Cannabis and Anxiety

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Anxiety

- Symptom:
 - Excessive, fear, stress, worry
 - Annual prevalence 18% of adults, 2:1 F:M
- Disorder:
 - Separation Anxiety Disorder
 - Specific Phobia
 - Social Anxiety Disorder (Social Phobia)
 - Panic Attack
 - Panic Disorder
 - Agoraphobia
 - Generalized Anxiety Disorder
 - Substance/Medication-Induced Disorder
 - Anxiety Disorder Due to Another Medical Condition
 - Unspecified Anxiety Disorder
- Not a qualifying condition in Utah or any other state except New Jersey

Patient-reported use of medical cannabis for pain, anxiety, and depression symptoms: Systematic review and meta-analysis. Kosiba JD, Maisto SA, Ditre JW.Soc Sci Med. 2019 Jul;233:181-192. doi: 10.1016/j.socscimed.2019.06.005. Epub 2019 Jun 8.

- Most common reasons for cannabis use:
 - Pain 64%
 - Anxiety 50%
 - Depression/Mood 34%

The Lancet Psychiatry Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis <u>Nicola Black, PhD ⁺ Emily Stockings, PhD ⁺ Gabrielle Campbell, PhD Lucy T Tran, BPsychSci(Hons) Dino Zagic, BPsychSci(Hons)</u> <u>Prof Wayne D Hall, PhD</u> et al. Published:October 28, 2019 DOI:https://doi.org/10.1016/S2215-0366(19)30401-8

Interpretation

There is scarce evidence to suggest that cannabinoids improve depressive disorders and symptoms, anxiety disorders, attention-deficit hyperactivity disorder, Tourette syndrome, post-traumatic stress disorder, or psychosis. There is very low quality evidence that pharmaceutical THC (with or without CBD) leads to a small improvement in symptoms of anxiety among individuals with other medical conditions. *There remains insufficient evidence to provide guidance on the use of cannabinoids for treating mental disorders within a regulatory framework.* Further high-quality studies directly examining the effect of cannabinoids on treating mental disorders are needed.

Review Eur Arch Psychiatry Clin Neurosci. 2019 Feb;269(1):107-120. doi: 10.1007/s00406-018-0970-7. Epub 2018 Dec 19.

Cannabis and mental illness: a review

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Conclusions and Future Directions

• Individuals may be predisposed to developing an addictive disorder due to various biological and sociological factors. This may support vulnerability towards initial use as well as both the positive and negative reinforcement that follows. Having a comorbid psychiatric disorder further complicates this, as the initial positive reinforcement received and the later withdrawal alleviation may mask itself as 'self-medication'. The reality, however, is that the perception of self-medicating one's mental illness with cannabis is common in mentally ill patients. The evidence thus far supports more harmful effects of recreational cannabis use on mental illness, rather than therapeutic. The high prevalence of cannabis users self-reported therapeutic effects, however, creates a paradox that has negatively influenced societal and political perspectives, as well as contributed to polarized views on cannabis. Collection and analysis of prospective data is vital in order to disseminate accurate information to the public so that individuals can make informed choices, and evidence-based policies can be implemented.

Self Medication and Addiction

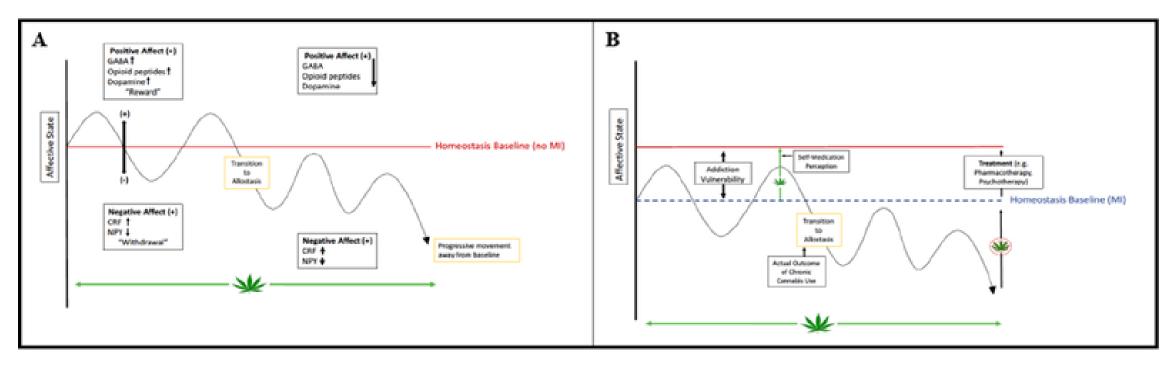


Figure 1.

nihms-1516933-f0001.jpg

Addiction Vulnerability and Allostasis Models Conceptualized for Cannabis Users with Mental Illness Individuals without mental illness (MI) (A) who use cannabis transition to an allostatic state, leading to neurobiological changes that induce a continuous reduction in positive affect that is associated with further use in attempts to regain original homeostatic levels. Individuals with MI (B) already have a lowered set point for positive and negative hedonic homeostasis, promoting addiction vulnerability, as substances are used in attempts to normalize an already altered (reduced) set point. Addiction in How effective and safe is medical cannabis as a treatment of mental disorders? A systematic review. Hoch E, Niemann D, von Keller R, Schneider M, Friemel CM, Preuss UW, Hasan A, Pogarell O.Eur Arch Psychiatry Clin Neurosci. 2019 Dec;269(8):995.

- Diagnoses were: dementia, cannabis and opioid dependence, psychoses/schizophrenia, general social anxiety, posttraumatic stress disorder, anorexia nervosa, attention-deficit hyperactivity disorder, and Tourette`s disorder.
- THC- and CBD-based medicines were associated with improvements of several symptoms of mental disorders, but not with remission. Side effects can occur, but severe AEs were mentioned in single cases only. The overall confidence in the evidence is low. To provide reliable treatment recommendations, more high-quality RCTs with larger sample sizes are requested.

Cannabis and Cannabinoids in Mood and Anxiety Disorders: Impact on Illness Onset and Course, and Assessment of Therapeutic Potential

Am J Addic. 2020 Jan;29(1):9-26. doi: 10.1111/ajad.12963. Epub 2019 Oct 2.

- Considered Generalized Anxiety Disorder, Social Anxiety Disorder, Panic Disorder, Agoraphobia, and Specific Phobia
- 12 studies, few studies distinguished between individual anxiety disorders
- Onset: 9 studies found no significant association between cannabis use and developing a future anxiety disorder. 1 study found cannabis use increased the odds of new diagnosis of Social Anxiety Disorder. And 2 studies with long follow-up times, adolescence to adulthood, demonstrated significantly increased odds of anxiety symptoms in those with cannabis use.
- Course: No statistically significant outcomes between cannabis users and non-users.
- Therapeutics: Only one study of a single 600 mg dose of CBD showed reduction in Social Anxiety Disorder symptoms in a public speaking test

J Transl Med 2020 Oct 2;18(1):374. doi: 10.1186/s12967-020-02518-2. Cannabis, a cause for anxiety? A critical appraisal of the anxiogenic and anxiolytic properties

Lara Sharpe¹, Justin Sinclair¹, Andrew Kramer¹, Michael de Manincor¹, Jerome Sarris²³

- Acute doses of CBD were found to reduce anxiety in both animals and humans, without having an anxiogenic effect at higher doses.
- Conversely, the available human studies demonstrate a common anxiogenic response to THC (especially at higher doses)
- Epidemiologic evidence suggests that 50% of cannabis users are using it for anxiety, second only to pain (64%), and greater than depression/mood (34%).

Treating Anxiety With Cannabis

- Cannabis preparations high in CBD and lower in THC would be more successful
- THC levels in cannabis have increase 212% between 1995 and 2015
- The epidemiologic data is in contrast to the findings of clinical trials
 - Even with increasing levels of THC users continue to use cannabis to treat their anxiety, some even decreasing or going off prescribed anxiolytic medication
 - Age, sex and background of exposure may have an impact on how an animal or human reacts to THC or CBD
- Continuing research may reveal that THC and CBD are not the only cannabinoids of clinical interest in anxiety
- Terpenes and terpinoids have also shown significant anxiolytic action.
- It is plausible that many phytochemicals could be contributing to the anxiolytic activity of cannabis