Evidence for a Categorical-Dimensional Hybrid Model of Autism Spectrum Disorder Revealed in Functional Network Connectivity

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TARGET AUDIENCE We sought to provide a new model for researchers and clinicians to conceptualize autism spectrum disorders (ASD) and potentially other brain disorders.

PURPOSE ASD is characterized by complex neuropsychiatric symptoms related to social interaction deficits and repetitive or stereotyped behaviors. Recent studies have revealed the dimensional nature of ASD symptoms, which exist along a continuum of severity across both ASD and typically-developing children (TDC) [1], as well as across the various ASD subtypes [2, 3]. However, it remains unknown whether the neural bases of an ASD diagnosis or ASD-like behaviors also follow a continuum or are better characterized categorically. Therefore, we investigated potential categorical and dimensional brain mechanisms of ASD.

METHODS In this study, resting-state functional magnetic resonance imaging scans were obtained from the Autism Brain Imaging Data Exchange (ABIDE) database for 107 typically-developing control children and 109 children with an autism spectrum disorder. Seed-based functional connectivity defined four large-scale higher-order cognitive networks (i.e., the dorsal attention network (DA), the default-mode network (DM), the salience network (SAL), and the executive control network (CON)). Social Responsiveness Scale scores, measuring the severity of social impairment related to the autism spectrum, provided a dimensional measure of ASD whereas clinical diagnoses defined ASD categorically. Linear regression analyses were applied to this dataset to delineate the effects of categorical and/or dimensional measures of ASD on the functional connectivity of each network. One model tested the separate effects of ASD diagnosis (1 or 0) and SRS score, covarying for age and site, as predictors of network functional connectivity. This model was designed to identify those categorical effects associated with an ASD diagnosis that were not driven by differences in symptom severity scores. Additionally, this model identified effects of ASD-related behaviors that were not due to effects of categorical diagnosis. A second model included the interaction of ASD diagnosis and SRS scores as a predictor in order to test whether there are categorical effects in the relationship of ASD-related behaviors to functional connectivity.

RESULTS For each of the four neural networks, our results revealed three distinct categories of neural mechanisms of ASD represented by 1) categorical differences in network-level functional connectivity strength between children with and without a diagnosis of ASD, supporting the existence of categorical mechanisms; 2) congruent quantitative relationships between network-level functional connectivity and behavioral measures across the two groups of children, indicating dimensional mechanisms; and 3) incongruent quantitative relationships between network-level functional connectivity and behavioral measures across the two groups of children, suggesting qualitatively different behavioral representations in the brain, reinforcing the categorical differences (Figure 1).

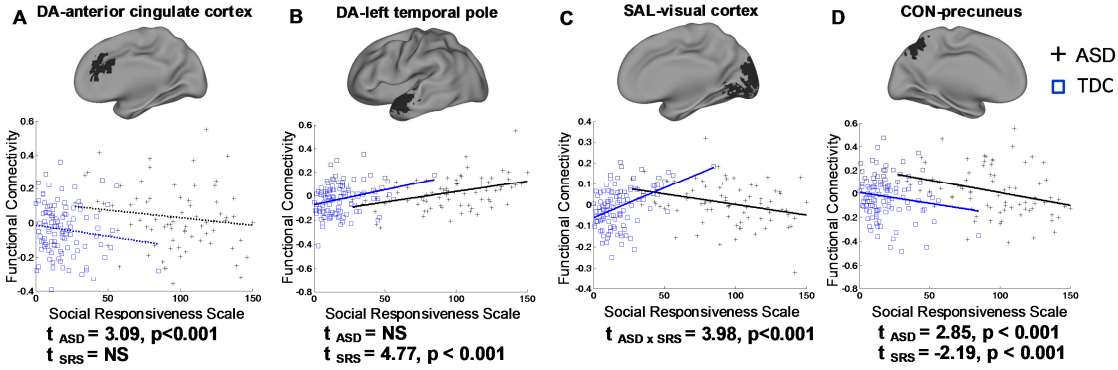

Figure 1. Scatter plots of the relationship between SRS scores and functional connectivity for TDC and ASD for selected regions depicting (A) categorical effects only, (B) dimensional effects only, (C) an interaction of categorical and dimensional effects, and (D) both dimensional and categorical effects.

DISCUSSION The detection of shared brain-behavior relationships across both ASD children and TDC supports a dimensional characterization of ASD based on symptom severity. On the other hand, functional connectivity deficits associated with a categorical ASD diagnosis or diagnosis-by-behavior interaction suggest that ASD children are also categorically distinct from TDC. Therefore, these data best support a hybrid categorical-dimensional model of ASD.

CONCLUSION These outcomes suggest that a characterization of ASD as a purely categorical or purely dimensional disorder in neuroimaging research studies would yield an incomplete understanding of the neural underpinnings of this complex disorder. Furthermore, while clinical diagnostic criteria have recently embraced the dimensional nature of ASD driven by symptom severity, this study validates the use of clinical cutoffs for categorical diagnoses as well.

REFERENCES

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