Contribution ID: 98 Type: Talk in simposio

Parsing autism heterogeneity by non-core features: developmental and neurobiological implications

Tuesday, September 24, 2024 4:15 PM (20 minutes)

The current diagnostic criteria for autism spectrum disorder (ASD) focus on the characteristics individuals share in terms of social-communicative difficulties and the presence of restricted and repetitive behaviors. However, phenotypic heterogeneity in non-core features, such as early language, intellectual, motor, and adaptive functioning (LIMA), is among the most prominent aspects that distinguish different functional types of autistic individuals. Furthermore, heterogeneity in LIMA features may be crucial in explaining the variability we observed in biology, outcomes, and treatment responses. In this work, we parsed autism heterogeneity using non-core LIMA features to aid in distinguishing types of autisms characterized by peculiar developmental trajectories, and distinct underlying biology. Applying stability-based relative cluster validation analysis to a large (n=615) publicly available dataset of clinical tests measuring LIMA features in young autistic children (24-68 months), we can identify two robust and replicable clusters with high generalization accuracy (98%). These clusters identify two subtypes of autism (e.g., type I vs type II) with opposite functional profiles defined by relatively high versus low LIMA feature scores. Furthermore, the subtypes exhibit different developmental trajectories throughout the early years of life, and they are sensitive to significant differences in functional and structural neuroimaging phenotypes and their relationships with gene expression. Finally, to promote future applications of our stratification model in research settings, we implemented a free online tool to help distinguish autism type I from autism type II.

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Psychophysiological Markers in Autism Spectrum Disorder: Current Evidence and Clinical Perspectives

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Yes

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Session Classification: Symposia