



The role of the hippocampal complex in long-term episodic memory

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1. Introduction

That the hippocampal complex plays a critical role in memory is no longer in dispute. Several essential questions remain unanswered, however, nearly 50 years after the seminal work of Scoville and Milner [1]. These include: what aspects of memory require hippocampal participation, when hippocampal participation is needed, and how various parts of the hippocampal complex are involved in these memory processes. Though there are provisional answers to each of these questions, vigorous debate continues in each case. To make matters more complicated, these questions are not independent of one another—the role played by various parts of the hippocampal complex may change over time, and with respect to the kind of memory involved. Answers to these questions force a consideration of the interactions between the hippocampal complex and the neocortex, as we will see.

We begin with a brief overview of the current status of each of these debates, present some data that bear on them, and finally outline our current approach to these issues. Some definitions, however, are essential at the outset. First, what exactly is meant by the term “hippocampal complex”? Starting from the core, the hippocampus consists of the CA fields and the dentate gyrus, the hippocampal formation incorporates the subiculum, and the hippocampal complex further includes the parahippocampal region, which incorporates the entorhinal cortex, the perirhinal cortex, and the parahippocampal gyrus.

Second, what is meant by the term “memory”? This seemingly innocent question is actually quite tangled in ways that have contributed to some of the debates in the field. The

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broadest definition views memory as any residue of experience that can influence subsequent behavior, and thereby includes such things as habituation, priming, habits, skills, etc. A more narrow definition would restrict itself just to those residues of experience that can be explicitly referred to by the individual who holds them. This latter definition was the one behind most analyses of memory until the 1970s, creating a situation in which animals did not have “memories” *per se*. At present, most investigators work with the broader definition, but it is important to keep in mind that different kinds of experience might leave behind residues that vary in important ways, not least of which include differences in underlying brain mechanisms.

2. What aspects of memory require hippocampal participation?

Given the broad definition just noted, there is now widespread agreement that there are multiple types of memory, only some of which require the participation of the hippocampal complex. This understanding was hard won over the course of 25 years of research that began with the assumption, based on work with HM [1], that memory as a whole was impaired after medial temporal lobe resection. Shortly thereafter, an early attempt to model the “memory” disorder through ablation of the hippocampus in primates failed [2]. A hint of what was to come appeared in the early work of Corkin [3], which showed that HM was capable of certain kinds of motor learning, even though profoundly amnesic for autobiographical events.

Animal models of hippocampal function, following from the early failure, concentrated on functions other than memory (however defined), such as response inhibition. A critical breakthrough came with the discovery by O’Keefe and Dostrovsky [4] of “place cells” in the hippocampus of the freely moving rat, which led to the suggestion that the hippocampus was indeed essential for learning and memory, but only when it involved the formation and use of spatial/cognitive maps [5,6]. Similar suggestions, also based on animal research, were made by Hirsh [8] and Gaffan [7], giving serious impetus to the view that there might be multiple neural systems responsible for different forms of learning. This idea offered a way to explain the apparent discrepancy between human and animal results—namely, that comparable tasks had not been used, and when the right tasks are employed across species, memory impairments will be comparable.

O’Keefe and Nadel [9] built on the place cell result to suggest that the hippocampus was the key component of a “cognitive mapping system” that used space as the core of a certain kind of memory in both animals and humans. Taking a distinction first described by Ryle, they argued that the hippocampus was critical for “memory that” but not for “memory how”. This idea was, in turn, taken up by Cohen and Squire [10], who showed that amnesics can learn procedural skills.

The notion that there is a particular type of learning and memory dependent on the hippocampal complex, and others that can be relatively independent of this complex, is now well-entrenched in the literature [11]. In humans, the forms of memory engaging the hippocampus, often referred to as explicit, may include both episodic and semantic memory. Episodic memory refers to specific events in the life of the individual, and

includes information about both the content of that experience, and the spatial and temporal context in which it occurred. Semantic memory refers to the non-contextual content of experience, or knowledge about the world acquired during experience that contributes to the formation of concepts, categories, our storehouse of facts and word meanings, and so on. However, questions remain about whether the hippocampal complex is essential for the acquisition or retrieval of semantic memory or whether the hippocampal complex simply contributes to semantic memory when it is fully functional.

A related debate has ensued on animal memory. Here, the issue is whether or not the hippocampus plays a special role in spatial learning and memory, or whether spatial relations are but a good example of a more general “relational” memory function. Since episodic memory necessarily incorporates information about spatial context, the debates within both the human and animal literature seem to be about the same thing. We will return to this issue later.

3. When is the hippocampal complex required?

When first tested, HM appeared to have a retrograde amnesia of 18–36 months, and clearly retained a great deal of previously acquired knowledge, such as the meaning of words and world knowledge. This led to the assertion that the hippocampal complex was not the site of permanent memory storage, but rather played some time-limited but critical role in the transfer of information from short-term into long-term memory. The time window during which this role is played has been called the consolidation period, a concept that was first mentioned over a century ago.

Two broad possibilities about the process of consolidation have been entertained. By one account, the “memory” is first stored in the hippocampus and then “transferred” out to other structures (presumably neocortical) during consolidation. Alternatively, the “memory” is always stored in neocortical sites, but the hippocampus is needed to “bind” or “integrate” its various components during the period of consolidation, when damage to the hippocampal complex can cause retrograde amnesia. By either scenario, consolidation leads to the creation of a stable, independent, memory trace in neocortical sites. Thus, the initial answer to the question of when the hippocampal complex is required was that it was needed only for the duration of the consolidation period, after which it became unnecessary.

The concept of consolidation, however, is now further complicated by the newly developed ideas regarding multiple memory systems. Within this perspective, it is possible that the hippocampal complex is transiently required for forming some kinds of memory, and permanently required for others.

Until recently, accepted wisdom held that the hippocampal complex was not permanently required for any form of memory. In particular, it was assumed that both episodic and semantic memory initially depended upon the hippocampal complex, and both became independent of it during the course of consolidation (e.g., [12,13]). More recently, Nadel and Moscovitch [14,15] have suggested that the role of the hippocampal complex differs for episodic and semantic information, playing a permanent role in the storage and retrieval of the former, but only a temporary (and non-essential) role in the storage and

retrieval of the latter. This debate will be the central focus of most of the data we will present in this chapter.

4. How do the various parts of the hippocampal complex contribute to learning and memory?

The primary question to be considered here is whether the distinguishable parts of the hippocampal complex have distinctive memory functions. Three possibilities have been suggested: (1) these areas have quite distinct and differentiable functions; (2) these areas function in similar and indistinguishable ways; and (3) the functions of the various areas blend with one another, resulting in relatively vague but measurable differences that might best be described as a continuum. We will elaborate on these issues below.

5. What, when, and how

These three debates converge in the following way: how and when do various parts of the hippocampal complex contribute to episodic and semantic (explicit) memory. At the heart of this convergence is the notion of consolidation, and it is to that putative process we now turn.

6. Consolidation revisited

The standard view of consolidation, as outlined above, makes a number of predictions that can be readily submitted to empirical test. First, it asserts that once consolidation has been completed, the relevant structures in the hippocampal complex should be unnecessary for retrieval of a fully elaborated memory of past experience. Second, it asserts that not only is the hippocampus not required for such retrieval, but that it also cannot be involved, since the linkages between hippocampus and neocortical sites have been “erased” over the duration of consolidation. This assertion flows from the assumption that the hippocampal system has limited capacity and that its neurons must be used only temporarily and then recycled for use in coding future experiences. Third, it asserts that the same fate should obtain for episodic and semantic memory over the course of consolidation, e.g., the hippocampal complex should be critical for both at the outset, and unnecessary for both after consolidation is complete.

After many years of general acceptance, these assertions have come under closer scrutiny in recent years, as new and better methods for assessing old memories, and the role of hippocampal structures, have been developed. The new data suggest that all three assertions are either wrong or at a minimum considerably oversimplified. For example, most current estimates of the extent of retrograde amnesia after hippocampal complex damage range between 10 and 20 years, which does not fit well with the notions of “temporary” memory and the recycling of neurons.

In reaction to the apparent shortcomings of the standard model of consolidation, Nadel, Moscovitch et al. [14–17] proposed an alternative approach—Multiple Trace Theory (MTT)—that aims to account for both the facts of long-term memory and the pattern of memory impairments associated with medial temporal lobe damage. MMT’s assumptions are to some degree consistent with the standard consolidation model, but they also differ in several critical ways.

7. Central assumptions held by standard theory and MTT

Both approaches hold the following assumptions in common:

- The hippocampus complex and neocortex are in constant interaction.
- Information from disparate neocortical sources is linked together by means of the hippocampal complex, where an ensemble trace is rapidly created (via LTP or some similar synaptic plasticity mechanism).
- This hippocampal trace (H trace), or index, serves to “bind” the disparate neocortical traces (NC traces), and it is through this action that various parts of the memory, stored in widely dispersed neocortical sites, can be reactivated together and experienced as an integrated memory.

Standard theory makes the additional assumptions that are not held by MTT:

- Over time, during consolidation, the NC traces become directly linked, and the intervention of the H-trace is no longer needed for normal retrieval.
- Semantic and episodic memories are treated the same way within the hippocampal and neocortical systems.
- Crucially, the information content is the same whether or not the H-trace is involved in retrieval; that is, the H-trace is only an index, containing no information inherent in the memory per se.

MTT differs from the standard theory in making the following assertions:

- The hippocampal complex and neocortex are always jointly involved in the storage and retrieval of normal episodic memory—the combined regions together comprise the episodic memory system, regardless of the age of the memory.
- Each reactivation/retrieval of an episodic memory occurs in a different context and results in an altered trace; reactivation thus expands and strengthens the H trace and/or strengthens the links between H and NC traces.
- The hippocampus is not merely an index to neocortical representations of memories, but itself stores contextual information regarding the episode.
- Semantic and episodic memories are treated differently within the hippocampal and neocortical systems. Only episodic memory requires hippocampal participation and storage, but semantic memory normally engages hippocampal involvement, and hence

benefits from the presence of an intact hippocampal system. All aspects of semantic memory are typically stored outside the hippocampal complex.

8. Implications of MTT

Given the set of assumptions outlined above, MTT leads to several predictions that clearly differentiate it from the standard consolidation model. These predictions all flow from the central tenet of MTT, namely, that as memories age, they will either be forgotten or will benefit from the formation of stronger, expanded, memory traces.

Thus, MTT predicts that:

1. The hippocampal complex will be active during retrieval of episodic memories regardless of the age of the memory.
2. The hippocampal complex will be preferentially active during processing of spatial/contextual material.
3. The hippocampal complex plays a different role in the storage and retrieval of episodic and semantic memory.
4. Older memories will have stronger, more distributed traces within the hippocampal complex.
5. Partial hippocampal complex damage will affect memories in proportion to their age/strength, while complete hippocampal complex lesions will yield a flat gradient of RA for episodic memory. This follows from the fact that older episodic memories, having expanded traces within the hippocampal complex, will be increasingly resistant to hippocampal damage.
6. Memories that are retrieved by amnesics with hippocampal complex damage will be generic in nature; that is, they will be lacking in the normal detail that intact individuals typically provide. This lack of detail should be evident regardless of the age of the memory.

In the remainder of this chapter we will describe several studies that assess several of these predictions, after which we will return to a discussion of the “what”, “where”, and “how” questions raised at the outset.

9. Hippocampal activation during retrieval of remote episodic memory

MTT asserts that because the hippocampal complex is always involved in the retrieval of normal episodic memory, activation of this region should be observed when even quite remote episodic memories are retrieved. In order to test this assertion, Ryan et al. [17] carried out the following experiment. Participants between the ages of 56 and 74 were recruited for a functional magnetic resonance imaging (fMRI) study. Just prior to entering the scanner they were administered a questionnaire that involved a long list of events experienced by many people. The subjects were asked simply to indicate whether or not they would be able to retrieve a memory for such an event.

Included in this list were some things that would most likely have occurred many years earlier (such as “learning to drive” or “smoking your first cigarette”) and some things that could have occurred quite recently (such as “giving a talk at a conference” or “taking a camping trip”). For each memory they identified they were asked to specify the year in which the original event occurred.

Based on these questionnaires, an individualized list was made up for each participant containing cues to both recent and remote events that the subject could recollect, defined respectively as events that occurred within the past 2 years or at least 20 years ago. During

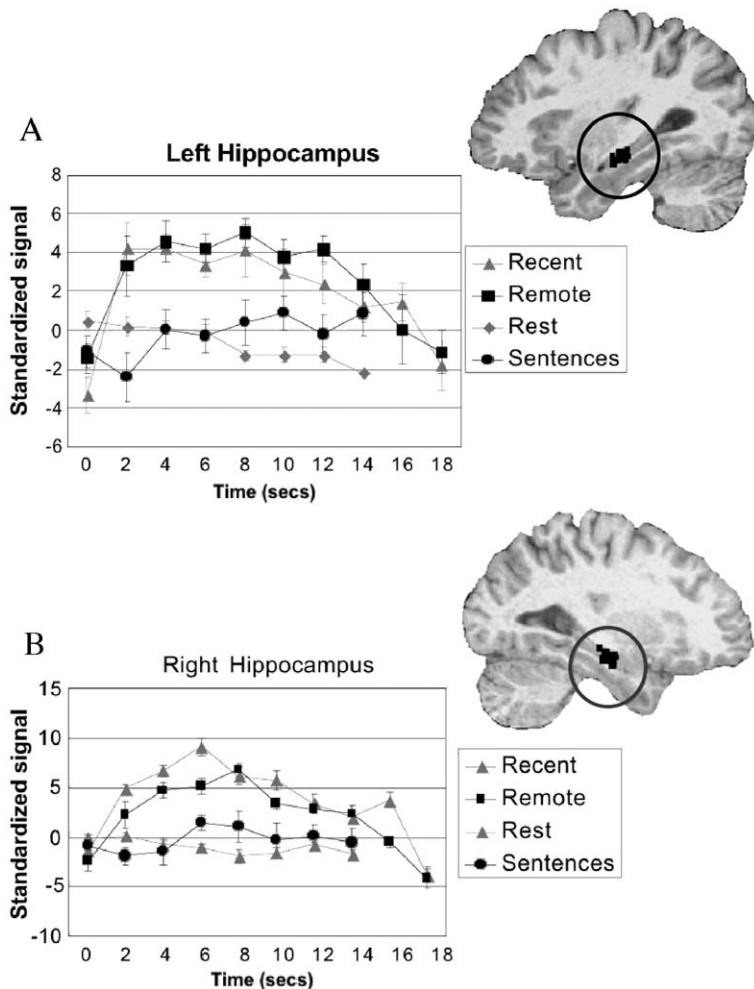


Fig. 1. (A, B) Activation in the left and right hippocampus during recollection of recent and remote memories, sentence completion, and relaxation.

a single fMRI session, each subject underwent five scans, each of which included four memory cues (two recent, two remote). Each memory cue was presented for 2 s, followed by a 20-s period during which the subject was instructed to recall the memory as thoroughly as possible. Recall of each event was followed by a 16-s relaxation period. After each scan, subjects were asked to provide detailed descriptions of the recalled events, including ratings for vividness, emotionality, importance, and arousal.

Regions of activation were first identified that were associated with memory retrieval. The mean hemodynamic responses for remote vs. recent memory retrievals were then compared within each region of activation.

The results (Fig. 1A and B) were clear: there was significant activation of the hippocampal complex in each of the seven subjects during memory recollection.

Most critically, the degree of activation was similar for recent and very remote memories.

Although these results seem quite compelling, there is an obvious alternate explanation. It is possible that the subjects were simply recalling the event that took place just prior to the fMRI session—the administration of the event questionnaire—and what we took to be hippocampal complex activation in response to remote memory retrieval was actually activation in response to recollection of a very recent event, namely the pre-scan procedures.

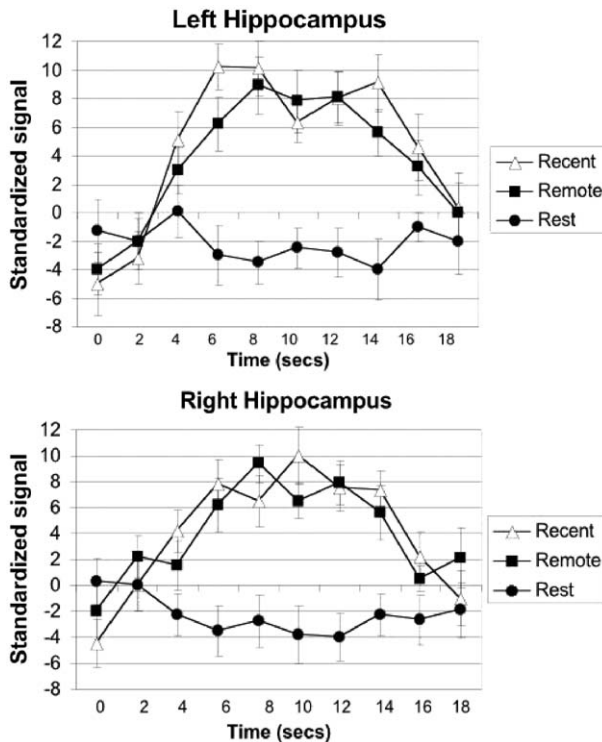


Fig. 2. Activation in the right and left hippocampus during recollection of recent and remote personal episodes in the “spouse” study.

In order to evaluate this possibility we carried out a follow-up study. We recruited couples married for at least 25 years. When they came into the laboratory, one member of the couple was taken into a separate room and administered the questionnaire. But now, instead of judging whether they could retrieve a particular event memory, they judged whether they thought their spouse could do so. Based on this information, a list of remote and recent “cues” was generated for each subject to be scanned, but in this case the subject had no reason to think about these particular events beforehand.

The results from these subjects (Fig. 2) were identical to those in the earlier study. Once again, there was robust activation of the hippocampus, and it was equivalent in the remote and recent memory conditions. We concluded that, as predicted by MTT, the hippocampus is active whenever an episodic memory is retrieved, be it a recent or remote memory.

10. What aspects of an episode activate the hippocampal complex?

MTT asserts that the hippocampal complex is activated during episodic memory retrieval for two reasons: first, episodes are defined by the context within which they occur, and MTT assumes that information about the context is stored in the hippocampal complex. Second, MTT assumes that this contextual trace is important in indexing and hence finding the rich details contained in an episodic memory. The richer this detail, the more dependent will episodic memory retrieval be upon the contextual trace.

Although the presence of contextual information distinguishes episodic from semantic memory, most previous neuroimaging studies of episodic memory retrieval have focused on the neural consequences of retrieving the contents, rather than the context, of an episode. For example, subjects might be trained on a paired associates task, or on a list of words, and are then asked only to recall the associates, or as many of the words as possible, but not to retrieve any contextual information. Such paradigms cannot assess the prediction made by MTT that it is the contextual aspects of episodic memory that engage the hippocampal complex.

To investigate this hypothesis, we recently designed a study to assess the role of the hippocampal complex during episode retrieval of content and contextual information (Hayes, Ryan, Nadel, and Schnyer, in preparation). In this way, we hoped to shed light on why the hippocampal complex remained active during retrieval of even quite remote memories.

In this experiment, participants aged 20–36 years viewed a 9 min videotaped walking tour through four houses. While in the scanner, participants viewed the study tour via a high-resolution goggles system. The tour began with a 5 s still picture of the outside of a house and continued by moving through a large distinctive room in the house, highlighting real-world objects and their locations (i.e., a vase on an end table). In each house, eight target objects and their locations were identified. The tour was narrated to ensure that participants were attending to aspects of the scene that would be important during subsequent memory testing, e.g., “notice what’s on the end table.” Participants viewed the videotaped tour twice in order to ensure adequate recognition accuracy.

Participants were then tested approximately 15 min later while undergoing fMRI for their memory for objects, the spatial relations amongst objects, and the temporal

ordering of objects and scenes viewed during the videotape. Testing consisted of self-paced, two-alternative forced choice recognition in which participants pressed a mouse button in their left or right hand to indicate their choice of the picture presented on the left or right side of the screen. There were four different test conditions, each composed of 60 trials. On the 60 OBJECT trials, participants were simultaneously shown two pictures of objects on a white background, one that they had seen during the tour, and one they had not. Subjects were instructed to choose the object they had seen during the tour. On the 60 TEMPORAL trials, they were shown either two objects or two scenes they had observed during the tour and indicated which of these they had observed first. On the 60 SPATIAL trials, they were shown two scenes and were instructed to choose the one they had viewed during the tour. The novel scenes on these trials were recombinations of aspects of scenes that had been viewed, so that the choice could not be based simply on recognition of the objects in the scenes. Finally, on 60 CONTROL trials, they were shown two unrecognizable scrambled pictures of targets and lures, one with a large “O” overlaid on it, and the other with a large “X”. The task simply alternated between indicating which picture contained the “X” or the “O”. The four trial types were presented to subjects in random order, and each trial was preceded by a 2-s cue indicating to the subject which trial type would appear next.

Preliminary work had demonstrated that after a single viewing, there were substantial differences in the accuracy scores for the three experimental conditions, which led us to

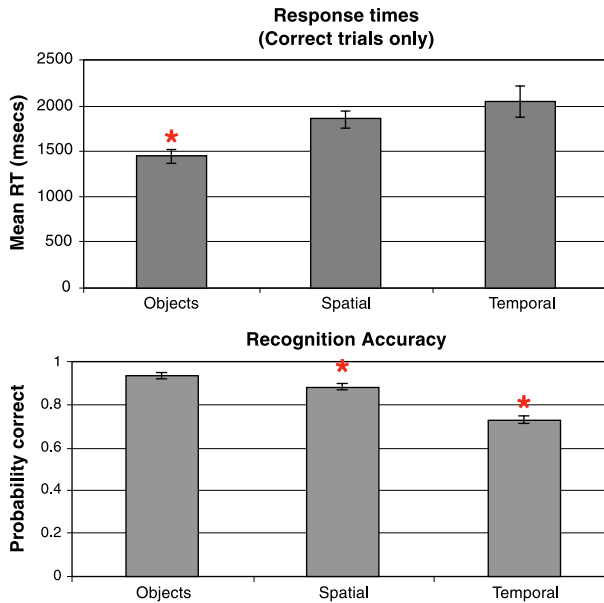


Fig. 3. Response times and recognition accuracy for the three types of recognition trials in the “house tour” study. Subjects responded faster on Object trials than on Spatial or Temporal trials, which did not differ from one another. Subjects were more accurate at retrieving Object information than either spatial or temporal information, and more accurate at spatial than temporal information (repeated measures, $N = 14$, p 's < 0.05 in both cases).

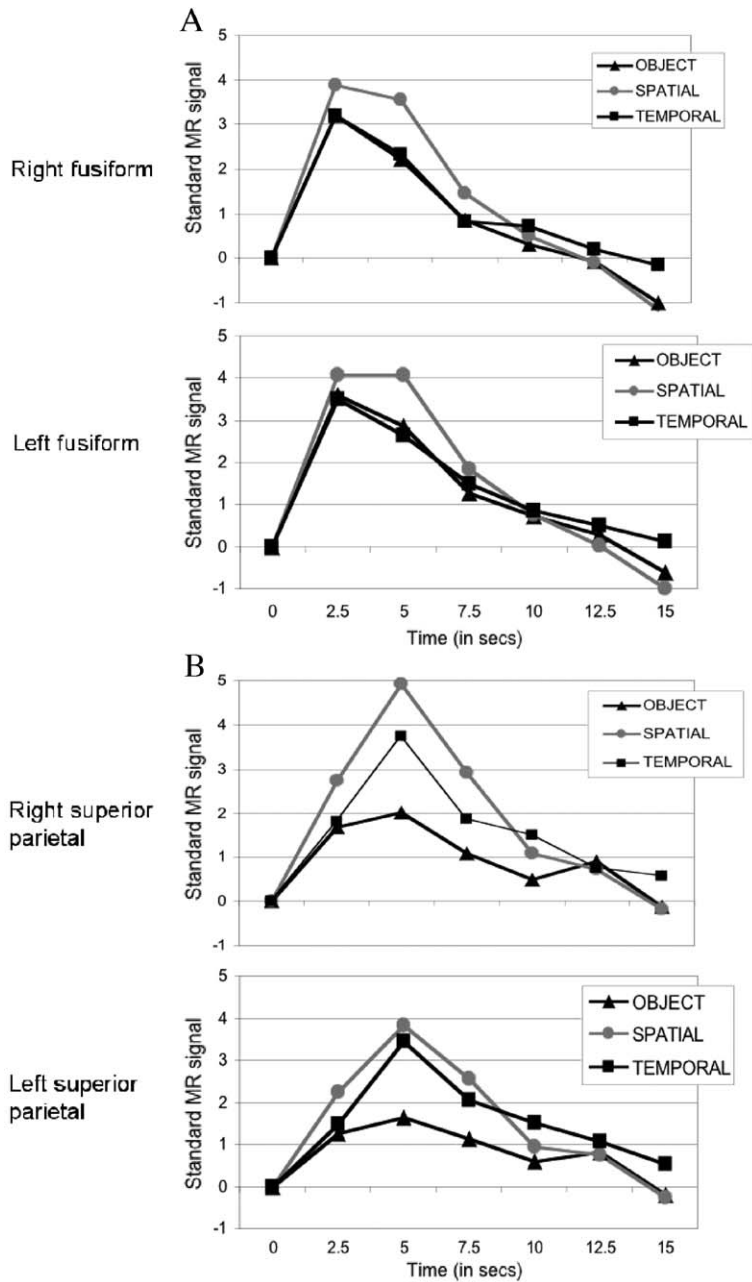


Fig. 4. (A) Right (R) and left (L) fusiform areas. (B) Right (R) and left (L) superior parietal areas. (C) Right (R) and left (L) parahippocampal gyrus. (D) Right hippocampus (9 of 14 subjects). (E) Right (R) and left (L) lateral prefrontal cortex (BA 44 and 45). (F) Right (R) and left (L) anterior middle frontal gyrus (BA 10 and 46).

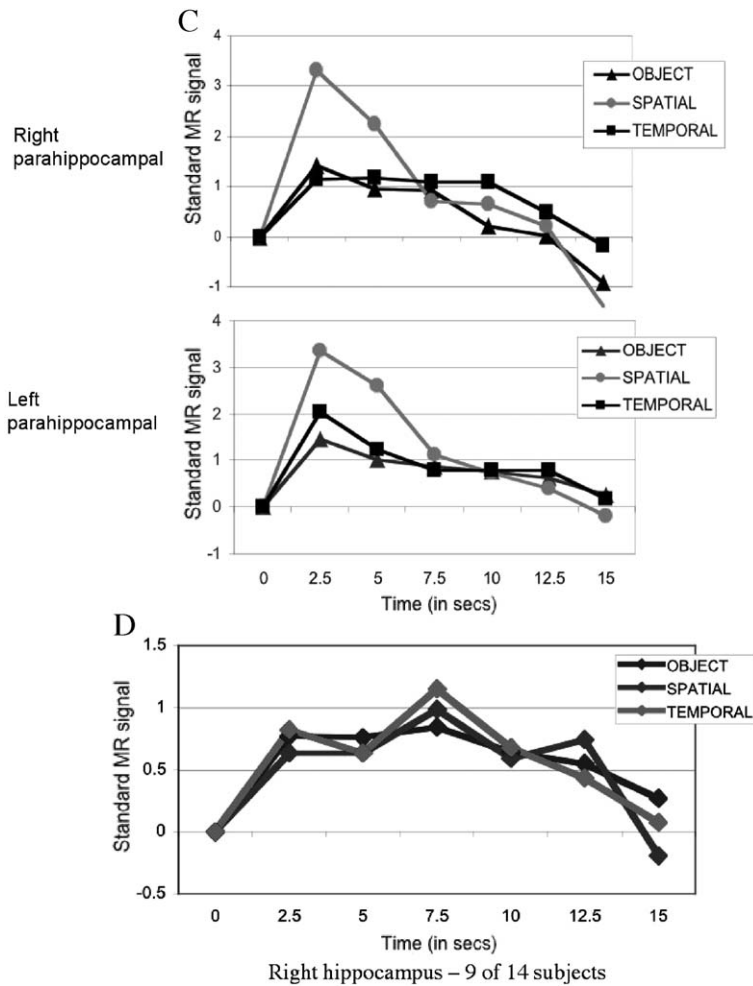


Fig. 4 (continued).

present the tour twice. This did not eliminate the differences completely, but it did raise performance on all trial types near 75% or higher (see Fig. 3).

Images were analyzed using a rapid presentation event-related technique developed and validated by Dale [18]. Only those trials on which the subject made a correct response were included in the analyses. An estimate of the hemodynamic response was obtained for each condition using the Control condition as the baseline. Regions of activation were identified in each individual by contrasting all three memory conditions with the control condition. The average amplitude of hemodynamic responses for the three conditions were compared within active regions using a repeated measures ANOVA (time by condition) across time points 2.5, 5, 7.5, 10, and 12.5 s post-stimulus onset.

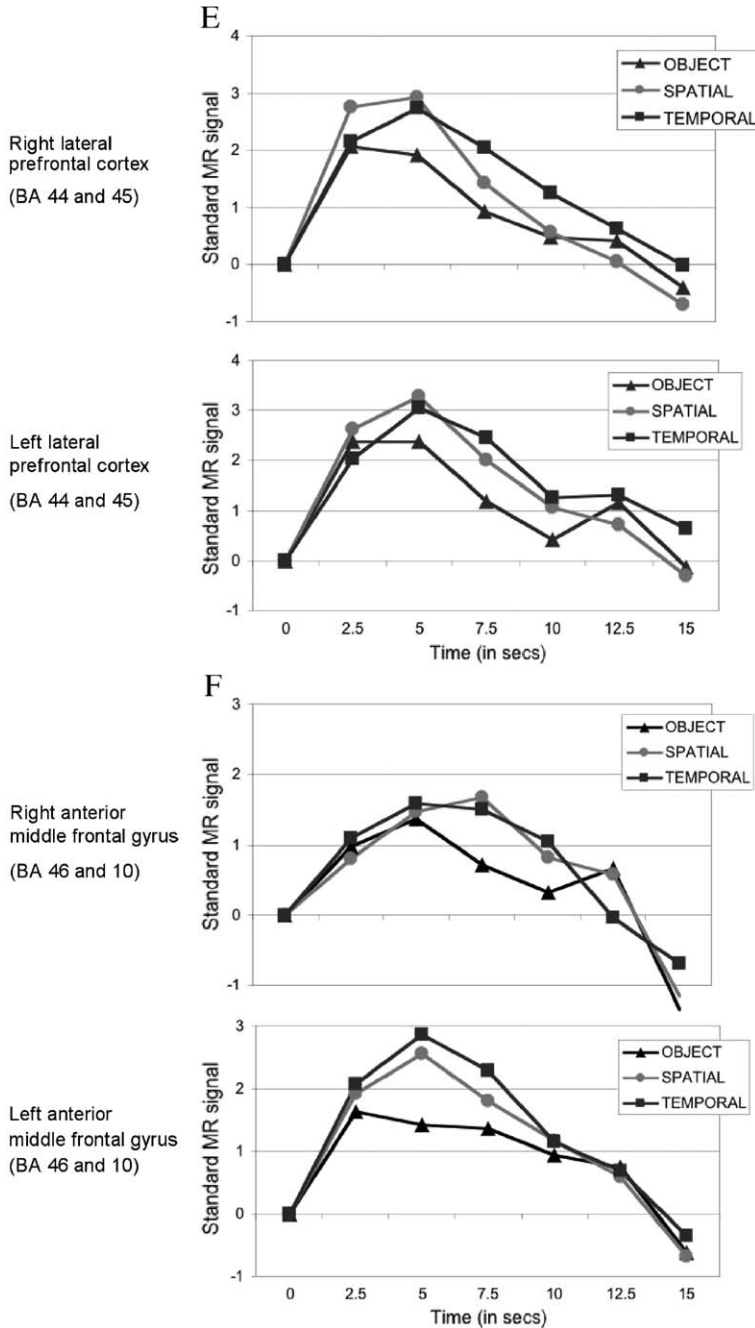


Fig. 4 (continued).

The results, presented in Fig. 4, indicated that the retrieval of episodic memory, in all its detail, activates a rich network of brain structures, some of which respond predominantly to the spatial information, some to the spatial and temporal information, and some to all three types of information tested.

There are a few points we wish to make about these data, which are still being analyzed. First, the hippocampus proper appears to have been activated during all types of recognition trials, although the level of activation of the hippocampus was relatively modest in all cases (note the scale change in Fig. 4D). Second, several areas were equivalently active in the spatial and temporal trials (context), but were less activated during the object trials. These areas, including the parietal and frontal regions, are candidates for playing an important role in episodic context. Finally, and most crucially from the present perspective, the parahippocampal region was activated mostly on the spatial trials.

These findings provide some support for MTT, in that one area within the hippocampal complex was preferentially activated during retrieval of spatial context information. However, the uniform though modest activation in the hippocampus proper during all three recognition conditions requires further discussion.

In their original formulation of the “cognitive map” theory of hippocampal function, O’Keefe and Nadel [9] suggested that all forms of information could gain access to the hippocampus, where they would be “enriched” by the imposition of a spatial framework. The consequence of this integration of information within the hippocampus itself was, in their view, the cognitive map. By this view, information about objects is not stored in the hippocampus, but activation of object representations, when attended, should lead to hippocampal activity. Information about spatial context, on the other hand, was assumed to be stored in the hippocampus, and thus activation of this structure when such information is retrieved is no surprise. The limitations of neuroimaging studies are manifested in this case. One cannot determine, from activation alone, whether a given brain structure is the site of storage, processing, retrieval, or all three. What we can apparently conclude from these data is that a part of the hippocampal complex, the parahippocampal region, is particularly interested in spatial contextual information. This conclusion is consistent with MTT, but we await converging evidence before we can definitely determine the role of the entire hippocampal complex in the retrieval of various aspects of an episode. Our data are consistent with the central tenets of MTT, but they do not prove the case yet.

11. Do memory traces expand within the hippocampus with time

MTT makes a fundamental claim that over time, with reactivation of a memory, its trace within the hippocampus should become more diffuse. This is the mechanism by which MTT accounts for the facts of graded retrograde amnesia as a function of partial damage in the hippocampal complex. This assertion has been tested in a recent study carried out by Gilboa, Grady, Winocur, and Moscovitch, preliminary results from which can be reported here.

In this study, middle-aged subjects (40–60 years old) were recruited and photographs from their life were obtained either from a spouse or close friends. In this way,

Coronal section showing left hippocampal activation

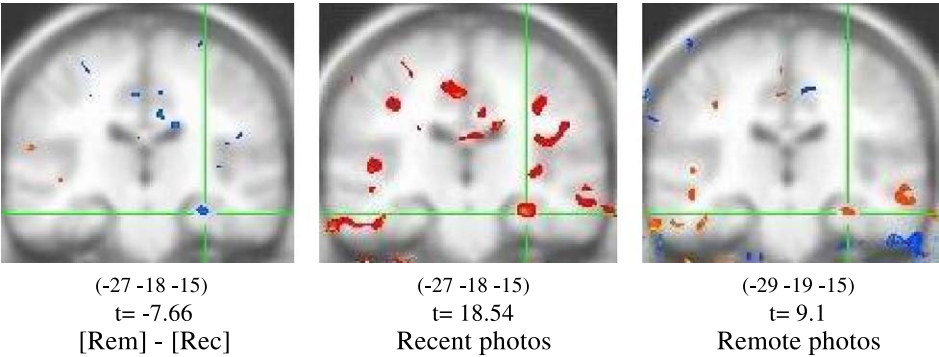


Fig. 5. Coronal activation in the left hippocampus during viewing of recent and remote “self” photos compared to “other” photos.

Direct comparison of old photos that were vividly remembered with photos that were not

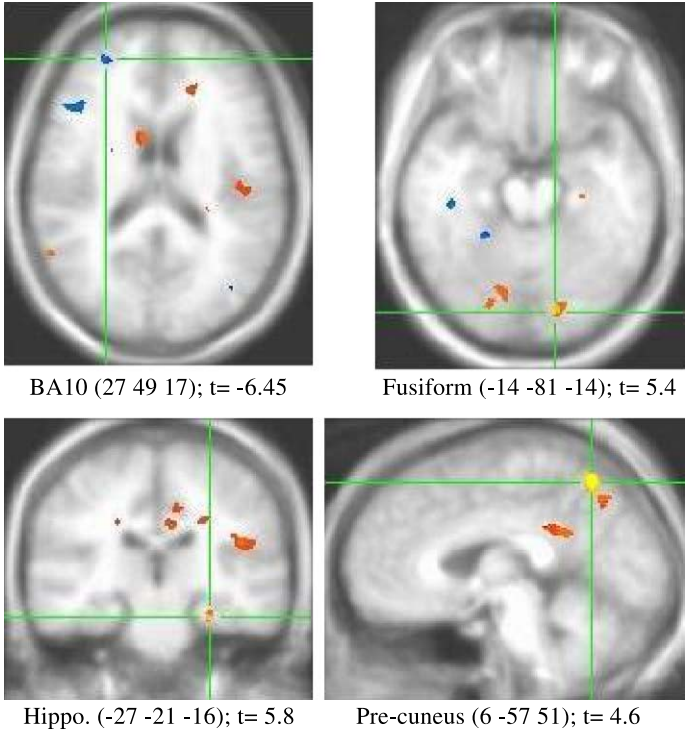


Fig. 6. Relation of activation to vividness.

Gilboa et al. considered the possibility that the increased activation observed for photos of more recent events reflected differences in the vividness of the retrieved memories. They compared levels of activation between old photos that were and were not vividly remembered, and indeed, it was the case that activation in several brain regions, including the lingual and posterior fusiform areas, the pre-cuneus, and the hippocampus, was positively related to vividness (see Fig. 6). Interestingly, activation in area BA10 (in particular the middle frontal gyrus) was inversely related to vividness. Thus, we can assume for the moment that remembering both recent and remote events portrayed in photos will activate the hippocampus (and other regions), but that the level of activation is, not surprisingly, a function of how vividly the event is recalled.

The most interesting result, and the one directly bearing on the prediction of MTT, is shown in Fig. 7. Here, the focus of activations within the hippocampus is plotted for both recent and remote memories. The figure makes it clear that memories of remote events activate a more diffuse zone of the hippocampus than do memories of recent events. This directly supports the critical prediction of MTT that as memories age they will benefit from expansion of their traces within the hippocampus.

12. Conclusion

In this chapter we have presented a series of studies aimed at contrasting predictions about memory consolidation from the Standard Model and the Multiple Trace Theory (MTT) of episodic memory consolidation. The results of each of the studies were consistent with the predictions of MTT, and call into question some long-held beliefs regarding the role of the hippocampal complex in episodic memory storage and retrieval. While much remains to be done, present evidence indicates that the hippocampal complex is always involved in the normal retrieval of episodes from the past, even the distant past. In these concluding remarks, we will focus on two issues that arise as a consequence of this conclusion: (1) what precise roles do the hippocampus and its related structures within the hippocampal complex play; and (2) does anything like consolidation occur within cortical circuits?

13. The role of the hippocampal complex

It is our view that the hippocampal complex contributes something essential to episodic memory that cannot be replaced by neuronal ensembles and their interconnections in the neocortex. While most of the content of any given episode is represented in neocortical circuits, spatial contextual elements are not. These elements are represented within the hippocampal complex as part of the “cognitive mapping” function of that system. It remains unclear whether this contextual trace is stored in the hippocampus itself, as O’Keefe and Nadel [9] originally supposed, or is instead stored in parahippocampal regions, as some recent data might suggest. Resolution of this question depends as much on clearer conceptualization of what it means to say

that some kind of information is “stored” in a given region of the brain as it does on more empirical data. What is unassailably the case is that the hippocampus itself is activated when any episodic memory is retrieved. Does this mean that spatial contextual elements are stored there, or does it mean that these elements are “sent” there from the parahippocampal region during retrieval, along with information about the other, non-spatial, elements of the episode. The fact that retrieval of any of the aspects of the episodes in our house tour study activated the hippocampus proper supports the latter view, but the present data alone are inconclusive.

14. Is there cortical consolidation?

The answer to this question almost certainly appears to be yes, but the nature of that consolidation is not quite what standard theory posited. To recapitulate: according to the standard view, all aspects of an episode memory are represented in neocortical circuits, but in the early stages of memory consolidation, these elements are either not linked together at all, or they are too weakly linked to permit retrieval of a fully elaborated episode memory. The purpose of cortical consolidation, in this view, is to slowly strengthen these linkages so that after some time period they can stand on their own and a rich episode memory, complete with all its contextual detail and elaborated content, can be retrieved without the intervention of the hippocampus.

We have already noted one of the serious problems with this view—namely, the length of time this process seems to require. A “temporary” memory trace that persists for 10 or even more years does not seem very temporary. Nor does it fulfill one of the functions of consolidation that was often mentioned in early treatments—the “recycling” of previously used hippocampal neurons into a pool of available elements to represent future episodes. This idea reflected the view that there was a capacity limitation on hippocampal neurons and that there surely could not be enough to represent all the episodes of an organism’s life. While this capacity issue remains to be resolved (and will only be so when we have clearer ideas on the memory capacity of neurons and all their dendrites, as well as a better sense of the importance of adult neurogenesis in the hippocampus), the multi-year duration of consolidation does not fit well with the notion of recycling.

There is another serious problem with this view, one that relates to computational issues within the neocortex itself, and the very nature of episodic memory. A defining feature of the episodic memory system is its ability to link together any possible combination of objects, actions, and events. This arbitrary nature of episodic experience is its hallmark, and it is what presents the greatest challenge to theory. How can a system be structured such that any two (or more) elements, among the many billions that are possible, can be attached to each other? Assuming that these elements are represented in the neocortex, the problem becomes one of understanding how any two neocortical elements (or ensembles) can be linked together, no matter how disparately located within the brain. For many, the role of the hippocampal system is to provide a solution to this very problem—by standing in a hierarchical relation to neocortex, it can serve to facilitate these arbitrary links from outside. The notion of the hippocampus as an “index” derives from this perspective. But, the assumption that during consolidation the neocortex becomes independent of the

hippocampal index, and does so in a way that fully preserves all the information comprising the original episode, demands that this linkage problem be solved within the neocortex itself. And there is no obvious way to understand how this can happen.

Consider three possibilities. First, connections might already exist between every possible pair of neurons in the neocortex. Second, such full connectivity might not exist, but new connections are formed over time between the relevant neurons. Or, third, connections are not really needed. Instead, “binding” of the relevant cortical sites happens by way of coherent oscillations, as some have suggested in the context of perception.

The first possibility seems implausible on its face. There are just too many neurons. The third possibility, while intriguing, lacks any empirical support at present. Nor is it at all obvious why consolidation should take so long under this scenario, since physical linkages are not being formed. The second possibility is at least conceivable, but there is very little support for the idea that entirely new connections are made within the neocortex on a regular basis. Most of the data support the idea that plasticity involves alterations in synaptic efficacy among already-connected neurons, rather than the establishment of new links.

We prefer to conclude that the basic premise is incorrect, and that consolidation within neocortical circuitry has an important but more limited role than standard theory supposed. We imagine that neocortical consolidation can permit the ongoing extraction of statistical regularities from experience, thereby permitting the acquisition of associations, and the formation of semantic knowledge such as word meanings, concepts, and categories. Developmental amnesics, and even HM, have demonstrated the capacity to form, however laboriously, semantic memories. There is no doubt that a functional hippocampal system contributes to this kind of cortical consolidation, hence to the normal establishment of semantic memories. But, it is not essential.

What the hippocampal system is essential to, we submit, is the representation of what is unique about episodic experience—its context. This aspect of an episode cannot be fully captured within neocortical circuitry, and in its absence, retrieved episodes and even remotely stored spatial maps are poorly detailed compared to the normal case. Somehow, in ways that remain to be specified, this hippocampal contextual trace makes it possible to retrieve sufficient details from neocortical storage sites such that an episodic memory can be reconstructed that is faithful to both the contents and context of our past experience.

These speculations about hippocampal and neocortical roles in memory consolidation provide a way forward in thinking about multiple trace theory. It remains for future research to fill in the missing details.

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