◆ Human Brain Mapping 33:1717–1726 (2012) ◆

Medial Temporal Contributions to Successful Face-Name Learning

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Abstract: The brain mechanisms that enable us to form durable associations between different types of information are not completely understood. Although the hippocampus is widely thought to play a substantial role in forming associations, the role of surrounding cortical regions in the medial temporal lobe, including perirhinal and parahippocampal cortex, is controversial. Using anatomically constrained functional magnetic resonance imaging, we assessed medial temporal contributions to learning arbitrary associations between faces and names. By sorting learning trials based on subsequent performance in associative and item-specific memory tests, we characterized brain activity associated with successful face-name associative learning. We found that right hippocampal activity was greater when corresponding face-name associations were subsequently remembered than when only a face or a name, but not both, were remembered, or when single-item information or associative information was not remembered. Neither perirhinal nor parahippocampal cortex encoding activity differed across these same conditions. Furthermore, right hippocampal activity during successful face-name association learning was strongly correlated with activity in cortical regions involved in multimodal integration, supporting the idea that interactions between the hippocampus and neocortex contribute to associative memory. These results specifically implicate the hippocampus in associative memory formation, in keeping with theoretical formulations in which contributions to across-domain binding differ among brain structures in the medial temporal region. *Hum Brain Mapp 33:1717–1726, 2012.*

Key words: memory; medial temporal lobe; fMRI; associative memory; hippocampus; perirhinal cortex

INTRODUCTION

Declarative memory is a term for memory for personally experienced events and facts, as assessed in recall or recognition tests. A consensus view about the neural basis of this type of memory is that brain structures in the medial temporal lobe (MTL) play an essential role by linking neocortical representations of memory fragments together [Eichenbaum and Cohen, 2001; McClelland et al., 1995; Paller, 1997, 2002; Squire et al., 1984]. However, it is unclear whether distinct areas within the MTL, such as the hippocampus and perirhinal cortex, play different functional roles in storing the associative information that is fundamental to declarative memory [Voss and Paller, 2010].

The content of declarative memories can be subdivided into item information and associative information. An example of an item memory from a museum visit could concern the specific form of a medieval knife. An associative memory formed on the same occasion could concern

Contract grant sponsor: National Science Foundation; Contract grant number: 0818912.

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Received for publication 6 August 2010; Revised 22 February 2011; Accepted 7 March 2011

DOI: 10.1002/hbm.21316

Published online 20 June 2011 in Wiley Online Library (wileyonlinelibrary.com).

the knife's relation to other items (such as other weapons in the same display case) or the knife's relation to the wider context of an autobiographical episode (such as the particular location and circumstances of the museum visit). Our study is designed to investigate whether MTL regions make distinct contributions to the successful formation of associative memories.

One influential view emphasizes differences between the hippocampus and perirhinal cortex, with associative memory more heavily dependent on the hippocampus than on perirhinal cortex [Aggleton and Brown, 1999; Eichenbaum et al., 2007]. In keeping with this view, patients with brain damage limited to the hippocampus can display impaired memory for associations with preserved memory for items [Giovanello et al., 2003; Holdstock et al., 2005; Mayes et al., 2002, 2004; Turriziani et al., 2004; Vargha-Khadem et al., 1997; Yonelinas et al., 2002]. In addition, results from functional magnetic resonance imaging (fMRI) have implicated hippocampal activity in associative memory, whereas activity in other MTL structures such as perirhinal cortex and/or parahippocampal cortex are thought to support memories comprised of fewer associative links [Davachi and Wagner, 2002; Davachi et al., 2003; Ranganath et al., 2004; Yonelinas et al., 2001].

Other evidence from neuropsychology and neuroimaging, however, conflicts with this hypothesis about medial temporal functions. For example, some patients with hippocampal damage show equivalent impairments in item and associative memory [Manns et al., 2003; Wixted and Squire, 2004], and some fMRI activation patterns span several MTL structures for single-item memories as well as for associative memories [Gold et al., 2006; Jackson and Schacter, 2004; Kirwan and Stark, 2004]. These findings have prompted the suggestion that both item and associative memory depend on integrated networks in the MTL, and that contributions from MTL structures cannot be sharply dichotomized in terms of contributions made to item versus associative memory [Squire et al., 2004, 2007; Wais, 2008]. Moreover, it has been suggested that some MTL regional dissociations may reflect confounds with memory strength [Kirwan et al., 2008].

The chief goal of the present investigation was to test the hypothesis that the hippocampus makes more substantial contributions to associative memory than does perirhinal or parahippocampal cortex, with respect to the common memory challenge of linking a name to a face. This hypothesis follows from several recent theories of MTL function that make predictions regarding regional contributions to memory based on the type of processing engaged for to-be-remembered information. These theories attempt to address the controversy regarding the ambiguous boundaries of associative memory. For example, when remembering an individual person, the item level might be one facial feature that uniquely identifies that person, or the item level might be the face (including the entire configuration of facial features), or the item level might even be the person's complete combination of constituent physical features. Thus, brain regions involved in memory for individual items may be sensitive to varying degrees of association between component parts. Moreover, a different type of associative processing may be operative when a set of parts is represented as a single item, as in a so-called "unitized" item [Haskins et al., 2008; Hayes-Roth, 1977; Quamme et al., 2007; Schacter and McGlynn, 1989].

Current theories differ in the type of associative memory processes ascribed to different parts of the MTL and in the specific ways in which MTL structures are proposed to accomplish item and associative memory. The Domain Dichotomy view posits that two types of associative memory are associated with different anatomical dependence [Mayes et al., 2007; Montaldi and Mayes, 2010]. By this view, perirhinal cortex is critical for forming within-domain associations involving two or more components within one stimulus domain (e.g., two faces), whereas the hippocampus is critical for forming across-domain associations (e.g., associations between faces and names). A variant on this view attributes memory for spatial contextual information to parahippocampal cortex [Davachi, 2006]. Another view is that perirhinal and parahippocampal cortex encode item and contextual information, respectively [Diana et al., 2007; Ranganath, 2010]. The contextual information in this account is not restricted to spatial information. Furthermore, the hippocampus is thought to be necessary for item-context bindings and for item-item bindings, regardless of domain, unless items have been unitized. Another view does not attribute different functions to different MTL regions [Shimamura, 2010; Shimamura and Wickens, 2009]. Rather, relational binding in the MTL is taken to be hierarchical in nature, with the hippocampus located at the top of the hierarchy. Therefore, complex bindings will depend more on the hippocampus, whereas low-complexity relations can be supported by MTL cortical regions. Further theoretical advancement in this area would be facilitated by additional evidence on the differential involvement of these regions in various types of associative challenges. Face-name associations thus provide a useful test case, as face-name memories clearly represent complex, across-domain associations.

We measured the extent to which fMRI activity varies during face-name associative learning as a function of subsequent memory performance. In particular, we examined neural activity in three MTL regions in each hemisphere-hippocampus, perirhinal cortex, and parahippocampal cortex. A secondary goal was to identify regions that may support face-name memory in conjunction with the MTL, and to uncover how this coordination differs across MTL regions. We therefore also examined the extent to which MTL activity was correlated with activity in other brain regions during learning while taking into account associative learning success. If the hippocampus is involved in across-domain binding, a logical prediction is that the set of cortical regions correlated with hippocampal activity

during successful association learning would be involved in multimodal integration, whereas the set correlated with perirhinal and parahippocampal activity would be involved with unimodal item representation.

Prior neuroimaging findings with face-name pairs generally fit with the notion that the hippocampus substantially contributes to the formation of across-domain associations [Chua et al., 2007; Kirwan and Stark, 2004; Small et al., 2001; Sperling et al., 2001, 2003; Zeineh et al., 2003]. Yet, the relevance of other MTL structures to forming face-name associations is debatable. Whereas cortical regions of the MTL are not typically thought to be essential for across-domain associations, there have been observations implicating entorhinal cortex [Chua et al., 2007; Sperling et al., 2001, 2003] and parahippocampal cortex [Kirwan and Stark, 2004]. In most of these prior studies, however, memory for individual faces and names was not directly contrasted with memory for associations between the two. Chua et al. [2007] assessed memory for both faces and face-name associations on each test trial. Subjects demonstrated associative memory by selecting the correct name from two choices. On the whole, then, it is unclear from previous studies whether activity in cortical regions of the MTL preferentially reflects the formation of memories for individual faces and individual names or for face-name associations. In the present study, we overcome this limitation by comparing activity associated with successful memory formation for face-name associations with pooled activity for successful memory formation for individual faces and names and unsuccessful face-name association memory.

Previous face-name association studies typically used standard procedures to align and coregister brains based on overall shape [although MTL features were used for alignment by Kirwan and Stark, 2004, and by Zeineh et al., 2003]. Because MTL regions are very small, regional boundaries can become blurred when data are averaged across multiple participants. To avoid this problem in the present study, neural activity in each MTL region was defined based on anatomical landmarks in individual brains [Fernandez et al., 1998; Kirwan et al., 2007; Reber et al., 2002; Small et al., 1999; Stark and Okado, 2003; Zeineh et al., 2000].

MATERIALS AND METHODS

Subjects

Eighteen right-handed individuals with normal or corrected-to-normal vision were recruited from the Northwestern University community. They received monetary compensation for their participation, and written informed consent was obtained in advance after all experimental procedures were explained. Twelve subjects were selected for analyses (ages 20–38 years, 9 female and 3 male), based on suitable motion parameters (< 5 mm change in x, y, or z directions) and robust memory performance (>20% correct on association test).

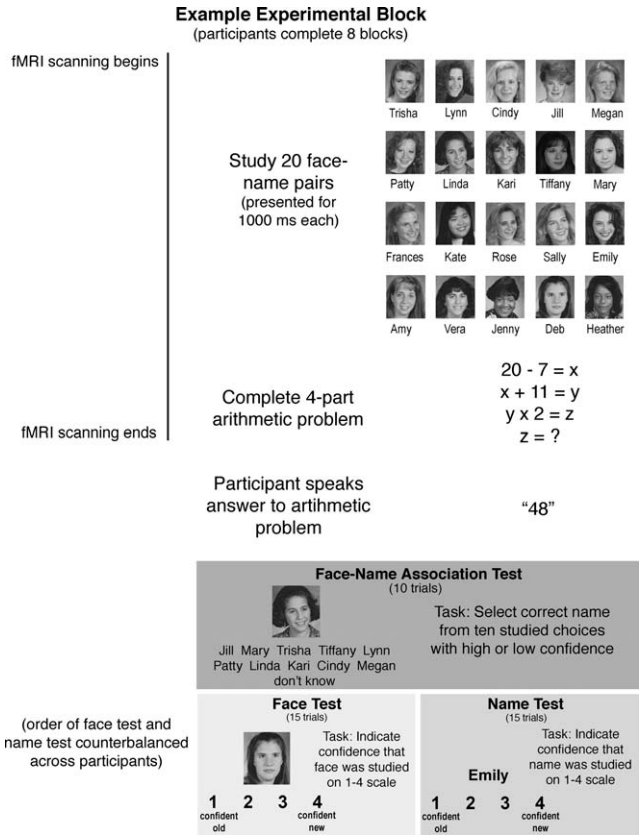

Figure 1.

During each block, participants studied face-name pairs presented one at a time. After completing a math problem, three memory tests were administered. In the face-name association memory test (FNA test), participants selected one of 10 studied names that appeared below a face to indicate which name went with each face. In the face and name memory tests (F and N tests), participants indicated whether or not a particular face or name had been presented during the study phase.

Materials and Procedure

The experiment consisted of eight study-test blocks conducted with the participant situated in the MRI scanner, a Siemens 3-Tesla whole-body Trio system with an eight-channel acquisition head-coil. Head movements were minimized with foam inserts placed on either side of the head. Visual stimuli were presented on a projection screen at the end of the scanner and viewed via a mirror mounted on the head coil. Auditory stimuli were played through headphones. Study and test procedures are shown schematically in Figure 1. Imaging data were collected only during the study phase.

Stimuli were 200 color images of faces from a high-school yearbook and 200 unique names spoken in a female

voice. Of these, 160 faces and 160 names were studied as face-name pairs. There were 20 trials per block, and each trial included one face and one name. An additional 40 faces and 40 names that did not appear during any of the eight study phases served as foils during the item memory tests (five faces and five names per block).

During each of the eight study phases, participants studied 20 face-name pairs presented one pair at a time with a variable interstimulus interval ranging from 3 to 7 s. During each study trial, a face appeared on the screen for 1 s while a spoken name was presented. Each face was presented with a gender-consistent name and all faces within a block were of the same gender (gender was randomized across blocks). A four-part arithmetic problem then appeared on the screen for 30 s, beginning 7 s after the last face-name pair was presented while the scanner continued to collect images. Participants verbally reported the answer to the math problem after scanning completed.

Each test phase began ~1 min after participants responded to the math problem, and each one included a face-name association memory test (FNA test) for 10 of the face-name pairs, followed by a face memory test (F test) and a name memory test (N test) for the other 10 pairs. No fMRI data were collected during the test phase. The FNA test was always administered first, because results from our previous experiments using similar procedures showed that testing associative memory first is important for achieving robust associative memory accuracy [Guo et al., 2004]. The order of F and N tests was counterbalanced across blocks and across participants.

With this procedure we avoided testing both item memory and associative memory for any specific face-name pair. Doing so would be problematic because of proactive interference from the first test, which would decrease the extent to which memory performance on the second test reflects brain activity from the time of initial encoding. Association memory for a study pair would potentially be corrupted if the items in the pair appeared in intervening item tests, and likewise, item memory would potentially be corrupted if an association test intervened.

In each of the 10 randomly ordered trials of the FNA test, one of the previously studied faces appeared at the top of the screen with 10 studied names below the face. The same 10 names in the same order were used in each of the 10 trials, and one name was always the correct one. Participants were asked to select the name that had been paired with the face via button press or to select "don't know." The face stayed on the screen until a name was selected. Decision confidence was measured for each trial in a second step by asking participants to indicate high or low confidence via button press.

The F test and the N test each comprised 10 items from the prior study phase (i.e., those not tested in the face-name association test) and five novel foil items (faces or written names, depending on the test), presented in random order. On each of the 15 test trials, an item appeared on the screen for 2 s and participants decided if it was old or new. Participants indicated their decision and confidence by pressing one of four buttons corresponding to the following scale: 1 = high confidence old; 2 = low confidence old; 3 = low confidence new; 4 = high confidence new.

By one account, each associative memory in this experiment is comprised of three pieces of information (a face, a name, and a link between the two), whereas an item memory is comprised of only one piece of information (a face or a name), but it is important to note that testing procedures effectively equated the amount of information participants were asked to retrieve. On the item tests, participants retrieved memory for a single piece of information. On the FNA test, participants were shown a previously studied face along with 10 previously presented names and were instructed that all stimuli presented in this test were presented during encoding and that one of the 10 names was always the correct answer. Thus, retrieval of one piece of information, the associative link between two items, is sufficient to complete this test.

Neuroimaging

During the study phase of each of the eight blocks, fMRI data were collected to monitor stimulus-locked neural activity, indicated by blood oxygen-level-dependent (BOLD) signal. Whole-brain gradient-recalled echo-planar images were obtained using the following parameters: TR = 2 s, echo = 25 ms, flip angle = 80°, field-of-view = 11 cm, 35 axial 3-mm slices, 0-mm gap, voxel size = $3.44 \times 3.44 \times 3\ mm^3$, 112 volumes per block. During each study phase, fMRI data were collected for 224 s. Each study phase began 20 s after the onset of fMRI data acquisition to allow T1 effects to stabilize. Data from this initial period were excluded from analyses. The scanner continued to collect images throughout encoding stimulus presentation (120 s) and for an additional 84 s, during which time participants attempted to solve the four-part arithmetic problem and kept the answer in mind until the scanner stopped running. At the completion of the eight experimental study-test blocks, a high-resolution T1 scan was obtained for anatomical localization (160 axial slices, voxel size = $0.859 \times 0.859 \times 1\ mm^3$).

All fMRI analyses utilized the AFNI software package [Cox, 1996]. An anatomical region-of-interest (ROI) approach was used to test a priori hypotheses concerning functional specialization across MTL structures. Preprocessing steps included motion correction, removal of voxels with low or erratic signal (less than 30% of the mean signal averaged across all brain voxels or greater than 30% change over one volume), and coregistration with the structural images. The six ROIs included left and right hippocampus, left and right perirhinal cortex, and left and right parahippocampal cortex (Fig. 2A). The methods used to identify the boundaries defining each of these regions followed those described by Reber et al. [2002]. ROIs were

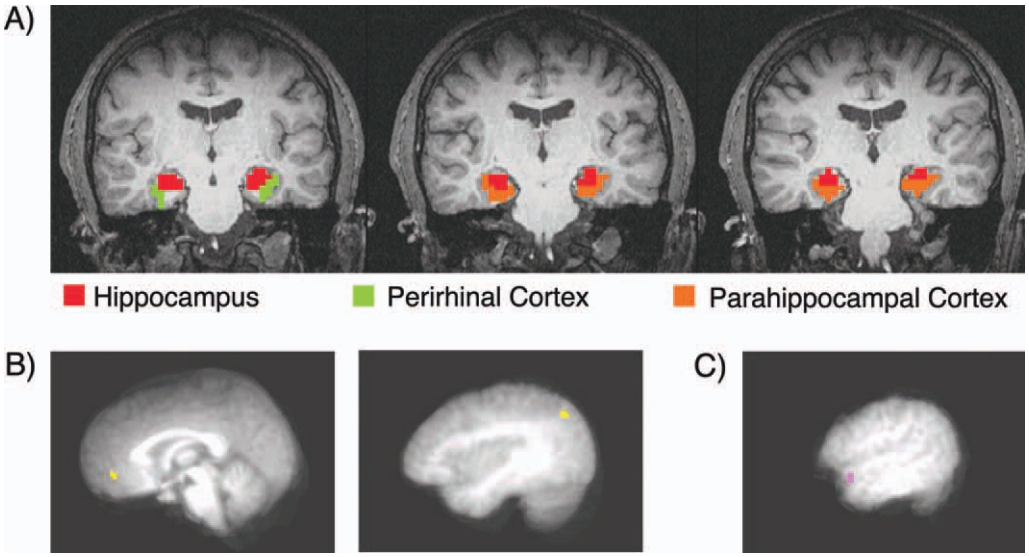

Figure 2.

(**A**) Medial temporal regions-of-interest included the hippocampus, perirhinal cortex, and parahippocampal cortex, shown here for a representative subject on four successive coronal slices (anterior to posterior) across the uncal apex. (**B**) Sagittal view of two regions (left inferior frontal gyrus and left inferior parietal lobule, respectively) showing activity significantly correlated with right hippocampal activity with regard to associative memory success. (**C**) Sagittal view of a region in the left superior temporal gyrus that showed significant correlated activity with right perirhinal and parahippocampal cortex with regard to associative memory success. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

drawn over structural images using voxels with the resolution of the functional data, such that each functional voxel was categorized as belonging to only one ROI.

After the MTL ROIs were identified on each participant, the time series for all blocks were concatenated, and the raw signal was averaged for all voxels within each ROI to provide within-ROI spatial smoothing. Data from each ROI were analyzed using a general linear model (GLM) to identify activity associated with study trials sorted by subsequent memory performance. Six nuisance variables to correct for head motion were also included in the GLM. Estimates of the average hemodynamic response to each stimulus category were made via deconvolution across a time period from 4 s prior to stimulus onset to 12 s after stimulus onset. Stimulus responses were quantified as the average estimated BOLD signal from 4 to 8 s poststimulus-onset, reflecting standard hemodynamic lag. The average response amplitude during the 4 s prior to stimulus onset was used as the baseline amplitude for comparing responses across conditions within each region.

To identify patterns of coordination between the MTL and other brain regions operative during successful face-name association encoding, two psychophysiological interaction analyses were completed. In one analysis, the seed region was the right hippocampus and in the other the seed was the combined right perirhinal and parahippocampal cortices. Perirhinal and parahippocampal seeds were also examined separately, but patterns of coordination with other brain regions did not differ significantly, so here we report results from the combined analysis. For each analysis, two additional regressors were added to a whole-brain deconvolution separating encoding trials based on whether subsequent face-name association memory was demonstrated (*association hit* trials versus the combination of *single-item hit* trials and *miss* trials; see definition of trial types below). Peak activity was measured at 4 to 8 s poststimulus-onset. One regressor was created from the deconvolution of the detrended seed region BOLD signal to estimate trial-locked activity within the seed region. The other regressor was the interaction term, created by multiplying the output of the seed region deconvolution with a vector of 1′s, 0′s, and −1′s, specifying encoding trials in which associations were correctly remembered or not. Following each whole-brain deconvolution, the correlation coefficient for the interaction term was converted to a *z*-score by Fisher transformation for each participant.

RESULTS

Memory Performance

Performance was accurate in each of the memory tests and is summarized in Table I. For the association test, 45% (SE = 0.05) of the pairings were correctly remembered compared to an expected guessing rate of ∼10%. For the face and name tests, d' was calculated by subtracting the *z*-transformed false-alarm rate from the *z*-transformed

TABLE I. Behavioral results in each memory test (proportion of responses, standard errors of the mean in parentheses)

	Correct with high confidence	Correct with low confidence	Incorrect	False-alarm rate
Association memory test	0.32 (0.05)	0.13 (0.02)	0.55 (0.05)	Not applicable
Face memory test	0.60 (0.04)	0.17 (0.01)	0.23 (0.03)	0.14 (0.03)
Name memory test	0.49 (0.04)	0.19 (0.03)	0.32 (0.03)	0.11 (0.03)

On the association memory test, incorrect includes trials when the wrong name was selected and trials when the "don't know" option was selected (10% of trials, on average). On the face and name memory tests, incorrect refers to the proportion of old items missed in the recognition test, and false-alarm rate refers to the proportion of new items incorrectly endorsed as old.

high-confidence hit-rate, to index the ability to discriminate between studied and new stimuli, where a d' value of 0 indicates chance performance and positive d' values indicate successful discrimination [Macmillan and Creelman, 2005]. Although the restriction to high-confidence hits influences d' in uncertain ways, the d' values are used only to compare performance across tests and not to support any further inferences. Mean d' scores did not significantly differ across the face (1.33, SE = 0.15) and name (1.17, SE = 0.15) tests [$t(11) = 0.45$, $P > 0.6$]. Paired t-tests verified that performance levels for the association, face, and name memory tests were significantly greater than chance [$t(11) = 6.85$, $P < 0.001$, $t(11) = 9.18$, $P < 0.001$, $t(11) = 8.30$, $P < 0.001$, respectively].

MTL Activations

Evoked activity in each MTL ROI was assessed based on categorizing study trials according to subsequent test performance. For the study trials tested with the FNA test (10 face-name pairs per block), correct responses judged as either high or low confidence were treated as recognition hits, leading to a roughly equal split between hits (45%) and misses (55%). For study items assessed with the F and N tests (the other 10 faces and 10 names from each block), only correct high-confidence old responses were counted as indicative of successful item memory (60% and 49% of the study trials for each test, respectively). Low-confidence old responses were counted as unsuccessful item memory, given that there was insufficient evidence that participants had acquired a strong item memory. It is unclear whether subjects reliably use the same metric for confidence judgments across tests, so any cross-test comparisons would potentially be influenced by confidence differences, but an advantage of our analysis method was that signal-to-noise ratios for hit encoding trials and miss encoding trials were roughly equivalent for the association, face, and name tests. Study trials were thus assigned to one of four categories: *association hit* (correctly recognized during the FNA test), *double-item hit* (both face and name correctly recognized on the F and N tests), *single-item hit* (either face or name correctly recognized but not both), or *miss* (not recognized on the association test, or not recognized on both of the item tests). Given the small number of encoding trials for which items were not recognized on both of the item tests (on average three trials per participant), we were unable to examine these misses separately from misses on the association test. Association misses examined separately did not reveal significant differences in any ROI compared with the pooled miss category (P values > 0.27). Note that this categorization goes beyond what would be possible if only association memory was tested because item memory was assessed for half the study items. However, this is not equivalent to a factorial design with item and associative memory, because each face-name pairing was tested with either the association test or with item tests. In particular, the *double-item hit* has an unknown level of associative memory (not necessarily less than for an *association hit*) and the association miss has an unknown level of item memory (not necessarily less than when one or both item tests yielded a hit). Testing each face-name pairing with all three tests, however, would have posed serious barriers for interpreting memory performance results due to carry-over effects.

To assess the involvement of each MTL region in associative memory, paired t-tests contrasted *association hit* trials with trials in which correct associative memory would be unlikely (*single-item hit* and *miss* trials). Greater associative activity was found in right hippocampal but not left hippocampal, perirhinal, or parahippocampal regions (see Fig. 3). Percent signal change was significantly greater for *association hit* trials than for *single-item hit* and *miss* trials in the right hippocampus [$t(11) = 2.74$, $P < 0.05$]. No such differences were observed in left or right perirhinal cortex, left or right parahippocampal cortex, or left hippocampus (P values > 0.15).

Whether associations were correctly remembered for encoding trials that subsequently appeared on the item tests is unknown, as associative memory for these trials was never tested. However, for trials in which subjects successfully recognized both the face and the name (*double-item hits*), there is a high likelihood that they would also have been able to recognize the face-name association. Indeed, no reliable differences in percent signal change were found in comparisons between *association hit* and *double-item hit* conditions in any of the six ROIs, all P values > 0.36. Furthermore, when we combined *association hit* trials with *double-item hit* trials, paired t-tests between these trials and *the single-item hit* and *miss* trials for each

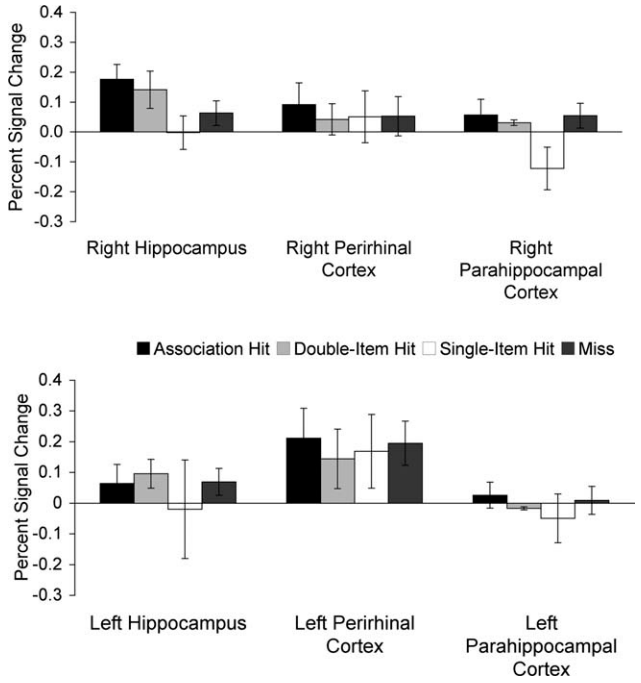

Figure 3.

Percent signal change in right and left hemisphere regions-of-interest for encoding trials successfully recognized on the face-name association memory test (association hits), encoding trials successfully recognized on both item tests (double-item hits), encoding trials successfully recognized on one but not both item tests (single-item hits), and encoding trials not correctly recognized on either of the item tests or on the association test (misses). Bars represent standard errors of the mean.

region revealed a pattern of results similar to those observed in the initial analysis. Percent signal change was significantly greater for *association hit* and *double-item hit* trials in the right hippocampus [$t(11) = 3.22$, $P < 0.01$]. No reliable differences were observed in the right or left perirhinal cortex, right or left parahippocampal cortex, or in the left hippocampus [P values > 0.10].

Psychophysiological Interactions With Other Brain Regions

Another aim of this study was to test the extent to which activity reflecting face-name association encoding in the hippocampus and surrounding cortical regions is coordinated with other brain regions. Psychophysiological interaction analyses contrasted regional cross-correlation during *association hit* trials with combined *single-item hit* and *miss* trials for the right hippocampus and with the combined right perirhinal/parahippocampal region. These analyses were completed to identify regions showing coordination of activity patterns based on subsequent memory performance. Only right hemisphere activity patterns were used as seed regions, as significant differences between *association hits* and other memory types were found in the right hippocampus only. For both analyses, *t*-tests were used to identify brain regions showing significant correlations; reliable clusters of voxels were identified using a voxel threshold of $P < 0.0003$ in a contiguous cluster of at least 150 mm^3. This combination of threshold and minimum cluster size ensured that false positive rates did not exceed $P = 0.05$, as determined by Monte Carlo simulations using random noise as data. Significant correlations with the hippocampus for the interaction were observed in the left inferior parietal lobule and left inferior frontal gyrus (Fig. 2B). A significant correlation with the perirhinal/parahippocampal seed for the interaction was present in the left superior temporal gyrus (Fig. 2C). A final *t*-test directly comparing correlation maps for the hippocampus versus the MTL cortical regions did not reveal any areas showing a significant difference in the degree of correlation with the two regions.

DISCUSSION

Our results support the hypothesis that the hippocampus is instrumental in the successful formation of face-name associations and that this type of across-domain binding depends on coordination between the hippocampus and relevant cortical regions, as posited by several recent theories of MTL function [Davachi, 2006; Mayes et al., 2007; Montaldi and Mayes, 2010; Shimamura, 2010; Shimamura and Wickens, 2009]. Perirhinal and parahippocampal cortex did not show different activity patterns for storing face-name associations compared with other trial types, suggesting that these regions may be less relevant for across-domain binding.

Additional support for these conclusions was derived from psychophysiological interaction analyses. Hippocampal activity during successful encoding of face-name associations was correlated with regions involved in multimodal integration, whereas perirhinal and parahippocampal cortex activity was not. As different regions of the cortex are specialized to represent different sorts of information, such as names or faces, coordination between the hippocampus and multimodal neocortical regions is consistent with the challenge of forming associations across domains.

The extraction of the functional signal from MTL regions identified from anatomical landmarks provided a level of anatomical specificity greater than that in many prior studies of face-name learning. Standard whole-brain analyses could miss effects in small MTL regions, because stereotactic locations in different individuals may not coincide with the same region after warping procedures are applied. The use of anatomical landmarks in individual brains is thus very important in this context [Kirwan and Stark, 2004; Zeineh et al., 2003].

Neural activity in the right hippocampus was greater for successful association memory than for item memory

or for unsuccessful memory. This finding is consistent with previous findings implicating the right hippocampus in successful face-name encoding [Chua et al., 2007; Kirwan and Stark, 2004; Sperling et al., 2003], and supports the Domain Dichotomy view and other theories that posit that hippocampal processing functions to bind information from diverse domains [Davachi, 2006; Diana et al., 2007; Mayes et al., 2007; Montaldi and Mayes, 2010; Ranganath, 2010; Shimamura, 2010; Shimamura and Wickens, 2009].

It has been previously proposed that anterior portions of the hippocampus are preferentially involved in successful encoding of associations relative to more posterior regions [Chua et al., 2007; Schacter and Wagner, 1999; Sperling et al., 2003], although not all results support this view [Kirwan and Stark, 2004; Small et al., 2001]. In the current experiment, we also examined anterior and posterior portions of the hippocampus separately, using the appearance of the uncal apex in the coronal plane to place the anterior/posterior boundary. These analyses failed to yield convincing differences across regions. Accordingly, we reported results collapsed across the anterior and posterior portions. Divergence in the location of encoding-related differences observed in hippocampal activity across different studies may be due to differences in the manner in which face-name associative memory was tested. For instance, studies that implicated the anterior hippocampus [Chua et al., 2007; Sperling et al., 2003] used a two-alternative forced-choice test that was administered following the encoding of 455 face-name pairs. In the current study, a 10-alternative forced-choice test was administered following the encoding of 20 pairs, and this procedure was repeated across eight separate blocks. Differences in the amount of time elapsed between study and test as well as in the number of face-name pairs participants were required to remember at one time could influence how the hippocampus stores associative information, but further studies are needed to test these speculations.

Recent theories posit that perirhinal cortex may support memory for within-domain associations and unitized items [Davachi, 2006; Mayes et al., 2007; Montaldi and Mayes, 2010]. This idea is consistent with results showing that perirhinal but not hippocampal activity predicts successful face memory [Chua et al., 2007], and with our finding of no significant activity difference in right perirhinal cortex between trial types. Although the individual faces and individual names can be broken down into component parts—a face comprises a set of facial features and a name comprises a set of phonemes—there is a sense in which these components are unitized into a single item [Haskins et al., 2008; Quamme et al., 2007; Schacter and McGlynn, 1989]. Although differences between trial types did not approach significance in the right perirhinal cortex, examination of overall activity levels indicated slightly higher activity levels for successfully remembered face-name associations than for other trial types in this region. This trend is consistent with the suggestion that perirhinal cortex could play a role in associative memory storage in some situations [Staresina and Davachi, 2008], and that contributions to face-name associations may differ in extent across individual MTL regions rather than in an all-or-none manner.

Although less is known regarding the nature of parahippocampal than perirhinal contributions to memory, parahippocampal cortex has been hypothesized to play a role in the encoding of contextual and/or item information and is not typically implicated in across-domain binding [Davachi, 2006; Diana et al., 2007; Shimamura and Wickens, 2009]. The present results are consistent with these views. There was no evidence that parahippocampal cortex is essential for the successful encoding of face-name associations.

The results from our psychophysiological analyses did not reveal any brain areas that showed significantly greater interaction correlations for hippocampus than for MTL cortical regions or vice versa. Thus, our results do support a strong division of labor in the MTL with regard to the extent of cross-talk with other brain regions during successful face-name association memory encoding. Yet, the significant correlational results using the right hippocampal seed are consonant with the idea that the hippocampal role in face-name associative memory involves specific interactions with neocortical regions. Variability in associative encoding-related hippocampal activity correlated with activity in the left inferior parietal lobule and in the left inferior frontal gyrus. Previous studies have implicated these regions with recollection requiring across-domain binding [Duarte et al., 2005; Eldridge et al., 2000; Henson et al., 1999; Vincent et al., 2006; Yonelinas et al., 2005], suggesting that these regions are involved in organizational and elaborative processing required for binding diverse types of information into a coherent memory. The emergence of these regions in our analysis suggests that coordinated activity between these regions and the hippocampus may be especially important in forming associations between faces and names. In contrast, variability in associative encoding-related perirhinal/parahippocampal activity produced increases in correlated activity in the left superior temporal gyrus only. This region may be specifically important for storing name information, as it has been previously linked to the processing of semantic information [Binder et al., 1994] and to names in particular [Tsukiura et al., 2002]. Accordingly, this correlational finding may reflect interactions between superior temporal gyrus and MTL cortex that are instrumental for learning a person's name.

CONCLUSION

Evidence from brain activity at the time of initial learning showed that the right hippocampus contributed to successfully forming face-name associations. Because our analyses contrasted item and associative memory, we can exclude the possibility that this hippocampal subsequent

memory effect reflects memory only for the two individual items rather than for the face-name association. Furthermore, reliable differences across subsequent-memory trial types were not observed in other regions of medial temporal cortex.

Outside the MTL, frontal and parietal activity typically associated with multimodal processing was correlated with hippocampal activity but not with MTL cortical activity, bolstering theories that the hippocampus is necessary in forming across-domain associations in conjunction with relevant neocortical regions. Yet, it remains possible that MTL cortical regions also support some types of associative memory, given the tendency for perirhinal activity to predict subsequent face-name association retrieval (though nonsignificant), and given the lack of evidence for a significant difference between MTL cortex and hippocampus in how neocortical activity was coordinated during successful association encoding.

When it comes to forming face-name associations, a major contribution comes from the hippocampus and its coordination with other brain regions, in contradistinction to perirhinal and parahippocampal cortex. Whether this principle also applies for all other types of associations is presently unknown. To gain further understanding of associative memory and the MTL, it will be important to examine MTL activity with a variety of different encoding situations and types of to-be-remembered stimuli.

ACKNOWLEDGMENTS

The authors thank Marwan Baliki and Helen Alexander for assistance with fMRI data collection and analysis.

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