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Genetic architecture and behavioral analysis of attention and impulsivity

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Abstract

Impulsive behavior and deficits in attention are hallmarks of several psychiatric diseases such as attention deficit hyperactivity disorder (ADHD) and addiction. Genetic predisposition is a major risk factor contributing to the development of these diseases. The aim of this thesis was to identify genetic mechanisms underlying impulsivity and attention. In human, rat and mouse, aspects of impulsivity and attention can be measured in similar behavioral tasks, enabling a swift translation of results obtained in animal models to the human condition. In mice, impulsivity in a response task and 'novelty seeking' behavior, both associated with addiction vulnerability, were genetically independent. This suggests that this variety of impulsivity and 'novelty seeking' contribute in different ways to addiction vulnerability, and insight into both is required to understand vulnerability. Impulsivity and attention were genetically independent as well. This is of importance in the treatment of ADHD, it supports the notion of patients with predominant attentional deficits and patients with predominantly symptoms of hyperactivity-impulsivity that benefit from different treatments. Research contained in this thesis has implicated several genes in impulsivity and attention, including genes involved in dopamine signaling. Interfering with dopamine signaling through these genes in the medial prefrontal cortex affected impulsive behavior. Follow up research on the identified genes will contribute to our understanding of molecular processes underlying disease and provide novel entries into the development of disease treatment.