Increased default-mode variability is related to reduced task-performance and is evident in adults with ADHD

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Abstract

Insufficient suppression and connectivity of the default mode network (DMN) is a potential mediator of cognitive dysfunctions across various disorders, including attention deficit/hyperactivity disorder (ADHD). However, it remains unclear if alterations in sustained DMN suppression, variability, and connectivity during a prolonged cognitive engagement are implicated in adult ADHD pathophysiology, and to which degree methylphenidate (MPH) remediates any DMN abnormalities. This randomized, double-blinded, placebo-controlled, cross-over clinical trial of MPH (clinicaltrials.gov/ct2/show/NCT01831622) explored large-scale brain network dynamics in 20 adults with ADHD on and off MPH, compared to 27 healthy controls, while performing a reward-based decision-making task. DMN task-related activation, variability, and connectivity were estimated and compared between groups and conditions using independent component analysis, dual regression, and Bayesian linear mixed models. The results show that the DMN exhibited more variable activation patterns in unmedicated patients compared to healthy controls. Group differences in functional connectivity both between and within functional networks were evident. Further, functional connectivity between and within attention and DMN networks was sensitive both to task performance and case-control status. MPH altered within-network connectivity of the DMN and visual networks, but not between-network connectivity or temporal variability. This study thus provides novel fMRI evidence of reduced sustained DMN suppression in adults with ADHD during value-based decision-making, a pattern that was not alleviated by MPH. We infer from multiple analytical approaches further support to the default mode interference hypothesis, in that higher DMN activation variability is evident in adult ADHD and associated with lower task performance.