Brain-behavior patterns define a dimensional biotype in medication-naïve adults with attention-deficit hyperactivity disorder.

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Abstract

BACKGROUND:
Childhood-onset attention-deficit hyperactivity disorder (ADHD) in adults is clinically heterogeneous and commonly presents with different patterns of cognitive deficits. It is unclear if this clinical heterogeneity expresses a dimensional or categorical difference in ADHD.

METHODS:
We first studied differences in functional connectivity in multi-echo resting-state functional magnetic resonance imaging (rs-fMRI) acquired from 80 medication-naïve adults with ADHD and 123 matched healthy controls. We then used canonical correlation analysis (CCA) to identify latent relationships between symptoms and patterns of altered functional connectivity (dimensional biotype) in patients. Clustering methods were implemented to test if the individual associations between resting-state brain connectivity and symptoms reflected a non-overlapping categorical biotype.

RESULTS:
Adults with ADHD showed stronger functional connectivity compared to healthy controls, predominantly between the default-mode, cingulo-opercular and subcortical networks. CCA identified a single mode of brain-symptom co-variation, corresponding to an ADHD dimensional biotype. This dimensional biotype is characterized by a unique combination of altered connectivity correlating with symptoms of hyperactivity-impulsivity, inattention, and intelligence. Clustering analyses did not support the existence of distinct categorical biotypes of adult ADHD.

CONCLUSIONS:
Overall, our data advance a novel finding that the reduced functional segregation between default-mode and cognitive control networks supports a clinically important dimensional biotype of childhood-onset adult ADHD. Despite the heterogeneity of its presentation, our work suggests that childhood-onset adult ADHD is a single disorder characterized by dimensional brain-symptom mediators.