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Abstract:

Drug addiction is a behavioral disorder characterized by impulsive behavior and continued intake of drug in the face of adverse consequences. Millions of people suffer the financial and social consequences of addiction, and yet many of the current therapies for addiction treatment have limited efficacy. Therefore, there is a critical need to characterize the neurobiological substrates of addiction in order to formulate better treatment options. In the first chapter, the striatal dopamine system is interrogated with [11C]raclopride PET to assess differences between chronic cannabis users and healthy controls. The results of this chapter indicate that chronic cannabis use is not associated with a reduction in striatal D2/D3 receptor availability, unlike many other drugs of abuse. Additionally, recent cannabis consumption in chronic users was negatively correlated with D2/D3 receptor availability. Chapter 2 describes a retrospective analysis in which striatal D2/D3 receptor availability is compared between three groups of alcohol-drinking and tobacco-smoking subjects: nontreatment-seeking alcoholic smokers, social-drinking smokers, and social-drinking non-smokers. Results showed that smokers had reduced D2/D3 receptor availability throughout the striatum, independent of drinking status. The results of the first two chapters suggest that some combustion product of marijuana and tobacco smoke may have an effect on striatal dopamine concentration. Furthermore, they serve to highlight the effectiveness of using baseline PET imaging to characterize dopamine dysfunction in addictions. The final chapter explores the use of [18F]fallypride PET in a proof-of-concept study to determine whether changes in cortical dopamine can be detected during a response inhibition task. We were able to detect several cortical regions of significant dopamine changes in response to the task, and the amount of change in three regions was significantly associated with task performance. Overall, the results of Chapter 3 validate the use of [18F]fallypride PET to detect cortical dopamine changes during a impulse control task. In summary, the results reported in the current document demonstrate the effectiveness of PET imaging as a tool for probing resting and activated dopamine systems in addiction. Future studies will expand on these results, and incorporate additional methods to further elucidate the neurobiology of addiction.

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