Recall without Hippocampal Engagement

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Summary

The hippocampus is considered pivotal to recall, allowing retrieval of information not available in the immediate environment. In contrast, neocortex is thought to signal familiarity, and to contribute to recall only when called upon by the hippocampus. However, this view is not compatible with representational accounts of memory, which reject the mapping of cognitive processes onto brain regions. According to representational accounts, the hippocampus is not engaged by recall per se, rather it is engaged whenever hippocampal representations are required. To test whether hippocampus is engaged by recall when hippocampal representations are not required, we used functional imaging and a non-associative recall task, with items (objects, scenes) studied in isolation, and item-parts used as cues. As predicted by a representational account, hippocampal activation increased during recall of scenes – which are known to be processed by hippocampus – but not during recall of objects. Object recall instead engaged neocortical regions known to be involved in object-processing. Further supporting the representational account, effective connectivity analyses revealed that recall was associated with increased information flow out of lateral occipital cortex (object recall) and parahippocampal cortex (scene recall), suggesting that recall-related activation spread from neocortex to hippocampus, not the reverse.

Keywords: Recall, Representational-Hierarchical, Medial Temporal Lobe, fMRI

Introduction

Dominant theories of memory hold that the hippocampus (HC) is critical for recall. Anatomical findings and computational models suggest that hippocampal circuitry is well-suited to the process of retrieving information not currently present, based upon a partial cue (Marr 1971; Teyler and Discenna 1986; McClelland et al. 1995; Rolls 2013). Under this view, recall begins when a cue activates the trace of an associated memory in hippocampus, and is completed when sensory details of the memory are subsequently reinstated in neocortex (Marr 1971; Teyler and Discenna 1986; McClelland et al. 1995; Danker and Davachi 2013; Bosch et al. 2014). Numerous mechanisms have been proposed to explain the privileged role of the hippocampus in recall, including pattern completion (McClelland et al. 1995; Norman and O'Reilly 2003; Rolls 2013), neurogenesis (Aimone et al. 2011) or the construction of sparse, high-dimensional representations (Marr 1971). In contrast, neocortex is assumed to employ different mechanisms, contributing to memory retrieval either by signaling the familiarity of previously encountered items or by providing sensory details when called upon by hippocampus during recall (Miller et al. 1991; Brown and Aggleton 2001; Ranganath 2010; Danker and Davachi 2013; Staresina et al. 2013).

We test an alternative account of declarative memory retrieval, which predicts that recall should be possible without engaging the hippocampus (Cowell et al. 2010). The representational-hierarchical (R-H) view rejects the notion that functional distinctions between HC and the surrounding neocortex can be defined in terms of specialized mechanisms for different stages or components of memory retrieval. Instead, functional distinctions between are assumed to correspond to differences in the information that each region represents (Bussey and Saksida 2002; Cowell et al. 2010; Graham et al. 2010; Ranganath 2010; Shimamura 2010). Many studies have found distinctions in representational content within the medial-temporal lobe, showing that perirhinal cortex (PRC) is engaged for processing

individual objects, whereas the parahippocampal cortex (PHC) and HC are engaged for processing spatial scenes (Lee et al. 2005, 2008; Barense et al. 2012; Hannula et al. 2013; Mundy et al. 2013; Staresina et al. 2013). In addition, HC appears to play a special role in representing associative relations (Eichenbaum et al. 1994; Rudy and Sutherland 1995; Diana et al. 2007). Accordingly, the R-H account suggests that the only reason that HC is so often implicated in recall is that recall is typically performed for episodic memories, and episodes are high-dimensional conjunctions of items and events within their spatio-temporal context: episodes are represented in HC. The R-H account therefore makes the striking prediction that recall will depend on neocortical regions, without engaging HC, if the recalled memories do not require hippocampal representations (Cowell et al. 2010).

This prediction has not been tested because no retrieval task has decoupled the process of recall from the content of the retrieved memory. That is, neuroimaging studies of recall have almost invariably employed associative material, in which arbitrarily paired items (e.g., an item and a context) are presented at study, and one item is used to cue recall of the other at test (Hannula et al. 2013; Staresina et al. 2013; Tompary et al. 2016). But, such tasks require retrieving information across a learned association. Consequently, previous reports of hippocampal engagement in cued recall could be explained either by traditional accounts in which HC employs specialized mechanisms for recall, or by a representational account in which HC represents associative relations.

To test the prediction that representational content, and not mnemonic mechanism, determines the involvement of medial temporal lobe regions in recall, we took a standard recall paradigm and manipulated the stimulus material (Figure 1A). Our critical test was a non-associative object recall task, in which subjects studied single images of everyday objects and were cued at test with circular patches taken from studied and unstudied images. Importantly, recall responses were associated with explicit recall of the object and were verified by asking subjects to give the name of the object in a post-scan test. In contrast to studies using associative stimuli, which have found activation in HC to be modulated

by mnemonic process (e.g., recall vs. familiar) but not stimulus type (e.g., objects vs. scenes), we predicted that HC activation would be modulated by the type of stimulus content being retrieved. Specifically, we expected that our non-associative object recall task would not engage HC despite requiring the retrieval of a whole memory from a partial cue, but would instead engage object-processing regions in neocortex, including PRC. As a control condition we used an analogous recall task with scene images and scene-patches, with the expectation that HC would be engaged, because the components of scenes are conjoined by arbitrary associations. In addition, because dominant theories of memory suggest that recall-related reinstatement in neocortex depends upon hippocampal feedback, we conducted effective connectivity analyses to determine whether recall-related activation spreads from neocortex to HC, or the reverse.

Materials and Methods

Subjects

Twenty-two (7 male) native English speakers from the University of Massachusetts Amherst and Dartmouth College communities were recruited. Two subjects were excluded from the analyses, one due to excessive motion during scanning, and the other because behavioral responses were not recorded for the majority of their scanned trials. The remaining subjects were between 18 and 32 years of age (M=22.9, SD=3.9) with normal or corrected-to-normal vision. Subjects were paid for their participation and informed consent was obtained in accordance with the University of Massachusetts Amherst and the Dartmouth College Institutional Review Board.

Materials

Stimuli were 240 color images, 125 objects and 125 scenes, with 5 of each type used as practice stimuli (example stimuli shown in Figure 1A). Object stimuli were color illustrations (600 x 600 pixels) of natural (e.g., seahorse) and manmade (e.g., accordion) objects taken from a freely available database (Rossion and Pourtois 2004). Scene stimuli were color photographs (600 x 800 pixels) of indoor (e.g., child's bedroom) and outdoor (e.g., beach volleyball court) scenes, selected to depict non-overlapping contexts (Oliva and Torralba 2001; Quattoni and Torralba 2009; Xiao et al. 2010; Martin Cichy et al. 2014). Cues were circular patches, 150 pixels in diameter, selected from object and scene images with an effort to minimize semantic information. For example, the cue for a baby carriage (object) did not include a whole wheel and the cue for a laundromat (scene) did not include a whole washing machine.

Procedure and Design

Subjects completed a practice session comprising an abbreviated version of the experimental session. The experimental session consisted of a study phase outside the scanner, a scanned test phase followed by a standard localizer task (face, house, object, scrambled-object), and finally a post-scan memory test outside the scanner (Figure 1A).

Study phase: Subjects viewed 180 images (90 objects & 90 scenes) sampled from the full set, with the remaining 60 images serving as foils at test (images served as foils a roughly equal number of times). There were 20 blocks of nine images, blocked and intermixed by image type (object, scene), with image order randomized across blocks of each type and block order counterbalanced across subjects. Blocks began with a 3s introduction screen indicating "objects" or "scenes". Each trial began with a 200ms fixation, followed by the study image and a text prompt that appeared on screen for 3s. For objects subjects indicated "natural or manmade" and for scenes subjects indicated "indoor or outdoor". After viewing all images, subjects saw half for a second time with the cue patch removed and replaced by a white circle.

Test phase: Subjects viewed 240 cues from the 180 studied images and the 60 unstudied images. Trials were grouped into 20 blocks of 12 cues, blocked by cue type (object, scene), with cue order randomized. There were 10 runs, each with one object block and one scene block. Within each block there were three baseline trials (Stark and Squire 2001), nine trials with cues from studied images, and three trials with cues from unstudied images. On baseline trials participants saw a small fixation point and pressed a button each time it flickered (once or twice), on all other trials a fixation-cross was shown for 250-750ms (M=500 ms; duration varied randomly on each trial), followed by a cue and text prompt. The cue and prompt remained on screen for 3s and were replaced by a fixation-cross for 3, 5 or 7s followed by a 1s blank screen. Subjects responded 'recall', 'familiar' or 'new' - selecting recall only if they remembered the whole image that a cue came from – with instructions to respond quickly but accurately.

Functional localizer: Upon completion of the test phase participants completed two passive viewing runs of a functional localizer. Localizer runs consisted of sequentially presented grayscale images of houses, faces, objects and scrambled-objects overlaid with a grid. Each image was presented for 700 ms, with presentation blocked by category; block order was randomized for the first presentation of each category and this order was subsequently repeated three times for a total of 12 blocks (3 per category).

Post-test phase: Block structure and trial order were identical to the test phase (without baseline trials). For each cue subjects were prompted to name or describe the whole object or scene to which the cue belonged – typing a response. On each trial, a fixation-cross appeared for 200ms, followed by a cue and text prompt that remained until the participant responded. If participants did not know which whole image a cue belonged to (i.e., they failed to recall) they were asked to guess.

Structural and Functional Magnetic Resonance Imaging (MRI)

Imaging was performed using a 3T Philips Achieva Intera scanner with a 32-channel head coil, at

Dartmouth College, NH. Each session began with a high-resolution T1-weighted anatomical scan, using

an MP-RAGE sequence to acquire 160 1.0mm sagittal slices, covering a field of view (FOV) of 240 x 120 x

188 mm (TR, 9.9 ms; TE, 4.6 ms; flip-angle, 8°). Functional scans were acquired using a T2-weighted

echo-planar imaging (EPI) protocol (TR, 2000 ms; TE, 30 ms; flip angle, 90°; 3 x 3 x 3 mm voxels; matrix

size, 80 x 80; FOV, 240 x 105 x 240 mm). Thirty-five axial slices and 142 volumes were acquired per run,

for a total run duration of 284 s.

Conventional Functional Data Analyses

Functional data were preprocessed and analyzed using BrainVoyager and custom MATLAB code

written using the NeuroElf toolbox. T1 scans were registered to the functional scans and data were

interpolated to 1mm isotropic space and warped to Talairach space (Talairach & Tournoux, 1988).

Preprocessing included slice acquisition time correction, 3D motion correction, linear trend removal,

temporal high-pass filtering (3 cycles per run) and spatial smoothing using a 6 mm Gaussian kernel.

MTL ROIs were defined in each subject using anatomical landmarks (Pruessner et al. 2000,

2002). In addition, a lateral occipital cortex (LO) ROI was defined by conducting an RFX GLM on the

functional localizer data, with regressors for the face, house, object and scrambled-object blocks, and

placing a sphere (radius 5mm) on the peak group-level activation following an object minus scrambled-

object contrast.

To examine the effects associated with cued object and scene recall, all trials were binned by

stimulus type (object, scene) and trials corresponding to studied objects or scenes were additionally

binned by subject memory response (recall, familiar, new). Each trial was modeled by boxcar functions

beginning at trial onset and ending when the subject made a response. The boxcar functions were then

convolved with a canonical hemodynamic response function (HRF) and entered into a design matrix

along with nuisance regressors for motion and a scrub regressors for time points in which the frame displacement exceeded 0.9 (< 5% of time points).

Dynamic Causal Modeling Analyses

We used effective connectivity analyses to determine the direction in which information flow between different brain regions was modulated by recall. Assuming that hippocampus and neocortex are functionally connected during a visual memory task, most accounts of memory would predict that this functional connection is modulated during successful recall, relative to trials on which recall does not occur. Because traditional accounts of memory have proposed that neocortical engagement during recall is mediated via hippocampal feedback, such accounts also predict the *direction* in which the connection is modulated: from HC to neocortex, since HC is the site of the pattern completion process underlying recall, which subsequently triggers neocortical reinstatement. In contrast, representational accounts assume that recall-related pattern completion occurs in whichever brain region contains the representations required for part-to-whole completion of the retrieved memory: either LO or PRC for objects, and either PHC or HC for scenes. Thus, representational accounts predict, for object stimuli, that the 'hub' from which information flow increases during successful recall is a neocortical ROI, rather than HC (Figure 4).

Dynamic Causal Modeling (DCM) permits an investigation of how the functional connections between brain regions are modulated by a particular cognitive process, e.g. recall, and in which direction the connection is modulated. We used DCM to test the opposing predictions of traditional and representational accounts of memory. DCM was carried out in SPM12 using the same ROI definitions and preprocessing steps used in the conventional functional analyses. Separate GLMs were conducted on each subject's data, using the spm_fmri_concatenate.m function to concatenate across runs. Object and scene trials were coded by independent 2x2-factorial design matrices defined by study status

(studied, unstudied) x memory response (recall, no recall). The event duration was set at 2 seconds to allow for sufficient sensitivity (Staresina et al. 2013) and motion parameters were included as nuisance regressors. Timecourses were then extracted from the left and right hemisphere LO, parahippocampal gyrus (PHG; corresponding to PRC for objects and PHC for scenes) and HC ROIs, by taking the first eigenvariate (similar to the mean timecourse; see Friston et al. 2006) from the 15 voxels with the greatest recall minus no-recall contrast – computed as the difference between the recall/studied beta weights and no-recall/studied beta weights (Stephan et al. 2010; Staresina et al. 2013).

A space of 42 fully intrinsically connected DCMs was constructed separately for objects and scenes in the left and right hemisphere, giving a total of 168 models for each participant (see Supplemental Figure S2). The models were grouped into six families, with each family defined by combination of driving input location – LO alone, or both LO and PHG – and the source ROI for the recall-modulated connections – LO, PHG or HC. Within each family we considered all 7 possible combinations of modulation of the connections emanating from the source ROI.

Model fitting was based on maximizing the free energy (Friston et al. 2003) which provides a measure of model evidence that naturally accounts for complexity, with timecourses fit separately for each participant, hemisphere (left, right) and stimulus type (object, scene). We then used random-effects (RFX) Bayesian model selection (BMS) to compare the different model families (Penny et al. 2010). In addition, we conducted a fixed-effects (FFX) model comparison to obtain an estimate of the parameters for each DCM and averaged the parameter estimates across the winning family (parameter estimates are reported in Table S1).

Results

Behavioral Performance

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Behavioral data from the scanned test confirmed that image patches successfully cued memory, eliciting a recall response on 36.8% of studied object trials versus 10.4% of unstudied object trials (paired t-test, t_{19}=10.6, p<.001) and on 29.0% of studied scene trials versus 8.79% of unstudied scene trials (paired t-test, t_{19}=8.52, p<.001). A repeated measures ANOVA indicated that the effect of study (studied, unstudied) on memory response (recall, familiar, new) was similar for objects and scenes ($F_{1.54,}$ $_{29.3}$=2.81, p=.088, $\hat{\epsilon}$=.77). To verify that recall responses corresponded to accurate retrieval, subjects completed the recall task a second time outside the scanner, typing a description of the study image for each image-patch (Figure 1B). Conditioning post-test naming accuracy on memory at test confirmed that naming was more accurate following a recall response than a familiar response, for objects (paired t-test, t_{19}=17.8, p<.001) and scenes (paired t-test, t_{19}=9.78, p<.001).

Recall of Objects without Hippocampal Engagement

According to the R-H account, the contributions to memory retrieval of subregions within MTL should differ based on representational content (e.g., objects or scenes), not based on mnemonic mechanism (e.g., recall or familiarity). Although it is widely assumed that HC is required for successful recall, we predicted that our patch-cued object recall task would not engage HC, but that our control task – patch-cued scene recall – would engage HC. To estimate the contribution of HC and PRC to recall we analyzed only trials in which the cue came from a previously studied image, contrasting trials on which recall was successful (i.e., recall response) with trials on which it was unsuccessful (i.e., familiar).

We fitted a general linear model (GLM) to the preprocessed functional data (see Experimental Procedures) and extracted mean parameter estimates from anatomically defined PRC and HC in each subject. Parameter estimates were then submitted to a repeated-measures ANOVA with factors ROI (PRC, HC), image-type (object, scene) and memory response (recall, familiar). A significant 3-way interaction, F(1, 19)=11.65, p=.003, confirmed that the engagement of HC and PRC during recall versus

familiar trials differed by image type (Figure 2; also see Figure S1). To investigate the factors driving this 3-way interaction, we conducted separate repeated-measures ANOVAs within HC and PRC, with factors image-type (object, scene) and memory-response (recall, familiar). Consistent with the predictions of an R-H account, we found a significant image-type x memory-response interaction in HC, $F(1, 19)=6.61$, $p=.019$, with paired t-tests indicating significantly greater activation during recall- than familiar-responses for scenes, $t(19)=4.10$, $p=.001$, but – critically – not for objects, $t(19)=1.78$, $p=.091$. Moreover, confirming that the 3-way interaction was driven by the absence of HC activation during object recall, an equivalent repeated-measures ANOVA conducted in PRC failed to find evidence of an image-type x memory-response interaction, $F(1, 19)=0.058$, $p=.813$, with paired t-tests revealing significantly more activation during recall- than familiar- responses for both objects, $t(19)=4.89$, $p<.001$, and scenes, $t(19)=3.19$, $p=.005$.

The Hippocampus at Finer Resolution: No Evidence for Engagement by Object Recall

Next, to investigate functional activity in HC more closely, we divided each subject's HC ROI longitudinally (see Figure 3A) to create three subdivisions corresponding to anterior, middle, and posterior HC (Staresina et al. 2011; Hannula et al. 2013). In line with the unitary HC ROIs, a repeated-measures ANOVA with factors subdivision (anterior, middle, posterior), image-type (object, scene) and memory-response (recall, familiar), revealed only a significant image-type x memory-response interaction, $F(1, 19)=6.51$, $p=.020$, but no interaction with subdivision, $F(2, 38)=0.012$, $p=.988$ (Figure 3B). Moreover, paired t-tests conducted separately for objects and scenes indicated that in all three subdivisions of HC there was significantly greater activation during recall- than familiar-responses for scenes but not objects: anterior-HC (scenes: $t_{19}=3.22$, $p=.005$; objects: $t_{19}= 0.920$, $p=.369$), middle-HC (scenes: $t_{19}=4.36$, $p<.001$; objects: $t_{19}= 1.96$, $p=.065$), and posterior-HC (scenes: $t_{19}=3.85$, $p=.001$; objects: $t_{19}= 1.82$, $p=.085$).

The Parahippocampal Gyrus: An Anterior-Posterior Gradient of Engagement by Object and Scene Recall

Prior studies have reported that subregions within the parahippocampal gyrus (PHG) – a

neocortical region running parallel to the longitudinal axis of HC and encompassing PRC (equivalent to

anterior-PHG) and PHC (equivalent to posterior-PHG) – respond differentially to object and scene recall

(Staresina et al. 2011, 2013; Hannula et al. 2013). To look for evidence for this subdivision in our data we

defined PHG in each subject using anatomical landmarks, creating three subdivisions along the

longitudinal axis, as with HC (Figure 3C). In line with previous studies we expected to find relatively more

activation associated with object recall than scene recall in anterior-PHG (corresponding to PRC) than in

posterior-PHG (corresponding to PHC). A repeated-measures ANOVA with factors subdivision (anterior,

middle, posterior), image-type (object, scene) and memory-response (recall, familiar), revealed a

significant 3-way interaction, $F(2, 38)=10.38$, $p<.001$ (Figure 3D). Separate ANOVAs conducted within

each PHG subdivision indicated that there was a significant image-type x memory-response interaction

only in posterior-PHG (PHC), $F(1, 19)=21.4$, $p<.001$, in which – confirming our expectations – significantly

more activation was associated with scene than object recall. This pattern reveals an asymmetry

between PRC and PHC: more activation was associated with scene than object recall in PHC, but

equivalent activation was observed during object and scene recall in PRC. We note that similar

asymmetries have been reported previously, perhaps because scenes (and scene parts) often contain

objects (Hannula et al. 2013; Staresina et al. 2013). Finally, to test whether each subdivision of PHG was

significantly engaged by recall we conducted paired t-tests separately for objects and scenes, which

indicated that in all three subdivisions, for both objects and scenes, there was significantly greater

activation associated with recall- than familiar-responses: anterior-PHC (objects: $t_{19}= 3.56$, $p=.002$;

scenes: $t_{19}=2.43$, $p=.025$), middle-PHC (objects: $t_{19}= 5.44$, $p<.001$; scenes: $t_{19}=5.91$, $p<.001$), and

posterior-HC (objects: $t_{19}= 5.28$, $p<.001$; scenes: $t_{19}=11.4$, $p<.001$).

Feedforward Connectivity from Neocortex to HC Increases during Object and Scene Recall

It is generally assumed that recall-related activation in neocortex is mediated by HC (e.g.,

Staresina et al. 2013; Danker et al. 2016). Although the conventional functional analyses revealed that

retrieved stimulus content, not mnemonic process, accounts for activation in MTL in our non-associative

recall task, it is possible that HC is necessary to mediate the retrieval of whole object representations

(e.g., in PRC) from object patches – Note that the conventional analysis revealed above baseline

activation during recall in posterior-HC (though it was not significantly greater than activation during

familiar responses; see Figure 3B).

To investigate whether recall-related activity in neocortex might be mediated by HC we used

dynamic causal modeling (DCM) to look for changes in effective connectivity associated with recall. Our

approach was to compare model families, with each family comprising three fully connected regions:

HC, PHG (PRC for objects and PHC for scenes) and lateral occipital (LO) cortex. Families differed in the

connections modulated by recall – connections out of LO, connections out of PHG or connections out of

HC (see Figure 4A & Figure S2) – allowing us to ask which region drives information flow during recall.

Families had driving inputs (studied item trials) either into LO only, or into both LO and PHG. The LO ROI

was chosen as common input region because it is known to be involved in the perception of both

objects and scenes, perhaps because it contributes to the recognition of objects whether presented

alone or embedded within scenes (MacEvoy and Epstein 2011). One sample t-tests performed on the

univariate measure of recall activation (i.e., the difference between GLM estimates for recall versus

familiar trials, as described above) confirmed that LO was involved in both object (t_{19}=5.03, p<.001) and

scene (t_{19}=5.08, p<.001) recall, with no difference in recall activation between image type in LO

(t_{19}=0.129, p<.899).

Random effects (RFX) Bayesian model selection (BMS) was conducted separately for the left and right hemisphere and the results averaged (Figure 4B). For objects, BMS strongly favored models with a driving input into LO and recall modulating the connectivity out of and within LO, exceedance probability (EP)=0.99. For scenes, BMS did not overwhelmingly favor any family of model. The winning family had driving input into both LO and PHC, with recall modulating the information flow out of and within PHC, EP=0.66. Importantly, even for scenes we found little evidence for families assuming feedback from HC to neocortex during recall (combined EP for families with recall modulating connectivity out of HC was <0.001). Looking at individual model EPs (rather than family EPs) confirmed that the most likely model for scenes had input to both LO and PHC, with recall modulating information flow out of and within PHC (EP=0.70; supporting PPI connectivity analyses and post-hoc DCM analyses are included in the Supplemental Information). An additional fixed effects (FFX) analysis was conducted and used along with Bayesian model averaging to recover estimated parameter values across the winning model families (see Table S1).

Discussion

We used fMRI and a non-associative recall task to ask whether the involvement of the HC in recall is mandatory. As predicted by the R-H view of memory, when participants studied isolated images and were cued to recall them with part of the image, HC was engaged during recall of everyday scene images but not during recall of individual objects. In contrast, PRC – known for its role in object processing – was engaged during recall of both objects and scenes. In addition, changes in effective connectivity during successful recall were consistent with the R-H account: Bayesian model comparison supported models in which information flow out of LO increased during object recall and information flow out of PHC increased during scene recall. Contrary to the predictions of traditional accounts of

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memory retrieval, we found almost no evidence to support models in which hippocampus drove increased activation in neocortical regions during recall. Together, these findings challenge dominant theories of memory, demonstrating that HC does not play a critical role in recall per se, but instead is engaged to the extent that its representations are required to retrieve the full memory given a partial cue.

Prior work has reported domain-specific contributions of neocortical MTL to recall (Hannula et al. 2013; Staresina et al. 2013; Vilberg and Davachi 2013), with PRC preferentially engaged by object recall and PHC by recall of scenes. Similarly, we found an interaction between neocortical ROIs within MTL (PHC, PRC) and stimulus category (object, scene), underpinned by greater recall activation for scenes than objects in PHC, but equivalent recall activation for objects and scenes in PRC. However, in contrast to claims that HC plays a domain-general role in recall, which has been evidenced by reports that HC is engaged by recall regardless of the stimulus material (Danker and Davachi 2013; Hannula et al. 2013; Staresina et al. 2013; Tompary et al. 2016), we found that HC contributed to scene but not object recall when the task does not involve paired associates. Moreover, our DCM analyses suggested that, even during scene recall, HC did not mediate neocortical activation. Critically, both the conventional analysis and the DCM are consistent with an account in which recall is supported by the brain region containing the type of representation necessitated by the task.

The literature on episodic memory contains many definitions of a process akin to recall, alternatively termed recollection (as opposed to familiarity; Brown and Aggleton, 2001; Diana et al., 2007), intentional retrieval (as opposed to automatic; Jacoby, 1991), or remembering (as opposed to knowing; Tulving, 1985). All of these definitions invoke either conscious awareness or intention, and a subset of them also stipulate that the process retrieves a specific type of information, such as context (Mandler 1980) or autobiographical, episodic details (Tulving 1985). While definitions of recall or recollection that invoke retrieval of context or personal information undoubtedly apply to recall in many

everyday situations, their utility for investigating brain function is limited by the fact that they confound

a mnemonic mechanism (recall) with the content of the memory (e.g., context). In order to discover

whether mnemonic mechanism or mnemonic content determines engagement of various brain regions,

it is necessary to deconfound the two. Accordingly, in this study we defined recall as an explicit process

that retrieves specific details not immediately present and confers a feeling of certainty about the past

occurrence of an item or event, without stipulating the nature of the retrieved details. In our object

recall task, the details that had to be retrieved were a sufficient number of object features that the item

could be identified and prior study of it remembered. Although item-based recall is rare in everyday life,

it provides a critical test of the two alternative accounts of how the brain supports cued retrieval. Using

this test, we demonstrated – contrary to widely-held beliefs – that the contribution of different MTL

regions to recall is better explained by mnemonic content than by mnemonic mechanism.

One characterization of the differential contributions of MTL structures to memory retrieval is

that the PRC represents intra-item associations by performing 'unitization' (Mayes et al. 2004; Quamme

et al. 2007). The present results are compatible with this hypothesis: perirhinal unitization of objects at

the time of study might facilitate later part-cued object recall, engaging PRC but not HC at test. Critically,

however, our task involved recall and not recognition. Only part of an image was presented at test,

rather than the whole item. Therefore any unitized, item-level representation could not be activated

without first retrieving its missing parts. Critically, the contrast defining our measure of recall activation

was trials on which participants retrieved the whole item versus trials on which the part seemed familiar

without eliciting retrieval. Post-scan behavioral testing verified that recall but not familiar responses

were associated with above baseline ability to name the item from the part (Figure 1B). Thus, recall

responses cannot be explained by familiarity. Consequently, while perirhinal unitization may play a role

in encoding, the contribution of PRC to the retrieval of object memories in our task is analogous to the

role of HC in the retrieval of episodic memories involving arbitrary associations—namely, a pattern completion process that retrieves information not present in the cue.

The notion that experience can induce neocortical regions to fill in information via pattern completion has parallels with the perceptual priming literature. Debate continues as to whether the processes and representations underlying visual priming are distinct from, or shared with, those underlying recognition memory (Tulving et al. 1991; Schacter 1992; Berry et al. 2008). A classic demonstration of priming involves the initial inability to comprehend degraded images such as Mooney figures (Mooney 1957) or the famous hidden Dalmatian dog (Gregory 1970), and the ease with which the image contents can be identified after exposure to a coherent version of the image. In such cases, post-priming identification involves cueing the observer with a degraded version of the full image to induce reinstatement of essential information such as global form, and there is evidence that the pattern completion underlying this process occurs in visual cortex (Gorlin et al. 2012). Although our object recall task is directly modeled on standard tests of episodic retrieval (e.g., cued recall of paired associates) it also parallels the part-to-whole completion process required to identify Mooney figures. We suggest that the principal difference between these tasks — Mooney figure priming, object recall and standard recall — is the complexity and specificity of the stimulus representation required for retrieval: representations in visual cortex support category-level identification based upon Mooney figure cues (Gorlin et al. 2012); representations in PRC underlie retrieval of specific objects in our part-cued object recall task; and hippocampal representations are critical for typical recall tasks in which participants must retrieve information arbitrarily associated with a test cue. Thus, neuroimaging data from both priming and recall tasks may be accounted for by a common pattern completion process acting upon representations at different levels in the ventral visual-perirhinal-hippocampal hierarchy.

Finally, we consider whether the objects in our task were recalled from their part-cues using semantic object knowledge or episodic memory. In line with previous fMRI investigations of episodic

memory (e.g., Hannula et al. 2013; Staresina et al. 2013; Danker et al. 2016), we adopted a content-neutral definition of episodic recollection, as the retrieval of stimulus specific details not immediately present and certainty about past occurrence, without the requirement that the details be contextual or personal. Our task was tailored to this definition by instructing participants to give a 'recall' response only when the part cue elicited explicit recollection of the studied item and a high degree of certainty that the item appeared in the study phase. Moreover, post-scan testing verified that participants identified part cues (e.g., "name or describe the object") at a much higher rate if they came from objects that were studied (36.8%, where naming rate is collapsed across participant response) than from unstudied objects (10.4%, collapsed across response). This indicates a significant contribution from the episodic memory trace acquired during at study to the ability to complete an object from its part. Naming rates were higher still for studied objects that were explicitly recalled in the scanner (75%), but we could not compare these rates to items that were unstudied-but-'recalled' because such events occurred too infrequently; both the higher naming rate for recalled items and the infrequency of recall responses to unstudied items suggest that participants were following instructions regarding 'recall' responses accurately. Thus, the knowledge used to retrieve objects from part-cues was at least in part episodic.

Nevertheless, just as semantic knowledge contributes to recall in episodic memory tasks employing more complex, associative information (Bartlett 1932; Bransford and Johnson 1972; Brewer and Treyens 1981) it is highly probably that semantic knowledge contributed in our task. But perhaps the distinction between episodic and semantic retrieval has been paid too much heed. Above, we argued for the existence of a continuous hierarchy from early visual regions through perirhinal cortex into hippocampus, across which a common pattern completion process is employed to retrieve whole representations based upon partial cues. The levels of the hierarchy differ not in terms of process (familiarity versus recollection) but in terms of representational content, with early regions contributing

only perceptual information, intermediate regions both perceptual and semantic knowledge, and later (medial temporal lobe) stations conferring perceptual, semantic and episodic content. A task requiring pattern completion – be it low-level priming, object recall, or episodic recall – will engage regions along this pathway only as far as the representational demands of the task require (Tyler et al. 2004).The contribution of perceptual, semantic or episodic information to retrieval will be determined by representational requirements in the same way.

In sum, the findings reported here suggest that the neural mechanisms underpinning recall do not occur exclusively and mandatorily in HC, and that representational content rather than mnemonic mechanism underlies the functional division of labor within MTL during cued retrieval of declarative memories.

Author Contributions

Conceptualization, D.A.R. and R.A.C.; Methodology, D.A.R. and R.A.C.; Investigation, D.A.R., P.S. and R.A.C; Data Curation, D.A.R. and D.M.W. Writing – Original Draft, D.A.R. and R.A.C.; Writing – Review & Editing, D.A.R., P.S., D.M.W. and R.A.C; Funding Acquisition and Supervision, R.A.C.

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Figure Legends

Figure 1.

Schematic of task and behavioral results. **(A)** Subjects studied 90 objects and 90 scenes, indicating

natural/manmade (objects) or indoor/outdoor (scenes). At test, subjects saw 120 object patches and

120 scene patches (90 seen, 30 unseen) and responded recall, familiar or new, with recall indicating that

they specifically remembered the whole item that a patch came from. Finally, subjects saw all 240 item

patches a second time and were asked to type the name of the item that the patch came from. If they

did not recall seeing the item they were encouraged to guess. **(B)** Proportion of items correctly named at

post-test, conditioned on subject response at test. Responses to seen and unseen items are shown

separately and the proportion of unseen items correctly named has been collapsed across test response.

Error bars show 95% CIs around the means.

Figure 2.

Functional activity during recall and familiar responses to objects and scenes. Parameter estimates

shown for perirhinal cortex (PRC; left) and hippocampus (HC; right). Significant (p<.05) interactions ($\otimes$)

and differences ($*$) are indicated. Error bars show 95% CIs around the means.

Figure 3.

Schematic of 3-part hippocampus (HC) and parahippocampal gyrus (PHG) ROIs and corresponding

functional activity from each region. **(A)** Schematic of the 3-part hippocampus ROI. **(B)** Functional

activity during recall and familiar responses to objects and scenes in anterior (left), middle (center) and

posterior (right) hippocampus. **(C)** Schematic of the 3-part parahippocampal gyrus ROI. **(D)** Functional

activity during recall and familiar responses to objects and scenes in anterior (left), middle (center) and
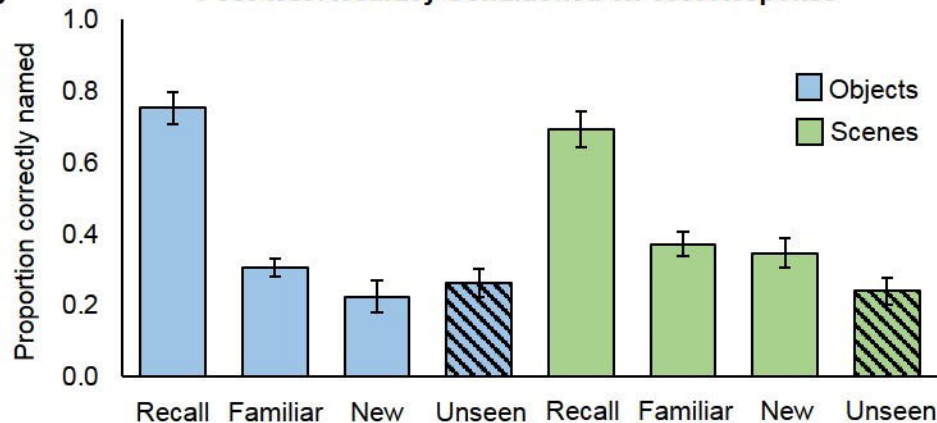
posterior (right) parahippocampal gyrus. Note, anterior and posterior parahippocampal gyrus roughly

correspond to PRC and PHC respectively. Significant (p<.05) interactions ($\otimes$) and differences ($*$) are

indicated. Error bars show 95% CIs around the means.

Figure 4.

Information flow between ROIs during the cued recall of objects and scenes **(A)** Predictions of traditional

and R-H accounts of memory and simplified schematic of the model family space (see Figure S2 for full

model space). All models had full intrinsic connectivity (grey dashed arrows). Model families were

defined by (1) the ROI from which outward connections were permitted to be modulated by recall (bold

circles) and (2) the location of the driving input (not shown here). **(B)** Results of the Bayesian model

selection for objects (left, blue) and scenes (right, green). Results are shown for the winning input family

(input into LO for objects, input into LO & PHC for scenes). For objects BMS strongly favored models in

which recall modulated information flow out of and within LO (family exceedance probability = 0.99).

For scenes, BMS favored models in which recall modulated information flow out of and within PHC

(family exceedance probability = 0.66). Parameter estimates for modulation by recall are reported in
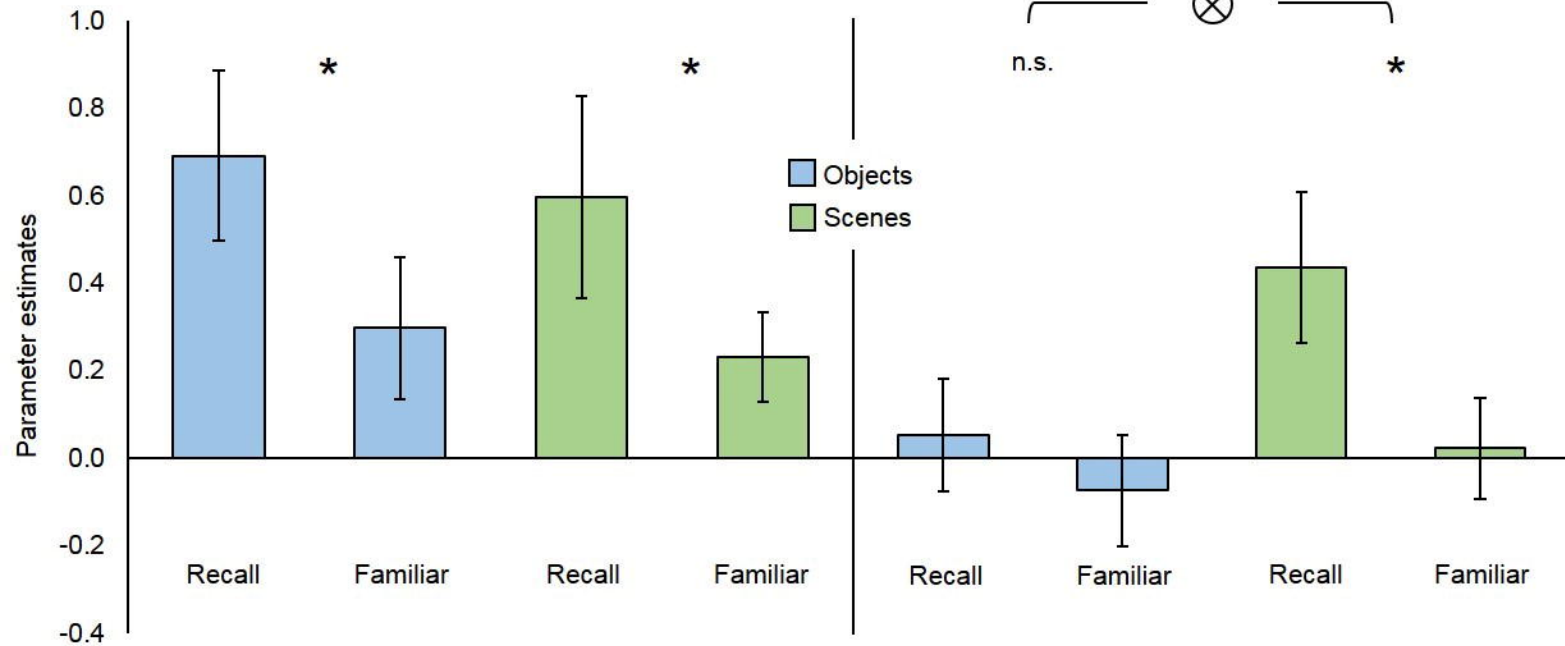
Table S1.

A Study | Test (scanned) | Post-test

Natural Manmade
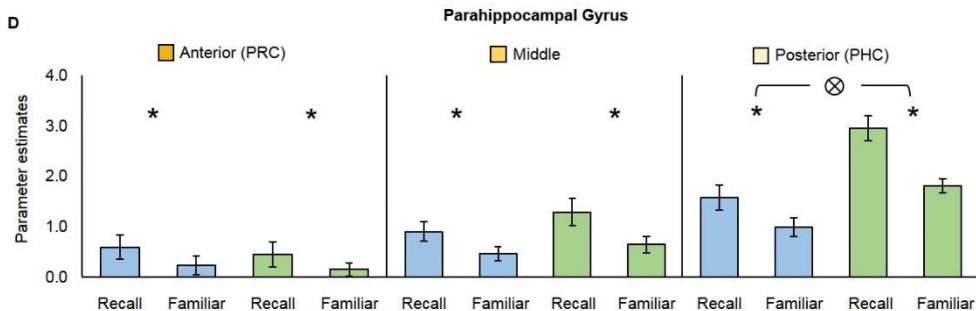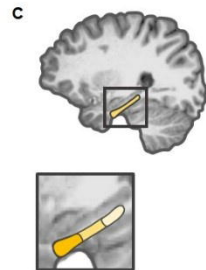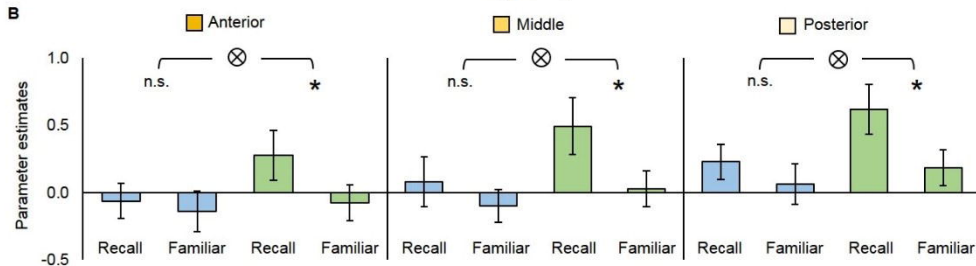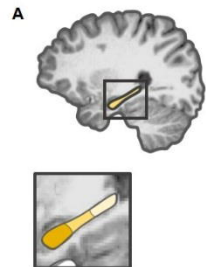
Indoor Outdoor

Recall Familiar New

Recall Familiar New
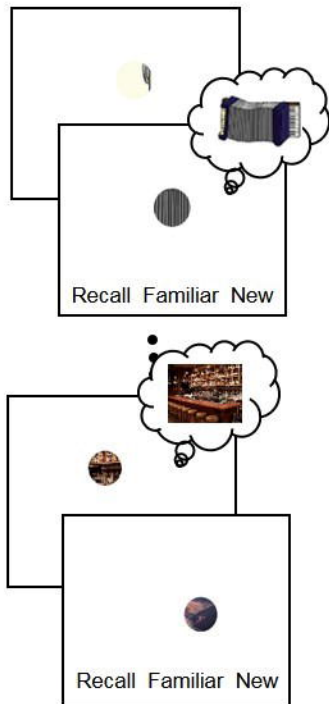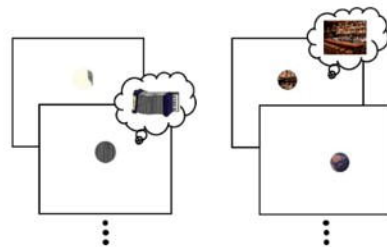
e.g. "name the object that this part came from. If you don't know then just guess"

B Post-test Accuracy Conditioned on Test Response

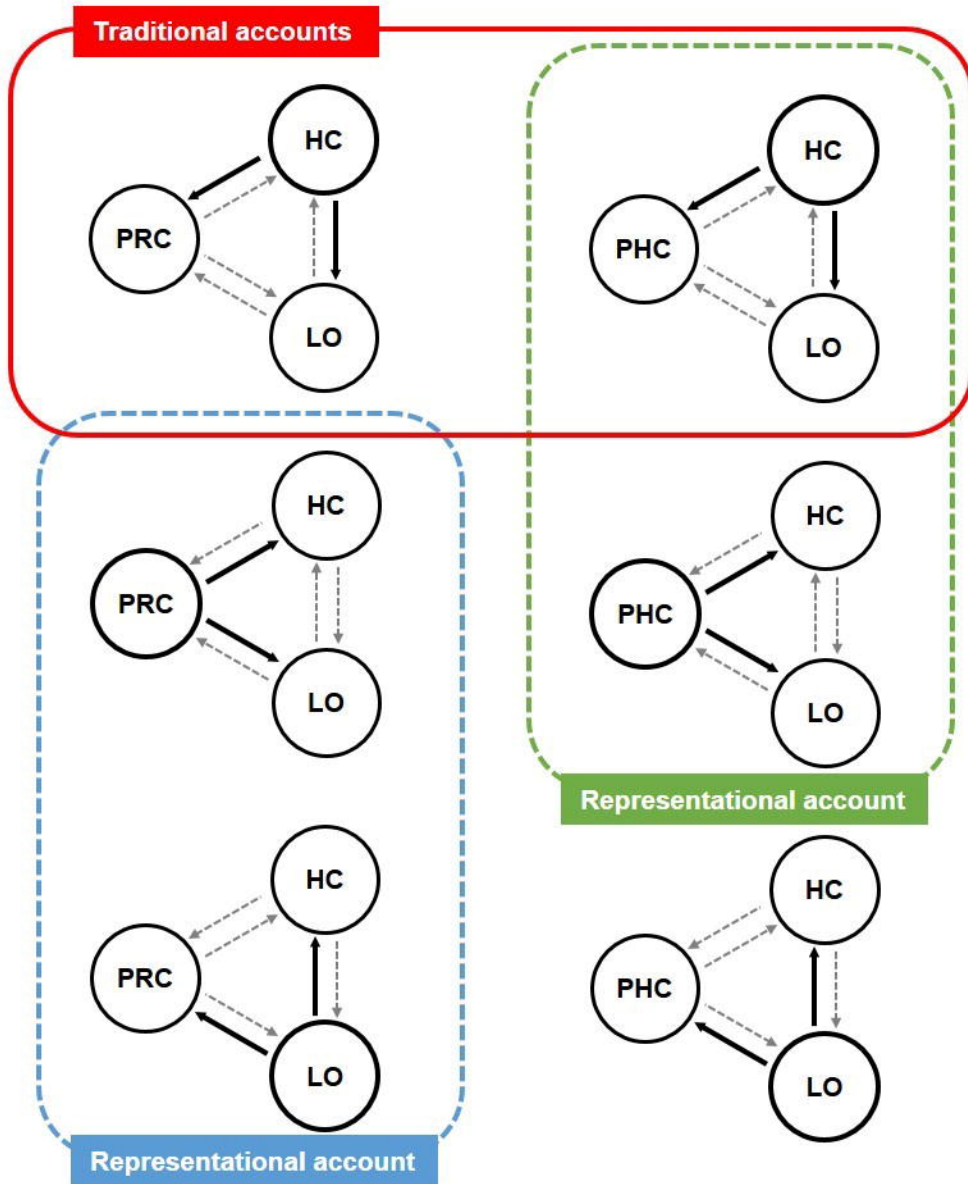Proportion correctly named

Objects
Scenes

Recall Familiar New Unseen Recall Familiar New Unseen

Hippocampus

A

Traditional accounts

Representational account

Representational account

B Bayesian model selection

HC

PHG

LO