White Matter Microstructure Correlates with Reading Ability in Healthy Subjects and Those with Fetal Alcohol Spectrum Disorder

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INTRODUCTION: Diffusion tensor imaging (DTI) studies of reading ability consistently highlight left temporal-parietal white matter in healthy individuals[1-3] and dyslexia[4-8]; the corpus callosum is also implicated by DTI[8-10]. Studies have also investigated DTI white matter - reading relationships in traumatic brain injury (n=41)[11] and preterm children (n=19)[12], demonstrating correlations in callosal areas. Individuals with fetal alcohol spectrum disorder (FASD), where brain injury is associated with prenatal alcohol exposure, often have cognitive deficits including reading[13]. DTI abnormalities in the corpus callosum and temporal lobe[14,15] are observed in FASD, yet their link to reading is unknown. The purpose of this study was to determine if white matter microstructure, measured by fractional anisotropy (FA), correlates with reading ability in subjects with FASD and how that relates to a healthy cohort.

METHODS: Subjects were 40 volunteers aged 5-19 years (22m/18f; mean age: 10.7±3.4 years) with FASD and 40 age- and gender-matched controls. All subjects were assessed with the Woodcock Reading Mastery Word ID test. An independent samples t-test evaluated group differences. DTI was performed on a 1.5T Siemens Sonata scanner using dual spin echo EPI, 40 3mm slices (no gap), image matrix 128x128 with 75% phase partial Fourier zero-filled to 256x256, TE/TR=98ms/6400ms, b=1000 s/mm^2, 8 averages and 6 directions, ~6 minutes. Non-diffusion weighted images were normalized to the ICBM EPI template with non-affine transformations in SPM8; fractional anisotropy (FA) maps were normalized with the same parameters and smoothed with a 4 mm kernel. Voxel-based correlation of FA, controlling for age, with age-normalized Word ID scores was performed in SPM8 for each group separately; only voxels considered to be white matter in all individuals (FA≥0.2) were included in the analysis. Positive and negative t-tests with $p<0.025$ per voxel and clusters size≥84 were used to determine significant clusters (overall alpha was <0.049).

RESULTS/DISCUSSION: Subjects with FASD had lower Word ID scores than controls ($mean_{FASD}$=92±13; $mean_{control}$=107±13; $p<0.001$). In the FASD group, 6 clusters with positive Word ID-FA correlations were observed: brainstem (595 voxels), two bilateral parietal (left: 103 voxels, right: 102 voxels), right internal capsule (137 voxels), and two left temporal (148 and 150 voxels). Three clusters in the FASD group had negative correlations: the right frontal/parietal (192 voxels) and two bilateral cerebellum (left: 210 voxels, right: 227 voxels). In the control group, no negative clusters and four positive clusters were observed: three in left temporal/parietal (209, 206, 136 voxels), and one in genu of corpus callosum (92 voxels). Figure 1 shows all clusters and plots of FA averaged over a left parietal cluster for each group (marked by *, #). There was no overlap between FASD and control clusters.

Significant FA-Word ID correlations in controls were focused in the left temporal-parietal region, with one cluster in the genu, supporting earlier findings in healthy individuals and dyslexia[2-8]. Similar left temporal-parietal clusters were observed in FASD, suggesting consistent involvement of this brain region despite known brain damage of this area in FASD. However, correlations in FASD differed in that they were more widespread than in controls, including right hemisphere white matter, and that there were 3 clusters with negative correlations. The more widespread, and notably symmetric correlations, in FASD individuals may be due to atypical brain development or compensation for the limited capacity of other brain regions. Some FASD clusters may simply reflect coincidental brain damage and poor general cognitive performance in the disorder rather than direct involvement in reading.

Brain structure - reading correlations in FASD are reported for the first time, highlighting the consistent involvement of the left temporal-parietal area for reading ability in healthy and abnormal populations, albeit with more widespread regions in FASD children/adolescents.

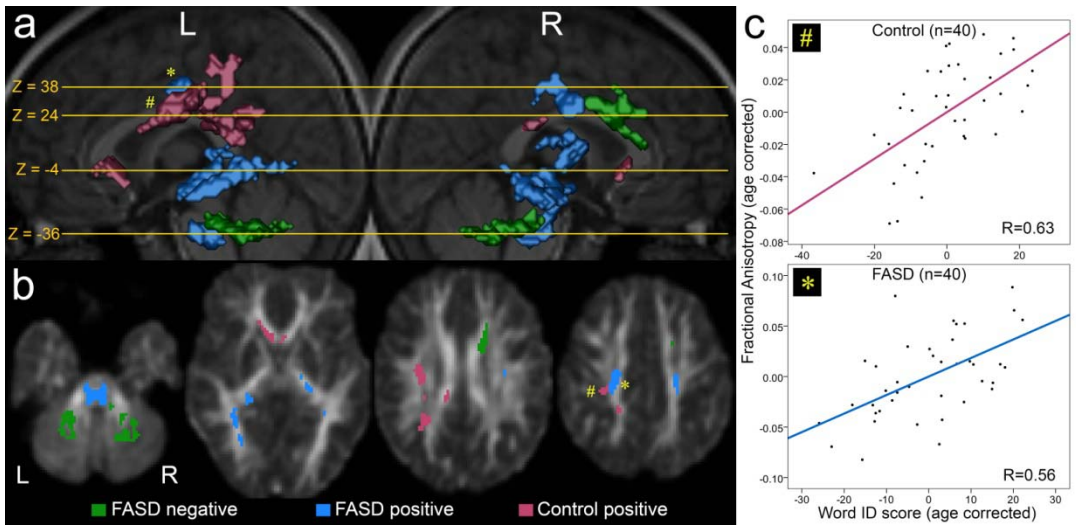

Figure 1: a: clusters with significant fractional anisotropy (FA) - Word ID correlations are shown for controls (n=40) and FASD subjects (n=40). b: clusters shown overlaid on normalized, smoothed FA maps. c: FA averaged across a left parietal cluster from each group (# for controls, * for FASD) is shown plotted against Word ID score, both corrected for age.

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