

## Cannabis Use and Psychosis: Current Perspectives

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### Abstract

Cannabis is the most commonly abused illicit drug in the United States. Its use, however, is not without its dangers. Mounting evidence has recently shown a possible link between cannabis use and the development of psychosis and a subsequent predisposition to developing schizophrenia. In this article, the authors review the literature related with cannabis use and the appearance of a psychotic disorder, data supporting the existence of cannabis-induced psychosis and the association between cannabis and schizophrenia along with the case of an 18-year-old white man with a severe cannabis dependence who developed schizophrenia-like symptoms.

**Key Words:** cannabis, schizophrenia, psychosis

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Cannabis abuse and dependence in the United States has been identified in approximately 4% of the general population, primary in the 18- to 29-year-old population.<sup>1</sup> Nearly half of US 12th-grade student have been exposed to cannabis.<sup>2</sup> With a peak in use of cannabis in 1979; the current consumption has been relatively stable since 1997 with 37% of Americans over the age of 12 having tried cannabis.<sup>2</sup>

Nowadays, there is much debate about the existence of cannabis-induced psychosis. Opponents suggest that cannabis use is unrelated to predetermined psychotic manifestations. However, there is a great deal of evidence supporting the belief that cannabis use and psychosis are related.<sup>3</sup> Symptoms of cannabis-induced psychosis include sudden onset of confusion, hallucinations, emotional lability, amnesia, disorientation, depersonalization, and paranoid symptoms.<sup>3</sup> The case for cannabis-induced psychosis has been strengthened by case reports showing the onset of symptoms after ingestion of large amounts of cannabis; the presence of symptoms in a subset of patients without any previous personal or family history of psychosis; a quicker onset of symptoms

with greater the potency of cannabis, and remission of symptoms after a period of enforced cannabis abstinence.<sup>3</sup>

Previous literature looked at the relationship between self-reported cannabis use by the age of 18 and the diagnosis of schizophrenia, and found that the relative risk of receiving a diagnosis of schizophrenia was 2.4 times higher among those who had tried cannabis by the age of 18, compared with those who had not.<sup>3</sup> There was also a dose-response relationship between a diagnosis of schizophrenia and the number of times that cannabis had been used by the age of 18.<sup>3</sup> Compared with those who had never used cannabis, the adjusted relative risk of a diagnosis of schizophrenia was 1.5 times greater for those who had smoked cannabis 1 to 10 times, and 2.3 times greater for those who had used >10 times.<sup>3</sup>

In patients with an established psychotic disorder, cannabis has a negative impact on illness course as shown by more recurrent and earlier relapses, more frequent hospitalizations, and worse psychosocial functioning.<sup>4</sup> About 15% of cannabis users indicated that they have experienced psychotic symptoms. Cross sectional studies support the emergence of psychotic symptoms in those who did not previously have psychosis.<sup>5</sup> In this regard, data suggests that among patients who develop schizophrenia, marijuana users have earlier onset of presentation, more psychotic symptoms, poorer response to medication, and worse outcomes than noncannabis using schizophrenic patients.<sup>6</sup> Since marijuana was initially legalized in California in 1996 for medical use, today there are >15 states that have enacted laws to legalized medicinal marijuana.<sup>6</sup> Currently, our population is pensive about the rights or wrongs of using

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cannabis for recreational purposes and moreover the consequences of abusing this drug.<sup>6</sup> It is prudent to be aware of the cost of marijuana use to mental health; especially, in adolescents as the cost that cannabis can have on society can be astronomical.<sup>6</sup> In 2001, >110,000 emergency department visits had marijuana as a contributing factor.<sup>6</sup> It has been shown that youth using cannabis perform lower on academic assessment scales compared with nondrug using peers, even after adjusting for other substance use.<sup>6</sup> In addition, cannabis use is higher among high school dropouts and later been associated with unemployment.<sup>2</sup>

Questions have been raised about the association between cannabis use and schizophrenia. Studies have found that marijuana use in adolescents increases the risk of early-onset schizophrenia in vulnerable patients.<sup>7</sup> Newer studies have shown that marijuana use in adolescents increases the risk of psychotic illnesses in adulthood even after accounting for prodromal symptoms and other drug use.<sup>7</sup> The risk increases with the amount of marijuana used and earlier onset of use.<sup>7</sup> An additional study looked at 169 patients with psychotic disorder, including schizophrenia, of which 77 had a diagnosis of cannabis use disorder (CUD), where 92% of CUD started using cannabis before the onset of their first psychotic episode. When looking at patients who used only cannabis versus no drug use, it was found that the cannabis group had a higher score on the Positive and Negative Syndrome Scale, which suggests an increase in severity of psychotic symptoms.<sup>7</sup> In approximately 49% of patients, cannabis use started before the onset of prodromal symptoms, whereas in 15.6% of the patients the prodromal period and cannabis use started together.<sup>7</sup>

Patients with pure CUD (other substances excluded) had significantly higher scores on positive symptom subscales compared with patients without any substance use disorder.<sup>7</sup>

## CASE REPORT

K.H. is an 18-year-old white male, single, enrolled in college who is living with his parents. He has a previous

diagnosis of cannabis dependence. He was brought to the psychiatric emergency room by his father because he was "acting erratic." On admission, he appeared internally preoccupied, hypervigilant, with pressured speech, suspicions about being followed, and anxious. There were no signs of acute withdrawal noted on admission, including vital signs that were within normal limits and clear sensorium. In regards to his substance use, he admitted to using marijuana at the age of 13 on an occasional basis; however, for the past 2 years he has been smoking approximately 3 to 4 g of marijuana daily by glass pipe. He denies other drug use and denies alcohol use on a regular basis. He also denies smoking tobacco.

K.H. was noted to have a brief anoxic event at birth with minor speech developmental delays, which eventually resolved. He reports that his mother has a history of bipolar disorder and alcohol dependence. No other mental illness was noted in his family. He was an excellent student during middle school; however, during high school he was transferred to an alternative school because of numerous violations for possession of cannabis. He is currently enrolled in college. His parents note that his grades have recently been declining and they are considering withdrawing him from classes for the semester. He has been arrested various times in the past because of cannabis possession and reckless driving.

During his first day on the unit, K.H. was found to be agitated and restless; he did not sleep overnight and was noted to be talking to himself. He appeared to be actively responding to internal stimuli and was noted to be laughing inappropriately at times. He continuously paced the unit, appeared anxious, and reported that he could hear his cell phone ringing inside his mattress despite his cell phone being locked with his belongings off the unit. He also believed that "someone was waiting for him outside the hospital." Despite his delusional thought content and perceptual disturbances, he continued to be oriented to person, place, time, and maintaining appropriate engagement with staff. His vital signs were stable during his hospitalization. He

was started on risperidone and lorazepam as needed for agitation. Within 5 days his psychosis resolved and he was discharged home. At 1-year follow-up, his family reported that he had been court ordered to complete a 30-day drug rehabilitation program, which he successfully completed. He continued to take medications, did not require further hospitalization, continued to see a therapist in the community for his addiction, and continued with his schooling.

## DISCUSSION

A possible hypothesis is that cannabis abuse precipitates the onset of episodes of psychosis in patients with schizophrenia. The neurobiological mechanism underlying this increased vulnerability to psychosis may be related to increased cannabinoid receptors (CB) in dorsolateral prefrontal cortex and increased release of dopamine in the mesolimbic pathway by tetrahydrocannabinol (THC).<sup>8,9</sup> Dopamine activation in the striatum involves direct interaction between the dopamine D2 receptors and CB1 receptors.<sup>10</sup> Functional interactions between the endogenous cannabinoid system are noted in disorders that involve dysregulated dopamine neurotransmission.<sup>10</sup>

The endocannabinoid system plays an important role in the modulation of other neurotransmitters, and thus it may indirectly influence dopamine firing as well. Exogenous cannabinoids, like THC could disrupt the fine tuning effects of endocannabinoids.<sup>4</sup> THC, in animal studies, has been shown to evoke burst firing in the ventral tegmental area, hence increasing dopamine concentrations in striatal regions in the brain.<sup>4</sup> Striatal dopamine plays an important role in attributing salience to stimuli in the environment; an increase in dopamine may facilitate psychotic experiences by enabling false attribution of significance to ambiguous stimuli.<sup>4</sup> Auditory hallucinations, therefore, may be the most prominent as they occur in the moment, whereas delusions may be understood as secondary interpretations of aberrant perceptions.<sup>4</sup>

Cerebrospinal fluid levels of endogenous cannabinoids have been

found to be elevated in patients with schizophrenia regardless of age, sex, or current medication.<sup>11</sup> This suggests that endogenous cannabinoids may play a role in the pathogenesis of schizophrenia.<sup>11</sup> Furthermore, post mortem studies have demonstrated increased binding of CB agonist in the dorsolateral prefrontal cortex in patients with schizophrenia, regardless of cannabis use.<sup>12</sup> Smoking cannabis induces an upregulation of CB1 receptors in motor areas, such as the caudate putamen, which is similar to what is found in the prefrontal cortex of schizophrenic individuals.<sup>1,8</sup>

A second hypothesis postulates that cannabis abuse and schizophrenia share a common etiologic factor such as genetic vulnerability or developmental neuropathology.<sup>13-15</sup> A longitudinal study from New Zealand, demonstrated a 4-fold increased risk to developing schizophrenia by the age of 26 in individuals who started using cannabis before the age of 15.<sup>5</sup> THC has been shown to exacerbate positive symptoms in patients with schizophrenia. Further, it has been shown to induce positive symptoms in control groups as well.<sup>16</sup> Analysis of neuroimages have shown that there are similarities between the functional networks that are affected by cannabis and those suspected to be involved in the pathogenesis of schizophrenia.<sup>12</sup>

## CONCLUSIONS

As per the above case and discussion, we are more certain today about the relationship that exists between early onset of cannabis abuse and the diagnosis of schizophrenia in young adults. Although this report documents the possible prognostic and development of schizophrenia related with the early onset of cannabis abuse, longitudinal studies are needed to establish whether cannabis abuse accelerates the beginning of schizophrenia or is a direct cause of this psychopathology. Research exploring the biological and genetic mechanism underlying this relationship could help health care providers in recognizing the importance of education and promoting healthy life styles as well as improved overall quality of life.

Today this issue is very polemic; although legalization activists and many marijuana users believe smoking cannabis has no negative effects, scientific research indicates that marijuana use can cause many health problems.

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