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Dysfunction and Dysconnection in Cortical-Striatal Networks during Sustained Attention: Genetic Risk for Schizophrenia or Bipolar Disorder and its Impact on Brain Network Function.

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Abstract

Abnormalities in the brain's attention network may represent early identifiable neurobiological impairments in individuals at increased risk for schizophrenia or bipolar disorder. Here, we provide evidence of dysfunctional regional and network function in adolescents at higher genetic risk for schizophrenia or bipolar disorder [henceforth higher risk (HGR)]. During fMRI, participants engaged in a sustained attention task with variable demands. The task alternated between attention (120 s), visual control (passive viewing; 120 s), and rest (20 s) epochs. Low and high demand attention conditions were created using the rapid presentation of two- or three-digit numbers. Subjects were required to detect repeated presentation of numbers. We demonstrate that the recruitment of cortical and striatal regions are disordered in HGR: relative to typical controls (TC), HGR showed lower recruitment of the dorsal prefrontal cortex, but higher recruitment of the superior parietal cortex. This imbalance was more dramatic in the basal ganglia. There, a group by task demand interaction was observed, such that increased attention demand led to increased engagement in TC, but disengagement in HGR. These activation studies were complemented by network analyses using dynamic causal modeling. Competing model architectures were assessed across a network of cortical-striatal regions, distinguished at a second level using random-effects Bayesian model selection. In the winning architecture, HGR were characterized by significant reductions in coupling across both frontal-striatal and frontal-parietal pathways. The effective connectivity analyses indicate emergent network dysconnection, consistent with findings in patients with schizophrenia. Emergent patterns of regional dysfunction and dysconnection in cortical-striatal pathways may provide functional biological signatures in the adolescent risk-state for psychiatric illness.

KEYWORDS: attention; bipolar disorder; brain networks; dynamic causal modeling abstract; schizophrenia

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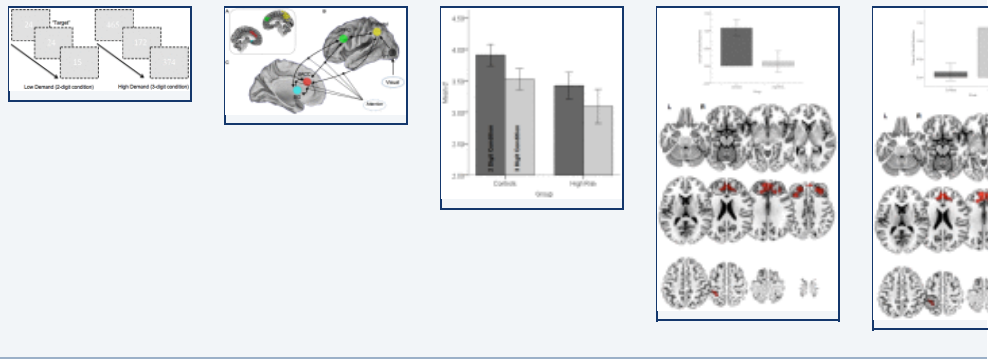

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