

# Memory: brain systems and behavior

Larry R. Squire and Stuart Zola-Morgan

Larry R. Squire and Stuart Zola-Morgan are at the Veterans Administration Medical Center, San Diego, CA 92161, USA, and the Department of Psychiatry, University of California, San Diego, La Jolla, CA 92093, USA.

*Certain questions about memory address a relatively global, structural level of analysis. Is there one kind of memory or many? What brain structures or systems are involved in memory and what jobs do they do? One useful approach to such questions has focused on studies of neurological patients with memory impairment and parallel studies with animal models.*

Memory impairment sometimes occurs as a circumscribed disorder in the absence of other intellectual deficits<sup>1-7</sup>. In such cases, the memory impairment occurs in the context of normal scores on conventional intelligence tests, normal immediate (digit span) memory, and intact memory for very remote events. The analysis of memory impairment can provide useful information about the organization of memory and about the function of the damaged neural structures. Clinically significant memory impairment, i.e. amnesia, can occur for a variety of reasons and is typically associated with bilateral damage to the medial temporal lobe or the diencephalic midline. The severity and purity of the amnesia can vary greatly depending on the extent and pattern of damage. Standard quantitative tests are available for the assessment of memory and other cognitive functions, so that the findings from different groups of study patients can be compared<sup>8-10</sup>.

The deficit in amnesia is readily detectable in tests of paired-associate learning and delayed recall. Indeed, amnesic patients are deficient in most tests of new learning, especially when they try to acquire an amount of information that exceeds what can be kept in mind through active rehearsal or when they try to retain information across a delay. This deficit occurs regardless of the sensory modality in which information is presented and regardless whether memory is tested by recall or recognition techniques. Moreover, the memory impairment is not limited to artificial laboratory situations, where patients are instructed explicitly to learn material that occurs in a particular episode and then are later instructed explicitly to recall the material. For example, patients can be provided items of general information with no special instruction to learn (e.g. Angel Falls is located in Venezuela); and later they can simply be asked factual questions without any reference to a recent learning episode (e.g. Where is Angel Falls located?). In this case, amnesic patients are impaired both in tests of free recall as well as in tests of recognition memory, in which the correct answer is selected from among several alternatives<sup>11</sup>. These aspects of amnesia show that the deficit is a pervasive one, affecting the new learning of both specific episodes and facts.

## Heterogeneity of symptoms

Not all amnesic patients exhibit the same deficits. For example, patients with alcoholic Korsakoff's syndrome are often emotionally flat, apathetic, and without insight about their memory impairment<sup>12</sup>. On the other hand, the well-known amnesic patient H.M.<sup>13,14</sup> (with bilateral surgical lesions that reportedly involved much of the medial temporal region)

has an agreeable personality, a sense of humor, and insight into his condition. The same is true for other (non-Korsakoff) amnesic patients<sup>15,16</sup>, such as those with amnesia due to an anoxic or ischemic episode. Formal testing has yielded a list of cognitive (and memory) disorders exhibited especially by the Korsakoff patient, that are not obligatory to amnesia. Thus, impaired memory is sometimes accompanied by disorders that influence the appearance of the memory impairment but that can be dissociated from it. These disorders include: (1) special difficulty with memory for the temporal order of recent events<sup>17</sup>; (2) source amnesia, i.e. a special problem in determining when and where information was acquired, quite apart from remembering the information itself<sup>11,18</sup>; (3) failure to release from proactive interference, i.e. failure to show the normal improvement in performance when subjects attempt to learn words belonging to a new category after attempting several word lists from another category<sup>17</sup>; and (4) impaired metamemory, as assessed for example by tests that ask subjects to predict their own performance on an upcoming multiple-choice test<sup>19</sup>. Finally, it has been reported that amnesic patients perform worse in recall tests than would be expected given their level of recognition performance<sup>20</sup>, but further work is needed to show whether this finding is common to all amnesias or is limited to certain kinds of patients.

Recently, a study was done of patients with circumscribed frontal lobe lesions<sup>21</sup>. These patients performed poorly on standard tests of frontal lobe function, including the Wisconsin Card Sort Test. The patients were clearly not amnesic, as they performed well on conventional memory tests. Yet they did show some of the above-mentioned deficits. For example, the frontal patients had impaired metamemory abilities, they exhibited source memory errors, and they had more difficulty with free recall than would be expected from their level of recognition performance. Earlier work with other frontal patients<sup>22</sup> showed that they had special problems with temporal order judgements. These findings suggest that amnesic patients who show these particular deficits may have frontal lobe damage in addition to the brain lesions that produce amnesia. Recently, using quantitative CT scan analysis, we found evidence of frontal lobe damage in patients with Korsakoff's syndrome<sup>23</sup>, who do exhibit these deficits.

## Retrograde amnesia

In addition to deficits in new learning and certain other non-obligatory deficits, amnesic patients also exhibit retrograde amnesia, an inability to remember information that occurred prior to the onset of the disorder. Retrograde amnesia affects both facts and episodes, particularly those that were encountered close to the time of the precipitating incident. We recently had the opportunity to study retrograde amnesia in five patients who became amnesic on a known date between 1976 and 1986 as the result of an anoxic or ischemic event. On tests of public events and famous faces that came into the news during a

particular decade (1940–1985), these patients exhibited a temporally-graded impairment affecting approximately the past 15 years (Ref. 24 and Squire, L. R., Haist, F. and Shimamura, A. P., unpublished observations) (Fig. 1). Performance was markedly impaired for the 1970s and 1980s but was at normal levels for items concerning the 1940s, 1950s, and 1960s. These findings show that the damaged brain regions cannot be the site of permanent representations. The data do not rule out the possibility that experience is initially recorded in the damaged regions and later moved elsewhere; nor do the data exclude the idea that there are two identical records of experience, a temporary one within the damaged area and a potentially permanent one elsewhere. While these are possibilities, it seems more likely that the critical structures damaged in amnesia perform a specific function for a limited period of time.

One proposal is that the critical structures are initially required for the establishment of memory and for retrieval from memory. When sufficient time has passed after learning, memory becomes independent of these structures. Synaptic change, occurring at disparate cortical sites, is considered to constitute initially the representation of a complex experience. Rehearsal, new learning events, or perhaps even quasi-random neural activity across time, might serve to maintain or strengthen some aspects of the originally established representation. Thus, while forgetting occurs, some aspects of the original representation may become stronger. A related possibility is that, as a result of rehearsal or encounters with similar material, additional representations of the original experience are established. As this process of reorganization and consolidation continues, representations gradually become independent of the structures damaged in amnesia.

### Spared learning abilities

What kind of memory requires the integrity of the brain structures damaged in amnesia? The answer to this question comes from studies of preserved learning in amnesic patients. Amnesia is a narrower syndrome than casual clinical observation would suggest, in that significant areas of learning and memory are intact. This idea was suggested by an early demonstration that the severely amnesic patient H. M. exhibited day-to-day improvement in a motor-skill task<sup>25</sup>. It now appears that amnesia spares not only motor skills, but also perceptual skills and certain cognitive skills<sup>26–30</sup>. In addition, amnesia spares word priming, e.g. presentation of a word increases the tendency to produce that same word when its initial letters or a closely related word are presented several minutes later<sup>6,31</sup>. Recently, we have extended this list of spared learning abilities in amnesia to include adaptation-level effects (Benzing, W. and Squire, L. R., unpublished observations). Control subjects and amnesic patients lifted a collection of weighted containers with one hand, judging their heaviness on a 1 to 9 scale. About 20 minutes later, working with the

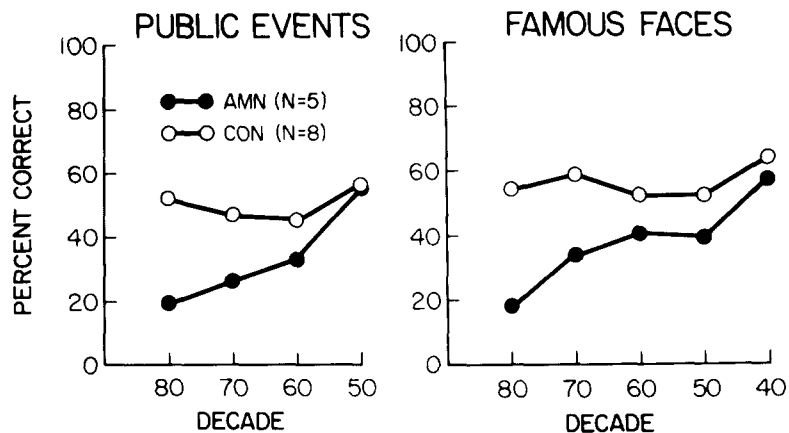


Fig. 1. Remote memory performance by five patients who became amnesic following an anoxic or ischemic episode (AMN) and eight control subjects (CON). The patients became amnesic between 1976 and 1986. Testing occurred in 1986 and 1987 when the patients averaged 52 years of age. The tests asked subjects either to recall news events that had occurred from 1950 to 1985 or to identify photographs of people who had come into the news from 1940 to 1985.

other hand, subjects judged a standard set of ten containers. Experience with the first set of containers influenced these later judgments. Subjects who lifted relatively heavy weights in the first session now judged the standard weights to be lighter than did subjects who lifted relatively light weights in the first session. This effect of prior experience was equivalent in amnesic patients and control subjects. Yet, on formal tests, the amnesic patients were quite poor at recalling and recognizing information about the first session.

These phenomena are all examples of implicit memory abilities. The information is accessible only in performance, not as a conscious recollection. If subjects are encouraged to use explicit memory strategies in these tasks, normal subjects often perform better than amnesic patients. These findings have suggested the existence of two or more separate memory systems or processes (Fig. 2). One of them affords the ability to store information explicitly, such that it is then available later as a conscious recollection. This ability is lost in amnesia. We have used the term declarative to describe this kind of memory ability. Declarative memory depends on the structures damaged in amnesia. This kind of memory can be declared, i.e. it can be brought to mind as a proposition or an image.

Non-declarative memory comprises a heteroge-

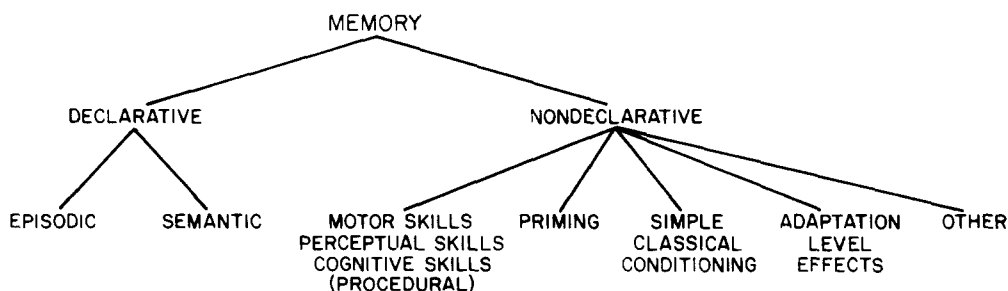
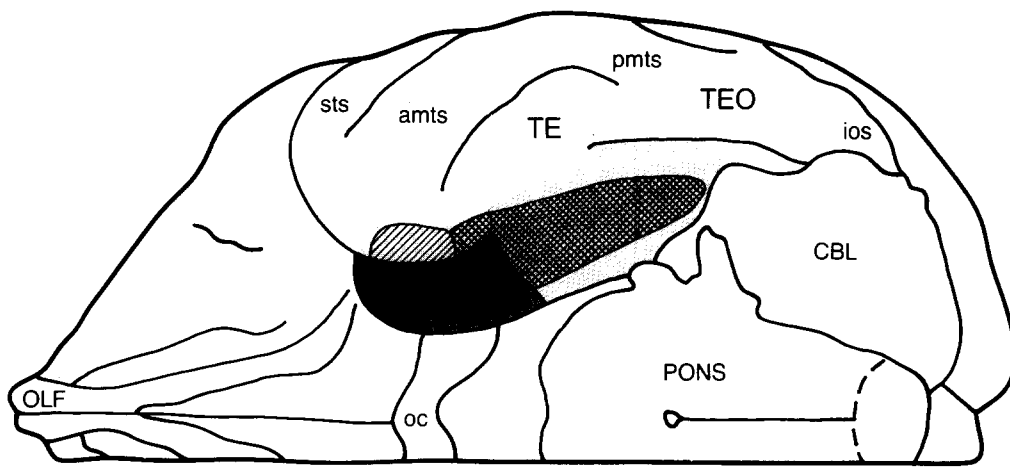


Fig. 2. A tentative memory taxonomy. Declarative memory includes what can be declared or brought to mind as a proposition or an image. It depends on the integrity of the hippocampus and related structures. Non-declarative memory refers to a heterogeneous collection of abilities: motor skills, perceptual skills, and cognitive skills (these abilities and perhaps others are examples of procedural memory); as well as simple classical conditioning, adaptation level effects, priming, and other instances where experience alters performance independently of providing a basis for the conscious recollection of past events.



**Fig. 3.** Ventral view of the left hemisphere of monkey showing location of the amygdala and hippocampus (cross-hatching) and the overlying cortical regions typically included in surgical removals of the medial temporal region damaged in the neurosurgical ablation of these structures. Dark grey = periamygdaloid cortex; light blue = perirhinal cortex; dark blue = entorhinal cortex; light grey = parahippocampal gyrus.

neous collection of learning and memory abilities, all of which afford the capacity to acquire information implicitly. For example, in the case of motor skill and perceptual skill tasks, subjects typically do not acquire much declarative knowledge about what they have learned. The information is available through performance, and subjects appear to access the information by engaging in the procedures in which the knowledge is embedded. Amnesic patients can acquire such skills at a normal rate and retain them at a normal level. We have used the term procedural to describe this skill-learning ability. Other kinds of memory abilities are also intact in amnesia, e.g. word priming and

adaptation-level effects. Because so little is known about the similarities and differences between these spared abilities, it is not clear whether the term procedural aptly describes them all. However, it is clear that declarative memory ability can be tied to the function of the structures damaged in amnesia and that the spared (non-declarative) memory abilities do not depend on these structures.

### The anatomy of memory

Information about which neural connections and structures belong to the functional system damaged in amnesia comes from two sources: well-studied cases of human amnesia in which neuropathological data are available; and attempts to develop an animal model of amnesia in the monkey.

It has long been known that bilateral damage to the midline diencephalon or bilateral damage to the medial temporal region causes profound amnesia in humans. Patients with lesions that involve structures of the basal forebrain can also have persisting memory impairment in conjunction with personality change<sup>32</sup>. With regard to the diencephalon, the two structures most frequently implicated by clinico-pathological data have been the mammillary bodies of the hypothalamus and the mediodorsal nucleus of the thalamus. The idea that the mammillary bodies are important derives from reports of its consistent damage in Korsakoff's syndrome<sup>33</sup>, the best studied example of diencephalic amnesia. Yet, it is commonly agreed that the mammillary bodies are not the only site of damage<sup>34</sup>. Other studies suggest that damage to the mediodorsal nucleus might be required to produce the amnesia of Korsakoff's syndrome either alone<sup>35</sup> or in combination with the mammillary bodies<sup>36,37</sup>. Additional clinical cases, including those that report amnesia in conjunction with infarction in the territories of the tuberothalamic or paramedian arteries, have also provided support for the importance of the medial thalamus in amnesia<sup>38</sup>. The complication here is that, although the damage does frequently involve the mediodorsal nucleus, other thalamic structures are also damaged and the mediodorsal nucleus is sometimes only minimally involved. Accordingly, the human cases leave considerable uncertainty about the specific diencephalic structures that must be damaged to cause amnesia.

One promising approach to the anatomy of amnesia is afforded by the recent development of an animal model of

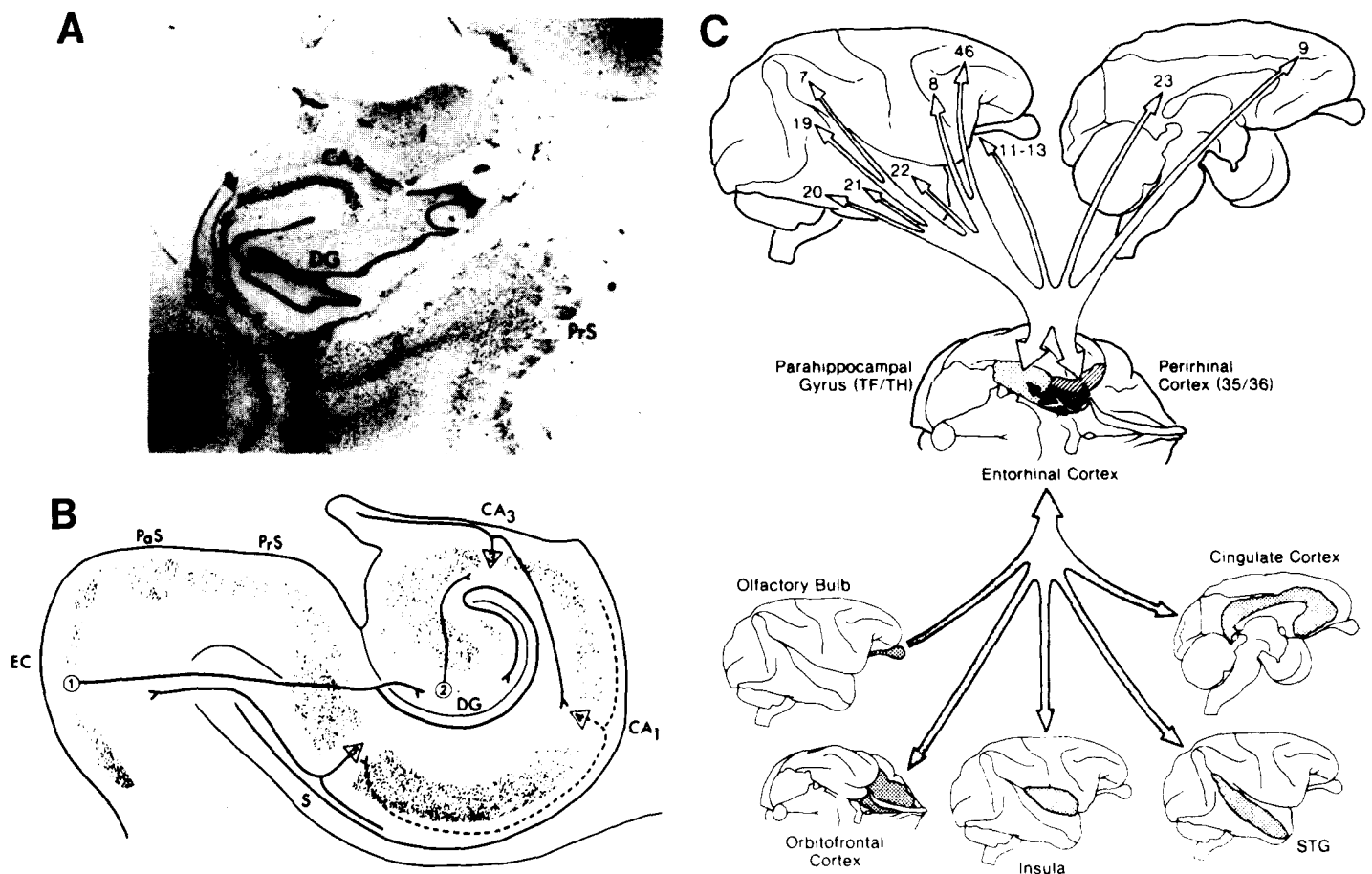
	2 Months → 1.5 Years					Pattern Discrimination	Motor Skills
	Delayed NMTS-I	Object Retention	8-Pair Concurrent	Delayed Response	Delayed NMTS-II		
H <sup>+</sup> A <sup>+</sup>	++	++	++	++	++	-	-
H <sup>+</sup>	+	+	+	++	+	-	-
H <sup>+</sup> A	+	+	+	++	+	-	-
A	-	-	-	-	-	-	-
FX	(+)	-	-	(+)	-	-	-
MB	+	-	-	-	-	-	-

**Fig. 4.** Performance of monkeys with bilateral lesions of the medial temporal or the diencephalic regions on four tasks sensitive to human amnesia (delayed non-matching to sample, retention of object discriminations, eight-pair concurrent learning, and delayed response), and two tasks analogous to those that are spared in human amnesia (pattern discrimination learning and motor skill learning). For description of tasks see Refs 58, 59. Delayed non-matching to sample was the first test given after surgery (delayed NMTS-I), and it was repeated 1.5 years after surgery (delayed NMTS - II). Abbreviations: H<sup>+</sup>A<sup>+</sup>, the conjoint hippocampus-amygdala removal - the structures removed bilaterally include the hippocampus proper, dentate gyrus, subicular cortex, entorhinal cortex, parahippocampal gyrus, perirhinal cortex, periamygdaloid cortex, and amygdala; H<sup>+</sup>A same as H<sup>+</sup>A<sup>+</sup>, but with sparing of perirhinal cortex, periamygdaloid cortex, and anterior entorhinal cortex; H<sup>+</sup>, same as H<sup>+</sup>A<sup>+</sup>, but with sparing of the amygdala, periamygdaloid cortex, and anterior entorhinal cortex; A, bilateral lesions limited to the amygdala; FX, bilateral lesions of the fornix; MB, bilateral lesion of the mammillary bodies; ++, severe impairment; +, moderate impairment; -, no impairment; (+) for NMTS - I, normal performance at delays of 8-60 s, moderate impairment at longest delay of 10 min; (+) for delayed response, only two of four FX monkeys impaired.

human amnesia in the monkey<sup>39-41</sup>. The memory tasks available for the monkey are sensitive to human amnesia<sup>42</sup>. This work has shown that bilateral lesions restricted to the mammillary bodies produce only negligible<sup>43</sup> or transient<sup>44</sup> memory impairment. Accordingly, mammillary body lesions alone are unlikely to be the cause of the severe and permanent memory impairment associated with alcoholic Korsakoff's syndrome and other diencephalic amnesias. Additional work has shown that medial thalamic lesions, including the mediodorsal nucleus, produce marked and enduring impairment<sup>45-47</sup>. Further work is needed to determine whether damage to the mediodorsal nucleus alone can cause amnesia, and to assess which other thalamic structures might be important.

With respect to medial temporal amnesia, it has long been believed that damage to the hippocampus is responsible for memory impairment in the human cases. Work with monkeys showed that bilateral damage to the medial temporal region caused severe memory impairment<sup>48</sup>. This lesion (here termed

[H<sup>+</sup>A<sup>+</sup>]; the bracketed terms in this section correspond to the lesion groups indicated in Fig. 4) approximated the removal sustained by the amnesic patient H. M. and involved the amygdala, the hippocampus (including the dentate gyrus and subicular cortex), as well as surrounding cortical regions: periamygdaloid cortex, perirhinal cortex, entorhinal cortex, and the parahippocampal gyrus (Fig. 3). This large removal is not required to produce significant memory impairment. A substantial, albeit less severe, deficit is readily detected when monkeys with bilateral hippocampal [H<sup>+</sup>] lesions (including dentate gyrus, subicular cortex, posterior entorhinal cortex, and most of the parahippocampal gyrus) are trained postoperatively and then tested at long retention intervals (e.g. after delays of 10 minutes)<sup>49</sup>. One possibility is that the more severe [H<sup>+</sup>A<sup>+</sup>] deficit depends on amygdala damage<sup>50</sup>; another is that it depends on damage to the perirhinal cortex, periamygdaloid cortex, and on anterior entorhinal damage, all of which occur with the larger H<sup>+</sup>A<sup>+</sup> lesion. Recently, in collaboration with David Amaral,



**Fig. 5.** (A) Photomicrograph of a thionin-stained coronal section through the left hippocampal formation of R. B.'s brain. The only pathology evident is the complete loss of pyramidal cells confined to the CA1 field of the hippocampus (indicated by arrows). Abbreviations: CA3, field CA3 of the hippocampus; DG, dentate gyrus; PrS, presubiculum; S, subiculum. (B) Schematic diagram of the primate hippocampal formation. The numbers and the solid lines connecting them show the unidirectional flow of information from (1) entorhinal cortex, to (2) dentate gyrus, to (3) the CA3 field of the hippocampus, to (4) the CA1 field of the hippocampus, and to (5) the subiculum. In case R. B., a lesion of the CA1 field (represented by cell 4 and the dashed lines) disrupted the sequence of information flow in the hippocampus. Abbreviations: EC, entorhinal cortex; PaS, parasubiculum; other abbreviations as in (A). (C) Summary of cortical afferent and efferent connections of entorhinal cortex, which is the major source of projections to the hippocampus. The major cortical input originates in the adjacent parahippocampal gyrus, and perirhinal cortex. These regions in turn receive projections from several polysensory associational regions in the frontal, temporal, and parietal lobes. The entorhinal cortex also receives cortical inputs directly from other presumed polysensory regions and one unimodal input from the olfactory bulb. With the exception of the olfactory projection, these projections are reciprocal. Patient R. B.'s lesion would have disconnected the hippocampus from putative memory storage areas.

we found that histologically confirmed lesions damaging all the components of the amygdala complex bilaterally, but sparing surrounding cortex [A], had no detectable effect on memory as measured by four different memory tasks. In addition, adding circumscribed amygdala damage to the hippocampal lesions just described [H<sup>+</sup>A] did not increase the memory deficit. These findings emphasize the importance for memory functions of the hippocampus and the surrounding cortical regions. Neuroanatomical data show that these cortical regions comprise one of two major efferent systems of the hippocampus and the major route by which information is exchanged between hippocampus and neocortex. Damage to the second efferent system of the hippocampus, the fornix [FX], and damage to one of its major targets, the mammillary complex [MB], produced only a transient effect on memory<sup>44</sup>.

This emphasis on the contributions of the hippocampus to normal memory functions is compatible with the suggestion that the amygdala also plays an important role. The amygdala has widespread connections to neocortex<sup>51</sup>, and a number of studies suggest that it is important in establishing affective associations to events<sup>52</sup> and in bringing together information from different modalities<sup>53</sup>. Amygdala damage could therefore be expected to affect performance on memory tasks that depend on these functions.

### **The hippocampus is an essential component of the memory system damaged in amnesia**

Recently, a favorable human case showed that damage limited to the hippocampus proper can cause a clinically significant memory impairment. Patient R. B. became amnesic in 1978 at the age of 52 when he suffered an ischemic event as a complication of open-heart surgery<sup>54</sup>. He survived the ischemia, but afterwards exhibited marked memory impairment. During the five years that he survived, he was tested repeatedly as part of ongoing work with amnesic patients in our laboratory. His Wechsler Memory Scale score was 90, and his Wechsler Adult Intelligence Score (IQ) was 110. He failed altogether on delayed prose recall, and he performed poorly on several other verbal and non-verbal tests of new learning ability. His memory impairment was easily noted, as he repeated the same stories within a short period of time and forgot incidents from each day's activities. He exhibited little retrograde amnesia, performing as well as or better than control subjects on tests of past public events. (A retrograde amnesia affecting as much as a year or two prior to his injury would not have been detected by these tests.)

When R. B. died in 1983 of congestive heart failure at the age of 57, we were encouraged by his family to conduct a thorough neuropathological examination. We obtained the brain within a few hours after death and examined it thoroughly for signs of pathological change. Approximately 4000 sections were cut, 400 of which were mounted on slides and stained for cells or fibers. The major finding was a complete bilateral depletion of neurons in the CA1 field of hippocampus (Fig. 5A). The lesion extended the entire rostrocaudal extent of the CA1 field, sparing the other hippocampal fields. Other important structures exhibited no signs of pathology (the amygdala, the mammillary complex,

the mediodorsal nucleus of the thalamus, and the basal forebrain nuclei). A small lesion was found in the left globus pallidus and in the right postcentral gyrus. There was also scattered loss of cerebellar Purkinje cells and some small acellular foci in neocortex. However, during five years of testing, we were unable to detect any signs of cognitive impairment except for memory dysfunction, and the CA1 lesion was the only lesion to which we could reasonably associate the memory impairment.

It is worth emphasizing that, whereas R. B.'s amnesia was clinically significant and easily detectable, amnesia can be more severe. For example, the surgical patient H. M.<sup>13</sup> has a more severe amnesia than did R. B., in agreement with the fact that H. M.'s damage involved not only the CA1 field but a large portion of the medial aspect of the temporal lobe. Moreover, our current study patients with amnesia resulting from an anoxic or ischemic event have more severe retrograde amnesia than did R. B. (Fig. 1). Because the hippocampal formation is particularly vulnerable to damage by anoxia or ischemia, and was damaged in R. B., it seems likely that the pathology in these other patients will include the CA1 field of hippocampus. However, because these patients are more severely impaired<sup>24</sup>, they probably have additional damage as well, perhaps within the medial temporal region. Because amnesia can vary in severity, it is important to be able to obtain quantitative data and to compare and contrast patients who have different lesions.

A carefully studied patient with severe amnesia caused by encephalitis (case D.R.B.) makes this point clearly<sup>55</sup>. D.R.B. has severe anterograde amnesia together with a severe, extensive retrograde amnesia spanning his entire life. He is reportedly unable to recall more than a few past experiences. Radiographic evidence showed that not only does this patient have bilateral damage encompassing the medial temporal structures linked to memory functions, but he also has bilateral damage involving most of the orbitofrontal cortex and all of the basal forebrain. In addition, the damage extends bilaterally into the anterolateral temporal lobes. It was suggested that the severe and extensive retrograde memory impairment is a consequence of damage to the basal forebrain and also to lateral temporal cortex, one of the regions likely to be involved in storing representations of permanent experience.

Findings from patient R. B., who had damage in the CA1 region, are especially useful because the neuroanatomy of the hippocampus is rather well understood. Although R.B.'s lesion was spatially limited, involving an estimated 4.63 million pyramidal neurons on each side of the human brain, such a lesion would 'open' the trisynaptic circuit (Fig. 5B). This circuit is an essentially unidirectional pathway that begins in the projection from entorhinal cortex to dentate gyrus and ends with return projections to entorhinal cortex from the CA1 and subicular fields. Some computation must occur in this circuitry if learning is to be accomplished in a normal way<sup>24,56</sup>. Recent pathological findings in Alzheimer's disease are consistent with this view. Prominent cell loss has been found in layers II and IV of entorhinal cortex, which would effectively isolate the hippocampus; and this pathology has been proposed as a cause of the

severe memory impairment that occurs early in the disease process<sup>57</sup>.

The output from hippocampus seems to be relayed to many areas of neocortex, that is, to areas believed to be involved in the processing and storage of acquired information (Fig. 5C). These cortical projections occur directly, by way of the entorhinal cortex, and indirectly by way of the parahippocampal gyrus and perirhinal cortex. Moreover, these projections are largely reciprocated – exactly what is needed if the hippocampus is to have access to activity occurring at information storage sites. It is perhaps through these connections that the hippocampus operates upon and participates in declarative representations. The relationship between hippocampus and neocortex begins at the time of learning and persists for a period of time after learning. During this time-limited period, representations become gradually independent of the hippocampus.

Information is accumulating about how memory is organized, what structures and connections are involved, and how they are involved. Facts and ideas developed at this level of analysis could guide quantitative, computational approaches, which could result in neural models and tests of specific mechanisms. In addition, information at this level of analysis should form a useful bridge between strictly psychological accounts of memory and neurobiological approaches that seek cellular and synaptic mechanisms of memory.

#### Selected references

- 1 Milner, B. (1972) *Clin. Neurosurg.* 19, 421–446
- 2 Weiskrantz, L. (1987) *Human Neurobiol.* 6, 93–105
- 3 Cermak, L. S., ed. (1982) *Human Memory and Amnesia*, Lawrence Erlbaum
- 4 Mayes, A. and Meudell, P. (1983) in *Memory in Animals and Humans* (Mayes, A., ed.), pp. 203–252, Van Nostrand Reinhold
- 5 Hirst, W. (1982) *Psychol. Bull.* 91, 435–462
- 6 Schacter, D. L. (1985) in *Memory Systems of the Brain: Animal and Human Cognitive Processes* (Weinberger, N., Lynch, G. and McGaugh, J., eds), pp. 351–379, Guilford Press
- 7 Squire, L. R. (1987) *Memory and Brain*, Oxford University Press
- 8 Squire, L. R. and Shimamura, A. P. (1986) *Behav. Neurosci.* 100, 866–877
- 9 Butters, N. et al. *Clin. Neuropsychol.* (in press)
- 10 Wechsler, D. (1987) *Wechsler Memory Scale – Revised*, The Psychological Corporation
- 11 Shimamura, A. and Squire, L. R. (1987) *J. Exp. Psych. Learn. Mem. Cog.* 13, 464–473
- 12 Talland, G. A. (1965) *Deranged Memory*, Academic Press
- 13 Scoville, W. B. and Milner, B. (1957) *J. Neurol. Neurosurg. Psychiatr.* 20, 11–21
- 14 Corkin, S. (1984) *Semin. Neurol.* 4, 249–259
- 15 Kaushal, P. I., Zetin, M. and Squire, L. R. (1981) *J. Nerv. Ment. Dis.* 169, 383–389
- 16 Squire, L. R. and Zouzonis, J. A. *J. Clin. Exp. Neuropsychol.* (in press)
- 17 Squire, L. R. (1982) *J. Exp. Psychol. Learn. Mem. Cog.* 8, 560–571
- 18 Schacter, D. L., Harbluk, J. L. and McLachlan, D. R. (1984) *J. Verb. Learn. Verb. Behav.* 23, 593–611
- 19 Shimamura, A. P. and Squire, L. R. (1986) *Behav. Neurosci.* 100, 165–170
- 20 Hirst, W. et al. (1986) *J. Exp. Psychol. Learn. Mem. Cog.* 12, 445–451
- 21 Janowsky, J., Shimamura, A. P. and Squire, L. R. (1987) *Soc. Neurosci. Abstr.* 13, 1454
- 22 Milner, B. (1971) *Br. Med. Bull.* 27, 272–277
- 23 Shimamura, A. P., Jernigan, J. L. and Squire, L. R. (1987) *Soc. Neurosci. Abstr.* 13, 1453
- 24 Squire, L. R., Shimamura, A. P. and Amaral, D. G. in *Neural Models of Plasticity* (Byrne J. and Berry W., eds), Academic Press (in press)
- 25 Milner, N. (1962) in *Physiologie de l'Hippocampe*, pp. 257–272, Centre Nationale de Recherche Scientifique
- 26 Brooks, D. N. and Baddeley, A. D. (1976) *Neuropsychologia* 14, 111–112
- 27 Corkin, S. (1968) *Neuropsychologia* 6, 255–265
- 28 Cohen, N. J. and Squire, L. R. (1980) *Science* 210, 207–209
- 29 Nissen, M. J. and Bullemer, P. (1987) *Cognitive Psychology* 19, 1–32
- 30 Cohen, N. J. (1984) in *Neuropsychology of Memory* (Squire, L. R. and Butters, N., eds), pp. 83–103, Guilford Press
- 31 Shimamura, A. P. (1986) *Q. J. Exp. Psychol.* 38A, 619–644
- 32 Damasio, A. R., Graff-Radford, N. R., Eslinger, P., Damasio, H. and Kassell, N. (1985) *Arch. Neurol.* 42, 263–271
- 33 Barbizet, J. (1973) *Human Memory and Its Pathology*, W. H. Freeman
- 34 Mair, W. G. P., Warrington, E. K. and Weiskrantz, L. (1979) *Brain* 102, 749–783
- 35 Victor, M., Adams, R. D. and Collins, G. H. (1971) *The Wernicke-Korsakoff Syndrome*, Blackwell
- 36 Butters, N. (1984) *Semin. Neurol.* 4, 1271–1273
- 37 Markowitsch, H. J. (1982) *Neurosci. Biobehav. Rev.* 6, 351–380
- 38 von Cramon, D. Y., Hebel, N. and Schuri, U. (1985) *Brain* 108, 993–1008
- 39 Mishkin, M. (1982) *Philos. Trans. R. Soc. London Ser. B.* 298, 85–95
- 40 Squire, L. R. and Zola-Morgan, S. (1983) in *The Physiological Basis of Memory* (Deutsch, J. A., ed.), pp. 199–268, Academic Press
- 41 Mahut, H. and Moss, M. (1984) in *Neuropsychology of Memory* (Squire, L. R. and Butters, N., eds), pp. 297–315, Guilford Press
- 42 Squire, L. R., Zola-Morgan, S. and Chen, K. *Behav. Neurosci.* (in press)
- 43 Aggleton, J. P. and Mishkin, M. (1985) *Exp. Brain Res.* 58, 190–197
- 44 Zola-Morgan, S., Squire, L. R. and Amaral, D. G. (1987) *Soc. Neurosci. Abstr.* 13, 1454
- 45 Aggleton, J. P. and Mishkin, M. (1973) *Neuropsychologia* 21, 189–197
- 46 Aggleton, J. P. and Mishkin, M. (1973) *Exp. Brain Res.* 188, 199–209
- 47 Zola-Morgan, S. and Squire, L. R. (1985) *Ann. Neurol.* 17, 558–564
- 48 Mishkin, M. (1978) *Nature* 273, 297–298
- 49 Zola-Morgan, S. and Squire, L. R. (1986) *Behav. Neurosci.* 100, 155–160
- 50 Murray, E. and Mishkin, M. (1986) *J. Neurosci.* 6, 1991–2003
- 51 Amaral, D. G. (1987) *Handbook of Physiology (Sect I: The Nervous System) (Pt V: Higher Functions of the Brain)* (Mountcastle, V. and Plum, F., eds), pp. 211–294, American Physiological Society
- 52 Mishkin, M. and Aggleton, J. (1985) *The Amygdaloid Complex* (Ben-Ari, Y., ed.), pp. 409–420, Elsevier
- 53 Murray, E. A. and Mishkin, M. (1985) *Science* 228, 604–606
- 54 Zola-Morgan, S., Squire, L. R. and Amaral, D. G. (1986) *J. Neurosci.* 6, 2950–2967
- 55 Damasio, A. R., Eslinger, P., Damasio, H., Van Hoesen, G. W. and Cornell, S. (1985) *Arch. Neurol.* 42, 252–259
- 56 McNaughton, B. L. and Morris, R. G. M. (1987) *Trends Neurosci.* 10, 408–415
- 57 Van Hoesen, G. W. and Damasio, A. R. (1987) *Handbook of Physiology (Section I: The Nervous System) (Pt V: Higher Functions of the Brain)* (Mountcastle, V. and Plum, F., eds), pp. 871–898, American Physiological Society
- 58 Zola-Morgan, S. and Squire, L. R. (1985) *Behav. Neurosci.* 99, 22–34
- 59 Zola-Morgan, S. and Squire, L. R. (1984) *J. Neurosci.* 4, 1072–1085

**Don't miss other TINS Special Issues!**  
**Subscribe now.**