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Cannabis Use and Mental Health: A Critical Analysis of Current Research

Kacper Rusiński
University Clinical Hospital in Poznan
Przybyszewskiego Street 49, 60-355 Poznań
kacper.rusinski1@gmail.com
https://orcid.org/0009-0005-4002-9267

Filip Klimas
SP ZOZ MSWiA Hospital in Kraków
Kronikarza Galla 25 street, 30-053 Kraków
e1filipklimas@gmail.com
https://orcid.org/0009-0000-5266-8676

Dorota Zatłoka-Mazur
Tytus Chałubiński Regional Hospital in Zakopane
Kamieniec 10 street, 34-500 Zakopane
zdorota811@gmail.com
https://orcid.org/0009-0003-3663-1891

Zuzanna Zięba
University Clinical Hospital in Poznan
Przybyszewskiego Street 49, 60-355 Poznań
E-mail: zuzia1997.z@gmail.com
https://orcid.org/0009-0002-1576-8058

Adriana Potoczek
University Clinical Hospital in Katowice
Medyków 14 street, 40-752 Katowice
adriana.potoczek@interia.pl
https://orcid.org/0009-0002-3981-3490

Iwona Pudełko University Clinical Hospital in Wrocław
Borowska 213 street, 50-556 Wrocław
i.pudelko.97@gmail.com
https://orcid.org/0009-0001-6403-4141

Izabela Kazubek-Fuksiewicz
Medical University of Silesia in Katowice
Poniatowskiego 15 street, 40-055 Katowice
kazubekiza@gmail.com
https://orcid.org/0009-0000-4433-2638

Klaudia Ostrowicz
Upper Silesian Medical Center of Prof, Leszek Giec SUM
Ziołowa 45/47 street, 40-635 Katowice
ostrowiczklaudia@gmail.com
https://orcid.org/0009-0008-4098-7213

Izabela Lekan
St. John Paul II Mazovian Provincial Hospital in Siedlce
Księcia Józefa Poniatowskiego 26, 08-110 Siedlce
izaabelalekan@gmail.com
https://orcid.org/0009-0000-5079-9795

ABSTRACT

Cannabis is one of the most widely used psychoactive substances globally. In several countries, including Canada, the Netherlands, certain U.S. states, and Australia, its possession is legal. With its growing popularity in recent years, the impact of cannabis on mental health has become a focal point of numerous scientific studies. The aim of this review was to summarize the current evidence-based knowledge on the impact of cannabis on mental health. This article explores the relationship between cannabis use and specific mental disorders. The reviewed literature was sourced from PubMed and Google Scholar using the keywords "mental health", "cannabis", "psychosis" "schizophrenia" "depression" and "cognitive functions".

Keywords: mental health, cnnabis, psychosis, shizophrenia, depression, cognitive functions

1. Introduction

The most popular drugs derived from the Cannabis sativa plant are marijuana and hashish. Marijuana comes from the leaves, stems, and dried flower buds of the cannabis plant, while hashish is the resin obtained from the flowering buds. The components of cannabis preparations are either smoked or taken orally after being mixed with other substances [1]. Cannabis is the most commonly used controlled substance (its manufacture, possession, and use are regulated by the government) in the world, following alcohol and tobacco. According to the United Nations Office on Drugs and Crime (UNODC), 3.9% of adults use cannabis, with a total of 180.6 million cannabis users worldwide [2]. The latest study in Poland from 2018 found that marijuana was the most commonly used drug overall, with a 12.1% usage rate. Among respondents aged 15-34, 7.8% used it. In the entire studied group (aged 15-64), usage was higher among men (16.4%) than women (7.7%) [3].

2. Materials and methods

A comprehensive literature review on the association between cannabis use and mental health was conducted using the PubMed and Google Scholar platforms. The search included the following keywords: "Mental Health", "Cannabis", "Psychosis", "Schizophrenia", "Depression", "Cognitive Functions". The collected data were analyzed to provide relevant insights into the relationship between cannabis use and mental disorders, drawing from review articles, bibliographic analyses, cohort studies, and meta-analyses.

3. Cannabis Compounds and Cannabinoid Receptors

Cannabis contains over 421 compounds, including more than 60 pharmacologically active cannabinoids. The two most well-known cannabinoids are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) [1]. Cannabinoids exerts its effects primarily through CB1 and CB2 receptors. CB1 receptors are mainly found in the brain—specifically in the basal ganglia, cerebellum, hippocampus, and association cortices—while CB2 receptors are primarily located in peripheral tissues, on cells of the immune system, in the hematopoietic system, and in the spleen. Both cannabinoid receptors, CB1 and CB2, are G-protein-coupled and become activated through the inhibition of adenylate cyclase. The activation of these receptors leads to the inhibition of neurotransmitter release, such as acetylcholine and glutamate, while indirectly affecting gamma-aminobutyric acid (GABA), N-methyl-D-aspartate (NMDA), opioid, and serotonin receptors. [4]. The impact on behavior and the negative effects of cannabinoid use

are primarily due to THC. Acting through CB1 receptors, it induces euphoria, relaxation, altered time perception, impaired concentration, impaired motor coordination and psychotic symptoms. In turn, by acting through CB2 receptors, it can cause immunosuppression.
Interestingly, CBD has a modulatory effect on CB1 receptors and, as a result, helps reduce the negative effects of THC [5].

4. Psychosis

Psychosis is a clinical syndrome characterized by a loss of contact with reality. The main symptoms of psychosis include delusions, hallucinations, and disorganized speech. Psychosis can be a component of other mental disorders, such as schizophrenia, major depressive disorder with psychotic features, and bipolar disorder with psychotic features. Psychosis can also be caused by certain pharmacological agents and substances. Numerous studies have shown that tetrahydrocannabinol (THC), the main psychoactive compound in cannabis, can cause psychotic-like symptoms. Cannabis increases the likelihood of psychotic episodes by increasing the synthesis and release of dopamine, while blocking the reuptake of dopamine, thereby creating a hyperdopaminergic state [3,4,6].
In most cases, these experiences are transotory and usually last a few hours. However, a certain group of people may experience lasting psychotic disorders, leading to functional impairment and significant suffering. Therefore, research has focused on identifying subgroups that may be particularly susceptible to the psychogenic effects of cannabis [7,8]. Furthermore, an increased risk of early onset of psychotic symptoms in association with cannabis use has been observed in the general population [9].
One established risk factor is early onset of cannabis use. One study found that the prevalence of psychotic symptoms among adolescent cannabis users was 31%, compared with 20% in nonusers. This is likely due to the fact that cannabis affects the maturation of the cerebral cortex [10].
Another critical factor is THC dosage, as the psychogenic effects of THC are dose-dependent. In recent years, there has been a significant increase in the THC content of cannabis worldwide, which may contribute to the increase in cannabis-related mental health disorders. In both the United States and Europe, THC levels have doubled over the past decade [4,11]. High-potency cannabis users were 1.6 times more likely to develop psychosis than nonusers. A Frequency of use also plays a significant role-daily marijuana users were 3.2 times more likely to develop psychotic disorders than nonusers [12]. Genetic predisposition also contributes significantly to

the risk of cannabis-induced psychosis. This is associated with several genotypes, most notably the AKT1 gene. AKT1 encodes a protein kinase involved in the dopamine signaling pathway that plays a key role in modulating dopaminergic neurotransmission and may influence susceptibility to psychotic disorders [13,14].

5. Schizophrenia

The risk of developing schizophrenia during one's lifetime is approximately 0.7%. It is a disease that leads to disability due to impaired functioning in society and is associated with a shortened life expectancy. The causes of schizophrenia are still not fully understood, which is why environmental factors that may increase the risk of developing the disorder are being investigated. One such factor appears to be the use of cannabis.[15]. Young people are particularly at risk, especially those with a genetic predisposition and those who take large doses. In addition, marijuana use increases the risk of relapse and exacerbation of symptoms. [7]. The results of an observational study involving 50,000 people showed that individuals who used cannabis before the age of 18 were twice as likely to receive a diagnosis of schizophrenia, and those who used it chronically were six times more likely to be diagnosed with schizophrenia compared to non-users. [16].

The relationship between cannabis use and the risk of developing schizophrenia remains controversial, as the results of observational studies may be flawed due to reverse causality – individuals affected by schizophrenia may be more prone to using cannabis. [17,18]

6. Depression

Depression is a condition that occurs more frequently in cannabis-dependent individuals than in the general population. Cannabis can trigger depression in susceptible individuals and lead to earlier onset of the disease. On the other hand, depression can influence the desire to reach for cannabis to improve the mood. Additional research is needed to establish a causal relationship between cannabis use and depression [19,20].

The role of oxidative stress and lower levels of known antioxidants such as tryptophan, vitamin E, tyrosine, and glutathione has been implicated in the pathophysiology of depression. In turn, cannabis increases oxidative stress in the body, which may be the cause of cannabis-induced depression [19,21].

The dose of THC once again plays a role in the development of depression in cannabis-dependent individuals. It has been found that people diagnosed with depression, anxiety or substance use disorders are more likely to use extremely high-potency cannabis [19].

The age of first use and higher frequency of cannabis use are key factors in the pathophysiology of cannabis-induced depression. Studies show that cannabis use during adolescence is associated with an increased risk of major depression in early adulthood and increases the risk of suicidal thoughts. Younger people's brains are still developing, making them more susceptible to the effects of THC, which affects brain plasticity [22,24]. Studies also show a link between cannabis dependence and anxiety disorders. The comorbidity rate of depression and anxiety disorders is three times higher among cannabis addicts [23].

7. Cannabis use disorder (CUD)

There is a common belief in society that cannabis is a relatively safe substance, as it is not considered to cause addiction. The Gallup Institute showed that public support for the legalization of marijuana in the United States increased from 16% to 68% over the years 1972-2020 [33]. However, the basis for the development of addiction is the effect of psychoactive substances on the dopaminergic and reward systems. THC present in cannabis has been proven to have an addictive potential, although it is lower in comparision to other psychostimulants. For example, methylphenidate or amphetamines cause a greater release of dopamine in the brain than THC [25].

Moreover, chronic cannabis use is associated with a decrease in the expression of the CB1 receptor, which leads to the development of tolerance and cause the need to increase the amount of cannabis consumed [26].

Cannabis dependence is classified in the DSM-5 as cannabis use disorder (CUD). Cannabis use disorder (CUD) is broadly defined as the inability to stop consuming cannabis, even when it causes physical or psychological harm.

The risk of addiction among cannabis users has been estimated at around 9%, rising to one in six among those who began using cannabis during adolescence. The corresponding risk for nicotine is 32%, for heroin 23%, for cocaine 17%, for alcohol 15%, and for stimulant use 11% [27]. Tolerance and withdrawal symptoms develop in 10% to 30% of cannabis use disorders. Cannabis use disorders are associated with declines in functional status, including lower income, greater need for social support, crime, unemployment, and reduced life satisfaction [25]. There is also additional evidence that cannabis exposure is detrimental to the developing

brain, making individuals more susceptible to other addictive substances. 44.7% of people with a history of cannabis use have started to use other illicit drugs at some point in their lives. Cannabis use is also associated with an increased risk of initiating and maintaining alcohol dependence [24].

8. Cannabis use and memory and cognitive functions

There are several studies indicating that regular cannabis use negatively affects memory and cognition, especially among adolescents. A dose-dependent correlation between cannabis use and neurodevelopmental abnormalities has been revealed in adolescents who regularly use cannabis. THC impairs neuronal connectivity, mainly in the frontal lobes and hippocampus. It has been shown that adolescents who regularly use cannabis score lower on IQ tests, around 6-8 points. Importantly, the decline in thinking and memory processes persists even in adulthood and after cessation of cannabis use. Among adults who use cannabis, significantly poorer cognitive performance was demonstrated compared to non-users, in areas such as attention and working memory, which affected information processing speed and executive functions [25]. A prospective study found that long-term cannabis users in midlife showed a decrease in IQ scores compared to their childhood levels and displayed a reduced hippocampal volume in neuroimaging assessments. [28].

Other studies suggest that IQ deficits may be a factor in the development of cannabis dependence, and that people with lower IQ may be more susceptible to addiction [26, 29].

9. Conclusion

Statistics clearly show that cannabis use is becoming increasingly popular in society. It is a substance that is more easily accessible, partly because some countries have legalized its possession. "Medical marijuana" is also available on the market. Cannabis legalization is gaining many supporters. There is a belief that this psychoactive substance is harmless, non-addictive, and its negative impact on health is comparable to that of alcohol. But is a liberal approach to cannabis legalization correct?

In our article, we summarized the negative effects that cannabis use can have on mental health. Scientific researches has proven the connection between cannabis use and the increased occurrence of psychoses, schizophrenia, and depression. Cannabis is also a substance with

addictive potential, which is another cause of suffering and social dysfunction. Cannabis use also negatively affects memory processes and cognitive functions.

The observed increase in mental health disorders associated with cannabis use is most likely linked to the rising concentration of THC in relation to CBD in cannabis products, as CBD acts antagonistically to THC and mitigates its negative effects. As we mentioned in our article, THC concentration have doubled over the past decade in cannabis.

The social group most vulnerable to the negative effects of cannabis is youths.The individuals who begin using cannabis before the age of 18 are more likely to develop the mental disorders we discussed in our article. THC use during adolescence disrupts brain development processes and leads to permanent changes, which have implications in adulthood.

In our article, we focused on the impact of cannabis use on mental health. However, let's not forget that THC can also cause somatic disorders. Cannabis weakens the immune and endocrine systems and can lead to a heart attack. [30,31]. Cannabis use is especially dangerous during pregnancy and may lead to premature birth and developmental disorders in the child [32].

In conclusion, there is evidence of the harmful impact of cannabis use on health. Due to its growing popularity and availability, as well as the belief in its harmlessness, social education is needed, especially among youth. THC concentrations in cannabis products should also be monitored, and further research on the dose-dependent harmful effects of THC on mental health is essential.

Disclosure

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Author's contribution

All authors contributed to the article.

Conceptualization: Zięba Z, Rusiński K, Klimas F

Methodology: Lekan I, Rusiński K, Kazubek-Fuksiewicz I;

Software: Potoczek A, Rusiński K, Ostrowicz K;

Formal analysis: Zięba Z, Potoczek A, Pudełko I;

Investigation: Kazubek-Fuksiewicz I, Ostrowicz K, Zięba Z;

Resources:, Pudełko I, Klimas F, Potoczek A;

Data curation: Zatłoka-Mazur D, Rusiński K, Lekan I;

Writing - rough preparation: Lekan I, Zięba Z, Zatłoka-Mazur D;

Writing - review and editing:, Rusiński K, Ostrowicz K;

Visualization: Zatłoka-Mazur D, Zięba Z, Lekan I

Supervision: Zatłoka-Mazur D, Pudełko I;

Project administration: Zięba Z, Klimas F, Potoczek A;

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