Aberrant Time-varying Cross-Network Interactions in Children with Attention-Deficit/Hyperactivity Disorder and Its Relation to Attention Deficits

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Abstract

Background
Attention-Deficit/Hyperactivity Disorder (ADHD) is thought to stem from aberrancies in large-scale cognitive control networks. However, the exact nature of aberrant brain circuit dynamics involving these control networks is poorly understood. Using a saliency-based triple-network model of cognitive control, we test the hypothesis that dynamic cross-network interactions among the salience (SN), central executive (CEN), and default mode (DMN) networks are dysregulated in children with ADHD, and investigate how these dysregulations contribute to inattention.

Methods
Using fMRI data from 140 children with ADHD and typically developing (TD) children from two cohorts (Primary cohort = 80; Replication Cohort = 60) in a case-control design, we examined both time-averaged and dynamic time-varying cross-network interactions in each cohort separately.

Results
Time-averaged measures of SN-centered cross-network interactions were significantly lower in children with ADHD compared to TD children and were correlated with severity of inattention symptoms. Children with ADHD displayed more variable dynamic cross-network-interaction patterns, including less persistent brain states, significantly shorter mean lifetimes of brain states, and intermittently weaker cross-network interactions. Importantly, dynamic time-varying measures of cross-network interactions were more strongly correlated with inattention symptoms than time-averaged measures of functional connectivity. Crucially, we replicated these findings in the two independent cohorts of children with ADHD and TD children.

Conclusions
Aberrancies in time-varying engagement of the SN with the CEN and DMN are a robust and clinically-relevant neurobiological signature of childhood ADHD symptoms. The triple-network neurocognitive model provides a novel, replicable and parsimonious dynamical systems neuroscience framework for characterizing childhood ADHD and inattention.