Abnormal functional network connectivity among spatially independent resting state networks in children with frontal lobe epilepsy

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Introduction: Functional connectivity is defined as the temporal synchronization of low-frequency fluctuations (0.01-0.1Hz) arising from spontaneous neuronal activities in distant brain regions. Resting state fMRI measures the spontaneous fluctuations in absence of a specific task. Although several studies have evaluated the resting state networks (RSNs) in adults with different types of epilepsy[1], there is currently minimal information available on functional connectivity and no published data on temporal coherence across the RSNs in children with epilepsy. This study aims to assess functional connectivity within RSNs and functional network connectivity (FNC) across several RSNs in children with frontal lobe epilepsy (FLE) using the independent component analysis (ICA) method.

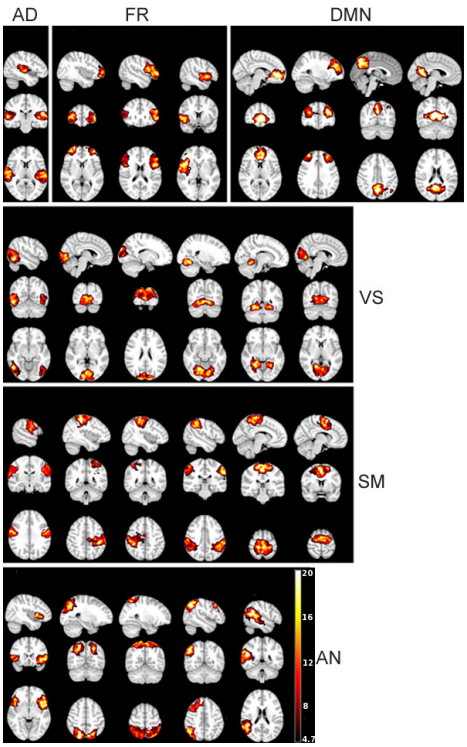

Fig 1. Spatial maps of the 25 components identified as RSNs plotted as T-maps ($p < 0.05$, FDR corrected) overlaid on MNI152 template. Top row (from left to right): components of the AD, FR, and DMN. 2nd, 3rd and 4th rows: VS, SM, and AN networks.

Subjects and MRI parameters: 15 patients with FLE (mean age: 13.9 yrs) and 14 age-matched healthy controls (mean age: 14.7 yrs) were recruited and written informed consents were obtained from participants. MRI was performed on a Philips 3T scanner with an 8-channel phased array head coil. High-resolution anatomical T1 and resting state fMRI (with closed eyes) images were acquired in all subjects.

Data Analysis: After a series of pre-processing steps[2], a 75 components ICA analysis (implemented in the GIFT software package[3]) was performed. By spatially correlating all components with existing RSNs[4], we were able to extract 6 RSNs: auditory (AD), sensorimotor (SM), visual (VS), attention (AN), frontal (FR) and default mode network (DMN), from all subjects. One and two-sample t-test analysis was performed on z-maps of all RSN components for within and between group comparisons. We then studied temporal correlations between RSN components by examining the time series of the components using the FNC toolbox (http://mialab.mrn.org/software/fnc/index.html). The correlation between all pair-wise combinations of independent components (ICs) of interest was calculated for both groups[5]. Statistical analysis was performed to identify IC pairs with significant temporal correlation differences between patients and controls.

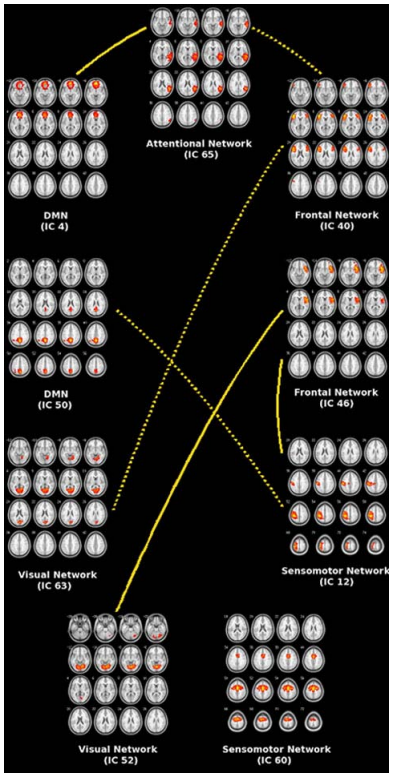

Fig 2. FNC between RSNs: Group comparison of pair-wise ICs revealed reduced FNC (solid line) between DMN-AN, FR-SM, and FR-VS, and increased FNC (dotted line) between FR-AN, DMN-SM and FR-VS in patients vs. controls.

Results and Discussion: Fig 1. shows the spatial maps of the 6 RSNs in controls. Based on two-sample t-test ($p < 0.005$ uncorrected), FR showed only reduced connectivity while the remaining five networks demonstrated both reduced and increased functional connectivity in patients relative to controls. Fig. 2 presents the results of group comparison of pair-wise ICs, which shows reduced FNC between DMN-AN (ICs 4-65), FR-SM (ICs 46-12), and FR-VS (ICs 46-52), and increased FNC between FR-AN (ICs 40-65), DMN-SM (ICs 50-12) and FR-VS (ICs 40-63) in patients relative to controls. The current results suggest that abnormal functional connectivity exists both within and across the RSNs in children with FLE. Epilepsy is considered a disorder of neural networks and the findings of this study support this concept and provide evidence on the effect of localization-related epilepsy, in this instance FLE, on several RSNs. We have also demonstrated both reduced and elevated functional connectivity within the RSNs and also in FNC across the RSNs, suggesting that brain plasticity may play a role in the reorganization of the networks, both within and across the networks.

References: 1. Waites AB, et al. Ann Neurol. 2006; 59:335-43. **2.** Widjaja E, et al. Am J Neuroradiol. in press. **3.** Calhoun VD, et al. Hum Brain Mapp. 2001; 14:140-51. **4.** Allen EA, et al. Front Syst Neurosci. 2011; 5:2. **5.** Jafri MJ, et al. Neuroimage. 2008; 39: 1666-81.

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