

Subtypes of functional brain organization are associated with autism symptoms

Sebastian Urchs, Montreal Neurological Institute

Abstract:

Autism Spectrum Disorder (ASD) is a prevalent neurodevelopmental disorder, characterized by social impairment and restricted behaviour, which begins very early in life. ASD and other neurodevelopmental disorders are characterized by a wide heterogeneity of symptoms and treatment response which may be associated with heterogeneous neurobiological aberrations. Here we present a novel analytic approach to characterize subtypes of brain organization in a sample of ASD patients and healthy controls and explore their association with symptom severity.

From the multisite ABIDE [1] dataset we selected 140 ASD patients with available ADOS severity scores and age-matched them with healthy controls (280 subjects, mean age 17.7, SD 7.2). Resting-state fMRI scans were preprocessed using the NIAK pipeline [2]. Individual seed based intrinsic functional connectivity (iFC) maps were computed for 20 previously identified functional brain networks [3]. For each network, we identified 5 subtypes of iFC by grouping subjects with similar iFC maps together through hierarchical agglomerative clustering. The average map across all individual iFC maps within a cluster is the subtype map. To highlight subtype differences, we subtracted the global average map from all subtype maps. We derived subtype weights for each individual using the spatial correlation of the individual iFC map and the corresponding subtype maps. To investigate the association of the identified subtypes with ASD symptom severity, we regressed the individual subtype weights together with cofactors of noninterest against ADOS severity scores using a general linear model. T-tests on the significance of the subtype weight factor were generated. We controlled the false discovery rate (FDR) at $q=0.05$.

We identified 11 subtypes of iFC organization that showed significant associations with ADOS severity scores. The majority of findings was localized in primary sensory and motor networks. Subtypes negatively associated with ADOS severity were characterized by above average within network iFC and above average iFC with higher visual areas in the occipital lobe. Conversely, subtypes negatively associated with ADOS severity exhibited below average within network iFC and below average iFC with occipital areas.

We were able to characterize the heterogeneity of functional brain organizations and distinguish subtypes of functional connectivity. Among these connectivity subtypes we identified several that were associated with a measure of ASD symptom severity. Together these results suggest that stratifying heterogeneous psychiatric samples by subtypes of functional brain organization may be a useful tool to better study distinct relationships of neuropathology and psychiatric symptoms.