Opinion TRENDS in Cognitive Sciences Vol.11 No.9

Imaging recollection and familiarity in the medial temporal lobe: a three-component model

Rachel A. Diana[1,2], Andrew P. Yonelinas[2] and Charan Ranganath[1,2]

[1] Center for Neuroscience, 1544 Newton Court, Davis, CA 95618, USA
[2] Department of Psychology, University of California, One Shields Avenue, Davis, CA 95616, USA

The medial temporal lobe (MTL) plays a crucial role in supporting memory for events, but the functional organization of regions in the MTL remains controversial, especially regarding the extent to which different subregions support recognition based on familiarity or recollection. Here we review results from functional neuroimaging studies showing that, whereas activity in the hippocampus and posterior parahippocampal gyrus is disproportionately associated with recollection, activity in the anterior parahippocampal gyrus is disproportionately associated with familiarity. The results are consistent with the idea that the parahippocampal cortex (located in the posterior parahippocampal gyrus) supports recollection by encoding and retrieving contextual information, whereas the hippocampus supports recollection by associating item and context information. By contrast, perirhinal cortex (located in the anterior parahippocampal gyrus) supports familiarity by encoding and retrieving specific item information. We discuss the implications of a 'binding of item and context' (BIC) model for studies of recognition memory. This model argues that there is no simple mapping between MTL regions and recollection and familiarity, but rather that the involvement of MTL regions in these processes depends on the specific demands of the task and the type of information involved. We highlight several predictions for future imaging studies that follow from the BIC model.

Introduction

Converging results from studies of individuals with amnesia, animal models and imaging research have shown that regions in the medial temporal lobe (MTL) have an essential role in supporting episodic memory (e.g. Refs [1,2]). Although there is broad support for the role of the MTL in memory, there is debate about the extent to which the hippocampus, parahippocampal cortex (PHc) and perirhinal cortex (PRc) support recollection and familiarity-based recognition. Recollection is the process of recognizing an item on the basis of the retrieval of specific contextual details, whereas familiarity is the process of recognizing an item on the basis of its perceived memory strength but without retrieval of any specific details about the study episode (Box 1).

Corresponding author: Ranganath, C. (cranganath@ucdavis.edu).
Available online 17 August 2007.

Here we review the results of neuroimaging studies that have examined neural correlates of recollection and familiarity in the MTL, and consider their theoretical implications. We present a three-component model, originally proposed by Eichenbaum *et al.* [3], which we refer to as the 'binding of item and context' (BIC) model. The original model was based on an overview of results from behavioral, neuropsychological and neuroimaging studies of recognition memory in humans and animal models. In this paper, we further specify the BIC model by examining the relevant neuroimaging evidence in more detail, by using the model to generate specific predictions for future neuroimaging studies, and by relating the model to other models of MTL function.

fMRI studies of recollection and familiarity

Event-related functional magnetic resonance imaging (fMRI) studies have used several different measures to disentangle recollection and familiarity. These measures include experiments in which subjects study individual items and are then given recognition tests that require remember/know responses, source memory responses or recognition confidence responses (Box 1). In general, results from contrasts that differentiate between remember and know, between source correct and source incorrect, and between the highest and lower confidence responses can be considered to be related to recollection. Familiarity contrasts typically examine activity differences between recognized, non-recollected items and non-recognized items ('misses'), or activity changes that are correlated with recognition confidence ratings. It should be emphasized that these contrasts are not expected to be completely process pure (Box 1). Given the limitations inherent in any particular method to identify a neural correlate of recollection or familiarity, the approach that we have adopted here is to determine whether there are consistent patterns in published studies that generalize across different measurement approaches.

An issue to consider when looking at the imaging results is that boundaries for the PRc and PHc are based on cytoarchitecture and anatomical connectivity, not on gyral and sulcal landmarks (note that susceptibility artifacts can cause signal loss in MTL, particularly in anterior regions, and results should be interpreted with this in mind). To be consistent with previous studies, we use the terms 'PRc'

 1364-6613/$ – see front matter doi:10.1016/j.tics.2007.08.001

Box 1. Familiarity and recollection in recognition

Several dual-process models have been developed to account for the observation that recognition memory judgments can be based on recollection (i.e. retrieval of qualitative information about a previous study event such as where or when an item was presented) or familiarity (i.e. assessment of memory strength) [12,55,56]. These models have been supported by experimental dissociations showing that some variables preferentially influence recollection, whereas other variables preferentially influence familiarity. For example, recollection is slower and requires more attention than does familiarity. Conversely, familiarity is more sensitive to perceptual changes across study and test, and is influenced by fluency manipulations such as subliminal masked priming.

Imaging studies have used several methods to identify neural correlates of recollection and familiarity. For example, the remember/know procedure requires participants to assess subjectively whether a recognized item elicits contextual recollection or whether it is based on familiarity in the absence of recollection. Another method is to obtain recognition confidence ratings. Because recollection reflects the retrieval of specific details of the study event, it is expected to lead to highly confident recognition responses; by contrast, familiarity is expected to contribute across a wide range of confidence responses because all items should elicit some level of familiarity strength. Lastly, tasks such as associative recognition (i.e. was A paired with B?) and source memory (i.e. was A studied with task 1?), in which participants are required to retrieve specific aspects of the study event, are thought to rely heavily on recollection. In addition to the imaging studies reviewed here, event-related potential and neuropsychological studies of humans, as well as lesion studies in rodents, have used these methods to reveal neural dissociations between recollection and familiarity (see Ref. [3] for details).

It should be noted that each method of assessing recollection and familiarity has its own strengths and weaknesses. For example, source memory tasks measure recollection as the ability to retrieve a specific detail about the study event (i.e. list membership). If the subject fails to recollect this specific detail, then that item will not be treated as recollected, even if the subject does recollect other details about it. This approach means that even incorrect source retrieval trials might include 'non-criterial' recollection, particularly when accuracy levels are high (see Ref. [12]). Thus, when assessing studies of recollection and familiarity, it is essential to look for convergence across various different measurement methods.

Box 2. Information flow in the MTL

The inputs and projections of MTL subregions provide some insight into the functions of the hippocampus, PRc and PHc. Figure 3 shows the locations of the regions within the MTL. PRc receives the majority of its inputs from unimodal visual association areas and roughly a third of its inputs from unimodal, non-visual, semantic association areas [40,58,59]. The PHc receives its strongest inputs from visuo-spatial areas in the dorsal stream, dorsolateral prefrontal cortex and retrosplenial cortex, in addition to unimodal inputs [58,59]. Both the PRc and PHc project to entorhinal cortex, but these input streams remain segregated (at least in the rodent brain), such that the PRc projects primarily to lateral entorhinal areas and the PHc projects primarily to medial entorhinal areas. It should be noted, however, that the PHc and PRc are also interconnected (although the connections are asymmetric such that the projections from the PRc to PHc are relatively weak) [59]. Entorhinal cortex provides the majority of the cortical input to the hippocampus, which in turn projects back to the PRc, PHc and entorhinal cortex.

Comparing the inputs to the PRc and PHc, it is apparent that the PRc receives more input from unimodal perceptual regions (the 'what' stream) that convey detailed information about item features, whereas the PHc receives more inputs from polymodal cortical areas (the 'where' stream) that convey integrative information about the context in which items are encountered. The hippocampus is the site of convergence of 'what' and 'where' information in the processing stream. This circuit of information flow might be central to understanding the encoding and retrieval of memories (see Ref. [40] for more details).

and 'PHc' to refer to activations observed in the anterior and posterior parahippocampal gyrus, respectively. Nonetheless, it should be kept in mind that typical imaging methods place limits on the ability to differentiate between these regions, and there is sometimes ambiguity regarding whether activation falls in one region or the other (Box 2). Lastly, although the amygdala has been implicated in recognition of emotionally arousing material, it has not been consistently identified in other studies that we reviewed, and thus we have not considered this region further (Box 3).

As shown in Table 1 and Figure 1, hippocampal activity during encoding [4–12] and retrieval [7,9,13–25] is reliably increased for items that are recollected, but is not sensitive to differences in item familiarity. A similar, but less robust pattern of results (greater activity for recollected items than non-recollected items but no sensitivity to familiarity) is apparent for regions corresponding to the PHc during both encoding [4,6–8,26] and retrieval [7,14,17,18,20,24,25,27].

Unlike the hippocampus and the PHc, however, activity in regions corresponding to the PRc is rarely observed by using contrasts examining recollection of items, but it is consistently correlated with familiarity. During encoding, activity in regions corresponding to the PRc is increased for items that are later judged as familiar [4,6–8,10,11,28]; during retrieval, by contrast, activity is decreased for items judged to be familiar relative to forgotten items [15,16,21,22,29]. This pattern of results is strikingly consistent with physiological studies of rodents and monkeys [30], and with one intracranial recording study in humans, which found that perirhinal neurons show decreased activity for familiar as compared with novel stimuli [31].

The results overwhelmingly support the claim that activity patterns in the hippocampus and PHc can be distinguished from those in the PRc. Furthermore, three studies have reported within-study double dissociations, linking activity in the hippocampus and PHc to recollection, and activation in the PRc to familiarity [4,6,8].

Box 3. Questions for future research

- What is the role of attention in determining which aspects of an event are treated as items and which are treated as context?
- How does the allocation of attention relate to whether activations or deactivations are seen in the MTL?
- Can contextual information influence how items are represented?
- What is the functional role of the strong, asymmetric projections from the PHc to the PRc?
- What are the necessary and sufficient conditions for unitization to occur?
- Is unitization dependent on attention? And is it necessary to hold two items in a single attentional window to unitize them?
- Does unitization necessarily create a new single representation for a novel association or does it create a direct link between the pre-existing representations of the two items?
- Do the PRc and PHc inputs to entorhinal cortex remain segregated in humans as they are in rodents?
- What additional mnemonic processes are implemented by entorhinal cortex, and how do these processes differ from the PRc and PHc?

Table 1. Activation of the MTL in studies of recollection and/or familiarity using single items

Study[a]	Method	Materials	Stage	Contrast	Hipp	PPHG	APHG
Recollection of items							
Davachi *et al.* [4]	SC/SI/Miss	Words	En	SC > SI	b	l	None
Gold *et al.* [55]	SC/SI/Miss	Words	En	SC > SI	None	None	l
Johnson and Rugg [26]	RKN	Words	En	R > K	None	l	None
Kensinger and Schacter [6]	SC/SI/Miss	Emotional pictures	En	SC > SI	l	r	None
Kensinger and Schacter [6]	SC/SI/Miss	Emotional words	En	SC > SI	l	None	None
Otten [12]	RKN	Words and pictures	En	R > F	r	None	None
Ranganath *et al.* [8]	SC/SI/1–6	Words	En	SC > SI	r	r	None
Staresina and Davachi [47]	Recall/SC/Item	Words	En	Recall > Item	b	None	None
Staresina and Davachi [47]	Recall/SC/Item	Words	En	Source > Item	None	None	l
Uncapher and Rugg [11]	RKN	Words	En	R > K	l	None	None
Uncapher *et al.* [10]	SC/SI/Miss	Words + two sources	En	Both SC > 1 or 2 SI	r	None	None
Cansino *et al.* [14]	SC/SI/Miss	Words	Re	SC > SI	r	l	None
Daselaar *et al.* [15]	1–6	Words	Re	6 > 1–5	l	None	None
Daselaar *et al.* [16]	1–4	Words and non-words	Re	4 > 1–3	l	None	None
Dolcos *et al.* [18]	RKN	Neutral pictures	Re	R > K	b	r	None
Dolcos *et al.* [18]	RKN	Emotional pictures	Re	R > K	b	b	b
Dobbins *et al.* [17]	SC/SI/Miss	Words	Re	SC > SI/Miss	b	l	l
Eldridge *et al.* [19]	RKN	Words	Re	R > K	b	r	None
Kahn *et al.* [27]	SC/SI/Miss	Words	Re	SC > SI	None	b	None
Montaldi *et al.* [21]	1–4R	Scenes	Re	R > all else	b	None	None
Sharot *et al.* [56]	RKN	Scenes	Re	R > K	None	r	None
Vilberg and Rugg [57]	RKN	Pictures	Re	R > K	l	l	None
Weis *et al.* [22]	SC/SI/Miss	Scenes	Re	SC > SI	b	None	None
Wheeler and Buckner [23]	RKN	Words	Re	R > K	b	None	None
Woodruff *et al.* [24]	RKN	Words	Re	R > K	r	r	None
Yonelinas *et al.* [25]	1–4R	Words	Re	R>4	b	l	None
Familiarity							
Davachi *et al.* [4]	SC/SI/Miss	Words	En	SC=SI > Miss	None	None	l
Gold *et al.* [55]	SC/SI/Miss	Words	En	SC=SI > Miss	l	b	r
Henson *et al.* [28]	RKN	Words	En	K > R	None	None	r
Kensinger and Schacter [6]	SC/SI/Miss	Emotional pictures	En	SI > Miss	None	None	l
Kensinger and Schacter [6]	SC/SI/Miss	Emotional Words	En	SI > Miss	None	None	l
Ranganath *et al.* [8]	SC/SI/1–6	Words	En	1–4 linear increase	None	None	l
Uncapher and Rugg [11]	RKN	Words	En	K > Miss	None	None	r
Uncapher *et al.* [10]	SC/SI/Miss	Words + two sources	En	All recognized > forgotten	None	None	l
Daselaar *et al.* [15]	1–6	Words	Re	1–6 linear decrease	l	None	l
Daselaar *et al.* [16]	1–4	Words and non-words	Re	4 > 3 > 2–1	None	None	l
Gonsalves *et al.* [29]	RKN	Faces	Re	R<K<Miss<CR	None	l	b
Montaldi *et al.* [21]	1–4R	Scenes	Re	1–4 linear decrease	None	None	b
Weis *et al.* [22]	SC/SI/Miss	Scenes	Re	SI < Miss	None	None	r
Yonelinas *et al.* [25]	1–4R	Words	Re	1–4 linear decrease	l	None	None

[a]Only experiments and contrasts that reported activation in at least one MTL subregion are included. In addition, contrasts not specific to familiarity or recollection (see text) have been excluded. Numbers 1–6 refer to recognition confidence ratings, in which higher ratings indicate higher confidence that an item was studied. Abbreviations: Hipp, hippocampus; PPHG, posterior parahippocampal gyrus; APHG, anterior parahippocampal gyrus; SC, source (and item) correct; SI, source incorrect but item correct; Miss, old item judged new; Assoc. rec., associative recognition; R, remember; K, know; N, new; En, encoding; Re, retrieval; l, left; r, right; b, bilateral.

Figure 2 presents data from one of the studies demonstrating a double dissociation [8]. Although some studies did not find significant activation differences among the MTL subregions for recollection and familiarity, only a few studies reported MTL activations that did not fit with the patterns described above. In addition, Table 1 suggests that there were no reliable differences in lateralization or anterior–posterior location of these activations related to encoding or retrieval [32], nor were there any differences between studies examining memory for emotional or neutral stimuli.

Findings from the fMRI studies (Table 1) have several implications for models of MTL function. First, the data are not consistent with models that do not differentiate among MTL subregions. If the hippocampus, PRc and PHc contribute equally to both recollection and familiarity [33,34], then one would expect to see similar patterns of MTL activation for both types of response. This is clearly not the case. Similarly, if these three regions contribute only to recollection [35,36], then one would expect to see MTL activation for recollection but not for familiarity, which is also not the case. The data are more consistent with models proposed by Eichenbaum and Cohen [37] and Aggleton and Brown [38,39], which link the hippocampus with recollection and the PRc with familiarity. These models, however, do not predict the dissociation between the PHc and the PRc that is evident in the published studies. Accordingly, these models cannot fully explain the complete pattern of results in the imaging literature without some modification. Below, we describe the BIC model and argue that this model can account for the imaging results.

The BIC model of MTL function

Anatomical studies of monkeys and rodents provide a foundation for the BIC model [3]. In general, these studies suggest that the PRc receives detailed information about specific items that are to be remembered, whereas the PHc

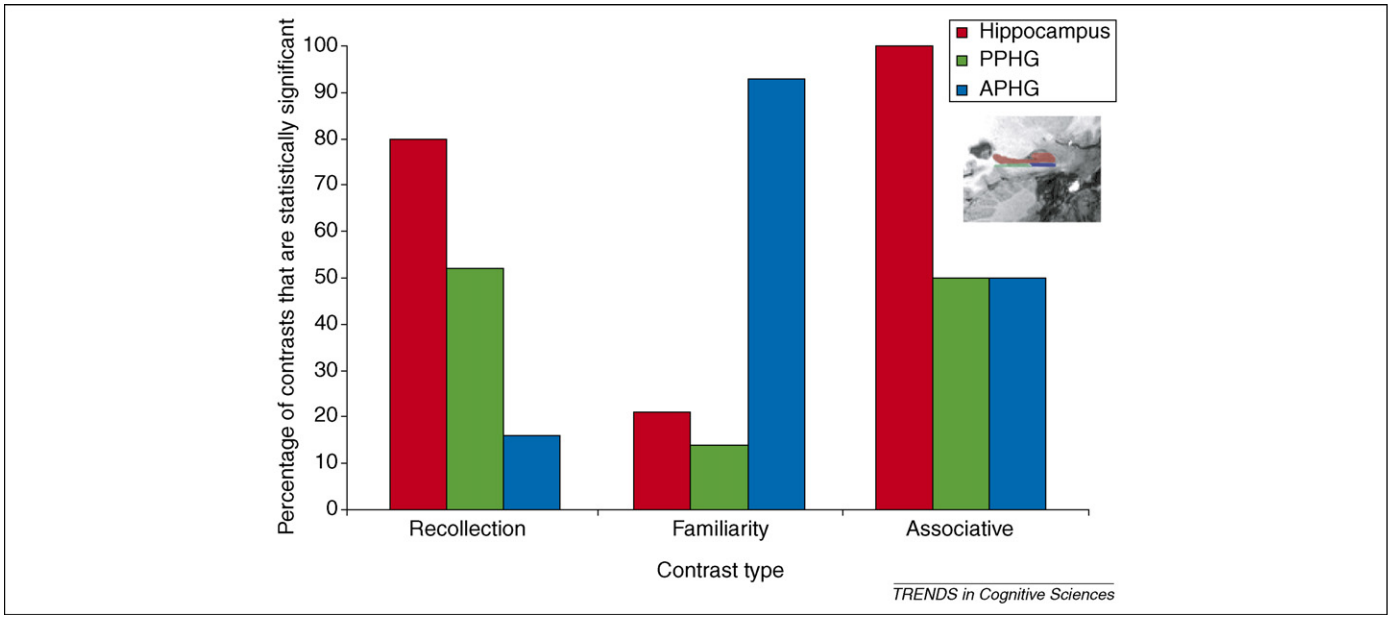

Figure 1. Activation of MTL subregions in studies of recollection and/or familiarity. Shown is the percentage of contrasts of each type (recollection, familiarity or associative recognition) in which activation was reported for the hippocampus, the posterior parahippocampal gyrus (PPHG) and the anterior parahippocampal gyrus (APHG). Data are summarized from Tables 1 and 2.

receives detailed information about the spatial context in which each item was encountered (Box 2). The information about 'what' and 'where' – two key attributes of episodic memories – converges in the hippocampus. Drawing on this framework, we suggest that the PRc and PHc encode item and context information and the hippocampus in turn encodes representations of item–context associations. Item representations can support familiarity in standard tests of item recognition because no specific contextual information is necessary to make a familiarity judgment.

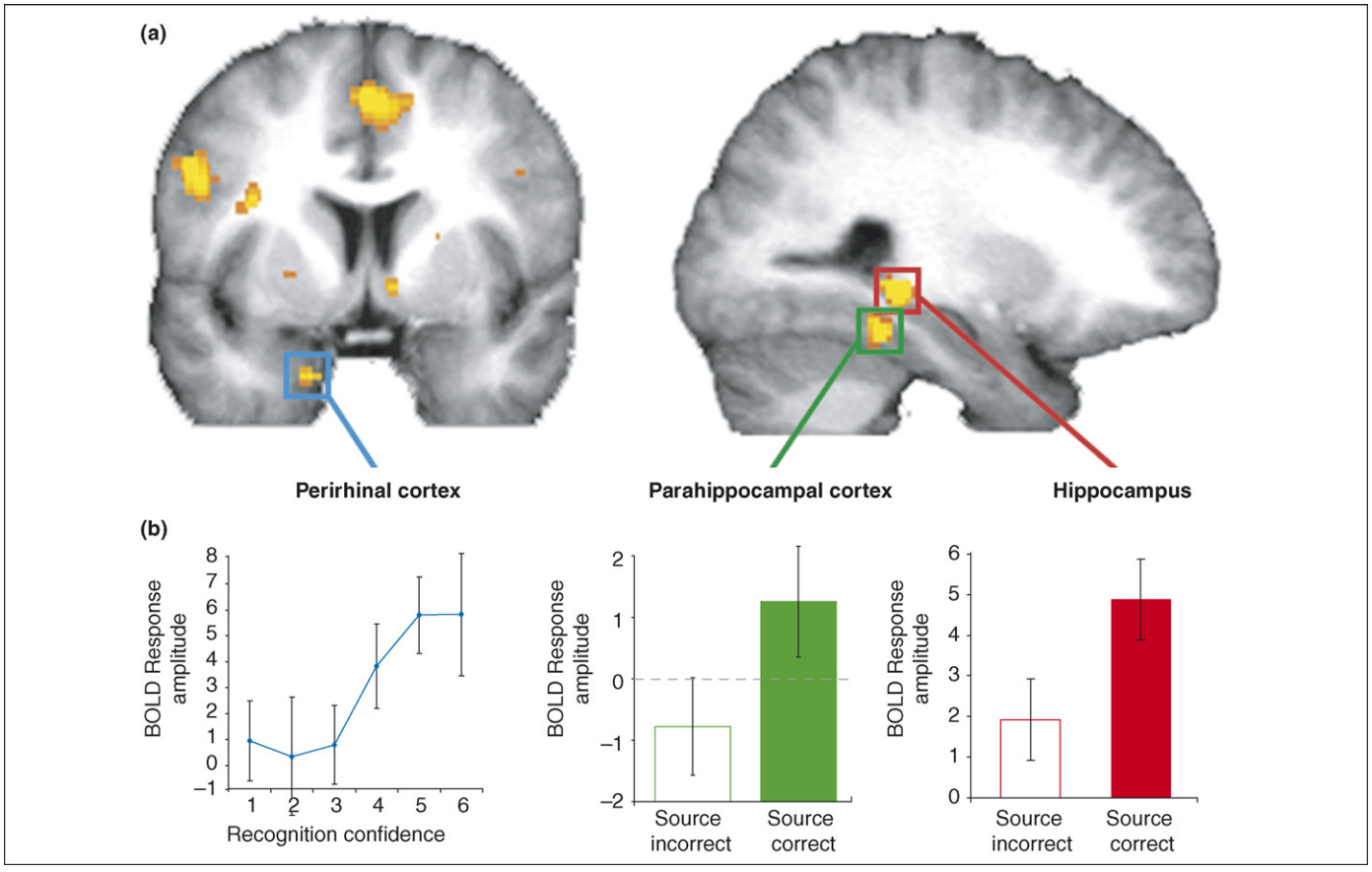

Figure 2. Double dissociation between neural correlates of recollection and familiarity in the MTL. **(a)** Location of recollection and familiarity effects in the MTL. **(b)** fMRI BOLD response amplitude in the perirhinal cortex (PRc), posterior parahippocampal cortex (PHc) and hippocampus. Results are taken from Ranganath and colleagues [8].

Therefore, similar to previous models [38–40], the BIC model predicts that the PRc is involved in familiarity-based recognition. Context representations and item–context bindings support recollection in tests of item recognition. As previous models suggest, this means that the hippocampus is important for recollection [37–39]; however, the BIC model is novel in that it suggests that the PHc is also important for recollection because it represents contextual information (Figure 3).

According to the BIC model, the pattern of activation in the MTL will depend on the type of processing that is occurring and the cues that are presented. During item encoding, the PRc will be more active for items that are subsequently judged as more familiar because increased processing is required to strengthen the item. The hippocampus and PHc will be more active in trials for which contextual information will be subsequently retrieved.

During item retrieval, the item cue will deactivate the PRc to the degree that the item is familiar. A more familiar item will lead to a larger deactivation because better encoding leads to a more efficient item representation. Thus, familiarity-based responses are expected to produce deactivations in the PRc. In addition, input to the hippocampus might trigger re-instantiation of the activation pattern that occurred during the learning event ('pattern completion'). Such hippocampal activity will in turn lead to reactivation of the associated contextual information in PHc networks, thereby leading to recollection. Thus, recollection-based responses are expected to produce activations in the PHc (and the hippocampus).

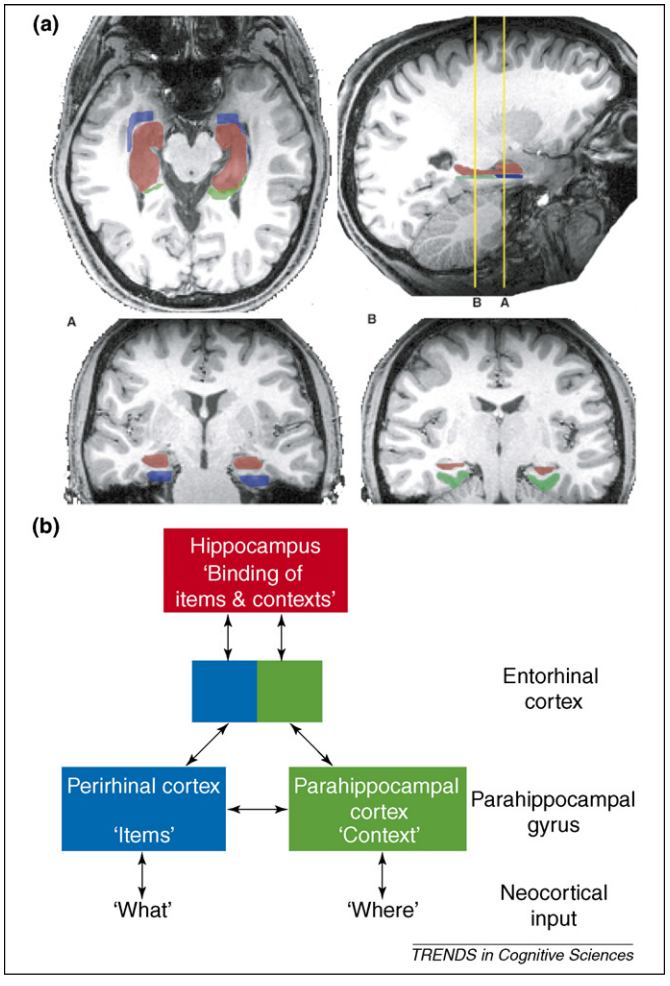

Figure 3. Anatomy of the MTL region. **(a)** Approximate locations of the hippocampus (red), the PRc (blue) and the PHc (green) shown on T1-weighted magnetic resonance images. **(b)** Representation of the anatomical connections among, and the proposed roles of, the hippocampus, PRc and PHc in episodic memory according to the BIC model. The arrow between the PRc and PHc indicates the anatomic connection between the two regions; the PRc receives more inputs from the PHc than vice versa. The connections shown here are based on results from anatomical studies of rats and monkeys [59].

In atypical recognition paradigms, we might see different patterns of activation and deactivation depending on the way in which item and context representations are retrieved. In general, we predict that the PRc and PHc should show deactivations during processing of familiar items or contexts when those items or contexts are represented at test. In addition, the PRc and PHc should activate during retrieval of items or contexts when those items or contexts are retrieved spontaneously, typically through pattern completion in the hippocampus.

The BIC model of recollection and familiarity provides an anatomically based explanation of existing fMRI studies of item recognition. The key innovation of this model is that recollection and familiarity are not thought to have a simple one-to-one mapping to regions of the MTL. Rather, MTL subregions are important for processing different types of information (items, contexts, and bindings). As we describe below, the demands of the encoding and retrieval tasks in a given experiment will determine which subregions will be recruited during recollection-based processing and familiarity-based processing.

Additional model predictions

The relatively simple assumptions described above lead to several predictions for more complex tasks, such as associative memory tasks. For example, tests of associative recognition in which pairs of items are studied and memory is then tested for the specific item pairings might lead to activations that are somewhat different from those seen in tests of single-item recognition. As in item recognition, recollection of inter-item associations should elicit hippocampal activation because hippocampal representations are required to link one item to the other or to the study context. In addition, if the study context is retrieved then PHc activation should be observed, and if one of the test items elicits recollection of the associated item then PRc activity might be observed. Table 2 presents the recollection effects observed in experiments involving pairs of items. Although there are few such published studies [5,7,20,41], the results are in agreement with the expectations and indicate that hippocampal activation is observed in nearly all contrasts, and that activation of both PRc and PHC is relatively common.

Another expectation derived from the model is that the PRc might be able to support associative recognition on the basis of familiarity if the associated items are encoded as a single unit (i.e. 'unitized') [42,43]. That is, the distinction between items and associations is determined by the manner in which the stimuli are processed (e.g. 'BIC' can be processed either as three separate letters or as a single word). Consequently, if two paired items are encoded as a single unit, PRc-mediated item familiarity signals should

Table 2. Activation of the MTL in associative studies of recollection and/or familiarity

Study[a]	Method	Materials	Stage	Contrast	Hipp	PPHG	APHG
Recollection of associations							
Jackson and Schacter [5]	Assoc. rec.	Word pairs	En	Intact hit > intact called recombined	l	None	l
Kirwan and Stark [7]	Assoc. rec.	Face–name	En	Intact hit > intact called recombined	r	r	None
Eldridge *et al.* [41]	RKN	Picture–word	Re	R > K	l[b]	None	b
Eldridge *et al.* [41]	RKN	Picture–word	Re	RK < Miss = CR	r[b]	r[b]	None
Fenker *et al.* [20]	RKN	Word–fearful face	Re	R > K	r	None	r
Fenker *et al.* [20]	RKN	Word–neutral face	Re	R > K	b	l	None
Kirwan and Stark [7]	Assoc. rec.	Face–name	Re	Intact hit > intact called recombined	r	r	b
Murray and Ranganath [43]	Assoc. rec.	Word pairs	En	High-confidence pairs > other pairs	l	None	None

[a]Only experiments and contrasts that reported activation in at least one MTL subregion are included. In addition, contrasts not specific to familiarity or recollection (see text) have been excluded. Abbreviations as in Table 1.
[b]These studies used a flat-mapping procedure to differentiate activations in different hippocampal subregions. Although data were collected during encoding and retrieval, the encoding data were contaminated by an unexplained artifact that precludes a clear interpretation of the data. Accordingly, only the retrieval data are summarized here. Within the hippocampus, recollection-related activation has been reported for the left subiculum and familiarity-related activation has been reported for the CA2/CA3/dentate gyrus region.

become useful in discriminating between studied pairings and pairs that consist of familiar items for which the pairings have been rearranged. Although published fMRI studies have not yet tested this hypothesis, some evidence from studies of individuals with amnesia is consistent with this idea [44,45]. For example, Quamme *et al.* [45] demonstrated that hippocampal amnesic individuals with deficits in recollection but normal familiarity showed severe impairment in associative recognition tests for unrelated word pairs. This impairment was markedly reduced if they had encoded word pairs as single units (i.e. they made up new compound words out of the random word pairs). This result suggests that the PRc might be sufficient to support familiarity-based recognition of unitized associations. Recent results suggest that unitization of item and source information can also support familiarity-based source recognition (R.A. Diana *et al.*, unpublished data). Consistent with the BIC model, under these conditions PRc activation was associated with correct source recognition, rather than the typical finding of PHc activation during source retrieval [46].

Given the complementary nature of the PRc and PHc, we might expect to see some parallels in activation patterns across these two regions. During encoding, for example, the PRc shows decreases in activity with repeated processing of the same item, and the PHc should show similar decreases in activity with repeated processing of the same contextual information [47]. Although this prediction has not been tested directly, some imaging studies have reported results that are broadly consistent with it. For example, activation in the posterior hippocampus and PHc is increased during processing of new arrangements of familiar items in a grid, whereas the anterior hippocampus and PRc are activated when unique objects are added to the grid but the spatial arrangement is unchanged [48].

The model also makes clear predictions for retrieval: that is, the retrieval or recall of item information should be associated with PRc activity, whereas the retrieval of context information should be associated with PHc activity. In addition, given adequate temporal and spatial resolution, it should be possible to observe dissociations in the time course of brain activation observed in the PHc, PRc and hippocampus during recollection. The model predicts that presentation of a studied context should first involve the PHc; this activation would then be followed by the association of item and context in the hippocampus, and completion of the pattern in the PRc, leading to item recognition. By contrast, presentation of an item should involve first the PRc, followed by the hippocampus and then the PHc, where the pattern is completed.

The nature of context in the PHc

A novel aspect of the BIC model is that it predicts that context representations, including both spatial and non-spatial information, are encoded by the PHc. Several studies have implicated the PHc in memory for spatial information [49,50]. These findings have led theorists to suggest that the PHc is important for encoding spatial context [51]. Several studies have demonstrated PHc involvement in a range of memory tasks, however, suggesting that it plays a wider role in memory formation. For example, Bar and Aminoff [52] have demonstrated that the PHc is more active during recognition of visual objects that are strongly associated with a specific context (e.g. roulette wheel or beach chair) than during recognition of objects that are not associated with a particular context. The authors claim that this is evidence for involvement of the PHc in more semantic or schematic types of context.

Additional insight into the nature of the contextual information supported by the PHc can be obtained by considering the studies of recollection reviewed above. The contrasts listed in Table 1 indicate that activation of the PHc is observed during recollection of spatial location, but that it is also involved in the recollection of information that is less easily described as spatial. For example, PHc activity is related to recollection of neutral and emotional pictures and words. These studies, of course, do not indicate the type of contextual information that was retrieved, so one could argue that they might have led to the retrieval of spatial information such as the room where the study was conducted. However, activation of the PHc has also been associated with retrieval of information, such

as the background color of the studied items and even the semantic processing task that was conducted with the items during study (i.e. whether subjects made a pleasantness versus concreteness judgment about a word). Although it is conceivable that even semantic judgments have some spatial processing component, a simpler explanation is that the PHc is able to support both spatial and non-spatial contextual information.

Although the available empirical evidence does not enable us to provide a definitive claim about exactly what types of contextual information the PHc supports, we can propose a provisional definition that includes visual, spatial and semantic, gist or schema information that is peripheral to the study item. Another way of describing the difference between item and context information is that the PHc supports a more global representation of the study event, whereas the PRc supports a more local representation of the event, such as those objects that fall within the immediate focus of attention. Regardless, if the PHc does represent spatial and non-spatial contextual associations, then PHc activity should be increased during retrieval of both kinds of information. This prediction can be tested in future studies.

Comparison of BIC with other recent models of MTL organization

Although the BIC model is similar to other recent models of MTL organization, it differs in some important aspects. For example, Fernandez and Tendolkar [40] referred to the PRc as the 'gatekeeper' of declarative memory, arguing that its role is to direct encoding resources towards less familiar items. This same familiarity signal is then relevant at retrieval for making item memory judgments. This model predicts the decreasing activation that is seen with repetition of items in the PRc; however, it does not make specific predictions for the hippocampus and PHc. In addition, Norman and O'Reilly's model [53] highlights the PRc and PHc as an intermediary between the hippocampus and the neocortex. However, the roles of the PRc and PHc are not differentiated, and thus this model provides little insight into the observed differences in activation across these regions.

Mayes *et al.* [54] have proposed the domain dichotomy model, which also argues that the hippocampus is essential for recollection, whereas the PRc is important for familiarity (no role for the PHc is specified). In addition, they suggest that hippocampally-dependent recollection is necessary to support memory for new associations between items from different processing domains (e.g. faces and words), but familiarity could support learning of new associations between items within processing domains (e.g. an association between two faces). The BIC model does not distinguish between within- and between-domain associations, but it does differentiate between item and contextual information. Thus, we predict that associations between items from different processing domains might be supported by familiarity, if items have been unitized. As noted above, the BIC model also predicts that PRc activity can be seen during recollection of an item–item association (i.e. if presentation of one item elicits reactivation of the associated item representation), whereas the domain dichotomy model restricts the role of the PRc to familiarity. Future studies testing the competing predictions of the two models will be important.

Lastly, Davachi [51] has proposed that the PRc is important for encoding specific visual and conceptual features of studied items, whereas the PHc might contribute to spatial contextual encoding. The object and spatial information encoded in the PRc and PHc, respectively, is then passed to the hippocampus and recombined into a domain-general relational representation. This model is similar to the BIC model except that it is not explicitly tied to recollection and familiarity processes and therefore does not make specific predictions about the graded nature of PRc activation (Box 1). Thus, the model does not explain why, for non-recollected items, activation of the PRc co-varies in a graded manner with increasing familiarity [8,15,21]. In addition, this model treats the PHc as a region supporting only spatial information, whereas we argue that the PHc is not limited to the processing of spatial information. These differences highlight the need for further experiments investigating the nature of item and context information as represented in the MTL.

Concluding remarks

Imaging data have provided significant insights into the functional organization of the MTL and, more specifically, into the way in which different MTL regions contribute to recollection and familiarity. Whereas activity in the hippocampus and PHc is correlated with recollection, activity in the PRc is correlated with familiarity. The results are not consistent with many existing models, but they can be explained by the BIC model. The BIC model is the first model of MTL function to propose a role for the PHc in encoding contextual information in general (without restricting such information to a specific domain). The model presents underlying mechanisms for the type of information that is encoded and the way in which it is processed to predict the involvement of the hippocampus, PRc and PHc in recollection and familiarity. Crucially, the model does not assume a simple mapping between MTL subregions and recollection and familiarity. Instead, it argues that there is an integrated system in which the involvement of each subregion depends on the type of information processing that is engaged. We hope that future studies that test the predictions of the model will lead to further progress in understanding how activity in these MTL regions supports different mnemonic processes.

Acknowledgements

This work was supported by the National Institute of Mental Health (grants MH068721 and MH059352) and the National Institute of Neurological Disorders and Stroke (grant NS40813). We thank the reviewers for their insights.

References

1 Eichenbaum, H. *et al.* (1992) The hippocampus – what does it do? *Behav. Neural Biol.* 57, 2–36
2 Scoville, W.B. and Milner, B. (1957) Loss of recent memory after bilateral hippocampal lesions. *J. Neurol. Neurosurg. Psychiatry* 20, 11–21
3 Eichenbaum, H. *et al.* (2007) The medial temporal lobe and recognition memory. *Annu. Rev. Neurosci.* 30, 123–152

4 Davachi, L. *et al.* (2003) Multiple routes to memory: distinct medial temporal lobe processes build item and source memories. *Proc. Natl. Acad. Sci. U. S. A.* 100, 2157–2162
5 Jackson, O. and Schacter, D.L. (2004) Encoding activity in anterior medial temporal lobe supports subsequent associative recognition. *NeuroImage* 21, 456–462
6 Kensinger, E.A. and Schacter, D.L. (2006) Amygdala activity is associated with successful encoding of item, but not source, information for positive and negative stimuli. *J. Neurosci.* 26, 2564–2570
7 Kirwan, C.B. and Stark, C.E.L. (2004) Medial temporal lobe activation during encoding and retrieval of novel face–name pairs. *Hippocampus* 14, 919–930
8 Ranganath, C. *et al.* (2004) Dissociable correlates of recollection and familiarity within the medial temporal lobes. *Neuropsychologia* 42, 2–13
9 Stark, C.E.L. and Squire, L.R. (2000) Functional magnetic resonance imaging (fMRI) activity in the hippocampal regions during recognition memory. *J. Neurosci.* 20, 7776–7781
10 Uncapher, M.R. *et al.* (2006) Episodic encoding is more than the sum of its parts: an fMRI investigation of multifeatural contextual encoding. *Neuron* 52, 547–556
11 Uncapher, M.R. and Rugg, M.D. (2005) Encoding and the durability of episodic memory: a functional magnetic resonance imaging study. *J. Neurosci.* 25, 7260–7267
12 Otten, L.J. (2006) Fragments of a larger whole: retrieval cues constrain observed neural correlates of memory encoding. *Cereb. Cortex* DOI: 10.1093/cercor/bhl156
13 Bunge, S.A. *et al.* (2004) Prefrontal and hippocampal contributions to visual associative recognition: interactions between cognitive control and episodic retrieval. *Brain Cogn.* 56, 141–152
14 Cansino, S. *et al.* (2002) Brain activity underlying encoding and retrieval of source memory. *Cereb. Cortex* 12, 1048–1056
15 Daselaar, S.M. *et al.* (2006) Triple dissociation in the medial temporal lobes: recollection, familiarity, and novelty. *J. Neurophysiol.* 96, 1902–1911
16 Daselaar, S.M. *et al.* (2006) Effects of healthy aging on hippocampal and rhinal memory functions: an event-related fMRI study. *Cereb. Cortex* 16, 1771–1782
17 Dobbins, I.G. *et al.* (2003) Memory orientation and success: separable neurocognitive components underlying episodic recognition. *Neuropsychologia* 41, 318–333
18 Dolcos, F. *et al.* (2005) Remembering one year later: role of the amygdala and the medial temporal lobe memory system in retrieving emotional memories. *Proc. Natl. Acad. Sci. U. S. A.* 102, 2626–2631
19 Eldridge, L.L. *et al.* (2000) Remembering episodes: a selective role for the hippocampus during retrieval. *Nat. Neurosci.* 3, 1149–1152
20 Fenker, D.B. *et al.* (2005) Recapitulating emotional context: activity of amygdala, hippocampus and fusiform cortex during recollection and familiarity. *Eur. J. Neurosci.* 21, 1993–1999
21 Montaldi, D. *et al.* (2006) The neural system that mediates familiarity memory. *Hippocampus* 16, 504–520
22 Weis, S. *et al.* (2004) Process dissociation between contextual retrieval and item recognition. *NeuroReport* 15, 2729–2733
23 Wheeler, M.E. and Buckner, R.L. (2004) Functional–anatomic correlates of remembering and knowing. *NeuroImage* 21, 1337–1349
24 Woodruff, C.C. *et al.* (2005) Content-specificity of the neural correlates of recollection. *Neuropsychologia* 43, 1022–1032
25 Yonelinas, A.P. *et al.* (2005) Separating the brain regions involved in recollection and familiarity in recognition memory. *J. Neurosci.* 25, 3002–3008
26 Johnson, J.D. and Rugg, M.D. (2007) Recollection and the reinstatement of encoding-related cortical activity. *Cereb. Cortex* DOI: 10.1093/cercor/bhl156
27 Kahn, I. *et al.* (2004) Functional–neuroanatomic correlates of recollection: Implications for models of recognition memory. *J. Neurosci.* 24, 4172–4180
28 Henson, R.N.A. *et al.* (1999) Recollection and familiarity in recognition memory: an event-related functional magnetic resonance imaging study. *J. Neurosci.* 19, 3962–3972
29 Gonsalves, B.D. *et al.* (2005) Memory strength and repetition suppression: multimodal imaging of medial temporal cortical contributions to recognition. *Neuron* 47, 751–762
30 Aggleton, J.P. and Brown, M.W. (2005) Contrasting hippocampal and perirhinal cortex function using immediate early gene imaging. *Q. J. Exp. Psychol. B* 58, 218–233
31 Viskontas, I.V. *et al.* (2006) Differences in mnemonic processing by neurons in the human hippocampus and parahippocampal regions. *J. Cogn. Neurosci.* 18, 1654–1662
32 Schacter, D.L. and Wagner, A.D. (1999) Medial temporal lobe activations in fMRI and PET studies of episodic encoding and retrieval. *Hippocampus* 9, 7–24
33 Squire, L.R. (1994) Declarative and nondeclarative memory: multiple brain systems supporting learning and memory. In *Memory Systems* (Schacter, D.L. and Tulving, E., eds), pp. 203–231, MIT Press
34 Squire, L.R. and Zola, S. (1998) Episodic memory, semantic memory, and amnesia. *Hippocampus* 8, 205–211
35 Huppert, F.A. and Piercy, M. (1978) The role of trace strength in recency and frequency judgments by amnesic and control subjects. *Q. J. Exp. Psychol.* 30, 347–354
36 Mayes, A.R. *et al.* (1985) Is organic amnesia caused by a selective deficit in remembering contextual information? *Cortex* 21, 167–202
37 Eichenbaum, H. *et al.* (1994) Two functional components of the hippocampal memory system. *Behav. Brain Sci.* 17, 449–517
38 Aggleton, J.P. and Brown, M.W. (2006) Interleaving brain systems for episodic and recognition memory. *Trends Cogn. Sci.* 10, 455–463
39 Brown, M.W. and Aggleton, J.P. (2001) Recognition memory: what are the roles of the perirhinal cortex and hippocampus. *Nat. Rev. Neurosci.* 2, 51–61
40 Fernandez, G. and Tendolkar, I. (2006) The rhinal cortex: 'gatekeeper' of the declarative memory system. *Trends Cogn. Sci.* 10, 358–362
41 Eldridge, L.L. *et al.* (2005) A dissociation of encoding and retrieval processes in the human hippocampus. *J. Neurosci.* 25, 3280–3286
42 Yonelinas, A.P. *et al.* (1999) Recognition memory for faces: when familiarity supports associative recognition. *Psychon. Bull. Rev.* 6, 654–661
43 Murray, L.J. and Ranganath, C. (2007) The dorsolateral prefrontal cortex contributes to successful relational memory encoding. *J. Neurosci.* 27, 5515–5522
44 Giovanello, K.S. *et al.* (2006) The contribution of familiarity to associative memory in amnesia. *Neuropsychologia* 44, 1859–1865
45 Quamme, J.R. *et al.* (2007) Effect of unitization on associative recognition in amnesia. *Hippocampus* 17, 192–200
46 Staresina, B.P. and Davachi, L. (2006) Differential encoding mechanisms for subsequent associative recognition and free recall. *J. Neurosci.* 26, 9162–9172
47 Grill-Spector, K. *et al.* (2006) Repetition and the brain: neural models of stimulus-specific effects. *Trends Cogn. Sci.* 10, 14–23
48 Pihlajamaki, M. *et al.* (2004) Visual presentation of novel objects and new spatial arrangements of objects differentially activates the medial temporal lobe subareas in humans. *Eur. J. Neurosci.* 19, 1939–1949
49 Suzuki, M. *et al.* (2005) Dissociable brain activations during the retrieval of different kinds of spatial context memory. *NeuroImage* 25, 993–1001
50 Epstein, R. and Kanwisher, N. (1998) A cortical representation of the local visual environment. *Nature* 392, 598–601
51 Davachi, L. (2006) Item, context and relational episodic encoding in humans. *Curr. Opin. Neurobiol.* 16, 693–700
52 Bar, M. and Aminoff, E. (2003) Cortical analysis of visual context. *Neuron* 38, 347–358
53 Norman, K.A. and O'Reilly, R.C. (2003) Modeling hippocampal and neocortical contributions to recognition memory: a complementary-learning-systems approach. *Psychol. Rev.* 110, 611–646
54 Mayes, A. *et al.* (2007) Associative memory and the medial temporal lobes. *Trends Cogn. Sci.* 11, 126–135
55 Gold, J.J. *et al.* (2006) Item memory, source memory, and the medial temporal lobe: Concordant findings from fMRI and memory-impaired patients. *Proc. Natl. Acad. Sci. U. S. A.* 103, 9351–9356
56 Sharot, T. *et al.* (2004) How emotion enhances the feeling of remembering. *Nat. Neurosci.* 7, 1376–1380
57 Vilberg, K.L. and Rugg, M.D. (2007) Dissociation of the neural correlates of recognition memory according to familiarity, recollection, and amount of recollected information. *Neuropsychologia* 45, 2216–2225
58 Eichenbaum, H. (2006) Remembering: Functional organization of the declarative memory system. *Curr. Biol.* 16, 643–645
59 Suzuki, W.A. and Amaral, D.G. (2004) Functional neuroanatomy of the medial temporal lobe memory system. *Cortex* 40, 220–222