

Age-related Changes of White Matter (WM) Microstructure in Autism Spectrum Disorder (ASD)

PURPOSE

Previous studies of WM microstructure in children with ASD were limited by relatively small cohort size. We analyzed diffusion metrics of WM microstructure in 583 subjects from four different cohorts in the National Database of Autism Research.

METHODS AND MATERIALS

All imaging and clinical data of study cohorts with T1-weighted and diffusion tensor imaging (DTI) scans were retrieved. Using FSL, we generated Fractional Anisotropy (FA), Mean Diffusivity (MD), and Radial Diffusivity (RD) maps. Tract-based spatial statistics and a voxel-wise analysis were performed to compare ASD and typically developing individuals; using general linear models, we assessed the influences of age and ASD diagnosis. We also analyzed cortical thickness using voxel-based morphometry (VBM). Age is reported as median (interquartile) months.

RESULTS

Subjects from 4 study cohorts were included: (1) Infants (“A Longitudinal MRI Study of Infants at Risk for Autism”; age: 7(1) m, 34/121 ASD/control, 12% female); (2) toddlers (“Biomarkers of Autism at 12 months”; age: 33(12) m, 57/45 ASD/control, 16% female); (3) adolescents (“Multimodal Developmental Neurogenetics of Females with ASD” age: 158(51.5) m, 106/124 ASD/control, 48% female); and (4) young adults (“Atypical Late Neurodevelopment in Autism” age: 242(128.5) m, 67/29 ASD/control, 1.5% female). We find a pervasive age-related increase in FA across majority of WM tracts in all age-groups. In voxel-wise analysis, we find reduced FA among ASD subjects compared to controls within anterior/middle commissural tracts of corpus callosum only in adolescents ($p=0.014$) and young adults ($p=0.007$), but not infants ($p=0.451$) and toddlers ($p=0.440$). Corresponding increases in ASD-related MD and RD were found in young adults ($p=0.003$). Tract-based analysis also showed reduced ASD-related FA in the corpus callosum, after adjusting for age as covariate, among adolescents ($p=0.026$) and young adults ($p=0.012$), but not younger children (infants: $p=0.316$, toddlers: $p=0.861$). In tract-based analysis, RD was increased in the corpus callosum of young adults after controlling for age ($p=0.023$). In VBM analysis, we found age-related decrease in cortical thickness of young adults, but without any significant differences related to ASD.

CONCLUSIONS

In a large dataset with an age range of 1 to 50 years, we showed an age-related impairment of microstructural integrity in anterior/middle corpus callosum commissural tracts among ASD patients compared to controls, starting in adolescence, and becoming more pronounced among young adults.

CLINICAL RELEVANCE/APPLICATION:

Age-adjusted microstructural correlates of ASD can improve diagnostic algorithms and provide potential objective biomarkers to monitor treatment response.