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THEORETICAL REVIEW

Mechanisms for Widespread Hippocampal Involvement in Cognition

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The quintessential memory system in the human brain—the hippocampus and surrounding medial temporal lobe—is often treated as a module for the formation of conscious, or declarative, memories. However, growing evidence suggests that the hippocampus plays a broader role in memory and cognition and that theories organizing memory into strictly dedicated systems may need to be updated. We first consider the historical evidence for the specialized role of the hippocampus in declarative memory. Then, we describe the serendipitous encounter that motivated the special section in this issue, based on parallel research from our labs that suggested a more pervasive contribution of the hippocampus to cognition beyond declarative memory. Finally, we develop a theoretical framework that describes 2 general mechanisms for how the hippocampus interacts with other brain systems and cognitive processes: the memory modulation hypothesis, in which mnemonic representations in the hippocampus modulate the operation of other systems, and the adaptive function hypothesis, in which specialized computations in the hippocampus are recruited as a component of both mnemonic and nonmnemonic functions. This framework is consistent with an emerging view that the most fertile ground for discovery in cognitive psychology and neuroscience lies at the interface between parts of the mind and brain that have traditionally been studied in isolation.

Keywords: memory, hippocampus, perception, learning, decision making

Memory, in all its forms, is what enables cognition. Without it, we would be unable to recognize people, places, or things; unable to speak, understand language, or plan. It is the root of our personal identities, the source of regret, pride, and nostalgia. Conceived of in this way, understanding how memory is organized and how it interacts with other aspects of the mind is essential for all areas of psychology.

The study of memory is an instructive example of how neuroscience can inform—and be informed by—psychology. This integration has a long history in animal behavior and neurophysiology, human neuropsychology, and, more recently, human neuroimaging. The resulting theories, particularly the multiple memory systems theory, have framed decades of research and are among the most publicly disseminated and well known throughout psychology.

This article is the first in a series of articles published as a special section of the *Journal of Experimental Psychology: General.* In the broadest terms, the goal of the special section is to encourage a continued dialogue with neuroscience among the readership of this influential journal in psychology. Although these articles are focused on memory, we hope that they demonstrate the general value of integrating psychology and neuroscience, which could apply across a wide range of topics.

Given the long-standing interaction between neuroscience and the psychology of memory, why a special section now? The purpose is to present cutting-edge findings and views that make a compelling case for reevaluating standard theories. Indeed, although there is an existing tradition of considering alternative conceptions of memory, the multiple memory systems framework has been dominant for more than 50 years.

Multiple Memory Systems

From the perspective of modern cognitive neuroscience, it is hard to imagine that scientists once thought that learning and memory were supported equally by all parts of the brain (Lashley, 1950). This notion was dramatically revised by an accidental discovery after a surgery gone wrong. In 1953, the now-famous patient H. M. underwent bilateral removal of the hippocampus and

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surrounding tissue as a treatment for intractable epilepsy. The result was a severe memory impairment (Corkin, 2013; Scoville & Milner, 1957; Squire, 2009): H. M. lost the ability to form new memories of his experiences, such as what he had done that morning or whom he had met recently. But not all forms of memory were affected. H. M. continued to be able to learn motor skills (such as mirror drawing) and continued to be vulnerable to automatic and unconscious influences of experience on behavior (such as priming).

The severity of the memory loss, combined with its selectivity, suggested that memory is not a unitary process, neither cognitively nor in the brain. Rather, it might be best understood in terms of a set of parallel and independent processes. Researchers began by differentiating between two broad forms of memory: declarative memory and nondeclarative memory (also known as procedural memory). Declarative memory has been used to refer to long-term conscious memories of general facts (semantic memory) and personal events (episodic memory). Nondeclarative memory has been used to refer to everything else, particularly nonconscious learning of skills and habits, perceptual information, emotional and skeletal responses, and reflexes (Squire, 2004). On the basis of cases like patient H. M., it was concluded that declarative memory depends on the hippocampus, whereas nondeclarative memory does not.

This theory of multiple memory systems opened the door for decades of research into the organization of memory. Much of this work has focused on developing a detailed understanding of the cognitive and neural mechanisms by which the hippocampus and surrounding medial temporal lobe (MTL) regions support declarative memory.

A prototypical task used to study declarative memory in humans involves presenting participants with a series of words or objects and later testing their memory. Tests can include asking participants to recall as many items as possible or to judge which items they recognize from the list. Neuroimaging has enabled substantial progress in understanding the organization of memory by examining what happens in the brain at the time of successful versus unsuccessful encoding (Paller & Wagner, 2002) and retrieval (Hutchinson, Uncapher, & Wagner, 2009). This has led to insights about the contributions of particular MTL subregions to declarative memory. For instance, encoding depends on binding items to the context in which they appear: The hippocampus is thought to be important for the binding process itself, and perirhinal and parahippocampal cortices represent the items and contexts, respectively (Davachi, 2006; Ranganath & Ritchey, 2012; Shimamura, 2010). Likewise, retrieval can be associated with a weak sense of familiarity or a full recollection of the encoding details, and there is evidence that these two modes can be mapped onto MTL cortex and hippocampus, respectively (Yonelinas, Aly, Wang, & Koen, 2010; cf. Smith, Wixted, & Squire, 2011).

In parallel, a search began for the cognitive and neural underpinnings of nondeclarative sorts of memory. Two forms of nondeclarative memory that have received considerable attention are priming and habit learning. Priming refers to a phenomenon wherein mere exposure to an item can facilitate later processing of that item or related items. In the task above, rather than asking for memory judgments at test, researchers might measure priming in terms of how easily participants detect or identify a degraded item based on whether it was presented earlier. By definition, priming involves some form of memory for prior experience, but it does not seem to require awareness and can be independent of declarative memory (Tulving & Schacter, 1990; cf. Turk-Browne, Yi, & Chun, 2006). In the perceptual domain, priming reflects automatic mechanisms in stimulus-selective cortical areas that attenuate neural activity (Grill-Spector, Henson, & Martin, 2006; Wiggs & Martin, 1998). Indeed, such perceptual priming has been found behaviorally in amnesic patients with declarative memory deficits (Hamann & Squire, 1997), part of a double dissociation where patients with occipital damage show no priming but have intact declarative memory (Gabrieli, Fleischman, Keane, Reminger, & Morrell, 1995).

Another domain of nondeclarative memory is the learning of procedures or habits. Habit learning is classically thought to occur slowly over many experiences and without conscious awareness. It is typically measured in terms of performance rather than memory, such as a tendency to learn to respond correctly to a stimulus across repeated attempts. Converging evidence suggests that habit learning is dependent on the striatum (Balleine & O'Doherty, 2010; Yin & Knowlton, 2006) and can occur independently of the hippocampus. For example, early studies showed that amnesic individuals with declarative memory deficits were capable of incremental learning of probabilistic stimulus–response associations despite having no conscious memory for the testing episode (Knowlton, Mangels, & Squire, 1996; Knowlton, Squire, & Gluck, 1994; cf. Hopkins, Myers, Shohamy, Grossman, & Gluck, 2004). By contrast, patients with disrupted striatal function due to Parkinson's disease were impaired at incremental learning of the task but had intact declarative memory for the testing episode (Knowlton et al., 1996).

These types of double dissociations between declarative and nondeclarative forms of memory were central in advancing the notion that memory is organized into multiple distinct and independent systems. Although this view has long been challenged in psychology (e.g., Crowder, 1989; Hintzman, 1990; Roediger, Rajaram, & Srinivas, 1990), it has had remarkably broad reach within and beyond the field of memory and is still taught in almost every introductory psychology and neuroscience course.

Scientific Serendipity

There is an extensive body of research on memory systems, conducted by several distinguished scientists, many of whom remain active to this day. How did the two of us come to be involved in organizing this special section?

A spontaneous conversation at Columbia University helped us recognize a synergy in our research. Although we both received some training in the field of memory, our interest in the hippocampus actually came from outside the field. In fact, it arose initially as somewhat of a surprise during studies of perception (N. T.-B.) and decision making (D. S.). These fields have not traditionally focused much on memory, and when they have, the emphasis has been on nondeclarative forms, such as priming and habit learning, that are thought to be subserved by other brain systems. Nevertheless, we each found ourselves grappling with empirical findings suggesting a role for the hippocampus in these domains. Below, we discuss this work from each lab separately and how these different lines of inquiry converged on the hippocampus.

The goal of perception is to recover the contents of the world from sensory input (light, sound, etc.). The environments we inhabit are generally stable over time, meaning that this sensory input contains widespread regularities. In high-level vision, this might correspond to the fact that we repeatedly encounter similar people, places, and things, and they tend to appear in similar spatial configurations and temporal sequences. The process of extracting such regularities is known as statistical learning (Aslin & Newport, 2012; Chun, 2000; Perruchet & Pacton, 2006).

In the Turk-Browne lab, much of our research on statistical learning has examined behavior (most recently, Zhao, Al-Aidroos, & Turk-Browne, 2013). But in the last few years, we have also begun investigating which brain systems might be responsible for this learning using functional magnetic resonance imaging (fMRI). The initial goals of this work were to use fMRI as a potentially more sensitive and online measure of statistical learning (Turk-Browne, Scholl, Chun, & Johnson, 2009) and to identify the functional consequences of such learning (Turk-Browne, Scholl, Johnson, & Chun, 2010). Beyond these goals, however, the studies also surprisingly and repeatedly found that the hippocampus was involved in statistical learning (see also Bornstein & Daw, 2012; Chun & Phelps, 1999; Curran, 1997; Durrant, Cairney, & Lewis, 2012; Harrison, Duggins, & Friston, 2006).

Why was this surprising to us? Because there are many reasons to think that statistical learning should not be hippocampally dependent. Consider the contribution of the hippocampus to declarative memory: It encodes single episodes, which can later be accessed consciously. In contrast, statistical learning requires computing probabilistic relationships across multiple episodes, and both the initial learning and the expression of knowledge are often automatic and implicit (e.g., Kim, Seitz, Feenstra, & Shams, 2009). More generally, the extraction of regularities over various time scales is typically viewed as a function of the neocortex (McClelland, McNaughton, & O'Reilly, 1995; Simoncelli & Olshausen, 2001).

We conducted a high-resolution fMRI study to more directly examine the role of the hippocampus in extracting regularities (Schapiro, Kustner, & Turk-Browne, 2012). Based on animal neurophysiology (Miyashita, 1993; Suzuki, 2008), this study tested the hypothesis that the hippocampus encodes regularities by shaping the similarity of object representations. Participants were incidentally exposed to a set of novel fractal-like objects (e.g., *A*–*H*; one letter per object), from which a distributed neural representation of each object was estimated in the hippocampus. Participants were then shown the same objects in a stream that, unbeknownst to them, contained temporal regularities (e.g., *ABEFCDABCGHD* . . .). When the hippocampal representations were estimated again after this exposure, objects that had followed each other with high probability (e.g., *AB*) came to be represented more similarly, relative to lower-probability (e.g., *CD*) and zero-probability pairs (e.g., *AH*). The hippocampus was playing a role beyond declarative memory.

When these results were presented in a brown-bag talk at Columbia University in the fall of 2011, an immediate connection was formed between us. Nearly identical stimuli were being used to investigate a completely different process, decision making. And once again the hippocampus was implicated.

Recent breakthroughs into the brain mechanisms of decision making have highlighted the important role of the striatum in learning to predict and obtain rewards (O'Doherty, Dayan, Friston, Critchley, & Dolan, 2003; see Daw & Doya, 2006). A key aspect of this discovery was that dopamine neurons in the midbrain—which modulate the striatum—signal the difference between expected and received rewards. This allows the brain to learn from experience to make choices that will increase the chances of reward in the future (Schultz, Dayan, & Montague, 1997; see Schultz, 2010). For example, imagine ordering one cookie at a coffee shop and receiving two. You would probably be more likely to go there again (and again). These findings align well with the idea from multiple memory systems theory that the striatum supports habit learning (Foerde & Shohamy, 2011b). Ideas about reward prediction in the striatum also suggested a neural mechanism by which habit learning could be accomplished.

Research in the Shohamy lab has drawn on such converging findings in learning and decision making to advance understanding of the role of the striatum in both behaviors. We found that rather than contributing broadly to probabilistic learning, the striatum selectivity supports learning when it is driven by immediate, trial-by-trial feedback—consistent with the reward prediction error coding in dopamine neurons. Learning the same information without feedback or with delayed feedback—even when this learning is not consciously accessible—depends instead on the hippocampus (Foerde, Race, Verfaellie, & Shohamy, 2013; Foerde & Shohamy, 2011a; Poldrack et al., 2001; Shohamy et al., 2004; cf. Clark & Squire, 1998). From a declarative memory perspective, these findings were surprising. They suggested that although the hippocampus and the striatum contribute to learning in different ways, they also have a lot in common. The hippocampus then seemed positioned to influence even reward-based decisions, behaviors typically ascribed to the striatum.

Most work in decision making had focused on how we make choices between familiar options, such as where to go for a quick lunch near the office. These decisions are informed by prior experience, such as an unexpectedly revelatory or disappointing meal in the past. In this situation, the assignment of value to options occurs through reward learning in the striatum. But what about when we have to decide between options with which we have no experience? Building on suggestions in the literature (Eichenbaum, 2000; Tolman, 1948), we examined the role of associative learning in this kind of "blind" decision making. The central hypothesis was that an efficient way to inform decisions between new options could be if, during reward learning, the reward value spreads beyond the cue to also enhance the value of other items associated with it in memory. This could be realized in the brain by associating the reward with the current stimulus via the striatum and also concurrently associating the reward with other stimuli reactivated via the hippocampus. In this way, preferences can arise not only from experience but also by association.

This hypothesis was tested in an fMRI experiment (Wimmer & Shohamy, 2012). Participants were incidentally exposed to a series of stimulus pairs (S_1S_2), where the first stimulus was a real-world image and the second was a fractal-like object. This stage is, in many ways, strikingly similar to the statistical learning task described above (Schapiro et al., 2012). But here, some of the objects (S_2+) were later paired with a monetary reward using classical conditioning, and the remaining objects were presented without reward (S_2-). In a final phase, some of the images previously paired with the rewarded objects (S_1+) were preferred over those paired with nonrewarded objects (S_1-), even though they had not themselves been rewarded. This value transfer occurred when the hippocampus was more active during the initial reward learning, reactivating the associated image such that it could be bound to the reward through functional connectivity with the striatum. But importantly, participants could not consciously identify the pairs, which suggested that this bias in decision making did not depend on declarative memory.

Thus, the research in our two labs unexpectedly led us to consider the role of the hippocampus in domains other than declarative memory. Our studies bore superficial similarity, as we were both using tasks in which participants learned about temporal associations between visual stimuli. We saw a deeper synergy too, whereby the hippocampus acts as a bridge between perception and decision making (see Figure 1): Schapiro et al. (2012) revealed the existence of shared representations in the hippocampus for associated perceptual objects, and Wimmer and Shohamy (2012) demonstrated that these representations can be leveraged to bias decisions. Here was a case where neuroimaging data seemed inconsistent with a psychological theory.

We credit Ran Hassin for refusing to let us handwave about the status of conventional views about declarative memory in the face of our results and for encouraging us to share this conversation with the broader community. There have been many other inconsistencies with and challenges to multiple memory systems far preceding our work (e.g., Crowder, 1989; Hintzman, 1990; Roediger et al., 1990). Although these issues have been noted and debated in the memory literature (e.g., Cohen & Eichenbaum, 1993; Henke, 2010; Suzuki & Baxter, 2009), the broader fields of psychology and neuroscience continue to treat multiple memory systems theory as dogma. We have both encountered reviewers and colleagues from other fields who express genuine surprise that we are studying the hippocampus, given our interests, or that we are finding a role for the hippocampus in learning and decision processes that often take place without conscious effort or awareness.

Our goal in organizing this special section was therefore to collect new developments about the cognitive functions of the hippocampus and MTL, many from outside the field of memory, to synthesize them for a broad audience, and to highlight possible new avenues for discovery. Time will tell whether these developments can be accommodated within current theories, or whether they demand a more wholesale course correction. Finally, we thank Isabel Gauthier for her amazing leadership throughout this process, Jenn Richler for her editorial guidance, and the special section authors for their hard work and exciting contributions.

The Case for a New Theory

It makes sense, when confronted with an unknown machine, to first identify the separate component parts and their specific functions. This is what pioneering neuropsychological and neuroimaging work has done in characterizing multiple memory systems. But once these components are identified, a whole new set of questions can be asked about how they work together to accomplish a more general function and what an understanding of such interactions tells us about the role of each component. We believe that this is where the field of memory stands now, as it starts to address new questions about what memory systems have in common and how they work together to support cognition more broadly. We need to confront the complexity of data that result from these investigations and to be open to reevaluating the traditional framework.

The strict division of labor into segregated systems may be mostly a useful simplification (see also Chun & Johnson, 2011;

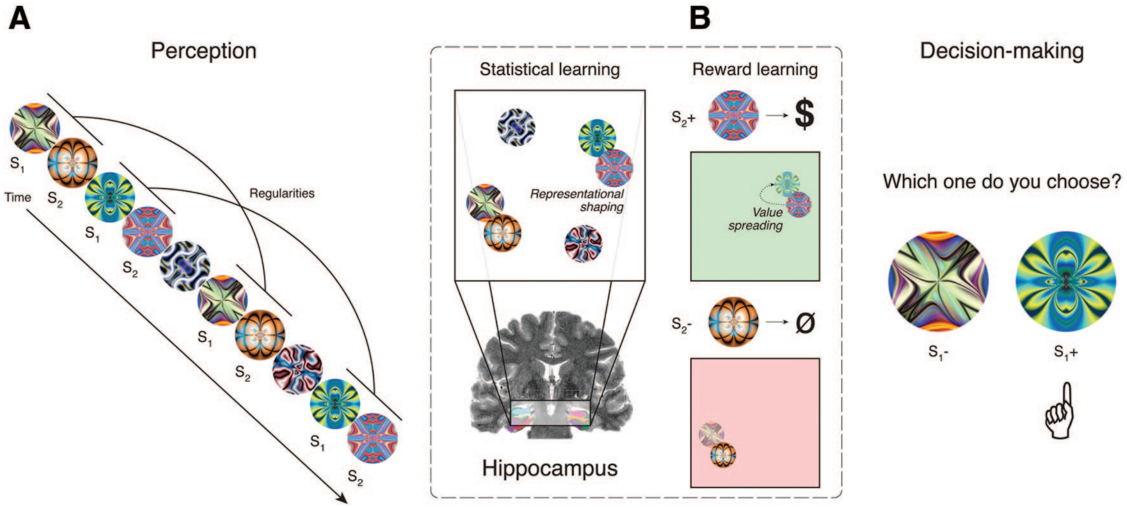

Figure 1. (A) Incidental exposure to temporal regularities increases the similarity of voxel patterns elicited by the associated objects within the hippocampus (Schapiro et al., 2012). This representational similarity allows the perception of one object to partially reactivate the hippocampal representation of the associate. (B) The extent to which this occurs during reward learning for one of the objects, as reflected in overall hippocampal activation, determines the value of the other associated object (Wimmer & Shohamy, 2012). This value is reflected in a higher likelihood of choosing this object later during decision making, even when it itself has never been directly rewarded. This figure is a conceptual depiction of the overlap of the studies in our two labs; in Wimmer and Shohamy (2012), S_1 images were actually faces, body parts, or scenes, rather than fractals. S_1 = Stimulus 1; S_2 = Stimulus 2.

Gaffan, 2002; Henke, 2010; Nadel & Hardt, 2011; Ranganath & Blumenfeld, 2005; Shanks & Berry, 2012). Although evidence of dissociations in patients provides an important first step in understanding how memory is organized, there are limitations in what logical conclusions can be drawn. For example, even if an aspect of memory function is preserved after damage—such as priming in amnesic patients—this does not mean that it is accomplished the same way as in the normal brain. Similarly, if some function is impaired after damage, this does not mean that the damaged area is the most essential or substantial component of that function.

The emphasis on differentiation of systems also encourages the labeling of single brain regions with single functions (a one-to-one mapping). But there can be parallel representations of the same event in multiple systems that all combine into one behavioral output (a many-to-one mapping). Moreover, any one brain system can contribute to multiple behavioral outputs (a one-to-many mapping). Indeed, there is much evidence from whole-brain imaging of the healthy brain for both of these possibilities in the case of memory and the hippocampus (see Figure 2).

Anatomically, the brain consists of highly interconnected networks, with both direct and indirect pathways between the hippocampus and other brain regions (see Figure 3). There are also common neuromodulatory inputs to areas thought to support distinct learning and memory processes, such as dopamine projections from the midbrain (Lisman & Grace, 2005; Shohamy & Adcock, 2010), by which motivation can influence memory (Adcock, Thangavel, Whitfield-Gabrieli, Knutson, & Gabrieli, 2006).

This all suggests that multiple systems can share information with each other and receive common input from other regions. Embracing the complexity of memory organization brings to light new questions about memory function: What is shared between memory systems? How do they interact? Are they competitive or cooperative? What is the significance of such interactions for behavior?

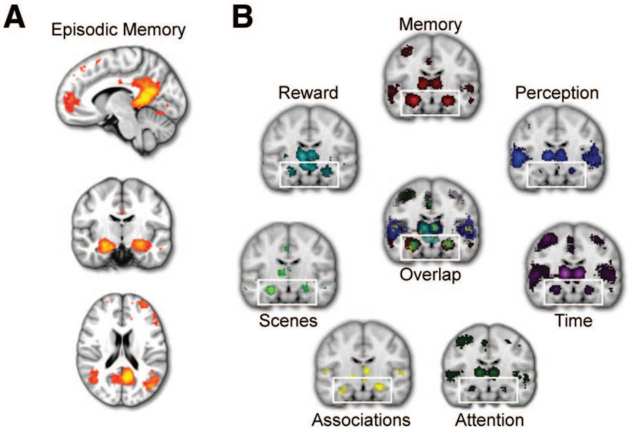

Figure 2. (A) Meta-analysis from http://neurosynth.org (see Yarkoni, Poldrack, Nichols, Van Essen, & Wager, 2011) of more than 4,000 published studies illustrating multiple brain regions associated with episodic memory. Colored voxels reflect a significant probability of the term *episodic* appearing in articles that reported activation in these voxels (reverse inference, corrected $p < .05$). (B) Meta-analysis of the same database illustrating multiple functions associated with the hippocampus and MTL (white frame). Colored voxels reflect a significant probability of activation in these voxels when an article contained each of the terms (forward inference, corrected $p < .05$). MTL = medial temporal lobe.

There is some evidence of interactions between the hippocampus and other memory systems, especially the striatum. For example, some studies in animals and humans have reported a negative relationship between these systems (e.g., Packard, 1999; Poldrack et al., 2001), suggesting that they compete for behavioral control. At the same time, other studies have reported a positive relationship, suggesting that these memory systems can guide behavior cooperatively (e.g., Sadeh, Shohamy, Levy, Reggev, & Maril, 2011; Wimmer & Shohamy, 2012; see Hartley & Burgess, 2005).

In fact, as evidenced by articles featured in the special section, the hippocampus is not exclusively dedicated to declarative memory. One of the clearest examples is the rich history of research on the function of the hippocampus in animals; by definition, it is difficult to test their ability to consciously report memories. This challenge has led to new theories of the hippocampus that emphasize the nature of the underlying representation, rather than the manner in which memory is expressed. For instance, relational memory theory places primary emphasis on the role of the hippocampus in building relations between items (Cohen & Eichenbaum, 1993; see also Horner & Burgess, 2013). Consistent with this theory—and inconsistent with multiple memory systems theory—the hippocampus supports relational processing over short intervals (Hannula, Tranel, & Cohen, 2006; Kurczek, Brown-Schmidt, & Duff, 2013; Olsen, Rondina, Riggs, Meltzer, & Ryan, 2013; Race, LaRocque, Keane, & Verfaellie, 2013), and relations can be deployed without awareness (Hannula & Ranganath, 2009; Ryan, Althoff, Whitlow, & Cohen, 2000). Relational memory is part of a broader class of theories about associative, contextual, and configural binding processes in the hippocampus (Hirsh, 1974; Johnson & Chalfonte, 1994; Milivojevic & Doeller, 2013; Nadel & Peterson, 2013; O'Keefe & Nadel, 1978; Sutherland & Rudy, 1989). In further support of these theories, the hippocampus is involved in incidental learning of temporal sequences (Curran, 1997; Durrant et al., 2012; Harrison et al., 2006; Schapiro et al., 2012; Turk-Browne et al., 2009) and spatial configurations (Chun & Phelps, 1999; cf. Manns & Squire, 2001), as well as in probabilistic reinforcement learning (Bornstein & Daw, 2012; Dickerson, Li, & Delgado, 2011; Foerde, Knowlton, & Poldrack, 2006).

Additional work in the special section reinforces a growing literature that challenges multiple memory systems theory by showing hippocampal involvement in cognition beyond basic notions of memory altogether. For example, the hippocampus has been implicated in imagining the future (Addis & Schacter, 2012; Peters & Büchel, 2010; cf. Kwan, Craver, Green, Myerson, & Rosenbaum, 2013), representing space (O'Keefe & Dostrovsky, 1971) and time (Howard & Eichenbaum, 2013), decision making during navigation (Johnson & Redish, 2007; Pfeiffer & Foster, 2013), transitive inference (Dusek & Eichenbaum, 1997), perception (Lee, Yeung, & Barense, 2012; Maguire & Mullally, 2013; Saksida & Bussey, 2010; see also Bainbridge, Isola, & Oliva, 2013; Yeung, Ryan, Cowell, & Barense, 2013), attention (Muzzio et al., 2009; see also Dudukovic, Preston, Archie, Glover, & Wagner, 2011; Reas & Brewer, 2013), and reward (Adcock et al., 2006; Wimmer & Shohamy, 2012; Wolosin, Zeithamova, & Preston, 2013).

How can the hippocampus be involved in such a broad range of behaviors? Is it involved because they all rely on similar mne-

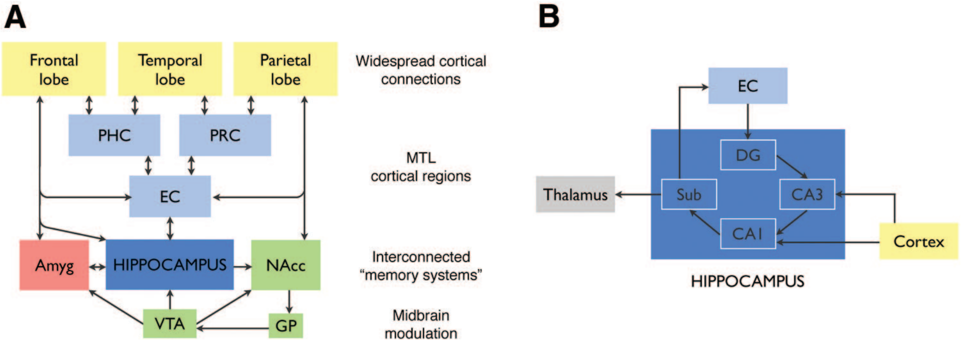

Figure 3. (A) The hippocampus is highly interconnected with many other cortical and subcortical brain regions, including those traditionally thought to support separate memory systems. These anatomical connections provide opportunities for shared and interactive cognitive processing. (B) Information processing circuit among subfields of the hippocampus. MTL = medial temporal lobe; Amyg = amygdala; CA# = cornu ammonis area #; DG = dentate gyrus; EC = entorhinal cortex; GP = globus pallidus; NAcc = nucleus accumbens; PHC = parahippocampal cortex; PRC = perirhinal cortex; Sub = subiculum; VTA = ventral tegmental area.

monic representations? Or, does the hippocampus contribute directly and essentially to nonmnemonic processes?

Mechanisms of Hippocampal Interaction

Here we make an initial attempt to reconcile these divergent findings theoretically. In the most general terms, we propose that the hippocampus shows up in such varied contexts because it is highly interactive. This is true at the neuroscientific level, with strong anatomical connections between the hippocampus and many other parts of the brain, including temporal cortex (Suzuki & Amaral, 1994), dorsolateral prefrontal cortex (DLPFC; Goldman-Rakic, Selemon, & Schwartz, 1984), visual cortex (Felleman & Essen, 1991), lateral parietal cortex (Rockland & Hoesen, 1999), and the midbrain and striatum (Shohamy & Adcock, 2010). As noted above, this is also true at the psychological level, with the hippocampus seemingly involved in most major cognitive functions. Examining the nature of these interactions—both within and between levels of analysis—holds tremendous potential for improving our understanding of cognition.[1]

To begin making progress in this endeavor, we propose two general ways in which the hippocampus can play such a widespread role. First, mnemonic representations in the hippocampus might modulate the operation of other systems. Second, specialized computations in the hippocampus might be recruited as a component of complex and distributed processes. We offer these two theoretical possibilities (henceforth the memory modulation hypothesis and the adaptive function hypothesis, respectively) as a platform for thinking about hippocampal interactions, abstracted away from the details of particular domains.

The memory modulation hypothesis (see Figure 4A) holds that mnemonic representations are the core function of the hippocampus. To guide behavior, these representations serve as a source of modulatory input to other brain systems. This input carries information that may not be currently available from the outside world but that appeared in, or was associated with, the same environment in the past. This is consistent with the important role for context in organizing memory (DuBrow & Davachi, 2013; Howard & Eichenbaum, 2013; Polyn, Norman, & Kahana, 2009; Smith, Hasinski, & Sederberg, 2013). The defining feature of our hypothesis is that memory traces, which might otherwise underlie declarative memory, influence processing elsewhere in the brain and that, like other forms of modulation, this influence is a bias rather than a necessary step in a causal process.

Perhaps the best example of this kind of mechanism is the role of DLPFC in cognitive control. When pursuing a behavioral goal, this region maintains a task representation that specifies how stimuli should be responded to in order to achieve that goal (Miller & Cohen, 2001). This control is actualized by DLPFC sending excitatory feedback to stimulus, response, and intermediary brain areas to guide activity along the corresponding task-relevant processing pathways.

In fact, the cognitive control literature has sometimes treated the hippocampus as a control region (Braver, 2012; O'Reilly, Braver, & Cohen, 1999). Whereas DLPFC exerts "activity-based" control—task-relevant pathways exist only so long as the task representation is active—the hippocampus can exert "weight-based" control (Miller & Cohen, 2001). That is, when rapid binding in the hippocampus is gradually consolidated into cortex (Ben-Yakov, Eshel, & Dudai, 2013; Tambini, Ketz, & Davachi, 2010), associations among cues are established as long-term pathways that do not require active maintenance elsewhere to be sustained. This may create abstract knowledge about the world, or schemas, that are represented in the neocortex and allow for rapid integration of new but related information (McClelland, 2013; van Kesteren, Ruiter, Fernández, & Henson, 2012; Wang & Morris,

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[1] In memory systems research, "interactions" between systems have been explored formally in terms of bidirectional influences of one system on another, especially between the hippocampus and the striatum (e.g., Packard, 1999; Poldrack et al., 2001). Here, we use the term *interaction* more generally to refer to possible mechanisms by which the hippocampus can influence or participate in multiple cognitive functions. There are both afferent (Suzuki & Amaral, 1994) and efferent (Lavenex, Suzuki, & Amaral, 2002) MTL projections throughout neocortex, and the precise circuits by which these mechanisms are implemented likely depend on the function in question.

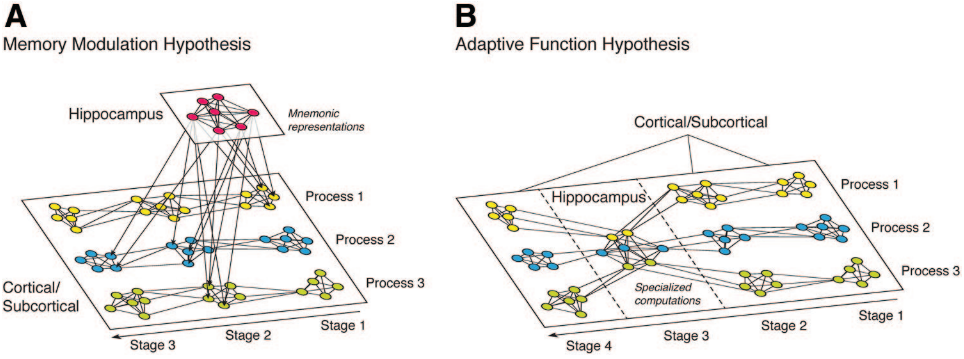

Figure 4. (A) The memory modulation hypothesis posits that mnemonic representations are the currency of the hippocampus and that these representations bias other cognitive processes. This can occur transiently, by reactivating related experiences from the past and making them available to active processes, or more permanently via offline consolidation of cortical and subcortical connections. (B) The adaptive function hypothesis posits that the hippocampus has special computational properties, such as recurrence, sparse coding, rapid binding, and massive interconnectedness, which make it useful for various mnemonic and nonmnemonic cognitive processes. Otherwise, however, it is like any other system: It receives input from upstream, performs certain computations, and sends output downstream. In both panels, the circles reflect neurons or neuronal ensembles, the lines reflect undirected synaptic connections, the processes subserve different cognitive functions, and the stages reflect different brain regions or the same brain region at different timesteps.

2010). Thus, over a long time scale, the hippocampus can come to control processing in the rest of the brain.

These permanent cortical changes are slow, but mnemonic representations in the hippocampus can also modulate brain systems more transiently (Miyashita, 2004). Such rapid modulatory effects could rely on a hippocampal computation known as *pattern completion*: When the hippocampus has bound the elements of an episode into a memory trace, subsequent experience of a subset of the elements causes the remaining elements to be reactivated by association (Leutgeb & Leutgeb, 2007; Marr, 1971; Norman & O'Reilly, 2003). This completion leads to the reinstatement of information during prediction (Turk-Browne et al., 2010; see also Smith et al., 2013) and recollection (Staresina, Henson, Kriegeskorte, & Alink, 2012; see also Diana, Yonelinas, & Ranganath, 2013; Polyn, Natu, Cohen, & Norman, 2005); guides attention to targets in repeated visual searches (Stokes, Atherton, Patai, & Nobre, 2012; see also Chun & Phelps, 1999); influences new learning and integration (Kuhl, Shah, DuBrow, & Wagner, 2010; Shohamy & Wagner, 2008; Zeithamova, Dominick, & Preston, 2012); and allows associated objects to benefit from reward learning in the striatum (Wimmer & Shohamy, 2012). These functions—perception, attention, reasoning, and decision making—can largely survive without this modulation, but the hippocampus may nevertheless bias them by injecting past experience.

The adaptive function hypothesis (see Figure 4B) holds that the hippocampus is an important part of the neural processing stream for various functions. This account places less emphasis on labeling the hippocampus as a dedicated system for memory. Rather, the hippocampus is viewed in terms of the repertoire of computations afforded by its unique architecture. Some of these computations can be borrowed from existing theories of memory, such as the ability of the hippocampus to bind two or more inputs (Cohen & Eichenbaum, 1993), but they can be used in the service of many processes, not just memory per se. If so, it might not be possible to identify the hippocampus with any single cognitive function. Instead, its function is defined by the role it plays in mediating between upstream and downstream processes (Eichenbaum, Dudchenko, Wood, Shapiro, & Tanila, 1999).

One way to think about this is to consider the position of the hippocampus with respect to the ventral visual stream (Nadel & Peterson, 2013). This stream consists of a hierarchy of interconnected areas in occipitotemporal cortex that transforms impoverished patterns of light on the retina into our rich experience of the world (Ungerleider & Mishkin, 1982). Each successive area takes the input it receives and produces a richer and larger representation: from low-level orientation and spatial frequency information, to mid-level textures and contours, to high-level objects that can be categorized and identified. Anatomical studies place the hippocampus at the very top of the hierarchy (Felleman & Essen, 1991).

The role of the hippocampus in visual processing is debated. On one hand, models of object recognition often perform well without accounting for the hippocampus (Riesenhuber & Poggio, 2000) and perception can be intact in patients with MTL damage (Lee, Barense, & Graham, 2005). On the other hand, hippocampal damage can impair scene discrimination (Lee et al., 2013; Maguire & Mullally, 2013), in addition to the impairment of object recognition caused by perirhinal damage (Saksida & Bussey, 2010; Yeung et al., 2013). These findings are controversial and sometimes unreliable (Kim et al., 2011; Suzuki, 2009). This may be related to the fact that visual discrimination is likely supported by multiple processes, only some of which depend on the hippocampus (Aly, Ranganath, & Yonelinas, 2013). A key candidate is *pattern separation,* a computation that allows the hippocampus to distinguish between similar inputs (Bakker, Kirwan, Miller, & Stark, 2008; Leutgeb & Leutgeb, 2007; Norman & O'Reilly, 2003).

Aside from perceptual and learning processes, perhaps the most basic computations in the hippocampus involve keeping track of space and time (Howard & Eichenbaum, 2013; Milivojevic &

Doeller, 2013). Certain hippocampal "place cells" fire whenever a rat passes through a specific location in an apparatus (O'Keefe & Dostrovsky, 1971). These neurons interact with the entorhinal cortex (Bonnevie et al., 2013) to produce a grid representation of space (Fyhn, Molden, Witter, Moser, & Moser, 2004), which also has been observed in humans (Doeller, Barry, & Burgess, 2010; Jacobs et al., 2013). There has been more work on spatial processing than temporal processing in the hippocampus, but a new literature is emerging. There are neuronal assemblies that track time during movement (Pastalkova, Itskov, Amarasingham, & Buzsáki, 2008) and "time cells" that code for elapsed time intervals irrespective of distance traveled or speed (Kraus, Robinson, White, Eichenbaum, & Hasselmo, 2013). This spatiotemporal information is clearly important for memory but also for other functions, such as navigation, decision making, and language (Johnson & Redish, 2007; Kurczek et al., 2013; Pfeiffer & Foster, 2013).

The memory modulation and adaptive function hypotheses are not mutually exclusive, and the hippocampus seems to have properties of both. Indeed, the hippocampus is ideally suited for both from a neuroanatomical perspective, because of its deep interconnection with several cortical and subcortical systems and its position at the apex of at least one major processing stream. Nevertheless, these hypotheses reflect different conceptions about the function of the hippocampus, raise different questions about the status of declarative memory and multiple memory systems theory, highlight different ways in which the hippocampus might interact with other brain systems, and invite different analogies when developing more elaborate theories.

Our goal in delineating these two mechanisms was to prevent them from being conflated and to provide a handle for formulating questions to stimulate new research. The memory modulation hypothesis suggests that the hippocampus may mediate certain forms of control. Although there has been a tremendous amount of work on this topic, it has focused nearly exclusively on frontal and parietal cortices. This work suggests many future studies to explore whether the hippocampus exerts control via similar or different mechanisms, including studies looking at feedback and functional connectivity. It also raises questions about the nature of the interaction of memory with other processes (cooperative versus competitive) and the neural mechanisms that mediate such interactions. The adaptive function hypothesis generates numerous predictions about behavior and brain activity as well. For example, superficially different processes that recruit the same hippocampal computations should interfere with each other behaviorally. Furthermore, nonmnemonic experimental manipulations of these computations would be expected to elicit hippocampal activation.

The special section sought to highlight the need for a new way of thinking about the interactive role of the hippocampus in cognition, but this is just the beginning. Much of the initial data relevant to this issue were obtained unexpectedly during whole-brain neuroimaging. More recent studies have started to examine the contribution of the hippocampus more systematically, such as with high-resolution fMRI of hippocampal subfields and MTL cortical areas (Carr, Rissman, & Wagner, 2010). But there is a need for additional behavioral, neuropsychological, and neuroimaging investigations to further develop the hypotheses proposed herein.

Conclusion

Research on the hippocampus and memory is at an exciting juncture. Looking back, the past several decades have been remarkably productive and have led to crucial breakthroughs in our understanding of neural and cognitive mechanisms of memory. Recent years have also begun to yield a wealth of new data and ideas that are pushing against the boundaries of standard theories. In particular, growing evidence suggests that rather than being treated as dedicated modules, memory systems should perhaps be considered as nodes in interactive networks with a wide influence across a range of cognitive functions. This view, in turn, raises questions about the mechanisms of these interactions and about the nature of mnemonic representations. Understanding how memory systems interact with other functions provides a framework for considering the broad effect of memory on many aspects of cognition, from perception to decision making. Ultimately, the hippocampus may be important not only for building relations between items but also for building relations across seemingly distinct functions.

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