Rapid retinotopic reactivation during spatial memory

Scott D. Slotnick

Department of Psychology, Boston College, McGuinn Hall, Chestnut Hill, MA 02467

Status: Under Revision for Brain Research

Text pages: 38 (including figures and tables)

Number of figures: 5

Number of tables: 1

Correspondence:
Scott D. Slotnick
Boston College, Department of Psychology
McGuinn Hall, Room 330
Chestnut Hill, MA 02467
URL: www2.bc.edu/~slotnics
E-mail: sd.slotnick@bc.edu
Phone: 617-552-4188
Fax: 617-552-0523
Abstract
Memories are thought to be constructed from features processed in different cortical regions. However, it is unknown how the retrieval process unfolds over time. The present investigation aimed to address this issue by combining evidence from functional magnetic resonance imaging (fMRI) and event-related potentials (ERPs). During study, abstract shapes were presented to the left or right of fixation and participants were instructed to remember each shape and its spatial location. At test, studied (old) and new shapes were presented at fixation and participants classified each shape as old and on the “left”, old and on the “right”, or “new”. Accurate memory for items previously presented on the left or right produced fMRI activity in right or left extrastriate cortex (BA18), respectively. ERP results revealed these retinotopic memory effects occurred within 100-250 ms after stimulus onset indicating memory construction can occur very rapidly (and supporting a mechanism mediated by the hippocampus).

Classification: Cognitive and Behavioral Neuroscience
Keywords: ERPs; fMRI; Hippocampus; Retrieval; Visual
1. Introduction

Retrieval has been described as a constructive process (Squire, 1992; Slotnick, 2004), where information processed in disparate cortical regions is combined to create a unified memory. Consistent with this view, memory for visual items can activate visual processing regions (Wheeler et al., 2000; Vaidya et al., 2002; Wheeler and Buckner, 2003, 2004) and memory for sounds can activate auditory processing regions (Wheeler et al., 2000; Schacter et al., 1996; Nyberg et al., 2000). However, such evidence provides relatively weak support for the constructive view of memory as it reflects information at the modality-specific level of processing which is far less specific than the detailed features that comprise our memories (e.g., within the visual modality, memory for color, shape, and spatial location).

There is very limited evidence that memory can activate cortical regions associated with processing specific features. During the study phase of an event-related potential (ERP) study (Gratton et al., 1997), line patterns were presented to the left or right of fixation. During the test phase, participants classified studied (old) and new items as “old” or “new”. Within 400-1400 ms after stimulus onset, old items previously presented in the left versus right visual field produced differential activity in right temporal regions and old items previously presented in the right versus left visual field produced differential activity in left temporal regions (similar results have been reported using words as stimuli; Fabiani et al., 2000). These retinotopic memory effects are consistent with the known retinotopic organization of striate and extrastriate cortex, where left visual field stimuli active right visual areas and right visual field stimuli activate left visual areas (Sereno et al., 1995; Slotnick and Yantis, 2003). Such visual sensory reactivation suggests memory can be specific at the detailed level of item features, where the previously lateralized stimulus is reexperienced. However, it is currently unknown how such detailed memorial information is constructed over time.
One aim of the present investigation was to confirm the presence of retinotopic memory effects using functional magnetic resonance imaging (fMRI). Fig. 1 illustrates the paradigm employed, where shapes were presented to the left or right of fixation during the study phase, and old and new shapes were presented at fixation during the test phase (during which participants responded “old-left”, “old-right”, or “new”). Retinotopic memory effects were identified by comparing accurate memory for old items previously presented in the left visual field versus right visual field and vice versa. In addition to assessing retinotopic memory effects, memory control regions (commonly associated with accurate memory, regardless of spatial location) were also identified and, based on previous studies, were expected to include the prefrontal cortex, the parietal cortex, and the medial temporal lobe (Buckner et al., 1998; Slotnick et al., 2003).

A second aim of the present investigation was to determine the earliest time at which retinotopic memory effects could occur using ERPs. There are three possible onset time ranges based on previous ERP results and depth electrode recording results. One hypothesis is that memory construction is a relatively slow process, such that retinotopic memory effects will first be observed starting 1000-1600 ms after stimulus onset, the time range corresponding to ERP activity in frontal regions during retrieval (Düzel et al., 1997; Curran et al., 2001; Nessler et al., 2001) believed to reflect post-retrieval monitoring (Goldmann et al., 2003). A second hypothesis is that retinotopic memory effects will occur starting 400-800 ms after stimulus onset, the time range corresponding to ERP activity in parietal regions during retrieval (Wilding and Rugg, 1996; Donaldson and Rugg, 1998) that has been associated with
memory for contextual information (Wilding, 2000; Vilberg et al., 2006). The third hypothesis is that retinotopic memory effects will occur very rapidly, starting 100-250 ms after stimulus onset, the time range corresponding to depth electrode activity in human and non-human primate hippocampus during retrieval (Rolls et al., 1989; Kreiman et al., 2000), a region that may bind information processed in different cortical regions (Squire, 1992; Manns and Eichenbaum, 2006).

2. Results

2.1. Spatial localization of retinotopic memory effects

Item memory accuracy during fMRI was 67.2 ± 1.6% correct while spatial location memory accuracy was 70.0 ± 2.0% correct (chance performance = 50%). Retinotopic memory effects were assessed by contrasting old-left-hit > old-right-hit, which was expected to activate right hemisphere early visual areas, and old-right-hit > old-left-hit, which was expected to activate left hemisphere early visual areas. Furthermore, in an effort to isolate memory related activity corresponding to perceptual reactivation, retrieval activity was required to overlap with encoding activity in early retinotopic visual regions. Fig. 2A illustrates the two regions of significant activity, one in the left hemisphere (cuneus, BA18, Talairach coordinate –9, –83, 18) and one in the right hemisphere (lingual gyrus, BA18, Talairach coordinate 24, –91, 6). Both of these activations reflect retinotopic memory effects, with memory for stimuli previously presented on the left and right visual fields preferentially activating the right and left visual regions, respectively. Analysis of event-related timecourses extracted from these regions (Fig. 2B) confirmed that both activations were lateralized to their respective hemisphere (hemisphere x condition interactions were both significant; left hemisphere p < 0.01, right hemisphere p < 0.05). Additionally, retinotopic memory effects were larger in the right than
the left hemisphere, as measured by differential effect size (i.e., old-left-hit – old-right-hit magnitude in the right hemisphere was greater than old-right-hit – old-left-hit magnitude in the left hemisphere; p < 0.05) and mean absolute magnitude versus baseline (p < 0.001).

Fig. 2 about here

Fig. 3A illustrates control regions associated with memory for spatial location (i.e., regions commonly associated with accurate memory). Consistent with previous findings, activity was observed in the prefrontal cortex, the parietal cortex, and the medial temporal lobe including the hippocampus (see Table 1 for a complete list of activations). To further characterize this activity, event-related timecourses were extracted from activity in the middle frontal gyrus, the intraparietal sulcus, and the hippocampus (Fig. 3B).

Fig. 3 about here

Fig. 3 about here

Table 1 about here

2.2. Timing of memory related retinotopic reactivation

Item memory accuracy during ERP recording was 63.0 ± 1.8% correct while spatial location memory accuracy was 66.5 ± 2.3% correct. Retinotopic memory effects were assessed by
testing for hemispheric lateralization within occipital and temporal ROIs (Fig. 4B). Differential ERP timecourses (computed from the average activity across electrodes within each ROI) preferentially associated with accurate memory for stimuli in the left visual field were computed from old-left-hit – old-right-hit ERPs and vice versa for stimuli in the right visual field. Such difference waveforms are analogous to those computed to isolate retinotopic attention effects in posterior electrodes (Heinze et al., 1994; Mangun et al., 1998), as activity common to both event types was subtracted out. Fig. 4A illustrates the waveforms corresponding to occipital and temporal ROIs within the 100-200 ms time range. Consistent with retinotopic memory reactivation, memory for items previously presented on the left produced greater activity in right as compared to left occipital and temporal ROIs (Fig. 4A, left), and memory for items previously presented on the right produced greater activity in left as compared to right occipital and temporal ROIs (Fig. 4A, right). Hemispheric laterality was evaluated at each 1ms timepoint using the mean activity at that time ± 6 ms. For a given occipital or temporal ROI and timepoint, significant hemispheric laterality required the following: 1) activity was significantly greater than zero (as only positive activity is known to reflect increases in neural activity), 2) activity was significantly greater than that of the occipital ROI in the opposite hemisphere, and 3) activity was significantly greater than that of the temporal ROI in the opposite hemisphere. As is typically done, frontal and parietal ROI activity that was concomitant with significant occipital and temporal ROIs was estimated using new-correct rejections as the baseline measure of activity (note that significant frontal and parietal ROI activity is reported without regard to hemisphere, as it is known that memory related activity in these regions can occur in either or both hemispheres). Fig. 4B illustrates the scalp voltage topographies associated with these significant retinotopic memory effects (at the median time point within each significant epoch). Fig. 4C shows the dipole source
locations corresponding to the voltage topographies, which confirmed a right hemisphere occipital source underlying the right posterior voltage topography and a left hemisphere occipital source underlying the left posterior voltage topography.

--------------------------

Fig. 4 about here
--------------------------

Fig. 5 shows significant lateralized ERP activity across the entire time range within temporal and occipital ROIs associated with memory for stimuli in the left and right visual fields (bottom of each panel) and concomitant activity within frontal and parietal ROIs (top and middle of each panel). Retinotopic memory effects occurred in the early (100-250 ms), middle (400-800 ms), and late (1000-1600 ms) epochs in both temporal and occipital ROIs, with memory for stimuli previously presented in the left and right visual fields evoking significant activity that was almost completely restricted to the right or left temporal and occipital ROIs, respectively. As the number of temporal and occipital ROI activations did not significantly differ, the number of activations in these regions were combined to yield significant retinotopic memory effects in both the right and left hemisphere (right hemisphere ROIs, 19 retinotopic, 0 ipsilateral, \( p < 0.001 \); left hemisphere ROIs, 9 retinotopic, 1 ipsilateral, \( p < 0.01 \)). Consistent with the fMRI results, the number of activations in the right hemisphere was greater than that in the left hemisphere (\( p < 0.05 \)). It is notable that there was significant frontal ROI activity within the middle and late epochs while there was significant parietal ROI activity within the early and late epochs. The early parietal ROI activity reflects visual sensory activity that spread beyond the occipital-temporal ROI boundaries, as the corresponding dipole sources were all localized to occipital cortex, so will not be considered further.
3. Discussion

Of relevance to the primary aim of the present study, the present fMRI results show that accurate memory for spatial location can reactivate retinotopic visual regions (i.e., produce retinotopic memory effects). In addition, memory control regions included the prefrontal cortex, the parietal cortex, and the hippocampus, consistent with previous findings (Buckner et al., 1998; Slotnick et al., 2003). As mentioned previously, parietal activity may reflect processing of contextual details (Wilding, 2000; Vilberg et al., 2006) while frontal activity may reflect post-retrieval monitoring (Goldmann et al., 2003). The present ERP results further characterized this memory control region activity and revealed significant activity in parietal and frontal ROIs (concomitant with retinotopic memory effects in occipital or temporal ROIs) during both the late epoch (400-800 ms) and middle epochs (1000-1600 ms), respectively. These results indicate that parietal and frontal lobe activations are not restricted to the middle and late epochs, which is consistent with previous findings (Ranganath and Paller, 1999; Allan et al., 2000, 2001; Tsivilis et al., 2001; Vilberg et al., 2006), and illustrates that the specific roles of these regions during retrieval are still under active investigation.

Of relevance to the second aim of the present study, retinotopic memory effects occurred within 100-250 ms after onset (Fig. 5), much faster than memory related activity typically attributed to parietal cortex or prefrontal cortex during retrieval, but well within the time range of memory related activity reported in the hippocampus (Rolls et al., 1989; Kreiman et al., 2000). Although ERPs are insensitive to activity in the medial temporal lobe,
hippocampal activity was observed with fMRI (Fig. 3). As such, the combined pattern of results supports a fast mechanism for retrieval of spatial location information that depends on the hippocampus.

The retinotopic memory effects, as assessed with both fMRI and ERPs, were significantly greater in the right than the left hemisphere. This may be due to hemispheric differences in visual spatial processing, as the left hemisphere has been shown to preferentially process categorical information, such as whether one item above or below the other, while the right hemisphere has been shown to preferentially process coordinate information, such as whether one item is greater or less than 2 cm away from the other (Kosslyn, 1987; Kosslyn et al., 1998; Slotnick et al., 2001). If accurate memory in the present paradigm depended on retrieval of the precise spatial location of the shape relative to fixation – a coordinate based process – there should be greater effects in the right hemisphere, as was observed. While this explanation is post hoc, it is also in accordance with the evidence that the right hemisphere is associated with memory for specific details (Koutstaal et al., 2001; Simons et al., 2003; Slotnick and Moo, 2006).

It should be underscored that the ERP retinotopic memory effects not only occurred in the early epoch, but continued to occur in the middle and late epochs (Fig. 5). These early retinotopic memory effects suggest retrieval can occur very rapidly, possibly via a hippocampal mechanism, but the continued retinotopic memory effects in the middle and late epochs suggest the memory representation persists or may be refined over time. It may be that the initial memory representation is relatively imprecise (although the behavioral results indicate it must have sufficient detail to make an accurate spatial memory judgment). Later during the retrieval process, activity in parietal cortex may enhance the memory representation through amplification or combining the component features, functions widely
attributed to this region during attentional processing (Mangun et al., 1998; Treisman, 1996). Finally, prefrontal regions may further enhance the memory representation or may be associated with monitoring or decision making functions. Although this model of retrieval is speculative, it highlights that a relatively detailed memory sketch can be retrieved very rapidly and then this representation may be refined over time. Future research will be needed to determine the precise operations that occur at each stage of retrieval process.

4. Experimental Procedure

4.1. Stimulus protocol and task

For both fMRI and ERP studies, participants completed multiple runs consisting of a study phase and a test phase. There were 2 initial practice runs followed by 6 experimental runs. The first practice run was 1/4 full-length and the second practice run was full-length. Data were only acquired in the subsequent 6 full-length experimental runs. In the study phase of each full-length run, 32 abstract shapes were presented 3° of visual angle to the left or right of fixation with random assignment of spatial location except for the constraint that no more than 3 shapes were sequentially presented on a given side (Fig. 1A). Shapes were constructed by connecting four Bezier curves filled with colored oriented lines, where the endpoints of each curve was placed on adjacent sides of a bounding square 5.5° of visual angle along each edge (details on shape construction have been described previously; Slotnick and Schacter, 2004). Shapes were never repeated and colors/line orientations were never repeated within a given run, except old items that were intentionally repeated during both study and test phases. Each shape was presented for 2.5 s followed by a 0.5 s fixation period. Participants were instructed to remember each shape and its spatial location while always maintaining central fixation. In the test phase of each full-length run, the 32 shapes from the study phase
in addition to 16 new shapes were presented at fixation in random order with the constraint that no more than 3 shapes of a given type (old-left, old-right, or new) were sequentially presented (Fig. 1B). For fMRI, shapes were presented every 4-12 s with a duration of 2.5 s (such temporal jitter allows for deconvolution of the hemodynamic response), and for ERPs shapes were presented every 6 s (with an extended duration of 4 s used to eliminate stimulus offset related activity). Participants made a button response with their left hand to indicate whether each shape was old and on the “left”, old and on the “right”, or “new” (a subsequent confidence rating was made during fMRI which was not considered in the present analysis). Shapes in each of the 3 conditions (old-left, old-right, new) were counterbalanced across participants using a Latin Square design.

4.2. Behavioral analysis

Item memory accuracy (Macmillan and Creelman, 2005) was defined as the percentage of old and new items that were correctly identified regardless of spatial location accuracy, weighted by the probability of each item type \( p(\text{old})*(\text{old-hit rate})+p(\text{new})*(\text{new-correct rejection rate}) \). Spatial location accuracy was defined as the percent of old items where spatial location was correctly identified, based on the total number of items correctly identified as old regardless of spatial location accuracy.

4.3. fMRI methods

Sixteen undergraduates with normal or corrected-to-normal vision provided informed and written consent to take part in the study. The experimental protocol had been approved by the Massachusetts General Hospital Internal Review Board. Analysis was restricted to the twelve participants who completed the experiment (7 females).
Imaging was conducted using a 3 Tesla Siemens Allegra scanner. Anatomic data were acquired using a multiplanar rapidly acquired gradient echo (MP-RAGE) sequence (TR = 30 msec, TE = 3.3 msec, 128 slices, 1 x 1 x 1.33 mm resolution). Functional data were acquired using an echo planar imaging (EPI) sequence (TR = 2 sec, TE = 30 msec, 64 x 64 acquisition matrix, 30 slices, 4.5 mm isotropic resolution). Imaging analysis was conducted using BrainVoyager QX (Brain Innovation B.V., Maastricht, The Netherlands). Functional data preprocessing included slice-time correction, motion correction, linear trend removal, high-pass temporal filtering (removal of temporal frequencies below 3 cycles/run), transformation into Talairach space, and re-sampling at 3 mm isotropic resolution. To maximize spatial resolution, no spatial smoothing was conducted. The anatomic volume of a representative participant was segmented at the gray-white matter junction, the cortical surface reconstructed, and then slightly inflated for display of the group functional results (Slotnick, 2005).

A random-effect general linear model approach was used to conduct the analysis. On an individual participant basis, a canonical hemodynamic response function was convolved with the protocol of each event – a series of square waves defined by each event onset and the subsequent behavioral response – to produce the corresponding hemodynamic response model. Events included encoding of shapes and locations (encoding-left, encoding-right), successful retrieval of shapes and previous locations (old-left-hit, old-right-hit), successful retrieval of shapes but not locations, unsuccessful retrieval of shapes, false memory of new shapes, correct rejection of new shapes (new-correct rejection), failures to respond, and a constant. It should be noted that old-hit, in the present study, refers to accurate item memory and accurate spatial location memory. Encoding trials and no response trials were assumed to be 2.5 s in duration. For each voxel, a general linear model was used to fit all event
hemodynamic response models to the activation timecourse resulting in the best-fit event model amplitudes (i.e. beta-weights). For a given statistical contrast, voxels were considered active when the difference between the associated beta-weights was significantly positive (using a one-tailed paired t-test, where variance was estimated using between participant variability).

Retinotopic memory effects were assessed by contrasting activity associated with accurate memory for stimuli in the left visual field with activity associated with accurate memory for stimuli in the right visual field (old-left-hit > old-right-hit) and vice versa for stimuli in the right versus left visual field (old-right-hit > old-left-hit). Furthermore, in an effort to minimize type I error, retinotopic memory effects were only considered within classic retinotopic regions (BA17, BA18) associated with perception/encoding. Specifically, a conjunction analysis (Nichols et al., 2005) was conducted to identify retinotopic regions that were activated at both retrieval and encoding, where the conjunction of (old-left-hit > old-right-hit) ∩ (encoding-left > encoding-right) and the conjunction of (old-right-hit > old-left-hit) ∩ (encoding-right > encoding-left) were used to isolate retinotopic memory effects. To investigate regions associated with memory control regions, old-hits were contrasted with new-correct rejections, as is commonly done, using the conjunction (old-left-hit > new-correct rejection) ∩ (old-right-hit > new-correct rejection). For each contrast entered into the conjunction, an individual voxel threshold of p < 0.01 was enforced, which corresponds to a joint p-value < 0.001 (computed using Fisher’s technique; Fisher, 1973). A minimum cluster extent threshold of at least 4 resampled voxels was also enforced.

Given that multiple statistical tests were computed, familywise (type I) error was controlled by limiting the false discovery rate (Benjamini and Hochberg, 1995; Genovese et al., 2002). For the memory control region results, a whole brain analysis, the individual voxel
threshold of p < 0.01 was selected to limit the false discovery rate to 0.05. For the retinotopic memory results, a region-of-interest analysis, false discovery rate was computed directly by dividing the number of false positives by the number of true positives and false positives (which was assumed equivalent to the number of contralateral and ipsilateral activations, respectively). The corresponding false discovery rate was also less than 0.05.

The functional results were projected onto the anatomic data of a representative participant. It is important to note that such activity should only be considered a reflection of the group results (precise activation coordinates are listed in Table 1). To further characterize the nature of activity in selected regions, event-related activity timecourses (computed from –2 to 12 seconds after stimulus onset) were extracted with the mean activity computed from voxels within a 5 mm sphere. Timecourses were additionally baseline corrected from –2 to 0 seconds after stimulus onset and linear drift corrected. When timecourse magnitudes were used to make statistical comparisons, mean activity from 6-8 seconds after stimulus onset was used (given that this is the time of the expected maximum of the hemodynamic response). Hemispheric asymmetry was assessed by comparing the magnitude of activity in a selected region with the magnitude of the homologous region in the opposite hemisphere (centered at the same y- and z-coordinates with the x-coordinate opposite in sign).

4.4. ERP methods

Twelve undergraduates (5 females) with normal or corrected-to-normal visual acuity were included in the analysis (3 additional participants completed the study but their data was not analyzed as it was corrupted). The experimental protocol had been approved by the Boston College Institutional Review Board with informed and written consent obtained from each participant before the experiment commenced.
Electrophysiological data was acquired in a shielded chamber (Global Partners in Shielding, Inc., Passaic, NJ) using a 128-channel NeuroScan system (Compumedics USA, Charlotte, NC) including SynAmps² amplifiers, a Quik-Cap with sintered silver/silver chloride electrodes, and the SCAN acquisition software program. All electrode impedances were maintained below 15 kΩ. Standard pre-processing was conducted using BESA analysis software on a run-by-run basis (MEGIS Software GmbH, Gräfelfing, Germany). Blink correction was conducted by removing the first principle component or the first and second principal components of the blink topography (the minimum number that explained at least 85% of variance) from the recorded waveforms. To further reduce noise, trials and electrodes associated with very high amplitudes or gradients were removed from the analysis (using the default threshold values in BESA). A low-pass (forward) filter cutoff of 0.5 Hz was implemented (6 dB/octave). No high-pass filter was used. Event-related averages corresponding to each item type in the study phase were computed from –100 to 500 ms after stimulus onset while event-related averages corresponding to each item type in the test phase were computed from –500 to 2000 ms after stimulus onset. For each participant, event-related averages associated with each event type were computed via a weighted average across runs. Dipole source localization was conducted at selected time points using a 4 shell ellipsoidal head model and dipoles that varied in magnitude, location, and orientation. To fit differential voltage topographies (e.g. old-left-hit – old-right-hit), a two dipole model was used to fit cortical activity as well as eye-movement activity (the latter of which was always localized just superior and posterior and not localized in cortex).

Analysis was conducted using the mean activity across 8 groups of electrodes that defined regions-of-interest (ROIs), defined a priori, over the left and right occipital, temporal, parietal, and frontal scalp. In an effort to maximize sensitivity to retinotopic memory effects,
Occipital and temporal electrodes were selected from those that evinced robust retinotopic activity during encoding (by contrasting encoding-left > encoding-right for right scalp electrodes and encoding-right > encoding-left for left scalp electrodes) and were also known to reflect retinotopic perception/attention related activity in striate and extrastriate cortex (Clark et al., 1995; Di Russo et al., 2002). In each hemisphere these regions were further divided into an occipital ROI and a temporal ROI to assess whether there were differential effects in these regions, based on limited evidence for preferential retinotopic memory effects in temporal electrodes (Gratton et al., 1997; Fabiani et al., 2000). Frontal and parietal ROI electrodes in each hemisphere were selected to match the regions of greatest activity associated with memory for specific or general details shown in two previous ERP studies that employed similar paradigms as the present study (Ranganath and Paller, 1999; Vallesi and Shallice, 2006). Electrode locations were labeled according to the 10-5 system (Oostenveld and Praamstra, 2001), a variant of the 10-20 electrode system (Jasper, 1958) with interpolated electrode positions. The left hemisphere occipital ROI included electrodes I1, O1, PO1, P1, PO9, PO7, PO5, P3, the temporal ROI included electrodes P9, P7, P5, CP3, TPP9, TPP7, CPP5, CP5, TTP7h, TP7, the parietal ROI included electrodes CPP1h, CP1h, CPP1, CP1, C1, CP3, and the frontal ROI included electrodes F3, AF3, AFp1, Fp1, FFC3, F5, AF5. Right hemisphere ROIs included the analogous electrodes. Occipital, temporal, and parietal ROIs are illustrated in Fig. 4B.

The 13 ms time window (± 6 ms) used to assess significance at each time point was computed based in part on the duration of significant encoding-related retinotopic activity, as it can be assumed that retinotopic memory reactivation should activate the same regions associated with encoding. However, it is known that encoding/perceptual activity has a much higher magnitude of activity than that associated with retrieval, such that the required duration
of activity at retrieval should be only some fraction of the encoding activation window. The duration of retinotopic encoding-related activity within the 60-200 ms time following stimulus onset (known to contain the extrastriate generated P1 visual sensory response) was determined to be 49 ms, computed by averaging the number of contiguous significant retinotopic encoding timepoints for the right occipital ROI (corresponding to differential activity associated with encoding-left – encoding-right) and left occipital ROI (corresponding to differential activity associated with encoding-right – encoding-left). The encoding-retrieval scaling factor of 4.45 was computed from the average event-related fMRI timecourses extracted from left and right BA18 at 6-8 ms following stimulus onset, the expected maximum (these regions and retrieval-related timecourses are shown in Fig. 2). Dividing the encoding time window by the encoding-retrieval scale factor was taken as the expected duration of retrieval related reactivation in retinotopic regions (49/4.45, with use of the next highest odd integer, 13 ms, to yield a relatively conservative measure).

The statistical threshold associated with each of the three tests used to assess hemispheric laterality was set such that the joint p-value was equal to 0.05, computed using Fisher’s technique (Fisher, 1973). A threshold p-value of 0.05 was also used to identify timepoints of significant frontal and parietal ROI activity (which were only considered when concomitant with significant occipital or temporal ROI activity). To control familywise error, false discovery rate was computed from the number of false positives divided by the number of true positives and false positives (Benjamini and Hochberg, 1995; Genovese et al., 2002), where true and false positives were assumed to be equal to the number of contralateral and ipsilateral visual activations, respectively (the same procedure used to correct for multiple comparisons with the retinotopic fMRI results). The corresponding false discovery rate was less than 0.05 (see
Results). Comparisons between number of activations over time (e.g., retinotopic versus ipsilateral) were computed using a Binomial test (with \( p = 0.50 \)).
Acknowledgments

I would like to thank Lauren Moo and Preston Thakral for stimulating discussions.
References


Heinze, H.J., Mangun, G.R., Burchert, W., Hinrichs, H., Scholz, M., Münke, T.F., Gös, A.,


Slotnick, S.D, Moo, L.R. 2006. Prefrontal cortex hemispheric specialization for categorical and coordinate visual spatial memory. Neuropsychologia 44, 1560-1568.


Vallesi, A., Shallice, T., 2006. Prefrontal involvement in source memory: an
electrophysiological investigation of accounts concerning confidence and accuracy. Brain
Res. 1124, 111-125.

specificity in episodic memory: memory-induced re-activation of picture processing areas.
Neuropsychologia 40, 2136-2143.

correlates of recollection and amount of information retrieved. Brain Res. 1122, 161-170.


knowing. Neuroimage 21, 1337-1349.


Wilding, E.L., 2000. In what way does the parietal ERP old/new effect index recollection?
Int. J. Psychophysioll. 35, 81-87.
Table 1

Neural regions commonly associated with accurate memory
(identified using the conjunction old-hit-left > new-correct rejection
∩ old-hit-right > new-correct rejection).

<table>
<thead>
<tr>
<th>Region</th>
<th>BA</th>
<th>x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left anterior prefrontal cortex</td>
<td>10</td>
<td>−23</td>
<td>49</td>
<td>8</td>
</tr>
<tr>
<td>Left inferior frontal gyrus</td>
<td>45/46</td>
<td>−40</td>
<td>34</td>
<td>7</td>
</tr>
<tr>
<td>Left inferior frontal sulcus</td>
<td>9/44/45/46</td>
<td>−43</td>
<td>13</td>
<td>25</td>
</tr>
<tr>
<td>Right inferior frontal sulcus</td>
<td>9/44/45/46</td>
<td>41</td>
<td>15</td>
<td>27</td>
</tr>
<tr>
<td>Left middle frontal gyrus</td>
<td>6/8/9/46</td>
<td>−38</td>
<td>9</td>
<td>45</td>
</tr>
<tr>
<td>Left superior frontal sulcus</td>
<td>6/8/9</td>
<td>−25</td>
<td>6</td>
<td>47</td>
</tr>
<tr>
<td>Right superior frontal sulcus</td>
<td>6/8/9</td>
<td>25</td>
<td>5</td>
<td>48</td>
</tr>
<tr>
<td>Left superior frontal gyrus</td>
<td>6</td>
<td>−19</td>
<td>2</td>
<td>57</td>
</tr>
<tr>
<td>Left medial prefrontal cortex</td>
<td>6/8/9/10</td>
<td>−4</td>
<td>28</td>
<td>36</td>
</tr>
<tr>
<td>Right medial prefrontal cortex</td>
<td>8</td>
<td>8</td>
<td>18</td>
<td>42</td>
</tr>
<tr>
<td>Left anterior cingulate</td>
<td>24/32</td>
<td>−4</td>
<td>28</td>
<td>21</td>
</tr>
<tr>
<td>Right anterior cingulate</td>
<td>24/32</td>
<td>6</td>
<td>28</td>
<td>18</td>
</tr>
<tr>
<td>Left posterior cingulate</td>
<td>23/31</td>
<td>−6</td>
<td>−54</td>
<td>28</td>
</tr>
<tr>
<td>Right posterior cingulate</td>
<td>23/31</td>
<td>6</td>
<td>−51</td>
<td>19</td>
</tr>
<tr>
<td>Left orbitofrontal cortex</td>
<td>11</td>
<td>−29</td>
<td>40</td>
<td>−6</td>
</tr>
<tr>
<td>Right orbitofrontal cortex</td>
<td>11</td>
<td>27</td>
<td>47</td>
<td>−3</td>
</tr>
<tr>
<td>Left insula</td>
<td>−</td>
<td>−37</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Right insula</td>
<td>−</td>
<td>30</td>
<td>21</td>
<td>3</td>
</tr>
<tr>
<td>Left basal ganglia</td>
<td>−</td>
<td>−8</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Right basal ganglia</td>
<td>−</td>
<td>10</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Left cerebellum</td>
<td>−</td>
<td>−25</td>
<td>−58</td>
<td>−24</td>
</tr>
<tr>
<td>Right cerebellum</td>
<td>−</td>
<td>20</td>
<td>−57</td>
<td>−24</td>
</tr>
<tr>
<td>Left superior parietal lobule</td>
<td>7</td>
<td>−18</td>
<td>−68</td>
<td>50</td>
</tr>
<tr>
<td>Region</td>
<td>BA</td>
<td>x</td>
<td>y</td>
<td>z</td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>-----</td>
<td>------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td>Right superior parietal lobule</td>
<td>7</td>
<td>16</td>
<td>-66</td>
<td>51</td>
</tr>
<tr>
<td>Left precuneus</td>
<td>7</td>
<td>-3</td>
<td>-61</td>
<td>40</td>
</tr>
<tr>
<td>Right precuneus</td>
<td>7</td>
<td>4</td>
<td>-62</td>
<td>41</td>
</tr>
<tr>
<td>Left intraparietal sulcus</td>
<td>7/19/39/40</td>
<td>-30</td>
<td>-60</td>
<td>37</td>
</tr>
<tr>
<td>Right intraparietal sulcus</td>
<td>7/19/39/40</td>
<td>37</td>
<td>-57</td>
<td>37</td>
</tr>
<tr>
<td>Left thalamus</td>
<td>-</td>
<td>-12</td>
<td>-25</td>
<td>12</td>
</tr>
<tr>
<td>Right thalamus</td>
<td>-</td>
<td>15</td>
<td>-25</td>
<td>10</td>
</tr>
<tr>
<td>Left striate cortex</td>
<td>17</td>
<td>-13</td>
<td>-72</td>
<td>7</td>
</tr>
<tr>
<td>Right striate cortex</td>
<td>17</td>
<td>9</td>
<td>-71</td>
<td>9</td>
</tr>
<tr>
<td>Left cuneus</td>
<td>18</td>
<td>-5</td>
<td>-68</td>
<td>18</td>
</tr>
<tr>
<td>Right cuneus</td>
<td>18</td>
<td>7</td>
<td>-70</td>
<td>17</td>
</tr>
<tr>
<td>Left lingual gyrus</td>
<td>18</td>
<td>-6</td>
<td>-71</td>
<td>-2</td>
</tr>
<tr>
<td>Right lingual gyrus</td>
<td>18</td>
<td>10</td>
<td>-72</td>
<td>0</td>
</tr>
<tr>
<td>Left superior occipital gyrus</td>
<td>19</td>
<td>-36</td>
<td>-72</td>
<td>32</td>
</tr>
<tr>
<td>Right superior occipital gyrus</td>
<td>19</td>
<td>37</td>
<td>-69</td>
<td>31</td>
</tr>
<tr>
<td>Left fusiform gyrus</td>
<td>19/20/37</td>
<td>-38</td>
<td>-51</td>
<td>-17</td>
</tr>
<tr>
<td>Right fusiform gyrus</td>
<td>37</td>
<td>43</td>
<td>-53</td>
<td>-13</td>
</tr>
<tr>
<td>Left collateral sulcus</td>
<td>20/36</td>
<td>-27</td>
<td>-44</td>
<td>-9</td>
</tr>
<tr>
<td>Left middle temporal gyrus</td>
<td>21/37</td>
<td>-48</td>
<td>-52</td>
<td>-2</td>
</tr>
<tr>
<td>Right middle temporal gyrus</td>
<td>21/37</td>
<td>56</td>
<td>-40</td>
<td>-2</td>
</tr>
<tr>
<td>Left retrosplenial cortex</td>
<td>26/29</td>
<td>-4</td>
<td>-41</td>
<td>14</td>
</tr>
<tr>
<td>Right retrosplenial cortex</td>
<td>26/29</td>
<td>4</td>
<td>-40</td>
<td>12</td>
</tr>
<tr>
<td>Left parahippocampal gyrus</td>
<td>30</td>
<td>-18</td>
<td>-41</td>
<td>-5</td>
</tr>
<tr>
<td>Left hippocampus</td>
<td>-</td>
<td>-16</td>
<td>-30</td>
<td>-3</td>
</tr>
<tr>
<td>Right hippocampus</td>
<td>-</td>
<td>23</td>
<td>-19</td>
<td>-4</td>
</tr>
</tbody>
</table>

BA refers to Brodmann area and Talairach coordinate (x, y, z) refers to the center of activation within each region.
Figure legends

Fig. 1. (A) During the study phase, shapes were presented to the left or right of fixation. (B) During the test phase, old shapes from the study phase (previously on the left, old-left, or previously on the right, old-right) or new shapes were presented at fixation and participants classified each shape as old and on the “left”, old and on the “right”, or “new”.

Fig. 2. (A) Spatial memory related fMRI activity in retinotopic visual regions projected onto a cortical surface representation (posterior view, with the right hemisphere to the right; gyri and sulci colored light and dark gray, respectively). Retinotopic memory effects were isolated by contrasting old-left-hit > old-right-hit (significant activity shown in red) and old-right-hit > old-left-hit (significant activity shown in blue). (B) Event-related timecourses extracted from the two significant regions of activity.

Fig. 3. (A) fMRI memory control regions projected onto a cortical surface representation (to the left, superior view) and a selected coronal slice (to the right, at the anterior-posterior position marked by the cyan dashed line on the left) identified using the conjunction (old-left-hit > new-correct rejection) ∩ (old-right-hit > new-correct rejection). (B) Event-related timecourses extracted from activity in the middle frontal gyrus, the intraparietal sulcus, and the hippocampus.

Fig. 4. (A) ERP differential activation timecourses in left occipital, left temporal, right occipital, and right temporal regions-of-interest (ROIs) computed to maximize sensitivity to retinotopic memory effects (i.e., memory for items previously presented in the left visual field activating right occipital-temporal ROIs and vice versa). To the left, old-left-hit – old-right-hit activity
within the 100-200 ms range is shown, with significant lateralized activity in right occipital and right temporal (retinotopic) ROIs demarcated between black vertical lines (significant lateralization in a given ROI was defined by activity that was significantly greater than zero and significantly greater than both occipital and temporal ROI activity in the opposite hemisphere). There was no lateralized activity in ipsilateral/left ROIs. To the right, old-right-hit – old-left-hit activity is shown, with significant lateralized activity in left occipital and left temporal (retinotopic) ROIs demarcated between black vertical lines (there was no lateralized activity in ipsilateral/right ROIs). (B) Posterior view of ERP voltage scalp topography with ROIs delimited by black ovals. Differential activation topography illustrates memory related retinotopic activation at the mean timepoint within the significantly lateralized epochs above (color scale in middle). (C) Posterior coronal view of occipital dipole sources underlying the voltage topographies above. Dipoles in the right and left hemispheres are colored red and blue, respectively.

Fig. 5. (A) In the lower component of each panel, lateralized temporal and occipital activity within 0-1600 ms associated with memory for stimuli in the left visual field (epochs with significant lateralization are demarcated by solid black vertical bars). In temporal and occipital ROIs, old-left-hit – old-right-hit activity was used for statistical assessment (the black vertical bar just preceding 200 ms in each of the right temporal and right occipital components of the right panels correspond to the epoch defined by the black vertical lines in the left panel of Fig. 4A). In parietal and frontal ROIs, old-left-hit – new-correct rejection activity was used for statistical assessment (only activity that overlapped the corresponding occipital or temporal ROI is shown). (B) Lateralized temporal and occipital activity associated with memory for stimuli in the right visual field. In temporal and occipital ROIs, old-right-hit – old-left-hit activity
was used for statistical assessment. In parietal and frontal ROIs, old-right-hit – new-correct rejection activity was used for statistical assessment.
Figure 2

A

- Old-left-hit > old-right-hit
- Old-right-hit > old-left-hit

B

Signal (% change)

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>0.05</th>
<th>0.10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (s)</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

Signal (% change)

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>0.2</th>
<th>0.4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (s)</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>
Figure 3

A

\[ \text{(Old-left-hit} > \text{new-correct rejection}) \cap \text{(Old-right-hit} > \text{new-correct rejection}) \]

B

---

<table>
<thead>
<tr>
<th>Signal (% change)</th>
<th>Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 2 4 6 8 10</td>
</tr>
<tr>
<td>Old-left-hit</td>
<td></td>
</tr>
<tr>
<td>Old-right-hit</td>
<td></td>
</tr>
<tr>
<td>New-correct rejection</td>
<td></td>
</tr>
</tbody>
</table>
Figure 5

A

Memory for stimuli in left visual field (old-left-hit > baseline)

B

Memory for stimuli in right visual field (old-right-hit > baseline)