Evidence for top-down dysregulation of primary visual processes in children and adolescents with schizophrenia

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Introduction: It has long been known that specific visual frequencies (i.e., 8 Hz) results in greater blood flow to the striate cortex (Fox and Raichle 1985; Singh et al 2003). This 8 Hz peak is thought to reflect synchrony in local neuronal firing. Evidence has supported disrupted neural connectivity as a possible etiology for schizophrenia. Much of the work supporting this hypothesis have come from studies measuring functional connectivity between distant brain regions. Since this synchrony is thought to reflect more localized connectivity, it was our plan to study local connectivity by evaluating entrainment in children and adolescents with schizophrenia. Disruption in entrainment could reflect disruptions in local connectivity, which could reflect localized disruptions in connectivity.

Methods: The subjects included 24 children and adolescents with schizophrenia and 24 age and gender matched controls (age range 9 to 19). The diagnostic assessment was performed using the K-SADS and measure of positive and negative symptoms were also obtained. Imaging was performed on a Siemens 3 Tesla Trio scanner. Subjects observed two runs of a block design, each run was three minutes in length, and consisted of a flashing checkerboard presented at either 1, 4, 8, or 12 Hz. Functional images were acquired using a gradient echo sequence in 16 contiguous axial slices with an in plane resolution of 3.5 x 3.5 mm and a 2 mm slice thickness; TE = 30 ms, TR = 1 sec, flip angle = 60^o, FoV = 224 mm and the FoV phase was 100%. A total of 180 measurements were obtained in each of the two runs. The post-processing pipeline included time shifting, motion-correction, normalization, and spatial smoothing using FSL. Images were then imported to MATLAB. The region of interest was obtained by first performing a voxel-wide Fourier transform along the time axis. This was used to create a voxel-wide map based on the frequency of the block paradigm (0.1 Hz). The largest cluster was selected from the Fourier map and all clusters were found to be centered on the V1 area of the occipital lobe. The time courses were detrended using a discrete cosine transform removing the DC component and the first three order polynomials. The average hemodynamic response for each frequency and group were generated and a group by frequency ANOVA was performed on the maximum percent signal change for the hemodynamic response curve.

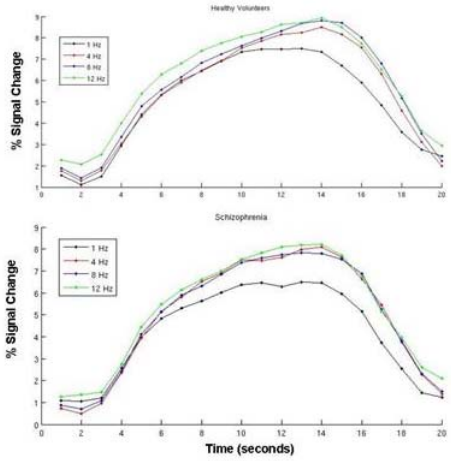

Figure 1 – Hemodynamic Response at Different Frequencies between Patients and Controls

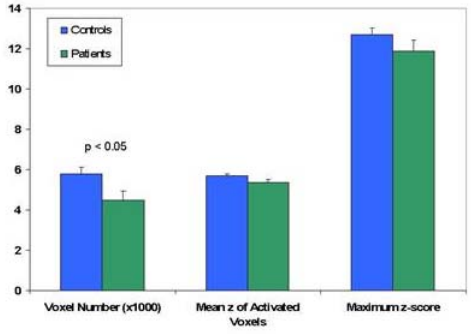

Figure 2 – Spatial Extent and Mean Level of Activation between Patients and Controls

Results: The average hemodynamic response for the patients and controls were quite similar (Figure 1). The hemodynamic response was greatest at 8 Hz and lowest at 1 Hz for both the patient and control groups and there were no patient/control differences. There was however, a significant difference in the number of activated voxels in the occipital lobe between patients and controls (Figure 2).

Conclusions: Children and adolescents with schizophrenia demonstrate significantly less activation in the occipital lobe during a multi-frequency flashing checkerboard task. However, there were no differences in the hemodynamic response function and maximum entrainment occurred in both groups at a frequency of 8 Hz. These results may reflect abnormal top-down control of visual networks in children and adolescents with schizophrenia, but with intact local neuronal connectivity.

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