Probability effects on the neural correlates of retrieval success: an fMRI study

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Event-related fMRI was employed to investigate the influence of the relative probability of old and new test items on the neural correlates of recognition memory. Twelve subjects undertook three study-test cycles, each consisting of an identical study phase in which a series of words was encoded in an incidental task, followed by a test phase in which yes/no recognition judgments were made to a mixture of studied (old) and unstudied (new) words. The ratio of old to new words differed in each test phase, and was either 25:75, 50:50, or 75:25. In lateral inferior and medial parietal cortex, and the posterior cingulate, greater activity was elicited by correctly classified old than new items independently of old:new ratio. By contrast, in other regions, including anterior, dorsolateral, and ventrolateral prefrontal cortex, differences in the activity elicited by old and new items varied according to old:new ratio, demonstrating in some cases a complete crossover interaction. The results suggest that differential activity elicited by old and new test items is likely to support successful recognition in only a subset of the regions identified in previous studies as exhibiting such differences. In other regions, most notably prefrontal cortex, differences in the activity elicited by old and new items appear to reflect processes that are contingent upon, rather than in support of, successful recognition.

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Introduction

Event-related fMRI has increasingly been employed to investigate the neural correlates of successful recognition memory (for a review, see Rugg and Henson, 2002; for subsequent studies see Cansino et al., 2002; Dobbins et al., 2002, 2003; Donaldson et al., 2001a; Rugg et al., 2003; Wheeler and Buckner, 2003). These studies have identified several regions where activity is greater for correctly classified old test items (hits) than for correctly classified new items (correct rejections)—so-called ‘old/new’ effects. The regions in which old/new effects were identified most consistently include inferior and superior parietal cortex [Brodmann Areas (BA) 39/40 and lateral BA7, respectively], medial parietal cortex (the precuneus or medial BA7), posterior cingulate cortex (BA23/31), and several prefrontal regions, notably bilateral anterior (BA10), right dorsolateral (BA9/46), and left ventrolateral (BA45/47) cortex.

The question arises as to the functional significance of these old/new effects. It does not necessarily follow that regions where such effects are found play a direct role in memory retrieval. For example, some old/new effects could reflect the greater salience of ‘old’ relative to ‘new’ items in recognition memory tests [see Neville et al., 1986, for a similar argument with respect to electrophysiological (ERP) old/new effects]. Differences in salience could arise out of a combination of the relatively low subjective probability of old items, and instructions that typically emphasise the importance of detecting old items in the context of a default ‘new’ response, thereby imbuing old items with the greater ‘targetness’ or ‘task relevance’.

The aim of the present experiment was to address this issue by investigating the sensitivity of fMRI old/new effects to differences in the relative probability of old and new recognition memory test items (the old:new ratio). By manipulating probability, it is possible to vary the relative salience of old and new items while holding constant the mnemonic demands and response requirements of the recognition task. Regions demonstrating old/new effects that are insensitive to the probability manipulation are candidates for supporting processing tied closely to recognition per se. By contrast, regions where old/new effects vary with old:new ratio likely support processes that, while contingent on successful recognition, contribute to functions such as target detection, adjustment of expectancies, overriding of prepotent response tendencies, etc. Although crucial for optimal recognition memory performance, such functions are extra-mnemonic in as much as they are also recruited in tasks that place no demands on long-term memory retrieval. Whether and how these functions are engaged is likely to be sensitive to strategic factors. By contrast, ‘core’ retrieval processes may largely be obligatory, or even automatic.

There is already reason to suspect that some of the prefrontal areas that have previously been demonstrated to exhibit old/new
effects fall into the second of the above categories. Preeminent among these areas are right dorsolateral and right anterior cortex. These regions have been implicated in memory retrieval since the earliest blocked-design PET studies (for review, see Desgranges et al., 1998; Fletcher et al., 1997). Although held to demonstrate sustained (‘state-related’) activity (Lepage et al., 2000; Nyberg et al., 1995; see Discussion) during retrieval tasks, findings from blocked studies contrasting different old:new ratios (e.g. Rugg et al., 1996, 1998) suggested that these regions also exhibit item-related old/new effects. This suggestion has been confirmed by recent event-related fMRI studies (for review, see Rugg and Henson, 2002). Two findings in particular suggest, however, that activity in these regions is only weakly coupled to successful recognition. First, in a block-design fMRI study, Wagner et al. (1998) reported that right anterior prefrontal activity could be modulated by manipulation of subjects’ expectations about the proportion of old items in a recognition test block, while holding the actual ratio constant. The authors argued from this finding that retrieval-related right anterior activity was modulated by cognitive ‘context’. In the case of right dorsolateral cortex, Henson et al. (2000) reported that event-related activity in this region was enhanced for test items attracting low-relative to high-confidence recognition judgments regardless of whether items were old or new. Henson et al. proposed that right dorsolateral activity reflected the engagement of postretrieval monitoring operations applied to the outcome of a retrieval attempt, rather than the recovery or representation of retrieved information.

The manipulation of old:new ratio has been employed previously in studies of electrophysiological (ERP) old/new effects (Friedman, 1990; Herron et al., 2003; Smith and Guster, 1993). The motivation for these earlier experiments arose from the proposal that ERP old/new effects, which primarily take the form of greater positivity in waveforms elicited by old than new items, reflect non-mnemonic processes engaged by ‘target’ items of low subjective probability, rather than processes associated with the actual ratio constant. The authors argued from this finding that retrieval-related right anterior activity was modulated by cognitive ‘context’. In the case of right dorsolateral cortex, Henson et al. (2000) reported that event-related activity in this region was enhanced for test items attracting low-relative to high-confidence recognition judgments regardless of whether items were old or new. Henson et al. proposed that right dorsolateral activity reflected the engagement of postretrieval monitoring operations applied to the outcome of a retrieval attempt, rather than the recovery or representation of retrieved information.

The critical stimuli consisted of 450 concrete nouns between four and nine letters in length, and with a frequency of occurrence between 30 and 100 counts per million (Kucera and Francis, 1967). The stimuli were randomly assigned to six different study lists, each of which contained 75 items. Each test list contained 100 critical items. The proportion of old items in the test lists was 0.25 in the ‘low old’ condition, 0.50 in the ‘equal’ condition, and 0.75 in the ‘high old’ condition. In the low old condition, 25 items were randomly selected from the preceding study phase and were presented together with 75 new items. In the equal condition, 50 randomly selected study items were presented together with 50 new items that were also randomly selected from one of the six lists. In the high old condition, 75 study items were presented together with 25 randomly selected new items. Twelve additional filler words were employed, two of which were added to the beginning of every study and test list. Across subjects, each critical word served with equal frequency as an old or new item in each probability condition. The presentation order of low old, equal, and high old study-test blocks was rotated across subjects to avoid order effects.

Stimuli took the form of white upper case letters (Helvetica 48 font) on a black screen, and were presented via a mirror fixed to the MR head coil at a viewing distance of approximately 30 cm. Both the stimuli and the fixation character (‘*’) were presented in central vision. Subjects responded on a hand-held button-box, with the thumbs of each hand resting on response keys. Subjects undertook three recognition memory blocks, each comprising a study and a test phase. An interval of approximately 1 min separated the study and test phases in each block, during which time a counting task was undertaken to prevent rehearsal and to clear short-term memory.

At the onset of each study and test list, the phrase ‘GET READY’ was presented in the centre of the screen before the first stimulus to prepare subjects for both study and test phases, each trial consisted of the presentation of the stimulus for 300 ms, followed by presentation of a fixation character (‘*’) for 2200 ms. At study, subjects were required to respond with one hand if the word depicted an animate object and with the other hand if it

Table 1
Hit and correction rejection (CR) rates, along with indices of discrimination (Pr) and response bias (Br), and RTs (ms), for each old:new ratio

<table>
<thead>
<tr>
<th>Old:new ratio</th>
<th>Hit</th>
<th>CR</th>
<th>Pr</th>
<th>Br</th>
<th>Hit</th>
<th>CR</th>
<th>Pr</th>
<th>Br</th>
<th>Hit</th>
<th>CR</th>
<th>Pr</th>
<th>Br</th>
</tr>
</thead>
<tbody>
<tr>
<td>25:75</td>
<td>0.89</td>
<td>0.76</td>
<td>0.49</td>
<td></td>
<td>0.83</td>
<td>0.72</td>
<td>0.40</td>
<td></td>
<td>0.86</td>
<td>0.69</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>50:50</td>
<td>0.83</td>
<td>0.72</td>
<td>0.40</td>
<td></td>
<td>0.84</td>
<td>0.69</td>
<td>0.56</td>
<td></td>
<td>0.85</td>
<td>0.69</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>75:25</td>
<td>0.84</td>
<td>0.72</td>
<td>0.40</td>
<td></td>
<td>0.85</td>
<td>0.69</td>
<td>0.56</td>
<td></td>
<td>0.86</td>
<td>0.69</td>
<td>0.56</td>
<td></td>
</tr>
</tbody>
</table>

Method

Subjects

Twelve subjects participated in the experiment (four males). All were right-handed, had English as their first language, and were between 18 and 30 years old. They gave informed consent before participating in the study, which was approved by an Institutional Ethics Committee. They were compensated at the rate of £7.50/h.

Experimental stimuli and procedure

The critical stimuli consisted of 450 concrete nouns between four and nine letters in length, and with a frequency of occurrence between 30 and 100 counts per million (Kucera and Francis, 1967). The stimuli were randomly assigned to six different study lists, each of which contained 75 items. Each test list contained 100 critical items. The proportion of old items in the test lists was 0.25 in the ‘low old’ condition, 0.50 in the ‘equal’ condition, and 0.75 in the ‘high old’ condition. In the low old condition, 25 items were randomly selected from the preceding study phase and were presented together with 75 new items. In the equal condition, 50 randomly selected study items were presented together with 50 new items that were also randomly selected from one of the six lists. In the high old condition, 75 study items were presented together with 25 randomly selected new items. Twelve additional filler words were employed, two of which were added to the beginning of every study and test list. Across subjects, each critical word served with equal frequency as an old or new item in each probability condition. The presentation order of low old, equal, and high old study-test blocks was rotated across subjects to avoid order effects.

Stimuli took the form of white upper case letters (Helvetica 48 font) on a black screen, and were presented via a mirror fixed to the MR head coil at a viewing distance of approximately 30 cm. Both the stimuli and the fixation character (‘*’) were presented in central vision. Subjects responded on a hand-held button-box, with the thumbs of each hand resting on response keys. Subjects undertook three recognition memory blocks, each comprising a study and a test phase. An interval of approximately 1 min separated the study and test phases in each block, during which time a counting task was undertaken to prevent rehearsal and to clear short-term memory.

At the onset of each study and test list, the phrase ‘GET READY’ was presented in the centre of the screen before the first stimulus to prepare subjects. For both study and test phases, each trial consisted of the presentation of the stimulus for 300 ms, followed by presentation of a fixation character (‘*’) for 2200 ms. At study, subjects were required to respond with one hand if the word depicted an animate object and with the other hand if it
depicted an inanimate object. At test, subjects were instructed to respond with one hand if the word had been presented in the immediately preceding study phase (‘old’), and with the other hand if it had not (‘new’). Subjects were told at the beginning of the experiment that the frequency of occurrence of old items during the test phase would be different in each block, and that they should try not to allow this to influence their recognition judgements. They were also instructed to respond as quickly as possible without sacrificing accuracy. The hand employed for each kind of response in the study and test phases was counterbalanced across subjects.

**fMRI data acquisition**

A Siemens 2T VISION MR scanner was used to acquire both T1-weighted anatomical volume images and T2*-weighted echo-planar (EPI) blood oxygenation level dependent (BOLD) images. Functional image acquisition parameters were: TE = 40 ms; TR = 1976 ms; slice thickness = 3.5 mm, skip = 1.5 mm. Each volume image comprised 26 axial slices. Scanning occurred during each of the three test sessions, and consisted of 142 volumes per session, the first 5 of which were discarded to allow tissue magnetisation to achieve a steady state.

**fMRI data analysis**

Analysis was performed with Statistical Parametric Mapping (SPM99, Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab5 (The Mathworks, Inc, USA). All volumes were realigned spatially to the first volume, and the time series for voxels within each slice realigned temporally to

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Fig. 1. Axial sections illustrating regions where activity elicited by old items exceeded that for new items independently of old:new ratio. Upper: bilateral inferior and medial parietal cortex. Lower: posterior cingulate. Results are shown superimposed on the normalized T1-weighted structural image of a randomly selected subject. Highlighted voxels are those identified by a two-sided $F$ test thresholded at $P < 0.001$ that survived exclusive masking with the outcome of the $F$ test for the old vs. new × old:new ratio interaction thresholded at $P < 0.05$.

Fig. 2. Coronal sections illustrating some of the prefrontal regions that demonstrated an old vs. new × old:new ratio interaction. Upper: bilateral anterior (BA10). Middle: right dorsolateral (BA46/10). Lower: bilateral posterior inferior (BA47). Results superimposed on the same structural image as in Fig. 1. Highlighted voxels were identified by an $F$ test of the interaction thresholded at $P < 0.005$ (upper section) and $P < 0.001$ (middle and lower sections).
acquisition of the middle slice. The movement parameters generated during realignment indicated that no subject moved more than 2 mm in any direction during each session. Resulting volumes were normalised to a standard EPI template based on the MNI reference brain in Talairach space (Ashburner and Friston, 1999) and resampled to $3 \times 3 \times 3$ mm voxels. The normalised images were smoothed with an isotropic 8 mm FWHM Gaussian kernel. The time series in each voxel were high-pass-filtered to 1/120 Hz to remove low-frequency noise and scaled within-session to a grand mean of 100 across both voxels and scans.

Statistical analysis was performed in two stages of a mixed effects model. In the first stage, neural activity was modelled by a delta function (impulse event) at stimulus onset. The ensuing BOLD response was modelled by convolving these neural functions with two haemodynamic response functions (HRF). The first, which we call the “early” response, represented a canonical HRF (Friston et al., 1998). The second, which we call the “late” response, represented a canonical HRF shifted 3 s later in time, and was included to capture possible delayed responses. The convolution was performed in a high-resolution time space, and downsampled at the midpoint of each scan to form covariates in a General Linear Model. The covariates for the “late” response were orthogonalised with respect to those for the “early” response, thereby attributing any shared variance to the “early” response. Unlike in some earlier studies (e.g. Rugg et al., 2003), analyses of the “late” covariate did not add any significant information to that obtained with the early response function, and so are not reported.

Five event types of interest were defined for each recognition test block; correct and incorrect responses to studied and unstudied items, plus missed responses or responses to filler items. Also included for each subject were six covariates to capture residual movement-related artefacts (the three rigid body translations and three rotations determined from the realignment stage). Parameter estimates for each condition and covariate were calculated from the least mean squares fit of the model to the data.

Linear contrasts of the parameter estimates for each subject comprised the data for the second-stage analyses, which treated subjects as a random effect. These contrasts were confined to correct responses to old and new items in each of the three conditions, and are described in Results. Stereotactic coordinates are reported in Talairach space and correspond to the standard MNI brain (Cocosco et al., 1997). These coordinates bear a close, but not exact, match to the atlas of Talairach and Tournoux (1998).

Results

Behavioral performance

Mean accuracy and RT are shown in Table 1 for each probability condition, along with a nonparametric estimate of response bias (Br; Snodgrass and Corwin, 1988). ANOVA of the discrimination index Pr (pHit–pFalse Alarm; Snodgrass and Corwin, 1988) failed to reveal any effect of probability, and the same held true for ANOVA of Br. ANOVA of the RT data revealed a main effect of response type ($F_{1,11} = 22.85; P < 0.001$), reflecting shorter RTs for hits than for correct rejection rejections, but gave rise to no effect of probability.

Table 2: Cortical regions demonstrating (A) old/new effects in the absence of an interaction with old/new ratio, and (B) an old/new ratio by old/new interaction.

<table>
<thead>
<tr>
<th>x, y, z</th>
<th>Z</th>
<th>Number of voxels</th>
<th>Region</th>
<th>BA</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Main effect</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>−12, −66, 39</td>
<td>3.83</td>
<td>26</td>
<td>l. medial parietal</td>
<td>7</td>
</tr>
<tr>
<td>−33, −72, 30</td>
<td>4.44</td>
<td>28</td>
<td>l. inferior parietal/temporal</td>
<td>39</td>
</tr>
<tr>
<td>9, −39, 18</td>
<td>3.92</td>
<td>16</td>
<td>r. posterior cingulate</td>
<td>29</td>
</tr>
<tr>
<td>9, −63, 33</td>
<td>3.62</td>
<td>29</td>
<td>r. medial parietal</td>
<td>7</td>
</tr>
<tr>
<td>36, −66, 36</td>
<td>3.57</td>
<td>13</td>
<td>r. inferior parietal</td>
<td>39</td>
</tr>
<tr>
<td>B. Interaction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>−36, 54, −6</td>
<td>3.28</td>
<td>2</td>
<td>l. anterior frontal</td>
<td>10</td>
</tr>
<tr>
<td>−6, 30, 42</td>
<td>3.74</td>
<td>23</td>
<td>l. superior frontal</td>
<td>8/24</td>
</tr>
<tr>
<td>−36, 24, −18</td>
<td>3.89</td>
<td>12</td>
<td>l. inferior frontal</td>
<td>47</td>
</tr>
<tr>
<td>−51, 21, −12</td>
<td>3.69</td>
<td>13</td>
<td>l. inferior frontal</td>
<td>47</td>
</tr>
<tr>
<td>−54, 12, 33</td>
<td>4.23</td>
<td>48</td>
<td>l. inferior frontal</td>
<td>9</td>
</tr>
<tr>
<td>−21, 0, 63</td>
<td>3.56</td>
<td>10</td>
<td>l. superior frontal</td>
<td>6</td>
</tr>
<tr>
<td>−39, −30, 54</td>
<td>4.12</td>
<td>26</td>
<td>l. superior parietal</td>
<td>40</td>
</tr>
<tr>
<td>−33, −57, 60</td>
<td>3.75</td>
<td>22</td>
<td>l. superior parietal</td>
<td>7</td>
</tr>
<tr>
<td>−24, −59, 9</td>
<td>3.69</td>
<td>19</td>
<td>l. occipital</td>
<td>18</td>
</tr>
<tr>
<td>36, 63, 6</td>
<td>3.97</td>
<td>20</td>
<td>r. anterior frontal</td>
<td>10</td>
</tr>
<tr>
<td>45, 45, 21</td>
<td>3.52</td>
<td>11</td>
<td>r. dorsolateral</td>
<td>46/10</td>
</tr>
<tr>
<td>36, 21, −6</td>
<td>3.89</td>
<td>51</td>
<td>r. inferior frontal</td>
<td>47</td>
</tr>
<tr>
<td>45, −63, 12</td>
<td>3.74</td>
<td>32</td>
<td>r. fusiform</td>
<td>37</td>
</tr>
<tr>
<td>24, −78, −9</td>
<td>3.69</td>
<td>14</td>
<td>r. occipital</td>
<td>18</td>
</tr>
</tbody>
</table>

Coordinates refer to the peak of each activated cluster. BAs are approximate only. l. = left, r. = right.

fMRI data

Analysis of the fMRI data was directed towards identifying voxels where (i) old/new effects were uninfluenced by old:new ratio, or (ii) item type and ratio interacted. Voxels demonstrating the latter effect were identified by an $F$ test of the interaction between the factors of item type and ratio. This two-sided contrast was thresholded at $P < 0.001$ (uncorrected for multiple comparisons), with degrees of freedom corrected for the effects of nonsphericity using the method proposed by Friston et al. (2002). Voxels exhibiting only a main effect of item type (and hence an old/new effect that did not interact with probability) were identified by exclusively masking the outcome of an $F$ test for the main effect of old vs. new items (thresholded at $P < 0.001$ uncorrected) with the outcome of the aforementioned $F$ test of the interaction, now thresholded at $P < 0.05$ uncorrected (note that the more liberal this threshold, the more stringent the test for the absence of an interaction). A spatial extent threshold of 10 voxels was applied to the outcome of both of the above analyses.

Old/new effects

Regions exhibiting a main effect of item type, unmodified by old:new ratio, are illustrated in Fig. 1 and detailed in Table 2A. All of these regions demonstrated a relative increase in activity for old items. As can be seen from the figures and table, the regions are all near the parietal cortex, and include both lateral and medial surfaces.1

1 With a reduced extent threshold, this analysis also identified a right anterior medial temporal region (4 voxels; peak 21, −6, −30) which showed relatively greater activity for new than old items. This finding is reported and discussed elsewhere (Henson et al., 2003).
Interaction effects

As detailed in Table 2B and Fig. 2, cortical regions demonstrating an item type \( \times \) ratio interaction included several areas of prefrontal cortex, along with occipital, fusiform, and superior parietal areas. One of the regions documented in Table 2B—left anterior prefrontal cortex—was identified only when the cluster extent threshold was reduced to 2. We have included this region, however, in view of the consistency with which left anterior prefrontal old/new effects have been reported in previous event-related fMRI studies of recognition memory, and the fact that the locus of the present effect \((-36, 54, 0\) vs. \(36, 63, 6\)). An ANOVA contrasting the patterns of old/new differences across these sites (factors of region, item type, and old/new ratio) revealed a reliable three-way interaction \(F_{1.7,19.1} = 7.34; P < 0.01\), indicating that the two regions did indeed respond differentially to the probability manipulation.

Discussion

Behavioral performance

As was also the case in our previous ERP study (Herron et al., 2003), the manipulation of old/new ratio had no effect on measures of recognition accuracy, response bias, or RT. The failure to find a probability effect on response bias is inconsistent with some previous reports (e.g. Ratcliff et al., 1992). As noted by Herron et al. (2003), a possible reason for the disparity between present and previous results lies in instructional differences. Whereas our subjects and those of Herron et al. (2003) were told merely that the old/new ratio would vary across blocks, in other studies, subjects were explicitly informed what the ratio in each block would be (e.g. Ratcliff et al., 1992). Irrespective of the reason for the absence of a behavioral effect, however, the fMRI and ERP findings (see below) clearly show that probability had a marked impact on how old and new items were processed in both the present study and that of Herron et al. (2003). These probability-dependent differences in brain activity may in part have supported strategic adjustments that permitted subjects to maintain a stable response bias across the different old/new ratios.

fMRI results

Many of the regions identified here were reported to exhibit old/new effects in previous studies of recognition memory. The present findings indicate that whereas in some of these regions, old/new effects are relatively invariant across different old/new ratios, in other regions the effects are strongly modulated by this manipulation. The findings have important implications for the interpretation of early fMRI and PET studies that investigated the neural correlates of retrieval success using blocked designs. To identify regions exhibiting old/new effects, these studies contrasted blocks of test trials containing a relatively high proportion of ‘old’ items with blocks containing mainly new items (e.g. Nyberg et al., 1995; Rugg et al., 1996; see Introduction). Such designs inextricably confound the probability of successful retrieval with changes in old/new ratio, the two factors that gave rise to strong interaction effects in the present study. Thus, the present results add further weight to previous suggestions that the findings of these older research were due to chance.

The results of the SPM analyses are available in full on request to the corresponding author.

2 The results of the SPM analyses are available in full on request to the corresponding author.

3 Degrees of freedom corrected for nonsphericity with the Geisser–Greenhouse procedure (Winer, 1971).
studies are ambiguous (Rugg, 1998; Rugg and Henson, 2002; see also Wagner et al., 1998).

The regions demonstrating probability-independent old/new effects in the present study were all identified in previous studies employing old vs. new contrasts (although it should be noted that the left inferior parietal old/new effect identified here is somewhat posterior to that reported in most earlier studies; see Rugg and Henson, 2002). It has been suggested that some of these regions, notably, inferior parietal cortex and the posterior cingulate, are associated specifically with successful episodic retrieval (recollection) rather than recognition based on an contextual sense of familiarity (Henson et al., 1999). The present findings are consistent with this proposal in as much as it implies that old/new effects in these regions should be uninfluenced by manipulations that act on processes ‘downstream’ of successful retrieval, rather than on retrieval processing per se (see Introduction). However, since old items were not segregated according to whether they elicited recollection, the findings do not speak directly to this issue. They do, however, serve to identify a set of candidate regions supporting a ‘retrieval circuit’ in posterior cortex (cf. Nyberg et al., 2000).

In contrast to inferior parietal cortex, old/new effects in left superior parietal cortex (BA7)—another region where such effects have consistently been reported—did interact with old/new ratio (the dissociation between these two parietal regions was confirmed by ANOVA of the parameter estimates from their respective peak voxels, which gave rise to a significant region × item type × old/new ratio interaction; \( F_{1,9,21.1} = 3.79; P < 0.05 \)). Thus, the retrieval-sensitive processes supported by this region appear to be dissociable from those supported by its more inferiorly located neighbour.

As noted above, several previous event-related fMRI studies of recognition memory have reported lateral parietal old/new effects near one or both of the inferior and superior regions discussed above (Rugg and Henson, 2002; see also Wheeler and Buckner, 2003). A good example of a study in which both regions were identified is given by Donaldson et al. (2001a), who reported lateral parietal old/new effects with peak loci at \(-37, -69, 33 \) and \(-40, -51, 54 \), close to the inferior and superior regions identified in the present study. To the best of our knowledge, however, the present findings are the first to suggest that these regions can be dissociated functionally. As discussed already, the more inferior area may play a role in the recovery or representation of retrieved information. The form of the old/new by probability interaction in the superior parietal region, where old/new effects were found only when old items were relatively infrequent (see Fig. 3), suggests that this region is sensitive to the salience of old items, and not just their study status, and thus reflects likely processes operating after successful retrieval.

Prefrontal cortex and old/new ratio

Most of the prefrontal regions reported to demonstrate old/new effects in previous studies of recognition memory were also identified in the present study. Remarkably, old/new effects varied with old/new ratio in every case. As illustrated in Fig. 3, the interactions took different forms in different regions. In every region, however, there was a tendency for a reduction or reversal in old/new effects when old items were relatively frequent. The findings have several implications for proposals about the functional role of different prefrontal regions in memory retrieval.

First, the findings suggest that none of the prefrontal regions identified here plays a necessary role in the initial reinstatement or representation of retrieved information—at least to the extent that such a role is indexed by the presence of an old/new effect. Instead, activity in several of these regions appears to be determined largely by the combination of an item’s study status and relative probability, such that processing is allocated preferentially to the rarer class of event. This pattern of activity is reminiscent of that elicited by ‘oddball’ stimuli in simple detection and discrimination tasks. It is perhaps no coincidence therefore that oddball-related activity has consistently been reported in a variety of prefrontal regions, including several near those identified in the present study (e.g. Ardekani et al., 2002; Clark et al., 2000; Kiehl et al., 2001; Kirimo et al., 2000). It will be of interest to determine the extent to which the probability-sensitive frontal activity elicited in these simple detection tasks, and the analogous activity identified in the present study, reflect the engagement of a common set of cognitive operations.

Unlike other prefrontal regions, left anterior prefrontal (BA10) activity did not exhibit a crossover interaction. As is evident from Fig. 3, left anterior old/new effects were present in two of the three probability conditions, failing to emerge only when old items were relatively frequent. The pattern is suggestive of processing engaged preferentially by old items, but modulated by the predictability or salience of these items relative to new ones. While it is unclear what this pattern implies about the functional role of left anterior cortex in memory retrieval, it may help explain why prefrontal old/new effects have been reported more consistently in this region than in any other in previous event-related studies of recognition memory (Rugg and Henson, 2002).

In contrast to the left anterior region, right anterior prefrontal cortex exhibited an almost symmetric item type × probability crossover. These different interaction patterns (a difference that was itself statistically significant) constitute the first direct evidence we are aware of that retrieval-related activity in left and right anterior prefrontal cortex can be dissociated (cf. Rugg et al., 2003). Furthermore, the present findings serve to qualify previous proposals that right anterior old/new effects are tied closely to successful retrieval (Henson et al., 2000; McDermott et al., 2000; Rugg et al., 2003). Rather, it appears that such effects are evident only to the extent that old items are more salient than new items, and that right anterior ‘retrieval success’ effects can actually be inverted by manipulations that imbue new items with the greater behavioral significance. The present findings may help explain why reports of right anterior old/new effects are less common than those for left anterior cortex (Rugg and Henson, 2002). Presumably, right anterior effects will be most in evidence when old items are rendered especially relevant or salient, by virtue either of their relative rarity (as here) or other circumstances that boost their salience above that of new items.

An early proposal concerning retrieval-related right anterior prefrontal activity was that it reflected the engagement of ‘retrieval mode’—a hypothesised cognitive state that biases subjects to process stimulus events as retrieval cues and to experience successful episodic retrieval ‘autonoetically’ (Tulving, 1983; Wheeler Stuss and Tulving, 1997; for supporting evidence, see Düzel et al., 1999; Lepage et al., 2000; Nyberg et al., 1995). According to this proposal, right anterior activity should be invariant in the face of variations in old/new ratio so long as subjects continue to treat test items as episodic retrieval cues. The present findings for right anterior prefrontal cortex might be taken to be inconsistent with the
retrieval mode proposal. In fact, the findings do not speak to this issue, since they were obtained by contrasting, within-task, the activity elicited by different classes of test item. Thus, it is possible that the modulation of item-related right anterior activity by old:new ratio was possibly superimposed upon a constant level of state-related activity (cf. Düzel et al., 1999). This interesting issue cannot be addressed by the present data, but could be investigated with a design optimised to detect both state- and item-related activity (e.g. Donaldson et al., 2001b).

The last of the prefrontal regions to be discussed specifically is right dorsolateral cortex. Right dorsolateral activity has been demonstrated previously to be dissociable from successful retrieval, and has been held to reflect the extent to which test items engage postretrieval monitoring operations (e.g. Henson et al., 2000; Rugg et al., 2003; see Introduction). From this perspective, the crossover interaction in this region between item type and old:new ratio could be accounted for by assuming that relatively rare ‘mnemonic events’, whether in the form of retrieval success or retrieval failure, invoke more monitoring than do relatively frequent events. This account is, however, post hoc. Moreover, since the same interaction pattern was also found in several other prefrontal regions, it is not clear why right dorsolateral activity should be singled out as showing a pattern consistent with a monitoring account.

Relationship between fMRI and ERP data

The fMRI data indicate that whereas activity in some posterior regions, notably medial and inferior lateral parietal cortex, may be tied closely to successful retrieval, retrieval-related activity in prefrontal cortex was invariably modulated by old:new ratio. A previously reported ERP study (Herron et al., 2003) showed analogous findings. As mentioned in the Introduction, the study employed a design essentially identical to the one adopted here, and focused on the effects of old/new probability on the ‘left parietal old/new effect’, which has been proposed as a correlate of episodic retrieval (Friedman and Johnson, 2000; Rugg and Allan, 2000). Consistent with this proposal, Herron et al. reported that the effect was insensitive to old:new ratio. This was in contrast to a later onsetting parietally distributed positivity, which, in an intriguing parallel with the present fMRI findings for superior parietal cortex, was larger when elicited by old words of low rather than medium or high probability.

Prompted by the present fMRI findings, we conducted further analysis of the ERP data of Herron et al. (2003). This led to the identification of an effect that was not described in the original report (see Fig. 4). From around 1200 ms post-stimulus, the waveforms over the frontal scalp appear to track the relative

Fig. 4. ERP data from Herron et al. (2003). (A) Grand average waveforms (N = 16) from a left prefrontal electrode elicited by old and new items for each old:new ratio (25:75 = low old). (B) Scalp topographies of the old/new effects averaged over the 1200–1900 ms latency region for the low old and high old conditions. (C) Magnitude of old/new effects during the 1200–1900 ms latency region collapsed across the four indicated electrode sites.
probability of old and new items, showing little difference in the 50:50 condition, but relatively greater negativity for the rarer item type in each of the other two conditions. ANOVA (factors of item type, probability, hemisphere, and electrode site) of the mean amplitude between 1200 and 1900 ms of the waveforms from the electrode sites indicated in Fig. 4 confirmed this impression, revealing a reliable item type × probability interaction ($F_{1,8,30.8} = 6.53; P < 0.005$).

Although it is not possible to identify any of the ERP effects described above with specific fMRI findings, the two data sets are nonetheless highly convergent. The insensitivity of the left parietal ERP old/new effect to old:new ratio strengthens the conclusion drawn from the present data that much of the activity elicited in posterior cortex by old items reflects processes that are closely related to the recovery and initial representation of retrieved information. In a similar vein, the frontal ERP effects, which mirrored the crossover pattern found for several prefrontal regions in the present study, add weight to the proposal that prefrontal activity reflects processes that are engaged during tests of recognition memory in a highly flexible manner. It is noteworthy that the frontal ERP effects did not vary with old:new ratio until around the time that subjects were making their responses (ca. 1 s; see Fig. 4). Thus, the probability-sensitive activity manifest by these effects is unlikely to reflect processes necessary for accurate recognition judgments. Rather, these processes may play a role in maintaining or updating a representation of the structure of the test list, perhaps in an effort to optimise future behaviour. An important unresolved question is the relation between the frontally distributed ERP effects described here, and the positive-going, right-lateralised effects occupying the same latency range that have been described in previous studies of recognition memory and its variants (for review, see Friedman and Johnson, 2000).

Concluding comments

The present findings point to a clear distinction between two classes of fMRI ‘old/new effect’ in recognition memory tests—sensitive and insensitive to old:new ratio, respectively. Regions where old/new effects were insensitive to old:new ratio—inferior and medial parietal cortex, along with the posterior cingulate—are arguably candidates for playing roles in support of successful recognition. Regions where the effects varied according to old:new ratio seem more likely to support processes that are sensitive to the outcome of a retrieval attempt, rather than acting directly on information that has been successfully recovered from memory. These regions appear to include most, if not all, of the prefrontal areas that have been implicated in memory retrieval by earlier functional neuroimaging studies. The present findings might very crudely be characterised as supporting a distinction between a parietal/posterior cingulate role in representing retrieved information, and a prefrontal role in tracking the outcome of successive retrieval attempts to maintain behavioural stability. It will be of interest to determine whether this distinction extends to retrieval tasks other than yes/no recognition memory.

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