A Summary of Selected Recent Research Concerning the Effects of Cannabis on Mental Health Conditions

Prepared for the Tompkins County Community by CCE Tompkins and Cornell University's Master of Public Health Program

Introduction

Cannabis, a widely debated and often controversial plant, has garnered significant attention within the realms of medicine and mental health. Its psychoactive properties, primarily attributed to delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), have sparked many studies investigating the potential therapeutic effects and risks associated with its consumption. Of particular interest is the relationship between cannabis use and mental health conditions, notably anxiety, depression, and post-traumatic stress disorder (PTSD). Understanding the implications of cannabis on these mental health disorders is important because of its relatively recent legalization in different parts of the US and the growing consideration of cannabis as a self-medication tool by individuals seeking relief from these conditions.

This literature review aims to review existing research on the effects of cannabis consumption on anxiety, depression, and PTSD, shedding light on potential benefits and drawbacks. We delve into the complexities of how cannabis, as a psychoactive substance, interacts with the human body and impacts mental health conditions. Moreover, we hope to critically evaluate the appropriateness of cannabis use as a form of self-medication for individuals grappling with mental health challenges. However, one significant limitation found in these sources was that they had mixed results and warranted further research, so much of what is written here is subject to change. We encourage individuals to consult official sources such as the New York Department of Health and other reputable sites for the latest research on this topic to form their own views.

The multifaceted nature of cannabis necessitates a comprehensive review to understand its effects accurately. Additionally, societal attitudes toward cannabis have evolved, influencing its legal status and societal acceptance, further shaping its potential role in mental health treatment. By reviewing and comparing what we already know about cannabis and its effects, this literature review aspires to contribute to a better

understanding of the complex relationship between cannabis and mental health, ultimately aiding in informed decision-making.

Review Strategy

The literature that was selected for review was based on several factors. All of the literature selected was about cannabis and either its legality, the social ideas surrounding it, or how it affects mental/physical/developmental health. The search terms used were truncated and Boolean searches of: “Cannabis,” “THC,” “CBD,” “Anxiety,” “Depression,” ”PTSD,” ”Stigma,” “consequences,” and “developmental health.” These words covered the majority of the topics that this literature seeks to discuss. Furthermore, literature from varying years in the past 30 years was employed to determine the changes in attitude towards cannabis use.

Is Cannabis Legal?

As of October 1st, 2023, Cannabis is Fully Illegal in six states (Idaho, Kansas, Nebraska, North Carolina, South Carolina, and Wyoming) and it is either partially or completely legal in the other 44 states.[1] Furthermore, Cannabis is medicinally available in these 44 states.[1]

How does Cannabis Work?

Cannabis has two active compounds that each have different effects: THC and CBD. The concentration of each of these compounds is strain-dependent. THC works through the endocannabinoid system, acting on two G-protein coupled receptors: CB_1 and CB_2.[2] THC is a partial agonist of CB1 and, in low doses, has been observed to have anxiety-reducing properties in some studies.[2] However, the opposite was observed in high doses of THC.[2] On the other hand, CBD, the other major component of cannabis and cannabis products, has been observed to lack the significant psychoactive, or “high-inducing,” effects of THC while displaying anti-inflammatory, pain-relieving, and anxiety-reducing properties in some studies.[2] At the moment, it is unclear how exactly CBD works in the body, but it is theorized that CBD is an antagonist to CB_1.[2]

Public Opinion about Cannabis

In the United States, opinions on the legalization of cannabis are multifaceted and often influenced by various social, economic, and health-related factors. Those against cannabis legalization often cite concerns regarding potential adverse health effects, particularly on cognitive development and mental health, especially among young people.[3] Critics worry that widespread legalization could lead to increased use, particularly among adolescents, and may consequently pose risks to their academic performance, overall well-being, and future prospects.[3] Additionally, opponents express

apprehensions about potential addiction and argue that legalizing cannabis might serve as a gateway to the use of more potent and harmful substances.[4]

Conversely, proponents of cannabis legalization point to its potential economic benefits, including job creation, tax revenue, and economic growth. They emphasize that a regulated cannabis market can diminish the black market, ensuring product safety, quality, and responsible consumption. Moreover, supporters highlight what they see as the medicinal benefits of cannabis, asserting that it can alleviate suffering for individuals with chronic pain, epilepsy, multiple sclerosis, and other medical conditions. One such organization that supports the use of cannabis for its medicinal benefits is the Multidisciplinary Association for Psychedelic Studies.[5] This organization developed the Zendo Project to help support people who are planning to use cannabis and offer them education and supportive care to reduce any possible harm.[5]

Furthermore, with the legalization of cannabis, health departments and organizations in the US have begun adding information about cannabis use to their websites. For example, the New York City Department of Health added a page about marijuana to its site.[6] This page talks about the legality of marijuana in the city, the Health Benefits and Risks, and some tips about using marijuana safely, such as keeping it away from minors and avoiding the consumption of other drugs while under the influence of cannabis.[6] The New York State Department of Health also added an FAQ page to its website that helps people find out how to register to get medical cannabis, where to find dispensaries, information about pricing, and information for health providers, caregivers, and organizations that can help them educate and prescribe cannabis to others.[7] In summary, the integration of comprehensive cannabis information and resources by health departments shows a growing acknowledgment of the complex landscape surrounding cannabis legalization, encompassing legal considerations, health benefits and risks, safe usage guidance, and accessibility to medical cannabis.

Can Cannabis be Used to Treat Anxiety, Depression, or PTSD?

When it comes to using cannabis to manage mental health conditions like anxiety, depression, and PTSD, the outcomes have been varied.

In a number of older papers and articles reviewed for this study, it is usually noted that cannabis use can be a cause of mental conditions such as anxiety and depression. For example, in a 1992 article about substance abuse disorders in juvenile delinquents, a positive association was found between the use of cannabis or alcohol and the development of misbehaving conduct, anxiety, and depression disorders.[8] In this paper, they noted that the likely reason that cannabis and alcohol were used by the participants was to deal with feelings of sadness and depression.[8] According to

Neighbors et al., “substance use, especially for those with depression or anxiety, may act as a negative reinforcer for their emotional distress.”(385)[8] Essentially, the juveniles were self-medicating using cannabis to deal with symptoms of depression, but this merely exacerbated their symptoms and led to an increase in the number of diagnoses of conduct disorders, anxiety, and depression.[8]

Another article that found that Cannabis was a cause of mental health conditions was a 2007 article from *The Lancet* that did a systematic review of studies that compared cannabis use with subsequent psychotic or affective mental health outcomes.[9] Their key discovery is a consistent increase in the incidence of psychosis in individuals who have used cannabis, indicating a significant association between cannabis use and psychotic symptoms.[9] Moreover, the risk of psychosis appears to escalate with higher frequency and heavier cannabis use, demonstrating a dose-response effect.[9] The authors, however, acknowledge the limitations and complexities in this field of study, including variations in study methodologies, challenges in measuring cannabis exposure accurately, and potential confounding factors.[9] They emphasize the importance of providing evidence-based public education to inform individuals about the potential risks associated with cannabis use, especially in light of the prevalent use of cannabis in the population.[9]

Despite the uncertainties, the evidence suggests that cannabis use may heighten the risk of psychotic disorders, underlining the need for cautious consideration of its impact on mental health.[9] This is further corroborated by a 2009 article that reviewed all studies from Medline, PsycLIT, and EMBASE up to August 2008.[10] According to the article, cannabis can cause anxiety and panic attacks and can exacerbate existing anxiety symptoms in new users.[10] However, it should be noted that Crippa et al. concluded that the effects of cannabis on anxiety were dose-dependent and that low doses had anxiolytic (anxiety-reducing) effects and high doses had anxiogenic (anxiety-causing) effects.[10] A major limitation of these older papers is that they all note that there is a distinct lack of evidence and that more research is needed to come up with a definite conclusion.[7,8,9]

In recent papers, there is a more positive view of cannabis use in self-medicating for mental health conditions. For example, in a 2017 article titled “Is cannabis treatment for anxiety, mood, and related disorders ready for prime time?,” Turna et al. discuss the effects of THC and CBD on eight mental health disorders.[2] In the case of Social Anxiety Disorder (SAD) treated with CBD, it was found that participants treated with CBD before giving a public speaking task were both less anxious and displayed reduced cognitive impairment.[2] Furthermore, participants who had taken CBD before the speech felt less discomfort giving the speech and had fewer negative self-evaluations than the other

participants.[2] For Generalized Anxiety Disorder, Turna et al. discussed a synthetic Cannabinoid known as Nabilone, which displayed effects similar to THC; in low doses, Nabilone was found to have anxiolytic effects, and in high doses, it was found to have anxiogenic effects.[2] When discussing Major Depressive Disorder (MDD), it was observed that plant-based cannabis may have had antidepressant effects on participants with varying results between individuals.[2]

On the other hand, treatment with THC was found to have no antidepressant effects on patients with MDD and was even found to cause dysphoria in some patients.[2] For Bipolar Disorder (BD), it was suggested that plant-based cannabis might be able to treat anxiety and insomnia in patients with PTSD, but the results were varied and inconclusive.[2] There simply was not enough information or evidence to definitively say whether CBD could treat BD.[2] When used to treat PTSD, plant-based cannabis and THC use was found to be effective at alleviating anxiety and stress-like symptoms.[2] The reason for this was because the hyperconsolidation of traumatic memories in individuals with PTSD is mediated by CB_1 receptors, which would have been kept occupied by THC and CBD in the participants that medicated with cannabis.[2] When observing Obsessive-Compulsive Disorder (OCD) and Trichotillomania, a synthetic cannabinoid known as dronabinol (a more active, synthetic form of THC) was found to be effective.[2] Finally, anecdotal information and retrospective studies involving patients with Tourette's Syndrome (TS) showed that plant-based cannabis and single-dose/short-term THC treatment reduced tic severity and intensity.[2]

In addition, in a 2011 article focused on investigating the effects of cannabis compounds, particularly CBD, on patients with social anxiety disorder (SAD) during a simulated public speaking task (SPST), the findings indicated that individuals in the SAD-placebo group exhibited heightened anxiety levels, cognitive impairment, discomfort, and alertness compared to healthy controls during the test.[11] However, pretreatment with CBD significantly reduced anxiety, cognitive impairment, and discomfort, resembling the results observed in healthy controls. The anxiolytic effects of CBD were linked to its action on limbic and paralimbic brain areas, associated with anxiety.[11] CBD was proposed to potentially act through 5-HT1A receptors, alleviating negative self-evaluation and subjective physiological abnormalities induced by SPST.[11] The study emphasized CBD's potential as a promising and rapid therapeutic intervention for SAD, presenting advantages over current pharmacological agents, warranting further extensive clinical trials to confirm its efficacy and safety.[11]

Likewise, a 2018 research article explained that the effects of cannabis, particularly in the context of pain relief, are multifaceted and involve the endocannabinoid system, which is distributed throughout the central and peripheral

nervous system.[12] This system interacts with various pain pathways, including inflammatory and endorphin/enkephalin pathways, among others.[12] THC, was stated to have potent analgesic and anti-inflammatory properties, acting primarily on CB_1 and CB_2 receptors.[12] It can modulate pain pathways involving opioid, serotonin, and N-methyl-d-aspartate (NMDA) receptors through various mechanisms.[12] CBD was also found to possess powerful analgesic and anti-inflammatory effects, mediated by multiple pathways, including serotonin receptors.[12] Cannabis strains, whether Sativa or Indica, may influence the entourage effects (the theory that all compounds in the cannabis plant work together to enhance their effects) due to varying ratios of cannabinoids, terpenes, and other compounds, resulting in different therapeutic benefits and user effects.[12] Notably, some studies suggest that cannabis can potentially reduce opioid use and aid in detoxification and weaning, contributing to combating the opioid epidemic.[12] However, Baron et al. determined that further research is needed to understand optimal combinations of cannabis constituents for specific therapeutic effects and to delineate strain-specific characteristics.[12]

In 2022, a study was published that delved into cannabis usage patterns and self-perceived symptom relief for insomnia among individuals dealing with depression, anxiety, and both conditions simultaneously.[13] The study analyzed self-reported scores before and after using cannabis, demonstrating a notable perceived improvement in insomnia symptoms with cannabinoids.[13] The findings align with early clinical trial outcomes, suggesting cannabis could be a potential future option for managing insomnia.[13] Notably, all cannabis strains were seen to reduce insomnia in individuals with these conditions, with indica-dominant, Indica hybrid, and Sativa-dominant strains more effective for insomnia in individuals with depression compared to CBD-dominant products.[13] The study urges the need for placebo-controlled trials to comprehensively evaluate the efficacy and safety of cannabinoids for sleep in those with mood and anxiety disorders.[13] Despite some limitations, this study's large, real-world sample contributes valuable insights into cannabis usage profiles for insomnia and sets the stage for more rigorous trials in the future.[13]

An article published in 2020 suggests that CBD holds promise as a potential therapy for anxiety, depression, schizophrenia, and related psychotic disorders.[14] Animal models demonstrated that CBD administration can reduce anxiety, depression, and stress-related behaviors, although effects varied based on factors like species, strain, age, gender, doses, and administration method.[14] CBD's complex molecular profile affects over 65 targets in the body, making it challenging to pinpoint the precise neurobiological mechanisms behind its behavioral effects.[14] However, the data suggests that receptors like 5-HT_{1A} and CB_1r, along with other elements crucial to emotional responses and cognitive processing, are involved in CBD's potential therapeutic effects

for these disorders.[14] While clinical trials display CBD's potential benefits, further comprehensive studies, especially on larger scales involving both animals and humans, are crucial to establish its safety and efficacy in treating psychiatric disorders like anxiety and depression.[14] Ongoing double-blind studies are anticipated to provide more clarity in the coming years regarding CBD's role in managing these psychiatric conditions.[14]

Additionally, a research article was published in 2020 that discussed the effects of cannabis, particularly CBD and THC, on anxiety using animal models and clinical trials.[15] In animal studies, the Elevated Plus Maze (EPM) is commonly used to assess anxiety levels.[15] CBD is generally described as anxiolytic in mice, with moderate doses showing anxiolytic effects, and higher doses having minimal effect.[15] THC, on the other hand, is generally seen as anxiogenic but has shown anxiolytic effects at high doses in certain studies.[15] Van Ameringen et al. also discuss the pharmacokinetic properties of CBD and ongoing clinical trials related to cannabis and anxiety.[15] Clinical trials in humans have produced largely inconclusive results regarding the anxiolytic effects of cannabis, but survey studies indicate a substantial number of individuals use cannabis to alleviate anxiety symptoms.[15] Van Ameringen et al also discuss the risks of cannabis use, including the potential for cannabis use disorder (CUD) and its association with anxiety and panic attacks.[15] Despite the emerging research, strong conclusions regarding the effectiveness of cannabis as an anxiolytic are yet to be drawn, and further research is needed to bridge gaps between animal models, clinical trials, and survey outcomes.[15]

Strains

The content set out above brings up the question of which strain of cannabis is best for treating different mental health disorders. According to a study from 2018, over the last 70 years, anxiety and other mental health conditions have typically been approached using reductionist medical models, focusing on physical brain changes and neurochemistry, and attempting to develop specific drugs to treat mental health issues.[16] However, this approach has not produced clinically highly effective drugs for mental illnesses.[16] The reductionist approach has also led to fragmentation in scientific research, isolating researchers into specialized factions, and hindering interdisciplinary understanding.[16]

By way of contrast, the 2018 study examines cannabis as a potential holistic solution for anxiety and other health problems.[16] Cannabis is increasingly acknowledged for its therapeutic potential in treating various health conditions, including anxiety.[16] The study explores different cannabis strains and their potential in treating anxiety, emphasizing that a one-size-fits-all approach may not be the most effective and that it

may require a case-by-case analysis.[16] The analysis of various strains reveals correlations between specific cannabinoids and terpenes with the anxiolytic effects of cannabis.[16] Notably, THC appears to be significantly correlated with increased anxiolytic activity, while certain terpenes like trans-nerolidol and caryophyllene also exhibit associations with enhanced anxiolytic effects.[16] However, Kamal et al. acknowledge the limitations of the study, including the need for controlled investigations to thoroughly understand the anxiolytic properties of different cannabis strains and chemotypes.[16]

Medically Approved Drugs

We can also look at an article from 2022 that talks about several medically approved cannabinoid drugs that have been rigorously tested for safety and efficacy and approved for use at the national level by regulatory agencies such as the Federal Drug Administration (FDA) and the European Medicines Agency (EMA). Dronabinol (Marinol®) is a synthetically produced THC used for anorexia, weight loss in AIDS patients, and chemotherapy-induced nausea and vomiting.[17] Nabilone (Cesamet™), a synthetic cannabinoid structurally similar to THC, is approved for treating chemotherapy-induced nausea and vomiting.[17] Rimonabant (Acomplia®), a potent synthetic CB1 receptor antagonist, was withdrawn due to serious side effects. Nabiximols (Sativex®), an oromucosal spray of Cannabis sativa extract with near-equal amounts of THC and CBD, is approved for spasticity treatment. Cannabidiol (Epidiolex®), a highly purified CBD solution, is approved for treating seizures associated with specific syndromes in pediatric patients.[17]

Each of these drugs has specific approved uses and potential side effects, contributing to the array of options within the medical cannabis realm.[17] Relatedly, , Legare et al. go on to discuss the potential therapeutic utility of cannabinoids in various diseases and conditions.[17] Chronic pain, especially neuropathy, stands out as a promising area, with cannabinoids demonstrating a significant reduction in pain.[17] In diseases of the central nervous system like multiple sclerosis and epilepsy, cannabinoids like Sativex and cannabidiol (Epidiolex) show efficacy in managing symptoms.[17] Additionally, cannabinoids may offer relief in disorders such as PTSD, anxiety, and sleep disturbances.[17] For cancer and related illnesses, cannabinoids have shown potential in reducing tumor growth and managing symptoms like nausea and pain.[17]

In 2014 there was a study that involved 102 patients using pharmaceutical-grade cannabis from the Netherlands.[18] Chronic pain was the predominant medical indication for use, and patients reported therapeutic satisfaction, irrespective of the strain of cannabis.[18] Interestingly, the study revealed that different strains with varying THC and CBD content led to distinct subjective effects.[18] The strain with high THC content

caused increased appetite but also higher levels of anxiety and dejection.[18] In contrast, the strain with low THC and high CBD content resulted in less appetite stimulation and reduced anxiety and dejection.[18] These findings provide valuable insights into selecting appropriate cannabis strains based on their pharmacologic composition for optimal therapeutic effects in different conditions.[18] However, federal regulations and pharmaceutical interests pose challenges in conducting comprehensive clinical trials to establish the effectiveness of cannabinoids definitively.[17]

What are the drawbacks/negative effects of Cannabis?

According to Legare et al., the adverse effects of cannabinoids, particularly high-THC cannabis, have been a subject of concern.[17] Heavy cannabis use in adolescents is associated with cognitive impairments, including reduced IQ and memory deficits, persisting even after cessation.[17] Psychological risks, including links to psychiatric disorders and an increased risk of psychosis, are evident with cannabis use, particularly high-THC varieties.[17]

Relatedly, a review was published in 2019 that extensively explored the effects of cannabis on mental illness, focusing on schizophrenia, manic depressive disorder (MDD), bipolar disorder (BD), anxiety disorders, and PTSD.[19] The findings in the review were far more negative than and contradictory to the previous articles and they raise significant concerns regarding the harmful effects of cannabis use, particularly in individuals with schizophrenia, where cannabis use is associated with an increased risk of psychosis and exacerbation of symptoms.[19] Additionally, cannabis use was linked to an elevated risk of MDD and worsening depressive symptoms, suggesting more evidence for harm than therapeutic benefits.[19]

The same pattern is also observed in BD, where cannabis use is associated with worsened symptoms, longer affective episode duration, and lower remission rates.[19] In the case of PTSD, cannabis use is prevalent, but the evidence regarding its therapeutic potential is mixed, necessitating further research.[19] The review also discusses the concept of self-medication, indicating that individuals may use cannabis to temporarily alleviate distressing symptoms, though it does not provide a true therapeutic effect.[19] The physical harms of cannabis use, including cognitive impairments, addiction, respiratory problems, and potential progression to other illicit drug use, are highlighted.[19] Lowe et al. emphasize the need for future research, rigorous clinical trials, and a better understanding of the relationship between cannabis use and mental illness to address the current gaps and discrepancies in the literature.[19]

In a 2020 article, the co-occurrence of cannabis use and depression was extensively studied, revealing a complex relationship.[20] Numerous studies reviewed in that article showed a higher likelihood of regular cannabis use among individuals with depression and vice versa.[20] Cross-sectional studies suggest a strong co-occurrence of depression and cannabis use. Longitudinal evidence indicates that while cannabis use may slightly increase the risk of developing depression, the stronger association is that depression may lead to increased cannabis use.[20] Factors such as age, gender, and genetic predispositions play a role in this relationship.[20] Cannabis use may have a stronger association with depression in younger individuals, and the genetic underpinnings suggest a common genetic association between cannabis use and MDD.[20] Regarding the use of cannabis as a treatment for depression, evidence is limited and primarily anecdotal, with some studies suggesting potential therapeutic effects, but robust clinical trials are lacking.[20] Pharmacological treatments for CUD are also an ongoing area of research, with medications like gabapentin and N-acetylcysteine showing promise.[20] Feingold and Weinstein conclude that, while there is a clear association between cannabis use and depression, the exact nature of this relationship and the potential for cannabis to effectively treat depression are areas that require further research and understanding.[20]

Effects on Developing Brains

A more well-documented consequence of cannabis use is its effects on developing brains, typically in adolescents and the children of pregnant/breastfeeding users. Something important to remember is that cannabis acts on the body and the brain through the endocannabinoid system, which is involved in various forms of synaptic plasticity, influencing neurotransmitter release and thereby affecting learning and memory.[21] Moreover, it interacts with the opioid system, with both systems sharing common features and modulating each other's effects, particularly in contexts such as drug abuse and pain management.[21] Moreover, the endocannabinoid system is also integral to brain development, with cannabinoid receptors and endocannabinoid ligands present even during fetal stages.[21] Exposure to cannabinoids during critical developmental periods can profoundly impact the maturation of neurotransmitter systems, including those involving catecholamines, serotonin, GABA, glutamate, and opioids, potentially leading to lasting alterations in brain function and behavior throughout life.[21]

In their 2008 paper, Trezza et al. discuss the behavioral consequences of cannabinoid exposure during pregnancy and lactation, as well as during adolescence, in both human and animal studies.[21] During pregnancy and lactation, exposure to substances like nicotine, alcohol, and cannabis can have lasting postnatal effects on behavior and cognition in offspring.[21] Research has shown that even moderate drug use

during pregnancy can lead to subtle yet long-lasting behavioral and cognitive alterations in children.[21] Maternal exposure to these substances can affect the developing nervous system, leading to functional abnormalities.[21] Cannabis is one of the most commonly abused drugs by pregnant women, and research has shown associations between prenatal cannabis exposure and neurobehavioral alterations in children, particularly in executive functions like attention and problem-solving.[21]

Animal studies also indicate that exposure to cannabinoid drugs during pregnancy can induce cognitive impairments and alter reward processing in the offspring.[21] During adolescence, cannabis use is prevalent and raises concerns regarding its potential impact on mental health and cognitive functions.[21] Studies suggest that early cannabis use during adolescence (by the age of 15) has an increased risk of psychotic symptoms later in life compared to individuals who start using cannabis later (Ages 18 and above).[21] Additionally, chronic cannabis use during adolescence may lead to cognitive deficits and alterations in reward pathways.[21] Animal studies support these findings, indicating that adolescent rats may be less sensitive to the aversive effects of THC but more susceptible to cognitive deficits and changes in opioid and dopamine systems.[21]

Many of these arguments are further supported by a 2019 paper from the Journal of Neuroscience that discusses the long-lasting effects of cannabis on the developing brain.[22] According to Hurd et al., maternal THC exposure during pregnancy affects the development of brain circuits, particularly the mesocorticolimbic system, which is regulated by dopamine.[22] Dopamine is a neurotransmitter linked to psychiatric and substance use disorders, and alterations in its receptors and gene expression can occur due to cannabis exposure.[22] This disruption can influence motivation, emotional regulation, reward, and cognition in offspring, potentially leading to psychiatric disorders later in life.[22] THC exposure during adolescence can also have detrimental effects on brain development, altering cognitive function, emotional behaviors, and socio-behavioral responses.[22] Studies in animals and humans show that THC exposure during crucial developmental periods like prenatal, perinatal, and adolescence can lead to behavioral and cognitive impairments.[22] These include alterations in synaptic function, changes in neurotransmitter systems, disruptions in GABAergic transmission, and shifts in gene expression and epigenetic regulation.[22] The effects of cannabis exposure can persist into adulthood, potentially increasing vulnerability to substance use disorders and other mental health conditions.[22]

Continuing on this theme, a 2019 paper from The American Journal of Drug and Alcohol Abuse discusses the effects of cannabis use on brain structure and function based on multiple studies.[23] The research primarily focuses on chronic and heavy

cannabis users, investigating their brain morphology and functional alterations.[23] Structural neuroimaging studies reveal morphological abnormalities in chronic users, particularly affecting brain regions with high densities of CB_1 receptors, such as the temporal lobe (including the hippocampus, amygdala, and olfactory system), cerebellum, and neocortex.[23] The hippocampus, a region rich in CB_1 receptors, has been extensively studied concerning cannabis use.[23] Individuals with chronic cannabis use have shown abnormalities in hippocampal volume and gray matter density, persisting even after months of abstinence.[23] Additionally, other brain regions like the amygdala and cortical areas have shown mixed results in terms of volume alterations.[23] There is also evidence suggesting potential damage to white matter, affecting brain connectivity and function.[23]

In terms of brain function, regular cannabis use has been associated with alterations in networks supporting working memory, attention, and cognitive control.[23] Functional MRI paired with cognitive testing has demonstrated changes in brain activity during various cognitive tasks.[23] Cannabis users often exhibit different patterns of brain activation, suggesting potential compensatory mechanisms to maintain performance.[23] Furthermore, Burggren et al. discuss the effects of cannabis use on cognition, encompassing both acute and chronic usage.[23] Acute administration of cannabis or THC is shown to adversely affect executive functions, such as planning, reasoning, and interference control.[23] Decision-making is also influenced, especially regarding risk-taking behavior.[23] Chronic, heavy cannabis use is linked to cognitive impairments extending beyond acute effects, particularly affecting memory, executive function, and processing speed.[23] Verbal learning and memory tasks are notably impaired, and the age and dose of THC exposure are considered significant factors in modulating memory and cognition.[23] Despite the potential cognitive deficits, cannabinoids are being explored for therapeutic purposes, such as in the treatment of epilepsy, ADHD, and autism spectrum disorder.[23] However, there is a need for further research to understand the specific neural and cognitive impact of medical marijuana use and its comparison to recreational use.

These indications of potentially negative impacts on developing brains is further corroborated by a 2021 article published in Nature Reviews Neuroscience that talks about how cannabis exposure during various developmental stages, including gestation, lactation, and adolescence, profoundly impacts neurodevelopment and has lasting effects on brain function and behavior.[24] Bara et al. explain that prenatal exposure to THC leads to disruptions in the gain and loss of synaptic efficiency, impairing normal neural network assembly.[24] During lactation, THC transfer to infants through breast milk affects synaptic pruning and the development of major neurotransmitter systems, potentially influencing early social communication and affective states in offspring.[24]

Second-hand cannabis exposure during childhood also poses risks, with documented THC metabolites in children's samples showing cognitive and emotional problems.[24]

In adolescence, a critical period of neurodevelopment, THC exposure affects the endocannabinoid system, excitatory-inhibitory balance, and neurotransmitter systems, potentially increasing susceptibility to psychiatric disorders, addiction, and altered drug sensitivity in adulthood.[24] Additionally, Bara et al. go into a discussion about the long-term consequences of developmental cannabinoid exposure on the brain and behavior, with a focus on epigenetic mechanisms.[24] Epigenetic factors, which modulate gene expression without altering the genetic code, are seen as key in explaining enduring phenotypic changes due to cannabinoid exposure.[24] The article outlines various epigenetic mechanisms, such as DNA methylation, histone modifications, and non-coding RNAs, that can be influenced by cannabis exposure during developmental stages, impacting synaptic plasticity and behavior.[24] It is highlighted that epigenetic modifications induced by cannabis may not only affect the individual exposed but could also be transmitted across generations through the germ line.[24] The findings underscore the importance of understanding how cannabis exposure during critical developmental periods can lead to lasting epigenetic changes, providing insights into potential prevention and intervention strategies.[24] Despite gaps in knowledge, the reversible nature of epigenetic modifications offers hope for mitigating the neurobiological and behavioral impacts of early cannabis exposure.[24]

Conclusion

The complex relationship between cannabis use and mental health, particularly anxiety, depression, and PTSD, presents a multifaceted picture. The literature illustrates a divergence in perspectives, with some studies suggesting potential therapeutic benefits, especially with compounds like CBD in managing symptoms of anxiety and stress. However, caution is warranted, especially considering the varying effects of different strains and cannabinoids, along with the lack of comprehensive clinical trials. On the other hand, there's a substantial body of evidence highlighting the potential negative consequences of cannabis use on mental health, especially when initiated during critical developmental periods. Prenatal exposure and use during adolescence are particularly concerning, given their potential to cause lasting alterations in brain structure, function, and epigenetic regulation, which may increase susceptibility to mental health disorders later in life.

For psychiatrists and therapists, it's essential to approach cannabis self-medication with a cautious and informed perspective. It is critical to educate patients about the potential risks associated with cannabis use, especially for vulnerable populations like pregnant individuals, adolescents, and those with a history of mental

health disorders. Encouraging open communication about cannabis use, assessing individual circumstances, and considering alternatives with established safety and efficacy should be a priority. Additionally, ongoing research and further clinical trials are essential to establish a clearer understanding of the potential therapeutic benefits and risks of cannabis use in mental health management. Until then, promoting evidence-based treatments and therapies for anxiety, depression, and PTSD remains paramount in ensuring the best possible outcomes for patients.

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