Aberrant cross-brain network interaction in children with attention-deficit/hyperactivity disorder and its relation to attention deficits: a multi- and cross-site replication study

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Background
Attention-Deficit/Hyperactivity Disorder (ADHD) is increasingly viewed as a disorder stemming from disturbances in large-scale brain networks, yet the exact nature of these impairments in affected children is poorly understood. We investigate a saliency-based triple-network model and test the hypothesis that cross-network interactions between the salience (SN), central executive (CEN) and default mode (DMN) networks are dysregulated in children with ADHD. We also determine whether network dysregulation measures can differentiate children with ADHD from controls across multisite datasets and predict clinical symptoms.

Methods
Case-control design. fMRI data from 180 children with ADHD and controls from three sites in the ADHD-200 database. We investigated between-group differences in resource allocation index (RAI; a measure of SN-centered triple network interactions), relation between RAI and ADHD symptoms and performance of multivariate classifiers built to differentiate children with ADHD from controls.

Results
RAI was significantly lower in children with ADHD compared to controls. Severity of inattention symptoms was correlated with RAI. Remarkably, these findings were replicated in three independent datasets. Multivariate classifiers based on cross-network coupling measures differentiated children with ADHD from controls with high classification rates (72%~83%) for each dataset. A novel cross-site classifier based on training data from one site accurately (62%~82%) differentiated children with ADHD on test data from the two other sites.

Conclusions
Aberrant cross-network interactions between SN, CEN and DMN are a reproducible feature of childhood ADHD. The triple-network model provides a novel, replicable and parsimonious systems neuroscience framework for characterizing childhood ADHD and predicting clinical symptoms in affected children.