Age Related Changes of the Interrelationships of White Matter in Autism Spectrum Disorder

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Target Audience: Researchers interested in autism spectrum disorders (ASD) and the use of diffusion tensor imaging (DTI) in understanding white matter changes in ASD.

Purpose: Brain imaging findings in children with autism spectrum disorder (ASD) suggest the disorder is associated with altered brain development and disrupted structural and functional brain "connectivity,"[1,2] which implies atypical white matter microstructure in at least some parts of the brain in ASD. However, it is unclear how homogeneous the structural organization of the white matter microstructure is within the brains of individuals with ASD at different ages. For example, does white matter microstructure across the brain become more or less variable with age in ASD compared to typical development? In this work, we examine the extent to which individual white matter tracts related to other white matter tracts between individuals in childhood and adulthood with ASD compared to typical development.

Methods: *MRI Acquisition*: Subjects for this study consisted of 100 males with ASD and 57 typically developing (TD) male controls between 3 and 39 years of age. DTI data were acquired from these participants on a 3 Tesla Siemens Tim Trio scanner. Diffusion weighted images were corrected for distortion and head motion and tensors were subsequently fit using the robust estimation algorithm (RESTORE[4]). Maps of fractional anisotropy (FA), mean diffusivity (MD), and radial diffusivity (RD) were calculated, however, only FA was used herein. *Analysis:* Median FA from 48 major white matter tracts[5] were extracted from each individual, and subjects were partitioned into two age groups. For each age and diagnosis group, the Pearson correlations between median FA for each of the 48 white matter tracts was generated. The mean of the correlation coefficients were then compared across age and group.

Results: Fig. 1a shows a visualization of the organization of white matter microstructure in ASD and TD age groups, with the nodes defined as the center of mass of each region and the color of the "edges" representing the strength of the correlation between region pairs. Correlations between white matter tracts above 0.8 are indicated with blue lines. Fig. 2 shows a scatter plot of the mean correlation coefficient as a function of the mean age of each group. Qualitatively, we see a dynamic relationship in the underlying white matter microstructure and a differential pattern between individuals with and without ASD.

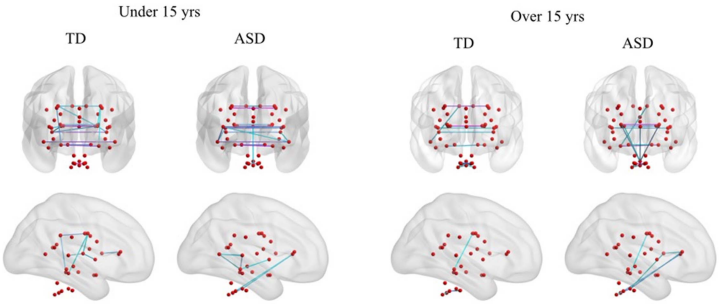

Fig. 1: Visualization of white matter correlations between ASD and TD age groups.

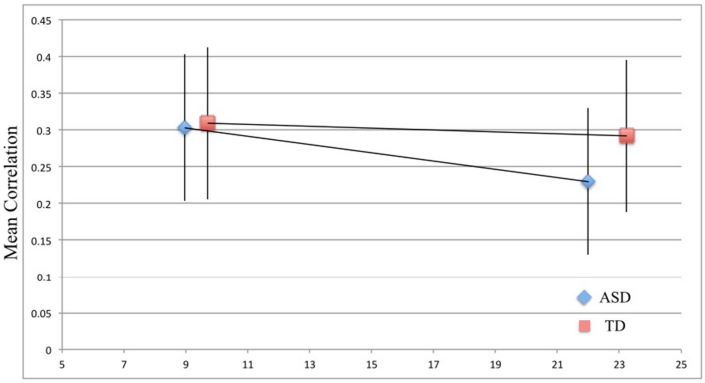

Fig. 2: Overall trends of white matter correlations between ASD and TD

Discussion: Previous studies have consistently indicated microstructural differences in at least some white matter tracts in ASD compared to typical development[2]. However, age-related changes in the homogeneity of the white matter microstructure among different tracts of the brain in ASD have not been examined previously. Our results suggest that the homogeneity of the white matter microstructure in typical development is similar in childhood and in adulthood. However, in ASD, there is decreasing homogeneity of the white matter microstructure across the brain from childhood into adulthood. These results possibly suggest that white matter tracts become structurally more independent in adults with ASD and less integrated into the neural networks of the brain. However, the biological processes underlying this dynamic pattern, such as changes in myelin content, remain unclear.

Conclusion: In this work, we have sought to examine the overall pattern of relatedness of the microstructure among different white matter tracts of the brain in individuals with and without ASD. Our results suggest the inter-relatedness of white matter microstructure is likely atypically changing with age in ASD. Moreover, our results highlight the need for more powerful longitudinal studies investigating the development and organization of white matter in the autistic brain.

References: [1] Rudie et al. Altered functional and structural brain network organization in autism. NeuroImage: Clinical. 2013; (2):79-94. [2] Travers et al. Diffusion tensor imaging in autism spectrum disorder: a review. Autism Research. 2012; 5: 289–313. [3] Barnea-Goraly et al. Similar white matter aberrations in children with autism and their unaffected siblings: a diffusion tensor imaging study using tract-based spatial statistics. Arch Gen Psychiatry. 2010;67(10):1052-60. [4] Chang et al. RESTORE: robust estimation of tensors by outlier rejection. MRM 2005 53:1088–1095. [5] Mazziotta J. et al. A four-dimensional probabilistic atlas of the human brain. J. Am. Med. Inform. Assoc. 2001;8:401–430.