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- Budding Psychosis: A Case of Tetrahydrocannabinol Precipitating Prolonged Psychotic Episode
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# Sentience and Psychedelics: The Promise of New Psychotherapy Catalysts

G rard Sunnen, MD

## Abstract

Links have been found connecting psychedelic phenomena to enhanced activity of selected brain neurotransmitter systems. Cortical activation of serotonin 5HT-2A receptor subtypes produces far-ranging effects ranging from changes in the configuration of consciousness to neurogenesis. Understanding heightened neuronal network fluidity and cortical cross-connectonomic communication presents exciting opportunities for integrating psychedelics in the treatment of a spectrum of clinical challenges to the human condition.

## INTRODUCTION

The new era of clinical psychedelic research is kindling a surge of new interest bordering on excitement. There is even a nascent notion that major discoveries will be made, leading to radically different ways of looking at self and humankind, maybe even piercing through one of the greatest questions facing the sciences today, namely the mind-body problem <sup>[1,2]</sup>.

In the fifties and sixties, psychedelic usage was fueled by the promise of facile spiritual discovery. Inspired by Eastern concepts offering novel philosophies of life, psychedelics became popular as potential accelerators of personal evolution.

So I also rode this wave, as did my parents, who were meditation students of a spiritual man, Paramahansa Yogananda, author of *Autobiography of a Yogi* <sup>[3]</sup>. We were inspired by Aldous Huxley's "Doors of Perception" <sup>[4]</sup> and Alan Watts' "Joyous Cosmology" <sup>[5]</sup>.

To illustrate the phenomena that commonly emerge during psychedelic explorations, I write on my first experience which took place in my late teens, using an established Native American recipe that called for three dried peyote cacti, while inviting a proper mindset, in a context of a supportive loving milieu. If it was time-tested by Native

Americans, I reasoned, they had paved the way, and I felt safe.

After an hour or so, the arduous visceral effects of the magic cacti evaporated. Situated near a trio of pines in the slowdown of a Sunday and with a soft breeze backdropped by a strikingly blue sky, I looked at the trees moving in the zephyr. Suddenly, I was jolted by a radically different perception. The trees, not only in their sway, but also in every branch, even down to each needle, were now registered and understood, as in a lifting fog's sudden clarity. Standing spellbound, I sensed nature's energies coursing through the tree trunks and the wonderment of passing birds in flight, all as if seen for the very first time.

My own self's perimeter was shifting as me/not-me demarcations fluidified. Sensations melded in a moving m lange that would later be understood as synesthesia. At this juncture, I realized that I had a choice to make: Either I would let things happen as they would, with acceptance and relaxation, or, feeling that these challenges could portend darker outcomes, I would now backtrack by ending my experiment, however I could. This juncture, commonly encountered during psychedelic therapies, speaks for the beneficial presence of a guide who, aware of this possible conundrum, will bolster patients' ego forces. They will then be more likely to emerge from their journeys with derived strength and aplomb.

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After several hours, I welcomed returning to the familiar sense of “Me.” Nevertheless, I remained deeply humbled by the realization that one’s so-familiar state of sentience could be so fundamentally transformed by ceremonial botanicals which, in mixing with brain dynamics, could dramatically influence perception, cognition, mood, and the highest qualia of the experiencing self. I would later appreciate that these experiences expressed the hallmarks of commonly shared psychedelic peregrinations. Knowledge in working with these phenomena embodies immense psychotherapeutic promise <sup>[6]</sup>.

### **THE FIRST PSYCHEDELIC SURGE AND THE NEW CONSCIOUSNESS ALCHEMY**

As a resident physician at New York’s Bellevue Psychiatric Hospital, the late sixties were a time for witnessing a new phenomenon. Half of our admissions were brought by the police, and our acute unit, with its safety rooms for agitated patients, was rarely idle. Within a few months, we saw our emergency population beginning to shift, as the classical DSM syndromes were now mixing with new and potent poly-pharmaceutical psychedelic brews.

That era was one for free-for-all “mind-expanding” mystical molecular magic and its new psychedelic alchemy. Our patients, to our wonderment, would detail how they had mixed, smoked, brewed, distilled, imbibed, and unfortunately injected, any permutation and combination of substances said to contain life-revealing properties. Blended with psilocybin in magic mushrooms were mescaline, LSD, unknown compounds derived in rogue laboratories, morning glory seeds, hashish, ibogaine, and then-mysterious plants from the Amazon and the Far East. In this age of experimentation, even psychiatric drugs, such as Thorazine and Elavil, easily obtained in street markets, found their way into

creative concoctions. We regularly pondered, is this psychiatric emergency a case of acute schizophrenic decompensation, schizoaffective psychosis, bipolar mania, delirium, a neurological problem, an intoxication, a wild mix of the above, or simply a “bad trip?”

### **THE CONTEMPORARY PSYCHEDELIC WAVE**

This first psychedelic wave subsided after some years. Decades later and present today, however, a second wave arrived, this one derived from the cumulated rich trove of discoveries into nervous system dynamics: Advances in brain imagery, neuronal circuitry mapping, psychosurgery and deep brain stimulation, neurotransmitter chemistry, all are leading to a birthing appreciation for the secrets psychedelic research could possibly unlock <sup>[7]</sup>.

Suppose impaired circuitries are putative in the creation of psychiatric pathologies. Could psychedelics, which appear to act at the very interface between brain chemistry and consciousness, be utilized to treat humankind’s psychic plagues, namely the spectrum of anxiety and trauma disorders, catastrophic depressions, thought pathologies, addictions, and end-of-life existential tribulations? Today, hundreds of psychedelics are identified, and the list is ever-growing <sup>[8]</sup>. On a more fundamental level, could the psychedelic keys that appear to open portals to the kingdom of sentience give us insights about how a palpable organ, the brain, can generate a phenomenon called *experiencing*, revealing how so many varieties of emotions can emerge from a mere physical entity? <sup>[9], [10], [11]</sup>.

### **CONNECTONOMICS OF CONSCIOUSNESS**

It has long been appreciated that the fullest expression of consciousness relies on the

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proper functioning of the cerebral cortex, in dynamic unison with subcortical arousal systems [9], [12]. Neuronal circuitries creating alertness, awareness, and attention, are referred to as the “consciousness system” [13].

Emerging from the brain stem are signals generated by billions of dense cells in net-like formations providing neural energies for ascending as well as descending signaling. The ascending reticular activating system (ARAS) is a prime provider for the tonus of alertness – indeed, lesions there lead to coma [14], [15], [16]. Several distinct arousal networks travel to the highest cortical centers via the pons, mesencephalon, thalamus and hypothalamus, each mediated by specific neurotransmitters: Glutamate, acetylcholine, GABA, norepinephrine, dopamine, serotonin, histamine, orexin and adenosine, a growing number of lesser-known neuromolecules, and even neurotransmitter gasses such as nitric oxide (NO) [17], [15]. From there, thalamocortical projections activate cortical connectomes to create the most delicate expressions of sentience [18].

The brain’s connectome is defined as the ensemble of all neurons that populate its universe [19]. Its outbound nerves eventually immerse their finest tendrils far into the substance of every bodily organ, from skin, muscle, and endocrine glands to immune networks, and back to the brain; as such, there are no clear boundaries to the brain’s connectome because it touches the intimate functions of all cells, determining the health of every organ. This principle forms the foundation for the practice of psychosomatic disciplines such as meditation and yoga, among others, that aim to harmonize all systems that contribute to our organism’s well-being.

Numerous sub-connectomes inhabit the greater brain connectome [20]. Sensory connectomes translate the constant messages of trillions of diverse bodily sensors into *experiencing*, while motor networks trace their circuitry from the elusive centers of volition, to

muscle activation. Other connectomes, visual, auditory, memory and language share space with abstract ones, as those dedicated to thinking, creativity, and the most complex, selfhood.

Although most connectomes function below the threshold of awareness, one connectome is granted special status; it could be named the “*Awareness Connectome*.” While consciousness derives from the energetic contributions of the total neuronal population, awareness expresses the ignition of selected neuronal circuits that can quickly respond to the milieu’s immediate demands. It thus embodies essential adaptation and survival value. The normal serial shifting of the mind’s attention reflects the scanning kinetics of this connectome. Fully able to center on incoming perceptions, it can also be dispatched omnidirectionally via the impetus of another connectome, one with nebulous provenance, namely volition [21]. This outgoing beam of awareness can delegate psyche into its soma, not only to expand its domain but also to influence internal bodily systems.

In Eastern perspectives, by contrast, awareness is interpreted as a form of transcendent energy. In the Tibetan Buddhist view, for example, the ultimate stuff of awareness belongs to a substance called the “subtle body” which can be conceived as belonging to a yet unidentified universal energetic dimension [22].

### **THE “ME CONNECTOME”**

Within the nebulae of neurons constantly pulsating with electro-chemical flux, resides an entity known as a *person*. Is personhood a neurological entity or a spiritual presence? Our brain’s language centers give it a name: “*Me*,” manifesting as a poignant sense of *experiencing* oneself in an instant of time, namely *qualia*. Drawing on the contributions of limbic connectomes, it is imbued with

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poignant feelings such as self-esteem and self-worth. This “Me” connectome, as the central experiencer and executor of mental functions, has the challenging task of negotiating all signals entering and exiting consciousness. In classical parlance, this refers to a delicate balancing act between conscious id, ego and superego forces. Could psychedelic therapies, via their propensity to assuage the usual perimeters of self, move this connectome in the direction of greater self-acceptance and self-appreciation, so commonly expressed as personal goals for psychotherapy?

### **PSYCHEDELIC NEUROTRANSMITTER DYNAMICS**

Brain connectomes use numerous neurotransmitter molecules to activate, facilitate, modulate, and inhibit their messages [23]. Cross-communication between all connectomes ensures that no one part of the nervous system is ever isolated from the others. Studies have consistently shown that activation of selected serotonin-based networks stimulates psychedelic actions on consciousness [24], [25], [26], [27]. Fourteen serotonin receptor subtypes grouped in seven families have been identified [28]. A consensus is reached that psychedelics’ core psychic effects are mediated via the engagement of 5HT-2A cortical receptors [29], [7], [30]. These authors posit that cortical serotonin circuits are of two types. 5HT1A receptors are involved in stress modulation. Their activation - by SSRI antidepressants, for example - leads to nervous system appeasement and relaxation. 5HT2A cortical receptor activation, on the other hand, leads to the altered configuration of sentience observed in psychedelic action. How can the activation of this connectome’s extensive ramifications be putative in producing such profound alterations in the expression of qualia?

### **SCULPTING SENTIENT CONNECTOMES WITH MEDITATIVE THERAPIES, THE POSSIBILITY OF “AWARENESS NEURONS,” ENHANCED NEUROPLASTICITY AND NEUROGENESIS**

What happens to the brain’s circuitry when meditation is consistently practiced? Considering discoveries showing the capacity of meditation-induced neuronal generation [31], [32], [33], [34], is it possible to stimulate brain awareness networks to expand their neuronal demographics? Research shows that meditation, which essentially involves the practice of directing awareness onto itself, can alter the morphology of selected brain structures [35], [36], [33], [37], [38].

How can these practices, developed by humanity for thousands of years [39], be utilized to bring about accelerated personal realization? In yogic practices, the awareness connectome is invited to forge links between high cortical functions and deep visceral systems. In this process, the *autonomic nervous system* becomes less robotic, as it is gradually invited into the domain of the sentient self. Since tapping into awareness networks via meditation increases the proliferation of neuronal cellular elements in selected brain structures, can we posit that such practices promote the genesis of specialized cell subtypes destined to produce awareness, namely neurons that, active in vast networks, could be called “awareness neurons?”

Studies point to the capacity of psychedelics to promote neuroplasticity. This is achieved by dendritogenesis, synaptogenesis, and the expression of plasticity-related genes via brain-derived neurotrophic factors. These authors privilege the prefrontal cortex and hippocampus as sites of the greatest psychedelic-induced fluidity [40].

In practices such as Zen Buddhism [41] and the “mental yogas,” as in Raja Yoga and Kriya Yoga, it becomes possible to attain



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coveted states of self that distinguish awareness-content from consciousness nature. In the profound experience of such special states, there are no thoughts, emotions, or memories; there is simply the raw energy of consciousness. This state is called “Pure consciousness” [42]. Experiencers attempting to describe this phenomenon use words like *ineffable and transcendental* [43]. Western languages have not yet ascribed words to these special states of qualia. However, one can appreciate that when *experiencing* is centered on the very energy that creates it, reports will often use terms that invoke the universal, cosmic, and divine.

Variations of “pure consciousness” states are regularly encountered in psychedelic therapy sessions as they can in the deeper stages of meditative hypnosis [48]. During these times, therapist/patient communications may become substantially altered, with long pauses and silences, the use of phrases rather than completed sentences, and novel choice of words. Those episodes represent times of greatest neuro-fluidity and, therefore, offer opportunities for establishing new and lasting modifications of personal constructs.

Experiencing “pure consciousness” can be as impactful as it is transformative because it teaches that notions of selfhood derived from a lifetime of family and social interactions may no longer satisfy the quest for personal *meaning*. Self-concepts emerging after experiencing “pure consciousness” connect to a seemingly more immutable base. The experience is therapeutic in the sense that it couples the sense of self to a more fundamental essence, namely personal *primal life energies*, which, at their foundation, remain perennially positive.

### **PSYCHEDELICS IN PSYCHOTHERAPY AND THEIR AUGMENTATION WITH PSYCHOSOMATIC TECHNIQUES**

Psychotherapy seeks to assist in the transformation of states of being from “lesser” subjective states to “higher” ones. Lesser states are usually ones of psychic malaise and existential pain, dysphoria in myriad forms, from persistent depressions and paralyzing anxieties to distressful self-image issues. On the contrary, the coveted states of consciousness imply relief and emancipation from these painful states.

As a technique of personal change, psychoanalysis undoubtedly holds the record for its tolerance for time in achieving coveted transformations. Its invaluable discoveries, however, opened portals leading to the understanding of the unconscious mind’s fascinating, complex mechanisms [45]. Modern psychotherapies have worked to become more quickly productive. While novel therapies claim faster improvements, the quest for transformative therapeutic results spawns poignant questions: What actualizes systemic personal change? Furthermore, in the context of new insights into neurodynamics, can the revelations gleaned from psychedelic clinical research assist in this task?

To accelerate therapeutic results, innovative approaches are integrating the assistance of augmenting therapies such as medical hypnosis [46], meditation, yoga, and Autogenic Training. These facilitators of well-being and therapeutic change become important in preparing patients for the full potential of their psychedelic experience.

### **ON PREPARING PATIENTS FOR PSYCHEDELIC-ASSISTED THERAPY**

Preparation for psychedelic therapy greatly enhances successful outcomes. In the context of understanding the patient’s psychodynamics and sources of psychic distress, a clear delineation of therapeutic objectives is agreed upon in a collaborative patient/therapist

dyad. Indeed, patients encountering psychedelic-induced confusion, who were then gently refocused on their goals, were invariably returned to calmer, more productive states.

Prior to embarking on psychedelic assistance, it is suggested that patients receive training in a selected mind-body discipline, may it be self-hypnosis<sup>[47]</sup>, yoga, meditative breathing, progressive relaxation, meditation, even Tai Chi and Qigong.

Herewith also suggested is *Autogenic Training*, sometimes called “Western Yoga,” which offers advantages for the fact that it has quantifiable progress objectives. Developed by European clinical researchers more than a century ago, *Autogenics* initially sought to replicate the phenomena observed in deep hypnosis, without the assistance of a hypnotist<sup>[49]</sup>. Deep autonomic nervous system relaxation is a priority goal for this practice, but like other yoga systems of personal growth, it ultimately develops higher ego-syntonic experiences of self<sup>[50]</sup>.

A calm-down may be needed during a psychedelic experience. The therapist, familiar with the patient’s chosen relaxation method, may suggest that it be practiced during the session. The therapist may also propose guided imagery, or a hypnotically induced calming trance state. Very effective are physiological breathing techniques; they, too, will need to be learned by the patient before exploring psychedelic therapy.

## **CONCLUSION**

Acting at the interface of the physical body and its consciousness, psychedelic agents embody unique properties to modulate perception, cognition, mood, and importantly, the experiential configuration of self. Via activation of 5-HT<sub>2A</sub> cortical circuitries and their subcortical ramifications, psychedelics link to the elaboration of sentience. Mounting evidence suggests that the therapeutic effects of psychedelics are connected to their

capacity to stimulate neuroplasticity. The mind-body problem remains unsolved, but the opportunities for its elucidation are ever increasing.

Psychological manifestations of activated 5-HT<sub>2A</sub> circuitry in cortical connectomes manifest as fluidities of selfhood that offer opportunities for accelerated therapeutic transformations. Techniques that develop heightened entente between mind and body easily complement psychedelic psychotherapies. Examples include medical hypnosis, meditation, progressive relaxation, yoga, mindful breathing, and Autogenics.

Psychedelic psychotherapies require planning. An understanding of patients’ psychodynamics and a clarification of objectives increase their productivity and successful outcomes. Embracing the promise of these therapies represents a dynamic movement toward an enlightened vision for their therapeutic promise.

A successful psychedelic experience will be expressed by beneficial ripple effects on several dimensions of functioning in a context of calmer and stronger qualia, all beckoning a brighter, more joyous personal cosmology.

## **AUTHOR INFORMATION**

Gérard Sunnen, MD  
([gsunnen@aol.com](mailto:gsunnen@aol.com))

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# Budding Psychosis: A Case of Tetrahydrocannabinol Precipitating Prolonged Psychotic Episode

Geoffrey Green, D.O. and Gualberto Morco, D.O.

## Abstract

This case report details a 14-year-old African-American male with ADHD who developed substance-induced psychosis and possible early-onset schizophrenia following cannabis use. After presenting with hallucinations, delusions, and aggressive behavior, he was diagnosed and treated in an inpatient psychiatric unit. His treatment included Risperdal, Vyvanse, Clonidine, and Propranolol, leading to some improvement in symptoms. The patient's unstable home environment, history of parental substance abuse and psychiatric illness, and recent traumatic experiences likely contributed to his condition. Despite ceasing cannabis use, the patient continued to experience mild paranoia and disorganization, indicating a complex interplay of genetic and environmental factors in the development of his psychosis. The case underscores the potential for cannabis to trigger psychosis in vulnerable adolescents and highlights the need for further research into these risk factors.

## INTRODUCTION

Schizophrenia, a neurodevelopmental condition characterized by auditory and visual hallucinations, delusions, and negative symptoms, can have a deleterious impact on a patient's functional status. Symptoms typically emerge in the early 20s, with two-thirds of cases presenting between the ages of 20-40<sup>[1]</sup>. The prevalence of this condition is rare, affecting 1-2 people in 10,000 with a lifetime prevalence of 1%.<sup>[1]</sup> Of all cases of schizophrenia, only 4% emerge before the age of 15<sup>[1]</sup>. Cannabis use, particularly at a younger age, has been linked to doubling the risk of future schizophrenia development, with daily use of high-potency THC increasing the risk of psychotic disease development five-fold.<sup>[2]</sup> The prognosis of patients with early-onset schizophrenia is worse than adult-onset. However, an acute onset tends to be more favorable compared to an insidious course<sup>[1]</sup>.

While there have been numerous studies regarding cannabis-induced psychosis, there is a dearth of literature demonstrating cannabis use as a direct instigator for first-episode psychosis and schizophrenia development rather than a risk factor for the future

development of the condition. Here, we present a case of prolonged substance-induced psychosis and possible early-onset schizophrenia with a timeline linking cannabis use and first-episode psychosis together.

## CASE

A 14-year-old African-American male with a history of ADHD presented to the emergency department for concern for hallucinations and delusions. Initial interview revealed he last smoked marijuana seven days prior to his arrival at the emergency department. At that same time, his mother endorsed observing behaviors not typical of the patient developing, including believing someone is going to kill him, claiming to have seen the devil, and endorsing the need to "pay for his sins." His urine drug screen was noted to be positive for THC and amphetamines, which were reasonably explained by his home prescription of Vyvanse. He was uncooperative and aggressive toward emergency department staff, requiring several medications for agitation and restraints. After stabilization, he was then transferred to an inpatient adolescent psychiatric unit with a working diagnosis of

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substance-induced psychosis secondary to cannabis use, first-episode psychosis.

At admission, the patient was unable to give an accurate history. He was acutely anxious with pacing and demonstrated disorganized behavior, randomly pausing to pray and spontaneously doing pushups multiple times during the encounter. He was started on low dose Risperdal 0.5 mg nightly for psychosis with rapid titration to 2 mg twice daily by day 12. On subsequent interviews, his distractibility and impulsivity improved as his home dose of Vyvanse 40 mg daily and Clonidine 0.1 mg nightly was restarted on the second and third day of admission, respectively. With improvement and the ability to participate in interviews in a more organized manner, he was able to endorse symptoms of depression, anxiety with panic attacks, and intermittent suicidal and homicidal ideation without a plan. His delusions continued to vary daily, ranging from perseveration regarding people with cat stickers, breaking up with his “imaginary” girlfriend, and believing he is already dead and therefore does not need to eat. Propranolol 5 mg twice daily was added on day 15 of his hospitalization due to continued anxiety related to his psychosis.

During his admission, it was discovered that his home situation was unstable. The patient’s mother had a history of drug abuse, and the patient had been staying intermittently with his godmother. Additionally, the mother had a history of psychiatric illness with a known prior prescription for Risperdal, though her specific psychiatric diagnosis remained unclear. The patient’s father was reportedly absent as he had been repeatedly jailed for sex-related offenses. Along with housing instability, recent traumatic events were revealed by the patient’s family, including a friend of the patient dying from gun violence and a separate criminal activity completed by a group of children he knew. The family believed the patient may have been aware of information related to this

criminal activity but was afraid of going to the police, fueling significant anxiety in the patient. This had been considered to potentially yield merit as the patient reported auditory and visual hallucinations of sirens and people pointing at him and calling him a “snitch” during his hospitalization.

At the end of his hospital course, he consistently denied having hallucinations but continued to have mild paranoia and disorganization. His final medication regimen at discharge included Risperdal 2 mg twice daily, Propranolol 5 mg twice daily, Clonidine 0.1 mg nightly, and Vyvanse 40 mg daily. Lab evaluation of the patient, including complete blood count, comprehensive metabolic panel, thyroid cascade profile, vitamin B12, antinuclear antibody, rapid plasma reagin, and HIV-1 and HIV-2 antibodies, were unremarkable. The patient was ultimately discharged after 22 days as he no longer demonstrated unsafe behavior on the unit with the coordination of continued care in the outpatient setting.

## **DISCUSSION**

This case highlights a unique instance where cannabis use can be directly traced to the onset of psychosis without remitting symptoms when the substance is no longer being consumed. The patient is suspected to have been at higher risk of developing psychosis and potential schizophrenia due to multiple factors. Of specific interest, he had frequent and early use of cannabis, which has been previously linked to a significantly higher risk of developing schizophrenia, particularly when used before the age of 15 [3]. He additionally has experienced housing instability with suspected other Adverse Childhood Events (ACEs), which approximately two-thirds of patients with schizophrenia have previously reported experiencing and has been linked to varying increased odds of developing the condition depending on exposure type [7, 8].



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Exposure to gun violence, as the patient's family endorsed him experiencing, has been shown to double the odds of reporting future psychotic experiences [9]. Finally, a family history of schizophrenia has been previously established as the strongest single indicator of individual schizophrenia risk, with approximately half of patients with early-onset schizophrenia reporting a family history of schizophrenia in a first or second-degree relative [10,11].

This case suggests that cannabis use puts adolescents at a higher risk of developing substantially long episodes of psychosis and potentially progressing to early-onset schizophrenia at young ages. As cannabis use does not precipitate psychosis and schizophrenia in all adolescent users, it would seem reasonable that there may be biological and social components that place certain individuals at heightened risk. In this case, the patient's combination of genetic risk factors, unstable home environment, and recent traumatic experiences combined with cannabis use are suspected to have increased his risk of experiencing his first psychotic episode. Further research is recommended to better identify which risk factors play a significant role in the development of psychosis and early-onset schizophrenia in the context of cannabis use.

### AUTHOR INFORMATION

Geoffrey Green, D.O.  
([ggreen2@capefearvalley.com](mailto:ggreen2@capefearvalley.com))

Gualberto Morco, D.O.

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## The FDA's Rejection of MDMA-Assisted Psychotherapy for PTSD: A Short-Sighted Decision with Far-Reaching Consequences

Tyler Kjorvestad, MD

The U.S. Food and Drug Administration's (FDA) recent decision to reject MDMA-assisted therapy (MDMA-AT) for the treatment of post-traumatic stress disorder (PTSD) has ignited a robust debate within both medical and psychological communities. This decision, rendered despite promising clinical trial results, underscores a pivotal moment in the evolving landscape of psychedelic medicine. In June 2024, the FDA's advisory committee expressed concerns over the study design, the potential for abuse, and the absence of long-term safety data, leading to a vote not to recommend MDMA-AT, which ultimately came to fruition at the August 2024 meeting<sup>[1]</sup>. The rejection comes at a time when mental health issues, particularly PTSD, are increasingly recognized as major public concerns, with conventional treatments often falling short, especially for severe cases.

In the general population, the lifetime prevalence of PTSD is estimated to be around 7-8%, with women being twice as likely as men to develop the disorder (Kessler et al., 2005). Annually, the incidence rate of PTSD can vary, but it is generally noted that approximately 3.5% of adults in the United States develop PTSD each year<sup>[2]</sup>. The annual economic impact of PTSD in the United States is estimated to be over \$42 billion, including direct medical expenses and indirect costs such as lost wages and decreased productivity<sup>[3]</sup>.

Furthermore, individuals with PTSD have a significantly increased risk of suicide. The lifetime suicide risk for individuals with PTSD is significantly higher than for the general population, with PTSD patients being up to six times more likely to attempt suicide<sup>[4]</sup>. Both the economic impact and elevated suicide risk necessitate the need for effective

interventions and support systems to adequately and effectively treat PTSD.

The treatment options for PTSD are limited and often inadequate for severe cases. Conventional treatments such as Selective Serotonin Reuptake Inhibitors (SSRIs), cognitive behavioral therapy (CBT), and prolonged exposure therapy are typically most helpful in mild to moderate PTSD and have diminishing returns in more severe and refractory PTSD patients<sup>[5]</sup>.

Additionally, the infrastructure supporting mental health treatment is under siege. Physician and nursing shortages, coupled with the underfunding of mental health services, only compound the issues of ineffective medication and psychotherapy options. MDMA, when used in a controlled therapeutic setting, has shown remarkable results in reducing symptoms of PTSD. MDMA facilitates the therapeutic process by reducing fear and defensiveness, allowing patients to revisit and process traumatic memories more effectively<sup>[6]</sup>. The drug's ability to enhance empathy and trust between the patient and the therapist provides a unique therapeutic benefit unachievable in traditional psychotherapy alone.

In a phase 3 trial, 86.5% of MDMA-AT participants demonstrated clinically meaningful improvement. Moreover, 71.2% of MDMA-AT participants no longer met DSM-5 criteria for PTSD by the study's end. The treatment led to more significant reductions in CAPS-5 scores and improved functional impairment as measured by the Sheehan Disability Scale<sup>[7]</sup>.

In contrast, SSRIs such as sertraline and paroxetine are commonly prescribed for PTSD, with studies suggesting that about 20-

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30% of patients achieve complete remission with these antidepressants alone <sup>[8,9]</sup>. While SSRIs can help reduce symptoms, they are often more effective when combined with psychotherapy. Trauma-focused therapies like Cognitive Behavioral Therapy (CBT) and Eye Movement Desensitization and Reprocessing (EMDR) have shown higher remission rates compared to antidepressants alone, ranging from 30% to 50%, with some studies reporting even higher rates depending on the duration and intensity of the therapy <sup>[10,11]</sup>. Combining antidepressants with psychotherapy often yields better outcomes than either treatment alone, with remission rates around 40-60% <sup>[12]</sup>. This combination approach, which is even more effectively demonstrated in MDMA-AT, highlights how leveraging the strengths of both pharmacological and psychological interventions provides a more comprehensive treatment strategy for patients suffering from PTSD.

## **CONCLUSION**

MDM-AT produces improvements beyond the standard of care for patients suffering from PTSD. MDMA-AT leverages MDMA's capacity to enhance empathy, trust, and emotional openness, facilitating a therapeutic process that traditional talk therapies might not <sup>[6]</sup>. The FDA's decision to not approve MDMA-AT affects patients' immediate access to a transformational treatment option and also sends a chilling message regarding the regulatory hurdles for psychedelic therapies. The rejection of MDMA-assisted therapy leaves a significant gap in treatment options, potentially condemning many to prolonged suffering or reliance on less effective or more side-effect-laden treatments. The medical community, policymakers, and patient advocates must continue to push for a reevaluation of MDMA-AT.

## **AUTHOR INFORMATION**

Tyler Kjorvestad, M.D.  
([tkjorvestad@kumc.edu](mailto:tkjorvestad@kumc.edu))

Kjorvestad, T. (2024, September). The FDA's Rejection of MDMA-Assisted Psychotherapy for PTSD: A Short-Sighted Decision with Far-Reaching Consequences. *The Journal of Psychedelic Psychiatry*, 6(3).

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