What is the Role of Cannabis in Psychotic Disorders?

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This issue of Primary Psychiatry examines a hot topic—the relationship of cannabis use to psychosis—from some novel perspectives, including that of the busy clinician treating patients with intractable dual diagnosis, and spanning prodromal research, challenge studies with drugs of abuse, and electronic tools for examining a “slice of life” in the experience of a young person with beginning substance use and emerging psychotic symptoms. Throughout, each article considers the evidence for the premise of a causal relationship of cannabis use to psychosis and then examines the implications of this for psychotic disorders—their course and prognosis, what may be safe and efficacious treatment, and a consideration of the biologic basis for an association of cannabis use and psychosis in a developmental context.

The first article is by Wilfrid N. Raby, MD, PhD, who has decades of clinical experience treating individuals comorbid for both psychotic disorders and substance misuse. Dr. Raby demonstrates that marijuana is not benign, especially for those with psychotic disorders who have less adherence to treatment; greater relapse rates; and higher levels of risk for violence, victimization, and self-harm. He focuses on the need for integrated treatment, including cognitive-behavioral therapy and motivational interviewing, with a reliance on long-term residential treatment for particularly intractable comorbid illness. He concludes with an impressive case for clozapine for “dually diagnosed” schizophrenia, which leads to a reduction of drug use in ~70% of cases and decreases in relapse risk as well.

Michael T. Compton, MD, MPH, and Claire E. Ramsay, MPH, provide a conceptual framework for considering the co-evolution of cannabis misuse and psychotic symptoms in adolescence, specifically the stress-diathesis model in which vulnerability interacts with exposures to lead to symptoms. They make a strong case for the premise that cannabis use hastens the inevitable onset of psychosis in vulnerable individuals, which is not negligible in import given how strongly associated earlier onset of psychosis is to poor course and outcome in schizophrenia and related disorders. They carefully examine how cannabis use and prodromal symptoms may influence one another among vulnerable teens, agnostic as to any conclusions about causality. They enumerate the several caveats to keep in mind in considering any causal association, including multiple drug use, consideration of potential confounders and moderators (eg, gender and family history), and methodologic concerns, specifically with retrospective assessments.

David Kimhy, PhD, and colleagues tackle this very concern raised by Ramsay and Compton, namely the limitations of retrospective assessments in examining the relationship of cannabis use to psychotic symptoms and disorders. They enumerate the many problems with retrospective assessments (identified as problematic also by the Food and Drug Administration), which include problems with accuracy due to memory impairments and biases in recall due to affective states and cognitive reframing. These problems may be particularly salient for phenomena such as thoughts and feelings in the context of normal and altered states, which can be transitory. They describe a methodology which obviates many of these problems seen with retrospective assessments in the laboratory, specifically Computerized Experience Sampling Methodology (ESM), which involves the use of Palm pilots outside of the laboratory, electronic devices which prompt study participants several times per day (with a beep) to answer screen queries as to feelings, thoughts, stresses, and drug use. Such frequency of sampling in ESM enables the use of time-lag analyses to examine the presence...
of temporal sequence, a condition for causality. Namely, does cannabis use precede psychotic-like symptoms? Do psychotic-like symptoms precede cannabis use? Further, as Palm Pilots are carried outside the laboratory, data are collected in real time in the real world, and are “ecologically valid.” ESM enables the examination of motivations for drug use as well as the social contexts in which drug use occurs. The use of ESM has proven feasible in youths both who use drugs and who are vulnerable to psychosis, and can be used as a clinical tool which improves the efficacy of cognitive-behavioral therapy (CBT) through its use in “homework.” The hope is that ESM and CBT together might reduce cannabis use in vulnerable teens, such that psychosis onset is forestalled and outcome improved.

Nehal P. Vadhan, PhD, and colleagues address the thorny issue of causation through reviewing studies in the experimental manipulation of drug exposure, specifically cannabis challenge in the laboratory. Challenge studies eliminate confounds and permit the evaluation of biologic correlates of drug effects. A leading theory of pathophysiology in schizophrenia and its related disorders highlights the importance of working memory deficits in mediating the various symptoms of the illness. Outside of the realm of research on psychotic disorders, it has been observed that the active ingredient of cannabis, specifically Delta 9-tetrahydrocannabinol, when administered in the laboratory, can induce transient working memory deficits in otherwise healthy individuals. In a sense, cannabis challenge is a transient functional lesion study of the normal brain and its cognitive function. Whereas a few studies have examined symptoms and affective sequelae of cannabis challenge in individuals with psychosis vulnerability, it remains to be learned whether these effects are mediated by perturbation of working memory.

The question of a causal association between cannabis use and psychosis carries great import as cannabis use may be a uniquely modifiable risk factor for psychosis. Data suggest that for vulnerable young people, cannabis use can precipitate psychosis and have lifelong consequences in terms of subsequent illness. For individuals with psychosis, continued use of cannabis is related to a heightened risk of injury and harm, as well as poor outcome. With methodologies outside of traditional clinical interview, such as experience sampling and laboratory challenge, we may respectively develop a better understanding of the motivation and context of use, and the biologic underpinnings of its effects, such that more efficacious interventions can be developed. PP