Cortical and sub-cortical networks in children with absence epilepsy.

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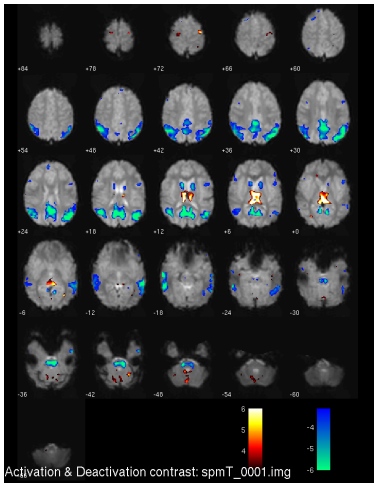
Background: Absence seizures (AS) are a common childhood seizure type and can affect cognition and interfere with learning. Physiological thalamo-cortical oscillations which underpin perception, cognition and arousal are also believed to be the substrate for AS generation REF. Recent data in animal models has implicated focal cortical regions as a trigger for instability in thalamo-cortical interactions[1]. Combining EEG with functional MRI (EEG-fMRI) provides a non-invasive method to study absence seizures.
Aim: The aim of this study is to identify regions of the cortex and sub-cortical structures involved in the generation of absence seizures using simultaneous EEG with functional MRI in a cohort of children with untreated absence seizures.

Subjects: Ten children (4 males, from 5 to 11 years of age) with typical absence seizures identified on history and routine EEG were recruited from the local EEG departments after institutional ethical clearance was granted. They were studied prior to commencing medication. Children were selected on the basis of a history of staring spells consistent with AS, EEG showing typical AS with 3 – 4 Hz spike wave, age less than 12 years, and an absence of other seizure types. All subjects were therefore able to be classified as Childhood Absence Epilepsy.

Methods
EEG acquisition: Eighteen non metallic scalp electrodes with carbon fibre leads were attached to the scalp in the conventional '10-20' locations (with the exception of Fz). ECG was recorded from 2 chest electrodes. EEG data were acquired using a custom built amplifier with fibre optic transfer of data to a computer in the MR control room. MR gradient artefacts and ballistocardiogram were removed from the EEG signal off line[2]. AS and other epileptic discharges were marked off line by two electroencephalographers (PWC, DF).
fMRI acquisition: fMRI data were obtained using a 3-T GE Signa LX whole body scanner (General Electric, Milwaukee, Wisconsin). Images were continuously acquired as a series of gradient-recalled echo planar image volumes (TR = 3200ms, TE = 40ms, flip angle = 80º with axial oblique slices 3.2mm thick + 0.2mm gap, 22 cm FOV; 64x64 matrix). fMRI data were acquired for 18-60 minutes (average 48 minutes).
Statistical Analysis: fMRI data were analysed using SPM8b (Statistical Parametric Mapping, Welcome Department of Imaging Neuroscience, London, United Kingdom). fMRI data were pre-processed prior to analysis (motion correction, slice-timing correction, spatial normalisation and smoothing by convolution with an 8-mm isotropic Gaussian kernel). Motion was modelled as an event of no interest. A second order group analysis was performed on the 10 subjects.



Results Figure 1: Statistical parametric map of 2nd order group analysis of 10 subjects ($p<0.001$). overlaid on single subject mean EPI image. Positive BOLD response is seen in the mesial and dorsal aspects of the thalamus (image -6 to +12) as well as a restricted region anterior to the central sulcus most prominent on the left. Negative BOLD is seen in the posterior midline structures of the precuneus and posterior cingulate (+42 to +6), lateral parietal lobe (+54 to +6) bilateral caudate nuclei (+18 to +6) and pons and midbrain (-30 to -48).

Conclusion: The results of this study support the findings of previous studies of EEG-fMRI in AS [3]. Prominent thalamic and restricted neo-cortical positive BOLD supports a role for thalamo-cortical connections in absence seizures. Negative BOLD response seen in the posterior rest network, (midline parietal lobule and lateral parietal cortex) and subcortically in the caudate nuclei and pons. A robust Negative BOLD response in the pons and midbrain has not been previously described and further expands the networks involved in AS generation.

References:
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