



Review

Memory formation, consolidation and transformation

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ABSTRACT

Memory formation is a highly dynamic process. In this review we discuss traditional views of memory and offer some ideas about the nature of memory formation and transformation. We argue that memory traces are transformed over time in a number of ways, but that understanding these transformations requires careful analysis of the various representations and linkages that result from an experience. These transformations can involve: (1) the selective strengthening of only some, but not all, traces as a function of synaptic rescaling, or some other process that can result in selective survival of some traces; (2) the integration (or assimilation) of new information into existing knowledge stores; (3) the establishment of new linkages within existing knowledge stores; and (4) the up-dating of an existing episodic memory. We relate these ideas to our own work on reconsolidation to provide some grounding to our speculations that we hope will spark some new thinking in an area that is in need of transformation.

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These are exciting times in memory research. Just as with memory itself, what seemed settled and fixed has become unsettled. The idea that memory formation is a highly dynamic process is hardly new, but the implications of this dynamism were largely ignored for 50+ years. That has changed in the past decade, overturning some well-established ideas, upsetting many apple-carts, and opening the door to new ideas. In this review we first detail traditional views of memory and then, in a frankly speculative way, offer some ideas about the nature of memory formation and transformation. We relate these ideas to our own work on reconsolidation to provide some grounding to the speculation. It is our hope that this flight of fancy will spark some new thinking in an area that is in need of transformation.

1. The nature of memory formation

The textbook view of memory formation goes something like that shown in Fig. 1 below.

That is, we experience an event, some aspects of this event get encoded, this encoding initiates a series of processes, typically labeled “consolidation”, that take time, leading to a permanent memory trace. Memory consolidation plays a key role in this sequence, as it determines both what will be preserved after initial encoding, and how long this process takes. Once consolidation is over, by definition, the permanent memory trace that results cannot be disrupted in the normal course of events. It is crucial to the very notion of consolidation that this end result be a fixed memory trace. Absent this, it would be impossible to state when consolidation has finished, since the operational definition of that end-point is precisely when some agreed-upon manipulation no longer disrupts memory.

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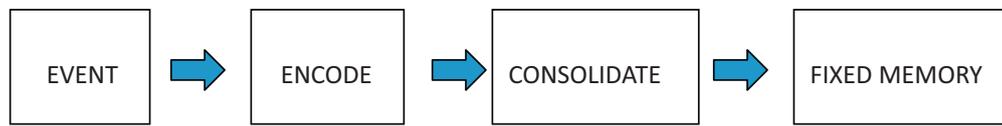


Fig. 1. Memory encoding – traditional view.

2. Problems with the textbook view

The problem with this view of memory formation is that it appears to be wrong. As Fig. 2 shows, when an apparently fixed memory is reactivated, some process is initiated that renders what initially seemed fixed once again labile (Nader et al., 2000; see also Lewis et al., 1968 and Misanin et al., 1968). A reactivated “consolidated” memory, that has become labile, is open to change in ways that a non-reactivated “consolidated” memory is not. This change can take any of several forms, including weakening or even erasure (Nader et al., 2000; Walker et al., 2003), strengthening, or alteration (Hupbach et al., 2007). Perhaps the most typical outcome is that the reactivated and thus temporarily fragile memory will become restabilized, and that will be that. However, under other conditions that perturb the system, a different result can be seen. In experimental work with animals, for example, the injection of protein synthesis inhibitors at this stage can disrupt the memory – an effect that is not seen in animals that received the same injections but without the prior memory reactivation (Nader et al., 2000). Another outcome, that we have explored (see below), involves the updating of the memory as a function of some novel experience. Thus, reactivation of an already consolidated memory is more than just

a “read-out” of the memory trace. Instead, reactivation initiates a process, labeled “reconsolidation”, that under some circumstances can lead to a changed (Hupbach et al., 2007) or even obliterated memory (Nader et al., 2000).

This is not a small problem that can be handled by tweaking one or another parameter of the textbook story. This problem goes to the very heart of the textbook story, which helps explain why the re-emergence of the idea of memory “reconsolidation” was met with such fierce resistance.

3. What next

Our view is that the facts alluded to above represent not just a challenge to the classic story concerning memory formation. They also create an opportunity to re-evaluate some basic assumptions about memory. The remainder of this paper is devoted to doing exactly that, in a spirit of what we hope is productive speculation. We consider the following questions:

- If memory consolidation is not about permanently fixing a memory trace, what is it about?

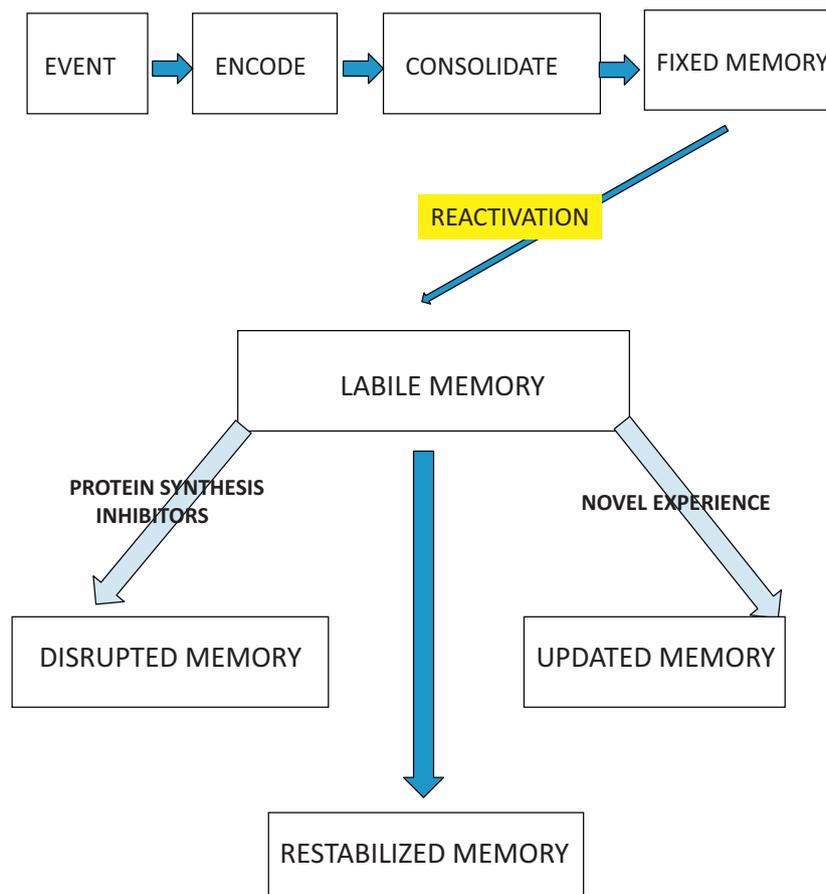


Fig. 2. Possible effects of reactivation induced memory trace lability: disruption (in this case caused by inhibition of protein synthesis; no change, other than restabilization of the trace, possibly in strengthened form; updating of the trace resulting from incorporation of novel information).

- What forms of memory transformation are possible, and how do these different forms of memory transformation map onto brain systems?
- What role does sleep play in the normal progression of memory formation?

Before addressing these questions we must spend some time talking about memory itself: what shape does it take in the brain? There is no single answer to this question, and indeed drawing careful distinctions between several forms of memory is crucial to understanding what consolidation is all about. A systematic analysis of memory is beyond the scope of this paper; readers are pointed to a recent review (Nadel and Hardt, 2011) that goes into considerably more detail on the following major points we will simply sketch out here:

1. While psychologists have made some progress sharply distinguishing processes such as perception, short-term memory and long-term memory, considerable neuroscientific evidence now suggests that such separations may make little sense in the brain (e.g., Barense et al., 2011).
2. Instead, the brain seems to be organized into representational systems distinguished by the qualitative nature of the information they represent (Nadel and Hardt, 2011). The idea that brain circuits are organized in this qualitative way is not new – similar ideas have been expressed for nearly 200 years: the doctrine of “specific nerve energies” first promulgated by Johannes Muller in the early 19th century, “labeled-line” theory, and content addressability are three manifestations of this idea.
3. Within this view, any given brain system represents a particular type of information, and is accessed whenever that kind of knowledge is deployed for any psychological process, such as attention, perception, short-term memory, or long-term memory.
4. We focus in this article on two kinds of memory and the representations that seemingly underlie them: episodic memory and semantic memory (e.g., Tulving, 1983). We experience the world “episodically” – acquiring knowledge from specific experiences in particular contexts (spatial and temporal). These experiences yield representations that at least at the outset allow us to recall both the context-bound episodic experience and the context-free knowledge that can be extracted from experience.
5. Current evidence suggests that information is processed simultaneously in multiple representational systems, such that representations supporting several kinds of “memory” are created in parallel, including episodic and semantic memories (see below).
6. It is misleading to talk about memories, either episodic or semantic, as being “retrieved”. This word implies a fixed entity that is accessed in its entirety. A better word is “remembered” or “recalled” – where the literal sense of those words is implied. That is, an episodic memory is stored in the brain in “dismembered” form, as bits and pieces represented in distinct brain systems. As Bartlett (1932) and many others have argued, recalling an episodic memory involves “reconstruction” – putting together these bits and pieces (accurately or not).

Most discussions of memory consolidation are concerned with episodic and semantic memory and the representations that underlie them, and how these forms of memory interact over time after an experience. As noted above, what makes things complicated is that the retrieval of either form of memory (episodic or semantic) typically engages brain systems important to both.

With these assumptions about memory in place, we can now turn to our three questions, starting with the very purpose of memory consolidation itself.

4. What is memory consolidation all about?

In contrast to the standard textbook story, we assume that consolidation is not only, or even primarily, about permanently fixing an isolated memory trace. Taking into account the points raised above about the nature of memory, we see memory consolidation as accomplishing a number of different things, depending on what aspect of memory one is looking at.

Consider what happens when an organism experiences a novel episode, which we can view as consisting of a set of entities (individuals, objects) interacting with each other in space and time. Let us leave aside, for present purposes, the various processes involved in “parsing” this episode into its constituent parts, although these are themselves fascinating and important. There is a consensus view of what happens in the nervous system during encoding: (1) representations of the various entities involved in the episode are activated, largely in cortical systems; (2) the conjunction of these entities activates representations within higher-order contextual systems, including the hippocampal formation. Representations in the hippocampal system encode spatial and temporal contextual attributes, while at the same time providing an “index” that can allow the system to access, and hence retrieve, the entities that played a role in a given episode. This much appears to be non-controversial, at least at the outset. What happens next during the phase of memory consolidation is not so clear, partly because there are two levels of memory representation, and the linkages within and between them that need to be considered, as seen in Fig. 3.

First, there are the various dispersed representations in cortex that capture the entities involved in the episode. These representations appear to involve distributed overlapping coding mechanisms that promote generalization. To put this in concrete terms, within this system kitchens can be distinguished from living rooms, but all kitchens are lumped together. Cortical systems appear to be specialized to extract the semantic features of entities, their statistical regularities, and to form categories and concepts.

Second, there is the representation formed within the hippocampal system that captures contextual attributes of the episode, most particularly the spatial context. These representations in the hippocampus appear to use sparse, distributed coding mechanisms that allow the system to separate closely related representations. This allows for sharp boundaries between quite similar contexts, and there is considerable evidence that hippocampal dysfunction manifests as, amongst other things, a loss of the ability to encode contexts and to discriminate amongst them (Nadel, 2008). This system can distinguish between my kitchen and that of my neighbor.

Then, there are the linkages among the various parts of the hippocampal contextual representations, the various parts of the cortical representations, and, finally, the linkages between the hippocampal-contextual representation and the distributed-cortical representations of the entities involved.

Memory consolidation could in principle affect each of these representations and linkages. As a result of consolidation processes, contextual representations in the hippocampal system, and entity representations in cortical systems, could be strengthened through enhancement of the changes in synaptic connectivity that is assumed to underlie memory at the cellular level. Although consolidation involves such strengthening in both cases, the outcome in the two systems is likely to be different: given the sparse coding in hippocampus, consolidation should have the effect of enhancing the unique, context-specific, nature of its representations. Given the overlapping coding that exists within at least some cortical

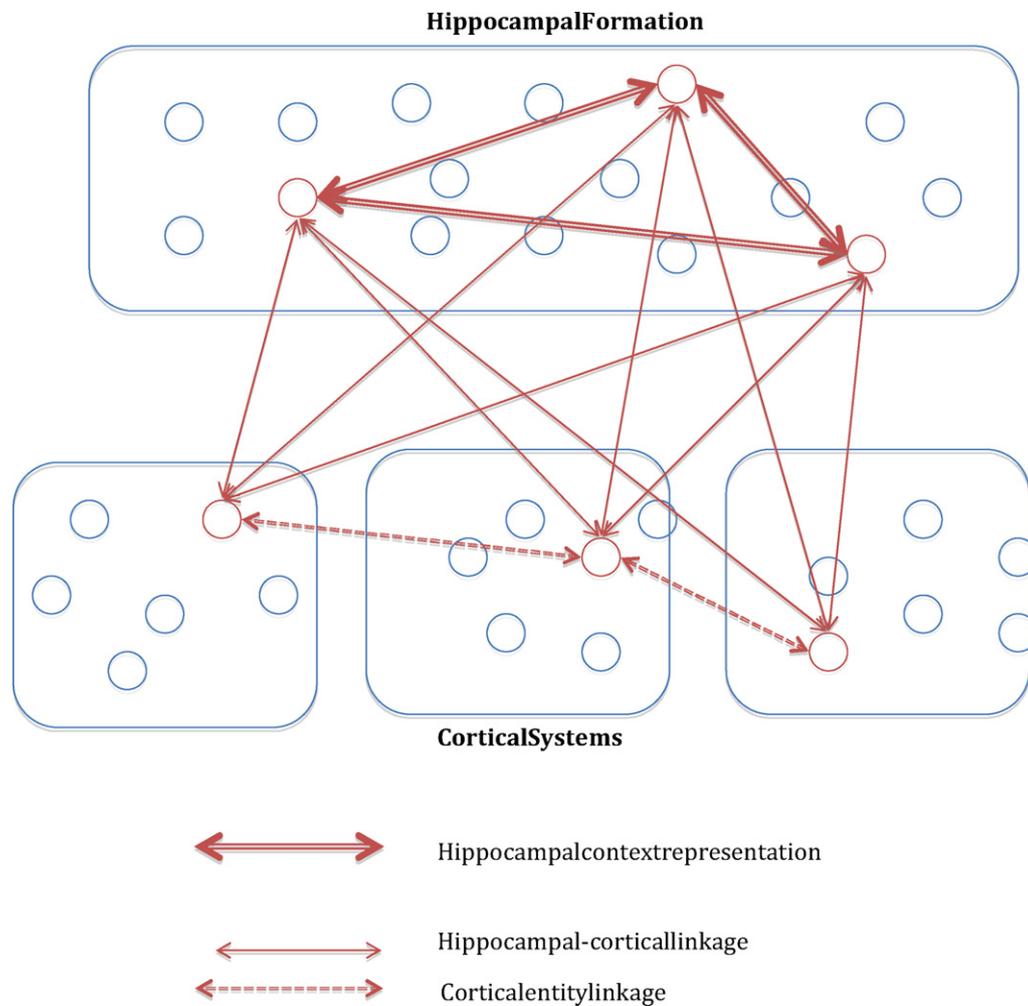


Fig. 3. Hippocampal and cortical representations.

systems, consolidation should have the effect of enhancing common elements at the expense of outliers. The result is the extraction of prototypes, or, to put it another way, the creation of semantic memory.

At the level of linkages other things are happening: creation of new linkages, or variations in the strength of linkages, within either the hippocampal or cortical systems result in memories that can be remembered or not. Such variations in the strength of linkages between hippocampal and cortical representations are at the heart of debates in the field of memory consolidation. Textbook models of consolidation presume that it is these linkages that fade with time, to be replaced by links within cortical networks (e.g., [Squire and Alvarez, 1995](#)). In this view, there is no necessary information loss associated with such a shift over time, since in this view the hippocampal representation is merely an “index” and captures no information other than which cortical nodes are part of the memory. In contrast, multiple trace theory (MTT, [Nadel and Moscovitch, 1997](#)) assumes that these linkages remain critical if one is to retrieve a detailed episodic memory, because the hippocampal representation is both an “index” and the bearer of specific spatial contextual information. Indeed, it is by virtue of being such a spatial representation that it can serve to index the entities that co-occurred in a particular spatial arrangement in the episode in question.

Thus, memory consolidation, and memory formation, involve the delicate interplay of all these factors, resulting in multiple representations, some of which represent the context, while others

represent the entities. What happens over time in these traces reflects the shifting fate of specific episodic knowledge and more generic semantic knowledge, about one’s experiences. It is hard to avoid the conclusion that we should be using the term memory transformation to describe these processes. Indeed, recent work building on multiple memory trace ideas uses this terminology to describe what happens to memories over time (e.g., [Winocur et al., 2010](#)).

5. What forms of memory transformation are possible? How are they instantiated in different brain systems? And what role does sleep play in the transformation process?

Following on from the analysis above, what can we say about the kinds of transformations that occur during memory consolidation and reconsolidation?

It would be instructive to work through the various stages of memory transformation in terms of an actual example for which some empirical data exist. [Fig. 4](#) portrays a paradigm we have recently been using to study episodic memory updating in humans. In brief, subjects learn a list of twenty common everyday objects, then two days later come back and are either actively reminded of that learning experience or not, then learn a second list of twenty objects. Again, two days later, they return and are asked to recall (or recognize) the objects from either the first or second list. In a series of studies ([Hupbach et al., 2007, 2008, 2009](#)) we have shown that when reminded prior to learning List 2, subjects routinely include

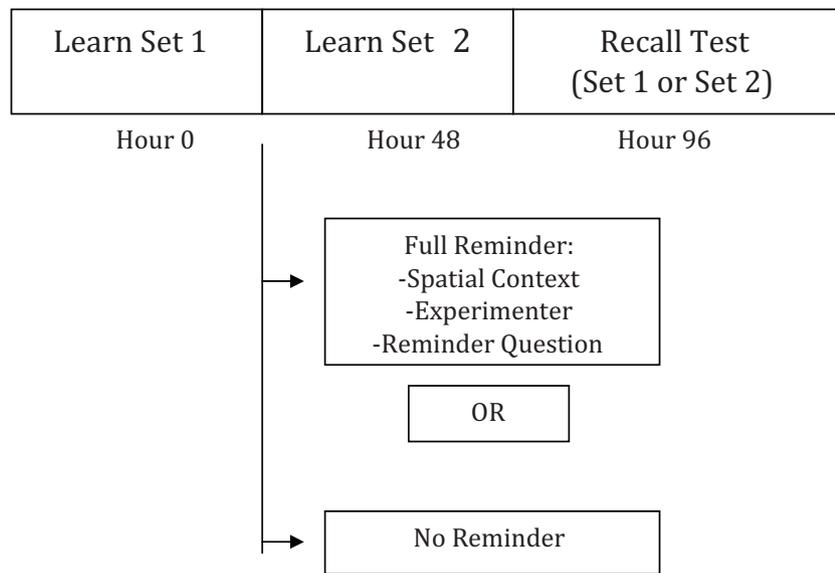


Fig. 4. Paradigm for the study of episodic memory reconsolidation. In the Full Reminder condition subjects are brought back to the same spatial context with the same experimenter and are asked if they remember what they were previously asked to do in the original session. Subjects in the No reminder condition go to a different location to learn List 2 with a different experimenter and get no reminder question.

(on the final test day) a number of the List 2 objects in their recall of List 1. They do not include List 1 items on a recall of List 2, so this is not a simple source confusion effect. And, although there is interference in recall of List 1 from having learned List 2 in terms of fewer List 1 items recalled, this interference is independent of the intrusions resulting from the reminder manipulation (Hupbach et al., unpublished data). Finally, the most effective reminder to elicit this memory updating effect is the initially rather unfamiliar spatial context in which the entire study is carried out (Hupbach et al., 2011).

Recently, the proponents of Temporal Context Models (TCM) of memory have simulated some of our results using a TCM-like model (Sederberg et al., 2011), but their approach cannot as yet account for the special role played by the spatial context (Hupbach et al., 2011). Further studies will allow us to determine the ultimate usefulness of this kind of approach to understanding the mechanisms underlying our updating effect.

Here, we would like to take another approach that is less about the mechanisms and more about the underlying systems-level processes we discussed above. Consider what is going on in the various representations and linkages when our subjects acquire a memory for List 1. We imagine that a number of things are happening in parallel: (1) representations of the objects in List 1, which presumably already exist, are activated in neocortical structures; (2) representations of all the other elements in the situation – the experimenter, the features of the room, etc. are also activated in neocortical structures; (3) linkages are formed between these various activated cortical traces and elements in the hippocampus; (4) the particular hippocampal elements activated become linked together to form a trace that encodes the spatial relations among the entities – this neural ensemble is the hippocampal-context representation; (5) linkages, however weak, are initiated between the representations of the entities in cortex (forming the distributed-cortex representation).

We assume that in the short run there are cellular changes that modulate the strength of these traces, a process typically labeled cellular consolidation (e.g., Mednick et al., 2011). In the long run, more substantial changes take place at the systems level, and as suggested above, many of these seem to take place

during sleep. In the course of a normal night of sleep, individuals experience periods of slow-wave sleep (SWS), followed by periods of rapid eye-movement sleep (REM). There are several notions about what happens during these two stages of sleep. According to the “active system consolidation” view (Diekelmann & Born, 2010), slow wave sleep repeatedly reactivates the hippocampal and neocortical traces resulting from an episode, leading to the strengthening of neocortical representations and the weakening of hippocampal representations. Such reactivations also act to incorporate information from the new episode into pre-existing cortical stores. Diekelmann and Born hypothesize that REM sleep may then play a role in stabilizing neocortical stores through synaptic consolidation.

Two other positions have been expressed concerning what happens to memory traces during SWS and REM. According to Tonini and Cirelli (2003, 2006), a process of synaptic rescaling renormalizes the hippocampal system during slow wave sleep without the loss of the hippocampal representation, a position more in line with our views than with the active system consolidation view. Walker and Stickgold (2010) further propose that REM is involved in memory integration, a process that goes beyond the initial consolidation mechanism Diekelmann & Born suppose happens during SWS.

These latter considerations suggest to us the following hypothesis: (1) in slow wave sleep, some selection process chooses amongst traces that have been formed during the day just those that deserve to persist; (2) following this, synaptic rescaling (cf. Tonini and Cirelli, 2003) renormalizes the hippocampal system, leaving only the “chosen” traces above threshold; (3) the stage having been cleared of extraneous actors, a second phase can now begin. In this phase the remaining above-threshold “traces” are replayed to the cortex; (4) we speculate that during this phase constraints on cortical plasticity are transiently lowered, facilitating the formation of new associations as well as the strengthening of those ensembles activated as a result of hippocampal replay; (5) in this way, information gathered during the episode in question can be integrated into existing cortical circuits; and finally (6) assimilation of connections among the different elements of the cortical representation occurs in REM.

Consider how this hypothesized sequence of events would play out in our memory updating paradigm: first, we assume that representations formed during the learning of List 1 survive the rescaling process. What is more, we assume that one result of rescaling these memory traces is their transformation into a form that allows later updating. We make this assumption because of some recent findings in our lab exploring the effects of sleep deprivation on memory updating. In this study (Newman-Smith et al., 2011) subjects learned List 1 and then were sleep deprived before learning List 2. In this case, subjects who were reminded of List 1 prior to learning List 2 did not misattribute List 2 items to List 1 (in contrast to what we find when subjects had a chance to sleep after List 1 encoding). By the time of this retrieval subjects had slept, so fatigue could not have been the cause of this seemingly anomalous result. There are two rather different ways of understanding this result. One possibility follows from the fact that Lists 1 and 2 are learned in very different mental contexts – one well rested, the other sleep deprived. List 1 is then recalled in a well-rested state, which matches the context in which List 1, but not List 2, was learned. It is possible that this context mismatch makes intrusions highly unlikely. Another possibility follows from the analysis offered above: during sleep a process unfolds that lowers constraints on plasticity and facilitates the formation of new connections. Until one sleeps, the traces established that day are protected from such change, and appear subject only to decay and consequent forgetting. Consistent with this idea is a study comparing paired-associate recall after 48 h during which one group of subjects slept during the first 24-h interval and a second group did not sleep until the second night after learning (Gais et al., 2007). The group that was sleep deprived forgot more associates than the group that slept and also showed less hippocampal brain activity during recall as measured by fMRI. This result suggests two things: first, sleep can both strengthen memory traces (thereby diminishing forgetting), and, perhaps as a function of hippocampal activity, transform memories into a format that permits subsequent updating.

In the account above we have attributed this effect to something that occurs during either slow wave or REM sleep. In our study subjects were deprived of both slow wave and REM sleep, so we cannot pin down which sleep stages are responsible at present.

To summarize, we believe memory traces are transformed over time in a number of ways, but that understanding these transformations requires careful analysis of the various representations and linkages that result from an experience. Many of these transformations occur in the normal course of events: (1) the selective strengthening of only some, but not all, traces as a function of synaptic rescaling, or some other process that can result in selective survival of some traces; (2) the integration (or assimilation) of new information into existing knowledge stores; (3) the establishment of new linkages within existing knowledge stores.

One class of transformations, however, only follows upon reactivation of previously established memory traces. These all involve the up-dating of an existing episodic trace that has been activated (cf., Lewis, 1979). It remains unclear what aspects of the episodic trace are actually changed as a function of updating. In principle there seem to be three possibilities: the hippocampal trace could be expanded to incorporate links to new (contextual) elements; cortical traces could be changed to incorporate associations between old and new elements; and, finally, the linkages between hippocampal and cortical trace systems could be expanded to include links to the newly incorporated elements. These three are by no means mutually exclusive; there are reasons to imagine that all are taking place.

As we indicated at the outset, this speculative analysis of the various processes involved in memory formation and reformation is offered with the view that we must, as a field, move away from current static understandings of memory to embrace the dynamics we now know to characterize this psychological capacity. We certainly do not expect our analysis to be right in all particulars, but rather hope that it will prove sufficiently interesting to propel new research and theories in the future.

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