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CURRENT VIEWS OF PSYCHEDELICS AND THEIR CONNECTION TO WELL-BEING

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ABSTRACT

This article provides an overview of the current views on psychedelics and explores their connection to well-being based on scientific research and anecdotal evidence. The article begins by examining the historical context of psychedelics. It then delves into the subsequent prohibition and resurgence of scientific interest in psychedelics, highlighting key studies that have shaped our understanding of their effects. The discussion then shifts to contemporary research on psychedelics, particularly focusing on their therapeutic potential in treating mental health conditions such as depression and anxiety. Studies utilizing psychedelics have shown promising results in facilitating transformative experiences and catalyzing lasting psychological benefits. Moreover, the article examines the neurobiological mechanisms underlying the effects of psychedelics, shedding light on how they modulate brain activity and alter perception. In addition to clinical applications, the article explores the growing interest in the potential of psychedelics to enhance well-being in healthy individuals. Anecdotal reports and preliminary research suggest that these substances may induce positive changes in personality traits, attitudes, and behaviors, leading to increased life satisfaction and a greater sense of connectedness with oneself, others, and the natural world. Lastly, the article discusses the public perception of psychedelic substances, the challenges, and the future directions in psychedelic research, including the need for rigorous clinical trials, the development of safe and responsible guidelines for their use, and the exploration of novel therapeutic approaches that integrate psychedelic experiences into psychotherapy.

KEYWORDS: *psychedelics, neuroplasticity, mental health, well-being, substance use, neuropsychopharmacology, therapeutic applications*

Psychedelics, a class of substances known for their profound effects on perception, cognition, and emotions, have gained increasing attention in recent years due to their potential therapeutic applications and their association with enhanced well-being. Throughout history, natural psychedelics derived from plants, like psilocybin (found in certain species of mushrooms), have been utilized for medicinal purposes. Following the publication of the initial report on lysergic acid diethylamide (LSD) in the English language in 1950, psychedelics briefly became intertwined with the fields of psychology and psychiatry [*Carhart-Harris RL, Goodwin GM, 2017*]. They were particularly explored as adjuncts to psychotherapy for addressing mood disorders and alcohol addiction, showing promising therapeutic potential. However, the progress of psychedelic research was curtailed in the mid-1960s due to restrictive legislation, effectively terminating most major research programs

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focused on these substances [*Grinspoon L, Bakalar JB, 1979*]. Over the past decade and a half, there has been a resurgence of scientific interest in studying psychedelic substances like LSD and psilocybin. These substances have gained recognition in clinical research, demonstrating potential benefits for mental health. Both in the general population as well as among individuals with various psychiatric conditions, there is evidence of notable improvements in mental well-being following a psychedelic experience. However, mental well-being is a multifaceted concept with intricate dimensions, and its significance extends beyond individual welfare to socioeconomic factors.

Recent findings regarding the positive impact of psychedelics on mental well-being suggest that these substances can have broad-ranging effects that are robust and long-lasting. Studies have demonstrated that substances such as LSD, psilocybin, and ayahuasca can induce profound and transformative experiences that can lead to lasting improvements in mental health outcomes. One of the remarkable aspects of psychedelics is their ability to produce robust and enduring effects on mental well-being [*Mans K et al., 2021*]. Unlike traditional psychiatric medications that often require regular and ongoing use, psychedelics have been found to elicit therapeutic benefits even after a single or limited number of doses. Participants in clinical trials and research studies have reported sustained improvements in mood, reduced symptoms of depression and anxiety, increased emotional openness, and enhanced overall well-being for weeks, months, or even years following a psychedelic experience [*Griffiths R et al., 2016*]. This suggests that the effects of these substances can be profound and long-lasting. The mechanisms underlying the positive impact of psychedelics on mental well-being are still being elucidated [*De Gregorio D et al., 2021*]. It is believed that these substances work by modulating serotonin receptors in the brain, particularly the 5-HT2A receptor, which is involved in various cognitive and emotional processes [*Vollenweider FX et al., 2007*]. Psychedelics are thought to induce a state of heightened plasticity and increased neural connectivity, allowing for novel perspectives, insights, and emotional processing. They can facilitate a deep exploration of one's thoughts, emotions, and beliefs, leading to a sense of self-reflection, personal growth, and the potential for transformative experiences. Moreover, the therapeutic benefits of psychedelics are not limited to specific mental health conditions. Research has shown their potential efficacy in treating a range of disorders, including treatment-resistant depression, anxiety disorders, post-traumatic stress disorder (PTSD), addiction, and existential distress in patients with life-threatening illnesses [*Tupper KW et al., 2015*]. These substances offer a unique approach to therapy by addressing the underlying psychological and existential aspects of these conditions rather than solely alleviating symptoms. However, it is important to note that the use of psychedelics for therapeutic purposes should be approached with caution and conducted under the guidance of trained professionals in controlled settings. Psychedelic-assisted therapy typically involves careful preparation, integration, and support to optimize the benefits and minimize potential risks.

In addition, when individuals approach the use of psychedelic compounds with a prior intention or purpose, such as for therapeutic or self-explanatory reasons, they are more likely to experience significant improvements in their mental well-being [*Gasser P et al., 2015*]. The exact mechanisms behind these positive effects are still being explored, but research suggests that psychedelics may promote neuroplasticity, enhance emotional processing, and facilitate introspection and self-reflection, and these substances have shown promising results in the treatment of various mental health conditions, including depression, anxiety, and PTSD [*Hasler, 2020*]. In terms of public policy implications, the growing body of research on psychedelics and their potential therapeutic benefits has sparked discussions and debates. Some argue for the need to reconsider existing drug policies and regulations to allow for expanded research and therapeutic applications. They advocate for a more evidence-based approach that acknowledges the potential benefits of these substances while ensuring appropriate safeguards and regulations are in place. Others express concerns about the potential risks and misuse associated with psychedelics, emphasizing the need for careful regulation and controlled access. They argue for a cautious approach that balances the potential benefits with the impor-

tance of public safety and preventing harm [*Mans K et al., 2021*]. Overall, the discussion of public policy implications surrounding psychedelics revolves around finding a balance between promoting research and therapeutic use while addressing potential risks and ensuring public safety. This ongoing conversation highlights the need for further scientific inquiry, rigorous clinical trials, and thoughtful policy considerations to fully understand and harness the potential benefits of psychedelics for mental well-being.

It is essential to have an in-depth examination of various potential mechanisms, analyzed from multiple perspectives, that contribute to the impacts and therapeutic possibilities associated with psychedelics. At the biochemical level, psychedelics primarily affect the 5-HT2A receptor, which is a subtype of serotonin receptor that is thought to play a crucial role in the psychedelic experience [*Passie T et al., 2008*]. Psychedelics such as psilocybin, LSD, and N,N-dimethyltryptamine (DMT) bind to and activate this receptor, leading to various psychotropic effects. When psychedelics such as psilocybin, LSD, and DMT interact with the 5-HT2A receptor, they initiate a cascade of effects within the brain that contribute to the unique and profound experiences associated with these substances [*López-Giménez JF, González-Maeso J, 2018*]. The 5-HT2A receptor is a subtype of the serotonin receptor family that is predominantly found in regions of the brain associated with perception, cognition, and mood regulation. Activation of the 5-HT2A receptor by psychedelics leads to alterations in neurotransmitter signaling, particularly with serotonin, which is involved in regulating various physiological and psychological processes [*Zhang G, Stackman RW Jr, 2015*]. By binding to and activating the 5-HT2A receptor, psychedelics modulate the release and uptake of serotonin in the brain. This results in an increased availability of serotonin and enhanced transmission of signals along serotonin pathways. These changes in serotonin signaling are believed to contribute to the characteristic effects of psychedelics, including changes in perception, sensory experiences, thought patterns, emotions, and consciousness. The activation of the 5-HT2A receptor by psychedelics triggers a cascade of downstream effects, including the activation of other neurotransmitter systems such as glutamate and dopamine. These interactions between different neurotransmitter systems contribute to the complex and multifaceted nature of the psychedelic experience. Furthermore, the precise mechanisms underlying the psychotropic effects of psychedelics are still not fully understood. It is believed that the activation of the 5-HT2A receptor leads to increased neuronal excitability, alterations in neural network connectivity, and changes in information processing within the brain. These changes may promote a state of heightened plasticity and allow for the emergence of novel connections and perspectives, leading to the unique and often transformative experiences reported by individuals who have taken psychedelics [*Vollenweider FX, Kometer M, 2010*].

Psychedelics increase neuroplasticity, which refers to the brain's ability to reorganize and form new connections between neurons. Research suggests that psychedelics may enhance neuroplasticity, which could potentially contribute to the therapeutic effects observed in conditions such as depression and mood disorders [*Olson, 2018*]. While research suggests that psychedelics can promote neuroplasticity and have therapeutic potential in certain areas, it's important to approach claims about their transformative and brain-enhancing effects with caution. Studies have indicated that psychedelics, such as psilocybin and MDMA (commonly known as ecstasy), may assist in overcoming fear and anxiety associated with past traumatic experiences. These substances have been explored as adjuncts to psychotherapy, showing promise in facilitating emotional breakthroughs and promoting healing in individuals with conditions like PTSD [*Elsouri KN et al., 2022*]. However, it's important to note that the extent of these effects and their generalizability to the average person's mental circuitry are still not well understood. Research has primarily focused on clinical populations and controlled settings, which may not fully reflect real-world scenarios. The response to psychedelics can vary widely among individuals, and factors such as mindset, environment, and individual differences can influence the outcomes of psychedelic experiences [*Garel N et al., 2023*]. Moreover, there is a need for more rigorous research on the long-term effects and potential risks associated with psychedelics. While the current body of evidence suggests

that psychedelics can be relatively safe when used responsibly and under professional guidance, there are concerns that certain individuals may be susceptible to adverse reactions or psychological distress during or after psychedelic experiences. Pre-existing mental health conditions, vulnerable personality traits, or a history of psychosis are some factors that may increase the risk of negative outcomes [*Schlag A, et al., 2022*]. Furthermore, claims about the cognitive-enhancing effects of psychedelics should be viewed with skepticism. While some anecdotal reports and preliminary research suggest possible cognitive benefits, such as increased creativity or enhanced problem-solving abilities, the evidence in this area is limited. It is crucial to differentiate between short-term perceptual and cognitive alterations experienced during the acute effects of psychedelics and long-term cognitive enhancement or changes in mental circuitry [*Nutt D, Carhart-Harris R, 2021*].

Psychedelics offer a critical period for social reward learning. Studies have indicated that psychedelics may create a "critical period" during which individuals are more receptive to social rewards, and this heightened sensitivity can potentially facilitate transformative experiences and promote positive changes in social behavior and relationships [*Nardou R et al., 2023*]. There is a connection between the restoration of social reward learning in adulthood and the re-establishment of oxytocin-mediated long-term depression in a specific brain region called the nucleus accumbens. The nucleus accumbens is a part of the brain that is associated with reward and motivation. It plays a crucial role in processing social rewards, such as social interactions and positive social experiences. Oxytocin, often referred to as the "love hormone," is a neuropeptide that is involved in social bonding, trust, and social reward processing. It is released in response to positive social interactions and contributes to feelings of bonding and connection. The term "metaplastic restoration" refers to the idea that there is a process of restoring or reestablishing a form of synaptic plasticity called long-term depression (LTD) in the nucleus accumbens. Synaptic plasticity refers to the ability of the connections between neurons to change and adapt in response to experience and learning. Long-term depression specifically refers to a weakening or decrease in the strength of synaptic connections over an extended period of time. The statement suggests that the ability to reinstate or restore social reward learning in adulthood is associated with the reestablishment of oxytocin-mediated long-term depression in the nucleus accumbens. This implies that changes in the neural circuitry and synaptic connections within the nucleus accumbens, specifically involving the release and effects of oxytocin, play a role in the restoration of social reward processing and learning in adulthood [*Musardo S et al., 2022*]. However, it's important to note that the specific mechanisms and processes involved in this metaplastic restoration are still not fully understood. Further research is needed to explore the intricate interactions between oxytocin, synaptic plasticity, and social reward learning in the nucleus accumbens to gain a more comprehensive understanding of this phenomenon.

Psychedelics also have anti-inflammatory properties. Some studies have found evidence suggesting that psychedelics possess anti-inflammatory properties, and this could be relevant to their potential therapeutic applications, as inflammation has been implicated in various psychiatric disorders [*Flanagan TW, Nichols CD, 2018*]. While traditionally known for their psychoactive and perceptual effects, psychedelics have also been found to exhibit anti-inflammatory properties. Inflammation is a natural immune response that occurs in the body as a defense mechanism against harmful stimuli, such as infections or tissue damage. However, chronic or excessive inflammation can contribute to the development and progression of various diseases, including autoimmune disorders, neurodegenerative conditions, and mood disorders. Recent research has suggested that certain psychedelics, such as psilocybin and LSD, may have anti-inflammatory effects. These substances have been shown to modulate the activity of the immune system and reduce the production of pro-inflammatory molecules [*Nichols DE et al., 2017*]. For example, studies have demonstrated that psilocybin can suppress the release of pro-inflammatory cytokines, which are signaling molecules involved in the inflammatory response. In addition, psychedelics may influence the activity of immune cells, such as macrophages and microglia, which play a crucial role in the regulation of inflammation in the body. The anti-inflammatory properties of psychedelics are thought to be medi-

ated by their interaction with various receptors and neurotransmitter systems in the brain [*Vorobyeva N, Kozlova AA, 2022*]. For instance, activation of the serotonin 5-HT2A receptor, which is a primary target for many psychedelics, can modulate immune responses and inflammation. It's important to note that while the anti-inflammatory effects of psychedelics show promise, more research is needed to fully understand the underlying mechanisms and their potential therapeutic implications. Clinical trials are currently underway to explore the potential of psychedelics in the treatment of conditions characterized by inflammation, such as depression, PTSD, and cluster headaches [*Sarris J et al., 2022*].

At the neural level, psychedelics have been associated with reduced efficacy of thalamo-cortical filtering, which refers to the brain's ability to regulate sensory information processing. Psychedelics have been found to disrupt this filtering mechanism, leading to an increased flow of sensory information to the cortex, which may contribute to the sensory distortions and heightened perception experienced during psychedelic states [*van Elk M, Yaden DB, 2022*]. When we perceive the world around us, our brain filters and processes incoming sensory information to create a coherent and manageable experience. This filtering mechanism allows us to focus on relevant stimuli while ignoring irrelevant or unnecessary sensory input. However, psychedelics have been found to disrupt this filtering mechanism, leading to an increased flow of sensory information to the cortex. The cortex is the outer layer of the brain responsible for higher-order cognitive functions, including perception, thinking, and consciousness. Individuals under the influence of psychedelics often experience sensory distortions and heightened perception. These effects can manifest in various ways, such as visual hallucinations, intensified colors, enhanced patterns, or increased sensitivity to sounds and textures. The amplification of sensory input can create an overwhelming and immersive experience, leading to a sense of expanded consciousness and altered perception of time and space [*Dos Santos RG et al., 2018*]. It is important to note that the specific effects of psychedelics on sensory processing can vary widely between individuals and depend on factors such as dosage, set (mindset and expectations), and setting (environment and social context) [*Aixalà M et al., 2018*]. Additionally, the overall subjective experience during a psychedelic state is influenced by a multitude of other factors, including personal disposition, mental state, and previous experiences. Understanding how psychedelics affect sensory processing and perception is an active area of research. Advances in neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and electroencephalography (EEG), have provided insights into the neural correlates of psychedelic experiences. These studies aim to unravel the complex interactions between psychedelics, brain networks, and subjective experience [*Mertens LJ, Preller KH, 2021*].

Psychedelic drugs have the potential to bring about enduring changes in behavioral patterns, learning abilities, and sensory functions that are typically affected in mental health conditions, suggesting that these drugs could offer a novel approach to treating and managing such conditions. Psychedelic substances like psilocybin, LSD, and MDMA have been a subject of growing interest in the field of mental health research. Studies have shown promising results in using these drugs to alleviate symptoms of various mental health disorders, including depression, anxiety, PTSD, and addiction [*Bogenschutz MP et al., 2015*]. The mechanism through which psychedelic drugs produce these therapeutic effects is not yet fully understood. Despite the potential benefits, it's important to note that the research on psychedelic drugs is still in its early stages, and further investigation is needed. Scientists emphasize the need for more rigorous studies to determine the safety, efficacy, and optimal dosage protocols for using these substances as therapeutic tools [*Barnes, 2003*]. Additionally, understanding the specific ways in which these drugs remodel brain connections will be crucial for developing targeted treatments for mental health conditions [*Reardon, 2023*]. Some current studies are aiming to delve deeper into the potential mental health benefits and associated outcomes of naturalistic psychedelic use. Previous research conducted through surveys had suggested that individuals who engaged in such use experienced positive effects on their mental well-being, similar to those observed in controlled clinical trials. However, the current study sought to provide further evidence and validation by examining a larger group of individuals who had re-

ported lifetime psychedelic experiences [*Cook N et al., 2015*]. According to Raison et al. (2022), one cross-sectional online survey was conducted, involving 2,510 adults who had at least one psychedelic encounter in their lifetime. This methodology allowed researchers to collect information from a diverse range of participants and obtain a snapshot of their experiences and perceptions related to psychedelic use. One unique aspect of this study was the exploration of the relationship between the amount of psychedelic use and behavioral outcomes. By examining the frequency and intensity of psychedelic use, researchers aimed to identify any potential correlations or patterns between usage levels and subsequent effects on behavior. Additionally, the study aimed to investigate the frequency of negative experiences or harms associated with psychedelic use. This aspect of the research aimed to provide a more comprehensive understanding of the potential risks and drawbacks that individuals might encounter when engaging in psychedelic experiences. Overall, the study sought to contribute to the existing body of knowledge on naturalistic psychedelic use and its impact on mental health and well-being. By utilizing a large sample size and incorporating novel aspects of analysis, the researchers aimed to provide valuable insights for both the scientific community and individuals interested in this subject matter [*Raison CL et al., 2022*].

The Hill-HarrisX poll in 2021 provides interesting insights into the American public perception of psychedelic substances and their medical potential. The results show a clear divide among voters regarding the perceived medical uses of psychedelics, particularly “magic mushrooms.” As shown in the research The Hill-HarrisX poll presents 1899 registered voters between May 21-23, 2021, the majority opinion, held by 65 percent of registered voters surveyed, is that psychedelic substances do not have medical applications. This indicates a prevailing skepticism or lack of awareness about the therapeutic properties of these substances. On the other hand, a significant minority, comprising 35 percent of voters, believes that psychedelic substances do possess medicinal benefits. One notable trend observed in the poll is the difference in opinions between age groups. Younger voters, specifically those aged 18-29, were more likely to recognize the potential medical uses of psychedelic substances. Among this age group, 53 percent agreed that “magic mushrooms” have medicinal benefits. In contrast, voters aged 30 and above were more inclined to perceive these substances as lacking medical utility [*The Hill, 2021*].

The generational difference in attitudes towards psychedelic substances may reflect evolving cultural perspectives and increased exposure to scientific research highlighting their therapeutic potential. Younger individuals may have greater access to information and be more open to alternative approaches to healthcare, leading to a higher acceptance of psychedelic substances as potential medical treatments [*Li I et al., 2023*]. These poll findings shed light on the public perception of psychedelic substances and can be valuable for understanding societal attitudes towards their legalization, regulation, and potential integration into healthcare systems. As the field of psychedelic research continues to grow, it will be interesting to observe how public opinion evolves and impacts future discussions and policies related to these substances [*Buranyi, 2015*].

Understanding the perspectives of individuals utilizing mental health services towards psychedelics and psilocybin therapy is crucial for comprehensive exploration. In another study published in the Irish journal of medical science in 2022, most people surveyed or studied expressed support for further research into the use of psilocybin therapy. Younger individuals were more likely to have positive views on psilocybin therapy. This could be attributed to a variety of reasons, such as greater openness to alternative treatments, increased exposure to discussions on psychedelic research and its potential benefits, and a general tendency among younger generations to question traditional approaches to mental healthcare. Also, those who had prior experience with recreational psychedelics were more inclined to support psilocybin therapy, suggesting that personal encounters with psychedelics may have influenced their perceptions and beliefs regarding the therapeutic potential of psilocybin. In addition, individuals with non-religious beliefs showed a higher likelihood of favoring psilocybin therapy. This correlation might be linked to the fact that some religious traditions hold conservative views on drug use, including psychedelics, which could influence attitudes to-

wards their therapeutic application [*Corrigan K et al., 2022*]. Overall, these findings provide insights into the demographic and experiential factors that may shape attitudes towards psilocybin therapy, and understanding these factors can help researchers and practitioners better tailor their approach and education efforts when exploring the potential benefits of psilocybin therapy for mental health treatment.

In summary, the emerging evidence suggests that psychedelic substances hold promise for inducing lasting changes in behavioral, learning, and sensory systems affected by mental health disorders. It is important to note that while initial findings are promising, further research is needed to fully understand the mechanisms underlying therapeutic effects of psychedelics on behavioral, learning, and sensory systems. Clinical trials are currently underway to investigate the safety and efficacy of psychedelics in the treatment of various mental health disorders, including depression, anxiety, and substance use disorders [*Sousa TR et al., 2022*]. Additionally, the therapeutic use of psychedelics is typically accompanied by a comprehensive and supportive therapeutic framework. This includes a carefully controlled environment, skilled therapists, and integration of experiences into the individual's daily life. The integration process allows individuals to make meaning of their psychedelic experiences and apply any insights gained to promote lasting positive changes. However, more research is required to fully comprehend their mechanisms of action and to establish their potential as safe and effective treatments in clinical settings [*Nutt DJ et al., 2010*]. This article presents a comprehensive overview of the current perspectives on psychedelics and their connection to well-being. While further research is warranted, the accumulating evidence suggests that psychedelics hold great promise as transformative tools for therapy and personal growth, offering new avenues for understanding consciousness and promoting mental health and well-being.

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