Supporting Information

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SI Results

Face-Name Correlation Analysis. Although PCA allowed isolation of what may be considered a more pure performance measure of relational memory that is not correlated with other cognitive measures (e.g., IQ), an additional whole-brain regression analysis was conducted using only the behavioral performance from the offline face-name memory task as a predictor. Across the whole brain, the only region to demonstrate any relationship to offline face-name learning was the hippocampus, bilaterally [supporting information (SI) Fig. S2, Experiment 1]. ROI analysis confirmed this result. Following removal of BOLD outliers, resting period activity in both the left [$R^2 = 0.29$, $F(1, 41) = 16.47$, $P < 0.001$] and right [$R^2 = 0.15$, $F(1, 41) = 7.48$, $P = 0.009$] hippocampus significantly correlated with face-name memory performance.

Experiment 2 – Whole-Brain Analysis. To further explore the relationship between the PCA memory scores and task-induced deactivation parameter estimates from Experiment 2, a whole-brain analysis was conducted. Specifically, following exclusion of those participants who were considered to be outliers based on their behavioral performance, task-induced deactivation maps were entered into a multiple regression analysis using participants' component scores as predictors of interest (MTL: $P < 0.005$, 5 voxel cluster threshold; whole-brain: $P < 0.001$, 5 voxel cluster threshold). This analysis confirmed and extended the results from the ROI replication analysis. Significant correlations were found between the memory component scores and voxels within the right MTL that overlapped with the MTL ROI identified in Experiment 1 (Fig. S3*a*). Furthermore, additional regions of bilateral MTL (encompassing portions of the hippocampus and parahippocampal gyrus) demonstrated a relationship with memory performance (Fig. S3 *b* and *c*). ROI analysis confirmed this result. Following removal of BOLD outliers, resting period activity in all MTL regions identified significantly correlated with face-name memory performance [right hippocampus/parahippocampal gyrus with memory component: $R^2 = 0.39$, $F(1, 43) = 27.60$, $P < 0.001$, left hippocampus/parahippocampal gyrus with memory component: $R^2 = 0.19$, $F(1, 42) = 10.03$, $P = 0.003$, right parahippocampal gyrus with memory component: $R^2 = 0.20$, $F(1, 41) = 10.16$, $P = 0.003$]. Subjects who demonstrated greater resting period MTL BOLD activity had higher PCA memory component scores. The remaining component coefficients were not significantly related to any of the MTL ROI's.

SI Methods

Subjects. Fifty participants between the ages of 18 and 32 (25 female; mean age = 20) were recruited from the Dartmouth community. All subjects were right-handed, reported no significant abnormal neurological history, and all had normal or corrected-to-normal visual acuity. Participants either received course credit or were paid for their participation, and all participants gave informed consent in accordance with the guidelines set by the Committee for the Protection of Human Subjects at Dartmouth College.

Data Acquisition

Apparatus. All imaging was performed on a 3.0T Philips Intera Achieva Scanner (Philips Medical Systems, Bothell, WA) equipped with a SENSE (SENSEitivity Encoding) head coil at the Dartmouth College Brain Imaging Center (Hanover, NH). Visual stimuli were presented using an Apple G3 Laptop computer running PsyScope software. Stimuli were projected to subjects with an Epson (model ELP-7000) LCD projector onto a screen positioned at the head end of the bore. Subjects viewed the screen through a mirror mounted on the head coil. Cushions were used to minimize head movement.

Imaging. Anatomical images were acquired using a high-resolution 3-D magnetization-prepared rapid gradient echo sequence (MPRAGE; 160 sagittal slices, TE = 4.6 msec, TR = 9.9 msec, flip angle = 8°, voxel size = 1 × 1 × 1 mm). For each experiment, functional data were collected in two runs using T2* fast field echo, echo planar functional images (EPIs) sensitive to BOLD contrast (TR = 2,500 msec, TE = 35 msec, flip angle = 90°, 3 × 3 mm in-plane resolution, sense factor of 2; Experiment 1: 108 sets of images; Experiment 2: 124 sets of images). Slices were acquired axially allowing whole brain coverage and were tilted parallel to the long-axis of the left and right hippocampal formation to optimize signal in the MTL and to minimize partial-volume effects in this region (45 slices; 3.5-mm slice thickness, 0.5-mm skip between slices).

Functional Neuroimaging. All experiments were collected in a single scan session and the order of experiments was counterbalanced across individuals.

Experiment 1. In a block-design experiment, subjects alternated between blocks of task (30 s per block) and blocks of fixation (i.e., passive rest; 30 s per block). During task blocks, subjects made odd/even judgments on a random set of numbers ranging from 1 to 1,000. Numbers were presented centrally at a rate of one every 1,250 msec and subjects made their responses using a two-button key press. During the passive rest blocks, subjects were told to simply maintain fixation on a crosshair that was presented at a central location on the screen.

Experiment 2. In an event-related design experiment, subjects were required to respond with a button-press when a stimulus appeared on the screen, and then respond with another button-press (opposite hand) when the stimulus disappeared. The stimulus was a large-field 8-Hz counterphase flickering checkerboard (black to white) that appeared at trial onset and lasted for 1,250 msec. Subjects were instructed to respond as quickly as possible to the onset and offset of the stimulus (button responses were counterbalanced across subjects). In each run, a total of 60 checkerboard trials were presented, and these task trials were interleaved with random periods of resting fixation. During the periods of fixation, subjects were instructed to simply maintain fixation on a crosshair that was presented at a central location on the screen. Fixation periods varied from 0 to 10 seconds (0–4 TRs) in duration.

Behavioral Testing

Standardized Tests. All standardized tests were administered and scored by a trained experimenter according to the procedure outlined in each test's respective manual and guidelines.

Wechsler Abbreviated Scale of Intelligence . The Wechsler Abbreviated Scale of Intelligence (WASI) is a reliable measure of general cognitive abilities, and is a means of estimating verbal, nonverbal, and general IQ. Subjects were administered all four subtests of this battery; this included the vocabulary, synonyms, block-design, and matrix reasoning subtests. Performance measures were verbal-IQ, performance-IQ, and full-IQ.

Wechsler Digit Span Subtest. This subtest of the Wechsler Adult Intelligence Scale (WAIS) is used as a measure of immediate auditory recall and working memory. Subjects were given a set of digits from an experimenter and were required to repeat them initially forwards and then backwards. Performance was calculated as the individuals' scaled digit-span score (as per WAIS scoring guidelines).

Nonstandardized Cognitive Tests. Cognitive tasks were administered using Apple Desktop computers running PsyScope Software (1). All tasks and stimulus lists were counterbalanced across subjects.

Choice Reaction Time. A choice reaction time task was used as a measure of visual-motor stimulus-response mapping. During each trial, one of four squares (the target square) was filled with an asterisk. Subjects were required to respond by pressing a corresponding key on a keyboard. Targets were presented in random order. Trials were presented in five blocks; each block consisted of 100 trials. The duration of each trial was self-paced and concluded with the subject's response. Subjects were instructed to respond as quickly as possible, without sacrificing accuracy. Performance was calculated as the average response time across all correct trials.

Repetition Priming. The facilitation in reaction time for classification of repeated objects was used as a measure of implicit memory. Subjects were presented with 50 colored objects obtained from an updated set of Snodgrass and Vanderwart line-drawn objects (2). Each object was presented individually at the center of the screen for 500 msec, at a rate of one every 2,000 msec. The 50 objects were each presented three times in random order, for a total of 150 trials. Subjects indicated whether each object was living (e.g., a monkey) or nonliving (e.g., a shoe) by responding with a key-press and were told to make this decision as quickly as possible, without sacrificing accuracy. Performance was calculated as the average difference in response time between the first and third repetition of each object (behavioral priming).

Verbal Recognition Memory. Recognition memory for verbal materials was used as a measure of verbal declarative long-term memory. During study, subjects made abstract/concrete judgments on a set of 100 words (i.e., incidental encoding). Words were presented once every 2 seconds (500-msec inter-trial interval) during which time subjects were required to respond by key press. Following a brief delay period (5 min), subjects were administered a surprise recognition memory test. During this test, subjects were presented with the 100 previously studied words and 100 novel words (foils). Subjects were required to indicate whether they thought the word was old (had been classified during the abstract/concrete judgment task) or new (had not been classified during the abstract/concrete judgment task) with a key-press, and were given as much time as they needed to complete the test. Words were high-frequency nouns (min K to F frequency: 20 per million) of three to six letters and one to two syllables. Word lists were matched for frequency, length, number of syllables, number of letters, and concreteness. Performance was calculated as d', which represents an individuals ability to discriminate between items that had actually been presented at study and those that had not.

Face-Name Relational Memory. Face-name learning was used as a measure of relational declarative long-term memory. The face stimuli consisted of a standardized set of unfamiliar male and female faces that were used in previous studies (3, 4). Names were chosen from the United States Social Security Administration's most popular first names for births in the United States from 1970 to 1979 (http://www.ssa.gov/OACT/babynames/1999/top1000of70s.html).

Subjects intentionally memorized a set of 50 unfamiliar face-name pairs over three repetitions of study (each face-name was presented simultaneously for 4,500 msec, with the name presented directly below the face; face-name pairs were followed by a centrally presented fixation cross-hair that lasted 500 msec). Following the study session, memory was assessed using a cued recall test of memory where subjects were presented with each of the studied faces and were required to provide the corresponding name that had been previously paired with that face. Performance was calculated as percentage of faces correctly named during this cued-recall test of memory.

Data Analysis

Behavioral. All behavioral data were examined for presence of outliers (>2.5 SD from the mean). Participants who demonstrated performance outside of this range on any behavioral measure (including all scanned task variables and offline behavioral testing measures) were removed from analysis. After removing all such outliers, 45 participants remained and were carried forward into subsequent analyses

A separate exploratory PCA was conducted for each of the two experiments. PCA produces a set of orthogonal "metavariables." These metavariables are associated with factor loadings that represent the weighting of each of the contributing measures onto each respective PCA component, thus allowing one to identify what each component may represent, and potentially isolating more pure performance measures that are not correlated with one-another.

Each analysis included all offline behavioral measures collected during the two postscan behavioral sessions, as well as two behavioral measures collected during each experiment's scanned controlled tasks (the average response time and the percentage of number of items not responded to). These latter two variables were included to serve as indices of inter-subject variability in attention or vigilance that may have been present during performance of the control tasks at the time of scanning. Behavioral measures from the two postscan behavioral sessions were: verbal-IQ, performance-IQ, full-IQ, the scaled digit-span score, average response time for correct trials during the choice-reaction time task, behavioral priming from the repetition priming task, d' from the verbal recognition memory test, and percentage of faces correctly named from the face-name pair relational memory task.

As per standard PCA analysis (5), the eigenvalues describing the variance matrix of these variables were extracted, and components with eigenvalues greater than 1 were selected for additional analysis. The factor loading structure from the selected components were rotated with the Varimax algorithm for interpretation. Finally, factor scores from each of these components were derived for every subject to be used in fMRI regression analyses. These factor scores represented estimations of the actual individual subject values (i.e., the relative contribution of each component to the variance of their behavior both within and across subjects) for each of the components.

MRI-Preprocessing of Functional Images. fMRI data were analyzed using SPM2. Each experiment was preprocessed separately. For each functional run, data were preprocessed to remove sources of noise and artifact. Preprocessing included realignment within and across runs to correct for head movement, unwarping to correct for susceptibility-by-movement interactions (field-disturbances), normalization to a standard anatomical space (3-mm isotropic voxels) based on the SPM2 EPI template, which approximates Talairach and Tournoux atlas space, and spatial smoothing (6-mm full-width-at-half-maximum) using a Gaussian kernel.

MRI-Statistical Images. Parameter estimates and statistical images were computed in an identical fashion for each experiment separately. For each subject, a general linear model incorporating onsets for the periods of task (modeled as events with durations convolved with the canonical hemodynamic response function) and covariates of no interest (a session mean, linear trends to account for low-frequency noise, and six movement parameters obtained from realignment) was used to compute a parameter estimate (β) corresponding to the periods of task, and treating the unspecified periods of rest as an implicit baseline or reference. The β-image was used to compute two weighted parameter estimate images (t-contrast images). These weighted parameter estimates allowed identification of those voxels demonstrating greater activity during periods of task relative to periods of rest (+1 weighting), and importantly, those voxels demonstrating greater activity during periods of rest while treating periods of task as the reference (−1 weighting). As we were interested in resting period BOLD activity as defined relative to periods of task, the latter weighted-parameter estimate (rest versus task) was used in subsequent analyses.

Experiment 1–MRI-Multiple Regression Analysis. Each subject's weighted-parameter estimate image representing BOLD activity during periods of rest relative to periods of task from Experiment 1 was carried forward into a multiple regression analyses. Subjects' PCA component scores for each of the identified PCA components were used as covariates of interest to predict this parameter estimate in default network voxels.

Anticipating the likelihood that regions of the default network would exhibit considerable variability in task-induced deactivations across subjects (6), and that this may lead us to potentially miss regions demonstrating a systematic relationship to offline cognitive measures, rather than using an inclusive whole-brain mask, this was done by manually identifying peak ROI locations obtained in the regression analysis against both a relatively liberally threshold-weighted parameter-estimate image isolating task-induced deactivations (rest versus task; $P < 0.01$) and previous reports of task-induced deactivations (7–9). Specifically, analysis was focused on regions of the medial prefrontal cortex, lateral parietal cortex, posterior cingulate gyrus and retrosplenial cortex, anterior portions of the lateral temporal cortex, and the MTL.

To explore the relationship between the resting period parameter values and the PCA component variables, a ROI analysis was conducted on foci that fell within regions of the default network. An automated peak-searching algorithm was used to identify foci of activity that demonstrated a significant relationship between each of the components and the resting period parameter estimate (F-map of whole brain: $P < 0.001$, F-map of MTL: $P < 0.005$, minimum contiguous voxel cluster size of 5). Significantly active voxels surrounding these foci were identified, and the mean parameter value of each ROI was extracted from each subject's resting period parameter estimate image. Following extraction of the mean parameter estimate from each ROI, the ROI data were interrogated for the presence of BOLD outliers (>2.5 SD from the mean). These outliers were removed. Finally, each ROI was submitted to regression analyses using the behavioral measures (subjects PCA component scores) as predictors of interest to assess the direction of relationship.

A more lenient threshold for MTL analysis was adopted for a number of reasons. First, as outlined in the introduction, the MTL was a theoretical site of interest. The current experiment was motivated by earlier studies exploring the relationship between resting period activity and MTL activity (10–12). As such, these previous reports initially motivated us to perform a pilot study using a smaller sample of subjects ($n = 21$), using only a single experimental paradigm (block-design number-judgment), and a single memory measure [face-name learning, (13)]. This pilot study uncovered a correlation between hippocampal deactivations and memory ability, thus leading us to follow up this study with the more extensive study reported in the present report. Second, although slice prescription was set so as to optimize signal within temporal lobe structures (i.e., slice orientation was parallel to the long-axis of the hippocampus so as to minimize partial-volume effects), this region is still susceptible to greater signal loss because of its close proximity to medial cavities (14). To this end, the replication analysis using an independent data set (Experiment 2) was a critical step in verifying the validity of the empirical results (see also *SI Results*).

Experiment 2–MRI Replication Analysis. To assess the reliability and generality of results across Experiments 1 and 2, the MTL ROIs found to demonstrate a significant relationship between resting period BOLD activity and subject's memory component scores that were identified in the Experiment 1 data set were formally tested for replication using the Experiment 2 data set. The rationale for the replication approach is based on the assumption that reproducibility of activations across data sets is the strongest indication that activations generalize and are not attributable to spurious artifact (e.g., motion). As such, a relationship between resting period parameter estimates and memory component scores in regions found to survive this stringent analysis can be considered highly reliable, as they are replicating across both independent data sets.

The MTL regions identified in Experiment 1 (i.e., hypothesis generation data set) were used as functional ROIs in Experiment 2 (i.e., hypothesis testing data set). For each subject, mean resting period weighted parameter estimates (treating the checkerboard detection task as the reference) were extracted from each of the ROIs from the Experiment 2 data set in same manner as that which was used in Experiment 1, and were submitted to a simple regression analyses using the Experiment 2 PCA memory-component scores as predictors of interest.

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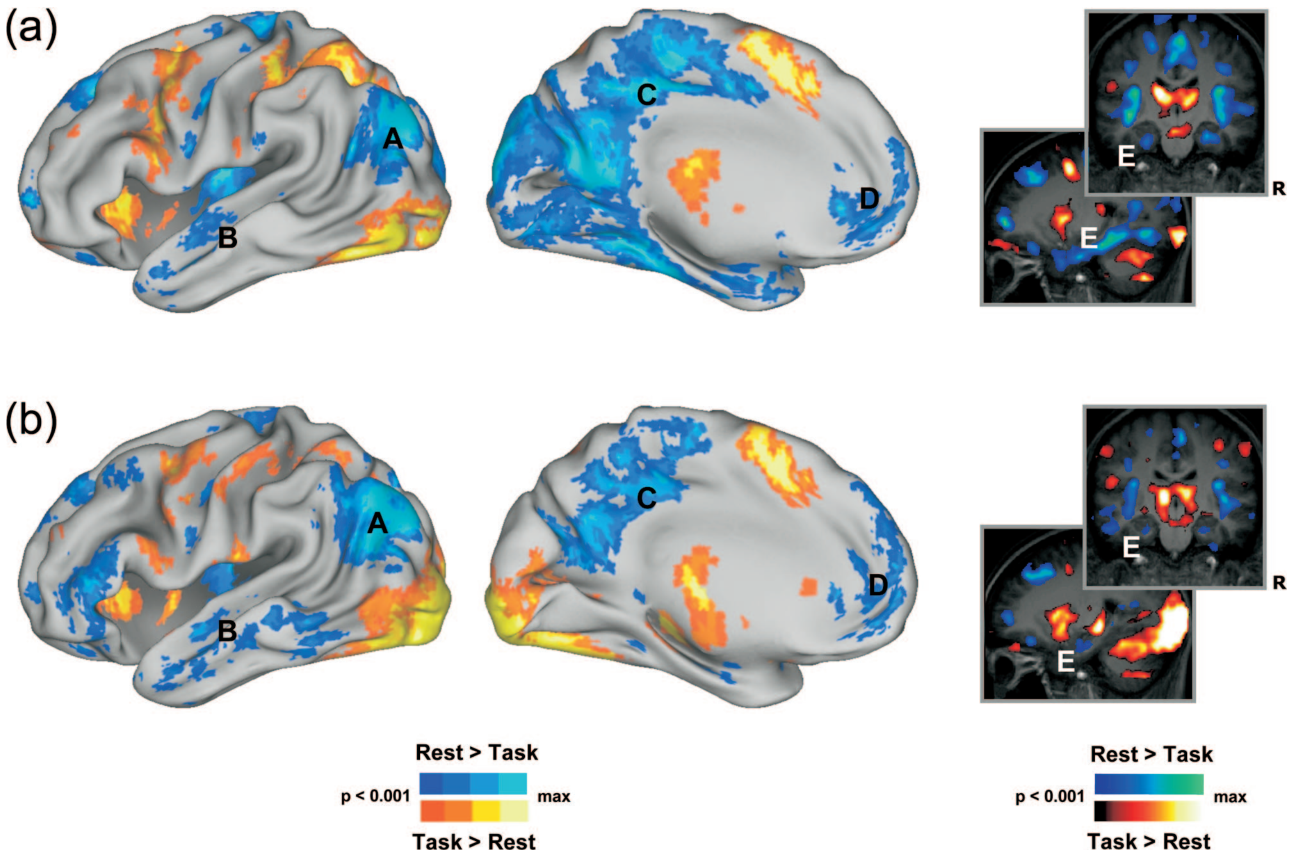

Fig. S1. Whole brain BOLD activity. Activation maps depict regions of the brain that demonstrated greater activity during periods of rest relative to periods of the control task (*blue*) ($P < 0.001$, minimum cluster size = 5 voxels) and those that demonstrated greater activity during periods of the control task relative to periods of rest (*yellow-orange*) ($P < 0.001$, minimum cluster size = 5 voxels) during (*a*) Experiment 1 and (*b*) Experiment 2. In both experiments, periods of rest elicited greater activity in A: Lateral parietal cortex, B: Middle temporal gyrus, C: Posterior cingulate gyrus, D: Medial prefrontal cortex, and E: Medial temporal lobes. Maps depict partially inflated cortical renderings (Caret Software: http://brainmap.wustl.edu/caret/) of the lateral and medial views of the left hemisphere, and slices obtained from a left-sagittal (*Bottom*) and coronal (*Top*) plane.

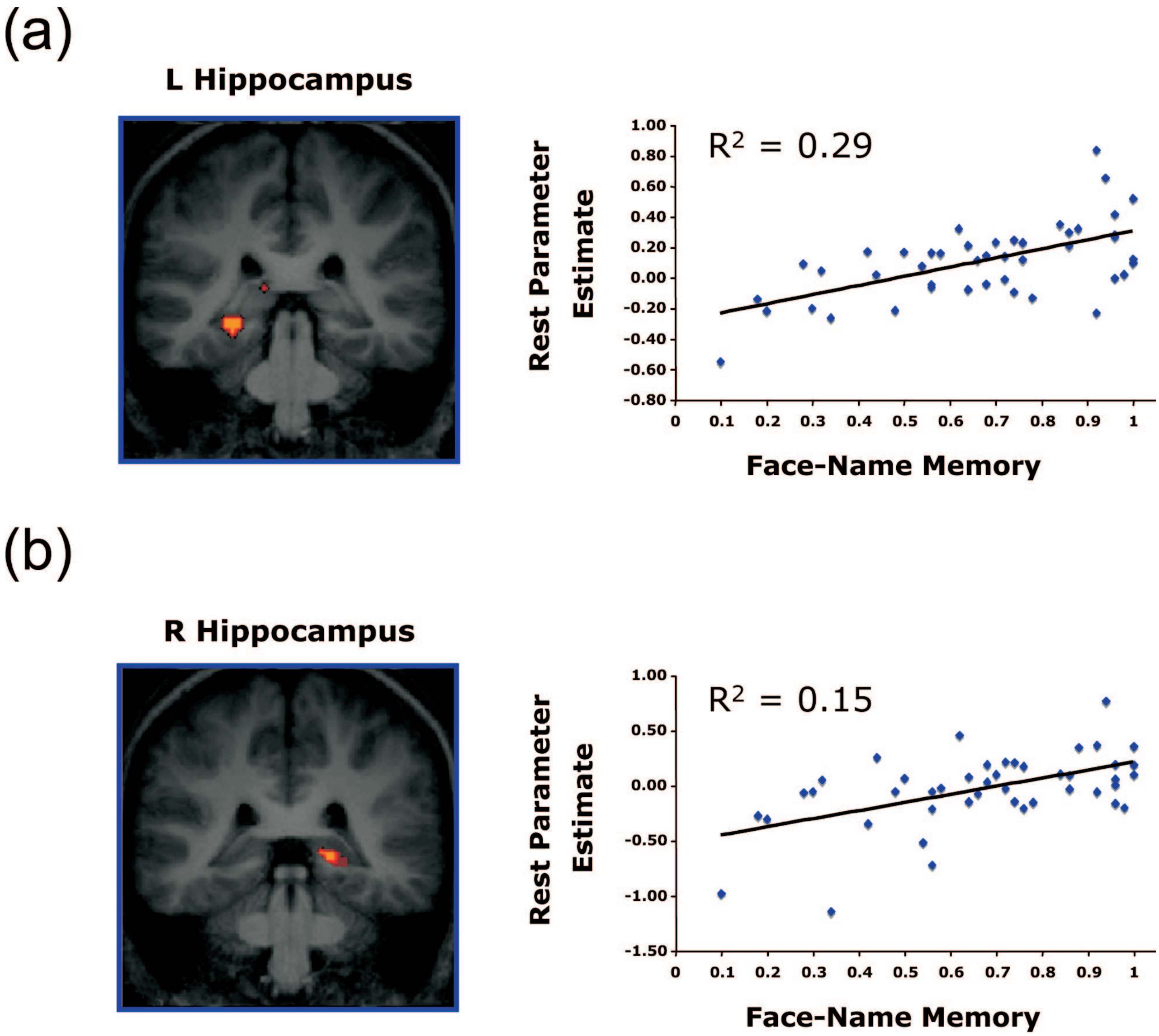

Fig. S2. Individual differences in resting period BOLD activity within the hippocampus predict face-name memory (Experiment 1). Subjects were scanned while periods of resting fixation (30 s) were interleaved with periods of an odd/even number judgment task (30 s) in a block-design experiment. Individuals evoking greater resting period hippocampal BOLD activity demonstrated better face-name memory performance during offline behavioral testing. (See *SI Results* for details.) Graphs depict subjects' mean resting period hippocampus ROI parameter estimates on the *y*-axis and their face-name memory performance (proportion correct) on the *x*-axis. Each point represents one subject. Refer to *SI Methods* and Fig. 1*A* for details of scanned task. (*a*) Left hippocampus (peak *xyz* Talairach coordinates: −27, −32, −6); (*b*) Right hippocampus (21, −32, −1).

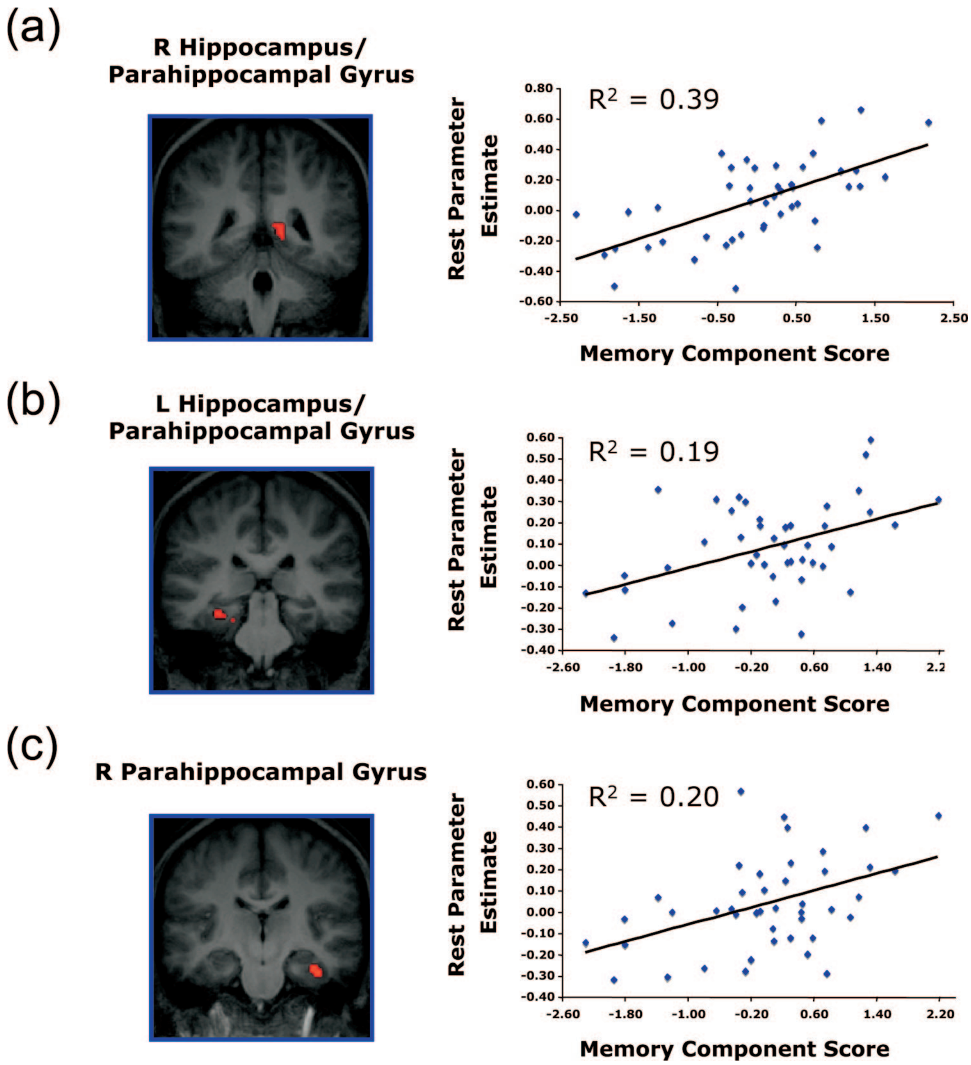

Fig. S3. Individual differences in resting period BOLD activity within regions of the left and right medial temporal lobes predict memory ability (Experiment 2). Subjects were scanned in an event-related experiment in which a checkerboard detection task (1.25 s) was interleaved with variable periods of resting fixation (0–10 s). Individuals evoking greater resting period MTL BOLD activity demonstrated larger PCA memory component scores during offline behavioral testing (see *SI Results* for details). Graphs depict subjects' mean resting period MTL ROI parameter estimates on the *y*-axis and their memory component scores on the *x*-axis. Each point represents one subject. Refer to *SI Methods* and Fig. 1*B* for details of scanned task. (*a*) Right hippocampus/parahippocampal gyrus (peak *xyz* Talairach coordinates: 12, −41, 5); (*b*) Left hippocampus/parahippocampal gyrus (−33, −30, −14); (*c*) Right parahippocampal gyrus (−39, −21, −19).

Table S1. Summary of the data from each behavioral measure in Experiments 1 and 2

Type of task	Behavioral measure	Mean	Std. dev.	Min.	Max.
Scanned tasks					
Odd/Even number judgment (Exp. 1)	Avg. reaction time, ms	597.4	54.1	267.1	459.9
Odd/Even number judgment (Exp. 1)	Number of items not responded to	3.8	5.9	1	31
Checkerboard detection (Exp. 2)	Avg. reaction time, ms	268.7	16.7	241.5	311.4
Checkerboard detection (Exp. 2)	Number of items not responded to	4.0	7.8	0	31
Offline behavioral tasks					
WASI	Verbal-IQ	120.9	8.5	99	136
WASI	Performance-IQ	116.2	8.2	96	129
WASI	General-IQ	121.1	7.9	100	134
Weschler digit span	Scaled digit-span score	13.1	2.6	8	18
Choice reaction time	Avg. reaction time, ms	352.4	53.7	267.1	459.9
Repetition priming	Behavioral priming, ms	49.1	33.3	−27.3	122.7
Verbal recognition memory	d′	1.9	0.7	0.6	3.4
Face-Name learning	Percent correct	67.2	24.8	10	100

Table S2. PCA analysis of behavioral measures from Experiment 1

Component	Rotated sum of square loadings		
	Eigenvalue	% of variance	% of cumulative variance
1	2.99	29.0	29.0
2	2.10	21.0	50.0
3	1.37	13.7	63.7

Table S3. Rotated factor loading structure (Experiment 1; see Table S2)

	Component		
Behavioral measure	1	2	3
Number judgment avg. RT	−0.2	**0.72**	−0.18
Number judgment no response	0.24	**0.61**	−0.36
Verbal-IQ	**0.8**	−0.16	−0.16
Performance-IQ	**0.84**	0.03	0.08
General-IQ	**0.97**	−0.07	−0.08
Digit-span	**0.56**	−0.21	0.3
CRT avg. RT	−0.1	**0.68**	0.17
Behavioral priming	−0.17	**0.69**	0.18
Verbal recognition d’	0.19	0.23	**0.87**
Face-Name memory	−0.37	−0.37	**0.51**

Table S4. PCA analysis of behavioral measures from Experiment 2

Component	Rotated sum of square loadings		
	Eigenvalue	% of variance	% of cumulative variance
1	2.80	28.0	28.0
2	1.59	15.9	43.9
3	1.55	15.5	59.4
4	1.39	13.9	73.3

Table S5. Rotated factor loading structure (Experiment 2; see Table S4)

	Component			
Behavioral measure	1	2	3	4
Checker avg. RT	−0.18	−0.03	**0.77**	0.14
Checker no response	−0.12	−0.07	**0.84**	−0.35
Verbal-IQ	**0.74**	−0.29	−0.31	−0.08
Performance-IQ	**0.85**	0.11	−0.04	−0.01
General-IQ	**0.93**	−0.13	−0.22	−0.07
Digit-span	**0.63**	−0.24	0.26	0.30
CRT avg. RT	−0.08	**0.76**	−0.11	−0.01
Behavioral priming	−0.14	**0.75**	0.03	0.07
Verbal recognition d’	0.24	0.36	−0.02	**0.79**
Face-Name memory	−0.41	−0.38	−0.16	**0.71**