435.043 - Neural Correlates of Autism Spectrum Disorder with Psychotic-like Symptoms in the Adolescent Brain Cognitive Development (ABCD) Cohort

Background: The neural correlates of autism spectrum disorder (ASD) and the psychotic disorder schizophrenia are divergent. However, the disorders are clinically associated, with ASD individuals at 3 to 4 times greater risk of developing schizophrenia than members of the general population. It is unknown whether ASD with co-occurring psychosis has a distinct neural signature, dissociable from those of ASD and schizophrenia alone. Identifying such a signature may help identify which youth with ASD are at risk of schizophrenia, allowing for individualized treatment and determination of prognosis.

Objectives: Using data collected from the Adolescent Brain Cognitive Development (ABCD) study (n = 11,875; 47.84% female; age mean = 9.91 years, SD = 0.62 years), we compared resting-state functional connectivity measures among three groups: 1) youth with ASD without psychotic-like symptoms, 2) youth with ASD and psychotic-like symptoms, and 3) youth with psychotic-like symptoms but not ASD. We hypothesized that each group would show a distinct pattern of connectivity among large-scale cortical networks.

Methods: To eliminate inter-scanner variability, we restricted the ABCD sample to participants with neuroimaging data collected by a Siemens scanner. We defined ASD by parent report during the screening interview, and defined psychotic-like symptoms by a Prodromal Questionnaire – Brief Child Version score ≥ 6, a cutoff based on previous literature. We then estimated random forest models to predict group status. The feature space for each model comprised 100 measures of resting-state connectivity strength between 10 large-scale cortical networks (auditory, visual, dorsal attention, ventral attention, default mode, salience, cinguloparietal, cingulo-opercular, frontoparietal, and retrosplenial-temporal). We addressed class imbalance using synthetic minority over-sampling and assessed performance using out-of-bag error scores. We calculated global feature importance using the Gini method, and compared top features across models, verifying model predictions by training local surrogate models to explain select predictions.

Results: 5,374 ABCD paricipants met our scanner criterion. 53 had ASD without psychotic-like symptoms, 16 had ASD with psychotic-like symptoms, and 737 had psychotic-like symptoms without ASD. All models predicted group status with low out-of-bag error rates (ASD without psychotic-like symptoms: 0.36%; ASD with psychotic-like symptoms: 0.21%; psychotic-like symptoms without ASD: 7.60%). ASD without psychotic-like symptoms was most strongly predicted by retrosplenial-temporal - salience, retrosplenial-temporal - fronto-parietal, and within-network retrosplenial-temporal connectivity. ASD with psychotic-like symptoms was predicted by dorsal attention network - cinguloparietal, salience - cinguloparietal, and cingulo-opercular - visual connectivity. Psychotic-like symptoms without ASD was predicted by within-network cingulo-opercular, cingulo-opercular - visual, and cingulo-opercular - auditory connectivity.

Conclusions: Within the ABCD cohort, ASD with psychotic-like symptoms, ASD without psychotic-like symptoms, and psychotic-like symptoms without ASD were characterized by distinct patterns of functional connectivity. Our finding that retrosplenial-temporal connectivity predicted ASD without psychotic-like symptoms is consistent with reports that retrosplenial-temporal connectivity is involved in social cognition and is altered in ASD. Our finding that dorsal attention and salience network connectivity predict ASD with psychotic-like symptoms is consistent with potentially altered interpretation of sensory cues in this sub-group. These results suggest that ASD with psychotic-like symptoms may be a sub-type of ASD with distinct neural correlates.

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