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Abstract

Methylphenidate is a first-line therapeutic option for treating attention-deficit/hyperactivity disorder (ADHD); however, elicited changes on resting-state functional networks (RSFNs) are not well understood. This study investigated the treatment effect of methylphenidate using a variety of RSFN analyses and explored the collaborative influences of treatment-relevant RSFN changes in children with ADHD. Resting-state functional magnetic resonance imaging was acquired from 20 medication-naïve ADHD children before methylphenidate treatment and twelve weeks later. Changes in large-scale functional connectivity were defined using independent component analysis with dual regression and graph theoretical analysis. The amplitude of low-frequency fluctuation (ALFF) was measured to investigate local spontaneous activity alteration. Finally, significant findings were recruited to random forest regression to identify the feature subset that best explains symptom improvement. After twelve weeks of methylphenidate administration, large-scale connectivity was increased between the left frontoparietal RSFN and the left insula cortex and the right frontoparietal and the brainstem, while the clustering coefficient (CC) of the global network and nodes, the left frontoparietal, cerebellum, and occipital pole-visual network, were decreased. ALFF was increased in the bilateral superior parietal cortex and decreased in the right inferior frontotemporal area. The subset of the local and large-scale RSFN changes, including widespread ALFF changes, the CC of the global network and the cerebellum, could explain the 27.1% variance of the ADHD Rating Scale and 13.72% of the Conner's Parent Rating Scale. Our multivariate approach suggests that the neural mechanism of methylphenidate treatment could be associated with alteration of spontaneous activity in the superior parietal cortex or widespread brain regions as well as functional segregation of the large-scale intrinsic functional network.