

Minnesota Psychiatric Society

Improving Minnesota's mental health care through education, advocacy, sound psychiatric practice and achieving health equity.

President Chinmoy Gulrajani, DFAPA (612-886-2516), Legislative Committee Chair Michael Trangle, MD, DLFAPA (612-859-4471), Executive Director Linda Vukelich (651-278-4241), Lobbyist Bill Amberg (612-260-9973)

RESPONSE TO THE PETITIONER'S REQUEST FOR THE MINNESOTA MEDICAL CANNABIS PROGRAM TO AUTHORIZE THE USE OF CANNABIS FOR THE TREATMENT OF ANXIETY –

The Minnesota Psychiatric Society, representing nearly 500 Minnesota psychiatric physicians, believes that all policy decisions impacting access to marijuana should be informed by scientific findings. Among the MPS members are experts in addiction medicine and experts in brain development. MPS opposes authorization of the use of medical cannabis for treatment of every and all anxiety disorders.

The membership has taken a position to caution the public and governmental agencies about the harms of cannabis, its lack of efficacy in anxiety, and current effective treatments of anxiety. Since Minnesota's medical cannabis program began, science has advanced our knowledge to demonstrate the lack of effectiveness, clinical impact and potential harms.

MPS Position:

- 1. Anxiety is a treatable condition.
- 2. It can be treated with non-addicting medications and psychotherapy. For some forms of anxiety, psychotherapy is the preferred treatment. Treatments are readily available through in-person or telemedicine.
- 3. Cannabis is not a benign drug. Its use causes a significant amount of addiction, and it also causes a number of psychiatric disorders.
- 4. Some psychiatric disorders are destabilized by cannabis to the point that the person may require hospitalization.
- 5. Cannabis may be a cause of psychosis.
- 6. Recent data suggests that there may be significant cardiovascular morbidity and mortality associated cannabis.
- 7. Cannabis has no proven efficacy in the treatment of anxiety or any other psychiatric disorder.

We base our position on the following points:

All anxiety is not the same. Anxiety disorders can be chronic disorders, and treatment may extend for weeks to months or years. Adjustment to a stressful experience or developmental issue can leave the person with worry and anxiety. These symptoms may likely pass when the situational issue resolves and psychological support is provided. These transient situational problems are best treated with support, compassion, understanding and psychological tools that are effective in time limited situations. Another serious concern is the choice of cannabis for one of the anxiety disorders namely separation anxiety disorder. MDH should be aware that separation anxiety is a common developmental issue in children around the age of two and three years. For some children a separation anxiety disorder may arise at the time of preschool. Significant emotional distress and limitations in community access may be a consequence. To suggest that this is one of the disorders that would be eligible for cannabis treatment is problematic. The scientific literature on the damage to the central nervous system to youth up to age 25 by cannabis is clear. (Bura et al)

There is a wealth of psychotherapeutic treatments which are effective and readily available.

- Recognized evidence-based therapies are diverse and effective. Psychotherapeutic treatments with response rates of 46–77% include cognitive-behavioral therapy, mindfulness, exposure therapy, meditation therapy, nonspecific behavior therapy, muscle relaxation therapy, computer platform cognitive-behavior therapy and others.
- Therapy is accessible and available in person and via telehealth. Investments in telemedicine and telepsychiatry provides care through virtual computer platforms have changed the accessibility and availability of therapy.
- Patient Centered Treatment is designed to best fit each person and adjust as needed. Therapists plan treatment and make modifications to fit each patient's needs, preferences, pace, processing and linguistic ability so that treatment is person centered. Also, behavioral interventions that may be less language based are readily available.

Medication treatments of SSRI/SNRIs are evidence based and definitive treatments for anxiety disorders. They are FDA approved including dosage guidelines. They are not intended to solely provide temporary relief of symptoms as argued in the petitioner's inaccurate and misleading statement. Using cure rather than effectiveness as a reason to authorize cannabis ignores the many years of research into the genetic, environmental and traumatic causes of mental illness and the thousands of clinical trials that have established the effectiveness of therapies for mental illness. Benzodiazepines are not the standard of care for the management of anxiety disorders due to lack of evidence for effectiveness as well as their potential for addiction. Clinical management of side effects is what clinicians do for anxiety or for treatment of high cholesterol with statins or many other conditions. Side effects from medications are not unique to mental illness or SSRIs: there are clear adverse effects from cannabis. Medical advances equip clinicians with a wide range of medication options. Physicians use genomic testing to identify specific metabolic pathways that may predispose some patients to side effects. Medications are effective. Physicians are aware of medication side effects, and they have time honored methods of mitigating them.

There are barriers to treatment, but that is a complex issue without a simple solution; cannabis is not the solution. There are campaigns to reduce the stigma surrounding mental illness so that people feel comfortable seeking help.

The neurobiologic basis for our position:

Studies of the neurobiology of anxiety disorders show that the transmitter glutamate plays a pivotal role in the development of anxiety disorders with acute stress enhancing glutamate release in the amygdala, the emotion center. Cannabis affects glutamate signaling in the human brain; it causes a perturbation of physiologically available glutamate. The neurophysiological model shows that the anxiety disorders are complex biological, emotional, and behavioral conditions but have a unifying neurobiological connection to glutamate transmission. The endocannabinoid system has an interaction with glutamate and an agonist of the endocannabinoid system is cannabis. The conclusion is that cannabis is a perturbation of physiologically available glutamate and has an adverse relationship to anxiety disorders.

The relationship of anxiety disorders to cannabis:

Little data is available that tests the efficacy of cannabis for people with generalized anxiety disorder and data for the other anxiety disorders are without empirical evidence. Literature reports cannabis to both increase and decrease anxiety.. At the same time, cannabis has been associated with adverse events including increased anxiety, psychosis, neurocognitive impairment, and addiction, which presents significant limitations to its use as a treatment. For instance, feelings of anxiety and panic often follow cannabis use, and are reported to drive the high rates of hospital emergency room visits in users. Unfortunately, neither the compound, nor users, have been characterized well enough to determine who will have an anxiogenic versus anxiolytic response following use. An additional concern with cannabis use relates to the increased risk of psychosis in those with a preexisting genetic vulnerability to schizophrenia with regular cannabis use. Similarly, there was moderate evidence to suggest a negative effect of regular cannabis use and incidence of social anxiety disorder and suicidal ideation, attempts and completions. A recent meta-analysis of 31 studies attempted to discern the temporal relationship between anxiety disorders and cannabis use. This analysis showed that a cohort of those using cannabis at baseline was significantly more likely to have symptoms of anxiety at follow-up in studies adjusted for confounders.

The opposite relationship was investigated in one study: there was no association between anxiety at baseline and regular cannabis use at follow-up. When assessed for cannabis use in this study among those with anxiety disorder, cannabis use did not increase suggesting in this naturalistic study that patients with anxiety disorder did not manage their anxiety with cannabis This evidence makes it clearer that cannabis may be a path to anxiety disorder and that anxiety need not be a path to cannabis use especially with effective treatments being available. (Kedzior and Laeb)

Cannabis statistics:

- 9% of all users get addicted to it. (Anthony et al. Lopez-quintero et al.)
- 17% of people who start using cannabis in their teens will develop a cannabis use disorder. (Anthony; Hall et al.)
- Cannabis can cause a number of disorders associated with frequent use including: cannabis induced intoxication, withdrawal, psychosis, anxiety disorder, sleep disorder, and delirium. (DSM-5 p 482; NIDA 2021.)

References:

- 1. Bura et al., Cannabis and Synaptic reprogramming of the developing brain; Nature Review Neuroscience 21 May 2021.
- 2. Bergink, H.J. van Megen, H.G. Westenberg Glutamate and anxiety Eur Neuropsychopharmacol, 14 (2004), pp. 175-183
- 3. Garakani, S.J. Mathew, D.S. Charney Neurobiology of anxiety disorders and implications for treatment Mt Sinai J Med, 73 (2006), pp. 941-949
- 4. E.P. Bauer, G.E. Schafe, J.E. Ledoux NMDA receptors and L-type voltage-gated calcium channels contribute to long-term potentiation and different components of fear memory formation in the lateral amygdala J Neurosci, 22 (2002), pp. 5239-5249
- 5. M.S. Fanselow, J.J. Kim, J. Yipp, O.B. De Differential effects of the N-methyl-p-aspartate antagonist DL-2-amino-5-phosphonovalerate on acquisition of fear of auditory and contextual cues Behav Neurosci, 108 (1994), pp. 235-240;
- 6. L.R. Reznikov, C.A. Grillo, G.G. Piroli, R.K. Pasumarthi, L.P. Reagan, J. Fadel Acute stress-mediated increases in extracellular glutamate levels in the rat amygdala: differential effects of antidepressant treatment Eur J Neurosci, 25 (2007), pp. 3109-3114
- 7. Cratty, D.L. Birkle, N-methyl-p-aspartate (NMDA)-mediated corticotropin-releasing factor (CRF) release in cultured rat amygdala neurons1810 Peptides, 20 (1999), pp. 93-100;
- 8. Millan The neurobiology and control of anxious states, Prog Neurobiol, 70 (2003), pp. 83-244
- 9. Cortese, K.L. Phan, The role of glutamate in anxiety and related disorders CNS Spectr, 10 (2005), pp. 820-830.)
- 10. EnriqueBaca-Garcia New perspectives in glutamate and anxiety Pharmacology Biochemistry and Behavior Volume 100, Issue 4, February 2012, Pages 752-7
- 11. Bara, Ferland, Rompala, Szutorisz, Hurd; Cannabis and Synaptic reprogramming of the developing brain, Nature Reviews in Neuroscience, 5/21.21.
- 12. MarcoColizzi, PhilipMcGuire, ;SagnikBhattacharyya Effect of cannabis on glutamate signaling in the brain: A systematic review of human and animal evidence Neuroscience & Biobehavioral Reviews Volume 64, May 2016, Pages 359-381
- 13. Turna Patterson, Ameringen, Is cannabis treatment for anxiety, mood, and related disorders ready for prime time? Jasmine *Depress Anxiety*. 2017;34:1006–1017.
- 14. Kedzior and Laeber, A positive association between anxiety disorders and cannabis use or cannabis use disorders in the general population- a meta-analysis of 31 studies BMC Psychiatry 2014, 14:136 http://www.biomedcentral.com/1471-244X/14/136
- 15. Anthony JC, Warner LA, Kessler RC. Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: Basic findings from the National Comorbidity Survey. Exp Clin Psychopharmacol. 1994;2(3):244-268. doi:10.1037/1064-1297.2.3.244
- 16. Lopez-Quintero C, Pérez de los Cobos J, Hasin DS, et al. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *Drug Alcohol Depend*. 2011;115(1-2):120-130. doi:10.1016/j.drugalcdep.2010.11.004
- 17. Anthony JC. The epidemiology of cannabis dependence. In: Roffman RA, Stephens RS, eds. *Cannabis Dependence: Its Nature, Consequences and Treat:ment.* Cambridge, UK: Cambridge University Press; 2006:58-105.
- 18. Hall WD, Pacula RL. Cannabis Use and Dependence: Public Health and Public Policy. Cambridge, UK: Cambridge University Press; 2003.
- 19. DSM-5 p. 482 Diagnoses associated with substance class
- 20. NIDA. 2021, April 13. Is marijuana addictive?. Retrieved from https://www.drugabuse.gov/publications/research-reports/marijuana/marijuana-addictive on 2021, September 13