

White Matter Abnormalities in Youth with High Functioning Autism or Asperger Syndrome Using DTI Tractography and Voxelwise Analyses

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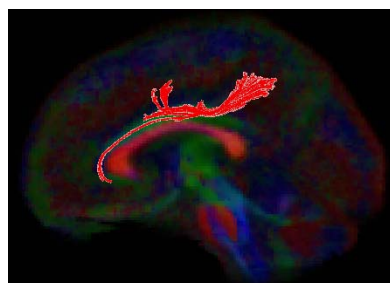
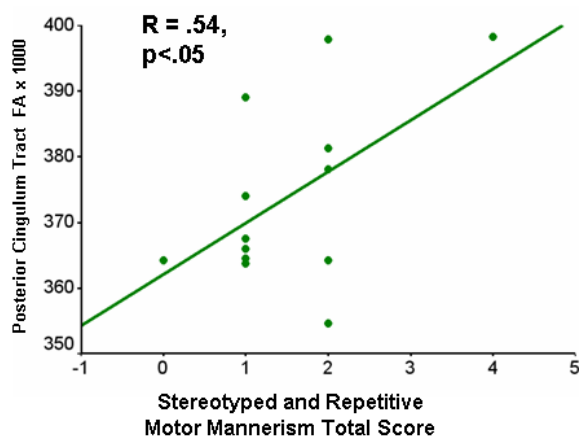
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Objective: Perform a whole-brain voxelwise analysis and tractography using diffusion tensor imaging (DTI) in high-functioning youth with Autism Spectrum Disorder (ASD) and demographically-matched healthy controls (HC) to examine the neural basis for deficits in social-emotional reciprocity in ASD.

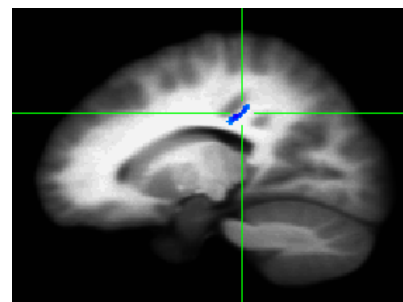
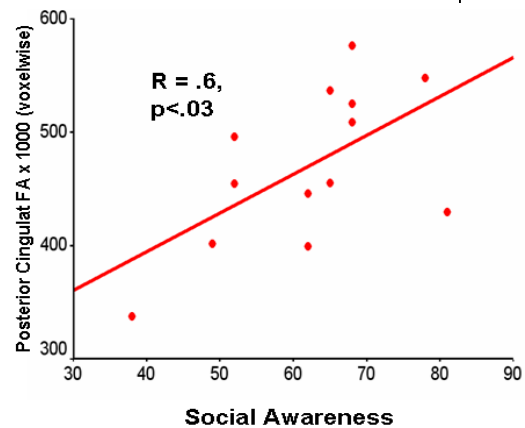
Method: ASD subjects were recruited from the Fay J. Lindner Center for Autism in Bethpage NY. All subjects met ADI-R & ADOS-G criteria for autistic or Asperger disorder. 13 ASD subjects (male only) and 12 age, gender, IQ, SES, and handedness-matched healthy controls underwent diffusion MRI. A 15-direction isotropic diffusion sequence was obtained with 50 isotropic (2.5x2.5x2.5 mm³) slices covering the whole brain. Following intra and inter-subject registrations of the fractional anisotropy, radial diffusivity, axial diffusivity and trace maps, voxelwise ANCOVA (VANCOVA) analyses was performed. Fiber tractography was performed on Talairach transferred averaged vector maps of all 25 subjects using DTIStudio and the average FAs and the 'average' principal eigenvectors. Since DTIStudio only uses the principle eigenvector to perform tractography, vector averaging was not applied to the remaining two radial eigenvectors. Placement of the initial seed ROI for tractography was based on the results of voxelwise analysis. The entire cingulum bundles on the left and the right hemispheres and a portion of the left posterior cingulum tract radiating to the parietal lobe were extracted. Correlation analyses were carried out between the results of voxelwise analyses and the diffusion parameters of all the extracted tracts and the social responsiveness scale (SRS) and the parent (ADI) and child (ADOS) diagnostic interview scores using the SPSS 11.0

Results: Compared to HC, ASD participants had increased FA values in the left posterior cingulate, pons, and the Rt. inferior frontal gyrus ($p < 0.002$, cluster size ≥ 100 voxels). Increased axial diffusivity was found in the bilateral posterior cingulate, left pre-frontal, and the left cerebellum ($p < 0.002$, cluster size ≥ 100 voxels). No significant changes in the radial and mean diffusivity parameters were found. Results of tractography showed increased average FA in the portion of the Lt. cingulum bundle radiating to the parietal lobe ($p = 0.05$). Within group analysis of ASD subjects showed positive correlations between the Lt. posterior cingulate FA cluster value and the SRS subscale of social awareness ($r = .6$, $p < 0.03$), and a trend in SRS autistic mannerism subscale ($r = .50$, $p < .08$). Extracted cingulate tract in this area also positively correlated with the ADI-R stereotyped and repetitive motor mannerism ($r = 0.54$, $p < .05$).

Conclusion: DTI voxelwise analysis and tractography results showed increased FA in several key brain areas in youth with ASD compared with HC. Among ASD subjects, increased FA of the post. cingulate gyrus (limbic circuit) was positively correlated with measures of social-emotional reciprocity and autistic mannerism. Our data suggest that alterations in the limbic system secondary to suboptimal connectivity may lead to core impairments of social interaction and behavior associated with the autism phenotype.



Tractography of the posterior portion of cingulate tract



Increased FA and axial diffusivity cluster in the posterior cingulate