# Early Reductions in Diffusion Anisotropy are Apparent in Pediatric Epilepsy

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## INTRODUCTION

Diffusion Tensor Imaging (DTI) is beginning to play a crucial role in elucidating the ultrastructural correlates of multiple cerebral disorders, including epilepsy. Reduced anisotropy of certain white matter regions has been shown for adult temporal lobe epilepsy[1] and grey matter diffusivity alterations have been implicated in both adult[2] and pediatric[3] epilepsy populations. However, the degree to which white matter DTI abnormalities are present in pediatric epilepsy remains to be determined and is the focus of the work presented here.

## MATERIALS AND METHODS

Sixteen pediatric epilepsy patients (age 15.69 +/- 3.45 years, 7 male and 9 female) and thirteen, matched control subjects (age 15.64 +/- 3.47 years, 4 male and 9 female) were administered DTI scans as part of a larger longitudinal study. The epilepsy patients were each scanned approximately two years after the first reported seizure. T1 weighted images used for anatomical referencing and diffusion weighted (DW) images (one with b=0 and 13 with different gradient directions with b=1000) were collected on a clinical 1.5T GE Signa LX MRI scanner. For DW images TR=4000 ms, TE =76.6 ms and the slice thickness was 4 mm with 8 mm spacing to allow for full brain coverage.

Images were transferred to an offline workstation for post processing and analysis with SPM5[4]. The diffusion II toolbox[5] was used for motion correction and calculation of the diffusion tensor. Fractional anisotropy (FA) maps were created and coregistered to the anatomical T1 images using SPM5 tools and all images were spatially normalized to a standard brain atlas. The maps were then smoothed using a Gaussian kernel with FWHM of 12 mm and two types of statistical tests were performed: 1) group analysis by two-sample t-test and 2) linear regression analysis within each group with age as the covariate. All tests were explicitly masked to include only voxels for which average FA >0.3. Significance was placed at P<0.01, uncorrected, with a threshold cluster size of 30 voxels.

## RESULTS AND DISCUSSION

*Between Groups Analysis.* Two sample t-tests between groups (Figure 1) showed reduced values of FA for the epilepsy group bilaterally in the anterior internal capsule and frontal lobe white matter as well as in several subcortical white matter regions. This reduction in anisotropy may indicate early excitotoxic injury, axonal degeneration, degradation of myelin or other structural damage in particular white matter regions for child-onset epilepsy populations. Because the duration of epilepsy was constant across subjects, there is an indication that white matter diffusion changes occur as early as two years after onset.

*Age as a Covariate.* The results from linear regression analysis (Figure 2) showed a more robust difference between the two groups, likely due to the inclusion of age as a covariate. Positive correlations were found between FA and age in control group corpus callosum (CC) regions. This was expected as maturation of the CC during childhood and adolescence is known to be accompanied by increases in anisotropy[6]. Interestingly, this anatomical correlation was not statistically evident in the pediatric epilepsy group, indicating a potential role for epilepsy in disruption of the development of white matter. Furthermore, between groups, CC regions were not shown to be statistically different, highlighting the importance of age considerations in the analysis of pediatric DTI data.

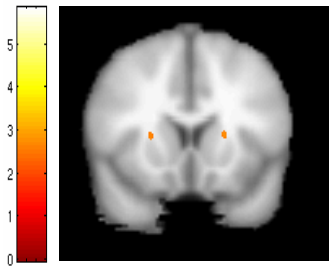


**Figure 1** Statistical map for control FA minus epilepsy FA overlayed on the MNI standard brain. Scale bar indicates the

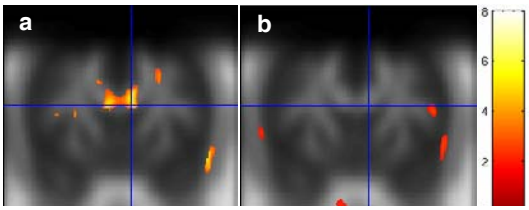


**Figure 2** Linear regression statistical map with age as a covariate overlayed on the average FA map for control subjects (**a)** and epilepsy subjects **(b)**. Scale bar indicates the T statistic

## CONCLUSION

Measures of diffusion anisotropy offer a powerful means to quantitatively examine white matter cellular and structural properties on a macroscopic scale. The work presented here indicates several fractional anisotropy differences between two-year post-onset pediatric epilepsy patients and controls, which evidence the neurodevelopmental impact of pediatric epilepsy. These results agree with previous volumetric studies of child-onset epilepsy that suggest an increased vulnerability in this group for reduced white matter volume[7], and extend these findings with further structural specificity to the affected regions. Because this structural damage has been correlated with cognitive performance deficits, it will be informative for future studies to investigate the relationships between diffusion abnormalities and neuropsychological test performance in child-onset epilepsy populations. Overall, the use of DTI indices to characterize structural abnormalities enhances our understanding of the correlates of pediatric epilepsy.

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