Orbitofrontal Signaling of Future Reward is Associated with Hyperactivity in Attention-Deficit/Hyperactivity Disorder

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Abstract

Alterations in motivated behavior are a hallmark of attention deficit hyperactivity disorder (ADHD), one of the most common psychiatric disorders in children and adolescents. The orbitofrontal cortex (OFC) plays a key role in controlling goal-directed behavior but the link between OFC dysfunction and behavioral deficits in ADHD, particularly in adolescence, remains poorly understood. Here we used advanced high-resolution functional magnetic resonance imaging (fMRI) of the human OFC in adolescents with ADHD and typically developing (TD) controls (N=39, age 12-16, all male except for one female per group) to study reward-related OFC responses, and how they relate to behavioral dysfunction in ADHD. During fMRI data acquisition, participants performed a simple decision-making task, allowing us to image expectation-related responses to small and large monetary outcomes. Across all participants, we observed significant signal increases to large vs small expected rewards in the OFC. These responses were significantly enhanced in ADHD relative to TD. Moreover, stronger reward-related activity was correlated with individual differences in hyperactive/impulsive symptoms in the ADHD group, whereas high cognitive ability was associated with normalized OFC responses. These results provide evidence for the importance of OFC dysfunctions in the neuropathology of ADHD, highlighting the role of OFC-dependent goal-directed control mechanisms in this disorder. DHD is characterized by alterations in motivated behavior which can be understood as diminished goal-directed control. The OFC plays a key role in controlling goal-directed behavior but its potential contribution to ADHD symptomatology remains poorly understood. Using high-resolution fMRI we show that adolescent ADHD patients display enhanced OFC signaling of future rewards and that these increased reward-related responses are correlated with the severity of hyperactivity/impulsivity. These findings suggest that an inability to adequately evaluate future outcomes may translate into maladaptive behavior in ADHD patients. They also challenge the idea that dysfunctions in dopaminergic brain areas are the sole contributor to reward-related symptoms in ADHD and point to a central contribution of goal-directed control circuits in hyperactivity.