Combined EEG, fMRI, and Cognitive Testing in Childhood Absence Epilepsy

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Introduction: The fundamental mechanisms of impaired attention in childhood absence epilepsy (CAE) are not known. Absence seizures consist of brief 5-10 s episodes of unresponsiveness, associated with a 3-4 Hz "spike-wave" discharges (SWD) on electroencephalography (EEG). In addition to the deficit during seizures, many children also suffer from milder impaired attention between absence episodes .

Our central hypothesis is that when SWD involve specific regions such as the anterior cingulate cortex and medial thalamus, attention is impaired, but when SWD do not involve these regions, attention is spared. Therefore, our main question is: which specific cortical and subcortical networks are selectively involved in absence seizures when patients show impaired attention?

Methods: We used simultaneous EEG and fMRI while testing attentional vigilance with a continuous performance task (CPT) and a simpler motor task (CPT-Control) in pediatric patients with typical absence seizures. To increase the chance of recording absence seizures, medications were held for up to 48 hours. The EEG recording system consisted of an EEG cap, carbon fiber cables, a 125 Hz analog low-pass Butterworth filter, and an EEG recorder (Neuroscan, NC, U.S.A.). EEG was recorded at 500Hz with 32 bit DC recording, utilizing a standard 10-20 montage with a linked mastoid reference. fMRI data were acquired using a 3T MR system (Siemens, Erlangen, Germany) with continuous EPI BOLD sequence, TR = 1550 mS, 25 slices per image, TE = 30 mS, FA = 80, slice thickness = 6 mm with no gap, FOV = 220 mm, matrix size = 64x64, BW = 2056 Hz. EEG artifact was removed by post-processing using temporal PCA-based gradient noise removal. fMRI data were analyzed using SPM2.

Results: We obtained a total of 34 seizures from 8 EEG-fMRI sessions in 7 patients between the ages of 11-14. Composite images of fMRI changes during the seizures for 5 of these patients are shown in Figure 1a-e. fMRI increases were seen most consistently in the thalamus, and in the occipital, paracentral, and lateral frontal and temporal cortex. Decreases were usually seen in the basal ganglia, as well as in the lateral parietal, anterior/posterior cingulate cortex and the precuneus. These changes were generally similar to those reported during SWD in more heterogenous populations of adult patients (Archer et al., 2003; Salek-Haddadi et al., 2003; Aghakhani et al., 2004), except the thalamus was perhaps more consistently involved in these pediatric patients with typical CAE. **RED = BOLD signal Increases** **GREEN = BOLD signal Decreases**

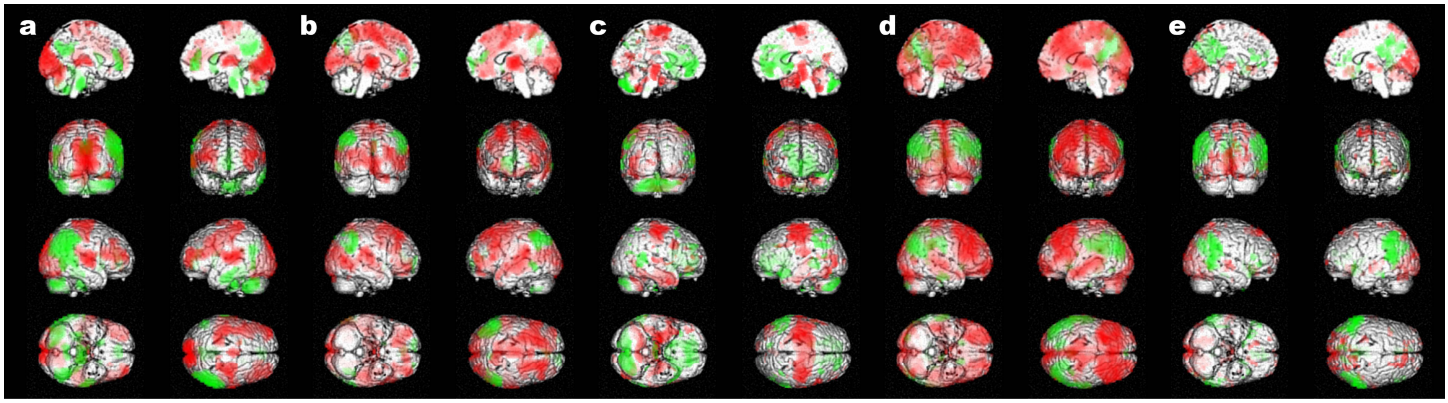

Fig. 1: BOLD fMRI changes during seizures vs baseline in 5 patients with typical CAE **a)** Patient 1, age 14 **b)** Patient 2, age 12 **c)** Patient 3, age 11 **d)** Patient 4, age 13 **e)** Patient 5**,** age 13**.** SPM voxel-level height threshold was p<0.01, and extent threshold k=3.

We also measured interictal fMRI changes during CPT in 20 CAE patients off-medication, and in 20 control subjects. Patients most commonly showed significant fMRI increases in the bilateral anterior frontal cortex, anterior cingulate, dorsolateral frontal and parieto-occipital cortex, left fusiform gyrus, bilateral medial thalamus, upper brainstem, and cerebellum. The CPT activated regions of the brain are consistent with other models of attention which involve interaction of cortical and subcortical functional pathways (Hage et al., 1998; Adler et al., 2001; Riccio et al., 2002), and overlapped with regions showing fMRI changes during absence seizures.

Conclusions: These results demonstrate the feasibility of obtaining high quality EEG-fMRI during behavioral testing in pediatric patients with CAE. As in adult patients, increases and decreases were seen in frontoparietal and thalamic networks. Our initial findings also suggest that the attentional networks involved in CPT overlap with thalamocortical networks affected by CAE. Further studies will relate the behavioral performance to specific regions involved in CAE.