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 event-related potentials (ERPs) and functional magnetic resonance imaging (fMRI). 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 the 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.

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Keywords: ERPs fMRI Hippocampus Retrieval Visual
The primary aim of the present investigation was to determine the earliest time at which retinotopic memory effects could occur using ERPs. 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 and the right visual field versus one another or versus each new item. 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 memory related ERP activity in frontal regions (Curran et al., 2001; Tsivilis et al., 2001) and depth electrode activity in human and non-human primate hippocampus (Rolls et al., 1989; Kreiman et al., 2000), where the hippocampus may bind information processed in different cortical regions (Squire, 1992; Manns and Eichenbaum, 2006).

A secondary aim of the present investigation was to identify the neural loci of retinotopic memory effects using functional magnetic resonance imaging (fMRI). Memory control regions (commonly associated with accurate memory) were also identified using fMRI 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).

2. Results

2.1. Retinotopic encoding/perception activations

ERP retinotopic encoding/perception effects were assessed by testing for hemispheric lateralization within occipital and temporal regions-of-interest (ROIs; Section 4.3 ERP methods). Differential ERP timecourses (computed from the average activity across electrodes within each ROI) associated with encoding/perception of stimuli in the left visual field were computed from encoding-left>encoding-right and timecourses associated with encoding/perception of stimuli in the right visual field were computed from encoding-right>encoding-left. Such difference waveforms are analogous to those computed to isolate retinotopic attention effects in posterior electrodes (Heinze et al., 1994; Mangun et al., 1998) with the aim of subtracting out activity common to both event types (e.g., if encoding-left and encoding-right both activate the same ventral temporal region the magnitude of differential timecourse activity will be zero). Fig. 2A illustrates the waveforms corresponding to occipital and temporal ROIs. Note that each ROI waveform in the right panel is simply the inversion of the corresponding waveform in the left panel which follows from subtracting the same activity in the opposite direction. The change in the magnitude of activity before stimulus onset can be attributed to anticipation effects (Sylvester et al., 2007; McMains et al., 2007) as participants could predict the time at which each stimulus would be presented given the constant inter-trial-interval. Consistent with known retinotopic perceptual effects, stimuli in the left visual field produced significant activations in the right occipital and temporal ROIs and stimuli in the right visual field produced significant activations in the left occipital and temporal ROIs. Hemispheric laterality was evaluated at each 1 ms timepoint using the mean activity at that time ±6 ms. For a given occipital or temporal ROI and timepoint, significant hemispheric laterality required all of the following: 1) activity was significantly greater than zero, 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. Fig. 2B illustrates the scalp voltage topographies and corresponding dipole locations associated with two retinotopic encoding/perception effects confirming a right hemisphere occipital source underlying the right posterior voltage topography and a left hemisphere occipital source underlying the left posterior voltage topography. Because each ROI waveform is inverted for encoding-left>encoding-right as compared to encoding-right>encoding-left, as mentioned above, it might be expected that the scalp voltage topographies should be mirror symmetric (at a given time point). However, it is important to keep in mind that laterality effects are driven by activation increases in right ROIs for one subtraction and activation increases in left ROIs for the other subtraction (i.e., activity in independent ROIs/electrodes underlie each of the two laterality effects). Fig. 2C shows the analogous fMRI retinotopic encoding/perception effects assessed by contrasting encoding-left>encoding-right and encoding-right>encoding-left. Robust retinotopic activations were observed in occipital and temporal cortex that were completely restricted to the contralateral hemisphere, with encoding/perception of stimuli in the left and right visual fields preferentially activating the right and left visual regions, respectively. Representative event-related timecourses were also extracted. These ERP and fMRI results indicate that retinotopic encoding/perception related activity is only observed in contralateral (and not ipsilateral) occipital and temporal regions. The results are also consistent with previous retinotopic attention extrastriate cortex effects reflected in the positive ERP P1 component that has maximum amplitude over occipital and temporal electrodes (Heinze et al., 1994; Mangun et al., 1998), as compared to the negative ERP N1 component that corresponds to deeper cortical sources that have more widely distributed maximal amplitude distributions (Clark and Hillyard, 1996; Di Russo et al., 2002). Critically, these encoding/perception results
indicate that if retinotopic reactivation occurs during retrieval it will be specifically manifested by an increase in activity within contralateral occipital and temporal ROIs.

2.2. Retinotopic memory activations

Item memory accuracy during ERP recording was 63.0±1.8% correct while spatial location memory accuracy was 66.5±2.3% correct (mean ± 1 se; chance performance = 50%). Item memory accuracy during fMRI was 67.2±1.6% correct while spatial location memory accuracy was 70.0±2.0% correct.

ERP retinotopic memory effects were assessed by testing for hemispheric lateralization within occipital and temporal ROIs. Differential ERP timecourses (computed from the average activity across electrodes within each ROI) associated with accurate memory for stimuli in the left visual field and right visual field were computed from old-left-hit–baseline and old-right-hit–baseline. Three event types were used to define baseline activity in an effort to fully characterize retinotopic memory effects: 1) the classic memory comparison, old-hit–new-correct rejection (although there is a notable item type confound), 2) to isolate activity associated with conscious remembering, old-hit–old-miss (where item type is constant), and 3) old-hit-left–old-hit-right and vice versa, where common neural activity will be subtracted out (which should maximize contralateral effects).

For the first comparison, accurate memory for stimuli in the left visual field was computed from old-left-hit–new-correct rejection and accurate memory for stimuli in the right visual field was computed from old-right-hit–new-correct rejection (see Johnson et al., 2008). Hemispheric laterality was evaluated at each 1 ms timepoint using the mean activity at that time±6 ms. For a given occipital or temporal ROI and timepoint, as with encoding, significant hemispheric laterality required all of the following: 1) activity was significantly greater than zero, 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. Fig. 3A and B illustrate the waveforms corresponding to occipital and temporal ROIs. As with the encoding waveforms, the change in activity before stimulus onset can be attributed to anticipation effects (Sylvester et al., 2007; McMains et al., 2007). Consistent with retinotopic memory reactivation, memory for items previously presented on the left (Fig. 3A) produced a greater number of activations in right occipital and temporal ROIs (red, dark yellow, and orange vertical bars) as compared to left occipital and temporal ROIs (blue, green, and cyan, vertical bars) and memory for items previously presented on the right (Fig. 3B) produced a greater number of activations in left (blue, green, and cyan, vertical bars) as compared to right occipital and temporal ROIs (red, dark yellow, and orange vertical bars).

Fig. 3C and D show the corresponding significant lateralized ERP activations (red vertical bars) within temporal and occipital ROIs associated with memory for stimuli in the left

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” (correct responses are shown to the right).
visual field and right visual field (bottom of each panel), respectively, with concomitant activations (red vertical bars) within frontal and parietal ROIs (top and middle of each panel; there were no negative-going effects within frontal and parietal ROIs). 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. Retinotopic memory effects occurred in the early (100–250 ms), middle (400–800 ms), and late (1000–1600 ms) epochs, with memory for stimuli previously presented in the left and right visual fields evoking activations that were largely restricted to the right or left temporal and occipital ROIs, respectively. Collapsing the activations across occipital and temporal ROIs in the right and left hemispheres yielded a significant retinotopic memory effect (26 contralateral, 9 ipsilateral, \( p < 0.01 \)). Hemispheric differences were also observed, with a significantly greater number of contralateral versus ipsilateral activations in the right hemisphere as compared to the left hemisphere (right hemisphere, 16 contralateral, 5 ipsilateral, \( p < 0.01 \); left hemisphere, 10 contralateral, 4 ipsilateral, \( p = 0.061 \)). The number of temporal and occipital ROI activations did not significantly differ (\( p > 0.20 \)). 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 it will not be considered further.

The second comparison aimed to isolate retinotopic memory effects associated with conscious remembering. Fig. 4A and B show significant lateralized ERP activations within temporal and occipital ROIs associated with remembered versus forgotten stimuli in the left visual field (old-left-hit – old-left-miss) and right visual field (old-right-hit – old-right-miss), with concomitant activations (red vertical bars) and negative-going effects (blue vertical bars) within frontal and parietal ROIs. Retinotopic memory effects occurred in the early (100–250 ms) and late (1000–1600 ms) epochs, with memory for stimuli previously presented in the left and right visual fields evoking activations that were largely restricted to the right or left temporal and occipital ROIs, respectively. Collapsing the activations across occipital and temporal ROIs in the right and left hemispheres yielded a significant retinotopic memory effect (21 contralateral, 7 ipsilateral, \( p < 0.01 \)). Hemispheric differences were also observed, with a significantly greater number of contralateral versus ipsilateral activations in the right hemisphere as compared to the left hemisphere (right hemisphere, 14 contralateral, 4 ipsilateral, \( p < 0.05 \); left hemisphere, 7 contralateral, 3 ipsilateral, \( p = 0.12 \)). Occipital–temporal differences were also observed, with a significantly greater number of contralateral versus ipsilateral activations in temporal ROIs as compared to occipital ROIs (\( p < 0.01 \); occipital ROIs, 4 contralateral, 3 ipsilateral, \( p > 0.20 \); temporal ROIs, 17 contralateral, 4 ipsilateral, \( p < 0.01 \)). These results support our previous results suggesting later as opposed to earlier visual processing regions are associated with conscious remembering (Slotnick and Schacter, 2004, 2006).

As has been done in previous studies to isolate retinotopic memory effects (Gratton et al., 1997; Fabiani et al., 2000), the third comparison employed difference waveforms between accurate memory for stimuli in the left versus right visual field (old-left-hit – old-right-hit) and accurate memory for stimuli in the right versus left visual field (old-right-hit – old-left-hit). This is analogous to difference waveforms computed to isolate retinotopic attention effects (Heineze et al., 1994; Mangun et al., 1998) with the aim of subtracting out activity associated with both event types. That is, the previous two comparisons employed baseline conditions that were not associated with item memory or spatial location memory. Because visual item memory has been associated with non-retinotopic/bilateral activity in ventral occipital–temporal cortex (Wheeler and Buckner, 2003, 2004), it can be argued that the previous comparisons (old-hit – new-correct rejection and old-hit – old-miss) produced bilateral activity due to differential item memory effects. It is notable that retinotopic memory effects were still observed in those comparisons despite such bilateral item memory related activity which may have masked the lateralized effects (the magnitude of visual item memory related activity may have been relatively small as it primarily occurs in more anterior ventral visual processing regions far from the ERP electrode sites; Slotnick, 2004b). The present comparison capitalizes on item memory being associated with both old-left-hit and old-right-hit such that subtracting these event types from one another can be expected to remove item memory related activity which should produce even more robust retinotopic memory effects. Fig. 5A and B show significant lateralized ERP activations within temporal and occipital ROIs associated with accurate memory for stimuli in the left versus right visual field and vice versa. Concomitant activations and negative-going effects within frontal and parietal ROIs are also shown. Retinotopic memory effects occurred in the early (100–250 ms), middle (400–800 ms), and late (1000–1600 ms) epochs, with memory for stimuli previously presented in the left and right visual fields evoking activations that were almost completely restricted to the right or left temporal and occipital ROIs, respectively. Collapsing the activations across occipital and temporal ROIs in the right and left hemispheres yielded a significant retinotopic memory effect (28 contralateral, 1 ipsilateral, \( p < 0.001 \)). Hemispheric differences were also observed, with a significantly greater number of contralateral versus ipsilateral activations in the right hemisphere as compared to the left hemisphere (right hemisphere, 19 contralateral, 0 ipsilateral, \( p < 0.001 \); left hemisphere, 9 contralateral, 1 ipsilateral, \( p < 0.001 \)). The number of temporal and occipital ROI activations did not significantly differ (\( p = 0.13 \)). Fig. 5C illustrates the scalp voltage topographies and corresponding dipole locations associated with two retinotopic memory effects confirming a right hemisphere occipital source underlying the right posterior voltage topography and a left hemisphere occipital source underlying the left posterior voltage topography.

Fig. 5D shows the analogous fMRI retinotopic memory effects assessed by contrasting old-left-hit > old-right-hit and old-right-hit > old-left-hit. 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. Only two regions of significant activity were observed, one in the right hemisphere (lingual gyrus, BA18, Talairach coordinate 24, –91, 6) and one in the left hemisphere (cuneus, BA18, Talairach coordinate –9, –83, 18). It is notable that although both of these activations occurred in BA18, they are not in homologous regions. In a previous spatial location memory fMRI
study, we reported contralateral memory effects in 5 of 5 BA18 regions tested, although the differential effects did not reach significance in 3 of these regions (Slotnick and Schacter, 2006). These results suggest that there may be sub-threshold retinotopic activations in homologous regions. Of primary importance, the significant activations observed did reflect retinotopic memory effects, with memory for stimuli previously presented in the left and right visual fields preferentially activating the right and left visual regions, respectively. Event-related timecourses were extracted from these regions (Fig. 5D). It should be noted that timecourse activity of negative magnitude, before and after each peak, can be attributed to a return to baseline following a previously active state (Slotnick and Schacter, 2004). Timecourse analysis
confirmed that both activations were lateralized to their respective hemisphere (hemisphere×old-left-hit/old-right-hit interaction, \( p < 0.001 \)). In the right hemisphere old-left-hit activity was greater than both old-right-hit activity (\( p < 0.001 \)) and new-correct rejection activity (\( p < 0.05 \)), and in the left hemisphere old-right-hit activity was greater than both old-left-hit activity (\( p < 0.05 \)) and new-correct rejection activity (\( p < 0.001 \)). 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, \( p < 0.001 \)) and mean absolute magnitude versus baseline (\( p < 0.001 \)).

2.3. Retinotopic memory negative-going effects

In addition to assessing memory related activations in occipital and temporal regions, it is also important to consider memory related negative-going effects (i.e., occipital and temporal ROI activity that is significantly less than...
zero and significantly less than activity in the occipital and temporal ROIs in the opposite hemisphere). Lateralized memory related negative-going effects were not observed for the old-hit–old-miss comparisons (5 contralateral, 7 ipsilateral, p=0.19) but were observed for the old-hit–new-correct rejection comparisons. Fig. 6A and B show significant lateralized ERP negative-going effects (blue vertical bars) within temporal and occipital ROIs associated with stimuli in the left visual field (old-left-hit–new-correct rejection) and right visual field (old-right-hit–new-correct rejection), with concomitant negative-going effects (blue vertical bars) within frontal and parietal ROIs (there were no concomitant activations in frontal and parietal ROIs). Lateralized memory effects were completely restricted to the right hemisphere during memory for right (ipsilateral) visual field stimuli, were associated with almost no frontal and parietal control activity, and occurred early and into the middle (400–800 ms) epoch. Collapsing the activations
across occipital and temporal ROIs in the right and left hemispheres yielded a significant lateralized memory effect (10 ipsilateral, 2 contralateral, \(p<0.05\)). Hemispheric differences were also observed, with a significantly greater number of ipsilateral versus contralateral activations in the right hemisphere as compared to the left hemisphere (\(p<0.01\); right hemisphere, 10 ipsilateral, 2 contralateral, \(p<0.05\); left hemisphere, 0 ipsilateral, 0 contralateral, \(p>0.20\)). The number of temporal and occipital ROI activations did not significantly differ (\(p>0.20\)). Based on the encoding results above (Section 2.1 Retinotopic encoding/perception activations), where retinotopic activity was associated with an increase in activity within contralateral occipital and temporal regions, these ipsilateral negative-going effects may reflect memory related inhibition during memory for stimuli in the right visual field.

### 2.4. Memory control regions

Fig. 7 illustrates fMRI control regions commonly associated with accurate memory (using the conjunction old-left-hit>new-correct rejection \(\cap\) old-right-hit>new-correct rejection).

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**Fig. 6** – (A) Old-left-hit–new-correct rejection lateralized temporal and occipital ROI ERP negative-going effects (blue vertical bars) with concomitant frontal and parietal ROI negative-going effects (blue vertical bars; there were no significant frontal or parietal ROI activations). Significant lateralization in a given ROI was defined by activity that was significantly less than zero and significantly less than both occipital and temporal ROI activity in the opposite hemisphere. (B) Old-right-hit–new-correct rejection lateralized temporal and occipital ROI ERP negative-going effects with concomitant frontal and parietal ROI negative-going effects (there were no significant frontal or parietal ROI activations).

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**Fig. 5** – (A) Old-left-hit–old-right-hit lateralized temporal and occipital ROI ERP activations (red vertical bars) with concomitant frontal and parietal ROI activations (red vertical bars) and negative-going effects (blue vertical bars). (B) Old-right-hit–old-left-hit lateralized temporal and occipital ROI ERP activations with concomitant frontal and parietal ROI activations and negative-going effects. (C) Toward the center, posterior view of differential ERP voltage scalp topographies (with ROIs delimited by black ovals) illustrate memory related retinotopic activation at the mean timepoint within select significantly lateralized epochs from above (color scale at center). Corresponding occipital dipole sources underlying these voltage topographies are also shown (dipoles in the right and left hemispheres are colored red and blue, respectively). (D) Toward the center, 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). Corresponding event-related timecourses extracted from the two significant regions of activity are also shown.
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).

3. Discussion

The present fMRI results showed that accurate memory for spatial location can reactivate retinotopic visual regions. In addition, memory control regions were identified and 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 the early (100–250 ms), middle (400–800 ms), and late epochs (1000–1600 ms). These results indicate that parietal and frontal lobe activations are not restricted to the middle and late epochs, respectively, which is consistent with previous findings (Ranganath and Paller, 1999; Allan et al., 2000, 2001; Tsivlis et al., 2001; Vilberg et al., 2006), and suggests that the specific roles of these regions during retrieval should be investigated further.

Of relevance to the primary aim of the present study, retinotopic memory effects occurred within 100–250 ms after onset (Figs. 3–5), much faster than memory related activity typically attributed to parietal cortex or prefrontal cortex during retrieval. This activity is within the time range of memory related activity reported in the frontal cortex (Curran et al., 2001; Tsivlis et al., 2001) and in the hippocampus (Rolls et al., 1989; Kreiman et al., 2000). Frontal ROI activity was in fact concomitant with nearly half of the early retinotopic memory activations in occipital and temporal ROIs (Figs. 3–5). In addition, although ERPs are insensitive to activity in the medial temporal lobe, hippocampal activity was observed with fMRI (Fig. 7). As such, the combined pattern of results supports a fast mechanism for retrieval of spatial location that may depend on both the frontal cortex and the hippocampus.

The retinotopic memory effects, as assessed with both ERPs and fMRI, 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 is 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 (Figs. 3–5). These early retinotopic memory effects suggest retrieval can occur very rapidly, possibly via a frontal–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. 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.

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).

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<th>y</th>
<th>z</th>
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<td>48</td>
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<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>-70</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>
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<td>20/36</td>
<td>-27</td>
<td>-44</td>
<td>-9</td>
</tr>
<tr>
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<td>-48</td>
<td>-52</td>
<td>-2</td>
</tr>
<tr>
<td>Right middle temporal gyrus</td>
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<td>56</td>
<td>-40</td>
<td>-2</td>
</tr>
<tr>
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<td>-4</td>
<td>-41</td>
<td>14</td>
</tr>
<tr>
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<td>4</td>
<td>-40</td>
<td>12</td>
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<tr>
<td>Left parahippocampal gyrus</td>
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<td>-30</td>
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<tr>
<td>Right hippocampus</td>
<td>-</td>
<td>17</td>
<td>-27</td>
<td>-4</td>
</tr>
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</table>

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

4. Experimental procedures

4.1. Stimulus protocol and task

For both fMRI and ERP studies, participants completed multi-run trials 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 the same trial (Fig. 1A). 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 the 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 were instructed to make a button response with their left hand on every trial to indicate whether each shape was old and on the “left”, old and on the “right”, or “new” (including low confidence responses where they had been encouraged to make their best guess). Given the moderate level of performance on the task, a proportion of accurate responses could be attributed to guessing which would tend to diminish the significance of the results; however, robust results were observed (indicating this was not a major concern). A subsequent confidence rating was made during fMRI (that was not considered in the present analysis). This protocol difference coupled with the different participants in the ERP and fMRI experiments is notable; however, the identical pattern of results was observed for both methodologies (so these differences did not substantially impact the results). 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 \( p(\text{old})^*p(\text{hit rate})+p(\text{new})^*p(\text{new-correct rejection rate}) \). 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. 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 were 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 were acquired in a shielded chamber (Global Partners in Shielding, Inc., Passaic, NJ) using a 128-channel NeuroScan system (Compumedics USA, Charlotte, NC) including SynAmps\(^2\) amplifiers, a Quik-Cap with sintered silver/silver chloride electrodes, and the Scan acquisition software program. All electrode impedances were maintained below 15 k\( \Omega \). The sampling rate was 1 ms. 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 the corresponding 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 high-pass (forward) filter cutoff of 0.5 Hz was implemented (6 dB/octave). No low-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 electrode system (Jasper, 1958) with interpolated electrode positions. The left hemisphere occipital ROI included electrodes 11, O1, P01, P1, O9, P07, P05, P3, the temporal ROI included electrodes P9, P7, P5, CP3, TpP9, TpP7, CP5, C5, TpP7h, Tp7, the parietal ROI included electrodes CP1h, 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. 2B.

The 13 ms time window 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; Heinze et al., 1994; Clark and Hillyard, 1996; Mangun et al., 1998; Di Russo et al., 2002) 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 s following stimulus onset, the expected maximum (these regions and retrieval-related timecourses are shown in Fig. 2 and Fig. 5). 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 \( p = 0.50 \)).

4.4. 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 T Siemens Allegra scanner. Anatomic data were acquired using a multiplanar rapidly acquired gradient echo (MP-RAGE) sequence (TR = 30 ms, TE = 3.3 ms, 128 slices, 1 x 1 x 1.33 mm resolution). Functional data were acquired using an echo planar imaging (EPI) sequence (TR = 2 s, TE = 30 ms, 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 pre-processing 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 (linear scaling based on Talairach landmarks), and resampling 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 (or event offset if there was no 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 (old-left-miss, old-right-miss), false memory of new shapes, correct rejection of new shapes (new-correct rejection), failures to respond, and a constant. 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 versus 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 (identified by contrasting encoding-left>encoding-right and vice versa). 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)\( \cap \) (encoding-left>encoding-right) and the conjunction of (old-right-hit>old-left-hit)\( \cap \) (encoding-right>encoding-left) were used to isolate retinotopic memory effects. To investigate regions associated with memory control, old-hits were contrasted with new-correct rejections, as is commonly done, using the conjunction (old-left-hit>new-correct rejection)\( \cap \) (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 encoding and memory control results, individual voxel thresholds of \( p < 0.001 \) and \( p < 0.01 \), respectively, were 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 image 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 were extracted with the mean activity computed from voxels within a 5 mm cube (encoding and retrieval timecourses were computed from −2 to 12 and −6 to 20 s after stimulus onset, respectively). Timecourses were additionally baseline corrected, as is standard with the BrainVoyager analysis software, such that the mean activity before and including stimulus onset was equal to 0. Mean activity from 6–8 s after stimulus onset was used to make statistical comparisons (given that this is the time of the expected maximum of the hemodynamic response).
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