Simultaneous EEG and fMRI of centro-temporal spikes in benign focal epilepsy of childhood

R. A. Masterton[1,2], A. S. Harvey[3], L. Lillywhite[1], J. S. Archer[1,4], D. F. Abbott[1,2], and G. D. Jackson[1,2]

[1]Brain Research Institute, Melbourne, Victoria, Australia, [2]The University of Melbourne, Melbourne, Victoria, Australia, [3]Royal Children's Hospital, Melbourne, Victoria, Australia, [4]James Cook University, Cairns, Queensland, Australia

Purpose: Benign focal epilepsy of childhood (BFEC) with centro-temporal spikes (CTS) is a common, age-limited, idiopathic focal epilepsy syndrome with characteristic electroclinical features. Seizure semiology suggests a focus in the central sulcus region close to the sylvian fissure, however the precise localisation of the generator of seizures and CTS in BFEC is not known. EEG and MEG source analyses also suggest a central sulcus focus - however, EEG and MEG only detect synchronised neuronal sources involving relatively large areas of superficial cerebral cortex, and are insensitive to other neuronal activity e.g. sub-cortical or asynchronous activity.

In this study, we performed simultaneous EEG and functional MRI (fMRI) in a group of children with well-characterised typical BFEC and CTS, to localise cortical and sub-cortical haemodynamic changes associated with these discharges.

Methods: We recruited nineteen children with recent-onset BFEC with CTS from multiple centres in Melbourne. Patients were only included in this study if they had one or more seizures of a type consistent with BFEC, were aged 7-13 years, had early milestones that were broadly within normal limits, were attending mainstream primary school, had typical CTS on EEG, and had no significant cerebral abnormality on MRI. Also only patients with unilateral CTS were included.

We acquired 30 minutes of simultaneous EEG and whole brain fMRI in a 3T GE Signa LX whole body scanner (General Electric, Milwaukee, WI, USA). fMRI images were acquired using a multi-slice gradient-recalled echo-planar imaging (EPI) sequence (TR = 3.0 s; TE = 40 ms; flip angle = 60°; 25 tilted axial slices 4 mm thick + 1 mm gap; field of view = 24 cm; 128 x 128 matrix). EEG was recorded with sixteen non-metallic disc electrodes with carbon fibre leads in standard 10-20 locations. EEG was reviewed off-line following fMRI acquisition in standard bipolar and referential montages. The EEG was filtered for magnetic gradient and motion artefacts using hardware and software developed in-house (*iBrain^{TM} EEG*). EEG was reviewed by two experienced EEGers independently and then together, with a consensus reached about events of interest.

The fMRI data was pre-processed (slice-timing corrected, realigned and smoothed) and analysed using SPM2 (www.fil.ion.ucl.ac.uk/spm/). The haemodynamic response was modelled using the event timings identified from the EEG convolved with three basis functions: the SPM canonical HRF and its temporal and dispersion derivatives. Motion correction parameters were included as effects of no-interest, and image volumes with a translational movement of greater than 1 mm (and the subsequent 3 volumes) were removed from the model using a delta function regressor in the design matrix.

The BOLD response was assessed using an F-contrast at a threshold of $p < 0.05$ corrected for multiple comparisons. The results were overlaid upon the subject's mean EPI and viewed using Brainsight^{TM} software (Rogue Research, Montreal, QC, Canada) in orthographic and 3D surface rendered views.

Results: Twelve children were excluded from this study: three did not meet our inclusion criteria; six had no CTS visible on their EEG immediately prior to and during the EEG-fMRI study; two studies were excluded for technical reasons (one due to excessive electrode artefact obscuring the EEG; one due to a problem with the acquisition software); and one child was unable to complete the 30 minute study due to restlessness.

Seven children had CTS on EEG: 4 left-sided and 3 right-sided. The mean number of CTS was 267±171. All children showed a BOLD signal change associated with their spiking.

Figure 1 shows the results from two children, with left-sided and right-sided CTS respectively. Figure 2 shows all the subject's individual results normalised into a common space and overlaid upon a single EPI image. All subjects showed remarkably consistent results with a common feature being BOLD signal change in the lower part of the post-central gyrus. Interestingly the BOLD changes were seen consistently on the anterior bank of the post-central gyrus, rather than the posterior bank of the pre-central gyrus as EEG studies have suggested. In 4 cases the BOLD changes were seen extending contiguously from the opercular part of the post-central gyrus to the circular sulcus. In one case, only a contra-lateral BOLD response was seen at a threshold of $p<0.05$ corrected, however at a lower threshold of $p<0.001$ uncorrected a bilateral BOLD response was observed.

Conclusion: Classical BFEC with CTS is a relatively homogeneous group based upon EEG/fMRI BOLD signal changes. They have in common BOLD signal changes associated with CTS in the lower part of the post-central gyrus on its anterior bank.

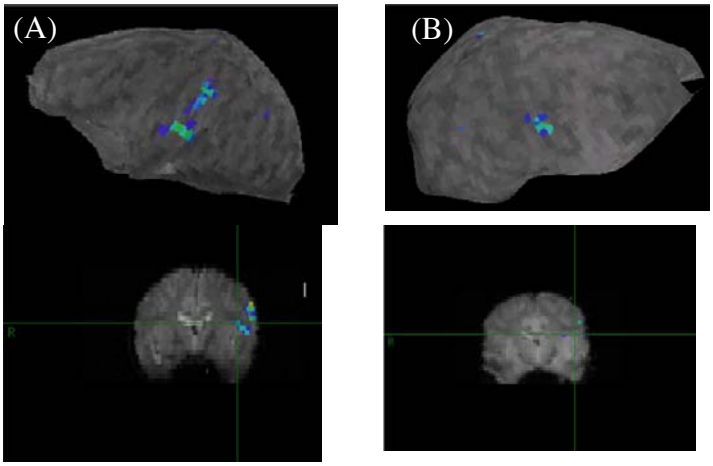

Figure 1 a): Example left CTS showing BOLD signal changes on the anterior bank of the post-central gyrus from the level of the inferior frontal gyrus into the sylvian fissure including the opercular bank of post-central gyrus.

Figure 1 b): Example right CTS showing BOLD signal changes on the anterior bank of post-central gyrus, at the level of the inferior frontal sulcus extending into the sylvian fissure to the circular sulcus but not including the insula cortex.

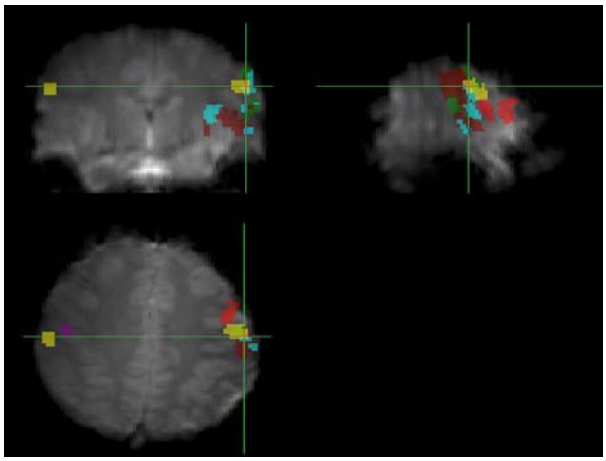

Figure 2: All subject SPMs normalized into a common space and overlaid upon a single EPI image, with the right-sided spike SPMs flipped from left to right. Each subject is represented with a unique colour. The SPMs are thresholded at $p<0.05$ corrected. One subject showed bilateral BOLD signal changes with some contra-lateral to the side of the EEG spiking. Another subject showed only a contra-lateral response at this threshold, with a bilateral response observed at a lower threshold of $p<0.001$ uncorrected.