secondary effects of disorganized retrieval strategies, impaired visual imaging, and/or a tendency to confabulate.

In the context of organic brain damage, retrograde amnesia is usually time-limited with a temporal gradient, such that the patient is better at recalling the more distant past than the more recent ([1,19,82,89]). The finding that retrograde amnesia after mesial temporal lobe damage extends backward in time for several years ([18,66,81]) gave rise to the proposal that memories are consolidated via the hippocampal region over a period of years [86]. This consolidation period is thought to be followed by storage of memories in diffuse cortical networks, independent of the hippocampal system ([68]). The fact that there are a number of patients with both anterograde and extensive retrograde memory impairment, but without other cognitive deficits to indicate widespread cortical dysfunction [20,23,31,72,98], suggests that in some cases, retrograde amnesia may result from blocked access to stored memories rather than from a destruction of diffusely stored representations. A role for the thalamus in coordinating and controlling the large scale cortical networks involved in conscious recollection has been put forward [9,39,61].

In patients with retrograde memory loss, the degree of impairment may differ according to type of to-be-remembered material. In some patients who were unable to recall autobiographical information, there was relative sparing of factual world knowledge [27,41,42,55,57,94], whereas the reverse pattern has also been documented [22,32,35,49]. These dissociations support cognitive theories that divide declarative memory processes into those involving semantic knowledge versus those involving episodic information ([11,78,86,93]). Markowitsch [61] has proposed that left sided lesions are more likely to cause deficient recall from the semantic knowledge system, whereas right sided brain lesions are particularly likely to disrupt autobiographical or episodic memory. There have also been some cases to indicate that dissociations in the ability to access different types of semantic knowledge can occur ([40,42]). It is not yet clear in what these differences consist, or whether such dissociations depend on lesion location.

In most patients with retrograde amnesia, procedural knowledge is thought to be preserved [48,62]. This aspect of memory for the past is often underexplored in amnesic patients, however, and there is at least one description of procedural knowledge being lost along with other types of memories by a patient with retrograde amnesia [64].

Although rarely seen in association with a focal brain lesion, a profound and isolated inability to recall past events is one of the most common presentations of simulated and psychogenic amnesia [56]. Psychogenic (or dissociative) amnesia is conceptualised as an amnesia of unconscious but psychological origin and is defined in the Diagnostic and statistical manual of mental disorders, fourth edition (p. 478) [24] as “an inability to recall important personal information, usually of a traumatic or stressful nature, that is too extensive to be explained by ordinary forgetfulness.” The disorder “is not due to the direct physiological effects of... a neurological or other general medical condition.” Recently, however, Kapur [47] has suggested that psychogenic amnesia can sometimes accompany a neurological disorder and he proposed a number of features to help distinguish psychogenic from organic retrograde amnesia.

Here we report a case of isolated retrograde amnesia following the extension of a previously asymptomatic, small bilateral thalamic lesion into the right medial thalamic region. In this patient, the amnesia affected memory for autobiographical information, and some aspects of procedural memory, as well as knowledge of famous people and famous events. Other aspects of semantic knowledge were spared. Strikingly, other areas of cognition including anterograde memory, frontal lobe functioning and visual imagery were intact. There were no indications from the patient’s background to suggest a psychogenic cause to the disorder and, 18 months after its onset, the condition remains stable, with no secondary gains having emerged. The case thus provides a unique opportunity to examine the role of the thalamus in the retrieval of stored memories.

2. Case presentation

JG was a 33 yr-old, right handed tradesman who presented with amnesia and disorientation. Ten days prior to his admission, he had developed a sore throat associated with coughing, sneezing and rhinorrhoea. Two days prior to admission, he became somnolent and difficult to rouse. On 29 July, 1998, JG woke complaining of a headache but showered and readied himself for work as usual. As he parted company with his wife, he stopped to ask her where he was working, and what he was supposed to be doing there. When she replied he appeared quite confused and was briefly tearful, saying “I’m so sorry, I don’t remember anything!” He was taken to his general practitioner who noted that he professed almost no knowledge of his past life. The doctor arranged hospital admission that same day.

On admission, JG was alert and had few complaints. He was neither depressed nor anxious although he seemed mildly perplexed by his memory loss. He knew

his name and date of birth, but did not know a number of other things about himself (e.g., whether he smoked). He did not know the year or the day. He had no recollection of two overseas trips taken during the previous year and was unable to say how they had celebrated his own or his wife's last birthdays. On further questioning, it became clear that he was unable to remember anything of his life in England (he had immigrated to Australia in 1993). For example, he could not give his parents' names, describe any aspect of his childhood or remember any details of his schooling. His last memory was of going to bed five days earlier and, when questioned, he thought that his current contract tradesman job was at a site where he had actually been working months earlier. In contrast to his poor retrograde memory, JG showed normal day-to-day anterograde memory. For example, a few days after admission, he was able to describe in detail the cerebral angiogram that he had undergone the previous day.

This profound and pervasive retrograde amnesia associated with very good day-to-day memory suggested psychogenic or simulated amnesia, so a formal psychiatric review was conducted. This revealed no evidence of a disturbance of mood, thought form or thought content. JG's general health was good. According to his wife, he smoked ten cigarettes per day and took modest amounts of alcohol. He used no illicit drugs. There was no personal or family history of migraine or psychiatric illness. His wife knew of no significant personal or financial stress. Formal psychiatric review was repeated on two occasions over the 18 months post-discharge. JG became mildly depressed and was treated successfully with Zoloft. At no time did he show evidence of malingering, confabulation or other significant psychopathology.

On neurological examination at the time of admission, JG's fine finger movements on the left were found to be clumsy. Laboratory investigations revealed a mild lymphopaenia ($1.16 \times 10^9/l$; $N = 1.5\text{--}4.0 \times 10^9/l$), consistent with viral infection and which returned to normal within two days. All other routine haematological and biochemical investigations were normal. The results of extensive investigations for the causes of stroke in a young person were negative.

JG's wife told us that over a few days in 1996 he had manifested similar symptoms. At that time he had been irritable, tearful (which was very out of character), forgetful and difficult to rouse, in association with flu-like symptoms. When we asked about JG's memory over the intervening 2 yr, his wife felt that there had never been any problem that compared to the one that he had developed recently. For example, no retrograde memory problems were noticed when he went home to England in 1997.

3. Neuroradiological findings

Computed tomographic (CT) scanning was carried out upon admission. This was initially reported as normal. Magnetic resonance (MR) imaging, first carried out on 30/7/98, revealed a bilateral (right > left) mesial thalamic lesion. In retrospect, this lesion could be seen on the CT scan as well. Higher quality MR images (as shown in Fig. 1) were obtained in April, 1999. There was no change in the lesion size or distribution between the two MR scans. We use terminology from the Mai et al. [58] brain atlas to describe the thalamic nuclei in this paper.

The MR scans demonstrated three areas of abnormal signal intensity in the thalami, two on the right and one on the left (Fig. 1). Only the more anterior lesion on the right had poorly defined borders and was thought to have occurred recently. This lesion involved the laterodorsal, ventroanterior, ventrolateral anterior, ventrointermedius, reticular, and dorsal part of the mediodorsal thalamic nuclei as well as the internal medullary lamina and part of the mammillothalamic tract. The second, more posterior area of abnormal signal on the right involved the posterior part of the mediodorsal nucleus, the centromedian, ventrolateral posterior, ventroposterior medial and parafascicular nuclei as well as the ventral internal medullary lamina and anterior tip of the medial pulvinar. Third, in the left thalamus, there was a small area of high signal intensity involving the posterior part of the mediodorsal nucleus and the paraventricular nucleus, as well as the posterior part of the internal medullary lamina and

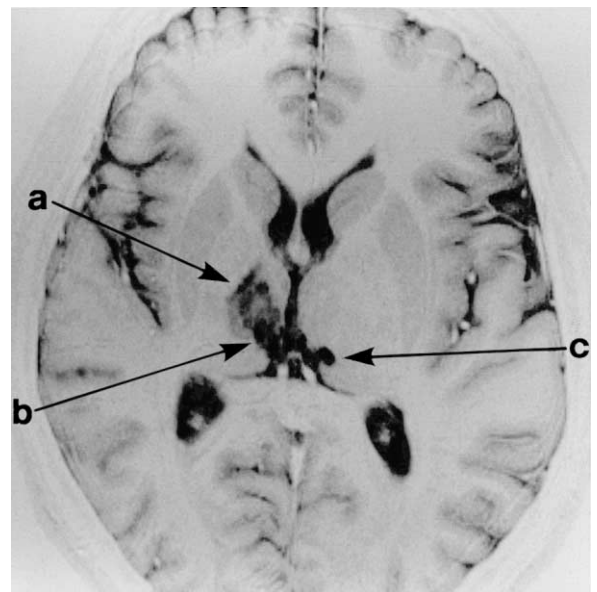


Fig. 1. MR image of JG's thalamic lesions taken at ≈ 9.7 mm above the anterior commissure–posterior commissure line. The right side of the brain appears on the left. (a) Recent right-sided lesion. (b) Old right-sided lesion. (c) Old left-sided lesion.

anterior tip of the medial pulvinar. The latter two regions were quite well defined and appeared to be of slightly higher signal intensity than the more anterior component on the right. Their appearance was judged to be nonacute. The estimated volume of the total lesion in the right thalamus was 772 mm³ and on the left it was 72 mm³. The mammillary bodies, anterior principal nuclei and fornices appeared normal bilaterally and showed no evidence of atrophy. Selective cerebral angiography was performed and was found to be normal.

The thalamic lesions were thought most likely to be the result of infarction. The findings suggested at least two episodes. The major radiological differential diagnosis was demyelination, but the distribution of the lesions was considered to be quite atypical and there was no evidence of lesions involving the corpus callosum. Recently, however, a case of encephalomyelitis affecting the thalamus has been described [74] and this aetiology must be considered a possibility.

4. Neuropsychological assessments

4.1. Initial assessment (1 day, 5 days and 3 months following admission)

On formal testing, JG's autobiographical memory was exceptionally poor (Table 1). On the autobiographical memory interview [53], his recall (both of semantic details and autobiographical incidents) was significantly impaired for every period of his life with the exception of the last 5 yr, for which he showed some patchy recall. For example, he could remember the date of his wedding 5 yr earlier and some details of the occasion. He was also able to recall a number of details of games played by England in the Football World Cup in June, 1998.

To assess JG's ability to *recognise* autobiographical material, three multiple choice tests were created from information and photographs supplied by his mother, sister and wife. JG gave his informed consent to participate in these experiments. In the first test (Major Life Events), there were 18 questions about his previous life (e.g., name of former fiancée, place where he had his first job, school sport in which he had won prizes), each with four possible responses. In a second, two-step test involving personally familiar faces from the past, 29 photographs of faces of friends and relatives from Australia (9 "recent") and England (20 "remote" from 7–25 yr ago) were first presented one at a time amongst the photographs of three strangers. JG had to pick the face that was familiar. In the second part of this test, he was asked to match each photograph of his friends or family members to one of four Christian names. As can be seen in Table 1, with the exception of his perfor-

Table 1
Autobiographical retrograde memory tests: initial and 12-month follow-up scores

Measure	Initial	Follow-up
<i>Standardised measure</i>		
Autobiographical memory interview		
Personal semantic information		
Childhood	2.5/21 ^a	0/21 ^a
Early adult	7.5/21 ^a	11.5/21 ^a
Recent	9/21 ^a	21/21
Total	19/63 ^a	32.5/63 ^a
Autobiographical incidents		
Childhood	0/9 ^a	0/9 ^a
Early adult	3/9 ^a	0/9 ^a
Recent	6/9	6/9
Total	9/27 ^a	6/27 ^a
<i>Multiple-choice autobiographical memory tests</i>		
Major life events	3/18 ^b	5/18 ^b
Recognition of friends and relatives		
Choosing familiar faces		
Recent	9/9	9/9
Remote	5/20 ^b	8/20
Matching name to face		
Recent	9/9	9/9
Remote	4/20 ^b	8/20

^a Denotes impaired performance >2 SD from the published mean for normal control subjects.

^b Denotes performance ≤ chance.

mance on recently known faces, he was unable to recognise the correct answers on these multiple-choice tests.

JG's retrograde memory for some aspects of non-autobiographical information was also profoundly impaired. During his hospital admission, JG could not recognise ten famous people (e.g., Margaret Thatcher) either from their names or their pictures. Three months following his admission, JG's knowledge of famous people and world events was tested in more detail using new tests of famous people and famous events designed to be appropriate to his cultural background and age. For the Famous People test, there were three parts, one involving 30 famous faces, one involving 60 famous names and one in which the original 30 famous faces were re-presented with choices of famous names. For the most part, the famous people were alive and very much a part of current popular culture (e.g., Bill Clinton, Nicole Kidman), but some were well-known figures from the past (e.g., Adolph Hitler, Albert Einstein). On the Famous Events test, there were 32 items (e.g., What happened at Lockerbie, Scotland?) pertaining to events from the 1970s, 1980s and 1990s. For each of these tests, the correct answer was presented amongst three distractors and a forced choice procedure was used.

JG's scores on these new experimental measures were compared with those of three men with no known

neurological disorders, and from whom written consent was obtained. The study was approved by the Central Sydney Area Health Service Ethics Committee. These subjects were matched to JG for their country of origin (Great Britain), years of living in Australia (range = 2–7 yr), age (range = 29–34 yr) and estimated Full Scale IQ from the National Adult Reading Test [69] (range = 94–102). Results are presented in Fig. 2. On all of these measures, JG performed at near-chance levels. For famous people, he showed true recognition (i.e., choose the face, identify the profession and match the correct name) for only 4/30 and all four of these were people who had received ongoing media attention in the three months between the time of his retrograde memory loss and the time of testing. There was no difference between his ability to recognise the names or faces of people from before his life time and those of people who were famous during his life. In light of the patchy recall he demonstrated for recent autobiographical events, it is interesting to note that on the famous world events test, JG showed no sign of spared memory for events from any period in his life.

Other aspects of JG's semantic knowledge were intact. He performed normally on the Pyramids and palm trees test [43], Boston naming test [46], and Semantic category (Animal) fluency [70], as can be seen in Table

2. Similarly, his performance on a range of anterograde memory tests, including measures of both learning and delayed recall for visual as well as verbal material fell within two standard deviations of the normal mean for his age (Table 2).

As can be seen in Table 2, JG's attention, speed of processing, and problem solving were intact. Performance on the Wisconsin card sorting test [8,33], the Trail Making Test [2] and verbal fluency (Controlled oral word association test [85]) also fell within normal limits; thus, there was no evidence of executive dysfunction. In addition, JG performed normally on tests of visual imagery, including measures that asked him to make judgements concerning the shapes of letters [17], the shapes and sizes of objects [25,54] or the length of different animals' tails (Martha Farah, personal communication). He showed no problems with face perception in that he could easily match pictures of faces when a target was presented amongst distractors on the facial recognition test [6,7].

4.2. Follow-up assessment

At the time of writing, 18 months after his hospital admission, JG continued to display normal memory for day-to-day events, but severe problems with retrograde memory. He reported that over the intervening months, he had returned to previously frequented sites (e.g., a golf course on which he had played several times, old work sites) and found them unrecognisable. He had to re-learn the routes to previously familiar places. When tested at 12 months follow-up, his neuropsychological profile on standardised testing remained remarkably stable (second column of Table 2), with some improvement on word fluency.

With regard to autobiographical material, at 12 months follow-up, JG's recall of personal events and semantic details from childhood and young adulthood had not changed significantly on the Autobiographical Memory Interview (second column of Table 1). Only for the most recent period of his life did his scores fall within normal limits on this test, which was to be expected as he could draw on material he had experienced or re-learned in the past year. On multiple choice testing, he remained largely unable to recognise personally relevant details of his life or familiar faces from the more distant past.

JG's recognition of famous people improved somewhat by the second assessment, which was not surprising given his good anterograde memory and the fact that a number of the faces were very much a part of popular culture over the intervening year. For several of the faces that he was now able to identify, he could say where he had learned the information over the past year. In spite of this improvement, only his ability to pick out which face was famous (77% correct) im-

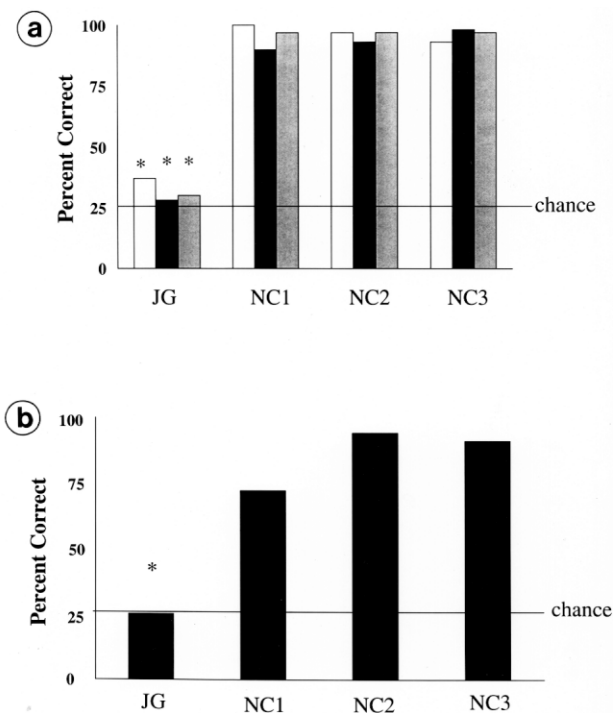


Fig. 2. Recognition memory tests of popular world knowledge. (A) Famous people tests (White bar: choosing a famous face, Black bar: choosing a famous name, Grey bar: matching a famous name to a famous face). (B) Famous events test (from past 30 yr). Asterisks indicate the tasks on which JG's performance fell more than two standard deviations from the mean obtained from the three normal control (NC) subjects.

Table 2
Neuropsychological test results

Measure	Initial	F-up ^a	Mean (SD)	Measure	Initial	F-up	Mean (SD)
<i>Semantic knowledge</i>				<i>Attention/speed of processing</i>			
Pyramids and palm trees	50	N/A	51 (1)	WMS-R digit span	20	20	16 (3)
Boston naming test	53	N/A	56 (4)	WMS-R mental control	6	6	5 (1)
Animal fluency	14	22	20 (4)	Trail making test – A	30 s	N/A	32 (13)
<i>Anterograde memory</i>				<i>General intellectual function</i>			
WMS-R				WAIS-R (Age scaled score)			
Logical memory I (Immed)	27	26	26 (8)	Similarities	8	N/A	10 (3)
Logical memory II (Delay)	22	23	22 (9)	Arithmetic	N/A	12	10 (3)
Paired assoc learning	18	18	21 (3)	Vocabulary	N/A	9	10 (3)
Verbal pairs II (Delay)	8	8	8 (1)	Picture completion	9	N/A	10 (3)
Visual reprod I (Immed)	39	N/A	33 (5)	National Adult Reading Test			
Visual reprod II (Delay)	39	N/A	30 (7)	Estimated FS IQ	102	N/A	100 (15)
Rey complex figure				<i>Executive function</i>			
Copy	35	33	33 (6)	Trail making test – B	60 s	N/A	69 (46)
Delayed recall	15	15	20 (7)	Verbal fluency (CFL)	29	34	37 (10)
Rey auditory verbal learning test				Wisconsin card sorting test			
Total trials 1–5	35	33	46 (11)		6 Cat ^b	N/A	max = 6
Recall list B	5	4	5 (2)	<i>Visual imagery/perception</i>			
Recall list A	6	6	10 (2)	Letter shapes	26	N/A	max = 26
Delayed recall list A	6	6	10 (2)	Eddy and Glass questions			
Recognition list A				Visual imagery	17	N/A	max = 18
Hits list A	13	14	14 (2)	Non-visual imagery	17	N/A	max = 17
False positives	2	3		Taller/Wider test	18	N/A	max = 20
Prospective memory				Animal tails			
	N/A	2	Max = 2	Benton Facial Recognition	20	N/A	max = 20
					N/A	45	41 (2)

(N/A = not assessed)

^a F-up = 12 month follow-up scores.

^b Cat = Categories.

proved enough to fall within two standard deviations of the mean achieved by the NC subjects. He continued to demonstrate a significant impairment on the recognition of famous names (35% correct) and the matching of names to faces (80% correct). Furthermore, no improvement was evident in his ability to recognise descriptions of famous events that occurred before the onset of his lesion (38% correct).

4.3. Procedural memory

Much of JG's long-standing procedural knowledge was intact. For example, when he left the hospital, he was able to drive and he knew how to play golf and billiards. When he returned to work four weeks later, he knew how to use his trade equipment. However, JG could not access some aspects of his prior procedural knowledge. He was uncertain as to which was his side of the bed. He had to re-learn how to use the cash register at the shop where he had worked for a few weeks prior to his admission and a coffee machine that he'd been using for about six weeks. Of interest, JG's

wife commented that he failed to recognise or appreciate music that he had previously enjoyed.

5. Discussion

JG is the first patient in whom isolated retrograde amnesia has been documented following a circumscribed thalamic lesion. His remote memory impairment extends over the course of his entire life, with some evidence of a reverse temporal gradient for autobiographical memories, such that more recent memory was slightly less impaired than more remote memory. Other aspects of JG's cognition including his attention, executive functioning, word finding ability and visual imagery were intact and thus could not be said to have contributed to his inability to access remote memories.

According to Kapur's [47] criteria, there were few aspects of JG's presentation to suggest simulated or psychogenic amnesia. The lack of an acute psychosocial stress, the persistence of the disorder and the presence of demonstrable thalamic lesions were all inconsistent

with the diagnosis of psychogenic amnesia. Furthermore, there was no apparent benefit to him from the patient role and neither extensive questioning of his family nor the passage of time has revealed circumstances that could be associated with malingering.

The MR images yielded evidence of at least two neurological events in the thalamus, with the more recent involving the medial region on the right side and the older incident(s) involving posteromedial regions bilaterally. The lesions lie in the territory of the thalamoperforate (also known as the paramedian) arteries. JG's wife gave a history of a short period of similar mild mood changes, somnolence, and memory problems occurring 2 yr prior to the present event. In light of the radiological findings, we believe that those symptoms were probably associated with an earlier episode of damage to the thalamus. It is important to note that the onset of JG's dense and persistent retrograde amnesia occurred only after the second episode, which involved extension of the lesion into more anterodorsal thalamic regions on the right, including the mammillothalamic tract, internal medullary lamina and anterodorsal part of the dorsomedial nucleus.

The anteromesial portion of the thalamus has rich projections to the frontal and temporal lobes and extensive hypometabolism has been found in these cortical areas as a consequence of a mediadorsal thalamic lesion [76]. A number of investigators [3,45,61,67,83,99] have proposed that these neocortical regions are crucial to remote memory retrieval. Thus, one might argue that JG's memory deficit is the result not of thalamic dysfunction per se, but of diminished functioning in these related cortical areas. This interpretation is difficult to sustain in view of JG's normal performance on neuropsychological measures sensitive to frontal and temporal lobe dysfunction.

A few previous patients have been reported with an extensive and persistent inability to access remote memories (along with anterograde amnesia) following bilateral thalamic infarction [42,71,90,97]. In addition, a patient described by Peru and Fabbro [77] initially showed both a retrograde and anterograde memory impairment after bilateral, anteromedial, thalamic venous infarction. Interestingly, their patient's retrograde memory impairment resolved in conjunction with shrinkage of the right-sided ischaemic region. Considering the overlap in site of lesion in these cases and in JG, we conclude that the thalamic regions most likely to be important to retrograde memory include the right mediadorsal nucleus, right mammillothalamic tract, postero-medial region of the left mediadorsal nucleus and internal medullary laminae bilaterally.

The lesion locus in JG differs from that of patients with isolated anterograde amnesia following thalamic damage [50,60,65,75,84,97]. In the latter cases, the common area of lesion involves the left mammillothalamic

tract and, in all but one [60], the left mediadorsal nucleus. The importance of the mammillo-thalamic tract in anterograde memory was emphasised in a recent review of neuropsychological deficits caused by thalamic infarction [95]. JG has no anterograde memory deficit and, in his case, there is relative sparing of the left mediadorsal nucleus and complete sparing of the left mammillothalamic tract.

JG was able to remember some details about the last few years of his life. In contrast, his more remote memories were completely lost to him. It has been postulated that transition from a predominantly hippocampus-dependent to a neocortex-dependent mnemonic representation takes years [79,86]. JG's pattern of memory loss in conjunction with the absence of any temporal lobe abnormalities indicates that he has some continued access to memories from the past 5 yr (i.e., according to this model, those presumably still being processed in the hippocampal network), but has lost access to more remote memories (i.e., those that have presumably been stored in the neocortex). Thus, his case provides support both for the view that the thalamus plays a key role in providing access to neocortically stored memories [9,39,61] and, indirectly, for a time-limited contribution of the hippocampus to memory consolidation (cf. [68,86]).

The pattern of spared versus inaccessible memory in JG adds to the growing body of evidence that the division of declarative memory into just two categories—episodic and semantic [13,87,93] is inadequate. JG was unable to remember famous people by their faces or names but displayed a good ability to access other aspects of semantic knowledge (e.g., names of objects, exemplars of categories, conceptual relationships between objects). Dissociation in the ability to recall different types of world knowledge has been noted previously [26,28,34,37,40,42,51]. Findings from these cases, and now also from JG, indicate that knowledge pertaining to people, events, and possibly to other types of unique material (e.g., famous buildings [26,72]) differs in some critical way from other types of factual knowledge such as words and meanings. The nature of this difference has not been much explored but may have something to do with the extent to which information about the world is linked or tagged to autobiographical events or to particular points in time [10,52]. Furthermore, JG's surprisingly incomplete recall of previously learned procedural information indicates the need to study the ways in which this knowledge may be subdivided, and differentially stored or accessed. We are currently exploring these issues.

The lack of concern demonstrated by JG over his loss of past memories has been noted in other patients with retrograde amnesia caused by thalamic infarction [15,80,92]. If this attitude is prevalent in patients with isolated retrograde amnesia, it may help to explain why

the diagnosis is so rare. In JG's case, the initial CT scan was reported as normal and within a few weeks of his hospitalization, he had returned to work and to some of his previous sporting interests. His wife said he had no significant problems in carrying out his activities of daily living. Had he had not complained of loss of memory for his past life and had MR scanning not been conducted, the remarkable features of his case could easily have been missed. It may also be important that much of his past life had occurred in a different physical context involving different people than those with whom he was presently familiar. Because of the relative preservation of JG's recent memory and his ability to recognise those with whom he had had recent contact, this pattern of retrograde amnesia might have been less apparent in someone who had remained in the same place all his life.

Overall, the findings from JG provide unique evidence that the right mesiodorsal region of the thalamus plays a crucial role in the ability to access remote memories, including those pertaining to autobiographical semantic details, autobiographical incidents and to some aspects of world knowledge. These findings are consistent with the proposals put forward by Markowitsch and colleagues [29,61] that the right hemisphere has a special role in autobiographical memory. We hypothesize that the right mediodorsal nucleus, right mammillothalamic tract and right internal medullary lamina (and possibly parts of the left mediodorsal nucleus and left internal medullary lamina) comprise the central processing mechanism referred to by McClelland [63] and Markowitsch [61] as responsible for inducing and coordinating the recall of cortically stored memory engrams.

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