Theories of episodic memory

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Theories of episodic memory need to specify the encoding (representing), storage, and retrieval processes that underlie this form of memory and indicate the brain regions that mediate these processes and how they do so. Representation and re-representation (retrieval) of the spatiotemporally linked series of scenes, which constitute an episode, are probably mediated primarily by those parts of the posterior neocortex that process perceptual and semantic information. However, some role of the frontal neocortex and medial temporal lobes in representing aspects of context and high-level visual object information at encoding and retrieval cannot currently be excluded. Nevertheless, it is widely believed that the frontal neocortex is mainly involved in coordinating episodic encoding and retrieval and that the medial temporal lobes store aspects of episodic information. Establishing where storage is located is very difficult and disagreement remains about the role of the posterior neocortex in episodic memory storage. One view is that this region stores all aspects of episodic memory *ab initio* for as long as memory lasts. This is compatible with evidence that the amygdala, basal forebrain, and midbrain modulate neocortical storage. Another view is that the posterior neocortex only gradually develops the ability to store some aspects of episodic information as a function of rehearsal over time and that this information is initially stored by the medial temporal lobes. A third view is that the posterior neocortex never stores these aspects of episodic information because the medial temporal lobes store them for as long as memory lasts in an increasingly redundant fashion. The last two views both postulate that the medial temporal lobes initially store contextual markers that serve to cohere featural information stored in the neocortex. Lesion and functional neuroimaging evidence still does not clearly distinguish between these views. Whether the feeling that an episodic memory is familiar depends on retrieving an association between a retrieved episode and this feeling, or by an attribution triggered by a priming process, is unclear. Evidence about whether the hippocampus and medial temporal lobe cortices play different roles in episodic memory is conflicting. Identifying similarities and differences between episodic memory and both semantic memory and priming will require careful componential analysis of episodic memory.

Keywords: episodic; representation; consolidation; recollection; familiarity; priming

1. INTRODUCTION

Episodic memory is memory for personally experienced events. The person who later remembers these events always consciously experiences them as an observer and also often as an actor. Most typically, events comprise interactions (including the experimenter's actions) over limited periods of time between various animate and inanimate objects in a specific context. They are experienced as a continuous series of linked scenes, each made up of several objects (which include the experimenter), located in particular spatial positions. The original experience may involve emotional arousal (e.g. fear) that was associated with the event and this emotion may be remembered when the linked scenes, constituting the episode, are later retrieved. The experimenter may also be vaguely aware during the episode itself of the more general spatio-temporal context in which the event is set and how it fits into his or her life story. Nearly always, events are automatically interpreted in a meaningful way through the use of available semantic knowledge. Events that are later remembered are, therefore, initially consciously experienced, either in association with emotion

or not, as a series of perceptual and semantic representations of objects, including the experimenter, that interact in space and time within a larger spatio-temporal context.

The rememberer is not only aware of the scenes that constituted an experienced event, but is usually also aware that s/he experienced these scenes at an earlier date, i.e. s/he has the conscious feeling that the scenes are being remembered. Rememberers will often know where an event fits into their life story by inference rather than by directly remembering their awareness of the event's general context at the time when it was originally experienced (there may have been no such awareness). Although episodic memory usually involves recall of a previously experienced event, it can sometimes involve recognition that something was personally experienced even when nothing extra is recalled. Thus, one can recognize that one experienced a particular event from a photograph or video of the occasion even though one may not recall anything else about it.

The boundaries of what counts as remembering an episode are, however, blurred. For example, one can recollect in detail the experience of learning each

component of a recently heard news story or word list. Such recollection clearly involves episodic memory. However, when specifically asked to recall recently encountered news stories or word lists, then it seems possible that just these things are remembered with very little, if any, reference to the episode in which the information was learned. Such remembering seems to be at least mainly of semantic, rather than episodic, information. Most people seem to assume that word-list or story recall are obviously examples of episodic memory. Their assumption is probably based on the belief that in order to know which word list or story to retrieve, one needs to retrieve some contextual (episodic) information. However, even if no specific cue is given (e.g. what was the story you just heard or what words were in the word list you just heard?), people may find that the recently encountered factual information just pops into their minds without the need to retrieve associated information about the learning context. The issue is an empirical one although it is difficult to resolve. Two related questions need to be answered. What proportion of the retrieved information is semantic and what proportion is episodic? How much, if at all, does retrieval of semantic information critically depend on cueing provided by retrieved and associated episodic information? Although the proportion of specifically episodic information that is retrieved, and how much it increases the retrieval of semantic information, should be influenced by instructions and the kind of cueing given, its role in story and word-list recall may be considerably less than is commonly assumed.

Any theory of episodic memory should characterize: (i) the encoding, storage, and retrieval processes that mediate this complex form of memory; (ii) the brain regions that perform each of these processes and how these regions interact with each other so that the processes work in an integrated manner; (iii) how the neurons within each relevant brain region interact so as to perform specific processes, and how the neurons in different regions interact so as to integrate the various processes that mediate episodic memory; (iv) how these episodic memory processes are similar to and/or differ from the processes that mediate other putative forms of memory, and to what extent the same brain regions mediate memory for episodes and other kinds of information.

This paper focuses on theoretical characteristics (i), (ii) and (iv) and has the following structure. First, the processes and information involved in making episodic representations at encoding will be outlined and the underlying brain regions considered. Second, major views about the psychological and physiological processes underlying consolidation and long-term storage of episodic representations will be outlined and differing views concerning where these processes are located in the brain are discussed. Third, views about how retrieval is achieved and the feeling that retrieved episodes are being remembered is produced. Which brain structures mediate these processes will be discussed. Where relevant, the similarities and differences between episodic memory and both semantic memory and priming will be discussed whilst assessing these theories. Each section will highlight where there are theoretical disagreements, or processes

and their neural bases that have been poorly specified, and will consider how lesion and functional neuroimaging research is helping with theory development in these problem areas.

2. REPRESENTING EPISODES AT ENCODING: PROCESSES, INFORMATION AND BRAIN REGIONS

Encoding episodes typically involves representing a sequence of linked scenes that occur over a short period of time. As such, it requires the representation of objects perceived from the observer's perspective in different positions that change across time. In episodes experienced by humans, visual information is usually most salient. However, information from other senses often plays a key role and all this sensory information is likely to be interpreted automatically by the observer in terms of available semantic knowledge, and may be coloured by emotion. These experiences are usually meaningfully interpreted. The major feature of episodic representations, therefore, is that they associate together very different kinds of information, which include perceptual and semantic aspects of objects and how these are located in space and time relative both to each other and the self. The experimenter deploys attention so that only some components of the episode will reach consciousness. How attention is deployed will determine how well aspects of the episode get into memory. It seems likely that spatial and temporal information will be represented in more than one kind of way when episodes are experienced. Spatial locations will, of course, be experienced from the observer/actor's perspective, i.e. egocentrically, but there may also be an allocentric awareness of objects' positions in each scene. A temporally ordered sequence of scenes will be experienced, but the observer/actor will also be aware of the duration of the different scenes constituting an episode.

Tulving (1995) has argued that episodic encoding depends on information being processed successfully through semantic memory. So if semantic memory is deficient, as in semantic dementia, episodic memory will be impaired. However, although it is trivially true that subjects will not remember semantic features of episodes that were not represented in the first place, there is good evidence that memory for perceptual aspects of episodes is relatively normal even when much of the episode cannot be meaningfully represented. Thus, patients with semantic dementia, who cannot meaningfully interpret episodes, can encode and later recognize the perceptual features of experienced objects relatively normally (e.g. Graham *et al.* 1997). It seems likely that spatio-temporal contextual features of experienced episodes can also be encoded and later remembered relatively normally in patients with semantic memory deficits, although this remains to be shown. Adequate representations of perceptual features and spatio-temporal context can probably be made without semantic processing. However, meaningfully interpreting an episode should help to link its components in an integrated representation, which may facilitate later recall more than recognition.

Functional neuroimaging evidence is consistent with the widely held view that the representations of episodes and their components, made during encoding, are based on complex patterns of neural activity that are primarily

located in distributed sites within those parts of the posterior neocortex that represent both meaningfully interpreted and relatively uninterpreted sensory information (e.g. Montaldi *et al.* 1998a). Episodes are, however, not only complex but highly variable in their information content, so which posterior neocortical regions are activated at encoding depends on the nature of the experience (see Mayes & Montaldi 1999). The precuneus has often been found to activate during episodic retrieval (e.g. Fletcher *et al.* 1995) so it is interesting that it has also been found to activate during the encoding of complex scene pictures and that its level of activation correlates with subsequent memory for the pictures (Montaldi *et al.* 1998b). This study's findings suggest that: (i) episodic retrieval may reactivate the posterior neocortical structures that were activated during the episode's initial representation, and (ii) the richer the initial representation as indicated by the level of precuneus activation the better the memory. What information precuneus activation represents is unresolved, but the activation was relative to that produced by the matching of similar pictures—so it may involve an association between visual images and their verbal semantic interpretation. Future work needs to identify more precisely where different episodic components are represented in the posterior neocortex, and how inter-component associations are represented. Also, the degree to which encoding activations are regenerated at retrieval needs to be determined.

It is unknown how awareness of scenes and their components is generated by the brain. It also seems likely, however, that neocortical activity is vital for such awareness even if subcortical activity is also essential. Emotional arousal, which may be experienced during an episode, is believed to depend on activity not only in neocortical sites but also in limbic system regions such as the amygdala (e.g. Gloor *et al.* 1982).

The frontal neocortex is also known to be active when episodes are represented (e.g. Kapur *et al.* 1994). It is widely believed that this activity controls executive functions, such as how attention is directed, which through 'top-down' influences on the more posterior sensory cortices coordinates which components of an episode are represented. It has been suggested that these 'top-down' influences play a key role in integrating the sensory and contextual components of the episodic representation (see Squire & Kandel 1999). Whether the frontal neocortex also plays a more direct role in representing some aspects of episodes, notably certain contextual components such as their temporal features, is uncertain. Although the neural mechanisms of spatial representation are quite well understood (see Burgess *et al.* 1997), those underlying the perception of temporal order and duration are much less so. It remains an interesting possibility that components of complex episodic representations are represented together through their spatiotemporal relationships within the frontal neocortex.

The medial temporal lobes have also been related to processing that leads to contextual memory (see Mayes 1988). However, although this region is often activated when episodic information is encoded (e.g. Montaldi *et al.* 1998a,b), it is unclear whether this activation reflects the processes involved in representing context and other

kinds of episodic information or the early consolidation processes that put this information into long-term memory. Even if the activation does reflect representational processes, this does not prove that either the hippocampus or the medial temporal lobe cortex plays a critical role in making episodic representations. Nevertheless, Murray & Bussey (1999) have argued exactly this in their proposal that the perirhinal cortex plays an essential role in the making of high-level visual object representations. According to this proposal, without a perirhinal cortex this information cannot be represented at all and there will be a high-level visual agnosia. This cortex certainly receives an appropriate convergence of high-level visual object information from the ventral stream (as well as inputs from other sensory modalities) to enable it to perform the postulated integrative operations efficiently. As indicated above, this does not establish that the perirhinal cortex plays a critical role in high-level visual perception. To do this, one needs to show that high-level object information does not converge at neocortical sites as well because these structures may be able to perform the appropriate integrative operations in a sufficiently similar way. This has not been shown convincingly. Also, at least in humans, there is some preliminary evidence that patients with extensive bilateral lesions to the medial temporal lobe cortices show normal short-term memory, let alone preserved matching abilities, for complex non-meaningful visual stimuli despite having very severe recognition deficits at longer delays (Buffalo *et al.* 1998). Murray & Bussey (1999) have questioned whether this task tapped the high-level integrative functions that they believe are performed by the perirhinal cortex alone, so further work with human patients is needed to ensure that these functions are tapped in an unequivocal way.

An argument similar to that of Murray & Bussey (1999) could be made about the hippocampus and entorhinal cortex. This region receives a convergence of spatial and object-related information, which may remain separate in the perirhinal and parahippocampal cortices, so it might be argued that associations, such as those necessary for representing scenes, can only be made in the hippocampus and entorhinal cortex. Information represented in different neocortical regions may particularly converge in the hippocampus–entorhinal cortex complex. If so, hippocampal–entorhinal cortex lesions should cause an inability to perceive associations between these kinds of information unless the reciprocal connections which exist between the perirhinal and parahippocampal cortices are sufficient to integrate spatial and object information outside the hippocampus–entorhinal cortex complex (Suzuki & Amaral 1994). However, even amnesics with lesions that include the perirhinal and parahippocampal cortices as well as the hippocampus–entorhinal cortex complex often show preserved intelligence and can answer questions about the locations of object pictures, following brief presentations, as accurately as control subjects when tested immediately (Mayes *et al.* 1993). This suggests that neocortical regions may also be able to perform basically similar object-location integrative operations. Nevertheless, as with the perirhinal cortex encoding hypothesis, it may prove difficult to detect subtle encoding deficits because subjects may use

compensatory strategies based on slightly less appropriate neocortical representations.

3. CONSOLIDATION AND STORAGE OF EPISODIC REPRESENTATIONS

(a) *Psychological and physiological storage processes*

Only a tiny fraction of experienced episodes are put into long-term memory storage and, even with those that are, only a small proportion of the experienced episode is later retrievable. As already discussed, the extent to which one retrieves episodic (contextual) information when trying to remember a recently heard story, and how memory of the story is improved by the availability of episodic information, is uncertain. However, if given appropriate instructions and cues (e.g. 'tell me about the story involving the woman who was robbed'), very little, if any, episodic information may need to be recalled, so the rememberer may be showing relatively pure semantic memory. The extent to which story memory is affected by context-dependent forgetting may provide one indication of how much, if at all, retrieval of semantic story information is being influenced by the availability of episodic information. The boundaries of episodic memory are, therefore, vague and hard to identify, but one must surely show some remembering of the original experience, i.e. perceptions, their temporal and spatial features, and usually their interpretations. In other words, however feebly, episodic memory must involve re-experiencing or reliving the original episode. The degree to which long-term episodic memory is typically attenuated requires further exploration. Although one can later recall that certain sensations and emotions were felt in a remembered episode, and that this episode occurred in a specific context within one's life story, it is unclear how much this ability derives directly from being able to retrieve the contents of the earlier episodic experience and how much it derives from inferences partially based on personal semantic knowledge.

Episodic memories, however fragmentary, can be formed without deliberate intent on the basis of the single experience of the episode, although memories are often strengthened by subsequent rehearsals. Part of an experienced episode may be retained in memory for life and memory is present from immediately after the occurrence of the episode. It is, therefore, of interest that Baddeley (2000) has recently proposed that working memory probably includes an episodic buffer that can hold episodic information for a few seconds or perhaps minutes. It is plausible to postulate that working memory buffers may be mediated by a continuation of the pattern of neural activity that originally represented the experience of the speech pattern, visual pattern or episode. Unless one believes, as some do (e.g. Miller & Matzel 2000), that a relatively stable memory store can be largely created in less than a second, one must postulate a short-term storage mechanism like continued neural activity, which can come into existence immediately, and maintains the memory until a more stable store is produced. The postulate is supported by single unit recording studies in monkeys which indicate that activity in sensory neocortical regions such as the TE and certain frontal regions continues for some seconds following stimulus presenta-

tion. Whereas continued activity in the TE was found to be disrupted by presenting further visual stimuli during the delay, this was not found with frontal cortex activity (see Squire & Kandel 1999). The frontal region may play a 'top-down' controlling role that enables the sensory representations produced in the TE and other posterior neocortical sensory regions to be sustained across filled delays for a short period, the duration of which cannot yet be specified. With an episodic buffer, frontal regions might also integrate the representation, particularly the linked sequence of scenes.

Evidence from extensive animal research suggests that long-term episodic memory depends on the growth of new synapses, a process which is mediated by the synthesis of new proteins (Bailey *et al.* 1996). This consolidation process will take some time to complete, but there is evidence that memories can be maintained for intermediate durations by subtler changes in synaptic efficacy (such as shifts in the location of vesicles in relation to the active zone), which do not depend on new protein synthesis and can be achieved relatively rapidly (see Squire & Kandel 1999). The strength of episodic memories varies greatly. Some of this variation will relate to the richness and coherence of the original representation, but it will also depend to a large extent on the strength of the consolidation changes that lead to the growth of new synapses where the memory is stored. Emotional arousal and arousal generally is known to strengthen episodic memory (McGaugh 2000). There is evidence that such arousal slows forgetting in the first hour or so following learning (e.g. Kleinsmith & Kaplan 1963), which is consistent with the arousal enhancing the protein-synthesis-dependent consolidation process.

(b) *Neuroanatomy of storage processes*

Where do the storage changes that underlie long-term episodic memory occur in the brain? There is a widely held view that information is stored where it was originally represented in the brain (e.g. Gaffan & Hornak 1997) so that there should be a heavy overlap between the neural array that represents an episodic experience as it occurs and the array that is reactivated during later remembering of the episode. A corollary of this view is that basically the same array will be reactivated whether an episode is remembered immediately, after a short delay, or after a delay of days or even years, provided that the same information is retrieved. There is some direct support from functional neuroimaging studies that the arrays that represent and re-represent experienced episodes lie primarily in the posterior neocortex (e.g. Conway *et al.* 1999). However, there is no agreement about whether the storage changes are confined to these representing regions and whether storage locations change over time. Three broad views can be identified.

The first view is that the storage changes that enable episodic memory to be shown at any stage following experience primarily lie within neural arrays located in the posterior neocortex. This view is the least popular of the three broad positions because most researchers believe that organic amnesia is caused by a storage deficit. Amnesia is caused by brain lesions in any of a number of regions: the medial temporal lobes, the midline diencephalon, the basal forebrain, and possibly the ventromedial

frontal cortex (see Mayes 1988). One possibility is that although episodic information is not stored in the regions damaged in organic amnesia, these regions (perhaps particularly the hippocampus and the medial temporal lobes) are involved in orienting produced by the novelty that episodes usually involve (e.g. Gray 1982). Such orienting could lead to the arousal without which the key consolidation processes, which are critical for long-term episodic memory, do not occur. In other words, the regions implicated in organic amnesia, and perhaps particularly the hippocampus and the medial temporal lobes, modulate the consolidation that primarily occurs in the posterior neocortex.

If this view is correct, then damage to a structure such as the hippocampus should not impair memory storage. Hippocampal damage impairs the acquisition of episodic memory and also the retrieval of episodic memories acquired normally before the damage occurred, so it is hard to know whether the damage disrupts the representation of episodic information at encoding, its consolidation into long-term memory, its maintenance in long-term storage, its retrieval, or some combination of these processes. In particular, it is hard to establish from lesion studies whether the hippocampus is a site where at least some kinds of episodic information are stored (e.g. contextual information). One attempt to address this question has been developed by Riedel *et al.* (1999). These workers used a water-soluble antagonist of AMPA/kainate receptors to inactivate the dorsal hippocampus of rats in a reversible fashion. They were able to show that temporary inactivation during training in a water maze or later, during testing for memory of the maze, disrupted memory for the location of the hidden platform. This implies that the hippocampus plays a critical role in both the acquisition and retrieval of spatial memory. More strikingly, they showed that inactivating the dorsal hippocampus for seven days, beginning either 1 or 5 days after the end of training, disrupted memory even though this was tested when the hippocampus seemed to be working normally. Riedel *et al.* (1999) concluded that prolonged hippocampal inactivation was either disrupting a slow consolidation process that was stabilizing the spatial memory or it was degrading the already present synaptic changes underlying long-term spatial memory. However, it remains uncertain whether these slow consolidation or long-term storage maintenance processes occur in the hippocampus itself or in a connected brain region where they may be disrupted if the hippocampus is inactive for a prolonged time. Although the reversible inactivation method is excellent for identifying when the hippocampus is involved in memory processing, it alone cannot identify with confidence whether the hippocampus is a storage site for aspects of episodic information.

There is one way in which this uncertainty about where long-term storage is located can be addressed. This depends on the use of more effective brain transplant procedures involving the use of stem cells, which enable the lost neuronal architecture of damaged structures to be restored to a good approximation. If (i) lesioning the hippocampus causes loss of memory for a component of episodic memory, and (ii) transplanting tissue restores the lost hippocampal neuronal architecture and restores the lost memory, then that memory could not have been

stored within the hippocampus. This is because storage would involve altered synaptic connections in the storage site, and these could not be replaced by transplanting new tissue. An effect precisely of this kind has been found in monkeys. Thus, Virley *et al.* (1999) found that excitotoxic CA1 lesions impaired already learned conditional discriminations in which two different pairs of identical objects signalled reward in either a left or right food well. Foetal CA1 transplants as well as stem cell transplants were found to restore memory of these previously learned discriminations to apparently normal levels. More precisely, the animals in whom lost hippocampal CA1 tissue had been replaced by transplanted tissue relearned the preoperatively trained discriminations to criterion as fast as unlesioned control animals. Assuming that the transplant recipients and their controls relearned at the same rate, the former animals had recovered their memories to normal levels even if memory for the discrimination was not present on initial re-testing.

This result strongly suggests that the discrimination memory was not stored in the CA1 field of the hippocampus of these monkeys. It could, however, have been stored in another hippocampal field, e.g. CA3, and the memory not been expressible initially because the CA1 lesion disrupted the hippocampal circuitry. The conclusion that the memory was not stored in CA1 would not only apply if all of the following conditions obtained. First, the memory was earlier stored in CA1 and possibly other sites as well as in CA3 in a distributed fashion, but could not be expressed when storage in CA1 was removed by a lesion. Second, following the transplantation, all the continuously intact brain sites that contained the remaining distributed memory were somehow able to restore the missing memory to the virgin transplanted CA1 tissue so that the whole distributed memory could be fully expressed. Nevertheless, with this one possible exception, the principle is clear. Provided stem cell transplantation does enable lesioned neuronal architecture to be reasonably restored, then the procedure provides the first powerful means of determining whether storage rather than merely processing and representation are mediated by a specific structure. If transplantation fails to restore pre-lesion memories, but enables similar ones to be acquired normally, then the damaged structure is very likely to be the site of storage.

Despite the shortage of direct supporting evidence, it seems probable that the hippocampus and medial temporal lobes do play a role in storing certain kinds of episodic information. The region's possible role in upregulating episodic storage processes in the neocortex does not mean that it cannot also store other kinds of episodic information. It therefore seems likely that the medial temporal lobes do play a role in storing episodic representations but the possible storage role of the posterior neocortex has been insufficiently appreciated. The two regions may store different components of episodic information.

The second view, which is perhaps the most widely believed, is that long-term episodic memories, dependent on new protein synthesis and storage changes at synapses, initially occur in the medial temporal lobes and hippocampus but that, as a result of voluntary and involuntary rehearsal over long periods of time, storage changes gradually occur primarily in the posterior neocortex so

that retrieval ceases to depend on the medial temporal lobes (see Squire & Alvarez 1995). The view presupposes that whereas the medial temporal lobes are very plastic, at least some sites in the neocortex are much less so. Most frequently, it is interpreted as proposing that the medial temporal lobes initially store a kind of index. This index enables the different neocortical regions that represent the distinct components of a remembered episode to be activated together despite the fact that there are no direct links between them initially. Gradually, the associative links provided by the medial temporal lobes cease to be necessary because direct links develop slowly through the neocortical plastic process. There is no agreement about whether the medial temporal lobes cease to be involved in storage altogether and, if so, whether this is because the stored memory is overwritten by later memories or whether it fades rapidly even without such interference (e.g. Squire & Alvarez 1995). The time scale of this transfer in which memory storage gradually develops in the posterior neocortex is only loosely specified, as is whether the key factor is the number of rehearsals rather than the passage of time *per se*.

The third view states that some aspects of episodic information (e.g. spatial context) depend on the medial temporal lobes for their storage and retrieval for as long as they are in memory, whereas other aspects of episodic information (e.g. feature information) depend on the neocortex for their storage and retrieval for as long as they are in memory (see Nadel & Moscovitch 1997). According to this view, those aspects of episodic information which are initially stored in the medial temporal lobes are not transferred to neocortical storage as a function of rehearsal and time. Instead, it is proposed that rehearsal causes these kinds of episodic information to be stored within the medial temporal lobes in an increasingly redundant fashion so that episodic memory becomes less vulnerable to damage in this region as time passes. Transfer of storage does not occur with rehearsal and the passage of time presumably because the relevant components of episodic representations only converge in the hippocampus and, to a lesser extent, the parahippocampal and perirhinal cortices and so can only be stored in these structures. Although the view postulates that the medial temporal lobes store marker information (e.g. about spatial context), which coheres the feature information that is stored in the neocortex, it does not specify whether the medial temporal lobes are critical for the initial representation of spatial context. In other words, although the region is critical for encoding spatial context into long-term memory (i.e. consolidation), it is not clear whether it is critical for experiencing and representing spatial context normally during episodic experience (encoding *per se*).

The three views about where episodic memories are stored do not specify in much detail where and how the components of episodic representations are stored and associated together, although this is beginning to be done by neural network models (e.g. O'Reilly *et al.* 1998). It has also been argued that the perirhinal cortex mainly receives high-level sensory object-related inputs from the posterior association neocortex and plays an important role in object memory, whereas the parahippocampal cortex mainly receives spatial information inputs and plays an

important role in spatial memory (Zola-Morgan & Squire 1993). Spatial and object information may be linked together in memory in the hippocampus and perhaps in the entorhinal cortex (see Mayes *et al.* 2001; Vargha-Khadem *et al.* 1997). However, much more needs to be specified about not only where, but also how the components of episodic memory are put into memory storage.

Most researchers believe that the hippocampus and medial temporal lobes are involved in storing episodic information and that long-term potentiation may indicate the mechanism of storage (e.g. Morris & Frey 1997) although proving these two proposals is very difficult. If the storage view is correct, determining whether episodic memories remain stored in the medial temporal lobes for as long as they last, or whether in time they transfer to the neocortex, is also likely to prove difficult. The Squire & Alvarez (1995) view predicts that amnesics with selective medial temporal lobe lesions, and particularly hippocampal lesions, should show relatively normal recall and recognition of pre-morbid episodic memories that were acquired sufficiently long before their trauma. Tests of this prediction have yielded conflicting results and although most studies find evidence of relative sparing of older memories, the time-scale is typically one of decades (see Mayes 1988). For example, on the one hand, Teng & Squire (1999) found that a 70-year-old amnesic with nearly total bilateral destruction of his medial temporal lobes was able to recall routes normally that had been learnt 50 years before, although his more recent route memories were grossly impaired. In contrast, Cipolotti *et al.* (2001) reported that a patient with damage apparently mainly confined to the hippocampus showed no relative sparing of episodic memories that were decades old. Conflicting results like this might arise because:

- (i) Subtle, but important, brain damage to neocortical structures is being missed. Such damage can cause retrograde amnesia with no sparing of older episodic memories and could do so because it disrupts representation and also possibly the storage of episodic information (see Nadel & Moscovitch 1997).
- (ii) Some patients have an atypical and perhaps reorganized neocortically based storage system for older episodic memories.
- (iii) Only some features of episodic memory show transfer whereas others do not. For example, it has been argued that older premorbid memories are not spared in amnesics when detailed episodic recall or memory for less prominent landmarks on routes is the measure, but sparing can occur for gist (e.g. Rosenbaum *et al.* 2000).

The time-scale of transfer suggested by the majority of studies of retrograde amnesia that do find sparing of older episodic memories is of the order of decades (see Nadel & Moscovitch 1997). If the transfer process were as slow as this, transfer would have taken longer than the typical human lifetime in prehistoric times. Other interpretations for very long temporal gradients with retrograde amnesia have therefore to be considered. If transfer does occur, it is surely likely to operate over a shorter period of between months and a few years rather than a few decades. Such shorter transfer times are supported by some animal studies. For example, rats were found to

show more hippocampal and less temporal and frontal neocortex activation when they retrieved five-day-old memories than when they retrieved 25-day-old memories (Bontempi *et al.* 1999). There is evidence for a subgroup of amnesics who show basically normal episodic and factual memory at delays of around one day and possibly longer, but then over a period of weeks show accelerated forgetting (e.g. Kapur *et al.* 1996). In unpublished work, the author and his colleagues found that one such patient, who had hippocampal sparing and major damage to her anterior temporal cortex, showed basically normal memory at delays of one day but severely impaired memory after delays of three weeks. She also showed impaired recall of information to which she had been repeatedly exposed over periods of several years. One interpretation of this memory impairment is that affected patients are unable to transfer episodic and factual memories to their posterior neocortices although initial storage in the medial temporal lobes is preserved.

Neuroimaging studies of retrieval of recent and remote episodic memories in humans have, however, typically looked at comparisons between memories years and decades old, respectively. An exception was a study which found that recognizing items studied immediately before testing produced no more medial temporal lobe activation than recognizing items studied one week before (Stark & Squire 2000a). If transfer occurs, it is unlikely that it could be completed in one week even if rehearsal is intense. Two other studies have found no difference in medial temporal lobe activation even when the older memories that subjects recalled were years older than the more recent memories. In the first study, young subjects recalled autobiographical incident memories formed roughly 20 years and just under a year earlier, respectively (Conway *et al.* 1999). In the second case, recall of similar memories formed between about one and four years earlier and over 30 years earlier, respectively, was compared (Ryan *et al.* 2001).

Mayes *et al.* (2000) found a similar lack of difference in the hippocampal and parahippocampal cortex activation produced when subjects recalled personally relevant routes learned about 30 years earlier and routes learned in the past few months. Although the results of this last study seem to conflict with evidence that remote spatial route recall may be relatively normal following extensive medial temporal lobe lesions (Teng & Squire 1999), there may be no conflict. The subjects in the neuroimaging study visualized following the remembered routes. Rosenbaum *et al.* (2000) have reported that patient K.C., who has extensive brain damage including severe bilateral atrophy of the hippocampus, showed relatively normal memory for the allocentric spatial features of the locality which had been his neighbourhood for almost 40 years. He was unable to remember details about local routes, however, which would probably have prevented him from visualizing remembered routes. If visualization does involve retrieval of aspects of spatial memory that are critically dependent on the medial temporal lobes for their storage, then the neuroimaging and lesion studies are not in conflict. However, the neuroimaging study did find that activity in a region that may have included the retro-splenial and posterior cingulate cortex was greater when more recent spatial routes were recalled.

In an unpublished neuroimaging study of episodic and semantic retrieval, however, the author and his colleagues have found that recalling recently acquired (weeks to a few months) episodic incident memories produced slightly, but significantly, more left hippocampal activation than recalling remote (5–10 years) episodic incident memories. Bilateral parahippocampal cortex activation relative to baseline remained unchanged, but activation in the retrosplenial–posterior cingulate cortex and precuneus also reduced. Although these results seem to support the view that episodic memory storage transfers to the posterior neocortex, interpretation is difficult. A potential problem with all neuroimaging studies of recent and remote memory retrieval is that retrieval is accompanied by re-encoding which may obscure retrieval-related changes in activation. There would be no problem if re-encoding and retrieval were physiologically identical in the hippocampus, and resolution may still be possible if Lepage *et al.* (1998) are correct to suggest that encoding occurs slightly more anteriorly in the hippocampus than retrieval. Nevertheless, it is safest to conclude that the case is still not proved that episodic storage transfers to the posterior neocortex with time and rehearsal.

There are several further areas of disagreement about how and where episodic storage is achieved, and key processes are not characterized in sufficient detail. First, it is unclear where and how episodic storage is modulated. Is episodic storage in both the posterior neocortex and medial temporal lobes modulated, and, if so, what structures mediate this modulation? It is also unclear what structures, as well as what psychological triggers (other than orienting to novel information), are involved in the modulation of episodic storage.

There is good evidence from lesion and functional neuroimaging studies that the amygdala modulates the activity of the hippocampus (as well as of other structures) in response to the presence of emotionally arousing stimuli during encoding so as to enhance later episodic memory. For example, Phelps *et al.* (1998) have found that a patient with bilateral amygdala damage, unlike control subjects, showed no slowing of forgetting for emotionally arousing words, although she showed a normal improvement of episodic memory when emotion provided an organizing principle at encoding. Relatedly, in a positron emission tomography (PET) study, Cahill *et al.* (1996) found that subjects who later showed better memory for emotionally arousing stimuli, but not neutral ones, showed more amygdala activation during encoding. Similarly, Hamann *et al.* (1999) found that the amygdala activation found during encoding of emotionally arousing stimuli correlated with the subsequent memory advantage shown for these stimuli relative to neutral, non-arousing stimuli. This correlation was not found with arousing but non-emotional stimuli. Amygdala activation was also found to correlate with hippocampal activation during encoding.

The amygdala may, therefore, modulate storage of episodic information by the hippocampus specifically in response to emotionally arousing stimuli. However, as already discussed, it is disputed whether or not the hippocampus itself modulates posterior neocortical storage sites, and whether the basal forebrain, midbrain and possibly the frontal neocortex (in a controlling role) are

involved with modulating posterior neocortical storage sites in response to different kinds of arousal. This latter possibility is supported by the finding that transection of the fornix, amygdala and anterior temporal stem, which disconnected the temporal cortex from the potentially modulating influence of the basal forebrain and midbrain, caused profound impairment in monkeys on several memory tests, including one that involved scene-related object memory (Gaffan *et al.* 2001). A companion study found that crossed unilateral lesions of the basal forebrain and either the inferior temporal or frontal cortex caused an impairment in memory for object–reward associations as severe as that produced by the fornix, amygdala, temporal stem transection (Easton & Gaffan 2001).

One interpretation of these results is that the frontal cortex controls the basal forebrain, which in turn upregulates the inferior temporal cortex's ability to store episodic memories. This claim, which is consistent with the view that initial storage of different components of episodes depends on both medial temporal cortex and temporal neocortex (see Mayes *et al.* 1985), warrants careful examination. It leaves open the possibility that the components initially stored by the medial temporal lobes are slowly transferred to the posterior neocortex.

Second, it is unclear to what extent the storage of semantic and episodic information differ from each other, both in terms of where storage occurs and how it is mediated. There are two issues here: (i) are there differences which relate to the kinds of information being stored and (ii) are there differences which relate to the amount of rehearsal which that information typically receives over long periods of time? Implicit in the view that storage and encoding sites for the same information are very similar is the universal belief that different information is processed and represented by different neural arrays. Semantic information comprises many kinds of knowledge, such as word meanings and knowledge about famous paintings, which are presumably stored in different brain regions. Therefore some kinds of semantic information are much more similar than others to episodic information (which also varies considerably), and so presumably show greater overlap of storage sites. Most typically, episodic memory involves retrieval of perceptual information in spatio-temporal settings, whereas semantic memory, albeit with important exceptions, does not. Episodic memory may also be coloured by emotion and some degree of self-awareness. It is unclear to what extent these two features will require storage in regions not involved in storing factual information. Also, although semantic memory cannot include self-awareness, it can surely be coloured by emotion without becoming episodic memory. For example, one's knowledge of certain historical characters, such as Hitler or Stalin, may be associated with disgust and hatred. The nature of this emotional colouring is, however, different from that involved with episodic memory because no specific emotional experience is being remembered.

Semantic information typically receives far more rehearsal than does episodic information over long periods of time, although episodic memories of great personal significance also typically receive a large amount of rehearsal over the years. Nadel & Moscovitch (1997) have argued that whereas episodic information

depends on hippocampal storage for as long as episodic memory lasts and regardless of how much rehearsal occurs, the storage of factual information may be re-organized over time until it depends only on the neocortex. In other words, they agree with Squire & Alvarez (1995) that semantic memory becomes independent of the medial temporal lobes with rehearsal over relatively long time periods because neocortical storage is gradually strengthened until it alone can effectively support semantic retrieval.

Vargha-Khadem *et al.* (1997) have reported that three young people, who suffered early and relatively selective hippocampal damage, showed impaired acquisition and retention of episodic memories. Despite this clear episodic memory deficit, these subjects developed relatively normal long-term semantic memories for facts to which they would have been repeatedly exposed over long time periods, as indicated by their relatively normal language, reading, writing and general knowledge. The subjects were impaired at recalling stories to which they had been exposed once only a short while earlier. Unless one cannot recall such stories except by recalling some of the experiential context in which they were learned, their recall is likely to depend on semantic memory. The findings, therefore, suggest that although semantic memory initially depends on the hippocampus, the slow repetition-rehearsal-dependent transfer process works normally without the hippocampus.

Two unpublished studies by the author and his colleagues, however, point to the need for caution in interpreting the findings. In the first study, a patient, who had suffered a relatively selective hippocampal lesion in her adult years, was, like the patients of Vargha-Khadem and her colleagues, impaired at recalling stories after a brief delay following study. This patient was further impaired at recalling new word meanings after a brief delay even when given up to ten learning trials. But the patient was also mildly impaired at recalling word meanings (e.g. MIR) to which she had been repeatedly exposed over a period of several years. That semantic memory in the patient should have been impaired for factual information repeatedly encountered in this way is plausible because the hippocampus is critical for recall, and hence rehearsal, and so should play a role in 'teaching' the neocortex.

In the second study, which used a block design functional magnetic resonance imaging (fMRI) procedure, it was found that even after healthy young male subjects had been given one week's intensive practice in learning new word definitions, their recall still produced a larger blood-oxygen-level-dependent (BOLD) response than a baseline condition on both sides of the hippocampus. Recall of equivalently practised and slightly older episodic memories also activated the hippocampus bilaterally and significantly more so on the right than did the verbal semantic retrieval. As with episodic memory, recall of these recently acquired semantic memories produced slightly more hippocampal activation (on the right) than did recall of remotely and heavily overlearned word meanings. Again resembling episodic memory, recall of the recent semantic memories activated the retrosplenial–posterior cingulate cortex and precuneus regions more than did recall of remote but similar

semantic memories. Activation of all these regions was less with semantic recall and it also reduced more over time in the retrosplenial–posterior cingulate cortex and precuneus regions. Interestingly, recall of recently acquired memories for geographical maps also activated the right hippocampus slightly more than recall of remote over-learned map memories. This neuroimaging study, therefore, suggests that both verbal and geographical semantic memory is similar to episodic memory in several ways. However, the study also found differences between the two kinds of memory, regardless of whether episodic memory involved recalling standard episodes or experiences in following specific routes and semantic memory involved recalling word meanings or maps. Episodic recall produced more activation than semantic recall in the hippocampus, parahippocampal cortex, inferior temporal neocortex, precuneus, posterior cingulate and medial frontal neocortex bilaterally and the ventrolateral frontal neocortex on the right. Whether these effects indicate qualitative or quantitative differences in what is stored requires further investigation.

Third, there is disagreement about whether primed information is stored in similar sites to episodic information. Humans show priming of semantic as well as perceptual information, so this form of memory involves retrieval of kinds of information that may sometimes form components of an episodic memory. However, in priming, memory is revealed by the efficiency with which previously experienced information is processed when re-encoded without the rememberer needing to be aware that this information has been encountered before. Retrieval of episodic memories, in contrast, is usually accompanied by the feeling that the episode has been experienced before. Both lesion and functional neuroimaging evidence has been used to argue that perceptual priming at least involves the posterior neocortex but not the structures damaged in organic amnesia (e.g. Moscovitch 2000). For example, it has been claimed that lesions in the right posterior neocortex disrupt certain kinds of perceptual priming but not explicit memory for the same nominal stimuli, and that a reverse pattern of deficit is found in amnesics (Gabrieli *et al.* 1995). However, it has also been argued that all forms of priming, whether for information that was familiar prior to the priming experience or novel, are disrupted in organic amnesia (Ostergaard 1999). This suggests that primed memories may at least be partially stored in structures, such as the hippocampus, which are implicated in amnesia. An intermediate position was supported by a recent meta-analysis (Gooding *et al.* 2000), which found that amnesics showed normal perceptual and semantic priming of information that was familiar prior to study, but impaired priming of items and associations that were novel at the time of study.

This meta-analysis suggests that storing new representations critically involves structures such as the medial temporal lobes regardless of whether the stored representation later supports priming or episodic memory. If this position is wrong and the priming of novel information does not need to involve the structures damaged in amnesia, as Moscovitch (2000) argues, then it must be possible for new memory representations of perceptual information to become established in the neocortex after

one learning trial. One possibility is that priming of certain kinds of intra-item association depends on neocortical storage, which is achieved rapidly and can be very long lasting. The storage of episodic experiences may depend on this rapid storage of at least some intra-component associations in the posterior neocortex. However, these episodic components, which are set up in the neocortex, may initially (and perhaps for as long as episodic memory lasts) only be associated together in memory in the hippocampus and medial temporal lobes. The inter-component linkage could be achieved by using some kind of index that perhaps uses spatio-temporal relations between the components.

4. EPISODIC RETRIEVAL: PROCESSES AND BRAIN REGIONS

Recall of episodic information is usually intentional and effortful, but it can occur unintentionally and automatically when a particular thought or perception directly triggers the recollection of an associated experience. Both recall and recognition of an earlier experience are accompanied by the feeling that one is remembering, pathology of which is displayed in *déjà vu* and *jamais vu* experiences. This feeling is not explained simply by the reactivation of previously stored information. It has been argued that priming, which does not involve this feeling, depends on storage changes within the representing neural array such that primed information is represented more efficiently possibly by fewer neurons so that the information can later be more efficiently processed (i.e. primed) (e.g. Wiggs & Martin 1998). This process, which presumably involves rapid strengthening of synaptic connections between a subset of the neurons in the encoding array, does not, however, explain why a feeling of remembering should be produced when this array is next activated as a result of recall or recognition. By itself, reactivation of the representation does not give any information about whether the representation has been encountered before or is new (e.g. imagined). The problem also applies to semantic memories because these often carry the feeling that they are true.

Moscovitch (2000) reviews different theoretical accounts of 'consciousness and memory'. However, most of the theories do not address the above problem. Moscovitch's own theory proposes that the memory trace comprises not just the information features of the episode but also components that constitute the consciousness of it, so that at retrieval not only the episode but the consciousness of it is reactivated. But it is hard to see how being conscious of the episodic information will produce the feeling that the episode has been previously experienced rather than imagined unless 'consciousness' is being used in an unusual sense. Moscovitch, however, does liken his theory to Milner's (1999) view. According to this view, episodic memory involves a trace in which a representation of the information that constitutes an episode is associated with a representation of a feeling of familiarity such that when the episodic representation is reactivated it feels familiar. If Moscovitch's theory is equivalent to Milner's, then it does address the problem of how a feeling of remembering is produced. Milner's theory also implies that priming and episodic memory may be

relatively independent of each other. This is because priming of previously new information depends entirely on a memory trace that links the information; episodic memory depends at least as much on the strength of the association between this representation and a representation of a feeling of familiarity. Milner proposed that this feeling is generated by the hippocampus (and perhaps also by the medial temporal lobe cortices) as the inverse of its function of triggering a feeling of novelty. Whether the medial temporal lobes are critical for episodic memory for this reason only, or because they also store, at least for a while, an index which interconnects the episode's components, is not specified by Milner. He also does not specify whether the representation of the familiarity feeling is stored in the medial temporal lobes or merely generated there and stored elsewhere.

Although Milner's theory is attractive it fails to give a convincing mechanism for how the association between the representations of the episode and the familiarity feeling is acquired in one trial. This is because when the episode is first experienced it is usually accompanied by a feeling of novelty rather than familiarity. If the theory is incorrect, the only other theory that provides a plausible mechanism for how the feeling that an episodic memory is familiar is generated is an elaboration of the attribution view (see Jacoby *et al.* 1989). According to this theory, when information is processed more fluently as a result of priming, subjects may be aware of the enhanced fluency and attribute it to the fact that the primed information has been previously encountered. In other words, the awareness of the enhanced fluency with which the information has been encoded automatically triggers a feeling that the information has been remembered. This theory has been used primarily to give an attributionist account of item familiarity, but it can be extended to cover all processes underlying episodic retrieval. The dual process theory of recognition (e.g. Mandler 1980) postulates that recognition depends not only on how familiar encoded item information feels but also on whether anything else can be recalled about the item and/or the episode in which it appeared. This latter process of recollection is a form of recall and, therefore, shares recall's defining feature, which is that non-encoded information is retrieved from memory. Extension of the attributionist theory to recall postulates that recall involves an organized search process in which the rememberer tries to retrieve appropriate cues, which when encoded will automatically and fluently elicit the target memory. The rememberer is aware of this fluency and automatically attributes it to the retrieved information coming from memory. The theory applies not just to item memory but to aware memory of the complex associations that constitute episodes (Mayes 2001).

Even the version of this theory that applies merely to item familiarity is controversial for two reasons. First, priming may be preserved in dense amnesics even when they show no item recognition (Hamann & Squire 1997; Stark & Squire 2000b). This observation is not fatal for the theory because extra conditions, which are not met in dense amnesia, may have to be present before memory attributions are made. For example, there may need to be a general memory of the context in which the item occurred, which dense amnesics lack. Second, it is

unclear whether subjects can detect that studied items have been more fluently processed than equivalent unstudied items would have been (see Mayes 2001). This is a serious problem for the theory, but it may be that the measure of enhanced fluency provided by behavioural priming is indirect and poor, or even that the kind of enhanced fluency relevant to memory attribution is distinct from what is measured in behavioural priming. It is clear, therefore, that there are currently no strongly supported theories of the mechanism that generates the aware feeling of memory for an episode.

Recall and, to a lesser extent, recognition of episodes typically involves a directed search for a target memory. This may involve several stages in which the rememberer retrieves cues, which then reactivate further memories until eventually it is judged that a retrieved memory corresponds to the correct episode. A good illustration of the operation of these monitoring processes is when someone experiencing *déjà vu* is quickly able to identify that the feeling of familiarity is false because other memories are all inconsistent with this one being true. The search and monitoring processes are widely believed to depend on activity in a number of frontal neocortical regions that control different executive processes. The belief is supported by extensive evidence from lesion and functional neuroimaging studies (see Mayes 1988; Nyberg 1999; Rugg & Wilding 2000). However, although variations in retrieval tasks have been shown to activate somewhat different regions of the frontal pole, dorsolateral frontal, ventrolateral frontal, as well as other frontal regions (e.g. orbitofrontal cortex), identification of the control functions of these regions is only just beginning (Fletcher & Henson 2001).

Although there is surprisingly little evidence that the processes of recall and recognition produce different patterns of brain activation (Cabeza *et al.* 1997), lesion evidence suggests that these two forms of retrieval are based on different processes that are mediated by different brain regions. For example, in a factor analysis of 50 memory impaired patients, Hunkin *et al.* (2000) found independent factors that loaded heavily on recall and recognition test scores, respectively. If the recollection that occurs in recognition is regarded as a kind of recall, then familiarity in which no additional information beyond that which is already encoded is retrieved may be regarded as the only true form of recognition. There is a widely held view, developed in its most complete form by Aggleton & Brown (1999), that recollection/recall depends critically on the hippocampus and the fornix, mammillary bodies and anterior thalamus that are linked to it (Aggleton & Brown 1999). Familiarity depends on a different neural array, which includes the perirhinal cortex, the dorsomedial thalamus and parts of the frontal neocortex. The neural network model of O'Reilly & Rudy (1999) postulates that this separation of recall/recollection and familiarity occurs because of the different way in which the hippocampus and neocortex/medial temporal cortices represent information in memory. The hippocampus rapidly makes memory representations that differentiate similar kinds of input (pattern separation), a process which facilitates the completion of memories from their encoded components (pattern completion). In contrast, the cortical structures

make memory representations that emphasize the common features of different inputs, although representations which do allow pattern completion to be achieved may develop through a slow process of learning.

The above view indicates that the hippocampus plays only a minor role in item recognition because although it plays a critical role in recollection, it is not involved in familiarity judgements. The view is supported by a recent fMRI study, which found that although recollection (as indicated by remember responding with the remember-know procedure) activated the hippocampus, familiarity (as indicated by know responding using this procedure) did not (Eldridge *et al.* 2000). However, findings with patients reported to have selective hippocampal lesions are conflicting. Vargha-Khadem *et al.* (1997) and Mayes *et al.* (2001) have found that four people with fairly focal hippocampal lesions showed relatively intact recognition not only for items but also for associations between similar kinds of items such as words or faces. In contrast, Reed & Squire (1997) have found clear item recognition impairments in patients with apparently similarly restricted lesions.

These differences are unlikely to relate to test differences because the patients with clear item recognition deficits differed from the relatively intact patients even when the same test was used. Nor are reorganizational changes likely to be the explanation for the relatively preserved item recognition of the patient of Mayes *et al.* (2001) because, like the patients of Reed & Squire (1997), this patient suffered adult onset damage (this explanation cannot be ruled out for the patients of Vargha-Khadem and her colleagues, however, because these patients suffered damage very early). Although the patients of Reed & Squire had generally more severe memory deficits than those of Vargha-Khadem, Mayes and their colleagues, the overall mildness of their memory deficits is also unlikely to be the explanation of the relatively preserved item recognition of the latter patients. This is because some of the patients, reported by Hunkin *et al.* (2000), who had equivalently mild overall memory deficits, showed item recognition deficits of similar severity to those of Reed & Squire (1997). Therefore, patients with mild overall memory deficits can have either clearly impaired or relatively intact item recognition depending on the nature of their neural dysfunction.

It is more likely that the differences between the patients with clearly impaired and relatively intact item recognition relate to variation in the extent of subtle, but functionally significant, damage or dysfunction outside of the hippocampus, which current imaging techniques have not detected. Interestingly, Baxter & Murray (2001) have reported a meta-analysis of three monkey studies of the effects of hippocampal lesions on object recognition. Although object recognition was significantly impaired, a negative correlation was found between the extent of hippocampal damage and the size of the object recognition deficit. Although one should be cautious in accepting this conclusion before it is checked further, it suggests that the greater the extent of residual hippocampus the more it disrupts neighbouring and perhaps intact structures, such as the perirhinal cortex, that mediate item familiarity memory. This interpretation is weakly supported because several of the patients of Reed & Squire (1997)

had smaller hippocampal volume reductions than did the patients of Vargha-Khadem, Mayes and their colleagues. If this interpretation is correct, then a negative correlation between severity of item recognition impairment and extent of hippocampal volume reduction should be found in larger groups of human patients with relatively selective hippocampal lesions, and patients with clearly impaired recognition should show abnormal functional activity in structures, like the perirhinal cortex, which are believed to be critical for familiarity memory.

Even when patients show relatively preserved item recognition, it has been found that they are clearly impaired at some forms of associative recognition. Thus, both Vargha-Khadem, and Mayes and their colleagues, have found that their patients had clear recognition deficits for associations between different kinds of information (such as location and objects, or words and temporal order), which are likely to be represented in distinct neocortical regions. This suggests that the hippocampus is most concerned with memory for associations between components that are likely to be represented in distinct neocortical regions. These associations notably involve spatial and temporal relationships, which play a critical role in the kinds of context memory that is central to recollecting episodes.

Although the brain regions supporting recall/recollection and familiarity, and the different memory representation systems on which they may be based, could well be partially distinct, they have still only been given a preliminary rough characterization. It is also still poorly understood how much overlap there is between the processes underlying retrieval and encoding and hence how much the brain regions underlying both will be the same. Although both retrieval and encoding have been shown to activate common anterior cingulate, frontal and insular regions bilaterally (Nyberg *et al.* 1996), it has been found repeatedly that they also activate different frontal regions (Tulving *et al.* 1994) and it has been argued that encoding episodes activates more anterior regions of the medial temporal lobes than does retrieval (Lepage *et al.* 1998), although this is disputed (Schacter & Wagner 1999). One would expect retrieval to reactivate only some of the neocortical regions that represented the original episodic experience, the amount depending on how much was retrieved. One would also expect that some of the search and monitoring processes may be specific to retrieval and, if the retrieved episode feels familiar, this may involve brain regions not involved in encoding.

5. CONCLUSION

Although it is agreed that the posterior neocortex, frontal neocortex and brain regions damaged in amnesics all play a role in encoding, storing and retrieval episodes, there is far less agreement about what the precise processing roles of these regions are. In particular, there is disagreement or uncertainty about several important issues. First, it is uncertain which regions represent the different components of an episode at encoding and retrieval. For example, although there is lesion and functional neuroimaging evidence that right-sided posterior neocortical regions are critical for retrieval (e.g. Markowitsch *et al.* 2001), some studies indicate the

importance of left-sided or bilateral activation (e.g. Conway *et al.* 1999). These differences probably relate to the kind of information being retrieved. Second, it remains unclear what regions are involved in storing the different components of episodes and how this changes across time. Third, there is disagreement about the extent of the processing differences in the medial temporal lobes, although it has been agreed since O'Keefe and Nadel's (1978) suggestion that the hippocampus plays an important role in episodic memory. For example, are the hippocampus and perirhinal cortex critical for encoding different kinds of association and/or do they store different kinds of association? Fourth, it is unclear how the feeling of episodic familiarity is produced by the brain. Fifth, the relationship of episodic memory to priming of complex associations is still unresolved, although there is some direct evidence that medial temporal lobe lesions can disrupt certain kinds of associative priming (Chun & Phelps 1999). Sixth, it is not agreed to what extent dissimilarities in the brain regions mediating semantic and episodic memory depend on rehearsal/repetition differences and to what extent they depend on differences in the information retrieved. Finally, even less is known about how the involved brain regions actually perform their functions.

Resolution of some of these issues will be helped by the use of animal models of amnesia, and also by the use of neuroanatomically constrained neural network models of episodic memory. The use of new techniques, such as the lesion followed by hippocampal transplant procedure adopted by Virley *et al.* (1999), will be valuable in providing more convincing evidence about whether specific regions are involved in storing components of episodic memory. Above all, it will be important to focus more on the components of episodic memory such as emotional feeling, perceptual representations, representations of oneself, representations of spatial location and temporal order and duration, different kinds of association, and how feelings of familiarity for an episode are produced.

This work was supported by a Programme Grant from the UK Medical Research Council. I am grateful to John Downes, Juliet Holdstock, Nikki Hunkin, Daniela Montaldi, QiYong Gong and Tom Spencer for their collaboration on some of the experimental work described.

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