Coherent Spontaneous Activity Identifies a Hippocampal-Parietal Memory Network

Justin L. Vincent,[1] Abraham Z. Snyder,[1,2] Michael D. Fox,[1] Benjamin J. Shannon,[3] Jessica R. Andrews,[3] Marcus E. Raichle,[1,2,4,5] and Randy L. Buckner[1,3,4,6,7,8]

[1]*Mallinckrodt Institute of Radiology,* [2]*Departments of Neurology,* [3]*Psychology,* [4]*Anatomy and Neurobiology,* and [5]*Biomedical Engineering, Washington University School of Medicine, St. Louis, Missouri;* [6]*Department of Psychology and Center for Brain Science, Harvard University, Cambridge, Massachusetts;* [7]*Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, Massachussetts;* and [8]*Howard Hughes Medical Institute, Chevy Chase, Maryland*

Vincent, Justin L., Abraham Z. Snyder, Michael D. Fox, Benjamin J. Shannon, Jessica R. Andrews, Marcus E. Raichle, and Randy L. Buckner. Coherent spontaneous activity identifies a hippocampal-parietal memory network. *J Neurophysiol* 96: 3517–3531, 2006. First published August 9, 2006; doi:10.1152/jn.00048.2006. Despite traditional theories emphasizing parietal contributions to spatial attention and sensory-motor integration, functional MRI (fMRI) experiments in normal subjects suggest that specific regions within parietal cortex may also participate in episodic memory. Here we examined correlations in spontaneous blood-oxygenation-level-dependent (BOLD) signal fluctuations in a resting state to identify the network associated with the hippocampal formation (HF) and determine whether parietal regions were elements of that network. In the absence of task, stimuli, or explicit mnemonic demands, robust correlations were observed between activity in the HF and several parietal regions (including precuneus, posterior cingulate, retrosplenial cortex, and bilateral inferior parietal lobule). These HF-correlated regions in parietal cortex were spatially distinct from those correlated with the motion-sensitive MT+ complex. Reanalysis of event-related fMRI studies of recognition memory showed that the regions spontaneously correlated with the HF (but not MT+) were also modulated during directed recollection. These regions showed greater activity to successfully recollected items as compared with other trial types. Together, these results associate specific regions of parietal cortex that are sensitive to successful recollection with the HF.

INTRODUCTION

Distinct regions within the parietal cortex are modulated during long-term memory retrieval (for a review, see Wagner et al. 2005). Specifically, greater activity in lateral and medial parietal regions has been repeatedly observed with functional magnetic resonance imaging (fMRI) when participants correctly recognize previously studied old items (hits) versus correctly identify new items (correct rejections). This parietal old/new effect (also called the "retrieval success effect") occurs regardless of whether the stimuli are lexical, graphic, or acoustic (Henson et al. 1999; Kahn et al. 2004; Konishi et al. 2000; Leube et al. 2003; McDermott et al. 2000; Shannon and Buckner 2004; Wheeler and Buckner 2003, 2004) and does not depend on response contingency (i.e., whether a motor response is made only to new vs. only to old items) (Shannon and Buckner 2004).

In the electrophysiological domain, event-related potential (ERP) experiments have demonstrated greater scalp positivity over parietal-temporal cortex in response to old versus new items (Donaldson and Rugg 1998; Rugg et al. 1998; Rugg and Wilding 2000).

Evidence further suggests that regions within parietal cortex are involved specifically in episodic retrieval. This possibility has emerged from studies employing the remember/know procedure (Gardiner and Richardson-Klavehn 2000; Tulving 1985), which distinguishes between trials eliciting recollection (when participants *remember* specific details of the earlier occurrence) versus trials eliciting only familiarity (when participants *know* that an item was encountered earlier but do not specifically remember its occurrence). Although there is debate in the recognition-memory literature regarding whether a categorical difference between recollection- and familiarity-based processes exists, both signal detection as well as dual-process models predict some form of increasing functional activity during retrieval of strong memories during remember judgments (Wixted and Stretch 2004). In line with this prediction, fMRI studies have demonstrated that specific regions within parietal cortex, including precuneus, posterior cingulate, and the inferior parietal lobule, show greater activity for remember relative to know judgments (Eldridge et al. 2000; Henson et al. 1999; Wheeler and Buckner 2004; see also Yonelinas et al. 2005). Likewise, it has been consistently observed that activity in medial and lateral parietal regions as well as parts of anterior temporal and medial prefrontal cortices are commonly associated with retrieval of autobiographical memories (i.e., episodic recall, remembering, or recollection) (Andreasen et al. 1995; Cabeza et al. 2004; Maguire and Mummery 1999; Maguire 2001).

Despite the preceding evidence, a role for parietal cortex is not contained in traditional accounts of memory impairment where results implicate medial temporal lobe and diencephalic structures (for reviews, see Aggleton and Brown 1999; Cohen and Eichenbaum 1995; Squire 1992). From the perspective of this more traditional view, it has remained tempting to ascribe changes in parietal cortex in memory paradigms to unaccounted-for elements of motor intention and/or visual-spatial attention. Thus despite evidence to the contrary, there remains a divide between traditional theories of episodic memory that focus on the

medial temporal lobe and associated diencephalic structures and human imaging studies, which expand this view to include contributions from the parietal cortex.

The present work sought to test the hypothesis that parietal cortex contains areas associated with the medial temporal lobe memory system in addition to the areas concerned with visual-spatial attention and sensory-motor integration (Andersen and Buneo 2002; Colby and Goldberg 1999; Corbetta and Shulman 2002; Heilman and Gonzalez Rothi 1993; Mesulam 1999). First, we determined whether there was coherent spontaneous activity between the hippocampal formation (HF) and regions of parietal cortex. The presence of such a correlation would establish a functional relationship between medial temporal and parietal structures. Second, we determined whether the functionally correlated regions in the HF and parietal cortex were also modulated during remembering. Together, these results would provide support for a hippocampal-parietal network associated with memory.

For this work we employed a novel approach based on the surprising observation that spontaneous, low-frequency (i.e., <0.1 Hz) fluctuations in the fMRI BOLD signal in the resting state exhibit patterns of coherence within specific networks of the human brain *in the absence of overt task performance* (e.g., Biswal et al. 1995; Fox et al. 2005; Greicius et al. 2003; Lowe et al. 2000). The presence of such precisely patterned spontaneous activity represents an important and underappreciated aspect of the brain's functional organization and provided us with an opportunity to assess in a new way the relationship between components of the brain systems important to memory, including the HF and parietal cortex.

More specifically, we sought to delineate the functional topography of parietal cortex by examining the voxel-wise correlations in spontaneous activity with seed regions of interest placed in the HF. We compared these results with correlations using seed regions of interest in the putative human middle temporal (MT+) complex. MT+ was chosen because of the known connections between MT and regions in posterior parietal cortex involved in sensory-motor integration and visual-spatial attention (Andersen et al. 1990; Maunsell and Van Essen 1983; Ungerleider and Desimone 1986). In this manner, cortical regions spontaneously correlated with the HF could be identified and distinguished from other parietal regions correlated with MT+ that likely relate to distinct processes. Functional response properties of the parietal regions identified from our analysis of spontaneous activity correlations then were explored in

a reanalysis of event-related fMRI studies of episodic memory retrieval. We hypothesized that parietal regions intrinsically correlated with the HF (as opposed to MT+) would be preferentially sensitive to episodic memory manipulations.

METHODS

Overview

A total of eight independent data sets and 111 participants were involved in the present study. We began by examining correlations in spontaneous BOLD fluctuations in four independent data sets (referred to as *data sets 1–4*), all of which only contained resting state data. No task was instructed. Correlation maps were computed for the HF and for MT+ to differentiate between regions associated with memory versus visual-motor processes. Across all four resting-state data sets, a qualitative dissociation between the MT+ and HF networks emerged, which were formally tested in *data sets 2* and *3* using regions of interest (ROI) defined in *data set 1*. These parietal regions identified from the spontaneous correlation maps then were used as a priori ROI in a reanalysis of two previously published event-related fMRI studies of recognition memory (Shannon and Buckner 2004; Wheeler and Buckner 2004). These two studies were selected because they contained manipulations that influenced the relative contributions of recollection and familiarity-based processes during retrieval. Finally, HF correlation maps were directly compared with a meta-analysis of four studies of recollection effects to determine the topographic overlap between spontaneous and evoked activity patterns (data from Dobbins et al. 2003; Kahn et al. 2004; Shannon and Buckner 2004; Wheeler and Buckner 2004; see Wagner et al. 2005). The correlation methods are described first and most extensively whereas methods used to reanalyze the previously reported event-related fMRI studies are described in less detail. All derived maps are shown in atlas space (Talairach and Tournoux 1988) either in slice format or projected onto the cortical surface using the software developed by Van Essen and colleagues (Van Essen 2005).

Participants

Forty-seven adults between the ages of 18 and 35 participated in the resting state correlation experiments yielding four independent data sets (Table 1). All participants had normal or corrected-to-normal vision and were right-handed, native English speakers. Participants were prescreened to exclude individuals with a history of significant neurologic or psychiatric conditions as well as those using psychoactive medications. All participants consented in accordance with the

TABLE 1. *Participants and MR scanning parameters*

	Data Set 1	Data Set 2	Data Set 3	Data set 4
n	12 (5 male)	13 (7 male)	12 (7 male)	10 (4 male)
Age, yr	23 ± 3.1	24 ± 2.3	24 ± 3	23.2 ± 2.6
Field strength, T	1.5	1.5	1.5	3
BOLD TR, s	2.5	2.36	2.36	3.01
BOLD TE, ms	37	37	37	25
BOLD flip angle, °	90	90	90	90
Voxel size, mm	3.75 × 3.75 × 8	3.75 × 3.75 × 8	3.75 × 3.75 × 8	4 × 4 × 4
Time points per run	128	110	110	110
No. runs	2	2	2	3

Data set 1 has been previously published as a control data set in Konishi et al. (2000). *Data set 4* has been previously published in Fox et al. (2005) for analysis of intrinsic correlations. The two scanners employed in these studies were the 1.5 T Vision scanner and the 3 T Allegra scanner manufactured by Siemens, Erlangen, Germany. Values for ages are means ± SD. MR, magnetic resonance; BOLD, blood-oxygen-level dependent; TR, repetition time; TE, echo time.

Washington University Human Studies Committee guidelines and received monetary compensation for participation.

Data acquisition and preprocessing

MR scanning was performed at the Washington University School of Medicine using either a 1.5 T Vision or 3 T Allegra scanner (Siemens, Erlangen, Germany) (Table 1). The fMRI data were acquired using an asymmetric spin-echo, echo-planar sequence sensitive to BOLD contrast (Kwong et al. 1992; Ogawa et al. 1992). All studies included whole brain coverage with contiguous slices. Sequence details for resting state correlation experiments are listed in Table 1. Structural data (for atlas transformation) included a high resolution sagittal, T1-weighted magnetization prepared rapid gradient echo (MP-RAGE) scan in all resting state data sets and additionally one T2-weighted fast spin echo scan in *data set 4.*

For the entire duration of all scans, participants simply fixated on a visual crosshair centered on a screen. No task was instructed. The visual stimulus was generated on an Apple Power Macintosh G4 computer (Apple Computer, Cupertino, CA) using PsyScope software (Cohen et al. 1993) and was projected onto a screen positioned at the head of the magnet bore. Participants viewed the screen through a mirror attached to the head coil. Headphones were used for communication and to attenuate scanner noise.

Resting-state data were preprocessed using procedures common in conventional fMRI studies to reduce scanner artifacts, correct for head motion, and transform the data into a standard atlas space. These preprocessing steps included compensation of systematic, slice-dependent time shifts using sinc interpolation, elimination of systematic odd-even slice intensity differences due to interleaved acquisition, rigid body correction for head motion within and across runs, and normalization for global mean signal intensity across runs. The third step provided a record of head position within fMRI runs that was later used as a nuisance regressor in the correlation analysis (see following text).

Atlas registration was achieved by computing affine transforms connecting the first image volume of the fMRI run (averaged over all runs after cross-run realignment) with the T1-weighted structural images (Ojemann et al. 1997). Our atlas representative template includes MP-RAGE data from 12 normal individuals and was made to conform to the Talairach and Tournoux atlas (1988) according to the spatial normalization method described by Lancaster and colleagues (Lancaster et al. 1995; Maccotta et al. 2001). The final preprocessing step combined motion correction and atlas transformation in one step to yield a motion-corrected volumetric time series resampled to 2-mm cubic voxels.

Correlation analysis

The objective of the correlation analysis was to identify regions of cortex intrinsically correlated with either the HF or area MT+. The basic procedure consisted of computing, for all brain voxels, the correlation coefficient against the BOLD time series extracted from a particular seed region (Biswal et al. 1995; Fox et al. 2005). We computed correlation maps for HF and MT+ seed regions in each hemisphere (4 seed regions in total). All seed regions were ~2 cm³ spheres centered on coordinates in stereotaxic atlas space (Table 2). The MT+ seed regions were centered on coordinates obtained from a previous fMRI study of coherent motion detection (Corbetta et al. 2002). The HF seed regions were centered on coordinates in the anterior hippocampus identified by peak search of the correlation map of retrosplenial cortex obtained in a separate data set (Lustig and Buckner 2004) using the present techniques (see following text). Limitations of resolution, spatial blurring as well as our method of defining the regions make their true boundaries ambiguous. For instance, the HF seed regions likely included the dentate gyrus, subiculum, posterior entorhinal cortex, and the parahippocampal gy-

TABLE 2. *Regions of interest*

	x	y	z	Volume, cm³
MT + seeds				
Left middle temporal (L MT+)	−45	−69	−2	2.01
Right middle temporal (R MT+)	45	−69	−4	2.01
MT + correlated regions				
Left post-central gyrus	−51	−27	32	3.71
Right post-central gyrus	55	−23	40	3.50
Left superior parietal cortex	−25	−53	52	3.72
Right superior parietal cortex	25	−57	52	3.73
Left ventral intraparietal cortex	−25	−81	22	3.58
Right ventral intraparietal cortex	27	−73	28	3.58
HF seeds				
Left hippocampal formation (L HF)	−21	−25	−14	1.99
Right hippocampal formation (R HF)	23	−23	−14	1.92
HF correlated regions				
Left inferior parietal lobule	−39	−73	42	3.67
Right inferior parietal lobule	45	−69	40	3.74
Left posterior cingulate	−5	−37	36	3.52
Left ventral precuneus complex	−3	−63	24	3.86
Left retrosplenial cortex	−5	−51	8	3.52

rus in addition to hippocampus proper where the region was centered. The MT+ seed regions may include areas surrounding the MT+ complex.

Correlation maps were computed for all four seed regions in each of four separate data sets. Use of multiple data sets allowed assessment of the reliability of intrinsic correlations across a variety of data samples and acquisition conditions. In particular, resting state *data sets 1–3* were acquired at 1.5 T using relatively coarse spatial resolution (8 mm slices; 2.36 or 2.50 s volume TR), whereas *data set 4* was acquired at 3 T using higher spatial resolution (4 mm slices) but somewhat lower temporal sampling density (3.01-s volume TR; Table 1). *Data sets 2* and *3* were combined for some purposes as they represent an age- and gender-matched split of one homogenous experimental group. The *data set 4* contained greater spatial resolution and therefore was used to examine correlation maps in individual subjects.

Correlation maps were generated following procedures of Fox and colleagues (2005). Briefly, the preprocessed functional data (in atlas space) were passed through an additional series of processing steps, the effects of which are illustrated in Fig. 1. First, for each voxel, temporal filtering removed constant offsets and linear trends over each run while retaining frequencies in the 0.009- to 0.08-Hz band. Data were spatially smoothed using a 6-mm full-width half-maximum Gaussian blur. Several sources of spurious or regionally nonspecific variance then were removed by regression including: six parameters obtained by rigid body head motion correction, the signal averaged over the whole-brain, the signal averaged over the lateral ventricles, and the signal averaged over a region centered in the deep cerebral white matter. Temporally shifted versions of these waveforms were also removed by inclusion in the linear system of the first temporal derivatives (computed by backward differences). In this manner, variance unlikely to be involved in spatially specific regional correlations was removed from the data. The global (whole brain) signal has recently been shown to correlate with respiration-induced fMRI signal fluctuations (Birn et al. 2006). Removing the global signal has two consequences: the distribution of correlation coefficients throughout the brain is shifted such that there are roughly equal numbers of positive and negative correlations and as a result of this process, testing a positive correlation coefficient for statistical significance against the null hypothesis of $r = 0$ becomes appropriate. Removing signals correlated with ventricles and white matter is an additional means of reducing nonneuronal contributions to BOLD correlations (Bartels and Zeki 2005; Fox et al. 2005).
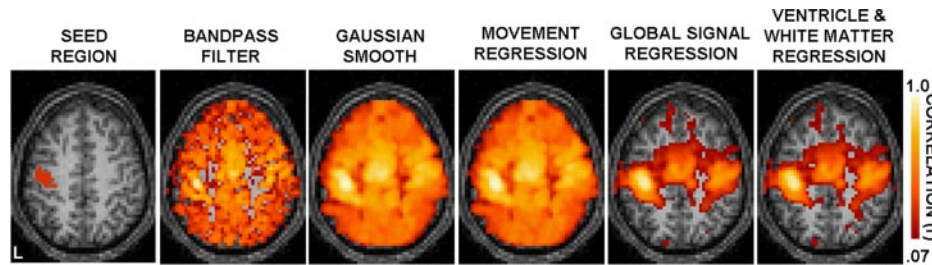
FIG. 1.   Correlation processing steps are illustrated for a motor region. Data from a representative participant are displayed in the atlas space of Talairach and Tournoux (1988) ($z = 48$ mm). The left side of the brain is on the left. Correlations with the seed motor region are shown after each successive processing step as follows band-pass temporal filter (0.009 Hz $< f <$ 0.08 Hz), Gaussian spatial smooth (6 mm FWHM), removal by regression of movement, mean global signal, and mean ventricle and white-matter signals. Each successive step increases the sensitivity and specificity of the correlations. Transverse correlation images in this paper are shown in similar atlas format following completion of all processing steps.

Several closely related formulas were used in the present correlation analyses. In what follows, $s(t)$ represents the signal averaged over a given seed region and $I(x, t)$ represents the signal at locus x and time t. The regression map, $\beta(x)$, was computed as

$$\beta(x) = \frac{(1/T)\int s(t)I(x,t)\mathrm{d}t}{\sigma_s^2}$$

where T is the duration of the entire time series, generally including several concatenated runs (excluding pre-steady-state time points at run starts). Correlation maps were computed as

$$r(x) = \frac{\sigma_s\beta(x)}{\sigma_{I(t)}} = \frac{(1/T)\int s(t)I(x,t)\mathrm{d}t}{\sigma_s\sigma_{I(x)}}$$

where $r(x)$ is the correlation of locus x against $s(t)$. The factors, σ_s and $\sigma_{I(x)}$, are the SDs of their respective signals, e.g., $T\sigma_s^2 = \int s^2(t)\mathrm{d}t$. Inclusion of these factors in the $r(x)$ formula ensures that $r(x)$ is dimensionless and confined to values in the range ± 1 (Schwartz inequality). The band-pass-filtering step causes the time average of the signal at every locus to be identically zero ($\int I(x, t)\mathrm{d}t = 0$). Accordingly, the present $r(x)$ formula omits differences from the mean, as is written in the preceding text.

Correlation maps were converted to z values using Fisher's r-to-z transformation (Zar 1996)

$$z(x) = 0.5 \ln\left(\frac{1 + r(x)}{1 - r(x)}\right)$$

This transformation generates voxel-wise values that are approximately normally distributed across individuals in a homogenous population. Individual $z(x)$ maps were averaged over subjects to obtain correlation maps representing the four data sets listed in Table 1.

To assess voxel-wise statistical significance at the group level, individual regression coefficient maps, $\beta(x)$, were entered into conventional random effects analyses. A significance map was computed for each data set and thresholded at a significance level of $P < 0.05$. We chose a liberal threshold to allow full exploration of the correlation network with the additional caveat that all interpreted patterns were consistent across data sets. For this analysis, a convergence map then was constructed by counting, at each voxel, the number of data sets in which the correlation with the seed region was statistically significant. Voxels meeting this criterion in two of four data sets were projected on the left cerebral hemisphere of the average fiducial PALS surface using Caret software (Van Essen 2005). As the results will show, the topography of the correlation patterns is highly reliable across data sets (usually independently reaching significance in all 4 data sets) and individual subjects.

Localization of a priori regions of interest

A central goal of the analysis was to identify parietal regions intrinsically correlated with either the HF or MT+. Regions were defined from the *data set 1* correlation maps and then used for regional statistical analyses in additional independent data sets. This strategy represents a conservative approach to the problem of multiple comparisons and allows for unbiased measurement of correlation strength (Buckner et al. 1995).

A group-averaged, Fisher's z transformed correlation map was generated for left HF, right HF, left MT+, and right MT+ in *data set 1*. These maps were collapsed over hemisphere by arithmetic averaging to obtain two maps, one derived from intrinsic correlations with the HF, the other derived from intrinsic correlations with area MT+. Peak search of the HF and MT+ correlation maps identified several local maxima within parietal cortex. ROI were defined around these peaks to include volumes of $\sim$3.6 cm^3. Two sets of parietal cortex regions were created (Table 2): one set (5 regions) represented parietal regions correlated with HF; the other set (6 regions) represented parietal regions correlated with MT+. These regions then were carried forward as a priori ROI for hypothesis-driven tests on the remaining 1.5 T resting state data (*data sets 2 and 3*) as well as the event-related fMRI data (see following text).

ANOVA was used to formally test several features of the regional correlation results in the combined *data sets 2 and 3*. For all parietal ROI identified from *data set 1* correlation maps (Table 2), a one-way ANOVA was conducted to test the effect of seed region (HF vs. MT+). For each region, secondary Bonferroni-Dunn analyses tested the effect of lateralization, i.e., dependence of correlation on the hemisphere containing the seed. Next, we asked if there was a interaction between the parietal networks and the seed regions with a two-way ANOVA, including parietal ROI class (HF correlated regions vs. MT+ correlated regions) by seed class (HF vs. MT+).

Regional analysis of remembering

As the results will show, HF and MT+ correlation maps were reliable in dissociating regions of parietal cortex. We then asked if the regions in parietal cortex intrinsically correlated with the HF were modulated by successful memory retrieval (Wagner et al. 2005). This question was directly addressed using the a priori ROI localized from the correlation maps obtained from *data set 1* (Table 2). More generally, we tested the hypothesis that regions defined based on correlations in spontaneous fluctuations of the BOLD signal have predictive value regarding the localization of task-related functional responses.

We reanalyzed two previously published event-related fMRI studies of episodic memory retrieval using regions defined from the intrinsic correlation maps obtained from *data set 1*. The first study (Wheeler and Buckner 2004) was based on the remember/know procedure, which distinguishes between recollection (remember) ver-

sus familiarity (know) (Gardiner and Richardson-Klavehn 2000; Tulving 1985). Participants ($n = 20$) studied words paired either with pictures or sounds. During fMRI, the subjects viewed words and indicated, by pressing one of three buttons, whether each item was recognized and accompanied by recollection of the paired picture or sound (remember), recognized without recollection of the paired associate (know), or new (correct rejection). Only correct responses were analyzed. Additional details are given in Wheeler and Buckner (2004).

The second study (Shannon and Buckner 2004) examined old/new recognition after manipulating levels of processing in an incidental encoding task. In the encoding phase, participants ($n = 16$) were shown a series of words and performed either deep (abstract/concrete) or shallow (uppercase/lowercase classification) encoding tasks. The deep versus shallow encoding procedure was used to encourage recollection- versus familiarity- based retrieval (Yonelinas 2002). During fMRI, the subjects were presented with a mixed list of old and new items and indicated by button press whether each items was old or new. The deep/shallow experiment thus yielded three types of event related responses (excluding errors): deep hit, shallow hit, and correct rejection. Additional details are given in Shannon and Buckner (2004).

Event-related fMRI responses were constructed over eight time points by selectively averaging modulations relative to the (fixation only) baseline (Dale and Buckner 1997). These responses were averaged within each region in Table 2 to obtain regional waveforms expressed as percent signal change. Quantitative estimates of response magnitude were calculated for each participant (for each trial type) as the difference between time points $3 + 4$ (representing the peak) minus time points $1 + 8$ (representing the baseline). Response magnitude estimates for each participant then were entered into ANOVA that explored effects of trial type.

R E S U L T S

MT+ and HF correlate with distinct cortical networks

The four seed regions and their associated correlation maps are shown for all four data sets in Fig. 2. In all data sets, regions strongly correlated with MT+ extended from the ventral intraparietal sulcus to the postcentral gyrus. Additional regions of strong MT+ correlation included parts of the precentral gyrus corresponding to the putative frontal eye fields. In contrast, the HF seed regions were correlated with the inferior parietal lobule, retrosplenial cortex extending into posterior cingulate and precuneus, medial prefrontal cortex, superior frontal cortex, and lateral temporal cortex extending to the temporal pole. Three features of MT+ versus HF correlation maps are evident in Fig. 2. First, the patterns of correlations were highly similar in all 4 data sets. The reliability of intrinsic correlations will be more formally addressed in the following text (Figs. 4 and 5). Second, seed regions in MT+ versus HF gave rise to very different correlation maps. This result will shortly be made more explicit in Figs. 3–5. Third, in overview, the intrinsic correlation maps were largely symmetric regardless of the hemisphere containing the seed region.

MT+ and HF correlations are robust in individual participants

Figure 3 shows significance maps for the correlations of left MT+ and left HF in four representative participants from *data set 4* (3 T data). Overall, individuals demonstrated similar patterns of correlation to the group maps shown in Fig. 2. Minimal overlap of left MT+ and left HF correlation maps is
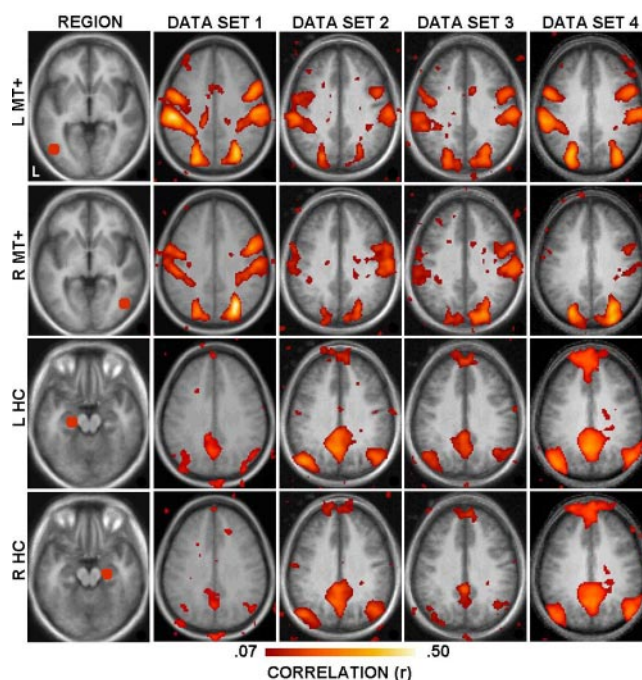

FIG. 2. Correlation maps are illustrated for the 4 seed regions. L MT+ and R MT+ are left and right regions defined around the MT+ complex; L HF and R HF are left and right regions defined within the hippocampal formation. Each image shows the mean voxel-wise correlation to the specific region displayed on the left. Four independent participant groups were analyzed (*data sets 1–4;* Table 1). Group means were obtained after within-subject transformation using Fisher's *r-*to-*z.* The mean *z* then was converted back to an *r* value for display purposes. Only positive correlations are shown. Correlation maps are overlaid onto the average anatomic image for each group (z = 32 mm). Note the consistency of the difference between correlation with MT+ vs. HF seed regions and also the reproducibility of the topography across independent data sets.

apparent in Fig. 3*C*. Correlations with MT+ were found along the intraparietal sulcus, the precentral sulcus, and dorsolateral prefrontal cortex. The HF was correlated with the retrosplenial, posterior cingulate, precuneus, medial prefrontal cortex as well as posterior parietal regions that were largely lateral to the intraparietal sulcus. These individual analyses demonstrate that correlations are robust even in single participants. Moreover, close inspection of the maps suggests that individual variation in gyral anatomy is reflected in the detailed correlation map topography (e.g., compare, in row 2, the configuration of the labeled intraparietal sulcus in relation to left MT+ correlation maps).

Maps of MT+ and HF correlation are reliable

A convergence analysis was performed to visualize the cortical topography of regions that were significantly correlated with either the left MT+ or left HF across all four data sets. Figure 4 displays the results of the left MT+ and HF convergence analysis (see also supplementary Figs. 1 and 2.[1]) Regions consistently correlated with left MT+ included MT+ extending in an arc along intraparietal and superior parietal cortex to postcentral gyrus, premotor cortex, insula, dorsolateral prefrontal cortex, and extrastriate cortex. In contrast, the

---

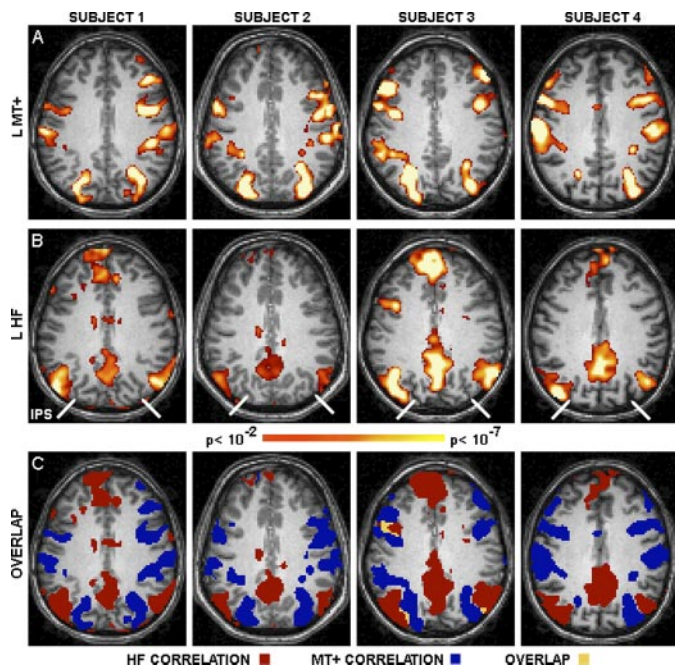[1] The online version of this article contains supplemental data.

FIG. 3. MT+ and HF correlations are robust in individual participants and reveal anatomic dissociation. The intrinsic correlation maps of 4 representative participants from *data set 4* are superimposed on their own anatomical images (z = 32 mm). Correlation maps are shown for the left MT+ complex (L MT+; *A*), left hippocampal formation (L HF; *B*), and the overlap of L MT+ and L HF (*C*). The HF and MT+ complex correlate with topographically distinct regions in lateral parietal cortex. The location of the intraparietal sulcus (IPS) is provided for reference (white lines in *B*). Note that the MT+ correlation map closely matches the configuration of the IPS. In contrast, parietal correlations with the hippocampal formation are largely lateral to IPS and along the midline.

left HF convergence analysis included the hippocampus, the retrosplenial cortex, posterior cingulate gyrus, precuneus, medial prefrontal cortex, lateral temporal cortex extending to the

temporal pole as well as dorsal prefrontal regions (including BA 8 and 9). Critically for the primary focus of this paper, the left HF was correlated with a region of the posterior parietal cortex lateral to the intraparietal sulcus in all four data sets. Note that this region is almost completely surrounded by regions correlated with MT+.

Localization of a priori regions

Parietal regions derived by peak search in resting state *data set 1* are listed in Table 2. MT+ correlated regions included the postcentral gyrus, superior parietal cortex (at or near putative human lateral intraparietal cortex, LIP), and ventral intraparietal cortex bilaterally. HF correlated regions in parietal cortex included bilateral inferior parietal lobule, posterior cingulate, ventral precuneus complex, and retrosplenial cortex. These regions were used in subsequent regional analyses of spontaneous and event-related fMRI data.

Specific parietal regions are selectively correlated with HF but not MT+

Figure 5 displays quantitative results obtained in resting state *data sets 2* and *3* evaluated in regions defined on the basis of *data set 1* (Table 2). The *top* and *bottom* panels (*A* and *B,* respectively) show regions predicted to correlate with MT+ and the HF. The bar graphs reflect mean *z* values (after Fisher's *r*-to-*z* transform) averaged over subjects. All regions predicted to associate with MT+ did so and vice versa for the HF.

Regional ANOVA revealed a significant main effect of seed region in all parietal ROI (all $P < 0.001$). Post hoc Bonferroni-Dunn analyses explored the six possible pairwise seed region comparisons. Comparison of left versus right MT+ and left versus right HF yielded no statistically significant effect of hemisphere in any ROI. In contrast, all four pairings of MT+ with HF seed regions were significant in all ROI (all $P < 0.001$). The two-way, parietal ROI class (HF correlated vs.
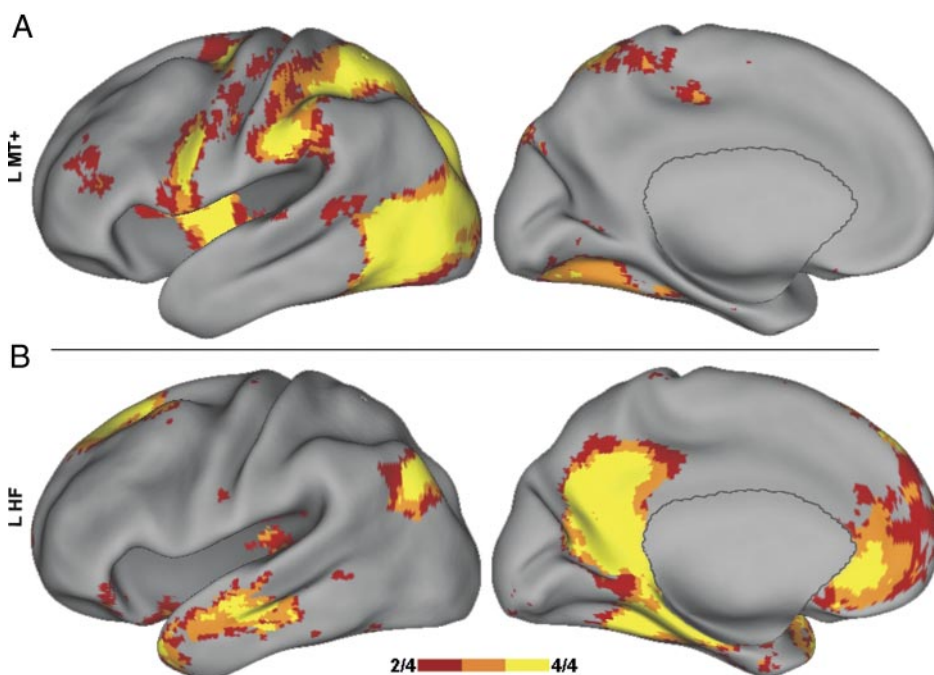

FIG. 4. Convergence analyses illustrate the cortical topography of regions that correlate with left MT+ complex (*A*) and the left hippocampal formation (L HF; *B*). Convergent correlations are displayed on the lateral and medial surface of the left cerebral hemisphere. The correlation with seed regions were identified at a threshold of $P < 0.05$ in each of the 4 independent data sets. Voxels over threshold in 2 of 4 data sets are shown in dark red; 3 of 4 data sets are shown in orange; 4 of 4 are shown in yellow. L MT+ convergence is observed in dorsolateral prefrontal cortex, premotor cortex, insula, as well as MT+ extending along the intraparietal and superior parietal cortex to postcentral gyrus. L HF convergence is observed in the inferior parietal lobule, ventral medial prefrontal, lateral temporal, as well as along the medial surface extending from the retrosplenial cortex into posterior cingulate.
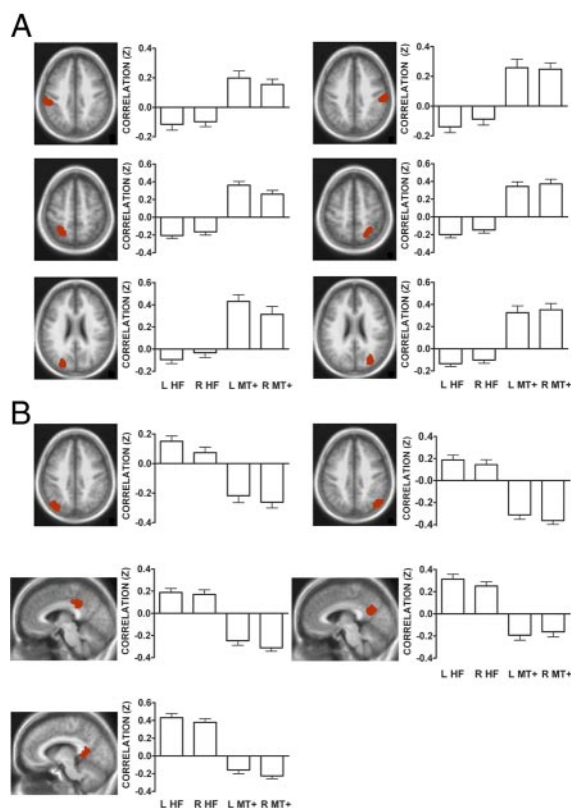
FIG. 5. Correlation strengths reveal a double-dissociation between distinct parietal regions correlated with the hippocampal formation (HF) and the MT+ complex. Bars represent the correlation strength (mean *z* after within-subject transformation using Fisher's *r*-to-*z*) for data combined over *data sets 2* and *3* (composite *n* = 25). Error bars show SE. Each panel represents the correlation strengths for a distinct parietal region defined independently from *data set 1* (Table 2). Regions are grouped according to those positively correlated with L MT+ and R MT+ (*A*) or those positively correlated with L HF and R HF (*B*). All images are transverse sections except those on the midline, which are displayed on the mid-sagittal plane to illustrate the topography along the posterior cingulate, ventral precuneus, and retrosplenial cortex.

MT+ correlated) × seed class (HF vs. MT+) ANOVA yielded a significant interaction [$F(1,24) = 123.18$, $P < 0.001$]. This result is not surprising given the robustness of the effects but is not mandated as the regional definitions were constructed independently (*data set 1*) from the test data (*data sets 2* and *3*). These results formally demonstrate that the identified lateral and medial parietal regions dissociate based on their differential correlation with HF and MT+. Moreover, we found that the parietal regions that correlated with the HF were negatively correlated with MT+ (Fig. 5, supplementary Figs. 1 and 2), which is concordant with the results of Fox and colleagues (2005) and Fransson (2005).

Parietal regions correlated with the HF are selectively activated by recollection

The preceding analyses revealed a specific set of parietal regions intrinsically correlated with the HF. We hypothesized that these regions would be recruited during episodic memory retrieval. Other parietal regions correlated with MT+ were hypothesized to be part of a separate network involved in visual-spatial attention and not episodic memory. We tested these predictions by using the ROI defined from the intrinsic correlation maps obtained

from *data set 1* (Table 2) to reanalyze two prior event-related fMRI studies of episodic memory retrieval (Shannon and Buckner 2004; Wheeler and Buckner 2004).

The regional response time courses are shown in Fig. 6. In the remember/know experiment, all five HF correlated regions showed a significant effect of trial type (memory condition). Importantly, all showed greater REMEMBER minus KNOW responses (all $P < 0.05$). The REMEMBER minus CR contrast also was significant ($P < 0.05$) in four of five of the HF correlated regions, including left and right inferior parietal lobule, retrosplenial cortex, and posterior cingulate. In contrast, there was neither a main effect of trial type nor a direct effect of REMEMBER minus KNOW or KNOW minus CR in any MT+ correlated region.

In the deep/shallow experiment, four of five HF correlated regions including left inferior parietal lobule, retrosplenial cortex, posterior cingulate, and ventral precuneus showed a significant effect of trial type. Significantly greater DEEP minus SHALLOW responses were found in posterior cingulate and ventral precuneus (both, $P < 0.05$). The DEEP minus CR comparison yielded significantly greater positive BOLD modulation in four of five HF correlated regions including left inferior parietal lobule, retrosplenial cortex, posterior cingulate, and ventral precuneus (all $P \leq 0.001$). The SHALLOW minus CR contrast was generally positive in these regions but this effect was statistically significant only in the left inferior parietal lobule [$t(15) = 2.19$, $P < 0.05$]. The regions correlated with MT+ showed neither a main effect of trial type nor a direct effect of DEEP minus SHALLOW, DEEP minus CR, or SHALLOW minus CR.

HF is activated by remembering

We also explored fMRI responses in the HF and MT+ seed regions themselves to directly test whether they are modulated by episodic memory demands. The regional response time courses are shown in Fig. 7. This analysis defined the HF region on the basis of functional correlations with retrosplenial cortex. It therefore is of general interest to know whether this type of HF localization accurately identified regions modulated by memory demands in conventional event-related fMRI. The HF was strongly modulated by remember/know paradigm. In the remember/know study, both the left and right HF showed a significant effect of trial type ($P < 0.001$). The REMEMBER minus CR contrast yielded significantly positive responses for the HF bilaterally (both $P < 0.05$). The KNOW condition produced significantly less activity than CR (both $P < 0.05$). The REMEMBER minus KNOW contrast therefore was significant in the HF bilaterally (both $P < 0.001$). With respect to MT+ in the remember/know experiment, there was a significant main effect of trial type in the left hemisphere. The KNOW condition produced significantly less activity than CR ($P < 0.001$) on the left, whereas the REMEMBER minus KNOW contrast was significantly positive ($P < 0.05$). Otherwise, MT+ showed no significant task dependencies in the remember/know experiment in either hemisphere. In the deep/shallow experiment, none of the seed regions showed a significant effect of trial type.
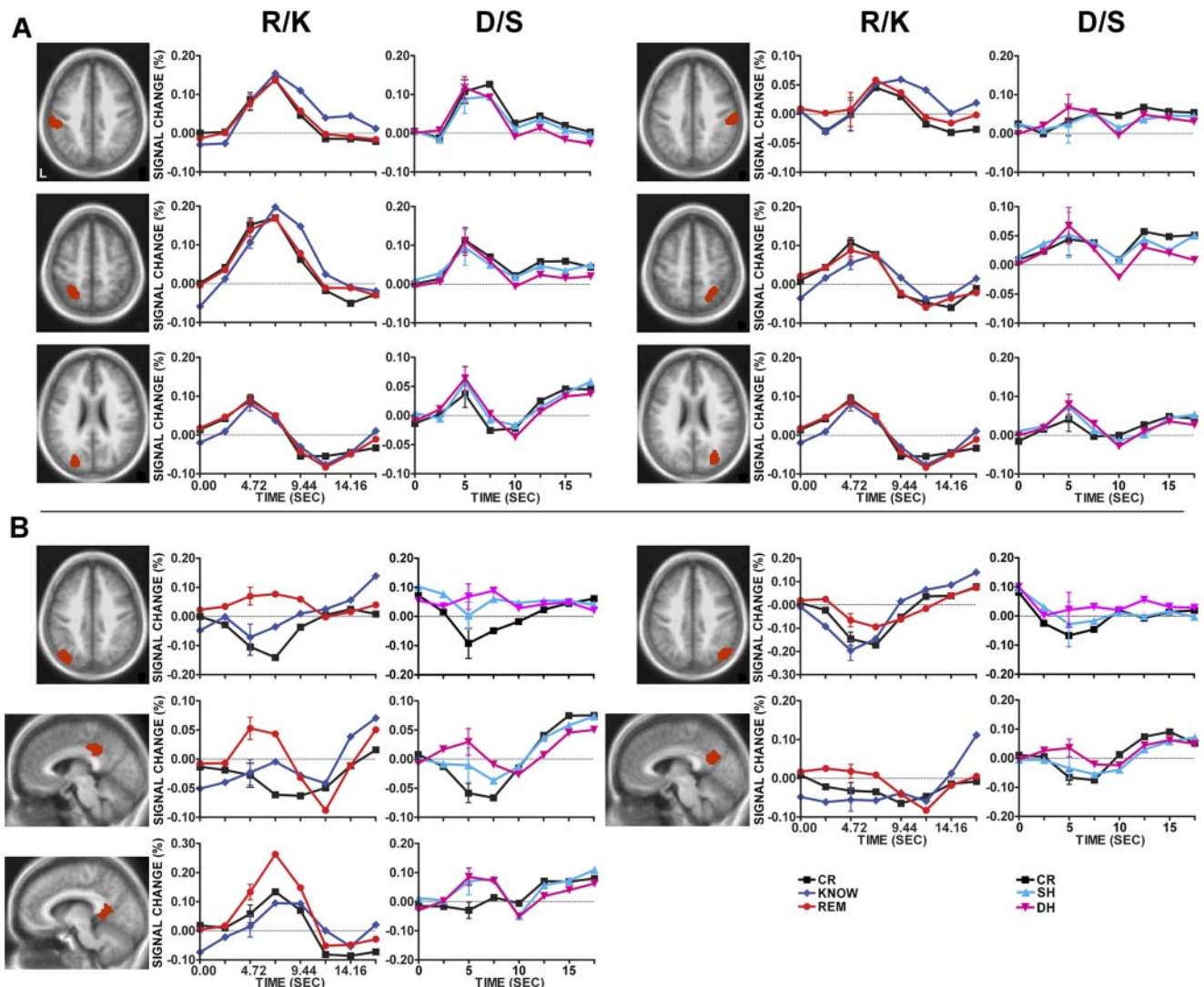
FIG. 6. The 2 groups of parietal regions demonstrate differential event-related fMRI responses during remembering. Regions are from Fig. 5 and include those that correlate with L MT+ and R MT+ (*A*) and those that correlate with L HF and R HF (*B*). Retrieval responses are plotted for each region using data from a remember/know paradigm (Wheeler and Buckner 2004) and a recognition paradigm following deep and shallow encoding (Shannon and Buckner 2004). For each experiment, the time courses of responses evoked by three event types are shown. Error bars over time point 3 show standard error of the mean. Remember/know (R/K) experiment: correct rejection (CR), know (KNOW), remember (REM). Deep/shallow (D/S) experiment: correct rejection (CR), shallow hit (SH), deep hit (DH). Responses are in percent signal change from a fixation baseline estimated for 8 time points. Note that parietal regions intrinsically correlated with MT+ show minimal differential responses to memory manipulations. In contrast, parietal regions derived from correlation with HF consistently show differential modulation during remembering. Statistical analyses are given in RESULTS.

HF correlation map overlaps with regions responsive to recollection success

The preceding analyses demonstrate that parietal regions correlated with the HF during maintained fixation (Rest) are modulated by memory demands in event-related fMRI. These results additionally provide evidence that parietal regions correlated with the HF include those involved in episodic memory. However, the results presented to this point leave unclear the degree to which those regions showing event-related effects associated with successful recollection overlap those associated with HF correlation. To address this issue, we compared the present left HF correlation convergence map to a meta-analysis of four event-related fMRI studies of successful recollection (displayed in Fig. 3 of Wagner et al. 2005). For the meta-analysis of successful recollection, a map was con-

structed that showed regions responding with greater activity for remember versus know recognition trials (Wheeler and Buckner 2004), source-hit versus source-miss trials (Dobbins et al. 2003; Kahn et al. 2004), and recognition following deep versus shallow encoding (Shannon and Buckner 2004). Results are displayed in Fig. 8 and reveal a high degree of topographic overlap between the intrinsically defined HF network and the recollection success maps.

DISCUSSION

This work reports an extensive investigation of the spontaneous activity correlations of seed regions in the HF and area MT+. The main finding is that specific regions within parietal cortex are correlated with the HF as opposed to MT+ and modulated by memory demands in event-related fMRI para-
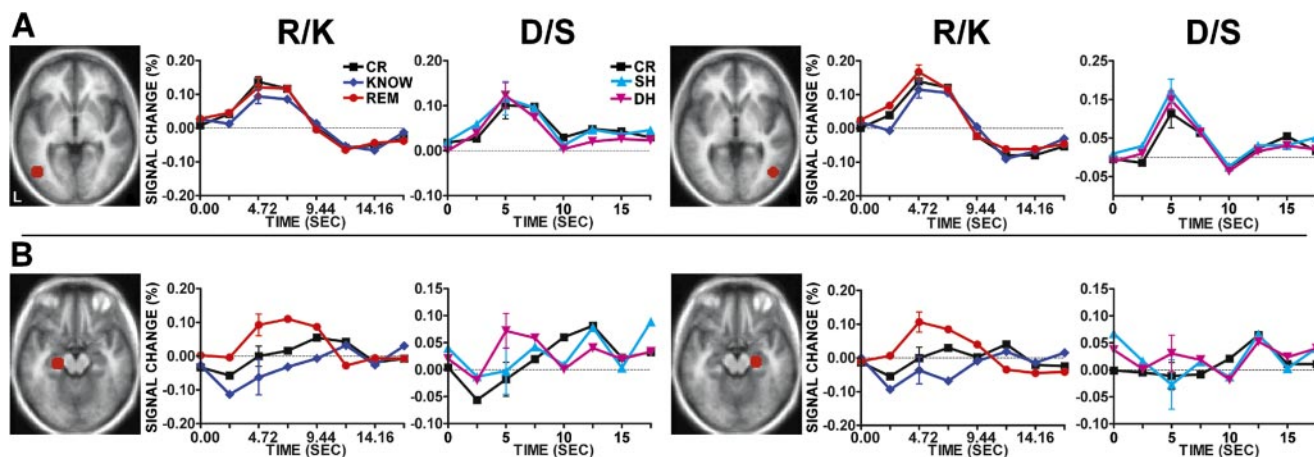
FIG. 7. MT+ and HF demonstrate differential event-related fMRI responses during remembering. The format is identical to Fig. 6. The seed regions used to drive the correlation analyses show dissociation based on mnemonic responses. The HF was consistently more sensitive to mnemonic task manipulations than MT+. Statistical analyses are given in RESULTS.

digms. These networks were visualized in individual participants (Fig. 3), group averages (Fig. 2), and were convergent across multiple data sets (Fig. 4). The HF and area MT+ were associated with clear, reproducible, and disjoint cortical networks.

Using independent component analysis during a low-level sensory-motor paradigm, Greicius and colleagues (2004) first noted that the HF appeared in the same component as medial parietal, lateral parietal, and medial prefrontal cortex, a network of brain regions that has been repeatedly noted to decrease its activity during the performance of a wide variety of goal directed tasks (Andreasen et al. 1995; Binder et al. 1999; Mazoyer et al. 2001; McKiernan et al. 2003; Shulman et al. 1997; for discussion, see Raichle et al. 2001). This initial observation was reinforced by the presence of HF correlations arising from spontaneous BOLD signal fluctuations when seed regions were placed in the posterior cingulate, precuneus, lateral parietal, and medial prefrontal cortices (Fox et al. 2005; Fransson 2005). Our results compliment these earlier studies by demonstrating that when a seed region is placed in the hippocampal formation itself, a similar topography of medial and lateral parietal as well as medial prefrontal and anterior temporal regions emerges.

Our observed correlations with a seed region in MT+ are also consistent with previous results with an MT+ seed (Fox et al. 2005) and correspond well with the correlations associated with seed regions in the intraparietal sulcus and the frontal eye fields (Fox et al. 2005). This network includes the dorsal frontoparietal system associated with goal directed (external) attention (Corbetta and Shulman 2002) and likely includes the putative human homologue of LIP (Sereno et al. 2001).

These resting state activity patterns suggest an ongoing functional relationship between regions in parietal cortex and the hippocampal formation. These regions are spatially distinct from those traditionally associated with visual-spatial attention and motor intention as revealed by comparing them with the functional correlations associated with MT+.

Spontaneous BOLD fluctuations and spontaneous cognition

Because our findings are based in significant measure on a novel imaging approach (i.e., the use of spontaneous fluctuations in the fMRI BOLD signal to probe network coherences in the resting brain), we anticipate that some will have concerns regarding their interpretation. This relates to the possible role of spontaneous cognition occurring in our subjects.
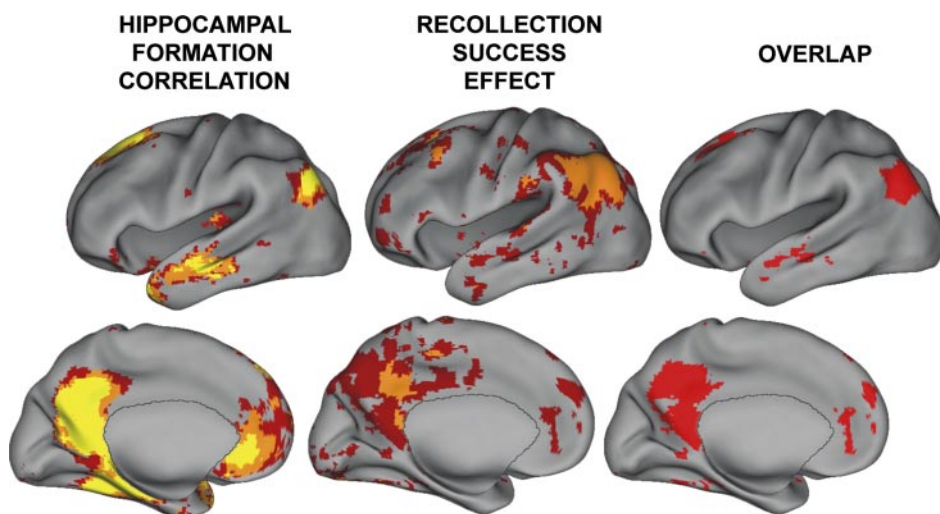

FIG. 8. Correlations with the hippocampal formation are topographically similar to recollection success effects. Images display the convergence map of hippocampal formation correlation (*left;* from Fig. 4), a convergence analysis of event-related fMRI studies that target recollection success (*middle*), and the overlap of the hippocampal formation correlation and recollection success effect (*right*). The recollection success effect is defined as greater activation during retrieval associated with a high level of recollection as compared with hits based preferentially on familiarity (adapted from Wagner et al. 2005). Four independent event-related fMRI data sets contributed to the recollection success effect. Color scale is the same as in Fig. 4. Regions of overlap extend to the superior prefrontal cortex, inferior parietal lobule as well as prominently along the medial surface extending from the retrosplenial cortex into posterior cingulate.

Some have argued that spontaneous and task-evoked activities represent much the same thing, functional activations. As a result, that which we learn from the former is not particularly interesting or unique and suffers from the fact that we do not know what type of cognition we are studying. We recognize that this concern is shared by many who have worried that using states such as visual fixation or eyes-closed "rest" in awake individuals injects uncertainty in the interpretation of data when comparisons are made with tasks involving specific stimuli and measured outputs (e.g., see Martin 1999; Stark and Squire 2001). Here we use such unconstrained states, and, in some sense consistent with these concerns, we observe the presence of highly organized networks typically found in brain-mapping studies involving specific tasks and constrained control states. In our case, functional imaging studies of episodic recall/recollection have documented much the same network architecture we see reflected in patterns of spontaneous BOLD activity (e.g., see review material in Cabeza et al. 2004; Maguire 2001; Wagner et al. 2005).

Although unconstrained cognition or behavior may well account for some part of spontaneous BOLD activity, there are reasons to believe that this activity likely reflects additional phenomena as well. We offer several observations in support of this assertion. *First*, coherent spontaneous activity is continuously present throughout the CNS even under anesthesia (Haider et al. 2006; Kenet et al. 2003; Kiviniemi et al. 2000). *Second*, coherent spontaneous fluctuations have been observed within systems associated with specific functions in the absence of those functions, such as the visual system in the absence of vision (Cordes et al. 2001; Nir et al. 2006) or the motor system in the absence of movement (Biswal et al. 1995; Cordes et al. 2001; Fig. 1, present manuscript). *Third*, under some conditions, task-evoked activity due to a specific behavior seems to be distinct from and appears to superpose approximately linearly with underlying spontaneous activity (Arfanakis et al. 2000; Arieli et al. 1996; Azouz and Gray 1999; Fox et al. 2006). This suggests that in some circumstances, unconstrained behavior during resting runs would result in BOLD modulations that are in addition to, not the source of, coherent spontaneous BOLD fluctuations. *Fourth*, spontaneous activity persists in vitro (Shu et al. 2003b). *Finally*, extant evidence (for a review, see Raichle and Mintun 2006) suggests that the majority of the brain's very considerable energy budget is spent on intrinsic functional activity not directly related to the execution of a particular task. It follows that these intrinsic processes, as revealed in part by spontaneous fluctuations in the fMRI BOLD signal, can be differentiated from the task-related or evoked responses that have been traditionally studied. fMRI provides a unique experimental opportunity to examine coherent spontaneous activity across the entire cortical extent that overcomes the technical challenges and limited coverage of multi-electrode recording (Leopold et al. 2003).

Thus we believe that the networks revealed through patterns of coherent activity in the spontaneous fMRI BOLD signal represent a unique and underappreciated aspect of brain functional organization present within identifiable systems even in the absence of observable behaviors normally attributed to those systems. The substrate that gives rise to coherent spontaneous activity (or the phenomenon of coherent spontaneous activity itself) may facilitate the coordination of neuronal

processing or relate to state transitions (Buzsaki and Draguhn 2004; McCormick 2005; Salinas and Sejnowski 2001). Self-sustained activity coherently fluctuating in distributed functional networks is a likely mechanism for supporting complex mental states (involving working memory or recollection). As a result of this ongoing activity, neuronal systems are dynamically transitioning through a range of physiological states. These states may provide the context that determines neuronal responsiveness to external stimuli (Shu et al. 2003a) as well as the content of the internal milieu (Polyn et al. 2005). However, the degree to which these spontaneous activity patterns are associated with conscious awareness is an open question and, in some ways, separable from the question of whether ongoing activity has important functional consequences. We discuss in the following text some possible interpretations of the observed spontaneous activity patterns recognizing that other interpretations are possible.

Functional versus anatomical connectivity

The presence of HF network-specific, spontaneous activity fluctuations raises the possibility that these are based on network-specific patterns of anatomical connectivity. Although we lack sufficient data in humans to evaluate such a hypothesis, some anatomical tract tracing work in monkeys is available and informative, albeit incomplete.

With regard to medial parietal cortex, retrosplenial cortex contains dense reciprocal projections with both the parahippocampal gyrus and entorhinal cortex (Insausti et al. 1987; Kobayashi and Amaral 2003; Lavenex et al. 2002; Suzuki and Amaral 1994; Vogt et al. 1992). In addition, there are strong connections among the presubiculum, subiculum, and parahippocampal gyrus and retrosplenial cortex (Morris et al. 1999). A more recent study demonstrates that the posterior cingulate (including areas 31 and 23) has connections to entorhinal cortex as well as the inferior parietal lobule (Parvizi et al. 2006).

In lateral parietal cortex, the inferior parietal lobule (i.e., monkey area 7a) has reciprocal connections with parahippocampal cortex (Cavada and Goldman-Rakic 1989; Kobayashi and Amaral 2003; Lavenex et al. 2002; Suzuki and Amaral 1994) and direct projections to the hippocampus (Rockland and Van Hoesen 1999). Further, the CA1 region of the hippocampus sends projections to area 7a in the inferior parietal lobule, implying that the hippocampus may have a significant influence on activity in the inferior parietal lobule (Clower et al. 2001). Intriguingly, maps of the cortical connectivity of macaque area 7a produce a network similar to the network we identify as intrinsically correlated with the HF in humans (see Fig. 7 of Cavada and Goldman-Rakic 1989).

Despite these intriguing anatomical results from studies in monkeys, the connectional anatomy of the lateral parietal component of our HF correlation map remains unclear for the following reason. The lateral parietal region shown in Fig. 4 is most likely at or near BA 39, a region that may have no homologue in the monkey (Karnath 2001). Thus it remains to be determined whether the human region is an expansion of macaque area 7a or an entirely new functional area in the human. Future fMRI and cytoarchitectonic studies that directly

compare human and monkey data in light of our findings may facilitate understanding this important evolutionary issue.

In addition to parietal cortex, our HF correlation map reveals important components in lateral temporal and medial prefrontal cortices. In this regard, parahippocampal cortex has been shown to have reciprocal connections to medial prefrontal cortex (BA 24, 25, 32, 11, and 10) (Kondo et al. 2005; Lavenex et al. 2002) as well as the lateral temporal cortex extending to the temporal pole, including areas TE, TEO, and STS (Kondo et al. 2005; Lavenex et al. 2002; Price 2005; Suzuki and Amaral 1994).

As mentioned in METHODS, the present HF seed regions likely included parts of entorhinal (BA 28) and perhaps parahippocampal (BA 35/36) cortex in addition to hippocampus proper. The preceding reviewed macaque anatomy may therefore account for correlations of the HF seed regions with retrosplenial, lateral parietal, medial prefrontal, and lateral temporal cortices. These areas correspond to the core of the HF correlation map shown in Fig. 4.

Finally, the bilateral character of the observed correlation maps obtained with unilateral seed regions suggests that correlations in spontaneous activity may extend beyond direct (monosynaptic) axonal connectivity. While bilateral connections exist, a model of correlations based purely on direct monosynaptic connections might predict stronger ipsilateral than contralateral correlations, which we did not observe.

Evidence for a parietal network associated with episodic memory retrieval

The notion that areas of parietal cortex may play a role in episodic memory may seem surprising because traditional views suggest that parietal cortex subserves processes associated with sensory-motor integration and visual-spatial attention (Andersen and Buneo 2002; Colby and Goldberg 1999; Corbetta and Shulman 2002; Heilman and Gonzalez Rothi 1993; Mesulam 1999). Therefore it is important to ask whether the activity modulations in parietal cortex during memory experiments are confounded by motor or attentional components of the tasks.

To address this possibility, Shannon and Buckner (2004) manipulated both stimulus modality and response contingency to look for interactions between the parietal memory (old/new) effect and visual-spatial attention or motor intention. To assess whether visual-spatial attention could account for memory effects in parietal cortex, the stimulus modality was varied by including both visual and auditory stimuli. To address the possibility that memory effects are confounded with motor intention, the response contingency was manipulated. Subjects were asked to make button-press responses to new items and not respond to old items. The memory effect was robust regardless of stimulus modality or response contingency, and there were no interactions between the old/new effect and manipulations of stimulus modality or motor intention.

Here, we present three additional lines of evidence suggesting that specific regions in parietal cortex play a role in episodic memory. First, specific regions within the parietal lobe are intrinsically correlated with the HF (Figs. 2–5), a structure that has a well-established role in declarative memory including episodic memory. Second, we show that these same parietal regions are differentially modulated by memory demands with the greatest activity occurring during recollection (Figs. 6 and 8). Finally, we show that the regions of parietal cortex that are coherent with the HF in the resting state and modulated by memory demands are spatially distinct from the parietal regions associated with visual-spatial attention and sensory-motor integration.

An unresolved issue is how to reconcile the present functional analyses that suggest parietal contributions to episodic memory and the absence of documented impairment of memory in patients with parietal lesions, at least insofar as lateral regions of posterior parietal cortex are concerned. Rare lesions of midline regions near retrosplenial cortex can cause memory difficulties (Valenstein et al., 1987; see Kobayashi and Amaral 2003 for review), but to our knowledge, there have been no reported lesions of the posterior cingulate or precuneus region in humans. The paucity of information in the neuropsychology literature with regard to the lateral parietal lesions and memory has been discussed previously (Wagner et al. 2005), and we raise it here again because the divergence remains unresolved. Because parietal cortex has not traditionally been considered important for episodic memory, it seems likely to us that patients with parietal lesions are rarely if ever actually investigated for memory disturbances. Also left parietal damage in particular is likely associated with language impairment too severe to permit detailed assessment of memory. However, it is notable that patients with Alzheimer's disease, a degenerative dementia the hallmark of which is early memory loss (Albert 1997), manifest amyloid deposition, hypometabolism, and structural atrophy in a cortical distribution that is qualitatively similar to the network intrinsically correlated with the HF (Buckner et al., 2005; Friedland et al. 1983; Herholz 1995; Reiman et al. 1996; see Fig. 6 of Buckner et al. 2005 for an image of convergence across methods). Further study will be required to elucidate the specific role of parietal cortex in recollection. Uncommon patients with focal and bilateral parietal lesions (e.g., patients with Balint's syndrome; Rafal 1997) or transcranial magnetic stimulationt in humans may also be informative.

Consideration of the larger correlated network: Implications for episodic and specifically autobiographical memory

Although this study focused on the relationship between parietal cortex and the HF, the intrinsically defined HF network showed strong correlations in the medial prefrontal and lateral temporal cortices. Medial prefrontal cortex, unlike the HF and parietal cortex, is conventionally associated with emotional and motivational processes ventrally (Bechara et al. 2000; Critchley 2005; Damasio et al. 1994; Gusnard et al. 2003; Schultz et al. 2000; Simpson et al. 2001a,b) and self-referential thought and "mentalizing" dorsally (Frith and Frith 1999, 2003; Gusnard et al. 2001; Kjaer et al. 2002). This result is intriguing because episodic memory is theoretically linked to self-referential processes (James 1890; Tulving 1983, 2001) and by some considered to be a uniquely human attribute (Tulving 1983, 2001).

It is therefore of interest that neuroimaging studies investigating autobiographical or personally relevant memories often report increased activity in medial prefrontal cortex (Andreasen et al. 1995; Cabeza et al. 2004; Maguire and Mummery 1999; Maguire 2001). For example, Cabeza and colleagues

(2004) directly contrasted retrieval for autobiographical and laboratory events. The most prominent difference between the two conditions was a relative increase in activity of medial prefrontal cortex for the autobiographical memories. Similarly, Maguire and Mummery (1999) incorporated personally relevant materials into a memory study and obtained a functional map that bears a remarkably strong resemblance to the HF correlation map illustrated in Fig. 4, including regions in medial prefrontal cortex as well as the temporal pole. These studies, combined with the present HF correlation results suggest that a complete understanding of episodic memory, particularly as it occurs in a more naturalistic setting with real-world stimulation, likely will include parietal as well as temporal and medial prefrontal cortices. This perspective is consistent with the possibility that typical real-world use of brain systems that support episodic memory may involve remembering past events of consequence to the self and evaluating these recollections in relation to one's own perspectives and future needs (Ingvar 1985).

Relationship of the HF correlation map to a default mode of brain function

The existence of a "default mode" of human brain function (Raichle et al. 2001) was inferred from the observation that a particular set of cortical regions is more active in the unconstrained resting state than during performance of most attention demanding tasks (Andreasen et al. 1995; Binder et al. 1999; Mazoyer et al. 2001; McKiernan et al. 2003; Shulman et al. 1997). However, a notable exception to this phenomenon occurs when subjects engage in recollection (Wagner et al. 2005). Accumulating evidence indicates that the posterior components of this network (posterior cingulate, precuneus, and lateral parietal cortex) closely correspond to the regions involved in recollection. As mentioned earlier, this topographic convergence supports the possibility that recollection of personally relevant memories is a component of the cognitive content of the default state as previously suggested (Andreasen et al. 1995; Buckner et al. 2005; Greicius et al. 2003, 2004; Gusnard and Raichle 2001; Raichle et al. 2001; Stark and Squire 2001). Alternatively, spontaneous activity associated with the HF may relate to learning processing independent of conscious awareness. Recording from the hippocampus, Foster and Wilson (2006) recently noted that rats replay recent event sequences spontaneously during stopped periods. It is possible that the patterned spontaneous activity between hippocampal and parietal cortex constitutes related phenomenon and represents a mechanism of experiential learning.

Spontaneous activity predicts the topography of task-evoked responses

A noteworthy aspect of our results is that correlation analysis of spontaneous BOLD fluctuations recorded in the absence of behavioral events predicts the anatomical location of fMRI responses in paradigms targeting memory. Correlations in spontaneous activity localized functional brain regions much in the same way task-based localizers have been used previously (e.g., Kanwisher et al. 1997; Tootell et al. 1995).

The correspondence between spontaneously emerging and task-evoked networks has also been demonstrated outside of fMRI. For example, Kenet and colleagues (2003) found that the spontaneous activity in extrastriate cortex observed with voltage-sensitive dye imaging in the anesthetized cat is spatially organized in patterns corresponding to orientation maps. Thus assemblies of neurons showing correlated spontaneous activity in the absence of visual stimuli preferentially responded to the same orientation of grating. On a more cellular level, MacLean and colleagues (2005) have demonstrated the existence of spontaneous activity patterns that mimic patterns evoked by thalamic stimulation. Such examples imply that certain aspects of the functional architecture of the brain can be discerned in its intrinsic activity.

Conclusions

These data support in a unique way the hypothesis that specific regions within parietal cortex play a role in memory functions associated with the HF. Furthermore, those regions of parietal cortex associated with the HF are anatomically distinct from regions of parietal cortex traditionally associated with spatial attention and motor intention. More broadly, the HF network defined in this manner appears to be very similar, if not identical, to a group of areas posited to constitute a "default network." The fact that the posterior parietal components of this network are specifically modulated by recollection would be consistent with the putative self-referential nature of this network's other components. On a more technical level, this work extends past studies of coherence patterns revealed in spontaneous fluctuations of the fMRI BOLD signal by demonstrating their robustness in individual subjects, their convergence across multiple data sets, and their ability to predict task-induced, local activity changes.

REFERENCES

Aggleton JP and Brown MW. Episodic memory, amnesia, and the hippocampal-anterior thalamic axis. *Behav Brain Sci* 22: 425–444, 1999.
Albert MS. The ageing brain: normal and abnormal memory. *Philos Trans R Soc Lond B Biol Sci* 352: 1703–1709, 1997.
Andersen RA, Asanuma C, Essick G, and Siegel RM. Corticocortical connections of anatomically and physiologically defined subdivisions within the inferior parietal lobule. *J Comp Neurol* 296: 65–113, 1990.
Andersen RA and Buneo CA. Intentional maps in posterior parietal cortex. *Annu Rev Neurosci* 25: 189–220, 2002.
Andreasen NC, O'Leary DS, Cizadlo T, Arndt S, Rezai K, Watkins GL, Ponto LL, and Hichwa RD. Remembering the past: two facets of episodic memory explored with positron emission tomography. *Am J Psychiatry* 152: 1576–1585, 1995.
Arfanakis K, Cordes D, Haughton VM, Moritz CH, Quigley MA, and Meyerand ME. Combining independent component analysis and correlation analysis to probe interregional connectivity in fMRI task activation datasets. *Magn Reson Imaging* 18: 921–930, 2000.

Arieli A, Sterkin A, Grinvald A, and Aertsen A. Dynamics of ongoing activity: explanation of the large variability in evoked cortical responses. *Science* 273: 1868–1871, 1996.

Azouz R and Gray CM. Cellular mechanisms contributing to response variability of cortical neurons in vivo. *J Neurosci* 19: 2209–2223, 1999.

Bartels A and Zeki S. The chronoarchitecture of the cerebral cortex. *Philos Trans R Soc Lond B Biol Sci* 360: 733–750, 2005.

Bechara A, Tranel D, and Damasio H. Characterization of the decision-making deficit of patients with ventromedial prefrontal cortex lesions. *Brain* 123: 2189–2202, 2000.

Binder JR, Frost JA, Hammeke TA, Bellgowan PS, Rao SM, and Cox RW. Conceptual processing during the conscious resting state: a functional MRI study. *J Cogn Neurosci* 11: 80–95, 1999.

Birn RM, Diamond JB, Smith MA, and Bandettini PA. Separating respiratory-variation-related fluctuations from neuronal-activity-related fluctuations in fMRI. *NeuroImage* 31: 1536–1548, 2006.

Biswal B, Yetkin FZ, Haughton VM, and Hyde JS. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magn Reson Med* 34: 537–541, 1995.

Buckner RL, Petersen SE, Ojemann JG, Miezin FM, Squire LR, and Raichle ME. Functional anatomical studies of explicit and implicit memory retrieval tasks. *J Neurosci* 15: 12–29, 1995.

Buckner RL, Snyder AZ, Shannon BJ, LaRossa G, Sachs R, Fotenos AF, Sheline YI, Klunk WE, Mathis CA, Morris JC, and Mintun MA. Molecular, structural, and functional characterization of Alzheimer's disease: evidence for a relationship between default activity, amyloid, and memory. *J Neurosci* 25: 7709–7717, 2005.

Buzsaki G and Draguhn A. Neuronal oscillations in cortical networks. *Science* R 304: 1926–1929, 2004.

Cabeza R, Prince SE, Daselaar SM, Greenberg DL, Budde M, Dolcos F, LaBar KS, and Rubin DC. Brain activity during episodic retrieval of autobiographical and laboratory events: an fMRI study using a novel photo paradigm. *J Cogn Neurosci* 16: 1583–1594, 2004.

Cavada C and Goldman-Rakic PS. Posterior parietal cortex in rhesus monkey. I. Parcellation of areas based on distinctive limbic and sensory corticocortical connections. *J Comp Neurol* 287: 393–421, 1989.

Clower DM, West RA, Lynch JC, and Strick PL. The inferior parietal lobule is the target of output from the superior colliculus, hippocampus, and cerebellum. *J Neurosci* 21: 6283–6291, 2001.

Cohen JD, MacWhinney B, Flatt M, and Provost J. PsyScope: a new graphic interactive environment for designing psychology experiments. *Behav Res Methods Instrum Comput* 25: 257–271, 1993.

Cohen NJ and Eichenbaum H. *Memory, Amnesia, and the Hippocampal System.* Cambridge, MA: The MIT Press, 1995.

Colby CL and Goldberg ME. Space and attention in parietal cortex. *Annu Rev Neurosci* 22: 319–349, 1999.

Corbetta M, Kincade JM, and Shulman GL. Neural systems for visual orienting and their relationships to spatial working memory. *J Cogn Neurosci* 14: 508–523, 2002.

Corbetta M and Shulman GL. Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci* 3: 201–215, 2002.

Cordes D, Haughton VM, Arfanakis K, Carew JD, Turski PA, Moritz CH, Quigley MA, and Meyerand ME. Frequencies contributing to functional connectivity in the cerebral cortex in "resting-state" data. *Am J Neuroradiol* 22: 1326–1333, 2001.

Critchley HD. Neural mechanisms of autonomic, affective, and cognitive integration. *J Comp Neurol* 493: 154–166, 2005.

Dale AM and Buckner RL. Selective averaging of rapidly presented individual trials using fMRI. *Hum Brain Mapp* 5: 1–12, 1997.

Damasio H, Grabowski T, Frank R, Galaburda AM, and Damasio AR. The return of Phineas Gage: clues about the brain from the skull of a famous patient. *Science* 264: 1102–1105, 1994.

Dobbins IG, Rice HJ, Wagner AD, and Schacter DL. Memory orientation and success: separable neurocognitive components underlying episodic recognition. *Neuropsychologia* 41: 318–333, 2003.

Donaldson DI and Rugg MD. Recognition memory for new associations: electrophysiological evidence for the role of recollection. *Neuropsychologia* 36: 377–395, 1998.

Eldridge LL, Knowlton BJ, Furmanski CS, Bookheimer SY, and Engel SA. Remembering episodes: a selective role for the hippocampus during retrieval. *Nat Neurosci* 3: 1149–1152, 2000.

Foster DJ and Wilson MA. Reverse replay of behavioral sequences in hippocampal place cells during the awake state. *Nature* 440: 680–683, 2006.

Fox MD, Snyder AZ, Vincent JL, Corbetta M, Van Essen DC, and Raichle ME. The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proc Natl Acad Sci USA* 102: 9673–9678, 2005.

Fox MD, Snyder AZ, Zacks JM, and Raichle ME. Coherent spontaneous activity accounts for trial-to-trial variability in human evoked brain responses. *Nat Neurosci* 9: 23–25, 2006.

Fransson P. Spontaneous low-frequency BOLD signal fluctuations: an fMRI investigation of the resting-state default mode of brain function hypothesis. *Hum Brain Mapp* 26: 15–29, 2005.

Friedland RP, Budinger TF, Ganz E, Yano Y, Mathis CA, Koss B, Ober BA, Huesman RH, and Derenzo SE. Regional cerebral metabolic alterations in dementia of the Alzheimer type: positron emission tomography with [18F]fluorodeoxyglucose. *J Comput Assist Tomogr* 7: 590–598, 1983.

Frith CD and Frith U. Interacting minds—a biological basis. *Science* 286: 1692–1695, 1999.

Frith U and Frith CD. Development and neurophysiology of mentalizing. *Philos Trans R Soc Lond B Biol Sci* 358: 459–473, 2003.

Gardiner JM and Richardson-Klavehn A. Remembering and knowing. In: *The Oxford Handbook of Memory*, edited by Tulving E and Craik FIM. New York: Oxford, 2000, p. 229–244.

Greicius MD, Krasnow B, Reiss AL, and Menon V. Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. *Proc Natl Acad Sci USA* 100: 253–258, 2003.

Greicius MD, Srivastava G, Reiss AL, and Menon V. Default-mode network activity distinguishes Alzheimer's disease from healthy aging: evidence from functional MRI. *Proc Natl Acad Sci USA* 101: 4637–4642, 2004.

Gusnard DA, Akbudak E, Shulman GL, and Raichle ME. Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. *Proc Natl Acad Sci USA* 98: 4259–4264, 2001.

Gusnard DA, Ollinger JM, Shulman GL, Cloninger CR, Price JL, Van Essen DC, and Raichle ME. Persistence and brain circuitry. *Proc Natl Acad Sci USA* 100: 3479–3484, 2003.

Gusnard DA and Raichle ME. Searching for a baseline: functional imaging and the resting human brain. *Nat Rev Neurosci* 2: 685–694, 2001.

Haider B, Duque A, Hasenstaub AR, and McCormick DA. Neocortical network activity in vivo is generated through a dynamic balance of excitation and inhibition. *J Neurosci* 26: 4535–4545, 2006.

Heilman KM and Gonzalez Rothi LJ. Apraxia. In: *Clinical Neuropsychology*, edited by Heilman KM, and Valenstein E. Oxford, UK: Oxford Univ. Press, 1993, p. 141–163.

Henson RN, Rugg MD, Shallice T, Josephs O, and Dolan RJ. Recollection and familiarity in recognition memory: an event-related functional magnetic resonance imaging study. *J Neurosci* 19: 3962–3972, 1999.

Herholz K. FDG PET and differential diagnosis of dementia. *Alzheimers Dis Assoc Disorders* 9: 6–16, 1995.

Ingvar DH. "Memory of the future": an essay on the temporal organization of conscious awareness. *Hum Neurobiol* 4: 127–136, 1985.

Insausti RA, Ameral DG, and Cowan WM. The entorhinal cortex of the monkey. II. Cortical afferents. *J Comp Neurol* 264: 356–395, 1987.

James W. *Principles of Psychology.* New York: Holt, 1890.

Kahn I, Davachi L, and Wagner AD. Functional-neuroanatomic correlates of recollection: implications for models of recognition memory. *J Neurosci* 24: 4172–4180, 2004.

Kanwisher N, McDermott J, and Chun MM. The fusiform face area: a module in human extrastriate cortex specialized for face perception. *J Neurosci* 17: 4302–4311, 1997.

Karnath HO. New insights into the functions of the superior temporal cortex. *Nat Rev Neurosci* 2: 568–576, 2001.

Kenet T, Bibitchkov D, Tsodyks M, Grinvald A, and Arieli A. Spontaneously emerging cortical representations of visual attributes. *Nature* 425: 954–956, 2003.

Kiviniemi V, Jauhiainen J, Tervonen O, Pääkkö E, Oikarinen J, Vainionpää V, Rantala H, and Biswal B. Slow vasomotor fluctuation in fMRI of anesthetized child brain. *Mag Reson Med* 44: 373–378, 2000.

Kjaer TW, Nowak M, and Lou HC. Reflective self-awareness and conscious states: PET evidence for a common midline parietofrontal core. *NeuroImage* 17: 1080–1086, 2002.

Kobayashi Y and Amaral DG. Macaque monkey retrosplenial cortex. II. Cortical afferents. *J Comp Neurol* 466: 48–79, 2003.

Kondo H, Saleem KS, and Price JL. Differential connections of the perirhinal and parahippocampal cortex with the orbital and medial prefrontal networks in macaque monkeys. *J Comp Neurol* 493: 479–509, 2005.

Konishi S, Wheeler ME, Donaldson DI, and Buckner RL. Neural correlates of episodic retrieval success. *NeuroImage* 12: 276–286, 2000.

Kwong KK, Belliveau JW, Chesler DA, Goldberg IE, Weiskoff RM, Poncelet BP, Kennedy DN, Hoppel BE, Cohen MS, Turner R, Cheng HM, Brady TJ, and Rosen BR. Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proc Natl Acad Sci USA* 89: 5675–5679, 1992.

Lancaster JL, Glass TG, Lankipalli BR, Downs H, Mayberg HS, and Fox PT. A modality-independent approach to spatial normalization of tomographic images of the human brain. *Hum Brain Mapp* 3: 209–223, 1995.

Lavenex P, Suzuki WA, and Amaral DG. Perirhinal and parahippocampal cortices of the macaque monkey: projections to the neocortex. *J Comp Neurol* 447: 394–420, 2002.

Leopold DA, Murayama Y, and Logothetis NK. Very slow activitiy fluctuations in monkey visual cortex: implications for functional brain imaging. *Cereb Cortex* 13: 422–433, 2003.

Leube DT, Erb M, Grodd W, Bartels M, and Kircher TT. Successful episodic memory retrieval of newly learned faces activates a left frontoparietal network. *Brain Res Cogn Brain Res* 18: 97–101, 2003.

Lowe MJ, Dzemidzic M, Lurito JT, Mathews VP, and Phillips MD. Correlations in low-frequency BOLD fluctuations reflect cortico-cortical connections. *NeuroImage* 12: 582–587, 2000.

Lustig C and Buckner RL. Preserved neural correlates of priming in old age and dementia. *Neuron* 42: 865–875, 2004.

Maccotta L, Zacks JM, and Buckner RL. Rapid self-paced event-related functional MRI: feasibility and implications of stimulus- versus response-locked timing. *NeuroImage* 14: 1105–1121, 2001.

MacLean JN, Watson BO, Aaron GB, and Yuste R. Internal dynamics determine the cortical response to thalamic stimulation. *Neuron* 48: 811–823, 2005.

Maguire EA. Neuroimaging studies of autobiographical event memory. *Philos Trans R Soc Lond B: Biol Sci* 356: 1441–1451, 2001.

Maguire EA and Mummery CJ. Differential modulation of a common memory retrieval network revealed by positron emission tomography. *Hippocampus* 9: 54–61, 1999.

Martin A. Automatic activation of the medial temporal lobe during encoding: lateralized influences of meaning and novelty. *Hippocampus* 9: 62–70, 1999.

Maunsell JH and Van Essen DC. The connections of the middle temporal visual ara (MT) and their relationship to a cortical hierarchy in the macaque monkey. *J Neurosci* 3: 2563–2586, 1983.

Mazoyer B, Zago L, Mellet E, Bricogne S, Etard O, Houde O, Crivello F, Joliot M, Petit L, and Tzourio-Mazoyer N. Cortical networks for working memory and executive functions sustain the conscious resting state in man. *Brain Res Bull* 54: 287–298, 2001.

McCormick DA. Neuronal networks: flip-flops in the brain. *Curr Biol* 15: R294–R296, 2005.

McDermott KB, Jones TC, Petersen SE, Lageman SK, and Roediger HL 3rd. Retrieval success is accompanied by enhanced activation in anterior prefrontal cortex during recognition memory: an event-related fMRI study. *J Cog Neurosci* 12: 965–976, 2000.

McKiernan KA, Kaufman JN, Kucera-Thompson J, and Binder JR. A parametric manipulation of factors affecting task-induced deactivation in functional neuroimaging. *J Cognit Neurosci* 15: 394–408, 2003.

Mesulam MM. Spatial attention and neglect: parietal, frontal and cingulate contributions to the mental representation and attentional targeting of salient extrapersonal events. *Philos Trans R Soc Lond B Biol Sci* 354: 1325–1346, 1999.

Morris R, Petrides M, and Pandya DN. Architecture and connections of retrosplenial area 30 in the rhesus monkey (*Macaca mulatta*). *Eur J Neurosci* 11: 2506–2518, 1999.

Nir Y, Hasson U, Levy I, Yeshurn Y, and Malach R. Widespread functional connectivity and fMRI fluctuations in human visual cortex in absence of visual stimulation. *NeuroImage* 30: 1313–1324, 2006.

Ogawa S, Tank DW, Menon R, Ellermann JM, Kim SG, Merkle H, and Ugurbil K. Instrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging. *Proc Natl Acad Sci USA* 89: 5951–5955, 1992.

Ojemann JG, Akbudak E, Snyder AZ, McKinstry RC, Raichle ME, and Conturo TE. Anatomic localization and quantitative analysis of gradient refocused echo-planar fMRI susceptibility artifacts. *NeuroImage* 6: 156–167, 1997.

Parvizi J, Van Hoesen GW, Buckwalter J, and Damasio A. Neural connections of the posteromedial cortex in the macaque. *Proc Natl Acad Sci USA* 103: 1563–1568, 2006.

Polyn SM, Natu VS, Cohen JD, and Norman KA. Category-specific cortical activity precedes retrieval during memory search. *Science* 310: 1963–1966, 2005.

Price JL. Free will versus survival: brain systems that underlie intrinsic constraints on behavior. *J Comp Neurol* 493: 132–139, 2005.

Rafal RD. Balint Syndrome. In: *Behavioral Neurology and Neuropsychology*, edited by Feinberg TE, and Farah MJ. New York, NY: McGraw-Hill, 1997, p. 337–356.

Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, and Shulman GL. A default mode of brain function. *Proc Natl Acad Sci USA* 98: 676–682, 2001.

Raichle ME and Mintun M. Brain work and brain imaging. *Annu Rev Neurosci* 29: 449–476, 2006.

Reiman EM, Caselli RJ, Yun LS, Chen K, Bandy D, Minoshima S, Thibodeau SN, and Osborne D. Preclinical evidence of Alzheimer's disease in persons homozygous for the epsilon 4 allele for apolipoprotein. *Eng J Med* 334: 752–758, 1996.

Rockland KS and Van Hoesen GW. Some temporal and parietal cortical connections converge in CA1 of the primate hippocampus. *Cereb Cortex* 9: 232–237, 1999.

Rugg MD, Mark RE, Walla P, Schloerscheidt AM, Birch CS, and Allan K. Dissociation of the neural correlates of implicit and explicit memory. *Nature* 392: 595–598, 1998.

Rugg MD and Wilding EL. Retrieval processing and episodic memory. *Trends Cognit Sci* 4: 108–115, 2000.

Salinas E and Sejnowski TJ. Correlated neuronal activity and the flow of neural information. *Nat Rev Neurosci* 2: 539–550, 2001.

Schultz W, Tremblay L, and Hollerman JR. Reward processing in primate orbitofrontal cortex and basal ganglia. *Cereb Cortex* 10: 272–284, 2000.

Sereno MI, Pitzalis S, and Martinez A. Mapping of contralateral space in retinotopic coordinates by a parietal cortical area in humans. *Science* 294: 1350–1354, 2001.

Shannon BJ and Buckner RL. Functional-anatomic correlates of memory retrieval that suggest nontraditional processing roles for multiple distinct regions within posterior parietal cortex. *J Neurosci* 24: 10084–10092, 2004.

Shu Y, Hasenstaub A, Badoual M, Bal T, and McCormick DA. Barrages of synaptic activity control the gain and sensitivity of cortical neurons. *J Neurosci* 23: 10388–10401, 2003a.

Shu Y, Hasenstaub A, and McCormick DA. Turning on and off recurrent balanced cortical activity. *Nature* 423: 288–293, 2003b.

Shulman GL, Fiez JA, Corbetta M, Buckner RL, Miezin FM, Raichle ME, and Petersen SE. Common blood flow changes across visual tasks. II. Decreases in cerebral cortex. *J Cognit Neurosci* 9: 648–663, 1997.

Simpson JRJ, Drevets WC, Snyder AZ, Gusnard DA, and Raichle ME. Emotion-induced changes in human medial prefrontal cortex. II. During anticipatory anxiety. *Proc Natl Acad Sci USA* 98: 688–693, 2001a.

Simpson JRJ, Snyder AZ, Gusnard DA, and Raichle ME. Emotion-induced changes in human medial prefrontal cortex. I. During cognitive task performance. *Proc Natl Acad Sci USA* 98: 683–687, 2001b.

Squire LR. Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. *Psychol Rev* 99: 195–231, 1992.

Stark CE and Squire LR. When zero is not zero: The problem of ambiguous baseline conditions in fMRI. *Proc Natl Acad Sci USA* 98: 12760–12766, 2001.

Suzuki WA and Amaral DG. Perirhinal and parahippocampal cortices of the macaque monkey: cortical afferents. *J Comp Neurol* 350: 497–533, 1994.

Talairach J and Tournoux P. *Co-Planar Stereotaxic Atlas of the Human Brain.* New York: Thieme Medical Publishers, 1988.

Tootell RB, Reppas JB, Kwong KK, Malach R, Born RT, Brady TJ, Rosen BR, and Belliveau JW. Functional analysis of human MT and related visual cortical areas using magnetic resonance imaging. *J Neurosci* 15: 3215–3230, 1995.

Tulving E. *Elements of Episodic Memory.* New York: Oxford, 1983.

Tulving E. Memory and consciousness. *Can Psychol* 26: 1–12, 1985.

Tulving E. Episodic memory and common sense: how far apart? *Philos Trans R Soc Lond B Biol Sci* 356: 1505–1515, 2001.

Ungerleider LG and Desimone R. Cortical connections of visual area MT in the macaque. *J Comp Neurol* 248: 190–222, 1986.

Valenstein EE, Bowers D, Verfaellie M, Heilman KM, Day A, and Watson RT. Retrosplenial amnesia. *Brain* 110: 1631–1646, 1987.

Van Essen DC. A population-average, landmark- and surface-based (PALS) atlas of human cerebral cortex. *NeuroImage* 28: 635–662, 2005.

Vogt BA, Finch DM, and Olson CR. Functional heterogeneity in cingulate cortex: the anterior executive and posterior evaluative regions. *Cereb Cortex* 2: 435–443, 1992.

Wagner AD, Shannon BJ, Kahn I, and Buckner RL. Parietal lobe contributions to episodic memory retrieval. *Trends Cogn Sci* 9: 445–453, 2005.

Wheeler ME and Buckner RL. Functional dissociation among components of remembering: control, perceived oldness, and content. *J Neurosci* 23: 3869–3880, 2003.

Wheeler ME and Buckner RL. Functional-anatomic correlates of remembering and knowing. *NeuroImage* 21: 1337–1349, 2004.

Wixted JT and Stretch V. In defense of the signal detection interpretation of remember/know judgments. *Psychon Bull Rev* 11: 616–641, 2004.

Yonelinas A. The nature of recollection and familiarity: a review of 30 years of research *J Mem Language* 46: 441–517, 2002.

Yonelinas AP, Otten LJ, Shaw KN, and Rugg MD. Separating the brain regions involved in recollection and familiarity in recognition memory. *J Neurosci* 25: 3002–3008, 2005.

Zar JH. *Biostatistical Analysis.* Upper Saddle River, NJ: Prentice-Hall, 1996.