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Introduction

fMRI methods are increasingly used in the pre-surgical study of focal epilepsy patients. Data obtained regarding the localisation of memory and the assessment of the functional integrity of brain structures is important for predicting cognitive outcome following surgical resection of epileptogenic tissue. Current paradigms for assessing memory lateralisation have largely focussed on verbal memory, which reliably recruit left hemisphere structures. The development of visuospatial paradigms has proved more challenging with left hemisphere processing biases and verbalisation strategies preventing development of a right hemisphere task. The current task aimed to determine the merit of a newly-designed visuospatial paradigm in maximising BOLD asymmetry to the right by placing a preferential load on spatial memory.

Methods

Both healthy controls (n = 20, age M = 24.7 years, range = 18-40) and 10 patients *(see below Table 1) with temporal lobe epilepsy underwent a forced-choice visuospatial recognition task that tested memory for orientation of a novel stimulus, whilst undergoing fMRI. The experiment involved an encoding (WATCH) phase, a retrieval (CHOOSE) phase and a rest phase (see example images on the right). During each trial, participants had to attend to novel visual stimuli and were asked to pay particular attention to the spatial layout. Stimuli were presented in blocks of 20 consecutive images. Subsequent recognition blocks were presented comprising 8 images from the immediately preceding block and images from earlier blocks. Behavioural data was recorded through the presentation software (Neurobehavioural Systems) and test performance scores were explored for both healthy controls and patient samples. fMRI data was obtained using a 3T Siemens Skyra MRI Scanner with standard 20 channel head and neck coil. The functional scans consisted of 250 volumes collected using gradient-echo echo-planar imaging (EPI) with a TR=2800 ms, TE=30ms and 90 degree flip angle. 40 contiguous axial slices were collected, with 3mm thickness, 192 mm field of view and a voxel size of 3x3x3mm. T1 structural scans were also obtained (192 volumes) with a 256 x 256 matrix, voxel size 1x1x1 mm.

Conclusions and Future Directions

Encoding/retrieval versus rest series statistical analyses were carried out using defined models examining encoding/retrieval versus rest, with local autocorrelation correction (Woolrich, 2001). Participant specific T1 was co-referenced with a MN112 T1 2mm brain, which was used to co-register the BOLD signal. Standard motion parameters were applied and MCLFIRMT correction was used with spatial smoothing set at 2mm. 2 (Gaussianised T/F) statistical images were thresholded using clusters (p = 2.3) and a (corrected) cluster significance threshold of p = 0.05 (Worsley, 2001). ROI analysis was conducted using FSL Expert Analysis Tool v6.00 - FLAT Query with the aid of The Harvard-Oxford Cortical Atlas to define ROIs (right/left hippocampus). T-tests were used to examine differences between the right and left ROIs. Total percentage correct for behavioural data were calculated and t-tests were used to examine differences in performance between healthy controls and patient samples.

Analysis

fMRI data processing was carried out using FEAT (FMRI Expert Analysis Tool), part of FSL (FMRI’s Software Library, www.fmrib.ox.ac.uk/fsl). Registration to high resolution structural and/or standard space images was carried out using FLIRT (Jenkinson, 2001, 2002). Time-series statistical analyses were carried out using defined models examining encoding/retrieval versus rest, with local autocorrelation correction (Woolrich, 2001). Participant specific T1 was co-referenced with a MN112 T1 2mm brain, which was used to co-register the BOLD signal. Standard motion parameters were applied and MCLFIRMT correction was used with spatial smoothing set at 2mm. 2 (Gaussianised T/F) statistical images were thresholded using clusters (p = 2.3) and a (corrected) cluster significance threshold of p = 0.05 (Worsley, 2001). ROI analysis was conducted using FSL Expert Analysis Tool v6.00 - FLAT Query with the aid of The Harvard-Oxford Cortical Atlas to define ROIs (right/left hippocampus). T-tests were used to examine differences between the right and left ROIs. Total percentage correct for behavioural data were calculated and t-tests were used to examine differences in performance between healthy controls and patient samples.

Results

Behavioural analysis (see Figure 3) demonstrated healthy controls (M=64.6 SD=11.1), performed significantly better (p<0.05) on the mirror memory task than the patient sample (M=41.3, SD=19.7), with no individuals in either group hitting near ceiling (100% correct) or floor (0% correct) for performance.

In healthy controls, successful recruitment of right hippocampus was demonstrated during spatial encoding of visual scenes (see Figure 2), with the right hippocampus being activated significantly more than the left (p<0.001) and region of interest analysis demonstrating right-sided dominance (LI = -0.13). However, there were no differences between left and right hippocampal activation on retrieval (p>0.05).

Preliminary findings for patient data are presented in Table 1. Global deactivation of hippocampal regions were seen in some patients, therefore lateralisation could not be determined. For all remaining patients with a left temporal pathology, the MMF encoding phase demonstrated right hippocampal dominance for visuospatial memory, as would be predicted. The results were more inconsistent for the retrieval phase, similar to that for controls.

Table 1. Patient Demographics

<table>
<thead>
<tr>
<th>PI</th>
<th>Age</th>
<th>Gender</th>
<th>Onset</th>
<th>Duration</th>
<th>Handedness</th>
<th>Pathology Features</th>
<th>Left Visitation Activation M (SD)</th>
<th>Right Visitation Activation M (SD)</th>
<th>Left vs Right Significance</th>
<th>Laterality Index (SD)</th>
<th>Lateralisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1G</td>
<td>51.4</td>
<td>M</td>
<td>5.4</td>
<td>46</td>
<td>R</td>
<td>Left hippocampal temporal abnormalities on MR and sharp wave spikes on right EEG</td>
<td>EN = .09 (0.09)</td>
<td>RE = .18 (0.15)</td>
<td>EN p&lt;0.0001**</td>
<td>RE p&lt;0.0001**</td>
<td>EN = -0.36</td>
</tr>
<tr>
<td>P2E</td>
<td>12.9</td>
<td>M</td>
<td>2.5</td>
<td>10.3</td>
<td>L</td>
<td>Left antememorial temporal lobe resection</td>
<td>EN = .11 (0.19)</td>
<td>RE = .31 (0.79)</td>
<td>EN p&lt;0.0001**</td>
<td>RE p&lt;0.0001**</td>
<td>EN = -0.48</td>
</tr>
<tr>
<td>P3F</td>
<td>12.2</td>
<td>F</td>
<td>4.3</td>
<td>3.8</td>
<td>L</td>
<td>Left temporal dominance</td>
<td>EN = -3.15 (1.12)</td>
<td>RE = -0.96 (0.67)</td>
<td>EN p&lt;0.015**</td>
<td>RE p&lt;0.0001**</td>
<td>EN = -0.27</td>
</tr>
<tr>
<td>P4U</td>
<td>22.1</td>
<td>M</td>
<td>10.6</td>
<td>10.4</td>
<td>R</td>
<td>Right side of left hippocampus</td>
<td>EN = -0.1 (0.11)</td>
<td>RE = -0.18 (0.74)</td>
<td>EN p&lt;0.02**</td>
<td>RE p&lt;0.0001**</td>
<td>EN = -0.36</td>
</tr>
<tr>
<td>P5C</td>
<td>3.1</td>
<td>M</td>
<td>21</td>
<td>10.1</td>
<td>R</td>
<td>Shrunken left hippocampus</td>
<td>EN = -0.01 (0.03)</td>
<td>RE = -0.84 (0.71)</td>
<td>EN p&lt;0.0001**</td>
<td>RE p&lt;0.0001**</td>
<td>EN = -0.45</td>
</tr>
<tr>
<td>P6H</td>
<td>56.7</td>
<td>F</td>
<td>9</td>
<td>47.2</td>
<td>R</td>
<td>Sharp wave spikes within right on EEG</td>
<td>EN = .07 (0.14)</td>
<td>RE = -0.84 (0.84)</td>
<td>EN p&lt;0.0001**</td>
<td>RE p&lt;0.0001**</td>
<td>EN = -0.64</td>
</tr>
</tbody>
</table>

*Only 6 patients scans were able to be analysed due to scan acquisition difficulties, such as too much movement artefact.

Figure 1. Example of Mirror Memory Task

Figure 2. Single participant’s activation maps for scene encoding (24, -18, -27). (A) Anatomical segmentation of the hippocampus in blue, (B) activation map for the main effect of scene encoding in red-yellow.

Figure 3. Average performance of controls versus patients on MBT