



Adaptation to cognitive context and item information in the medial temporal lobes

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ARTICLE INFO

Available online 27 July 2012

Keywords:

Parahippocampal cortex
Perirhinal cortex
Adaptation
Context
Memory

ABSTRACT

The medial temporal lobes (MTL) play an essential role in episodic memory, and accumulating evidence indicates that two MTL subregions—the perirhinal (PRc) and parahippocampal (PHc) cortices—might have different functions. According to the binding of item and context theory (Diana, Yonelinas, & Ranganath, 2007; Eichenbaum, Yonelinas, & Ranganath, 2007), PRc is involved in processing item information, the target of memory encoding, whereas PHc is involved in processing context information, peripheral information that identifies the circumstances of the episode. Here, we used functional magnetic resonance imaging (fMRI) adaptation to test the roles of different MTL subregions in the processing of item and context information. Participants were scanned while viewing a series of objects. Each object was presented with a unique semantic encoding question that elicited a salient cognitive context. The object picture, the encoding question, both, or neither were immediately repeated. We found that PRc activity was sensitive to repetition of the object but not the encoding question whereas PHc activity was sensitive to repetition of the encoding question but not the object. These data are consistent with the idea that the PRc and PHc are differentially involved in the representation of item and context information and additionally suggest that the role of the PHc extends to nonspatial, cognitive context information.

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1. Introduction

It is well established that the hippocampus is critical for episodic memory, but substantial evidence suggests that cortical regions in the medial temporal lobes (MTL), including the perirhinal cortex (PRc) and parahippocampal cortex (PHc), also play a critical role.¹ Unfortunately, the specific roles of these regions in episodic memory are not well understood, although several plausible theories have been proposed.

One view that has emerged from both functional magnetic resonance imaging (fMRI) and lesion studies is that the two areas show a category-specific division of labor, with PHc specialized for processing of scene information and PRc specialized for processing of faces and other objects (e.g. Barense, Gaffan, & Graham, 2007; Graham, Barense, & Lee, 2010; Taylor, Henson, & Graham, 2007).

Converging with this view, fMRI studies show that an area within the PHc, called the “parahippocampal place area” (Epstein, Harris, Stanley, & Kanwisher, 1999; Epstein & Kanwisher, 1998), is more active during processing of visual scenes compared to objects. Furthermore lesion studies suggest that damage to the right PHc is associated with deficits in spatial memory (Bohbot et al., 1998), whereas damage to the PRc and anterior hippocampus is associated with deficits in object recognition and perception (Barense et al., 2007; Lee & Rudebeck, 2010). Although the category-specificity view has a great deal of empirical support, it does not provide an adequate explanation for recruitment of PHc and PRc in tasks that do not involve visual object or scene stimuli. For example, these areas show activation that is sensitive to successful encoding and retrieval in verbal memory experiments (Cansino, Maquet, Dolan, & Rugg, 2002; Davachi, Mitchell, & Wagner, 2003; Eldridge, Knowlton, Furmanski, Bookheimer, & Engel, 2000; Kahn, Davachi, & Wagner, 2004; Ranganath et al., 2004; Woodruff, Johnson, Uncapher, & Rugg, 2005; Yonelinas, Otten, Shaw, & Rugg, 2005).

A second plausible interpretation of the function of PHc is that it processes a fused representation of the object of study and its background information (Eichenbaum & Bunsey, 1995; Pascalis, Hunkin, Bachevalier, & Mayes, 2009). This combined representation can be likened to a “snapshot” of the object in its

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¹ For the purposes of this experiment, we remain agnostic with respect to the existence of a clear border between PHc and PRc as opposed to a more gradual anterior–posterior gradient in function. The imaging methods used here cannot conclusively distinguish between these two possibilities, but notably, the implications of our results remain similar regardless of this issue.

surroundings. This role is in contrast to the hippocampus, which is thought to process a flexible, relational binding between object and background information such that the two types of information remain separate. Pascalis et al. (2009) speculated, based on their results, that PRc might support recognition of an object provided the background information was identical to that seen at study. This snapshot hypothesis predicts that separating the background information from the object of study renders the background information unrecognizable to PHc and separating the object of study from its background information renders the object of study unrecognizable to PRc. The hippocampus might then be unique in its ability to retrieve the original object information or background information via pattern completion. Therefore the representation of information in PHc and PRc is inflexible as compared to the hippocampal representation (Pascalis et al., 2009, p. 2108).

Another theory of MTL organization, the Binding of Item and Context theory (BIC) (Diana, Yonelinas, & Ranganath, 2007; Eichenbaum, Yonelinas, & Ranganath, 2007), provides an interpretation of the roles of PHc and PRc that is consistent with some aspects of the “snapshot” and category-specificity hypotheses, but proposes that PRc and PHc process different types of information at a more abstract level. According to the BIC theory, the PRc processes item information, PHc processes context information, and the hippocampus binds item and context information.

The BIC theory is partially compatible with the category-specificity view described above in that stimulus category can be seen as a powerful way to manipulate the processing of context (a spatial layout/scene) or item (a face/object) information. However, unlike other theories, BIC theory additionally proposes a role for the PHc in processing nonspatial context information, including aspects of the time, situation, and one’s cognitive state during an event. For example, when remembering the initial introduction to a new acquaintance, one might retrieve that it occurred: last week, in your office, via your boss, interrupting your preparations to leave for lunch. The internal cognitive state in this example includes mood (relaxed), train of thought (“Do I want Thai food today?”), opinions about the event (“This is an inconvenient time to meet a new colleague.”), and future planning (“I should add this person to the office e-mail list.”). Each of these items may become part of the encoded context that can be retrieved when the event is remembered. We will call these internal thoughts “cognitive context”. The term cognitive context is meant to distinguish internally produced contextual details from information contained in the external environment, such as the scene/room in which the event takes place, temporal information, or speech and actions by others present during the event.

BIC theory is also partially compatible with the “snapshot” theory of PHc function in that context/background information, or details outside the focus of attention, are thought to be processed in PHc while item/object information is thought to be processed in PRc. The primary difference between these two views is in the flexibility of the representations in these regions. The snapshot view suggests an “inflexible” or “fused” representation of associations between items and contexts in PHc such that recombinations of studied items and contexts are seen as novel events and an item presented without its context is seen as a novel event. At least some versions of this view (Pascalis et al., 2009) propose a similarly inflexible representation existing in PRc. BIC theory does not directly suggest the form of PRc and PHc representations but does predict that PHc will respond to a studied context as familiar, even without the associated item, and that PRc will respond to a studied item as familiar, even without the associated context.

Some support for the BIC theory comes from fMRI studies that have investigated distinctions between recollection and

familiarity-based recognition memory as defined by dual-process theory (see Aggleton & Brown, 2006; Yonelinas, 2002 for reviews). For example, several fMRI studies (Dobbin, Rice, Wagner, & Schacter, 2003; Kensinger & Schacter, 2006; Ranganath et al., 2004) have shown that PHc activation is associated with successful encoding or retrieval of the semantic processing task performed during encoding of specific words (e.g., pleasantness vs. concreteness judgments). In contrast, PRc activation has been associated with familiarity for items, irrespective of whether one can retrieve associated context information (Davachi et al., 2003; Kensinger & Schacter, 2006; Montaldi, Spencer, Roberts, & Mayes, 2006; Ranganath et al., 2004). The experience of recollection is defined by successful encoding and retrieval of context information that was previously associated with an item. According to the BIC theory, this encoding and retrieval of context information should be associated with activation in the hippocampus and PHc. In contrast, the experience of familiarity is defined by the strength of an item representation alone. The BIC theory proposes that these judgments based on the encoding and retrieval of item information alone should be associated with modulations of PRc activation. BIC theory therefore builds upon the work of dual-process theories of recognition memory (Aggleton & Brown, 2006; Yonelinas, 2002), but additionally can make predictions even in studies in which recollection and familiarity are not directly assessed.

As described above, many studies have characterized the functions of MTL subregions by examining differential brain activation related to the successful encoding/retrieval of item vs. context information. A complementary approach to characterizing the nature of information processed in PRc and PHc is fMRI adaptation. Adaptation paradigms are based on findings demonstrating that cortical pyramidal cells show diminishing responses when they are repeatedly stimulated in a short interval (Maffei, Fiorentini, & Bisti, 1973; Miller, Gochin, & Gross, 1991; Movshon & Lennie, 1979). In an adaptation paradigm, if a neural population is responsive to a particular feature (e.g., an item or context), repetition of that feature will cause a reduction in the firing rate of those neurons, these reduction in firing rate might manifest in fMRI data as a reduction in blood-oxygenation-level-dependent (BOLD) signal. Thus, in an fMRI adaptation study, reduction in BOLD signal following immediate repetition of a particular stimulus feature is taken as evidence that neural representations in the brain region code for the repeated information (Grill-Spector, Henson, & Martin, 2006; Grill-Spector et al., 1999; Grill-Spector & Malach, 2001; Kumaran & Maguire, 2007, 2009).

Consistent with both the category-specificity view and the BIC model, previous fMRI adaptation studies have consistently found that PRc is sensitive to the novelty of objects, whereas PHc is sensitive to the novelty of spatial relationships (Aminoff, Gronau, & Bar, 2007; Kohler, Danckert, Gati, & Menon, 2005; Pihlajamaki et al., 2004), object relationships (Aminoff et al., 2007; Kohler et al., 2005), and scenes (Goh et al., 2004; Howard, Kumaran, Ólafsdóttir, & Spiers, 2011). Additionally, there is some evidence that PHc sensitivity might also vary such that posterior PHc is sensitive to novel spatial information while anterior PHc is sensitive to novel object relationships and/or novel objects (Aminoff et al., 2007; Kohler et al., 2005). However, the studies described above examined adaptation of visual stimulus properties (object vs. spatial or scene context), so it is unclear whether the PRc and PHc play differential roles in the representation of *cognitive* context and item information. A single prior study examined MTL adaptation to repeated verbal objects and contexts, finding both PRc and PHc adaptation, but did not assess adaptation based on novel verbal contexts in addition to novel verbal items (O’Kane, Inslar, & Wagner, 2005).

Accordingly, in the current study, we used an fMRI adaptation paradigm to assess adaptation of both PHc and PRc to repeated objects or the cognitive context of those objects. We presented

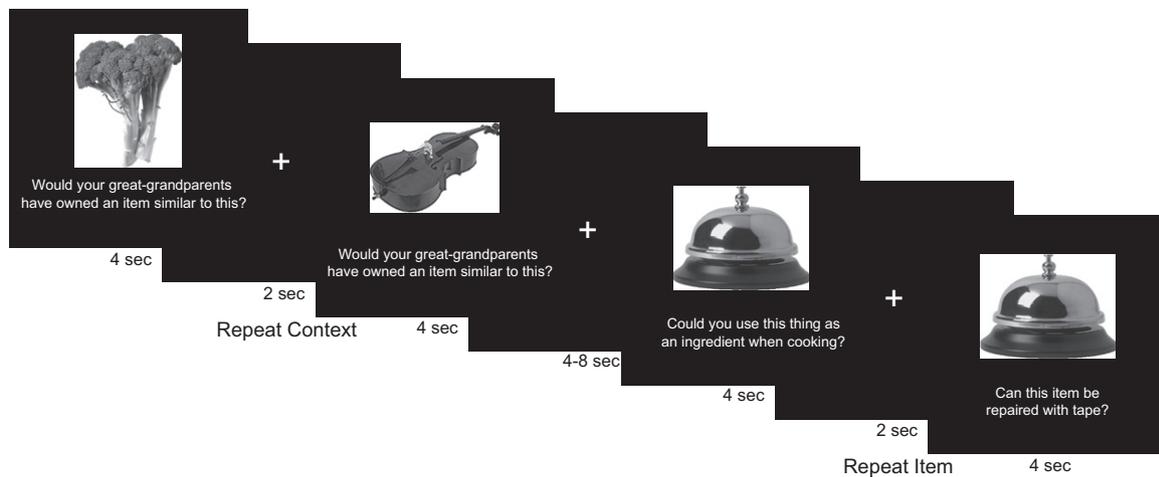


Fig. 1. Sample trial layout for RC and RI conditions. RC indicates repeated presentation of a semantic encoding question, as seen in the frames on the left. RI indicates repeated presentation of an object picture, as seen in the frames on the right. (Actual object stimuli were presented in color.)

pictures of single, concrete objects that participants were explicitly instructed to remember for a later memory test. Each picture was presented with a unique semantic encoding question (see Fig. 1) that required the participant to think about the object in an unusual way. These semantic encoding questions formed the cognitive context for each item. We then independently varied repetition of the item picture or the cognitive context as compared to trials on which no information was repeated or all information was repeated. We predicted that repetition of item information would lead to reduced activation in PRC, whereas repetition of context information would lead to reduced activation in PHc. Finally, we predicted that the hippocampus, which we propose supports encoding of item–context bindings, would show the largest amount of adaptation when both item and context information was immediately repeated.

2. Materials and methods

Participants were 15 right-handed adults from the University of California, Davis community ranging in age from 18 to 24, with a mean age of 21. Seven participants were female. One participant was excluded from the analysis due to excessive movement during the fMRI scans (3 standard deviations above the mean movement parameters in both translational and rotational movement), thus 14 participants were included in the final data set. Stimuli for the experiment were 364 pictures of individual objects and 156 experimenter-created yes/no questions that require deep processing of the conceptual features of each item.

MRI images were recorded during encoding of item–question pairings. Participants viewed 104 trials over four runs with 26 trials in each of four conditions. Each trial consisted of a 4-s exposure to a novel encoding question presented above a novel object picture. Sample object and question stimuli are presented in Fig. 1. Participants were asked to respond yes or no to the question while the stimuli were on the screen. Following a 2-s fixation screen, a second set of stimuli were presented for 4 s. Depending on the condition, this second presentation included repetition of one or more stimulus attributes from the previous stimulus presentation. In the Repeat Item (RI) condition, the repetition portion of the trial used the same object picture as the beginning of the trial but this object picture was presented with an entirely novel encoding question. In the Repeat Context (RC) condition, the repetition portion of the trial used the same encoding question as the beginning of the trial but this question

Table 1

Peak voxel locations and peak cluster sizes for each MTL anatomical ROI.

	x	y	z	# Voxels
<i>Left</i>				
Hippocampus	−21	−9	−26	4
Parahippocampal cortex	−21	−30	−15	9
Perirhinal cortex	−30	−3	−31	24
<i>Right</i>				
Hippocampus	29	−4	−27	8
Parahippocampal cortex	24	−27	−15	5
Perirhinal cortex	36	−6	−45	6

was presented with an entirely novel object picture. In the Repeat All (RA) condition, the repetition portion of the trial used both the same encoding question and the same object picture as the beginning of the trial. Finally, we included a baseline condition (no repetition (NR)) in which both the object picture and encoding question were entirely novel in the repetition portion of the trial. A fixation screen appeared during the variable intertrial interval with an average length of 6 s, ranging from 4 to 8 s.

Participants were given explicit instructions that the object pictures were to be studied for a later memory test. They were told that the encoding questions were designed to help them remember the objects. We asked the participants to imagine that the pictured object was real and sitting in front of them and then make a yes/no judgment to the encoding question based on the object. They were also told that some of the information on each trial might repeat. Following MRI data collection, participants were given a memory test on the object pictures that had been studied.

MRI data were acquired at the University of California, Davis Imaging Research Center using a 3T Siemens Trio scanner equipped with an 8-channel phased array head coil. Pre-screening interviews ensured safety in the scanner, and earplugs were provided to attenuate acoustic noise from the scanner. Padding and adjustable head restraints were used to minimize head motion. Functional data were obtained with a gradient echoplanar imaging (EPI) sequence (repetition time, 2000 ms; echo time, 25 ms; field of view, 220 mm²; 64 × 64 matrix); each volume consisted of 34 axial slices, with a thickness of 3.4 mm and no interslice gap, resulting in a voxel size of 3.4375 × 3.4375 × 3.4 mm³. Inspection of the EPI images revealed substantial drop-out artifacts in entorhinal cortex preventing further assessment of adaptation in this region of MTL. Additionally, T1-weighted images coplanar with the EPIs were acquired using

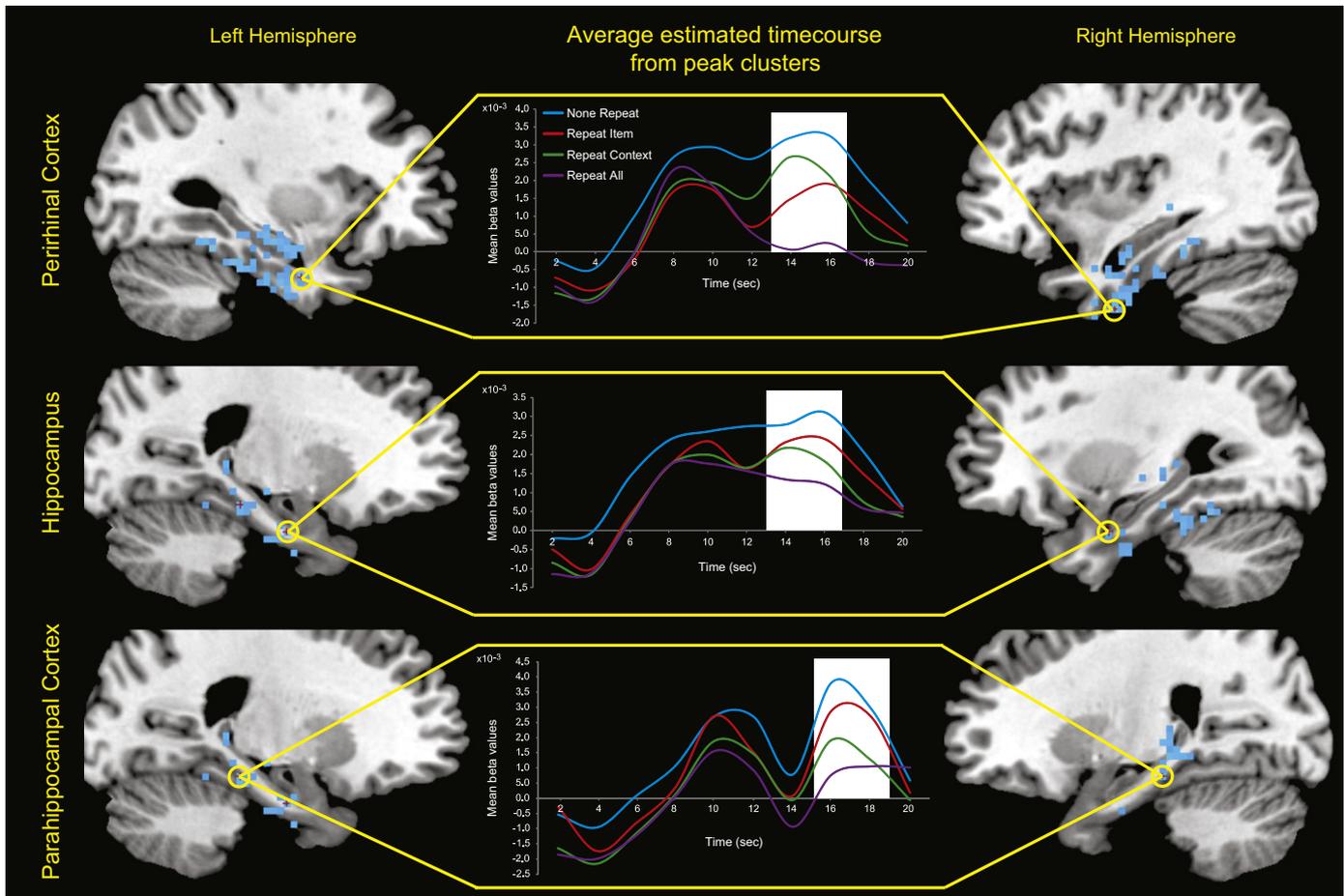


Fig. 2. fMRI adaptation effects and estimated timecourses in medial temporal lobe areas. Voxels showing overall adaptation effects (reduced activation in the RA condition as compared to the NR condition) are overlaid in blue on the brain images. FIR set analysis beta values were extracted from the peak cluster within each medial temporal lobe anatomical region, averaged across hemispheres, and are plotted as timecourses for the hippocampus, PRC, and PHC in the center. Interpolation between data points in the timecourse plots was based on the “smoothed line” algorithm implemented in Microsoft Excel (based on fitting a 4 point Bezier curve to the observed data). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

an MP-RAGE sequence (matrix size = 256×256 , voxel size = $1 \times 1 \times 1 \text{ mm}^3$, number of slices = 192). Preprocessing was performed using Statistical Parametric Mapping (SPM5) software. EPI data were slice-timing corrected using sinc interpolation to account for timing differences in acquisition of adjacent slices, realigned using a six-parameter, rigid-body transformation, spatially normalized to the Montreal Neurological Institute (MNI) EPI template, resliced into 3 mm isotropic voxels, and spatially smoothed with an isotropic 8 mm full-width at half-maximum Gaussian filter.

We modeled fMRI activity during the experimental task using a general linear model (GLM) with 15 finite impulse response (FIR) regressors for each condition (RI, RC, RA, and NR). Collectively, the set of FIR regressors estimate the BOLD response for 30 s after initial stimulus onset. This FIR analysis allowed us to compare the RA and NR conditions and identify MTL voxels in which adaptation effects were observed. The RA vs. NR contrast images were entered into a second-level one-sample *t*-test. Significant regions of adaptation were identified using an uncorrected threshold of $p < .001$.

Regions of interest (ROIs) were identified for the left and right hippocampus, PRC, and PHC, based on anatomical landmarks using criteria outlined in previous papers (Buffalo, Bellgowan, & Martin, 2006; Insausti et al., 1998).² The peak adaptation cluster

for the contrast between the RA and NR conditions was then identified within each subregion and hemisphere in order to further investigate adaptation effects in the RI and RC conditions. Table 1 lists the peak voxel location (also see Fig. 2) and peak cluster size within each anatomical region. These ROIs were used to extract trial-averaged timecourses from the FIR analysis. The peak of the HRF, as shown in the timecourses (see Fig. 2), varied slightly across the 3 MTL ROIs and we therefore selected the 2 peak TRs for each ROI based on an average of the RI, RC, and NR timecourses. The peak TRs occurred at timepoints 7 and 8 (i.e., 14–16 s following onset of the first object–sentence pair) for the hippocampal and PRC masks but across timepoints 8 and 9 for the PHC mask.

3. Results

Participant reaction times to the yes/no questions during MRI scanning reflected the influence of repetition. Mean reaction time

(footnote continued)

landmarks to identify these areas, combined with error introduced by spatial normalization, smoothing, and distortion due to magnetic susceptibility artifacts complicates localization of these areas in MRI data. That said, any error in identifying these regions would only be expected to reduce differences in adaptation effects across the three ROIs.

² It should be noted that the hippocampus, PRC, and PHC can only be conclusively identified through histological analysis. The use of anatomical

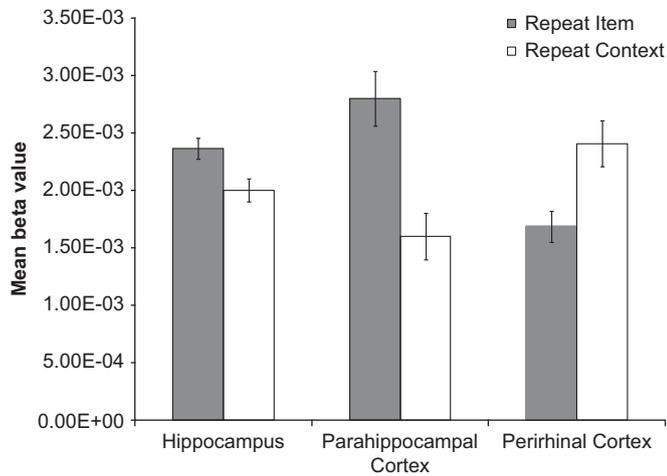


Fig. 3. PRC and PHc show qualitatively different patterns of adaptation during item vs. context repetition. Bar graphs illustrate mean beta values in PHc and PRC for the RI and RC conditions averaged across peak 2 TRs for each brain region.

during the initial presentation was 2.64 s and did not differ between conditions nor did it differ from the second presentation in the NR condition, when nothing was repeated ($M=2.59$, $p=.23$). Reaction time to the second presentation was 2.48 s in the RI condition, which was faster than the initial presentation, although this difference did not reach statistical significance ($t(13)=1.91$, $p=.08$). In the RC condition, reaction time to the second presentation was 2.13 s, which was significantly faster than the initial presentation, ($t(13)=7.56$, $p<.001$). In the RA condition, when the first and second presentations were identical, reaction time to the second presentation ($M=1.46$) was significantly faster than the initial presentation, ($t(13)=13.70$, $p<.001$), and significantly faster than the RC condition ($t(13)=5.48$, $p<.001$).

A follow-up memory test on the item pictures resulted in high rates of recognition, as expected due to repetition, with average hits at 86% and average false alarms at 3%. Differences in recognition hit rates amongst conditions were small, but significant, most likely because study time differed between conditions and therefore led to differences in overall accuracy. The conditions with the greatest number of item hits [the RI ($M=.91$; $t(13)=4.10$, $p<.01$, vs. NR) and RA ($M=.87$; $t(13)=1.80$, $p=.10$, vs. NR) conditions] also had the longest study duration (8 s) for each item. The conditions with the fewest number of item hits [the NR ($M=.83$) and RC ($M=.84$; $t(13)=1.29$, $p=.22$, vs. NR) conditions] also had the shortest study duration (4 s) for each item.

As described in the methods, the fMRI data analysis began with identification of regions in the MTL that showed overall adaptation effects in the RA condition as compared to the NR condition (peak cluster locations are shown in Fig. 2). These ROIs were then used to assess adaptation in the RI and RC conditions. Due to the method of selection, our ROI analyses maximize adaptation in the RA condition and thus it can be expected that the ROIs will show large activation differences between the NR and RA trial types. However, the critical question addressed in this ROI analysis was whether significant differences would be observed between the RI and RC conditions, and the ROI selection procedure was neutral with respect to this question. The RI and RC condition analyses are independent from the data used to select the ROIs. That is, any given trial in the data set was either used to select ROIs (NR and RA trials) or to extract timecourses and beta parameters (RI and RC trials). Therefore the following analyses of the RI and RC conditions are fully independent from the ROI selection procedure. Fig. 2 shows the estimated trial-

averaged timecourses extracted from an average of the right and left peak clusters in each anatomical ROI. It is important to note that, due to selection of the functional ROIs, all three regions show adaptation in the NR vs. RA contrast and that this adaptation is not independent from the voxel selection procedure and therefore cannot be assessed statistically. The hippocampus showed small adaptation effects due to repetition of the object picture and repetition of the encoding question, however there was no statistically significant difference between adaptation in the RI and RC conditions, $t(13)=1.50$, $p=.15$.

Our key predictions involved the PHc and PRC ROIs. We hypothesized that we would see qualitatively different patterns of adaptation effects across the two regions, such that repetition of the item picture (RI) would decrease activation in PRC while repetition of the context question (RC) would decrease activation in PHc. Consistent with this prediction, the results of a repeated measures ANOVA comparing the RI and RC conditions for the PRC and PHc peaks indicated no significant main effects of ROI or condition, but a significant ROI \times Condition interaction effect, $F(13)=12.90$, $p=.001$ (see Fig. 3). Follow-up t -tests based on this interaction identified a significant difference such that RI > RC in PHc, $t(14)=2.94$, $p<.05$ and a difference approaching significance such that RC > RI in PRC, $t(14)=1.78$, $p=.10$.

4. Discussion

In the current experiment, we used fMRI adaptation to test whether PHc and PRC are differentially involved in the processing of cognitive context and item information. We found a double dissociation between the adaptation effects in the two regions, as PRC activity was sensitive to repetition of a single-object picture (our operational definition of item information) whereas PHc was sensitive to repetition of a semantic encoding question (our operational definition of cognitive context information). This interaction effect provides evidence that PRC and PHc are functionally distinct, and the results are consistent with the idea that they support different aspects of memory (Davachi, 2006; Eichenbaum et al., 2007; Mayes, Montaldi, & Migo, 2007). We did not find a difference between the RI and RC conditions with respect to adaptation in the hippocampus. Below, we consider the implications of these findings.

4.1. PRC activation is preferentially sensitive to item repetition

Our findings with respect to PRC are consistent with extant reports in the literature and hypotheses regarding the role of PRC in episodic memory. Several theories propose that the PRC plays an essential role in supporting memory for visual objects (Barens et al., 2007; Graham et al., 2010) or more generally "items" such as abstract words (Davachi, 2006; Diana et al., 2007; Eichenbaum et al., 2007). Reductions in PRC activity during retrieval have been directly linked to increasing feelings of familiarity for a studied picture (Montaldi et al., 2006) and many studies of episodic familiarity judgments have identified a correlation between PRC activation and familiarity for item information (Davachi et al., 2003; Henson, Cansion, Herron, Robb, & Rugg, 2003; Kensinger & Schacter, 2006; Ranganath et al., 2004; Uncapher & Rugg, 2005; Weis et al., 2004). Theories of MTL function have identified a role for PRC in familiarity going back at least 10 years (e.g. Aggleton & Brown, 1999). Given these prior findings and theories, the current results can be seen as further evidence that PRC is a key region in encoding individual item representations, such as the object pictures used as the focus of attention in this study.

4.2. PHc activation is preferentially sensitive to context repetition

As noted earlier, a novel prediction of the BIC model, relative to other models of MTL function, is that the PHc may support representation of cognitive context. The paradigm introduced here represents a novel approach to investigation of cognitive context. By using over 150 semantic encoding questions, it was anticipated that a unique pattern of contextual thought could be elicited on each trial and then be flexibly applied to any given item. We found that repetition of such patterns of thought causes adaptation in PHc. This finding supports the claim that the key role of PHc in episodic memory is in processing context information. That is, although we know from previous studies that PHc is sensitive to visuospatial information, we found that context of a cognitive, nonspatial nature also produces adaptation in PHc.

The results are not entirely consistent with the claim that PHc is involved in the encoding of a “snapshot” of item–context associations such that the two types of information are inflexibly combined (Eichenbaum & Bunsey, 1995; Pascalis et al., 2009). If, as the “snapshot” theory predicts, item and context information are inextricably linked in PHc, then repeating either item or context information in the absence of its original partner would not produce adaptation in PHc. Rather, an inflexible binding between item and peripheral information suggests that an entirely new representation must be created in PHc when a repeated context is presented with a new item. Contrary to the “snapshot” theory’s predictions, our findings indicate that PHc treats repeated semantic encoding questions, even when presented with a new object picture, as familiar occurrences. At a minimum, our results suggest that any “snapshot” of item and context represented in PHc is relatively robust to changes in item information.

As noted earlier, several studies have demonstrated that PHc is involved in the processing of category-specific information, including scenes and spatial stimuli (Barens et al., 2007; Bohbot et al., 1998; Epstein et al., 1999; Stern et al., 1996; Taylor et al., 2007). For instance, Burgess, Maguire, Spiers, and O’Keefe (2001) tested retrieval of spatial source information (location) vs. nonspatial source information (identity of a person) and found that PHc activity was associated with memory for spatial source information but not nonspatial source information. Similarly, fMRI studies have found stimulus selectivity in MTL cortex such that PRC showed preferential activation for faces while PHc showed preferential activation for scenes (e.g. Litman, Awipi, & Davachi, 2009; Preston et al., 2010). In addition, one study reported that PHc activation predicts memory for the association of a word with an imagined scene, but not an imagined object, even when the physical stimulus is held constant (Staresina, Duncan, & Davachi, 2011). These findings demonstrate that the PHc is preferentially engaged under conditions that require processing of spatial context, but they do not indicate that PHc *exclusively* processes spatial stimuli. In fact, studies have consistently found that successful encoding or retrieval of nonspatial source information, such as a semantic encoding question, leads to greater PHc activation than unsuccessful source encoding or retrieval (e.g. Dobbins et al., 2003, pleasantness judgments vs. concreteness judgments; Kensinger & Schacter, 2006, animacy judgments vs. commonness judgments; Ranganath et al., 2004, size judgments vs. animacy judgments). We propose that the PHc is heavily involved in processing of visual gist, which is a significant and salient component of spatial context representation, but that PHc also incorporates other nonspatial features that denote behaviorally-significant contexts.

The current study is an improved assay of nonspatial processing in PHc because it does not rely heavily on spatial imagery. As seen in Fig. 1, the encoding questions used as context in this experiment were not primarily spatial in nature. These questions were designed to induce a unique cognitive state, such

that immediate repetition of the question with a new object would result in a similar cognitive state (e.g. semantic associations/knowledge such as “item availability in the previous 50 years” or “edibility”) directed at a new concept (e.g. “broccoli” vs. “bell”). Of course, given that PHc activation was related to the processing of these questions, one might be tempted to conclude post-hoc that these results reflect incidental spatial imagery. However, we contend that this explanation is unlikely to explain the current results. Although it is possible that simply making a semantic decision about an object could induce imagery, scenic imagery is not necessary to the task and may in fact distract from the specific question being asked. In addition, given that PHc is sensitive to *repetition* of the question, one would need to claim that similar spatial relationships are imagined on both repetitions, even when the object being assessed differs from the first to the second repetition. Finally, our experiment sets the verbal encoding question in opposition to a visual image of an object. Presumably an object picture would elicit more specific spatial imagery (Mullally & Maguire, 2011) than would an abstract encoding question due to its visual nature alone.

Our findings converge with several other studies suggesting that the role of PHc extends beyond that proposed by the category-specificity view (Bar & Aminoff, 2003; Bar, Aminoff, & Schacter, 2008). Bar and Aminoff have demonstrated in a series of studies that PHc is involved in processing context information such as: perception of objects with a strong context association (Bar & Aminoff, 2003; replicated by Epstein & Ward, 2010), memory for scenes with strong contextual associations (Bar, Aminoff, & Schacter, 2008), and memory for famous faces as opposed to nonfamous faces (Bar, Aminoff, & Ishai, 2008; but see also Epstein & Ward, 2010). Although follow-up studies have argued that these effects can be explained by spatial influences within the stimulus set (e.g. Mullally & Maguire, 2011), PHc activation has also been elicited by experimentally-created contextual associations that are based entirely on nonspatial information (Aminoff et al., 2007). In addition, multi-voxel pattern analysis has demonstrated that PHc is sensitive to category information that allows discrimination between categories of objects that do not contain spatial layout information (Diana, Yonelinas, & Ranganath, 2008). PHc also shows activation associated with successful source memory regardless of the type of stimulus being remembered, including words, objects, or scenes (Duarte, Henson, & Graham, 2011). Moreover, recent studies have found that PHc activation predicts memory for sequence information, which suggests a role for PHc in processing temporal context (Jenkins & Ranganath, 2010; Tubridy & Davachi, 2011). Finally, even studies of perception that do not test episodic context in particular suggest that PHc is sensitive to certain types of nonspatial information (such as the texture of a shape, wood vs. rock, rather than the identity of the shape, soccer ball vs. kiwi, Cant & Goodale, 2011).

4.3. Implications for theories of MTL organization

The finding that PHc is sensitive to repetition of semantic questions while PRC is sensitive to repetition of object images has implications for theories of MTL function in episodic memory. These data support theories that propose differing roles for PHc and PRC when information of different types is being processed (Cohen & Eichenbaum, 1993; Montaldi & Mayes, 2010) and conflict with theories that propose differing roles for PHc and PRC based purely on category-specificity (e.g. Barens et al., 2007; Taylor et al., 2007). These data are particularly consistent with the BIC theory (Diana et al., 2007; Eichenbaum et al., 2007) proposal that the functions of PRC and PHc in memory can be differentiated

according to the types of episodic information that are processed in MTL subregions (see also Montaldi & Mayes, 2010).

As noted earlier, evidence from studies of item and source recognition memory have indicated that PRC and PHC might differentially support familiarity and recollection-based recognition. The present results do not bear directly on this question, because this experiment was designed to directly manipulate repeated processing of item and/or context information, rather than to indirectly measure retrieval of item and context information via subjective reports. Selective repetition of item or cognitive context information might have influenced subjective experiences of recollection and familiarity, although it is not clear how such differences in recollection and familiarity would produce the present results, especially given that recollection is typically associated with increases in MTL activity rather than decreases (see Diana et al., 2007 for a review). In general, it is difficult to explain how recollection and familiarity might have driven the double dissociation between PHC and PRC observed here without invoking the idea that PHC and PRC are differentially involved in the representation of item and context information.

The current study adds to the growing body of evidence indicating that PRC and PRC play qualitatively different roles in memory. The findings also raise some important issues to be addressed in future studies. For instance, it will be important to determine how the brain differentiates between context and item information, and whether these factors also determine the relative recruitment of the PRC and PHC. Another question is the extent to which PHC is involved in processing of different contextual dimensions. The present results suggest that the PHC is sensitive to verbally-induced cognitive states, but further nonspatial manipulations of context must be tested in order to determine the scope and limits of PHC involvement in context processing.

Acknowledgments

This work was supported by NIMH grants MH083734 and MH059352 and K99 award MH083945 to R.A.D.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.neuropsychologia.2012.07.035>.

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