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REVIEW

Hippocampal Amnesia

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Abstract

This article reviews 147 cases of amnesia following damage including the hippocampus or fornix as reported in 179 publications. The aetiology, mnestic abilities and reference(s) are tabulated for each case. Consistent findings across cases include the association of bilateral hippocampal damage with a deficit in anterograde episodic memory combined with spared procedural and working memory. The limited nature of retrograde amnesia following lesions to the fornix is also noted. Less consistent and thus more controversial findings, include effects of lesion size or laterality, deficits in semantic memory or familiarity-based recognition and the extent of retrograde amnesia. The evidence concerning these issues is reviewed across cases.

Introduction

Amnesia is characterized by the profound loss of memory in the presence of relatively preserved cognitive abilities. Selective damage to a number of brain regions has been associated with amnesia, including a circuit comprising the hippocampus, the diencephalon and the fibres connecting them (Delay and Brion, 1969; Aggleton and Brown, 1999). This short review focuses on cases in the literature where amnesia occurs in the presence of hippocampal damage in particular.

Increasingly sensitive neuroimaging techniques have recently enabled a number of amnesic cases with apparently selective hippocampal pathology to be identified. With the study of hippocampal amnesics extending back over 100 years, it is interesting to know how these selective cases compare with other, often more famous, cases. In addition, because many of the latter have been extensively studied in multiple papers it can be difficult to determine what is known about each case and how they compare with one another. While not completely exhaustive, our review includes the aetiologies and memory abilities (where possible) of all the published cases of patients described as amnesic following damage including the hippocampus or fornix (147 cases in 179 publications). We briefly discuss the consistent findings across cases, as well as controversial issues awaiting resolution.

Types of lesion and aetiology

To aid the identification and comparison of individual amnesic patients, or groups of patients, this review is accompanied by seven tables, one for each category of lesion. The tables are ordered in terms of the specificity of the damage to the hippocampus as reported by the authors, starting with the most selective lesions in Table 1 (see also Fig. 1). We have chosen to use the anatomical terminology of Amaral (1999). In this definition, the *hippocampus* includes the hippocampus proper (fields CA1–CA4) and the dentate gyrus; the *hippocampal formation* includes the hippocampus, entorhinal cortex and the subicular complex; the *medial temporal lobe* includes the hippocampal formation, the perirhinal cortex (anterior parahippocampal gyrus) and the parahippocampal cortex (posterior parahippocampal gyrus). When reading the tables it is important to bear in mind that, although we have segregated the cases into groups with similar lesions, the variation in lesion size is continuous. Lesions in each case may completely or partially disrupt one or many structures in a network of brain regions.

Table 1 includes amnesic cases reported as having lesions that, within the temporal lobes, are selective to the hippocampus. This does not rule out additional damage outside of the temporal lobes as can be seen in Table 1. The other tables include amnesic cases with hippocampal lesions and addi-

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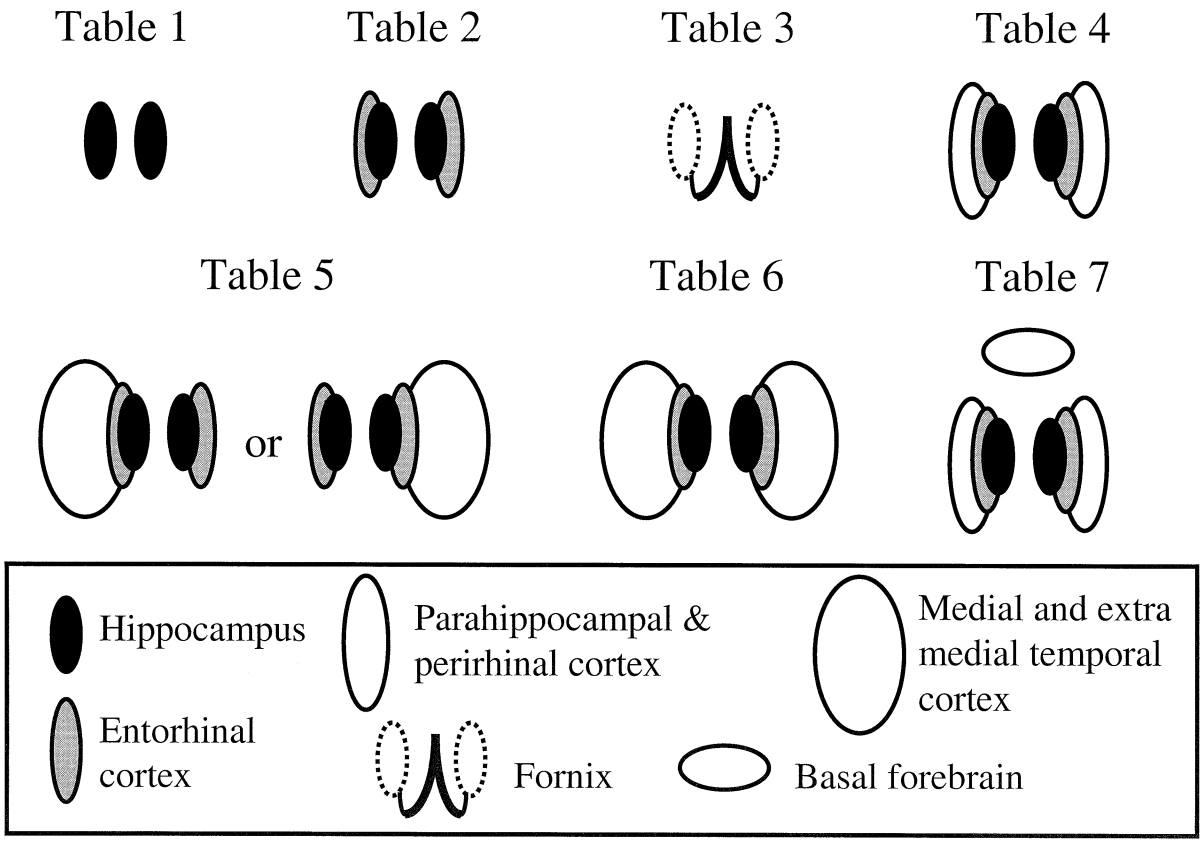

Fig. 1. Lesion locations for each of the seven tables.

tional temporal lobe damage, or lesions to the fornix (a large fibre bundle, second only to the corpus callosum, connecting the hippocampus to the subcortical brain). For inclusion in the tables a lesion to the hippocampus or the fornix must be demonstrated by autopsy, neuroimaging or surgical description. Damage to the amygdala, whilst noted where reported, was not a consideration in lesion categorization, given its acknowledged auxiliary role in memory (e.g. Aggleton, 2000).

The large number of amnesic cases described with damage including the hippocampus (Tables 1–7) reflects the susceptibility of the hippocampus to a range of pathological factors. Hippocampal cell damage can occur in a number of ways: loss of oxygen to the cells (anoxia, ischaemia and stroke cases), physical damage from surgery or head injury, viral attack (meningitis, encephalitis), and autoimmune responses (e.g. systemic lupus erythematosus). Examples of classic cases with particular aetiologies are the encephalic patient SS (Table 7), the ischaemic patient RB (Table 1), the bilateral temporal lobectomy patient HM (Table 6), the stroke patient RS (Table 5), the meningitic patient NM (Table 4), the closed head injury patient KC (Table 6) and the case described by Schnider *et al.* (1995) with systemic lupus erythematosus (Table 2). Of these aetiologies, encephalitis, ischaemia/anoxia and surgery are the most common. Surgery and encephalitis account for many of the cases with additional temporal lobe lesions (Tables 4–6), whereas ischaemia/anoxia accounts for more of the selective cases, although there has been some debate as to the possibility of extra-hippocampal 'hidden damage' following ischaemia (Bachevalier and Meunier, 1996; Squire and Zola, 1996).

Effects of lesion laterality and bilaterality

The question of whether bilateral lesions of the hippocampus are necessary for amnesia has been controversial. Patients undergoing temporal lobectomy were only found to become amnesic when a bilateral operation was performed (Scoville and Milner, 1957). However, a number of patients undergoing unilateral operations were also found to have amnesia (e.g. PB, Table 5). When these patients were examined at autopsy, many of them were found to have contralateral hippocampal damage, suggesting that amnesia was indeed caused by a bilateral lesion. However, when the lesion is caused by a stroke, amnesia can result from unilateral lesions involving the hippocampus (as determined from computed tomography or magnetic resonance imaging; Benson *et al.*, 1974; Ott and Saver, 1993). One possible explanation is that stroke causes additional hidden contralateral damage. It is also the case that in many unilateral stroke patients, and patients with asymmetric hippocampal damage resulting in amnesia, the damage is left lateralized. This may reflect a bias due to a preponderance of memory tests with a strong verbal component. However, there is also a greater tendency for left

hemispheric patients to suffer combined non-verbal and verbal problems than right hemispheric patients (Ott and Saver, 1993). Consistent with a dominant role for the left hippocampus in memory for personally experienced events ('episodic memory', see below), the majority of amnesic patients with unilateral temporal lobectomies or cases with asymmetric bilateral temporal lobe lesions in Table 4 have damage lateralized to the left. Functional neuroimaging in healthy control subjects shows a similar left lateralized hippocampal involvement in episodic or autobiographical memory involving verbal (Maguire *et al.*, 2000, 2001) and non-verbal (Burgess *et al.*, 2001; see also Spiers *et al.*, 2001b) material. However, the issue of laterality is not entirely clear, as Kopelman and Stanhope (1998) found a small number of patients with predominantly right-sided lesions to be impaired on episodic memory tasks.

The assumption that bilateral hippocampal lesions necessarily cause hippocampal amnesia has also been questioned. Two patients have been reported with bilateral hippocampal lesions who did not have the severe amnesia reported in the other cases [the case described by Fujii *et al.* (1999), Table 2, and patient KHJ, Table 6]. However, patient KHJ had grossly impaired performance on a delayed verbal recall test following an operation which removed extra left medial temporal lobe tissue, and the case reported by Fujii *et al.* (1999) was reported to have a severe retrograde episodic memory loss for at least 10 years. It is possible that in each of these cases insufficient bilateral hippocampal damage occurred to produce the profound amnesia seen in the other cases. Interestingly, Isaacs *et al.* (2000) found episodic memory to be somewhat impaired in children born preterm with significantly reduced hippocampal volumes (by approximately 10%), but not nearly as severely reduced as in the developmental amnesics reported with bilateral hippocampal reductions greater than 25% (Vargha-Khadem *et al.,* 1997, 2001).

Characterizing the deficit

Memory loss can occur for information encountered after the precipitating lesion, this is known as anterograde amnesia (see 'Anterograde performance' in Tables 1–7)—for information acquired before the precipitating lesion, this is known as retrograde amnesia (see 'Retrograde performance' in Tables 1–7). We consider anterograde amnesia first. A standard measure for assessing the extent of anterograde memory loss is the difference between the patient's intelligence and memory quotients (IQ and MQ, respectively; Scoville and Milner, 1957). These scores are given in the tables where available. Traditionally a difference of 20 points was used as a criterion for considering a case amnesic (Butters and Cermak, 1980). However, due to associated problems (e.g. patients with high IQ and normal MQ can be classed as amnesic), many patients are described as amnesic even though the difference is less than 20 points.

The episodic memory deficit and spared mnestic abilities

There is some debate regarding the nature of the memory loss that characterizes the amnesic syndrome. In the following we characterize 'hippocampal amnesia' as those deficits common to all the cases reported and then discuss the deficits that vary across cases. Amnesics are often first identified by their inability to remember personally experienced events. This type of memory is referred to as episodic memory and has been characterized as the ability to remember consciously the events and their unique spatiotemporal context (Tulving, 1972). Kinsbourne and Wood (1975) were the first to describe amnesia as a selective loss of episodic memory, and it is acknowledged that its impairment 'forms the basis of the classic amnesic syndrome' (Baddeley, 1995). Every case in Tables 1–7 shows some degree of impairment on tests of episodic memory (see 'Anterograde performance' in Tables 1–7).

While the loss of episodic memory is a constant feature of hippocampal amnesia, there are also a number of consistently spared mnestic abilities. None of the cases was reported to have impaired short-term memory (typically tested using digit span—the immediate recall of verbally presented digits) or to be impaired on tasks which involve learning skills or habits, priming, simple classical conditioning and simple category learning (for examples see 'Anterograde performance' in Tables 1–7). These latter spared abilities have been collectively described as non-declarative memory (Squire, 1992), implicit memory (Graf and Schacter, 1985) or procedural memory (Cohen and Eichenbaum, 1993), and there is good agreement that they do not depend on the hippocampus.

Beyond this basic distinction, a number of controversies remain. These include the effects of lesion size, how best to characterize the type of memory that is impaired and the extent of the anterograde and retrograde memory impairments. We consider these various issues below.

Semantic memory

One of the most contentious issues remains the involvement of the hippocampus in semantic memory. Semantic memory is defined as memory for factual knowledge, such as: Paris is the capital of France. Squire and others have argued that hippocampal amnesia includes a loss of both episodic and semantic memory, with the deficits present for both anterograde and retrograde semantic memory (e.g. Squire, 1992). Many cases do show anterograde semantic memory deficits. Impaired new semantic learning has been demonstrated in HM (Table 6), by his impaired learning of the definitions of words that had entered the general vocabulary after the onset of his amnesia (Gabrieli *et al.*, 1988). A similar pattern of impaired new semantic learning is observed in selective hippocampal patients GD (Table 1; Shimamura and Squire, 1987) and VC (Table 1, Cipolotti *et al.,* 2001). However, a number of early-onset hypoxic patients have been reported

by Vargha-Khadem *et al.* (1997) and Gadian *et al.* (2000) who show relatively preserved acquisition of semantic memory in the context of severely impaired episodic memory (see Table 1). It has been argued in the case of early-onset hypoxic patients that a functional re-organization of the brain may have occurred during development in which extra-hippocampal regions take on the role of the hippocampus. However, the late-onset selective hippocampal case PS (Table 1) also shows evidence of post-morbid semantic learning with vocabulary and famous faces (Verfaellie *et al.,* 2000). Even patients with more extensive lesions have been found to have normal post-morbid vocabulary and facts (e.g. case RS(ii), Table 5; Kitchener *et al.,* 1998). The involvement of the hippocampus in retrograde semantic memory loss is similarly controversial (see below). Patients who show semantic memory loss in the presence of normal episodic memory provide further evidence against a simple declarative account (Kapur *et al.,* 1994). Thus, the hippocampal role in semantic memory remains unclear and the testing of more patients with selective hippocampal lesions on standardized tests is required.

Familiarity-based recognition and lesion size

Another controversial issue is whether the hippocampus is necessary for recognition tests that can be solved by familiarity judgements. It has been suggested that the hippocampus, fornix and anterior thalamus are required for recollection of the context of events but not for familiarity-based item recognition, and that this latter function is served by the perirhinal cortex and the mediodorsal nucleus of the thalamus (Aggleton and Brown, 1999). By contrast, the declarative theory (e.g. Reed and Squire, 1997) states that recognition memory depends on the hippocampus and that tests of recognition are critical tests of hippocampal amnesia (even where the damage is selective). Similar to the issue of semantic memory, findings are not consistent between cases. Patients RB, GD, VC and PS (Table 1) all show deficits on tests of recognition, such as Warrington's Recognition Memory Test (Warrington, 1984). However, the developmental cases reported by Vargha-Khadem *et al.* (1997) and Gadian *et al.* (2000) all show spared recognition when the recognition test can be solved by a sense of familiarity. Spared recognition is not only found in developmental cases, but also in late-onset cases such as YR (Table 1) and DF (Table 2). A number of patients with bilateral fornix damage have also been reported with normal recognition (McMackin *et al.,* 1995; Table 3). In an alternative formulation to the declarative theory, Baddeley *et al.* (2001) suggest a link between semantic and recognition memory such that information may enter into the semantic store via repeated repetitions of stimuli which are held in a recognition system that is independent of the (hippocampal) episodic system. Although recent evidence from patient YR suggests this does not generalize to late-onset patients (Holdstock *et al*., 2001b). One possibility is that patients with impaired recognition memory have additional damage compared with those that do not. This hidden damage might be extra-hippocampal (e.g. Bachevalier and Meunier, 1996) or might relate to differences in the functional integrity of the residual hippocampal tissue itself (e.g. Maguire *et al.,* 2001; Table 1). Indeed, of the eight cases (WI, JL, LJ, PH, RM, HW, Table 1 and WH, LM, Table 2) identified as having hippocampal damage using the MRI method described in Squire *et al*. (1990), two cases (WH and LM) have had autopsies, and both also had entorhinal damage (Rempel-Clower *et al*., 1996).

Based on evidence from patients with selective hippocampal lesions (RB and GD, Table 1), patients with hippocampal formation lesions (e.g. WH and LM, Table 2), and patients with more extensive temporal lobe lesions (EP and GT, Table 6), Squire and colleagues have suggested that the larger the lesion the more profound the amnesia (e.g. Rempel-Clower *et al.,* 1996). While this assertion appears to be true for these cases, it is inconsistent with other cases. Selective cases YK (Table 1, IQ = 94) and BE (Table 1, IQ = 128) have MQs of 52 and 59, respectively, while the less selective case JT (Table 6, IQ = 126), who has a large bilateral medial temporal lobe lesion, has an above-average MQ score of 120. Such observations indicate that even selective lesions can cause a severe amnesia and that the location and completeness of a medial temporal lobe lesion are more important than its overall size.

Retrograde amnesia: extent and temporal gradients

In addition to the severe anterograde memory loss described above, a significant retrograde amnesia has been observed in a large number of cases of hippocampal amnesia (see 'Retrograde performance' in Tables 1–7). However, the duration of the retrograde amnesia is extremely variable, with some cases showing virtually no loss (e.g. RB, Table 1; Zola-Morgan *et al.,* 1986) and others reported as showing a complete inability to remember any information from any period of their lives (e.g. LD, Table 5; O'Connor *et al.,* 1992). Difficulties in determining the effect of hippocampal damage on retrograde amnesia arise from a number of sources. For many reported cases there was no attempt to characterize a loss of memories prior to the lesion (these studies are indicated by 'Not described' in the 'Retrograde amnesia' column of the tables). For many of the other cases there was no formal assessment with a standardized test. Even when standardized tests are applied there can be problems with validation of the results. While some tests match for the salience of the stimuli at all time periods (e.g. Sanders and Warrington, 1971), others do not (e.g. Reed and Squire, 1998). Low or varying motivation in some cases (e.g. GD, Table 1) can make the interpretation of performance difficult. For more discussion of the difficulties of testing retrograde amnesia see Warrington (1996) and Kapur *et al.* (1999).

A feature of retrograde amnesia that has attracted much attention is the existence of a temporal gradient (Ribbot,

1882) such that memories formed early in life are purported to be preserved relative to recent memories (e.g. HM, Table 6). To account for this it has been suggested that the hippocampus has only a time-limited role in memory, with memories becoming consolidated in neocortex after a certain time (Marr, 1971; Squire, 1992). It has been postulated by Squire and colleagues (Squire, 1987, 1992; Squire and Alvarez, 1995) that both semantic and episodic (i.e. declarative) memory are consolidated from hippocampus to neocortex, so that temporally extensive retrograde amnesia only occurs following temporal lobe lesions which extend beyond the hippocampus, with larger lesions producing more extensive retrograde amnesia. Evidence for this has come from the study of patients such as RB (Zola-Morgan *et al.,* 1986), GD, LM and WH (Rempel-Clower *et al.,* 1996). While findings with some selective hippocampal patients such as BE and LC (Table 1; Kapur and Brooks, 1999) support this hypothesis, findings from others do not. Two cases which provide evidence to the contrary are the case reported by Victor *et al.* (1961; Table 6) and patient VC (Cipolotti *et al.,* 2001; Table 1). The patient described by Victor *et al.* (1961) was found to have extensive temporal lobe lesions, but was described as having a well-defined retrograde amnesia for only 2 years prior to the damage. Selective hippocampal patient VC (Table 1) shows a virtually flat loss across all time intervals with extensive testing. The contrast between VC and patients RB and GD is puzzling. All three appear to have similar pathology and yet VC has an extensive retrograde amnesia, while the other two have a retrograde amnesia limited to 1–2 years. It is possible that subtle differences in pathology between the cases may play a decisive role: the hippocampal lesion is confined to CA1 region in GD and RB but is not in VC, but differences in the matching of the salience of cues over different time periods may also be a factor (Warrington, 1996).

Fractionating retrograde amnesia: alternatives to a simple consolidation hypothesis

As with anterograde amnesia, retrograde amnesia can be divided along similar lines into episodic (or autobiographical) memory and semantic memory. Semantic retrograde amnesia can be further subdivided into knowledge about one's personal past (autobiographical semantics) and general world knowledge (such as public events and famous faces). For a more detailed discussion see Kapur (1999). As with anterograde memory, inspection of Tables 1–7 shows episodic memory to be more consistently impaired in retrograde amnesia than semantic memory. There is often some semantic retrograde memory loss (for autobiographical semantic information, famous faces), but this is usually less severe than the autobiographical episodic retrograde amnesia (e.g. DRB, Table 7). Focusing on this dissociation, an alternative model of consolidation has been proposed in which semantic memories are consolidated to neocortex but episodic memories remain dependent on the hippocampal region for life (Nadel and Moscovitch, 1997; Fujii *et al.,* 2000). An interesting feature of the tables presented here is that retrograde amnesia appears to be limited in the few cases with fornix lesions that have been tested (Table 3). This is consistent with the suggestion that the afferent supply of acetylcholine to the hippocampus via the fornix is important for learning (e.g. Hasselmo, 1999). By contrast, efferents from the hippocampus to the entorhinal cortex and medial temporal lobe may have a greater role in the recollection of remote memories.

Conclusion

In summary, there is a great deal of variation in the memory impairments of hippocampal amnesics. One consistent feature is a severe loss of post- and often pre-morbid episodic memories in virtually all patients with bilateral hippocampal damage. Even apparently selective hippocampal patients can show a dramatic loss, such that the patient cannot remember any personal experience from before the lesion or any event they have encountered thereafter (e.g. VC, Table 1). The preservation of short-term memory and a number of mnemonic abilities which have been called procedural, implicit or non-declarative are also consistent features of hippocampal amnesia. Semantic memory and familiarity-based recognition may or may not be spared in hippocampal amnesics. The extent and types of retrograde amnesias are also extremely variable, with episodic memories being most affected. Future research with increasingly sophisticated neuropathological and neuroimaging techniques, combined with comprehensive neuropsychological testing will be required to identify the crucial factors and locations involved in these different patterns of impairment.

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Table 1. Case studies of hippocampal amnesics — where temporal lobe damage is restricted to the hippocampus (H) bilaterally[a]

Authors, published year	Cases	Aetiology (age at onset) — lesion (localization)	IQ	MQ	Retrograde performance (test if given)	Anterograde performance
Muramoto *et al.*, 1979[b]	1 case	Anaesthesia overdose (59) – BL H reduction by one third, slight dilation of third and fourth ventricles, EEG showed no abnormalities (CT, Pneumoencephalograph).	111	-	Stated as intact but unmeasured.	Anecdotal description; 'He could not recall what happened in the preceding few hours or few minutes'. Impaired recall of words on the Selective Reminding Test (Buschke, 1973). Had good insight into his condition, no confabulation. Normal digit span and mirror drawing, retention of mirror drawing at 1 month.
Cummings *et al.*, 1984	1 case	Anoxia - cardiopulmonary arrest, (53) – BL pyramidal cell loss in CA1–4; DG, subicular complex and MTL intact. Additional infarct in R parietal Cx and small infarcts in frontoparietal Cx and L thalamus were noted (**autopsy**).	-	-	Could not remember the current president. Reported his early AE and memory for political events as intact but AE for other events impaired.	Anecdotal description: He failed to remember a list of 3 words after 3 min. Normal intelligence, digit-span, perception and language. Consistently confabulated when asked about his activities. He also had a tendency to extinguish left-sided stimuli after bilateral stimulation.
Duyckaerts *et al.*, 1985	1 case	Hodgkin's disease, 2 generalized seizures (36) – BL H and Amyg. damage (**autopsy**).	113	74	Graded AE and AS, could comment on political events occurring 3 years prior to onset.	3/10 words remembered after short delay. Recognition memory was affected by an interference task. Normal language, digit span and problem solving abilities.
Zola-Morgan *et al.*, 1986	**RB**	Ischaemia (54) – total CA1 loss, minor damage to L globus pallidus, R postcentral gyrus, L internal capsule (**autopsy**).	111	91	Intact AE (**Crovitz**) and performance on the PE, FF tests. A test with television programmes showed a possible impairment for 1–2 years.	Impaired diagram recall (3/36). Very few items recalled on word lists, paired associates or story recall. Impaired word recognition.
Squire *et al.*, 1987 Squire and Shimamura, 1986 > Shimamura and Squire, 1987 > Squire *et al.*, 1988 > Janowsky *et al.*, 1989 > Shimamura and Squire, 1989 > MacKinnon and Squire, 1989 Squire and Frambach, 1990 > Shimamura *et al.*, 1990 (*1*) > Shimamura and Squire, 1991 > Cave and Squire, 1991(*2*) > Haist *et al.*, 1992 (*3*) > Knowlton *et al.*, 1992 (*4*) > Rempel-Clower *et al.*, 1996 > Reed and Squire, 1997 (*5*) >	**GD**	Ischaemia (43) – BL CA1 damage, with minor damage to L Amyg., L med. mammillary nucleus, L mediodorsal thalamic nucleus, R globus pallidus and the cerebellar vermis (**autopsy**).	92	85	Intact AE (**Crovitz**), some impaired public knowledge but hard to judge due to low motivation. Better recollection for childhood events.	Impaired diagram recall (7/36) and performance on episodic memory tests. Impaired yes/no recognition for words. Impaired new semantic learning and source memory. Impaired forced choice recognition of objects. Impaired forced choice recognition of sentences. Normal adaptation level effect. RMTW,F = 25,28. Normal skill learning, impaired 5-alternative forced choice recognition. Impaired yes/no recognition for words. Impaired 8-alternative forced choice for trivia facts. Impaired spatial location memory and 8-alternative forced choice for objects. Spared implicit memory for spatial sequences, impaired word pair recognition. Normal learning of artificial grammar, but impaired recognition of exemplars. Normal on tests sensitive to frontal and parietal lobe function. Impaired matching to sample task with a 5 min. filled delay.
Press *et al.*, 1989[c] Squire *et al.*, 1990 (*6*) > Cave and Squire, 1992a (*7*) > Cave and Squire, 1992b (*8*) > Polich and Squire, 1993 (*9*) > Musen and Squire, 1993 (*10*) >	**JL**	Suspected ischaemia (**65**) – BL H, identified as having Alzheimer's disease (MRI).	116	74	20 years impaired recall of PE, Spared recognition of PE.	Impaired diagram recall (1/36), paired associates, RMTW,F = 31,20. Impaired paired associates and word recall/recognition. Normal naming priming (up to 7 days) but impaired recognition for pictures. Verbal and non-verbal short-term memory impaired after a filled 24 s delay. Visual and auditory information processing normal, tested by ERP. Normal implicit Stroop task learning of colour-word associations

Kritchevsky and Squire, 1993 (*11*) > McKee and Squire, 1993 (*12*) > Knowlton and Squire, 1995 (*13*) > Knowlton *et al.*, 1996 (*14*) > See also refs 2,3,5						Impaired diagram recall (1/36). No reduction in the time spent examining previously seen pictures Impaired memory for both 'Remember' judgements and 'Know' judgements. Normal habit learning.
Squire and Frambach, 1990[c] Musen and Squire 1991 (*15*) > Squire and McKee, 1993 (*16*) > Knowlton and Squire, 1993 (*17*) > Knowlton *et al.*, 1994 (*18*) > Hamann and Squire, 1995 > Knowlton and Squire 1996 (*19*) > Hamann and Squire, 1996 (*20*) > Reber *et al.*, 1996 (21) Hamann and Squire, 1997 > Reed and Squire, 1998 > Clark and Squire, 1998 (22) > Buffalo *et al.*, 1998 > Reber and Squire, 1998 > Manns and Squire, 1999 (*23*) > Reed *et al.*, 1999 (*24*) > Reed and Squire, 1999 (*25*) > See also refs 1,3,4,5,7,9,10, 12,14	**LJ**	Unknown aetiology (51) – BL H (MRI).	98	69	Intact AE and AS (**AMI**). Impaired PE and FF for up to 10 years.	Impaired diagram recall (3/36), paired associates and word recall/recognition. Facilitated speed reading of non-words. Impaired subsequent recognition. Impaired yes/no recognition of names of people. Yes/no recognition of dot patterns. Normal probabilistic classification learning. Impaired semantic learning. Normal probabilistic classification, impaired ability to use it flexibly. Normal level of processing effects for recognition but not priming. Repetition of the task as used by Knowlton and Squire 1996. Spared perceptual memory but not conscious visual memory. RMTW,F = 33,29. Impaired eyeblink conditioning when awareness of the relationship is required. Less impaired abstract design recognition than patients EP and GT (Table 6). Normal implicit, but impaired explicit memory in a serial reaction time task. Visual and verbal recall and recognition deficits on the DPT. Normal classification learning but impaired recall of item features. Impaired transverse pattern learning and concurrent pair learning problems
Squire and Frambach, 1990[c] See also refs 2,7,8,10,12,14	**WI**	Possible Ischaemia (**69**) –BL H, identified as having Alzheimer's Disease (MRI).	98	60	Flat loss of PE recall, at least 20 years of impaired PE recognition.	Impaired delayed diagram recall (0/36) and performance on episodic memory tests.
Victor and Agamanolis, 1990	1 case	Anoxia, secondary to generalized seizures (**65**) – selective loss of H pyramidal cells, 50% cell loss in sup. DG, less in inf. DG and mild purkinje cell loss in the cerebellar vermis (**autopsy**).	114	96	Graded AE and AS for an undefined period.	'His greatest deficits were in learning disparate word associations and in his ability to retell short stories that had been read to him.'. Normal digit span and language.
Cave and Squire, 1991[c] Musen and Squire, 1992 > See also refs 4,5,7–10, 12–25	**PH**	Six year history of short epileptic attacks, became amnesic after a series of attacks (**65**) - BL H (MRI).	120	70	Not described.	RMTW,F = 33,41, impaired diagram recall (3/36). Normal priming of novel non-verbal material, but impaired 4 alternative forced choice recognition.
O'Connor *et al.*, 1995 Verfaellie *et al.*, 2000	**PS**	Anoxia – severe asthma attack and pneumonia (40)– selective BL H atrophy, possibly some mild cortical atrophy and ventricular enlargement (MRI).	104	90	Preserved recognition of some post-morbid FF and new vocabulary, although showed impaired recall of such information.	Impaired diagram recall (8/36) and performance on other tests of episodic memory. RMTW,F 29,33. Normal semantic learning, digit span and problem solving.

Table 1. *Continued*

Authors, published year	Cases	Aetiology (age at onset) – lesion (localization)	IQ	MQ	Retrograde performance (test if given)	Anterograde performance
Kartsounis *et al.*, **1995** Kapur *et al.*, 1999 Cipolotti *et al.*, 2001	**VC**	Ischaemia - 2 seizures (**67**) – BL H, slightly reduced L PHG (MRI). Some suggestion of possible R thalamic hypo-activation in a PET scan (Kapur *et al.*, 1999).	123	-	Impaired AE (3/27) and AS (**AMI**). Impaired FF and PE (**DoA**) for 40 years. Normal on a forced choice test of famous names and general semantics.	Impaired diagram recall (5/36), impaired post-morbid semantic learning. Impaired recall and recognition in the DPT. RMTW,F = 36,39. Normal language, perception, digit span, attention and executive performance. Examined over a 5 year period.
Hamann and Squire, 1996[c]	**RM**	Undescribed aetiology (**77** at test) – BL H (MRI).	102	56	Not described.	Normal level of processing effects for recognition but not priming. RMTW,F = 26,30.Impaired diagram recall (0/36) and performance on episodic memory tests.
Hamann and Squire, 1996[c] See also refs 16 and 18	**HW**	Undescribed aetiology (**76** at test) – BL H (MRI).	109	89	Not described.	Normal level of processing effects for recognition but not priming. RMTW,F = 23,22. Impaired diagram recall (6/36) and performance on episodic memory tests.
Vargha-Khadem *et al.*, 1997 Duzel *et al.*, 1999 > Gadian *et al.*, 2000 Baddeley *et al.*, 2001 > Maguire *et al.*, 2001 > Spiers *et al.*, 2001a >	**Jon**	Early hypoxic ischemia (**0–4**) – BL H 50% loss, see also Gadian *et al.* (2000) cases below (MRI-VBM). Activation (fMRI) in BL H during the retrieval of the few episodes he does 'remember' (Maguire *et al.*, 2001).	109*at*	93	Lesion acquired in childhood.	Impaired on diagram recall (1/36) and recall of stories and paired associates. Normal recognition but not recollective ERP measured responses. Normal language, digit and block span. semantic memory and item recognition. RMTW,F = 45,41, impaired recall but spared recognition on the DPT. Distinguishes between events he 'remembers' and those he 'knows' happened. Impaired navigation, map drawing and context-dependent episodic memorybut spared recognition of scenes and objects.
Vargha-Khadem *et al.*, 1997 Gadian *et al.*, 2000	**Beth**	Early hypoxic ischaemia (**0**) – BL H see also Gadian *et al.* (2000) cases below (MRI-VBM).	72*at*	83	Lesion acquired in childhood.	Impaired on diagram recall (3.5/36) and other tests of episodic memory. Normal language, digit and block span, semantic memory and item recognition.
Vargha-Khadem *et al.*, 1997	**Kate**	Early hypoxic ischemia (**9**) – BL H (MRI).	73*at*	66	Lesion acquired in childhood.	Impaired on diagram recall (1/36) and other tests of episodic memory. Normal, language, digit and block span.
Hirano and Noguchi, 1998[g] Hirano *et al.*, 1999	**YK**	HS Encephalitis (54) – BL H (MRI).	94	52	Impaired AE for whole life, AS impaired only for recent life (**AMI, Crovitz**). Impaired PE for 10 years.	Normal frontal functioning with no confabulation and a low normal digit span. Impaired diagram recall (0/36 after 5 min.) and performance on other tests of episodic memory. On the RAVLT he showed no learning and had impaired recall (3/15) and recognition (11/15).
Kapur and Brooks, 1999	**BE**	Encephalitis (45) – BL H (MRI).	128	59	Impaired AE for 2 years, normal on tests of AS (**AMI**). Impaired FP for 10 years.	RMTW,F = 39,42. Impaired list and design learning and delayed recall. Normal naming and problem solving.
Kapur and Brooks, 1999	**LC (i)**	HS Encephalitis (36) – BL H, small degree of L EC damage (MRI).	117	-	Impaired AE for a few years. Impaired PE and probably impaired FP for 7 years (**DoA**).	Disoriented for time, gave his age as 5 years younger. Very poor on subtests of WMS, and could not remember having been told a story after the delay. Some confabulation.

Holdstock *et al.*, 1999 Holdstock *et al.*, 2000a,b Mayes *et al.*, 2001a,b Holdstock *et al.*, 2001a,b	**YR**	Presumed ischaemia (58) – BL H atrophy, slight parietal lobe atrophy (MRI).	102	66	Not described.	Associations between different types of information impaired, but not between information of the same type. Impaired allocentric spatial memory but not egocentric spatial memory. Spared recognition on 35 tests, but impaired recall on the DPT. Impaired memory for temporal order. Impaired new semantic learning .
Gadian *et al.*, 2000	3 cases & Jon & Beth	Early hypoxic ischaemia (**0–9**) – BL H, subtle damage to BL putamen, ventral thalamus and midbrain (MRI-VBM).	85.8 *at* 83.8		Lesion acquired in childhood.	Impaired episodic memory, diagram recall (0–3.5/36). Normal language, digit and block span.

[a]Classification for the tables is based on the authors' designation of the lesion and impairments. The results listed next to a multiple case study apply to all the cases unless stated otherwise. The symbol > following a study indicates that the information on this line in the 'Anterograde performance' column is drawn from that study. Age of onset is in years (ages >60 or <18 are indicated in bold, perinatally acquired lesions = 0). The use of a recognized test of retrograde memory or of autopsy to localize the lesion are indicated in bold. Where a multiple case study is referred to more than once in the same table, an italicized number is added in parentheses to the 'Authors, published year' column of the first reference, and this number is then used for subsequent references to the study within the same table. MQ = general memory quotient, from the Wechsler Memory Scale (WMS—Wechsler, 1945, 1987). IQ, Full Scale IQ (FSIQ) or estimates of it using the National Averages Reading Test (Nelson and Wilson, 1991) or, in a small number of cases, the average of the Performance IQ and Verbal IQ.

Abbreviations: **LTL,** left temporal lobectomy; **RTL,** right temporal lobectomy; **H**, hippocampus; **HF**, hippocampal formation; **DG,** dentate gyrus; **PHG,** parahippocampal gyrus; **EC,** entorhinal cortex; **PHC,** parahippocampal cortex; **PrRC**, perirhinal cortex; **Amyg**., amygdala; **MTL**, medial temporal lobe; **TL**, temporal lobe; F, fornix; **Cx,** cortex; **BL,** bilateral; **L,** left; **R**, right; **ant.**, anterior; **med.**, medial; **sup.**, superior; **inf.**, inferior; **VBM**, voxel based morphometry; **AE**, autobiographical episodic memory; **AS**, Autobiographical semantic memory; **PE**, public event memory; **FF**, Famous Faces Test (Albert *et al.*, 1979); **AMI**, autobiographical memory interview (Kopelman *et al.*, 1989); **Crovitz**, Crovitz – Shiffman Autobiographical Memory Test (Crovitz and Shiffman, 1974); **DoA** Test, Dead or Alive Test (Kapur *et al.*, 1989); **RAVLT**, Rey Auditory Verbal Learning Test (Rey, 1964); **DPT**, The Doors and People Test (Baddeley *et al.*, 1994); ***at***, the age of the patient when IQ was tested below the range of ages for which the test is standardized which is assumed to have reduced the score by about 20 points see Vargh-Khadem *et al.* (1997); **RMTW,F,** Recognition Memory Test for Words and Faces (paired forced choice, max 50,50, Warrington, 1984); **FP**, famous people; **HS Encephalitis,** Herpes Simplex Encephalitis; **ERP,** Event Related Potential.

[b]This case had suffered anoxia from an anaesthesia overdose and as a result could not remember any new information for more than a few minutes or hours. However the imaging techniques used to measure the lesion, CT scanning and pneumoencephalography (which uses X-rays to image the brain after air has been used to displace fluid in the ventricles) are unlikely to have been able to detect any additional subtle pathology in the surrounding medial temporal cortex.

[c]This case was described as having a hippocampal formation lesion, but has been included in Table 1 because the authors reported that the entorhinal cortex was intact.

Table 2. Case studies of hippocampal amnesics – where the temporal lobe damage is restricted to the hippocampal formation (HF) bilaterally

Authors, published year	Cases	Aetiology (age at onset) – lesion (localization)	IQ	MQ	Retrograde performance (test if given)	Anterograde performance
Beatty *et al.*, 1987a,b > Shimamura and Squire, 1986 > Shimamura and Squire, 1987 > Squire *et al.*, 1988 > Press *et al.*, 1989 (*1*) Shimamura and Squire, 1989 > Benzing and Squire, 1989 > Janowsky *et al.*, 1989 (2) > Squire *et al.*, 1990 (*3*) > Squire and Frambach, 1990 (*4*) > Shimamura *et al.*, 1990 (*5*) > Musen *et al.*, 1990 > Shimamura and Squire, 1991(*6*) > Cave and Squire, 1991(*7*) > Musen and Squire 1991 > Musen and Squire, 1992 > Cave and Squire, 1992a > Cave and Squire, 1992b (*8*) > Haist *et al.*, 1992 > Squire and McKee, 1992 > Polich and Squire, 1993 > Musen and Squire, 1993 > Rempel-Clower *et al.*, 1996 (9) > Reed and Squire, 1997	**LM** (MRL)	Anoxia in epileptic state (54) – BL HF, and medial septum (**autopsy**).	109	90	Impaired AE over 25 years (**AMI**), impaired PE and FF for at least 15 years. Intact remote memory for floor plans.	Normal intelligence, impaired Rey-figure recall (6/36) and episodic memory. Impaired yes/no recognition of words. Impaired new semantic learning and source memory. Impaired forced choice recognition of objects. Normal attention, language and digit span. Normal word priming. Normal adaptation level effect. Impaired forced choice recognition of sentences. Impaired paired associates and word recall/recognition. Normal skill learning. Impaired yes/no recognition for words. Facilitated speed reading for words. Impaired recognition of story content. Impaired 8-alternative forced choice for trivia facts. Impaired spatial location memory and 8-alternative forced choice for objects. Facilitated speed reading of non-words. Impaired subsequent recognition. Normal priming of novel non-verbal material, but impaired recognition. Normal naming priming (up to 7 days) but impaired recognition for pictures. Verbal and non-verbal short-term memory impaired after a filled 24 s delay. Spared implicit memory for spatial sequences. Impaired yes/no recognition of names of people. Visual and auditory information processing normal, tested by ERP. Normal implicit Stroop task learning of colour–word associations. RMTW,F = 32,33.
Salmon *et al.*, 1988 Shimamura and Squire, 1989 > Knowlton *et al.*, 1992 > Kritchevsky and Squire, 1993 McKee and Squire, 1993 > Squire and McKee, 1993 > Knowlton and Squire, 1994 > Knowlton *et al.*, 1994 > Knowlton and Squire, 1995 > Knowlton *et al.*, 1996 > Also authors *1–9*.	**WH**	Ischaemia (**64**) – BL H and some cell loss in EC (**autopsy**).	113	67	Flat AE for approximately 30 years, graded thereafter (**Crovitz**).Graded loss of PE and FF for at least 25 years.	Severely impaired episodic memory. Normal on tests of executive functioning. Impaired associative priming in a word stem completion task. Normal learning of artificial grammar, but impaired subsequent recognition. Impaired diagram recall (1/36). No reduction in the time spent examining previously seen pictures. Impaired yes/no recognition of names of people. Normal prototype learning in a test of artificial grammar learning. Normal probabilistic classification learning. Impaired memory for both 'Remember' judgements and 'Know' judgements. Normal habit learning. RMTW,F = 29,24.

Yoneda *et al.*, 1994	Case 3 Case 4 Case 5 of 5	HS Encephalitis (48) – BL HF HS Encephalitis (43) – BL HF HS Encephalitis (24) – BL HF case 5: predominately L HF (MRI).	114 102 73	87 81 70	Retrograde amnesia varied between 1 year and 10 years, and correlated with the volume of the PHG.	High correlation was found between verbal learning and HF volume. Patients with selective damage had fewer amnesic difficulties.
Schnider *et al.*, 1995	1 case	Systemic lupus erythematosus (55) – swollen selective BL HF, blurring of cortical structure (MRI).	91	-	Temporal gradient of impaired AE 10–15 years. Relatively preserved AS (**AMI**). Impaired FP for 10–15 years.	Normal digit span and Corsi block span. Severe episodic memory loss on WMS, CAVLT, Rey-figure and design learning tests.
Eslinger *et al.*, 1998	**MR**	Status epilepticus (40) – BL HF (MRI).	117	56	Early and recent life AE impaired, recent life PS impaired (**AMI**).	Normal language, perception. 'could retain bits of information for only 3–4 min.'.
Eslinger *et al.*, 1998	**PD**	HS Encephalitis (40) – BL HF additional BL Amyg. damage (MRI).	91	68	Recent life AE, and recent and early life PS impaired (**AMI**).	Normal language, perception. 'Her retention of information was extremely limited'.
Henke *et al.*, 1999	**DF**	CO poisoning (28) – BLHF atrophy globus pallidus damage (MRI).	88	71	Normal knowledge of semantic categories, FF and FP. 1 year impaired AE (**Crovitz**).	Patient examined over a period of 1.5 years. Selective improvement of some episodic memory functions; immediate word recall and picture learning, recognition memory also improved. Other functions such as delayed verbal recall and spatial memory were not found to improve.
Fujii *et al.*, 1999	1 case	Encephalitis (51) – BL HF additional BL Amyg. damage (MRI).	93	93	All AE and recent life AS impaired (**AMI**) PE and FP (**DoA**) for 10 years.	Normal digit span, picture naming, frontal functioning. Mild episodic memory deficits Impaired diagram recall (10/36 after 3 min). Normal recognition, RMTW,F = 43,4.

Table 3. Case studies of hippocampal amnesics – cases with fornix (F) damage

Authors, published year	Cases	Aetiology (age at onset) – lesion (localization)	IQ	MQ	Retrograde performance (test if given)	Anterograde performance
Hassler and Reichert, 1957	1 case	Epilepsy – BL Fornix surgery **(autopsy)**	-	-	Not described.	Anecdotal description of a severe memory disorder.
Sweet *et al.*, 1959	1 case	Colloid cyst of the third ventricle (36) – BL F damage (surgical).	103	90	'there was no recall of events leading up to hospitalization', but 'memory for remote events is quite intact'.	Normal digit span. Persistent (2 years) loss of recent memory, which was as impaired as chronically hospitalized Korsakoff patients. The patient initially had problems with recognizing common objects, which resolved.
Christiansen *et al.*, 1971	1 case	Colloid cyst of the third ventricle – BL F damage (surgical).	-	-	Not described.	Anecdotal description of a severe memory disorder.
Mundinger *et al.*, 1976	2 cases of 3	Epilepsy – BL F surgery and commissurotomies (surgical).	-	-	Not described.	They 'experienced a temporary condition of confusion with short-period memory and confabulation'.
Heilman and Sypert, 1977	1 case	Tumor of third ventricle and L lat. ventricle (41) – BL post. F, L occipital craniotomy (CT, Pneumoencephalography).	108	72	Normal memory for the location of states on a map of the USA.	Tested at 5 months post surgery – severely impaired episodic memory. Normal digit span. Impaired forced choice face recognition, 6/12 faces correctly identified.
Jeeves *et al.*, 1979 Geffen *et al.*, 1980	**WF**	Colloid cyst of the third ventricle (22) – Callosotomy -BL F damage (surgical).	116	80	Not described.	In this study a similar patient with a transcallosal surgery but without BL damage to the F was not found to be as amnesic, providing the authors with evidence that the fornix damage is the cause of the memory impairment in transcallosal cases.
Cameron and Archibald, 1981	1 case	Colloid cyst of the third ventricle – L F damage (surgical).	-	-	Not described.	Verbal episodic memory deficits.
Rousseaux *et al.*, 1984	**VP**	Tumor of the third ventricle (**61**) – Tumor extended in the Fornix (CT).	94	89	Mostly preserved, but with temporal order problems.	Particularly impaired on the logical memory test of the WMS. The patient did not report any confabulation.
Carmel *et al.*, 1985	2 cases	Colloid cyst of the third ventricle - R F damage (surgical).	-	-	Not described.	'Significant' memory loss.
Tucker *et al.*, 1988	**KW**	Tumor (25) – L F, lesion extending from the pulvinar to the L lat. ventricle (MRI).	83	-	Not described.	Severe memory deficit for verbal but not nonverbal materials.
Rudge and Warrington, 1991	9 cases	Tumors of the splenium of the corpus callosum. F, Callosal, occipital lobe damage, 8 had additional parietal lobe damage, 4 had additional temporal lobe damage (7 CT, 2 MRI).	79-117	-	Not described.	Spared language skills. Impaired recognition on the RMTW,F and impaired spatial and perceptual skills.

Gaffan *et al.*, 1991	2 cases	Colloid cyst of the third ventricle			Less than 1 year in both cases.	Normal digit span, impaired scene recognition, concurrent pattern/object recognition and delayed matching to sample.
Hodges and Carpenter, 1991						
	Case 1	(45) – L F damage (MRI).	107	-		Impaired Rey-figure recall (19/36), RMTW,F = 42,41.
	Case 2	(33) – L F damage (MRI).	110	-		Impaired Rey-figure recall (20/36), RMTW,F = 42,41.
Botez-Marquard and Botez, 1992	1 case	Hematoma (47) – Damage to the ant. comissure and F (CT).	120	94	Not described.	Loss of visual memory, Rey-figure copy (5/36), visual imagery, topographical memory and a cessation of dreaming. Mild impairments of verbal memory. Smell and taste were diminished.
Von Cramon and Schuri, 1992	**DC**	Surgical removal of angioma of the L lat. ventricle (25) – Post. cingulate Cx, longitudinal bundle and F (surgical).	112	-	AE impaired - mild for 1 year but dense for the month prior onset. Intact profession-specific semantic knowledge.	Normal digit span, and implicit learning tests. Corsi block span and world list recall impaired. Immediate diagram recall (0/36), RMTF = 44.
Araki *et al.*, 1994	1 case	Transcalloscal tumor removal (59) – BL ant. F damage (MRI).	-	-	Not described.	Impaired episodic memory, which improved post-operatively. Spared procedural and semantic memory.
McMackin *et al.*, 1995	5 cases of 6	Third ventricle colloid cysts – BL F (MRI).	-	-	Not described.	Of the 6 cases 5 had BL F damage and all had persistent episodic memory problems. The other case had damage to the L F only and did not suffer a severe memory deficit.
D'Esposito *et al.*, 1995	1 case	Missile penetrating head injury (32) – L parietal crainiotomy, and hydrocephalus - BL F (CT).	-	-	Some impaired FP across all decades, with spared AE.	This patient had a large number of varied problems. Left visual field problems, hemiparesis, dysphasia, mild left neglect, problems with working memory, and episodic memory. Normal recognition memory and procedural learning.
Calabrese *et al.*, 1995	**NC**	Tumor in third ventricle (**14**) – Fronto -Parietal craniotomy and trancallosal Interfornicalottamy – BL F (MRI).	110	56	Transient RA which resolved after 1 month. No AE or AS impairments (**AMI**).	Diagram recall (5/36), normal digit span, attention, procedural memory and priming.
Vuilleumier and Assal, 1995	**JPC**	Closed head injury (29) – complete destruction of the corpus callosum probable damage to the BL F (MRI).	-	-	Dense retrograde amnesia for both AE and PE extending back at least 8 years.	Normal digit span, severe impairments in recognition and recall, 3/10 words recalled after a few minutes. There were also non-memory deficits from the callosal damage.
Yasuno *et al.*, 1999	1 case	Tumor (51) – Ant. thalamus and Ant. BL F (MRI).	91	79	Impaired temporal order for AE.	Impaired temporal order memory. Normal digit span and executive functions.

Table 3. *(Continued)*

Authors, published year	Cases	Aetiology (age at onset) – lesion (localization)	IQ	MQ	Retrograde performance (test if given)	Anterograde performance
Aggleton *et al.*, 2000	3 cases of 12	Third ventricle colloid cysts -			Not described.	Amnesia was present in only the cases with fornix damage and not found to be related to the enlargement of the ventricles
	Case 4	(50) R frontal surgical approach, moderate ventricular enlargement.	101	77		RMTW,F = 35,48.
	Case 5	(27) L frontal surgical approach moderate ventricular enlargement, small BL H and mammillary bodies.	73	71		RMTW,F = 44,39.
	Case 7	(30) Callosal surgical approach, small BL H and mammillary bodies. (MRI).	100	91		RMTW,F = 48,39.
Moudgil *et al.*, 2000	1 case	Ischaemic Infarct (**71**) – Ant. F (MRI).	-	-	Not described.	Severe anterograde episodic amnesia with some improvement on follow up. Normal confrontation naming and problem solving.

Table 4. Case studies of hippocampal amnesics – where the temporal lobe damage is restricted to the medial temporal lobe (MTL) bilaterally

Authors, published year	Cases	Aetiology (age at onset) – lesion (localization)	IQ	MQ	Retrograde performance (test if given)	Anterograde performance
Von Bechterew, 1900	1 case	Unknown (60) – BL softening of H, uncunate gyrus and hippocampal gyrus (**autopsy**).	-	-	Not described.	Anecdotal description of memory problems, including confabulation. Showed that the hippocampus is not the taste center in the brain.
Yoneda *et al.*, 1994	Case 2 of 5	H.S. Encephalitis (55) – BL MTL damage with moderately enlarged ventricles (MRI).	97	70	Densely impaired for 5 years AE, AS and PE.	More impaired on the WMS and RAVLT than the more selective cases in this study, see table 2.
Mayes *et al.*, 1997	Cases 3,9,10 of 10	case 3 : Head injury (**12**), case 9: Encephalitis (19), case 10: Encephalitis (**13**) – MTL (unspecified brain scan).	101.0	-	All cases had impaired PE and FF, and AE and AS, with the recent past more affected (**AMI**).	Impaired on tests of non-verbal and verbal recall and recognition. Best correlation between the non-childhood AE and post morbid episodic memory tests.
Postle and Corkin, 1998 > Hood *et al.*, 1999 >	**PN**	H.S. Encephalitis (58) – Abnormalities in BL HF, PHG and PrRC (MRI).	121	83	Not described.	Impaired word stem completion priming but spared perceptual priming. Impaired concurrent learning of object reward, 1–2 h inter-trial interval.
Holdstock *et al.*, 1999 > Holdstock *et al.*, 2000b >	**RS (i)**	Encephalitis (34) – BL reductions in H, thinning of L PGC, PrRC and EC. Possible R PrRC damage. Slight gyral and cerebellar atrophy (MRI).	107	74	Not described.	Impaired allocentric spatial memory but not egocentric spatial memory. Impaired delayed non-matching to sample with abstract designs after filled delays of > 10 s.
Holdstock *et al.*, 1999 > Holdstock *et al.*, 2000b >	**NM**	Meningitis (**17**) – BL MTL slight additional pathology in sup. frontal, parietal Cx and cerebellum (MRI).	84	77	Not described.	Impaired allocentric spatial memory but not egocentric spatial memory. Impaired delayed non-matching to sample with abstract designs after filled delays of > 10 s.

Table 5. Case studies of hippocampal amnesics – where the temporal lobe damage is restricted to the hippocampal formation bilaterally and unilaterally to medial and extra-medial temporal regions[a]

Authors, published year	Cases	Aetiology (age at onset) – lesion (localization)	IQ	MQ	Retrograde performance (test if given)	Anterograde performance
Milner and Penfield, 1955	case 1 case 2	Epilepsy, **L**TL bilateral EEG suggesting BL H damage (surgical).	104 120	- -	'past memory seemed normal'.	Memory for daily events is very seriously impaired. 'the major defect in these patients is the loss of the ability of record on going experience'. Impaired story recall, drawing recall and numeric recall. Normal in attention, concentration and reasoning ability.
Walker, 1957	4 cases	Epilepsy, 2 **L**TL (40,40), 2 **R**TL (53,57). All had additional complications suggesting extra pathology (surgical).	-	-	'preservation of the ability to remember remote happenings.'	'loss of memory for recent events'. Immediate digit span was normal but recall was affected by distracting the patients concentration. Normal acquisition and retention of motor skills. Impaired recall of newspaper articles.
Penfield and Milner, 1958 Milner, 1966	**FC**	Epilepsy, **L**TL (12) (28at op) – Possible EEG bitemporal disturbance (surgical).	104	72	Not described.	Severe verbal and non-verbal memory loss. Normal digit span, executive functions and mental arithmetic.
Penfield and Milner, 1958 Milner, 1966 Corkin, 1965 Penfield and Mathieson, 1974	**PB**	Epilepsy, **L**TL (35) (41at op) – L anterior TL,most of L Amyg. ant. L H, diffuse **R** H damage (**autopsy**).	119	97	He failed to remember events from up to 4 years prior to the operation.	This patient had 2 operations. Following the first operation the patient showed no episodic memory loss, but after the second operation, in which the anterior H was removed. Showed some improvement following the second operation but could still not remember the names of his work colleagues.
Stepien and Sierpinski, 1960 Stepien and Sierpinski, 1964	**HK**	Severe epilepsy (**6months**) EEG spreading from frontal to TL – **R** partial frontal and RTL (age 15). Spreading resolved (surgical).	-	-	Not described.	Patient showed impaired performance on a delayed recognition of visual and auditory stimuli after a delay of more than 60 s. This impairment resolved following the operation, which stopped the ictal spreading from frontal to temporal cortex.
Stepien and Sierpinski, 1964	4 cases	Epilepsy 3 **L**TL, 1 **R**TL – BL dysfunction indicated by EEG (surgical).	-	-	Not described.	All patients had unilateral lesions generating an after-discharge on the contra-lateral side causing presumed bilateral dysfunction on the test described above. In three of the patients this resolved after the operation stopped the after-discharge.
Dimsdale *et al.*, 1964 Sanders and Warrington, 1971 Sanders and Warrington, 1975 Warrington and Duchen, 1992	**NT**	Epilepsy **R**TL (54) – sclerosis of **L** HF (**autopsy**).	110	94	Flat loss of AE, PE and FF. cued recall of words. RMTW,F = 35,25.	Impaired episodic memory, normal perceptual learning and performance on the Korsakoff's patients.
Drachman and Arbit, 1966	**VF**	Epilepsy, **R**TL (51) – BL temporal slowing in EEG (surgical).	120	93	Not described.	Normal immediate digit and visuo-spatial span, but impaired following a delay.
Jones, 1974	**HB**	L temporal tumor **L**TL (41) – Tumor thought to extend to across the midline hippocampal commisure (surgical).	100	62	Not described.	Severely amnesic and unable to use visual imagery to aid verbal recall.

Benson *et al.*, 1974	4 cases of 10	Posterior artery occlusion - **L** med. temporal occipital area (CT).	case 2: 92	76	Normal recognition of FF	All patients showed severe amnesia suggesting that amnesia can arise from unilateral L lesions.
Woods *et al.*, 1982	1 case	Stroke (57) – **L** HC, PHG and fusiform gyrus, R mid and ant. regions of the HF (**autopsy**)	88	77	Had some unmeasured retrograde memory loss. Intact naming of FF.	'She remembered 6–7 items from a short story after 5 min, but after 15 min could not even recall that she had been told the story.' She recalled 0/3 objects after 5 min. Normal digit span and language.
Ostergaard, 1987 Ostergaard and Squire, 1990	**CC**	Cerebral odema and convulsions (**10**) – damage to **L** MTL, occipital lobes, temporo-occipital junction and infracalcarine area and R ant. H, orbitofrontal and PHG (CT).	96	-	Lesion acquired in childhood.	Severe episodic and semantic memory loss but normal procedural memory.
Beatty *et al.*, 1988	**JN**	Gliobastoma - **R**TL (CT)	-	-	Intact AE, including visuo-spatial information and geographical knowledge.	Severely impaired on memory for visual and verbal material.
O'Connor *et al.*, 1992	**LD**	Encephalitis (18) – Large RTL lesion and R ventromedial frontal. Partial L HC lesion (MRI).	82	84	Impaired AE for whole life with Relatively preserved AS (Test similar to **AMI, Crovitz**). Impaired PE for 5 years.	Mild/moderate deficits on verbal episodic memory tests.
Ott and Saver, 1993	4 cases of 6	Stroke – All **L** MTL damage, no evidence of contralateral damage from scans (MRI).	-	-	Case 6 is described as having a >2 years retrograde amnesia.	Normal immediate recall of 3 objects but no recall of objects after 5 min. Other reports were anecdotal e.g. 'the patient did not recall the events of the day before'.
O'Donnell *et al.*, 1993	Case B of 2	H.S. Encephalitis (59) – **L** H and post. amyg. damage (MRI).	103	93	'showed a dense RA'	Normal digit span. Impaired with both verbal and visual material. Altered dipole orientation in an ERP auditory odd ball task.
Loring *et al.*, 1994	1 case	Epilepsy (onset at **9**) **R**TL, R hemisphere dominant, (21) – L H volume reduced (MRI).	81	59	Not described.	Impaired on all memory measures of the WMS, diagram recall (15/36 after 30 mins).
Oxbury *et al.*, 1997	**CG**	Epilepsy (28) – **L**TL with R HF damage (**autopsy**).	117	~70	AE impaired for up to 8 years, AS for early life was borderline (**AMI**).	RMTW,F = 33,37, Normal executive functions. Rey-figure recall (9/36). Preoperative, post-operative and post-amnesia neuropsychology recorded.
Kitchener *et al.*, 1998	**RS (ii)**	Stroke (34) – **L** MTL, R post. H, sup. L thalamus, L BFB and L medial frontal Cx (MRI).	105	<50	No AE for any events for any time period and some AS from all time periods (**AMI, Crovitz**). Some spared learning of FP, impaired FF and FP, but to a lesser degree than other impairments.	Severe loss of episodic memory function, delayed recall of the Rey-figure (0/36). RMTW,F = 25,24. Severely impaired recognition and no recall on the DPT. New semantic learning relatively spared.

[a]Laterality is indicated in bold for clarity.

Table 6. Case studies of hippocampal amnesics – with bilateral temporal lobe (BTL) damage within and beyond medial areas

Authors, published year	Cases	Aetiology (age at onset) – lesion (localization)	IQ	MQ	Retrograde amnesia (test if given)	Anterograde performance
Glees and Griffith, 1952	**RH**	Suspected vascular accident – L hemisphere examined: Damage to ant. and med. TL, fusiform and lingual gyri, H and fornix (**autopsy**).	-	-	Not described.	Anecdotal – amnesia, dementia and loss of emotional drive. First to suggest that bilateral H damage required for severe loss of recent memory.
Scoville, 1954 > Scoville and Milner, 1957 > Corkin, 1965 > Milner, 1966 > Drachman and Arbit, 1966 > Milner *et al.*, 1968 > Sidman *et al.*, 1968 > Wickelgren, 1968 > Jones, 1974 > Marslen-Wilson and Teuber, 1975 > Huppert and Piercy, 1979 > Eichenbaum *et al.*, 1983 > Corkin *et al.*, 1984 Hebben *et al.*, 1985 > Freed *et al.*, 1987 > Freed and Corkin, 1988 > Smith, 1988 > Gabrieli *et al.*, 1988 > Sagar *et al.*, 1990 > Gabrieli *et al.*, 1990 > Sullivan and Sagar, 1991 > Woodruff-Pak, 1993 > Gabrieli *et al.*, 1993 > Keane *et al.*, 1995 > Corkin *et al.*, 1997 Postle and Corkin, 1998 > Shadmehr *et al.*, 1998 > Hood *et al.*, 1999 > Kensinger *et al.*, 2001 >	**HM**	Epilepsy, from age 16 (27) – Ant. med. TL, HF, EC, Amyg. damage posterior 2cm of HF spared but atrophic. Cerebellar atrophy and shrunken mammillary nuclei. Caudal PrRC and PHG, mediodorsal thalamic nuclei spared (MRI).	112	67	Impaired AE for 11 years, Impaired PE and FP.	Severe loss of recent memory. Normal intelligence, attention and language. Unimpaired motor skills, on rotary pursuit, bimanual tracking and tapping. Performance incompatible with a unitary process of memory. Normal immediate memory, impaired at delay. Little improvement in performance 14 years after operation. Impaired delayed match to sample, worse for non-verbal material. Impaired long-term but not short-term memory for digits and tones. Unable to use visual imagery to aid verbal recall. Some sparing of remote memory for famous faces. Initial evidence of a faster forgetting rate for pictures than controls. Able to detect odors but not discriminate them. Diminished ability to interpret and report internal states. Normal forgetting rate for pictures at delays of less than 24 h. Recognition comparable to controls at 6 months, but not on a standard yes/no test. Impaired incidental and intentional object location memory. Impaired anterograde but not retrograde semantic memory. Frequency discriminations are less impaired than content recognition. Intact priming for visual patterns. Short term, but not long-term memory, spared on non-verbal tests. Normal eyeblink conditioning. Retention of the mirror drawing skill one year later. Impaired recognition but spared visuo-perceptual priming. Impaired word stem completion priming but spared perceptual priming. Time-dependent changes in motor memories. Impaired concurrent learning of object reward, 1–2 h intertrial interval. No decrement in lexical or grammatical processing.
Scoville, 1954 Scoville and Milner, 1957	**MB**	BL TL surgery for manic depression (55) - 8 cm lesion (surgical). Similar to H.M.	-	-	'She gave the year as 1950 and and appeared to recall nothing of the last 3 years.'	'She showed a global loss of recent memory similar to that of HM'.
Terzian and Dalle Ore, 1955	1 case	BL TL removal (19) - Similar to H.M., but includes lat. TL (surgical).	-	-	Not described.	Anecdotal description of lesion effect. Amnesia with recognition, sexual, dietary and emotional problems.
Scoville and Milner, 1957	**DC**	BL TL surgery for paranoid schizophrenia (47) – 5.5cm lesion, with orbital undercutting (surgical).	122	70	'could give minute details of his early life and medical training (accurately, far as we could tell)'.	'This patient presented exactly the same pattern of memory loss as HM.'.

Scoville and Milner, 1957	**AZ**	BL TL surgery for paranoid schizophrenia (35) – 5cm lesion (surgical).	96	84	The patient had a memory loss for the whole period of her illness following the operation.	Severely impaired verbal and non-verbal memory but not as impaired as HM and DC.
Scoville and Milner, 1957	**MR**	BL TL removal for paranoid schizophrenia (40) – 5cm lesion, with orbital undercutting (surgical).	123	81	'showed little knowledge of recent events'.	Similar level of impairment to AZ.
Scoville and Milner, 1957	**AR**	BL TL removal for hebeprenic Schizophrenia (38) – 4.5cm lesion, additional orbital undercutting (surgical).	-	-	'she appeared to recall recent happenings quite well.'.	'we conclude that this patient has a memory impairment identical in type to the other patients in the group, but somewhat milder. It is interesting that she had a relatively small excision.'.
Scoville and Milner, 1957	**CG**	BL TL removal for schizophrenia (44) – 5.5cm lesion (surgical).	-	-	'it was possible to show that she remembered some recent events.'	'formal testing revealed the same deficit as that shown by AZ and MR.'.
Scoville and Milner, 1957	**AL**	BL TL for schizophrenia (31) – 6cm lesion, additional orbital undercutting (surgical).	-	-	Not described.	No recall of stories and drawings after a filled delay, however 'he did not show the severe memory loss typical of the patients in Group 1' (e.g. HM).
Victor *et al.*, 1961	1 case	Stroke (54) – BL inferomedial TL damage and damage to the mammillary bodies. (**autopsy**).	115	-	Well defined remote memory loss to 2 years.	Severe anterograde memory loss, had problems learning new facts.
Gol and Faibish, 1967	3 of 7	BL TL removals for intractable pain				
	case 1	(27) marked cerebral atrophy	66	-	'He knew the year but not the date'.	'fairly well oriented in time and space.'
	case 3	(46) relatively selective R H lesion	-	-		
	case 5	(55) 25% BL damage to H greater BL MTL damage outside H. (**autopsy**).	-	-	'he was not able to give his age'.	He was 'able to name the hospital and town correctly, but he was confused in time'.
Gol and Fabish, 1967	case 7 of 7	Surgery for intractable pain (37) – BL temporal and ant. frontal removals (surgical).	105	91	Unmeasured RA observed.	Problems with recent memory. He also showed poor judgement. No decline in memory following an initial unilateral operation.
DeJong *et al.*, 1969 DeJong, 1973	1 case	Ischaemia (32) – BL (L greater) HF, additional damage to PHG, fusiform cortecies and calcarine sulcus greater on L (**autopsy**).	111	-	Not described.	Anecdotal description, loss of both episodic and semantic information, memory was worse when it contained a strong emotional element.
Starr and Phillips, 1970	**MK**	Encephalitis (43) – excess dilation of third and lateral ventricles, BL TL damage. (Pneumoencephalograph).	126	80	Impaired AE for at least 5 years.	Impaired verbal learning. Spared motor learning. Some degree of confabulation.
Van Buren and Borke, 1972	3 cases	Cerebral infarcts – (**autopsy**)	-	-	Graded impaired AE.	All showed amnesia and spatial orientation problems, the unilateral patient recovered from the amnesia after 7 weeks.
	case 1	BL MTL and lingual gyri.				
	case 2	BL MTL and lingual gyri.				
	case 3	L H, PHG and lingual gyri.				

Table 6. *(Continued)*

Authors, published year	Cases	Aetiology (age at onset) – lesion (localization)	IQ	MQ	Retrograde amnesia (test if given)	Anterograde performance
Hierons *et al.*, 1978	10 cases	Encephalitis – large BL TL lesions. Common to all cases was the virtual destruction of the H (**autopsy**).	-	-	Patient 2 showed dense AE up to 20 years using family photos.	All had severe episodic memory problems.
Volpe and Petito, 1985	2 cases	Ischaemia - myocardial infarct –				
	Case 1	(**66**) Mild cortical atrophy, BL damage to CA1, subiculum, basolateral Amyg. and ant. inf. TL.	-	-	Could not recall recent current events.	Could not remember 4 unrelated items after 10 s and had problems with describing the differences between various items of the same semantic category.
	Case 2	Moderate cortical atrophy, BL damage to CA1, subiculum, presubiculum, Amyg. and PGH (**autopsy**).	-	-	Unable to describe the events of the preceding month; could not name the current president; thought she was younger than she was.	She could not remember unrelated items or calculate, and had problems performing complex everyday tasks.
Warrington and McCarthy, 1988 McCarthy and Warrington, 1992	**RFR**	Encephalitis (53) - BL TL (CT).	118	-	Impaired AE, spared context-independent information about people. Impaired PE for at least 15 years, impaired FF for at least 25 years.	Preserved language, and perception, RMTW,F = 27,26, Camden Topographical Recognition Memory Test = 8/30.
Tulving *et al.*, 1988 Tulving *et al.*, 1991 Rosenbaum *et al.*, 2000 Westmacott *et al.*, 2001	**KC**	Closed head injury (30) – BL MTL lesions, L med. occipital infarct, L fronto-parietal lesion, some swelling of the ventricles (MRI).	95	79.5	Flat severe loss of AE and PE, relatively preserved remote semantic memory. Intact remote topographical memory.	Spared new semantic learning. Very good short term memory, no story recall, chance performance on the RMTW,F.
Squire *et al.*, 1990 Knowlton and Squire, 1993 Squire and Knowlton, 1995 (*1*) > Hamann *et al.*, 1996 (*2*) > Reed and Squire 1998 (*3*) Clark and Squire, 1998 > Reber and Squire, 1998 > Buffalo *et al.*, 1998 (*4*) > Teng and Squire, 1999 > Reed *et al.*, 1999 > Reed and Squire, 1999 > Stefanacci *et al.*, 2000 Stark and Squire, 2000 >	**EP**	H.S. Encephalitis (**70**) – BL lesion of the ant. and med. TL (MRI).	103	61	Impaired AE and AS for almost entire life (**AMI, Crovitz**). Impaired PE and FF for at least 40 years. Intact remote topographical memory and memory for very early life.	No diagram recall, no recall of paired associates, RMTW,F 24,28 (at 24 h delay). Normal item classification, but impaired recall of items. Normal classification of novel stimuli. Normal emotional responses. Impaired post-morbid semantic learning. Impaired eyeblink conditioning when awareness of the relationship is required. Normal implicit but impaired explicit performance in a serial reaction time task. More impaired than L.J. on the recognition of abstract designs. Impaired learning of new large-scale environments. Normal classification despite impaired recall of item features. Impaired transverse patterning learning and concurrent pair learning problems. (worse than LJ and PH see table 2). Impaired recognition for items that the he had shown repetition priming for.
Schnider *et al.*, 1992 > Schnider *et al.*, 1994 >	1 case	Infarct (**66**)– BL MTL and L inferotemporo-occipital Cx. intact temporal stem and Amyg. (MRI).	-	-	Extensive ungraded impairments of AE, FP, PE. A few vague memories recalled. Names of family members remembered. Severe topographical memory loss, only oriented in his own premises.	Unable to match colours to objects in verbal or visuo-verbal tasks. Normal digit span, language and mirror drawing. Some anomia. Impaired diagram recall (0/36).

Ahern *et al.*, 1994 O'Connor *et al.*, 1995 O'Connor *et al.*, 1997	**JT**	Epilepsy and encephalitis (32) – BL MTL damage additional L anteromedial temporal lobe atrophy, ventricular dilation and BL Amyg. (MRI).	127	120	Impaired AE (**Crovitz**), PE and FF.	Variable performance on tests of episodic memory. Normal digit span and executive functioning. Average or low average on recognition tests.
See refs *1, 2, 3* and *4*	**GT**	H.S. Encephalitis (54) – large BL TL Lesion (MRI).	92	<50	No AE recalled (**AMI, Crovitz**). Impaired PE and FF for at least 40 years.	One of the most severe amnesias reported. The patient is anomic, but with normal word fluency.
Henke and Wieser, 1996	**KHJ**	Developmental BL arachnoid cyst with epilepsy from age 18, L HF and Amyg. removal at age 55 – BL TL damage greater on the left (MRI).	-	-	Not described.	Not described as amnesic but postoperatively recalled 0/15 words in the RAVLT.
Schmidtke and Vollmer, 1997	case 8 of 24	Encephalitis – large BL TL lesion (MRI).	86.5	54.5	Not described for this case.	As a group: MQ correlated with recent life AE and semantic memory performance with childhood AE.
Kopelman and Stanhope, 1998	13 cases of 44	9 Cases: encephalitis (MRI) 4 Cases: hypoxia – varying sizes of BL TL lesions (MRI).	95.9	68.4	Not described.	Word recall and recognition performance was no different from that of frontal lobe or diencephalic patients, where performance was titrated. Patients with predominately right lesions were more impaired on episodic memory tasks.

Table 7. Case studies of hippocampal amnesics – where the temporal lobe damage is restricted to the medial temporal lobe bilaterally but with additional basal forebrain (BFB) damage

Authors, published year	Cases	Aetiology (age at onset) – lesion (localization)	IQ	MQ	Retrograde amnesia (test if given)	Anterograde performance
Drachman and Adams, 1962 Drachman and Arbit, 1966 O'Donnell *et al.*, 1993	**LC (ii)**	H.S. Encephalitis (**16**) – BL inf. and med. TL, L worse than R. ant. worse than post., both sylvian fissures were enlarged and damage to BFB (MRI).	121	92	'her memory for distant past events was preserved'.	Normal digit span. Impaired supra-span memoranda even after multiple repetitions. Spared executive functions, but problems with affect, ideation and social withdrawal. Her procedural memory for playing the flute was still intact, 'although she was not able to remember what she had played after she completed a piece of music'. Months after onset she had learned some new facts. MQ had improved to 99 in 1993. Altered dipole orientation and reduced N1 and N2 ERP measures in a auditory oddball task.
Cermak, 1976 Cermak and O'Connor, 1983 Beatty *et al.*, 1988 O'Connor *et al.*, 1995 Verfaellie *et al.*, 2000 >	**SS**	Encephalitis (50) – BL TL lesion, greater on the left. and L BFB(MRI).	130	102	Flat loss of AE for whole life. Graded (30 – 40 years) loss of PE and FP.	Normal verbal working memory but severe loss of long-term memory. No post-morbid learning of famous faces or new vocabulary.
Damasio *et al.*, 1985a Damasio *et al.*, 1985b	**DRB** a.k.a. Boswell	Encephalitis (55) – Destruction of both MTLs and anterolateral regions of temporal lobe, and BFB (CT).	84	62	Impaired AE for all time periods, AS relatively spared. Dense loss of FF for whole life.	Severe visual and verbal memory loss, impaired diagram recall (4/36) , problems with temporal context, frequently confabulated.
O'Donnell *et al.*, 1993	Case A of 2	H.S. Encephalitis (**16**) – BL TL and BFB lesions.	122	99	Not described.	Normal digit span. In addition to the amnesia the patient showed a flat affect and social withdrawal. Altered ERP responses in an auditory oddball task.
Yoneda *et al.*, 1994	Case 1 of 5	Encephalitis (37) – BL MTL, BFB Lat. and Third ventricles enlarged (MRI).	72	72	Retrograde amnesia for 10 years when initially assessed and 5 years on follow up.	0/15 recalled words on the RAVLT, patient also had Kluver-Bucy syndrome.