

Cortico-hippocampal systems involved in memory and cognition: the PMAT framework

Maureen Ritchey^{*,1}, Laura A. Libby^{*,1}, Charan Ranganath^{*,†,1}

**Center for Neuroscience, University of California, Davis, CA, USA*

†Department of Psychology, University of California, Davis, CA, USA

¹Corresponding authors: Tel.: +530-757-8865; Fax: 530-757-8640,

e-mail address: meritchey@ucdavis.edu; lalibby@ucdavis.edu; cranganath@ucdavis.edu

Abstract

In this chapter, we review evidence that the cortical pathways to the hippocampus appear to extend from two large-scale cortical systems: a posterior medial (PM) system that includes the parahippocampal cortex and retrosplenial cortex, and an anterior temporal (AT) system that includes the perirhinal cortex. This “PMAT” framework accounts for differences in the anatomical and functional connectivity of the medial temporal lobes, which may underpin differences in cognitive function between the systems. The PM and AT systems make distinct contributions to memory and to other cognitive domains, and convergent findings suggest that they are involved in processing information about contexts and items, respectively. In order to support the full complement of memory-guided behavior, the two systems must interact, and the hippocampal and ventromedial prefrontal cortex may serve as sites of integration between the two systems. We conclude that when considering the “connected hippocampus,” inquiry should extend beyond the medial temporal lobes to include the large-scale cortical systems of which they are a part.

Keywords

Episodic memory, Medial temporal lobes, Perirhinal cortex, Parahippocampal cortex, Retrosplenial cortex, Functional connectivity, Default network

Millions of words and hours have been devoted to characterizing the role of the hippocampus in long-term memory, the results of which have established a strong foundation of knowledge about this structure and its neighboring cortical areas, the entorhinal cortex, perirhinal cortex (PRC), and parahippocampal cortex (PHC). These areas have been collectively referred to as the medial temporal lobe (MTL)

memory system (Squire and Zola-Morgan, 1991). Over the past 25 years, accumulating evidence has indicated that, like memories themselves, MTL regions have diverse properties. Some neurobiological models of memory have incorporated this evidence by redrawing the MTL as a collection of functionally heterogeneous structures (Aggleton and Brown, 1999; Davachi, 2006; Diana et al., 2007; Eacott and Gaffan, 2005; Eichenbaum et al., 2007; Montaldi and Mayes, 2010; Ranganath, 2010), in which the hippocampus binds together representations from PRC and PHC into an episodic memory trace. These models have considerably advanced our understanding of the unique contributions of MTL regions, but have maintained a focus on the MTL as a memory system apart from other brain systems, albeit with connections to perceptual processing streams. Thus, they are limited in their ability to explain the mnemonic functions of regions outside of the MTL, as well as the contributions of MTL structures to domains of cognition outside of memory.

We recently proposed an alternative framework, in which the PRC and PHC participate in two cortical systems for memory-guided behavior (Fig. 1; Ranganath and Ritchey, 2012). In this framework, the PHC and closely related retrosplenial cortex (RSC), are part of a posterior medial (PM) system that also includes the posterior cingulate, precuneus, angular gyrus, anterior thalamus, and mammillary bodies (aThal), and medial prefrontal cortex (mPFC).

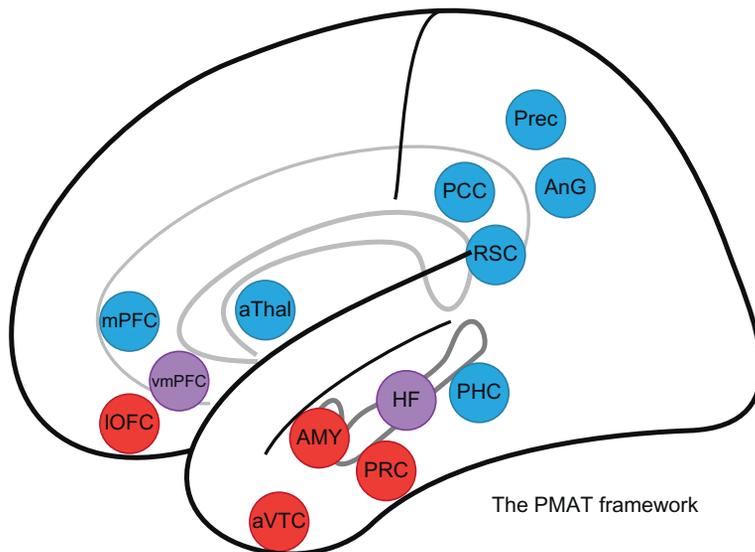


FIGURE 1

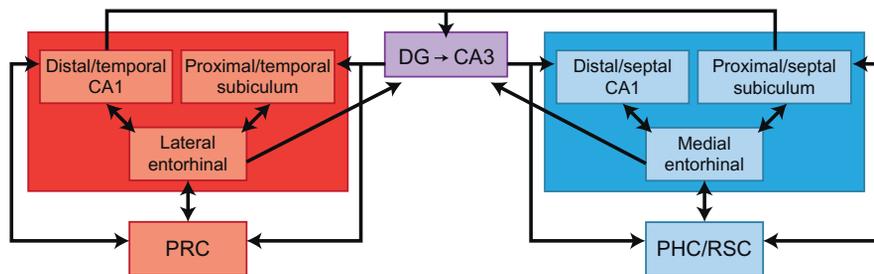
The PMAT framework. Regions of the PM system include the PHC, RSC, posterior cingulate (PCC), angular gyrus (AnG), precuneus (Prec), anterior thalamus and mammillary bodies (aThal), and medial prefrontal cortex (mPFC). Regions of the AT system include the PRC, anterior ventral temporal cortex (aVTC), amygdala (AMY), and lateral orbitofrontal cortex (IOFC). Possible sites of integration include the hippocampal formation (HF) and ventromedial prefrontal cortex (vmPFC).

bodies, and medial prefrontal cortex. The PRC is part of an anterior temporal (AT) system that also includes the ventral anterior temporal cortex, lateral orbitofrontal cortex, and amygdala. In this “PMAT” framework, the PM system is involved in on-line processing of context information and long-term storage of previously learned contexts in the form of situation models. The AT system is involved in processing item information and long-term storage of previously learned items in the form of concepts. As we have argued previously (Ranganath and Ritchey, 2012), the PMAT framework accounts for profiles of anatomical and functional connectivity and for the roles of these structures in a myriad of cognitive and memory-related functions. In this chapter, we review these findings and offer some new ideas about the implications of this framework for understanding hippocampal and medial prefrontal contributions to memory.

1 ANATOMICAL AND FUNCTIONAL CONNECTIVITY OF THE PM AND AT SYSTEMS

The foundation of the PMAT framework is an extensive body of literature documenting differences in anatomical connectivity among MTL structures (Aggleton, 2011; Burwell, 2000; Kondo et al., 2005; see Ranganath and Ritchey, 2012 for review). The PHC is extensively interconnected with both the PRC and RSC, but PHC and RSC show highly overlapping patterns of cortical and subcortical connectivity that diverge from the PRC. The PHC and RSC are major targets of the cingulum bundle, a white matter pathway that links these regions with the posterior cingulate, anterior cingulate, angular gyrus, precuneus, and ventromedial prefrontal cortex (vmPFC) (Morris et al., 1999; Mufson and Pandya, 1984; Schmahmann et al., 2007). These regions are often collectively described as the “default network” (Raichle et al., 2001). Subcortical targets identified in tracer studies include the anterior thalamus and mammillary bodies, regions known to play an essential role in episodic memory and spatial cognition (Aggleton and Brown, 1999; Aggleton and Nelson, 2014). The PRC is interconnected via the uncinate fasciculus with the temporopolar cortex, amygdala, and lateral orbitofrontal cortex (for reviews, see Suzuki and Naya, 2014; Von Der Heide et al., 2013), and subcortical connections include the mediodorsal thalamic nucleus. Finally, although the PHC, RSC, and PRC are heavily interconnected with the hippocampal formation (primarily entorhinal cortex), the connections can be organized into two parallel streams (Agster and Burwell, 2013, Knierim et al., 2006; Naber et al., 1999, 2001; Witter et al., 2000), with PHC and RSC primarily targeting the medial entorhinal cortex and PRC primarily targeting lateral entorhinal cortex (Fig. 2). PRC and PHC, along with these entorhinal areas, have different connections along the longitudinal and transverse axes of CA1 and subiculum.

Analyses of intrinsic functional connectivity measured with functional magnetic resonance imaging (fMRI) have revealed results that converge with the framework described above (Kahn et al., 2008; Libby et al., 2012). Whereas PRC shows strong

**FIGURE 2**

Parallel cortico-hippocampal pathways link the PM and AT systems with the entorhinal cortex, CA1, and subiculum. These pathways converge on the dentate gyrus (DG) and CA3.

functional connectivity with the ventral temporopolar cortex, amygdala, and lateral prefrontal cortex, PHC shows strong functional connectivity with the RSC, angular gyrus, posterior cingulate, and precuneus (Fig. 3A). Furthermore, two recent high-resolution fMRI studies have revealed functional connectivity dissociations that are strongly consistent with the parallel cortico-hippocampal streams identified in anatomical studies. These studies reported a distinction between posterior-medial and anterior-lateral regions of the entorhinal cortex, showing that these areas are differentially connected with the PRC and PHC (Maass et al., 2015) and with the extended AT and PM systems (Navarro Schroeder et al., 2015). PRC and PHC also exhibit different patterns of functional connectivity with hippocampal subfields (Libby et al., 2012; Maass et al., 2015), in that the PRC shows preferential connectivity with anterior CA1 and subiculum, whereas the PHC shows preferential connectivity with posterior CA1 and subiculum.

2 RELATIONSHIP BETWEEN CONNECTIVITY AND FUNCTION

A core assumption of the PMAT framework is that connectivity and task function are intimately related; that is, the function of its region will be constrained by its connectivity with other structures, sometimes referred to as its “connectional fingerprint” (Passingham et al., 2002). In one recent study, we directly tested whether the PMAT framework could explain the recruitment of different cortical areas during memory encoding (Ritchey et al., 2014). Using a data-driven, graph theoretic analysis of resting-state functional connectivity data, we identified networks that strongly resembled the PM and AT systems (Fig. 3B). We then measured the responses of these regions while participants learned different kinds of associations (i.e., associations between an item and its feature or an item and its context). Strikingly, for every participant in our sample, regions in the same functional connectivity-defined network exhibited more similar profiles of activation than

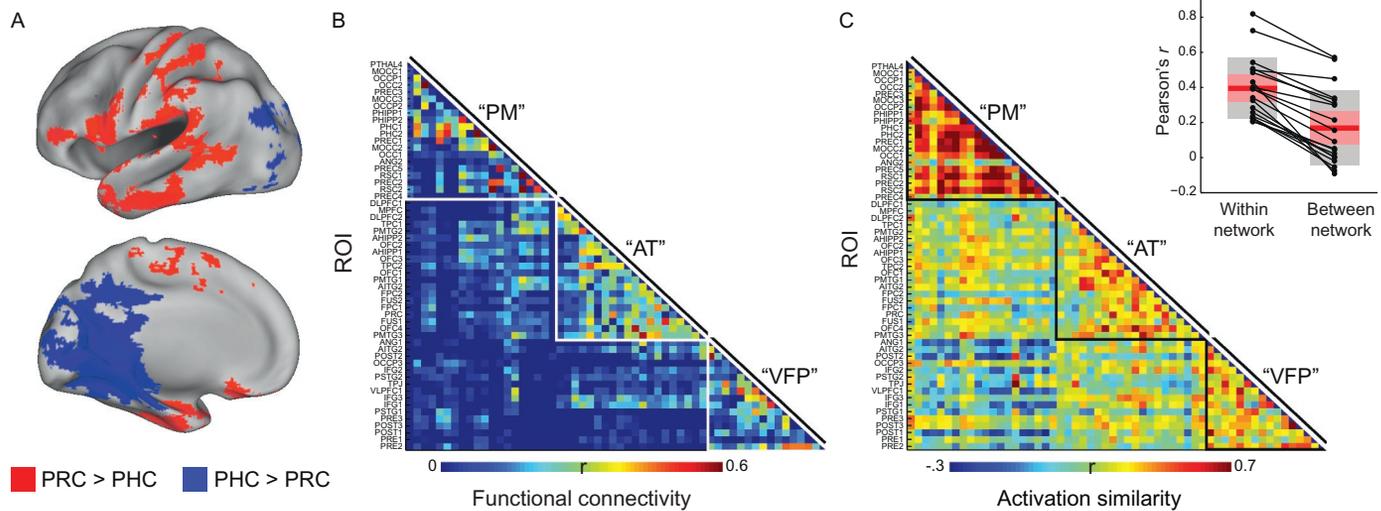


FIGURE 3

Functional connectivity and task similarity among regions in the PM and AT systems. (A) AT areas have stronger functional connectivity with the PRC than with the PHC (overlaid in red; gray in the print version), and PM areas have stronger functional connectivity with the PHC than with the PRC (overlaid in blue, dark gray in the print version). Results from left hemisphere seeds and targets are shown. (B) In an independent dataset, graph analyses of the functional connectivity among peaks from (A) revealed networks resembling the PM and AT systems, in which connectivity was stronger within a network than between networks. An additional network included mostly ventral frontal and parietal (VFP) regions. (C) Relative to regions in different networks, regions within the same functionally defined network made similar contributions to an associative memory encoding task, measured in terms of the similarity of their activation profiles. This difference was observed for each participant (see inset).

(A) Data from Libby et al. (2012). (B) and (C) Adapted from Ritchey et al. (2014).

regions in different networks (Fig. 3C). In fact, the functional connectivity networks accounted for more variability in the task data than information about whether the regions were part of the MTL memory system (Ritchey et al., 2014). In a related approach, Navarro Schroeder and colleagues (2015) demonstrated that regions within the AT and PM systems were differentially connected with the entorhinal cortex and that this entorhinal organization followed differences in object and scene responsiveness during an animacy judgment task. These findings are consistent with the idea that the functional specializations of the AT and PM systems are inextricably linked with the shared connectivity relationships of regions within each system.

Because numerous studies have reported increased activation in the default network during episodic memory retrieval, many recent studies have focused on relating connectivity within the PM system to memory performance (Andrews-Hanna et al., 2010, 2014; Fornito et al., 2012; King et al., 2015; Kragel and Polyn, 2015; Sestieri et al., 2011; St Jacques et al., 2011). For instance, in a study combining convergent results from three independent datasets, functional connectivity between core components of the PM system was shown to increase during episodic recollection (King et al., 2015). Moreover, the changes in connectivity, but not activation itself, were correlated with individual differences in recollection (King et al., 2015). These findings, along with other related results (Fornito et al., 2012; Foster et al., 2013; Kragel and Polyn, 2015; Schedlbauer et al., 2014; Watrous et al., 2013), indicate that contextual retrieval involves changes to the network dynamics of the PM system. Some evidence additionally suggests that modulating the network may be sufficient to alter memory function. Experiments using noninvasive brain stimulation techniques, such as transcranial magnetic stimulation, have shown that stimulation of the PM system can lead to changes in episodic memory performance (Bonni et al., 2015; Jones et al., 2014; Wang et al., 2014a; Yazar et al., 2014). In one study, lateral parietal stimulation was linked to widespread changes in cortico-hippocampal functional connectivity, including functional connectivity among medial and lateral parietal components of the PM system (Wang et al., 2014a). Studies of the network-level organization of memory, and our ability to perturb these networks, may reveal important insights into memory dysfunction and pathways toward improvement.

3 ROLES OF THE PM AND AT SYSTEMS IN MEMORY AND COGNITION

The work described above demonstrates clear links between connectivity and function within the PM and AT systems. Here, we will summarize evidence regarding the kinds of tasks that tend to recruit these systems, focusing first on the PHC, RSC, and PRC (those cortical areas most closely affiliated with the hippocampus), and then considering how these differences extend to other components of the PM and AT systems.

3.1 THE PM SYSTEM

3.1.1 *Episodic and Autobiographical Memory*

The PM system has been repeatedly linked to memory for the context of an event. For instance, areas in the PM system, including the PHC, RSC, and angular gyrus, have been collectively referred to as a “core recollection network” (Johnson and Rugg, 2007; Vilberg and Rugg, 2008), because these regions show enhanced activation when participants retrieve information about the context in which an item was studied or when they report spontaneous recollection of details from a study episode (for reviews, see Davachi, 2006; Diana et al., 2007; Eichenbaum et al., 2007; Spaniol et al., 2009). The involvement of the PHC, RSC, and other default network regions in episodic retrieval extends to retrieval of autobiographical events (Andrews-Hanna et al., 2014; Cabeza and St Jacques, 2007; Svoboda et al., 2006), which are often rich in contextual detail. Complementing these neuroimaging findings, neuropsychological studies have revealed deficits in autobiographical memory in patients with damage to the RSC (Maguire, 2001; Valenstein et al., 1987), the angular gyrus (Berryhill et al., 2007; Simons et al., 2010), or the thalamus and mammillary bodies (Mayes et al., 1987).

3.1.2 *Space and Time*

A rich body of evidence based on experiments with rodents, monkeys, and humans has linked the PM system, especially the PHC and RSC, to memory for spatial information. For instance, rodents with lesions to the postrhinal cortex (the likely rodent homologue of the PHC) are impaired at discriminating between novel and familiar object–context configurations, despite normal object recognition (Norman and Eacott, 2005). Related deficits have been observed for rodents with RSC lesions (e.g., Vann and Aggleton, 2002). The finding that PHC damage is associated with spatial memory impairments has also been observed in nonhuman primates (Alvarado and Bachevalier, 2005; Bachevalier and Nemanic, 2008) and human patients (Bohbot et al., 2000). Human neuroimaging work has complemented these findings, showing that responses in the PHC and RSC are related to memory for object–location associations (Cansino et al., 2002; Libby et al., 2014; Ross and Slotnick, 2008; Sommer et al., 2005; Uncapher et al., 2006) and that the RSC, in particular, carries information about location and first-person perspective during spatial memory retrieval (Marchette et al., 2014). In addition to spatial memory, some recent findings have implicated the PM system in memory for temporal context (Hsieh et al., 2014, submitted). Using analyses of multivoxel activity patterns during retrieval of learned temporal sequences, Hsieh et al. (2014) found that activity patterns in PHC carried information about the temporal or ordinal position of an object in a learned sequence. Similar results were found for other PM system regions, including the angular gyrus, posterior cingulate, and vmPFC (Hsieh and Ranganath, under review).

The PM system also plays a key role in spatial navigation. Cells within the PHC appear to code for specific navigational landmarks (Ekstrom et al., 2003), and some

PHC cells have place fields that are larger and more sensitive to environmental cues than hippocampal place cells (Burwell and Hafeman, 2003). Head direction cells, which selectively respond when the animal's head is oriented toward a particular direction in space, are distributed across the RSC, lateral mammillary bodies, anterior thalamus, and presubiculum (Yoder et al., 2011). Human patients with damage to the RSC also exhibit a form of topographical amnesia (Aguirre and D'Esposito, 1999; Epstein, 2008; Maguire, 2001), in which they are unable to use landmarks to orient oneself. The coordinated actions of components of the PM system have been previously described as integrating information about one's position within a global spatial context to construct a first-person spatial representation (Bird and Burgess, 2008).

3.1.3 Scene Perception

Outside of the memory domain, the most posterior part of the PHC (along with portions of the nearby lingual gyrus) has been referred to as the parahippocampal place areas, due to its responsiveness to scene information relative to other categories of visual stimuli (reviewed by Epstein, 2008). The RSC also shows some sensitivity to scene information (Huffman and Stark, 2014; O'Craven and Kanwisher, 2000; Park et al., 2007), although, as described previously, its involvement may specifically contribute to using scene information to orient oneself in context. One recent study showed that categorical selectivity in the PHC, measured as the discriminability of multivariate patterns to scenes versus faces, correlated on a trial-by-trial level with selectivity in the RSC (Huffman and Stark, 2014), suggesting that these regions may work together to support scene perception.

3.1.4 Social Cognition

Meta-analytic analyses have demonstrated considerable overlap between areas involved in autobiographical memory (including much of the PM system) and areas involved in social cognitive processes such as theory of mind, or the ability to infer the thoughts or motivations of others (Andrews-Hanna et al., 2014; Spreng et al., 2009). Andrews-Hanna et al. (2010, 2014) have recently argued that the default network comprises two subsystems, a ventral subsystem associated with mnemonic or contextual processing and a dorsal subsystem associated with theory of mind operations—the combination of which can support complex autobiographical memory retrieval. Indeed, the detailed representations of context that support autobiographical memory should include information about one's position as well as relationships to other agents within an environment.

Altogether, these findings and others (reviewed by Ranganath and Ritchey, 2012) suggest that regions in the PM system are involved in processing online context information, referencing it to the perspective of one's self, and storing that information into long-term memory.

3.2 THE AT SYSTEM

3.2.1 *Recognition and Associative Memory*

Several studies have implicated the PRC in recognition of objects or other items. For instance, PRC lesions have been shown to severely impair visual object recognition memory in monkeys (Alvarado and Bachevalier, 2005; Baxter and Murray, 2001; Nemanic et al., 2004) and rats (Aggleton et al., 2010; Ennaceur et al., 1996; Norman and Eacott, 2004). Research in humans has emphasized the idea that item recognition can be supported by contextual recollection or assessment of an item's familiarity and that the latter process is supported by the PRC (see Diana et al., 2007 for review). In human patients, lesions that disproportionately affect the PRC are rare, but one such patient showed severe impairments in familiarity-based item recognition memory (Bowles et al., 2007).

Beyond encoding individual objects, it is clear that PRC is also critical for learning associations between objects and their features or with other objects. For instance, many single-unit recording studies have shown that PRC neurons can encode associations between objects that have been repeatedly paired together (Miyashita, 1988), and PRC lesions severely impair learning of object–object associations (Murray et al., 1993; Norman and Eacott, 2005). Imaging studies of humans have also shown that PRC activity during learning predicts the degree to which people can learn to associate an item with an arbitrary feature (Diana et al., 2010; Staresina and Davachi, 2008; Staresina et al., 2011) or with another item (Haskins et al., 2008). Although most investigations of item recognition have centered on the PRC, there is some evidence that other components of the AT system may be involved in certain aspects of recognition memory. For instance, the activity of amygdala neurons is modulated by the novelty/familiarity of objects (Wilson and Rolls, 1993), and amygdala lesions in rats were shown to disrupt recognition memory in a manner consistent with a selective familiarity deficit (Farovik et al., 2011).

3.2.2 *Affective Processing*

The AT system seems to play a role in mediating associations between items and their affective or motivational significance. The amygdala is crucially involved in enhancing memory for emotional salient information (LaBar and Cabeza, 2006), especially emotional items and their features (reviewed by Kensinger, 2009). Under one account, the amygdala may support the binding of item and emotion information in memory through its strong reciprocal connections with the PRC (Yonelinas and Ritchey, 2015). Lateral orbitofrontal cortex, in contrast, signals the learned value of items (Lara et al., 2009; Tsujimoto et al., 2009) and is critical for making decisions based on past experience with item–reward associations (Noonan et al., 2011; Walton et al., 2010). There is also some evidence that the PRC is involved in coding associations between objects and rewards (Liu and Richmond, 2000; Liu et al., 2000) or aversive outcomes (Furtak et al., 2007).

3.2.3 *Semantic Processing*

Several lines of evidence have linked the PRC and temporopolar cortex to processing of semantic features of objects. For instance, damage to the PRC and left anterior temporal cortex in patients with semantic dementia is associated with a loss of conceptual knowledge about objects (reviewed by [Martin and Chao, 2001](#); [Murre et al., 2001](#)). Additionally, conceptual priming for words is associated with modulations of field potentials recorded in PRC ([Nobre and McCarthy, 1995](#)) and of left PRC activity measured with fMRI ([Dew and Cabeza, 2013](#); [Wang et al., 2010, 2014b](#)). Patients with lesions to the left PRC, in turn, show significant reductions in conceptual priming ([Wang et al., 2010](#)). Some evidence suggests that PRC contributions to conceptual priming and item recognition are related, in that reductions in PRC activity have been observed in overlapping regions during item recognition and after conceptual priming ([Dew and Cabeza, 2013](#); [Wang et al., 2014b](#)).

The role of the PRC in semantic processing may be bounded by the specificity of the semantic representation. Using a technique that enabled them to fit models of stimulus similarity to observed estimates of neural similarity, [Clarke and Tyler \(2014\)](#) demonstrated that responses in the PRC were best explained by a model that emphasized object-specific semantic features as opposed to visual or categorical information. Tyler and colleagues have proposed that PRC and temporopolar regions are specifically needed for fine-grained conceptual processing that is needed in order to resolve semantic confusability. Consistent with this idea, [Wright et al. \(2015\)](#) compared patients with and without PRC damage on naming and word–picture matching tasks and found that PRC damage was related to impair processing of highly confusable concepts. Finally, although not typically associated with semantic cognition, even the amygdala may make some contributions to conceptual knowledge, such as supporting the generalization of conditioned fear responses to other exemplars from the same semantic category ([Dunsmoor et al., 2014](#)).

3.2.4 *Object Perception*

The PRC has been often described as the terminal area of the ventral visual stream, and thus, perhaps not surprisingly, there is considerable evidence suggesting that the PRC is important for object perception ([Bussey et al., 2005](#); [Graham et al., 2010](#)). Damage to the PRC impairs performance on perceptual discrimination tasks that require fine discriminations between objects, particularly those objects that share multiple features in common ([Barense et al., 2005](#); [Bussey et al., 2002](#); [Lee et al., 2005, 2006](#)) or require integration of features across modalities ([Taylor et al., 2006](#)). Responses to objects in the PRC, amygdala, and anterior temporal cortex appear to be view-invariant ([Barense et al., 2010](#); [Nakamura et al., 1992, 1994](#); [Sato and Nakamura, 2003](#)), and multivoxel patterns in these regions are sensitive to item repetitions ([Hsieh et al., 2014](#); [Libby et al., 2014](#)), even when view is not maintained ([Libby et al., 2014](#)).

Altogether, these findings and others (reviewed by [Ranganath and Ritchey, 2012](#)) suggest that regions in the AT system are involved in processing and storing information about items, including their semantic and perceptual features as well as their salience and value.

4 POSSIBLE SITES OF INTEGRATION

4.1 THE HIPPOCAMPUS

Perhaps not surprisingly, the PM and AT systems must work together in order to support the full complement of memory-guided behavior. The hippocampus is a clear point of connection between the two systems due to its strong connectivity with both systems. As noted above and in [Fig. 2](#), there are parallel cortico-hippocampal pathways linking the PM and AT systems with the entorhinal cortex, CA1, and subiculum ([Witter et al., 2000](#)). The dentate gyrus is a major convergence point within the hippocampal circuit, as it receives a balanced distribution of connections from medial and lateral entorhinal cortex, as well as PRC and PHC ([Burwell, 2000](#); [Libby et al., 2012](#)). Therefore, it might be best to think of the hippocampus as playing dual roles in its interactions with the PM and AT systems. Functional interactions that occur via the traditional trisynaptic circuit can facilitate functional integration between the two systems ([Knierim et al., 2006](#)). In contrast, connections via the temporo-ammonic pathway can allow for separable interactions ([Ranganath and Ritchey, 2012](#)), possibly with the anterior (temporal) hippocampus affiliating with the AT system and posterior (septal) hippocampus affiliating with the PM system. This organization has implications for understanding functional dissociations along the longitudinal axis of the hippocampus, including differences in contributions to emotional processing ([Fanselow and Dong, 2010](#)) as well as in the scale of contextual representation ([Poppenk et al., 2013](#), [Strange et al., 2014](#)).

4.2 THE VENTROMEDIAL PREFRONTAL CORTEX

Outside of the MTL, the AT and PM systems also converge in a region that may be particularly important for the control of memory-guided behavior—the vmPFC. This putative integration zone lies at the posterior junction of medial prefrontal and orbitofrontal cortex ([Price, 2007](#)), and comparative anatomy studies suggest that, in humans, this region is bordered superiorly by the rostral sulcus, anteriorly by BA11, and laterally by the orbital sulcus ([Carmichael and Price, 1996](#); [Ongür and Price, 2000](#)). Rodent and nonhuman primate anatomical studies have shown that vmPFC has a profile of connectivity that spans the AT and PM systems. Compared to other prefrontal areas, the vmPFC is uniquely connected directly with both PRC and PHC ([Hoover and Vertes, 2011](#); [Kondo and Witter, 2014](#); [Kondo et al., 2005](#); [Price, 2007](#)), as well as the hippocampus ([Barbas and Blatt, 1995](#); [Beckmann et al., 2009](#); [Swanson, 1981](#); [Verwer et al., 1997](#)). Additionally, although the prefrontal nodes of the AT and PM systems (lateral orbitofrontal cortex and medial prefrontal cortex, respectively) have largely distinct whole-brain connectivity profiles and few direct interconnections ([Carmichael and Price, 1996](#); [Kondo and Witter, 2014](#); [Saleem et al., 2008](#)), both regions have strong reciprocal connections with vmPFC ([Carmichael and Price, 1996](#); [Price, 2007](#)). Thus, vmPFC can be thought of as the site of convergence between prefrontal and MTL components of both the AT and PM systems.

The functional properties of the vmPFC have been reviewed elsewhere (see [Euston et al., 2012](#); [Nieuwenhuis and Takashima, 2011](#); [Rushworth et al., 2011](#)). In brief, evidence suggests that vmPFC receives information about the intrinsic and/or learned value of items via PRC and lateral orbitofrontal cortex, as well as information about the demands and predictability of internal and environmental contexts from PHC and medial prefrontal cortex. As an integration zone, vmPFC in turn represents the value of items and their associated actions as a function of what is known about the current context ([Euston et al., 2012](#); [Rushworth et al., 2011](#)). Via reciprocal connections, vmPFC may also operate as a top-down control mechanism on the MTL, inhibiting or updating mnemonic representations that are behaviorally irrelevant ([Bunce and Barbas, 2011](#), [Ghashghaei and Barbas, 2002](#), [Nieuwenhuis and Takashima, 2011](#)). This region could mediate between item and context representations, controlling the extent to which these sources of information guide action selection. Additionally, some findings suggest that memory consolidation processes could lead to greater reliance on vmPFC interactions with cortical systems during retrieval of remote memories ([Frankland et al., 2004](#); [Tse et al., 2011](#)) and that interactions between the vmPFC and hippocampus could support the integration of new information with existing representations within the AT and PM systems ([Schlichting and Preston, 2015](#); [van Kesteren et al., 2012](#)).

5 CONCLUSIONS

Adopting the PMAT framework encourages one to think about the hippocampus not as an endpoint, but as a critical interface between two cortical systems that contribute to cognition in fundamentally different ways. These contributions can be understood as the product of complex interactions between brain areas, constrained by anatomy and optimized to support rapid learning in the service of perception, action, and cognition. Although the PMAT framework can explain an extensive body of evidence, more research is needed to resolve some important questions. One issue concerns functional specialization within each network. That is, network function depends on the coordinated actions of individual regions, and further work is needed to better understand the extent to which these regions make independent versus interactive contributions to cognition. Another important issue concerns communication between networks. The systems do not operate in isolation but rather interact to support a wide range of memory-guided behavior, and research is needed to understand how the hippocampus, vmPFC, or other linking nodes mediate these interactions. Finally, research will be needed to understand how neurodegenerative diseases progress within the AT and PM systems (cf, [Das et al., 2015](#); [La Joie et al., 2014](#); [Seeley et al., 2009](#)), and more importantly, whether interventions to enhance connectivity within these networks can be used to treat cognitive deficits in aging and dementia.

REFERENCES

- Aggleton, J.P., 2011. Multiple anatomical systems embedded within the primate medial temporal lobe: implications for hippocampal function. *Neurosci. Biobehav. Rev.* 36, 1579–1596.
- Aggleton, J.P., Brown, M.W., 1999. Episodic memory, amnesia, and the hippocampal-anterior thalamic axis. *Behav. Brain Sci.* 22, 425–444, discussion 444–89.
- Aggleton, J.P., Nelson, A.J., 2014. Why do lesions in the rodent anterior thalamic nuclei cause such severe spatial deficits? *Neurosci. Biobehav. Rev.* <http://dx.doi.org/10.1016/j.neubiorev.2014.08.013>. [Epub ahead of print].
- Aggleton, J.P., Albasser, M.M., Aggleton, D.J., Poirier, G.L., Pearce, J.M., 2010. Lesions of the rat perirhinal cortex spare the acquisition of a complex configural visual discrimination yet impair object recognition. *Behav. Neurosci.* 124, 55–68.
- Agster, K.L., Burwell, R.D., 2013. Hippocampal and subicular efferents and afferents of the perirhinal, postrhinal, and entorhinal cortices of the rat. *Behav. Brain Res.* 254, 50–64.
- Aguirre, G.K., D'Esposito, M., 1999. Topographical disorientation: a synthesis and taxonomy. *Brain* 122, 1613–1628.
- Alvarado, M.C., Bachevalier, J., 2005. Comparison of the effects of damage to the perirhinal and parahippocampal cortex on transverse patterning and location memory in rhesus macaques. *J. Neurosci.* 25, 1599–1609.
- Andrews-Hanna, J.R., Reidler, J.S., Sepulcre, J., Poulin, R., Buckner, R.L., 2010. Functional-anatomic fractionation of the brain's default network. *Neuron* 65, 550–562.
- Andrews-Hanna, J.R., Saxe, R., Yarkoni, T., 2014. Contributions of episodic retrieval and mentalizing to autobiographical thought: evidence from functional neuroimaging, resting-state connectivity, and fMRI meta-analyses. *NeuroImage* 91, 324–335.
- Bachevalier, J., Nemanic, S., 2008. Memory for spatial location and object-place associations are differently processed by the hippocampal formation, parahippocampal areas TH/TF and perirhinal cortex. *Hippocampus* 18, 64–80.
- Barbas, H., Blatt, G.J., 1995. Topographically specific hippocampal projections target functionally distinct prefrontal areas in the rhesus monkey. *Hippocampus* 5, 511–533.
- Barense, M.D., Bussey, T.J., Lee, A.C., Rogers, T.T., Davies, R.R., Saksida, L.M., Murray, E.A., Graham, K.S., 2005. Functional specialization in the human medial temporal lobe. *J. Neurosci.* 25, 10239–10246.
- Barense, M.D., Henson, R.N., Lee, A.C., Graham, K.S., 2010. Medial temporal lobe activity during complex discrimination of faces, objects, and scenes: effects of viewpoint. *Hippocampus* 20, 389–401.
- Baxter, M.G., Murray, E.A., 2001. Opposite relationship of hippocampal and rhinal cortex damage to delayed nonmatching-to-sample deficits in monkeys. *Hippocampus* 11, 61–71.
- Beckmann, M., Johansen-Berg, H., Rushworth, M.F., 2009. Connectivity-based parcellation of human cingulate cortex and its relation to functional specialization. *J. Neurosci.* 29, 1175–1190.
- Berryhill, M.E., Phuong, L., Picasso, L., Cabeza, R., Olson, I.R., 2007. Parietal lobe and episodic memory: bilateral damage causes impaired free recall of autobiographical memory. *J. Neurosci.* 27, 14415–14423.
- Bird, C.M., Burgess, N., 2008. The hippocampus and memory: insights from spatial processing. *Nat. Rev. Neurosci.* 9, 182–194.

- Bohbot, V.D., Allen, J.J., Nadel, L., 2000. Memory deficits characterized by patterns of lesions to the hippocampus and parahippocampal cortex. *Ann. N.Y. Acad. Sci.* 911, 355–368.
- Bonni, S., Veniero, D., Mastrospasqua, C., Ponzo, V., Caltagirone, C., Bozzali, M., Koch, G., 2015. TMS evidence for a selective role of the precuneus in source memory retrieval. *Behav. Brain Res.* 282, 70–75.
- Bowles, B., Crupi, C., Mirsattari, S.M., Pigott, S.E., Parrent, A.G., Pruessner, J.C., Yonelinas, A.P., Kohler, S., 2007. Impaired familiarity with preserved recollection after anterior temporal-lobe resection that spares the hippocampus. *Proc. Natl. Acad. Sci. USA* 104, 16382–16387.
- Bunce, J.G., Barbas, H., 2011. Prefrontal pathways target excitatory and inhibitory systems in memory-related medial temporal cortices. *NeuroImage* 55, 1461–1474.
- Burwell, R.D., 2000. The parahippocampal region: corticocortical connectivity. *Ann. N.Y. Acad. Sci.* 911, 25–42.
- Burwell, R.D., Hafeman, D.M., 2003. Positional firing properties of postrhinal cortex neurons. *Neuroscience* 119, 577–588.
- Bussey, T.J., Saksida, L.M., Murray, E.A., 2002. Perirhinal cortex resolves feature ambiguity in complex visual discriminations. *Eur. J. Neurosci.* 15, 365–374.
- Bussey, T.J., Saksida, L.M., Murray, E.A., 2005. The perceptual-mnemonic/feature conjunction model of perirhinal cortex function. *Q. J. Exp. Psychol. B* 58, 269–282.
- Cabeza, R., St Jacques, P., 2007. Functional neuroimaging of autobiographical memory. *Trends Cogn. Sci.* 11, 219–227.
- Cansino, S., Maquet, P., Dolan, R.J., Rugg, M.D., 2002. Brain activity underlying encoding and retrieval of source memory. *Cereb. Cortex* 12, 1048–1056.
- Carmichael, S.T., Price, J.L., 1996. Connectional networks within the orbital and medial prefrontal cortex of macaque monkeys. *J. Comp. Neurol.* 371, 179–207.
- Clarke, A., Tyler, L.K., 2014. Object-specific semantic coding in human perirhinal cortex. *J. Neurosci.* 34, 4766–4775.
- Das, S.R., Pluta, J., Mancuso, L., Kliot, D., Yushkevich, P.A., Wolk, D.A., 2015. Anterior and posterior MTL networks in aging and MCI. *Neurobiol. Aging* 36, S141–S150.
- Davachi, L., 2006. Item, context and relational episodic encoding in humans. *Curr. Opin. Neurobiol.* 16, 693–700.
- Dew, I.T., Cabeza, R., 2013. A broader view of perirhinal function: from recognition memory to fluency-based decisions. *J. Neurosci.* 33, 14466–14474.
- Diana, R.A., Yonelinas, A.P., Ranganath, C., 2007. Imaging recollection and familiarity in the medial temporal lobe: a three-component model. *Trends Cogn. Sci.* 11, 379–386.
- Diana, R.A., Yonelinas, A.P., Ranganath, C., 2010. Medial temporal lobe activity during source retrieval reflects information type, not memory strength. *J. Cogn. Neurosci.* 22, 1808–1818.
- Dunsmoor, J.E., Kragel, P.A., Martin, A., LaBar, K.S., 2014. Aversive learning modulates cortical representations of object categories. *Cereb. Cortex* 24, 2859–2872.
- Eacott, M.J., Gaffan, E.A., 2005. The roles of perirhinal cortex, postrhinal cortex, and the fornix in memory for objects, contexts, and events in the rat. *Q. J. Exp. Psychol. B* 58, 202–217.
- Eichenbaum, H., Yonelinas, A.P., Ranganath, C., 2007. The medial temporal lobe and recognition memory. *Annu. Rev. Neurosci.* 30, 123–152.
- Ekstrom, A.D., Kahana, M.J., Caplan, J.B., Fields, T.A., Isham, E.A., Newman, E.L., Fried, I., 2003. Cellular networks underlying human spatial navigation. *Nature* 425, 184–188.

- Ennaceur, A., Neave, N., Aggleton, J.P., 1996. Neurotoxic lesions of the perirhinal cortex do not mimic the behavioural effects of fornix transection in the rat. *Behav. Brain Res.* 80, 9–25.
- Epstein, R.A., 2008. Parahippocampal and retrosplenial contributions to human spatial navigation. *Trends Cogn. Sci.* 12, 388–396.
- Euston, D.R., Gruber, A.J., McNaughton, B.L., 2012. The role of medial prefrontal cortex in memory and decision making. *Neuron* 76, 1057–1070.
- Fanselow, M.S., Dong, H.W., 2010. Are the dorsal and ventral hippocampus functionally distinct structures? *Neuron* 65, 7–19.
- Farovik, A., Place, R.J., Miller, D.R., Eichenbaum, H., 2011. Amygdala lesions selectively impair familiarity in recognition memory. *Nat. Neurosci.* 14, 1416–1417.
- Fornito, A., Harrison, B.J., Zalesky, A., Simons, J.S., 2012. Competitive and cooperative dynamics of large-scale brain functional networks supporting recollection. *Proc. Natl. Acad. Sci. USA* 109, 12788–12793.
- Foster, B.L., Kaveh, A., Dastjerdi, M., Miller, K.J., Parvizi, J., 2013. Human retrosplenial cortex displays transient theta phase locking with medial temporal cortex prior to activation during autobiographical memory retrieval. *J. Neurosci.* 33, 10439–10446.
- Frankland, P.W., Bontempi, B., Talton, L.E., Kaczmarek, L., Silva, A.J., 2004. The involvement of the anterior cingulate cortex in remote contextual fear memory. *Science* 304, 881–883.
- Furtak, S.C., Allen, T.A., Brown, T.H., 2007. Single-unit firing in rat perirhinal cortex caused by fear conditioning to arbitrary and ecological stimuli. *J. Neurosci.* 27, 12277–12291.
- Ghashghaei, H.T., Barbas, H., 2002. Pathways for emotion: interactions of prefrontal and anterior temporal pathways in the amygdala of the rhesus monkey. *Neuroscience* 115, 1261–1279.
- Graham, K.S., Barense, M.D., Lee, A.C., 2010. Going beyond LTM in the MTL: a synthesis of neuropsychological and neuroimaging findings on the role of the medial temporal lobe in memory and perception. *Neuropsychologia* 48, 831–853.
- Haskins, A.L., Yonelinas, A.P., Quamme, J.R., Ranganath, C., 2008. Perirhinal cortex supports encoding and familiarity-based recognition of novel associations. *Neuron* 59, 554–560.
- Hoover, W.B., Vertes, R.P., 2011. Projections of the medial orbital and ventral orbital cortex in the rat. *J. Comp. Neurol.* 519, 3766–3801.
- Hsieh, L.-T., Gruber, M.J., Jenkins, L.J., Ranganath, C., 2014. Hippocampal activity patterns carry information about objects in temporal context. *Neuron* 81, 1165–1178.
- Hsieh, L.-T. & Ranganath, C. (under review). Cortical and subcortical contributions to sequence retrieval: schematic coding of temporal context in the neocortical recollection network.
- Huffman, D.J., Stark, C.E., 2014. Multivariate pattern analysis of the human medial temporal lobe revealed representationally categorical cortex and representationally agnostic hippocampus. *Hippocampus* 24, 1394–1403.
- Johnson, J.D., Rugg, M.D., 2007. Recollection and the reinstatement of encoding-related cortical activity. *Cereb. Cortex* 17, 2507–2515.
- Jones, K.T., Gozenman, F., Berryhill, M.E., 2014. Enhanced long-term memory encoding after parietal neurostimulation. *Exp. Brain Res.* 232, 4043–4054.
- Kahn, I., Andrews-Hanna, J.R., Vincent, J.L., Snyder, A.Z., Buckner, R.L., 2008. Distinct cortical anatomy linked to subregions of the medial temporal lobe revealed by intrinsic functional connectivity. *J. Neurophysiol.* 100, 129–139.

- Kensinger, E.A., 2009. Remembering the details: effects of emotion. *Emot. Rev.* 1, 99–113.
- King, D.R., de Chastelaine, M., Elward, R.L., Wang, T.H., Rugg, M.D., 2015. Recollection-related increases in functional connectivity predict individual differences in memory accuracy. *J. Neurosci.* 35, 1763–1772.
- Knierim, J.J., Lee, I., Hargreaves, E.L., 2006. Hippocampal place cells: parallel input streams, subregional processing, and implications for episodic memory. *Hippocampus* 16, 755–764.
- Kondo, H., Witter, M.P., 2014. Topographic organization of orbitofrontal projections to the parahippocampal region in rats. *J. Comp. Neurol.* 522, 772–793.
- Kondo, H., Saleem, K.S., Price, J.L., 2005. Differential connections of the perirhinal and parahippocampal cortex with the orbital and medial prefrontal networks in macaque monkeys. *J. Comp. Neurol.* 493, 479–509.
- Kragel, J.E., Polyn, S.M., 2015. Functional interactions between large-scale networks during memory search. *Cereb. Cortex* 25, 667–679.
- La Joie, R., Landeau, B., Perrotin, A., Bejanin, A., Egret, S., Pélerin, A., Mézenge, F., Belliard, S., de La Sayette, V., Eustache, F., 2014. Intrinsic connectivity identifies the hippocampus as a main crossroad between Alzheimer’s and semantic dementia-targeted networks. *Neuron* 81, 1417–1428.
- LaBar, K.S., Cabeza, R., 2006. Cognitive neuroscience of emotional memory. *Nat. Rev. Neurosci.* 7, 54–64.
- Lara, A.H., Kennerley, S.W., Wallis, J.D., 2009. Encoding of gustatory working memory by orbitofrontal neurons. *J. Neurosci.* 29, 765–774.
- Lee, A.C., Bussey, T.J., Murray, E.A., Saksida, L.M., Epstein, R.A., Kapur, N., Hodges, J.R., Graham, K.S., 2005. Perceptual deficits in amnesia: challenging the medial temporal lobe ‘mnemonic’ view. *Neuropsychologia* 43, 1–11.
- Lee, A.C., Buckley, M.J., Gaffan, D., Emery, T., Hodges, J.R., Graham, K.S., 2006. Differentiating the roles of the hippocampus and perirhinal cortex in processes beyond long-term declarative memory: a double dissociation in dementia. *J. Neurosci.* 26, 5198–5203.
- Libby, L.A., Ekstrom, A.D., Ragland, J.D., Ranganath, C., 2012. Differential connectivity of perirhinal and parahippocampal cortices within human hippocampal subregions revealed by high-resolution functional imaging. *J. Neurosci.* 32, 6550–6560.
- Libby, L.A., Hannula, D.E., Ranganath, C., 2014. Medial temporal lobe coding of item and spatial information during relational binding in working memory. *J. Neurosci.* 34, 14233–14242.
- Liu, Z., Richmond, B.J., 2000. Response differences in monkey TE and perirhinal cortex: stimulus association related to reward schedules. *J. Neurophysiol.* 83, 1677–1692.
- Liu, Z., Murray, E.A., Richmond, B.J., 2000. Learning motivational significance of visual cues for reward schedules requires rhinal cortex. *Nat. Neurosci.* 3, 1307–1315.
- Maass, A., Berron, D., Libby, L.A., Ranganath, C., Duzel, E., 2015. Functional subregions of the human entorhinal cortex. *eLife*, in press.
- Maguire, E.A., 2001. The retrosplenial contribution to human navigation: a review of lesion and neuroimaging findings. *Scand. J. Psychol.* 42, 225–238.
- Marchette, S.A., Vass, L.K., Ryan, J., Epstein, R.A., 2014. Anchoring the neural compass: coding of local spatial reference frames in human medial parietal lobe. *Nat. Neurosci.* 17, 1598–1606.
- Martin, A., Chao, L.L., 2001. Semantic memory and the brain: structure and processes. *Curr. Opin. Neurobiol.* 11, 194–201.

- Mayes, A.R., Meudell, R., Mann, D., Pickering, A., 1987. Location of lesions in Korsakoff's Syndrome: neuropsychological and neuropathological data on two patients. *Cortex* 24, 367–388.
- Miyashita, Y., 1988. Neuronal correlate of visual associative long-term memory in the primate temporal cortex. *Nature* 335, 817–820.
- Montaldi, D., Mayes, A.R., 2010. The role of recollection and familiarity in the functional differentiation of the medial temporal lobes. *Hippocampus* 20, 1291–1314.
- Morris, R., Pandya, D.N., Petrides, M., 1999. Fiber system linking the mid-dorsolateral frontal cortex with the retrosplenial/presubicular region in the rhesus monkey. *J. Comp. Neurol.* 407, 183–192.
- Mufson, E.J., Pandya, D.N., 1984. Some observations on the course and composition of the cingulum bundle in the rhesus monkey. *J. Comp. Neurol.* 225, 31–43.
- Murray, E.A., Gaffan, D., Mishkin, M., 1993. Neural substrates of visual stimulus-stimulus association in rhesus monkeys. *J. Neurosci.* 13, 4549–4561.
- Murre, J.M., Graham, K.S., Hodges, J.R., 2001. Semantic dementia: relevance to connectionist models of long-term memory. *Brain* 124, 647–675.
- Naber, P.A., Witter, M.P., Lopez da Silva, F.H., 1999. Perirhinal cortex input to the hippocampus in the rat: evidence for parallel pathways, both direct and indirect. A combined physiological and anatomical study. *Eur. J. Neurosci.* 11, 4119–4133.
- Naber, P.A., Witter, M.P., Lopes da Silva, F.H., 2001. Evidence for a direct projection from the postrhinal cortex to the subiculum in the rat. *Hippocampus* 11, 105–117.
- Nakamura, K., Mikami, A., Kubota, K., 1992. Activity of single neurons in the monkey amygdala during performance of a visual discrimination task. *J. Neurophysiol.* 67, 1447–1463.
- Nakamura, K., Matsumoto, K., Mikami, A., Kubota, K., 1994. Visual response properties of single neurons in the temporal pole of behaving monkeys. *J. Neurophysiol.* 71, 1206–1221.
- Navarro Schroeder, T., Haak, K.V., Zaragoza Jimenez, N.I., Beckmann, C.F., Doeller, C. F., 2015. Functional topography of the human entorhinal cortex. *eLife*, in press.
- Nemanic, S., Alvarado, M.C., Bachevalier, J., 2004. The hippocampal/parahippocampal regions and recognition memory: insights from visual paired comparison versus object-delayed nonmatching in monkeys. *J. Neurosci.* 24, 2013–2026.
- Nieuwenhuis, I.L., Takashima, A., 2011. The role of the ventromedial prefrontal cortex in memory consolidation. *Behav. Brain Res.* 218, 325–334.
- Nobre, A.C., McCarthy, G., 1995. Language-related field potentials in the anterior-medial temporal lobe: II. Effects of word type and semantic priming. *J. Neurosci.* 15, 1090–1098.
- Noonan, M.P., Mars, R.B., Rushworth, M.F., 2011. Distinct roles of three frontal cortical areas in reward-guided behavior. *J. Neurosci.* 31, 14399–14412.
- Norman, G., Eacott, M.J., 2004. Impaired object recognition with increasing levels of feature ambiguity in rats with perirhinal cortex lesions. *Behav. Brain Res.* 148, 79–91.
- Norman, G., Eacott, M.J., 2005. Dissociable effects of lesions to the perirhinal cortex and the postrhinal cortex on memory for context and objects in rats. *Behav. Neurosci.* 119, 557–566.
- O'Craven, K.M., Kanwisher, N., 2000. Mental imagery of faces and places activates corresponding stimulus-specific brain regions. *J. Cogn. Neurosci.* 12, 1013–1023.
- Ongür, D., Price, J.L., 2000. The organization of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans. *Cereb. Cortex* 10, 206–219.

- Park, S., Intraub, H., Yi, D.-J., Widders, D., Chun, M.M., 2007. Beyond the edges of a view: boundary extension in human scene-selective visual cortex. *Neuron* 54, 335–342.
- Passingham, R.E., Stephan, K.E., Kotter, R., 2002. The anatomical basis of functional localization in the cortex. *Nat. Rev. Neurosci.* 3, 606–616.
- Poppenk, J., Evensmoen, H.R., Moscovitch, M., Nadel, L., 2013. Long-axis specialization of the human hippocampus. *Trends Cogn. Sci.* 17, 230–240.
- Price, J.L., 2007. Definition of the orbital cortex in relation to specific connections with limbic and visceral structures and other cortical regions. *Ann. N.Y. Acad. Sci.* 1121, 54–71.
- Raichle, M.E., MacLeod, A.M., Snyder, A.Z., Powers, W.J., Gusnard, D.A., Shulman, G.L., 2001. A default mode of brain function. *Proc. Natl. Acad. Sci. USA* 98, 676–682.
- Ranganath, C., 2010. A unified framework for the functional organization of the medial temporal lobes and the phenomenology of episodic memory. *Hippocampus* 20, 1263–1290.
- Ranganath, C., Ritchey, M., 2012. Two cortical systems for memory-guided behaviour. *Nat. Rev. Neurosci.* 13, 713–726.
- Ritchey, M., Yonelinas, A.P., Ranganath, C., 2014. Functional connectivity relationships predict similarities in task activation and pattern information during associative memory encoding. *J. Cogn. Neurosci.* 26, 1085–1099.
- Ross, R.S., Slotnick, S.D., 2008. The hippocampus is preferentially associated with memory for spatial context. *J. Cogn. Neurosci.* 20, 432–446.
- Rushworth, M.F., Noonan, M.P., Boorman, E.D., Walton, M.E., Behrens, T.E., 2011. Frontal cortex and reward-guided learning and decision-making. *Neuron* 70, 1054–1069.
- Saleem, K.S., Kondo, H., Price, J.L., 2008. Complementary circuits connecting the orbital and medial prefrontal networks with the temporal, insular, and opercular cortex in the macaque monkey. *J. Comp. Neurol.* 506, 659–693.
- Sato, N., Nakamura, K., 2003. Visual response properties of neurons in the parahippocampal cortex of monkeys. *J. Neurophysiol.* 90, 876–886.
- Schedlbauer, A.M., Copara, M.S., Watrous, A.J., Ekstrom, A.D., 2014. Multiple interacting brain areas underlie successful spatiotemporal memory retrieval in humans. *Sci. Rep.* 4, 6431.
- Schlichting, M.L., Preston, A.R., 2015. Memory integration: neural mechanisms and implications for behavior. *Curr. Opin. Behav. Sci.* 1, 1–8.
- Schmahmann, J.D., Pandya, D.N., Wang, R., Dai, G., D’Arceuil, H.E., de Crespigny, A.J., Wedeen, V.J., 2007. Association fibre pathways of the brain: parallel observations from diffusion spectrum imaging and autoradiography. *Brain* 130, 630–653.
- Seeley, W.W., Crawford, R.K., Zhou, J., Miller, B.L., Greicius, M.D., 2009. Neurodegenerative diseases target large-scale human brain networks. *Neuron* 62, 42–52.
- Sestieri, C., Corbetta, M., Romani, G.L., Shulman, G.L., 2011. Episodic memory retrieval, parietal cortex, and the default mode network: functional and topographic analyses. *J. Neurosci.* 31, 4407–4420.
- Simons, J.S., Peers, P.V., Mazuz, Y.S., Berryhill, M.E., Olson, I.R., 2010. Dissociation between memory accuracy and memory confidence following bilateral parietal lesions. *Cereb. Cortex* 20, 479–485.
- Sommer, T., Rose, M., Weiller, C., Buchel, C., 2005. Contributions of occipital, parietal and parahippocampal cortex to encoding of object-location associations. *Neuropsychologia* 43, 732–743.
- Spaniol, J., Davidson, P.S., Kim, A.S., Han, H., Moscovitch, M., Grady, C.L., 2009. Event-related fMRI studies of episodic encoding and retrieval: meta-analyses using activation likelihood estimation. *Neuropsychologia* 47, 1765–1779.

- Spreng, R.N., Mar, R.A., Kim, A.S.N., 2009. The common neural basis of autobiographical memory, prospection, navigation, theory of mind, and the default mode: a quantitative meta-analysis. *J. Cogn. Neurosci.* 21, 489–510.
- Squire, L.R., Zola-Morgan, S., 1991. The medial temporal lobe memory system. *Science* 253, 1380–1386.
- St Jacques, P.L., Kragel, P.A., Rubin, D.C., 2011. Dynamic neural networks supporting memory retrieval. *NeuroImage* 57, 608–616.
- Staresina, B.P., Davachi, L., 2008. Selective and shared contributions of the hippocampus and perirhinal cortex to episodic item and associative encoding. *J. Cogn. Neurosci.* 20, 1478–1489.
- Staresina, B.P., Duncan, K.D., Davachi, L., 2011. Perirhinal and parahippocampal cortices differentially contribute to later recollection of object- and scene-related event details. *J. Neurosci.* 31, 8739–8747.
- Strange, B.A., Witter, M.P., Lein, E.S., Moser, E.I., 2014. Functional organization of the hippocampal longitudinal axis. *Nat. Rev. Neurosci.* 15, 655–669.
- Suzuki, W.A., Naya, Y., 2014. The perirhinal cortex. *Annu. Rev. Neurosci.* 37, 39–53.
- Svoboda, E., McKinnon, M.C., Levine, B., 2006. The functional neuroanatomy of autobiographical memory: a meta-analysis. *Neuropsychologia* 44, 2189–2208.
- Swanson, L.W., 1981. A direct projection from Ammon's horn to prefrontal cortex in the rat. *Brain Res.* 217, 150–154.
- Taylor, K.I., Moss, H.E., Stamatakis, E.A., Tyler, L.K., 2006. Binding crossmodal object features in perirhinal cortex. *Proc. Natl. Acad. Sci. USA* 103, 8239–8244.
- Tse, D., Takeuchi, T., Kakeyama, M., Kajii, Y., Okuno, H., Tohyama, C., Bito, H., Morris, R.G., 2011. Schema-dependent gene activation and memory encoding in neocortex. *Science* 333, 891–895.
- Tsujimoto, S., Genovesio, A., Wise, S.P., 2009. Monkey orbitofrontal cortex encodes response choices near feedback time. *J. Neurosci.* 29, 2569–2574.
- Uncapher, M.R., Otten, L.J., Rugg, M.D., 2006. Episodic encoding is more than the sum of its parts: an fMRI investigation of multifeatured contextual encoding. *Neuron* 52, 547–556.
- Valenstein, E., Bowers, D., Verfaellie, M., Heilman, K., Day, A., Watson, R., 1987. Retrosplenial amnesia. *Brain* 110, 1631–1646.
- van Kesteren, M.T., Ruiter, D.J., Fernández, G., Henson, R.N., 2012. How schema and novelty augment memory formation. *Trends Neurosci.* 35, 211–219.
- Vann, S.D., Aggleton, J.P., 2002. Extensive cytotoxic lesions of the rat retrosplenial cortex reveal consistent deficits on tasks that tax allocentric spatial memory. *Behav. Neurosci.* 116, 85–94.
- Verwer, R.W., Meijer, R.J., Van Uum, H.F., Witter, M.P., 1997. Collateral projections from the rat hippocampal formation to the lateral and medial prefrontal cortex. *Hippocampus* 7, 397–402.
- Vilberg, K.L., Rugg, M.D., 2008. Memory retrieval and the parietal cortex: a review of evidence from a dual-process perspective. *Neuropsychologia* 46, 1787–1799.
- Von Der Heide, R.J., Skipper, L.M., Klobusicky, E., Olson, I.R., 2013. Dissecting the uncinate fasciculus: disorders, controversies and a hypothesis. *Brain* 136, 1692–1707.
- Walton, M.E., Behrens, T.E., Buckley, M.J., Rudebeck, P.H., Rushworth, M.F., 2010. Separable learning systems in the macaque brain and the role of orbitofrontal cortex in contingent learning. *Neuron* 65, 927–939.
- Wang, W.C., Lazzara, M.M., Ranganath, C., Knight, R.T., Yonelinas, A.P., 2010. The medial temporal lobe supports conceptual implicit memory. *Neuron* 68, 835–842.

- Wang, J.X., Rogers, L.M., Gross, E.Z., Ryals, A.J., Dokucu, M.E., Brandstatt, K.L., Hermiller, M.S., Voss, J.L., 2014a. Targeted enhancement of cortical-hippocampal brain networks and associative memory. *Science* 345, 1054–1057.
- Wang, W.C., Ranganath, C., Yonelinas, A.P., 2014b. Activity reductions in perirhinal cortex predict conceptual priming and familiarity-based recognition. *Neuropsychologia* 52, 19–26.
- Watrous, A.J., Tandon, N., Conner, C.R., Pieters, T., Ekstrom, A.D., 2013. Frequency-specific network connectivity increases underlie accurate spatiotemporal memory retrieval. *Nat. Neurosci.* 16, 349–356.
- Wilson, F.A., Rolls, E.T., 1993. The effects of stimulus novelty and familiarity on neuronal activity in the amygdala of monkeys performing recognition memory tasks. *Exp. Brain Res.* 93, 367–382.
- Witter, M.P., Wouterlood, F.G., Naber, P.A., Van Haeften, T., 2000. Anatomical organization of the parahippocampal-hippocampal network. *Ann. N.Y. Acad. Sci.* 911, 1–24.
- Wright, P., Randall, B., Clarke, A., Tyler, L.K., 2015. The perirhinal cortex and conceptual processing: effects of feature-based statistics following damage to the anterior temporal lobes. *Neuropsychologia*. <http://dx.doi.org/10.1016/j.neuropsychologia.2015.01.041>. [Epub ahead of print].
- Yazar, Y., Bergstrom, Z.M., Simons, J.S., 2014. Continuous theta burst stimulation of angular gyrus reduces subjective recollection. *PLoS One* 9, e110414.
- Yoder, R.M., Clark, B.J., Taube, J.S., 2011. Origins of landmark encoding in the brain. *Trends Neurosci.* 34, 561–571.
- Yonelinas, A.P., Ritchey, M., 2015. The slow forgetting of emotional episodic memories: an emotional binding account. *Trends Cogn. Sci.* 19, 259–267.