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Preliminary findings of the clinical utility of an fMRI approach to visuospatial memory lateralization in paediatric and adult patients with epilepsy

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Introduction

fMRI methods are increasingly used in the pre-surgical study of focal epilepsy patients. Data obtained regarding the lateralisation 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 focused 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 the encoding phase, 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.

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

Table 1. Patient Demographics

<table>
<thead>
<tr>
<th>PI</th>
<th>Age (y)</th>
<th>Gender</th>
<th>Onset (y)</th>
<th>Duration (y)</th>
<th>Handedness</th>
<th>Left Hemisphere Pathology Features</th>
<th>Right Hemisphere Pathology Features</th>
<th>Left vs Right Activation (M (SD))</th>
<th>Laterality Index (L/R)</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>-</td>
<td>-</td>
<td>EN = 0.09 (RE = -0.15)</td>
<td>EN = -0.62 (RE = 0.13)</td>
<td>EN = R</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>-</td>
<td>-</td>
<td>EN = -0.11 (RE = -0.70)</td>
<td>EN = 0.16 (RE = 0.01)</td>
<td>EN = NA</td>
</tr>
<tr>
<td>P3F</td>
<td>12.2</td>
<td>F</td>
<td>8.4</td>
<td>3.8</td>
<td>L</td>
<td>-</td>
<td>-</td>
<td>EN = -3.12 (RE = -0.67)</td>
<td>EN = -0.07 (RE = 0.23)</td>
<td>RE = R</td>
</tr>
<tr>
<td>P4U</td>
<td>22.1</td>
<td>M</td>
<td>1.0</td>
<td>21.1</td>
<td>L/R</td>
<td>-</td>
<td>-</td>
<td>EN = -0.41 (RE = -0.57)</td>
<td>EN = -0.09 (RE = -0.29)</td>
<td>EN = NA</td>
</tr>
<tr>
<td>P5C</td>
<td>31.1</td>
<td>M</td>
<td>21</td>
<td>10.1</td>
<td>R</td>
<td>-</td>
<td>-</td>
<td>EN = -0.36 (RE = -0.50)</td>
<td>EN = -0.12 (RE = 0.01)</td>
<td>EN = NA</td>
</tr>
<tr>
<td>P6H</td>
<td>56.2</td>
<td>F</td>
<td>9</td>
<td>47.2</td>
<td>R</td>
<td>-</td>
<td>-</td>
<td>EN = 0.57 (RE = 0.14)</td>
<td>EN = -0.38 (RE = 0.10)</td>
<td>RE = R</td>
</tr>
</tbody>
</table>

Figure 1. Example of Mirror Memory Task

Figure 2. Single participant’s activation maps for scene encoding (A), retrieval (B) and contrast map (C, red-yellow)

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 MN1152 T2 2mm brain, which was used to register the BOLD signal. Standard motion parameters were applied and MCL菲尔RT function correction was used with spatial smoothing set at 5mm. 2 (Gaussianised T/F) statistical images were thresholded using clusters (z ≥ 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 = -0.12). However, there were no differences between left and right hippocampal activation on retrieval (p=0.05).

Conclusions and Future Directions

This paradigm stimulated significant activation of the right versus left hippocampus, demonstrating right-temporal dominance for encoding of visuospatial information in healthy controls of the 12 controls demonstrated deactivation of their hippocampal regions during retrieval phase. This is likely a consequence of poor signal to noise ratio and poor model fit. This may be accounted for by failed encoding, and thus retrieval, of tested stimuli that therefore would not have recruited hippocampal regions. Future research might focus on using behavioural data to generate a more specific event related design that examines only retrieval phases that were first successfully encoded.

Further future directions would include:

- Improving sample sizes of both clinical cases and healthy controls
- Recruiting patients with clear right sided-pathology
- Further definition of clinical groups into early and late onset of seizure, within the left and right groups to better predict likelihood of neoplasticity.
- Exploring predictive validity of fMRI results using pre and post-operative visuospatial memory performance data following right/left temporal resection
- Interrogating verbal memory areas and then using these to define parameters to better control for verbalisation strategies.