Failure of connectivity modulation during an attentional task in children with epilepsy is not explained fully by interictal activity

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Introduction: Patients with focal epilepsy often have cognitive deficits, but the role of controlling epileptic discharges and seizures on possible alterations in cognition is not well understood. Resting state fMRI studies in epilepsy have shown network abnormalities of various kinds[1,2] in particular default mode network abnormalities have been frequently reported. However, the processes underlying these and the role of interictal epileptiform discharges (IEDs) are unclear. We therefore decided to study alterations in network properties by 1) recording both during rest and during a 'natural stimulus' task, 2) recording simultaneous EEG with fMRI to enable the investigation of the role of interictal activity.

Methods: We collected simultaneous EEG-fMRI data at 1.5T using an MRI compatible EEG system. Subjects consisted of 16 pre-surgical drug-resistant patients with mixed localisation and 8 age-matched controls, all between the ages of 10-18. The fMRI data was obtained at 3.3x3x4mm resolution, TR=2160ms, TE=30ms, and 300 volumes. Four sessions of 10m48s duration were recorded: two sessions of rest, and two sessions of task. The task involved a video condition watching a cartoon and a condition presenting a screen with the words 'please wait'. EEG was corrected for in-scanner artefacts and interictal epileptic events (IEDs) visually identified by an expert clinician. Following standard pre-processing in SPM8 (www.fil.ion.ucl.ac.uk), each subjects' 4 sessions were entered into a general linear model containing the task, IEDs and effects of no interest. A general linear model (GLM) analysis was performed looking at blocks of task (video and 'please wait' conditions) which were entered as a regressor. In each individual a positive and negative T-contrast was used to show regions with greater activity in each condition. Group effects were subsequently tested between the groups in a second level analysis using these maps.

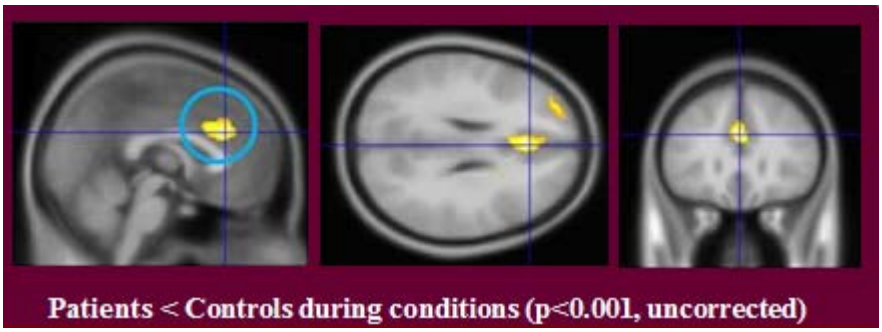

Figure 1: The DACC (circled) was the area of significant differences in the GLM between controls and patients.

The functional connectivity analysis was performed using conn (http://www.nitrc.org/projects/conn). Seed to voxel analysis used brain regions generated by the GLM group level differences to reveal network differences between patients and controls. We used a statistical threshold of p<0.001. We performed functional connectivity analysis 1) including and 2) excluding interictal activity as a covariate to remove the main effects of interictal activity from the connectivity.

Results: For the GLM analysis both patients and controls showed activity in the extrastriate visual cortex during video, and 'salience' network activations, which include areas such as the dorsal anterior cingulate cortex (DACC) and the parietal cortices[3], during 'please wait' task sessions. There was also increased activity during the please wait condition relative to the video which was significantly reduced in the DACC in patients (Figure 1). Significant differences in functional connectivity were found between groups in both 'task' and rest sessions. Higher connectivity was found during task in patients between the extrastriate visual cortex and the DACC, which is not present during rest sessions (Figure 2). These results were not strongly affected by the inclusion of interictal activity, making it unlikely that this is the direct factor influencing these results.

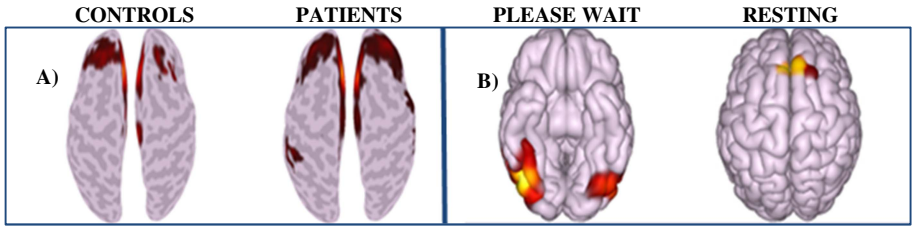

Figure 2: a) Functional connectivity analysis showing patients have more widespread brain recruitment than controls for the seeded region from the GLM where p=0.001. b) Functional connectivity analysis showing the significant differences between patients and controls during task and rest sessions where p=0.001.

Discussion: We have shown for the first time, the effect of epilepsy on a specific network during a low level attentional task despite a heterogeneous group of focal epilepsy patients. We found that patients did not modulate the connectivity between extrastriate and DACC between conditions as strongly as controls. Therefore it appears that they were unable to switch between tasks as efficiently. However, interictal activity does not appear to be the main factor responsible for this difference.

References: 1. Widjaja E, Zamyadi M, Raybaud C, et al. Abnormal Functional Network Connectivity among Resting-State Networks in Children with Frontal Lobe Epilepsy. AJNR Am J Neuroadiol. 2013. **2.** Laufs H, Hamandi K, Salek-Haddadi A, et al. Temporal lobe interictal epileptic discharges affect cerebral activity in "default mode" brain regions. Human Brain Mapping. 2006; 28(10): 1023-1032. **3.** Niendam T, Laird A, Ray K, et al. Meta-analytic evidence for superordinate cognitive control network subserving diverse executive functions. Cogn Affect Behav Neurosci. 2012; 12(2):241-268.