Title: Altered Visual Cortex Resting-state Functional Connectivity in Autism with Concomitant Cognitive Impairment

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Introduction: The Centers for Disease Control and Prevention (CDC, 2014) estimate that 54% of individuals with Autism Spectrum Disorders (ASDs) exhibit some measure of cognitive impairment (Full-scale Intelligence Quotient, FIQ ≤ 85). However, no studies of intrinsic Functional Connectivity (FC) using resting-state fMRI (rsfMRI) have been published in this population. Previous research using task fMRI involving social stimuli have shown reduced FC between social-processing regions and lower-order visual cortices in ASDs, suggesting that reduced feed-forward of visual information to higher-order social processing networks plays a role in social impairments characteristic of the disorder (Sato et al., 2012). Other research has suggested that the visual cortex is involved in a compensatory mechanism of cognition in ASDs (Simard et al., 2015). However, little is known about intrinsic Functional Connectivity (iFC) of the visual cortex in individuals with ASDs and cognitive impairment.

Method: The goal of the present study was to investigate iFC in individuals with ASDs with cognitive impairment. FIQ was measured using the Wechsler Abbreviated Intelligence Scale, Second Edition (Wechsler, 1999). T1-weighted anatomical and eyes-open fMRI resting-state scans from 66 children and adolescents with and without ASDs (ages 6-15, 44 ASD, 22 TD) were taken from in-house data (SDSU: n=27) and two sites (NYU: n=21; OHSU: n=18) from the Autism Brain Imaging Data Exchange (ABIDE). The full sample consisted of 3 groups of 22 individuals each (L-ASD [FIQ≤ 85] mean FIQ: 77±6; H-ASD [FIQ>105]: 123±8; TD: 99±7). All groups were matched within and across scanning-sites on head-motion, age, gender, and handedness. Following standard preprocessing, mean timeseries were extracted from seeds in the medial prefrontal cortex (mPFC), posterior cingulate cortex (PCC), and posterior superior temporal sulcus (pSTS), and entered into a subject-level GLM. Whole-brain iFC in the L-ASD group was contrasted with iFC in the H-ASD and TD groups using AFNI 3dttest++. All results were significant at a voxelwise p < .005, corrected to control for false-discovery rate (α < .05) using permutation testing.

Results: Compared to the H-ASD group, the L-ASD group showed significantly reduced positive iFC between pSTS and visual cortices, bilaterally, and between mPFC and PCC. Compared to the TD group, the L-ASD group showed a trend towards underconnectivity between the pSTS and primary visual cortex, which however did not reach statistical significance. The L-ASD group showed significantly increased connectivity between mPFC and intracalcarine (visual) cortex, both before and after controlling for FIQ. Effects were large and robust across scanning sites (Cohen’s d ranged from 1.46-2.0 for significant effects).

Discussion: The L-ASD group showed atypical patterns of iFC involving lower-order visual cortices compared to both comparison groups (H-ASD, TD). Reduced connectivity between primary visual cortex and one social-processing region (pSTS) in the ASD groups was more pronounced in the group with cognitive impairment (L-ASD). Conversely, the L-ASD group exhibited overconnectivity between the visual cortex and mPFC, a region of the default mode network considered to be important for both social and self-referential processing. This suggests that previous findings of atypical iFC involving the visual cortex in mostly high-functioning ASD cohorts may be more pronounced in individuals with lower levels of functioning. However, the exact functional relevance of atypical FC between visual cortex and social cognition networks in ASDs requires further investigation.

References/Citations: