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DMT: Mechanisms, Psychological and Physiological Effects, and Its Dual Role as a Drug of Abuse and Potential Health Benefit

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Introduction

N, N-Dimethyltryptamine (DMT) is a Schedule I prototypical indolethylamine hallucinogen that can be consumed orally, smoked, vaporized, injected intravenously, or snorted.[1,2] Being a Schedule I drug, this indicates that it's deemed to have a high potential for abuse and no accepted medical use. This substance is found in various plants, animals, and regions of the human body, including the brain, blood, urine, and cerebral spinal fluid.[2] DMT is a part of traditional South American snuffs and brewed drinks such as Ayahuasca.[1] In 1931 Canadian chemist, Richard Manske first synthesized DMT. [2] Later in 1946, microbiologist Oswaldo Gonçalves de Lima discovered its natural occurrence in certain plants. [2] It wasn't until 1956 that a Hungarian chemist and psychiatrist Stephen Szara revealed DMT's hallucinogen properties by extracting it from the plant Mimosa hostilis and self-administering it via intramuscular injection. [2] This pivotal discovery enabled scientists to explore how DMT alters human perception, emotion, and cognition. Following the discovery of its hallucinogenic properties, DMT gained significant popularity in the 1960s and was widely abused due to its intense effects and short duration of action.[1]

Mechanism of Action

DMT (N N-Dimethyltryptamine) primarily exerts its effects by acting on the serotonin receptors in the brain, particularly the 5-HT2A receptor. [3] Upon administration, DMT crosses the

blood-brain barrier and binds to these receptors, in the prefrontal cortex and other regions involved in sensory perception, cognition, and mood regulation. The activation of 5-HT2A receptors leads to a cascade of intracellular events, including increased release of glutamate, a key excitatory neurotransmitter. [3] This heightened glutamatergic activity contributes to the profound alterations in sensory perception and consciousness that characterize the DMT experience. Additionally, DMT's structural similarity to serotonin allows it to interact with other serotonin receptor subtypes, further modulating neural activity and contributing to its psychoactive effects. [4] The rapid onset and short duration of DMT's effects are likely due to its quick metabolism by the enzyme monoamine oxidase (MAO), which breaks down DMT into inactive metabolites. [4]

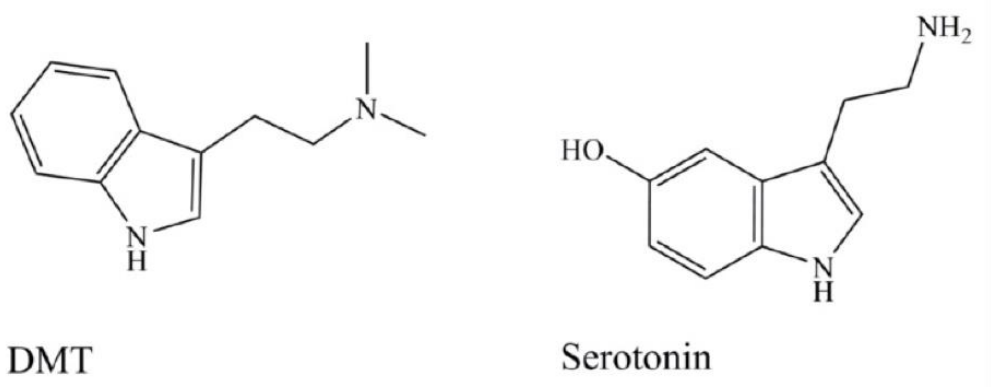

Figure 1: DMT (N, N-Dimethyltryptamine) and Serotonin Chemical Structures

https://europepmc.org/article/med/29366418

Psychological and Physiological Effects

DMT induces vivid visual and auditory hallucinations, complex geometric patterns, and encounters with autonomous entities, making users feel as if they have entered an alternate reality.

[5] These experiences often cause deep emotional responses, ranging from euphoria and a sense of oneness with the universe to fear and existential dread. [5] Users frequently describe a dissolution of the ego, leading to a temporary loss of self, which can be both enlightening and challenging. [5,6] When smoked or vaporized, the psychological effects typically occur rapidly, within seconds to minutes, lasting for around 15 to 30 minutes. But they can extend to several hours in ayahuasca ceremonies in combination with an MAO inhibitor. [6] Physiologically, DMT can cause increased heart rate and blood pressure, pupillary dilation, involuntary muscle movements, and sensations of bodily warmth or coldness. Gastrointestinal disturbances such as nausea are common, especially with oral consumption. [6,7] Despite these acute effects, DMT is generally considered to have a low toxicity profile. It does not produce significant long-term physiological harm, though its intense nature can lead to psychological distress or exacerbate existing mental health conditions in some individuals.

Risk and side effects

N, N-Dimethyltryptamine (DMT) impacts individuals differently based on factors like body size, weight, health, previous drug use, concurrent drug consumption, dosage, drug potency, and the environment. [8] This drug specifically can induce several risks and side effects that can be severe, particularly at higher doses. DMT, like all drugs, can cause both short-term and long-term

side effects, some of which may be dangerous. Short-term effects experienced during and immediately after use include increased heart rate, elevated blood pressure, dizziness, heart palpitations, dilated pupils, lack of coordination, agitation, nausea, loss of appetite, and even seizures, since DMT causes neurons of the brain to release serotonin. Excessive use of DMT, or combining it with other serotonin-containing drugs, can lead to serotonin syndrome that includes dry mouth and the previously mentioned (agitation, dilated pupils, confusion) and more. [9] The long-term effects are not well understood due to limited research, but users have reported experiencing psychotic-like episodes (flashbacks), which can occur days, weeks, or even months after the initial use.[10] Additionally, according to data from the Drug Enforcement Administration (DEA) and the American Association of Poison Control Centers (AAPCC), particularly in higher doses, it has been linked to severe adverse effects, including cardiac and respiratory arrest.[1] These risks and side effects highlight the potent nature of DMT being experienced in different magnitudes between users, which mandates more research being carried out on its effects, especially the long-term ones.

Potential Therapeutic Uses

Research into the therapeutic effects of DMT (N, N-Dimethyltryptamine) suggests it holds promise across various mental health treatments. It affects several key areas of the brain, primarily through its interaction with serotonin receptors, especially 5-HT2A receptors.[11] This interaction leads to profound alterations in brain activity, disrupting the default mode network involved in introspection and self-referential thoughts.[12] DMT shows potential in alleviating treatment-resistant depression and anxiety disorders by inducing profound mystical experiences that may

help patients confront and process trauma and existential distress.[13] Additionally, DMT-assisted therapy has shown promise in addiction treatment by facilitating insights that support recovery from substance abuse.[14] Its effects on neuroplasticity hint at potential applications in cognitive enhancement and treating neurodegenerative disorders.[15] Moreover, DMT's ability to induce spiritual experiences fosters personal growth and introspection, offering therapeutic benefits beyond conventional psychiatric approaches.[16] Ongoing research aims to clarify its therapeutic mechanisms and establish safe and effective protocols amidst legal and ethical considerations surrounding its use.

Legal Status and Safety

N, N-Dimethyltryptamine (DMT) is classified as a Schedule I substance in many regions, including the United States, signifying its high potential for abuse and lack of recognized medical use. This classification restricts research and therapeutic applications, though recent studies suggest DMT's promise in treating mental health disorders like depression and addiction.[18] Safety concerns are crucial due to DMT's intense psychoactive effects, such as hallucinations and significant changes in perception.[19] Physiological effects like increased heart rate and blood pressure pose risks for individuals with cardiovascular conditions.[19] While acute toxicity is low, improper use can lead to severe adverse effects, including serotonin syndrome when combined with other serotonergic substances.[19] To reduce these risks, DMT must be administered properly in a controlled setting, with strict safety rules and public education on responsible usage. Reviewing DMT’s legal status and expanding research opportunities are critical for discovering

its therapeutic potential while managing its risks.[20] Balancing regulation and research will help us better understand DMT's dual role as both a drug of abuse and a potential therapeutic agent.

Discussion

The exploration of N, N-Dimethyltryptamine (DMT) reveals a complex profile of both risks and potential benefits. The psychological effects of DMT, characterized by intense hallucinations and profound emotional experiences, suggest a significant impact on human cognition and perception. These effects, while offering potential therapeutic benefits, particularly in mental health treatment, also pose risks of psychological distress and exacerbation of existing mental health conditions. The physiological impacts showing a low toxicity profile include acute effects like increased heart rate and blood pressure that could be dangerous for individuals with preexisting conditions. Its severe adverse effects at higher doses emphasize the importance of controlled usage. Despite the historical context of DMT abuse, its potential for therapeutic applications, especially in treatment-resistant depression, anxiety disorders, and addiction, has sparked a new interest in research. Because DMT can be both a helpful treatment and drug abuse, we need a balanced approach to its study, regulation, and use.

Conclusion

DMT stands at the intersection of being a drug of abuse and a promising therapeutic agent, which calls for a detailed understanding of its mechanisms, effects, and applications. Societally, the therapeutic use of DMT could transform the treatment of certain mental health conditions, offering hope to individuals who have not responded to traditional therapies. Economically, this

could reduce healthcare costs associated with chronic mental health issues and addiction, along with the potential for a new area in the pharmaceutical market focused on psychedelics. Epidemiologically, while DMT use is currently limited, increased awareness and potential therapeutic legalization could influence its prevalence and patterns of use. Legally, the current Schedule I classification of DMT presents a significant barrier to research and therapeutic use. A shift towards a stricter regulatory framework and rigorous safety protocols could facilitate scientific exploration and controlled therapeutic application. Safety remains crucial, with the need for well-designed clinical trials to establish effective dosages, administration methods, and monitoring protocols to reduce risks. While DMT's intense psychoactive properties require careful management, its potential therapeutic benefits warrant rigorous scientific investigation and thoughtful consideration in healthcare and policymaking.

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