The Impact of Cannabis Use on Neuropsychological and Neural Biomarkers of Treatment Response in Schizophrenia Spectrum Disorders

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Dissertation

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Abstract

Cannabis use among patients with schizophrenia-spectrum disorders (SSD) is at significantly greater levels than in healthy populations but the impact of cannabis on neural mechanisms of clinical improvement is poorly understood. Cognitive functioning and neural connectivity are disrupted as a result of both SSD and cannabis use, and research indicates that neuropsychological capacity and connectivity of the striatum, a region involved in salience and reward processing, may be integral to effective antipsychotic drug (AP) treatment response, the primary pharmacological therapy for SSD. Despite this overlap, no previous research has investigated the effect of cannabis on the brain functions implicated in AP treatment response. The present study aimed to explicate the influence of recent cannabis use on previously established predictors of effective AP treatment outcomes for patients with SSD.

The study used a cohort of medication-naïve first-episode SSD patients who used cannabis at varying rates (i.e. both non-users (n=33) and users (n=43)). Patients were recruited from an ongoing treatment study that consisted of a baseline functional magnetic resonance imaging (fMRI) scan prior to beginning 12 weeks of standardized risperidone treatment, a common second-generation atypical AP drug. Clinical interview, urine toxicology screening, neuropsychological testing and resting-state fMRI were used to characterize the interaction between cannabis, cognitive functioning and striatal connectivity as related to clinical improvement. The study aimed to examine the extent to which the cumulative frequency of cannabis use prior to antipsychotic treatment influences previously established markers of treatment response, specifically: (1) neuropsychological functioning and (2) striatal connectivity. While the primary aims of the study were cross-sectional in nature, the longitudinal design of the parent study allowed us to explore the extent to which the cumulative frequency of cannabis use,
prior to and over the course of AP treatment, impacted the prognostic utility of: (1) baseline neuropsychological functioning and (2) baseline resting-state striatal connectivity in predicting treatment response following 12 weeks of treatment.

Our results demonstrated that there was no influence of cannabis use on baseline measures of neuropsychological functioning or striatal connectivity. There were also no differences between patients who responded to AP medications versus non-responders in neuropsychological functioning or striatal connectivity. However, there was evidence for a potential interaction effect between cannabis and striatal connectivity in regard to treatment response. Future research with a larger sample size is needed to further investigate the impact of cannabis on the utility of striatal connectivity in predicting treatment outcomes. As legalization of cannabis becomes increasingly widespread across the United States, it will be crucial to understand cannabis’ effect on treatment-related neural circuitry in order to create brain biomarkers that are generalizable to the large proportion of patients who use cannabis.