

Explore the effect of psilocybin on depression and anxiety

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Abstract:

Psilocybin, also known as “magic mushrooms,” is naturally found in psychedelic compound from different types of mushrooms. The utility of psilocybin for spiritual and therapeutic purposes has already go through several centuries. Scientific research on these compounds gained traction in the mid-20th century, the increasing interest in the possible therapeutic benefits of psilocybin has led to more discoveries, including its use in the treatment of major depression disorder, anxiety disorder, addiction, and end-of-life distress. Research on the effects and safety of psilocybin is ongoing, but preliminary studies have shown promising results. Psilocybin has the potential to revolutionize the way we treat mental health disorders and support overall well-being. Sewell and colleagues suggest that for patients with cluster headaches, psilocybin could make an effective use in the cure or prevention of the regular appearance of cluster headaches. Other than this exciting exploration, treatment of depression and anxiety disorder is also worth discussion. This essay suggests that psilocybin is useful in depression treatment, and is more suitable as a preventive rather than a therapeutic drug in the course of treatment.

Keywords: Psilocybin, psychedelics, depression, anxiety, pathology.

1. Introduction

Psilocybin, also known as “magic mushrooms,” is naturally found in psychedelic compound from different types of mushrooms. The term “psilocybin” is sometimes used interchangeably with the term “psychedelics”, referring to a wider range of substances that produce similar psychoactive effects. It has been used for centuries in various cultures for spiritual and therapeutic purposes. There are two main structural

categories of psychedelics: indoleamines: for example DMT, psilocybin, LSD, and phenylalkylamines: for example mescaline and DOI. Psilocybin is currently a hot topic among scientists for its potential use as a research tool to better understand psychosis and for its possible therapeutic benefits. Psilocybin might have the ability to totally change the way we treat mental health disorders and support overall well-being. Is psilocybin useful in depression treatment? How should we use it in order to make it the

most sufficient?

2. History of Psilocybin

2.1 History

Psilocybin is the main active compound of many species of the genus *Psilocybe*, commonly referred to as “magic mushrooms.” Hallucinogens can be classified into four broad groups based on their pharmacological properties: serotonin 2A (5-HT_{2A}) receptor agonists, empathogens or entactogens, dissociative narcotic psychedelics (NMDA misfits), and atypical stimulants, which have a wide range of neurotransmitter structural effects. Commonly referred to as “shrooms” or “magic mushrooms”, psilocybin will be able to produce a wide range of hallucinogenic effects: distorted perception of sights and sounds, loss of sense of time and space, and intense emotions ranging from joy to terror. Side effects like nausea or heart rate increasing sometimes occurs with them. The strength and time period of the effects of psilocybin are different between people, and is depended on other variables such as the dosage of the drugs, the setting of the environment, and the individual’s physiology (NIDA, 2024). These different hallucinogens have different mechanisms of action, producing distinct effects on the brain and body (Goldberg et al., 2020). What’s more, militaries took use of the potential use of psychedelics for various purposes, too. The reasons are not difficult to imagine: enhancing performance, suppressing fear, and even as a form of chemical warfare. The early research on psychedelics, particularly LSD, was initially conducted by the U.S. Army and the CIA in the 1950s and 1960s. The CIA’s MKUltra program investigated the effects of LSD as a mind-control agent, while the Army’s Special Operations Division experimented with the drug as a truth serum and a potential incapacitating agent (Gepfert, 2022). The current state of modern research on psilocybin has revealed significant therapeutic potential.

Psilocybin has been studied in the field of pharmacology because of the potential therapeutic use of it in several disorders, including depression, anxiety, addiction, and cluster headaches. As an antidepressant, psilocybin has been found to produce rapid and sustained reductions in depressive symptoms, possibly by modulating the activity of the brain’s default mode network. As an anxiolytic, it has been shown to have potential in treating anxiety disorders, including treatment-resistant anxiety in patients with cancer. Psilocybin was once used to deal with cancer patients, however, basic proof that antidepressant uses of psilocybin being non-restricted with cancer was provided by the study of treatment-resistant depression outside the background of cancer (Carhart-Harris RL et al., 2016). Of

particular note is the treatment of cancer-related psychiatric distress, by three placebo-controlled experiments yielding possible outcomes for psilocybin (Grob CS et al., 2011) (Carducci MA et al., 2016) (Ross S., et al, 2016). Psychedelics may be among the earliest psychoactive substances known to humanity (Schultes et al., 1998). There are two main structural categories of psychedelics: indoleamines (e.g., DMT, psilocybin, LSD) and phenylalkylamines (e.g., mescaline, DOI). These substances have been used for centuries by various cultures for therapeutic and spiritual purposes (Nichols, 2012). Psilocybin is currently a hot topic among scientists for its potential use as a research tool to better understand psychosis and for its possible therapeutic benefits. However, psilocybin is also a popular recreational drug and is often abused. (Tylš, F., Páleníček, T. & Horáček, 2014). Psilocybin and other classic psychedelics have long been used for spiritual and therapeutic purposes in indigenous cultures. Scientific research on these compounds gained attention in the mid-20th century but was left over due to their association with the non-mainstream movement in the 1960s and 1970s. Apart from this decline in interest, there is enthusiasm for the drugs’ potential as experimental therapeutics and tools for understanding human brain (Johnson & Griffiths, 2017). Sewell and colleagues suggest that for patients with cluster headaches, psilocybin could make an effective use in the cure or prevention of the regular appearance of cluster headaches. (Sewell et al., 2006).

Psilocybin was claimed to be effective in treating a wide range of conditions (Goldberg et al., 2020) including depression and anxiety associated with end-of-life issues (Yu et al., 2021), pain management (Whelan, A., & Johnson, M. I. 2018), obsessive-compulsive disorder (Moreno et al., 2006), and post-traumatic stress disorder (PTSD) (Varker et al., 2021). When talking about currently available psychedelic drugs, psilocybin has long be the first choice, and was considered safe relatively. There is still a lack of comparative studies on the efficacy of other psychedelic drugs for curing mood and anxiety disorders, but the existing data on solely psilocybin tells us that it is likely to be relatively effective among the psychedelic drugs in treating such disorders. This potential is an important consideration when making decision of the direction of further research into psilocybin-assisted therapy (Lowe et al., 2021)

2.2 Current Use

A study (Grandjean et al., 2021) explored the outcomes of psilocybin on functional connectivity (FC) throughout the brain in mice. The possible approach given by the researchers is to treat the antidepressant effects of psilocy-

bin, suggesting that it may interact with the default mode network (DMN) and alter it (Carhart-Harris et al., 2012). Resting state fMRI results showed that psilocybin decreased functional connectivity within the dopamine (DA) -associated striatal network, while also increasing FC between the 5-HT-associated network and cortical regions (Carhart-Harris et al., 2012). The results showed that psilocybin reduced functional connectivity of the dopamine (DA) -associated striatal network and demonstrated altered increased FC between the 5-HT-associated network and cortical regions (Grandjean et al., 2021).

Another study involving mice showed that psilocybin (a potent metabolite of psilocybin) caused an increase in dopamine and serotonin concentrations outside brain cells in the accumbens (Sakashita et al., 2015). This suggests another potential mechanism for the antidepressant effects of psilocybin and psilocybin, which may work by increasing dopamine levels (Coull et al., 2015).

3. Effect

Research suggests that psilocybin may have a variety of effects on the brain and nervous system, including changes in brain activity, mood, perception, and cognition. These effects can be both beneficial and potentially harmful, and people would need to learn more on this topic in order to fully understand the effects of psilocybin of different duration.

4. Psychological Effect

While psilocybin and similar hallucinogenic compounds are being investigated in human research, their potential for subjective side effects has hindered their acceptance for medical use. With limited knowledge of the full range of possible adverse reactions, these compounds continue to be controversial in the medical community (Studerus et al., 2011). Psilocybin works on human in special ways, and according to Dev, for example, the mPFC (medial prefrontal cortex) is often overactive in individuals with depression. Psilocybin's stimulating effects are believed to correct this imbalance by regulating activity in the prefrontal and limbic brain regions, including the amygdala. The amygdala plays a key role in the brain networks that process perception and emotion. Depressed individuals often become less sensitive to emotional cues, but psilocybin may help restore this sensitivity (Dev B Goel & Sarju Zilate, 2022).

From Preller, in order to find out the effects of psilocybin on brain connectivity, a double-blind, crossover study with 23 healthy participants being randomly assigned with drugs was conducted. Participants were given placebo and

0.2 mg/kg of psilocybin orally on separate days. Between three time points, magnetic resonance imaging will provide the image of administration and peak effects: at 20, 40, and 70 minutes after administration. This methodology allowed for a comprehensive assessment of psilocybin's impact on brain connectivity. Psilocybin was shown to decrease associative brain-wide connectivity, while from administration to peak effects, the sensory connectivity over time is always increasing. Additionally, the experiment suggests that the baseline connectivity was related to the amount of changes made by psilocybin-induced functional connectivity. Psilocybin-induced alterations in functional connectivity were also thought to be correlated with spatial gene expression patterns of the 5-HT_{2A} and 5-HT_{1A} receptors in a time-dependent manner (Preller et al., 2020). These findings provide valuable insights into the mechanisms by which psilocybin alters brain connectivity.

In another experiment, Wittmann et al. tried to find out the various doses of psilocybin effecting the time perceiving ability of healthy college students. The research shows that subjects are likely to experience a slower time compared to how it truly was when the time lasts longer than 2-3 seconds; with a shorter time period, on the other hand, their sense of time will be more accurate. These results tell us that even serotonergic substances only really affect our perception of time when duration is taken into account (Wackermann et al., 2008).

In addition to that, according to Felsch, a review of 30 experimental studies looking at the neurological effects of meditation found that psilocybin assisted meditation interventions may change the way people think about things associated with social anxiety disorder (SAD), such as a biased focus on threats. This may be achieved by altering the connectivity of the prominence network, balancing the movement and connectivity of the midline structure of the cortex, and increasing the number of amygdala responses controlled by the anterior parietal lobe. These findings suggest that psilocybin assisted meditation may have therapeutic potential for treating SAD and related disorders (Felsch, 2021).

5. Sociological Effect

In addition to its mental effects, psilocybin can also affect social behavior and interpersonal interactions. The possibility of using psilocybin assisted therapy to treat suffering that exists at the end of life has aroused interest around the world, but little is known about how socially acceptable such treatment is. A survey was conducted to assess the amount of societal acceptance of psilocybin for medical purposes in this context. This study aims to gain

insight into the social acceptability of this potential treatment option, including perceptions, attitudes and concerns about the treatment of existential suffering in this context. According to the study, the public is friendly and widely accepted towards the use of psilocybin to assist patients with grief at the end of life. These findings highlight the potential for this new therapy to be available in palliative and end-of-life care settings. This research helps mobilize resources and advocate for access to this new therapy for patients in need (Plourde et al., 2024). The trial provides the first empirical evidence of the effectiveness of psilocybin-assisted group therapy in reducing trauma symptoms. This novel approach to trauma treatment appears to be effective, and Valuable insights may involve into how psilocybin can aid in the healing process through further investigation of the psychological processes involved (Agin-Liebes et al., 2024).

6. Discussion

Neuroscience research has shown that psilocybin regulates key brain networks involved in emotion regulation, perception, and cognition. This has led to promising results in treating mood and anxiety disorders, particularly depression, and the ongoing studies examining psilocybin's potential therapeutic benefits in other situations such as addiction, PTSD, and end-of-life anxiety are progressing as usual. However, these effects can be both beneficial and potentially harmful, more research is needed in order to fully make use of both the short- and long-term effects of psilocybin.

7. Future Use

7.1 Prevention

Psilocybin should definitely continue to be used in the future. Psilocybin exert a great effect on thalamo-cortical neurotransmission (Woitas et al., 2022). According to an research by Raison, Montgomery-Asberg Depression Rating Scale (MADRS) was used as the criteria to measure the level of depression after the usage of either psilocybin or placebo. This scale ranges from 0 (no depression) to 60 (severe depression), from baseline to day 43. Participants in the study were individuals aged from 21 and 65 who have Major Depressive Disorder (MDD) for 60 days in minimum. These criteria will be able to ensure the severity of depressive symptoms that people experience. A key outcome measure was the change in the MADRS score from baseline to day 8.

Of the 104 participants (with an average age of 41 years; 52 women) randomly assigned to treatment (51 receiving

psilocybin and 53 receiving niacin), psilocybin treatment was associated with significantly lower MADRS scores compared to niacin, to be specific, from baseline to day 43 (with a mean difference of -12.3 [95% CI, -17.5 to -7.2]; $P < .001$), and from baseline to day 8 (with a mean difference of -12.0 [95% CI, -16.6 to -7.4]; $P < .001$). (Raison et al., 2023) In the study, psilocybin treatment was proved to have a relationship with a clinically significant decrease in depressive symptoms and functional disability with no severe adverse events. These results add to a growing body of evidence that psilocybin, in combination with psychological support, may provide a new and useful intervention for major depression. This research gives us promising insights into the potential benefits of psilocybin-assisted therapy with MDD for those patients.

7.2 Depression and Anxiety

Anxiety, depression and behavioral disorders are the leading causes of illness. Anxiety disorders often involve repeated episodes of intense anxiety and fear or panic attacks. These symptoms can seriously affect an individual's daily activities and can be difficult to control. Understanding the etiology of such mental disorders has gained more momentum in contemporary research. A major biological factor that contributes to depression and anxiety is altered activity in the amygdala. The amygdala is part of the limbic system which usually plays an important role in processing emotions, particularly those related to fear, anger, and anxiety. The nerve cell connecting the amygdala and the prefrontal cortex (PFC) are "depression circuit." Depression occurs when emotionally charged signals in it overpower the PFC to normalize the signals (hare&du-man, 2020). Biotherapy is one of the most widely used approaches, involving the use of drugs, genetic testing, or other biological methods to alter underlying physiological processes associated with mental health conditions. Medications such as Benzodiazepines are widely prescribed for short-term relief of anxiety symptoms (Tiffin et al., 2018). Client-centred therapy, pioneered by Carl Rogers, represents the humanistic approach of positive psychology. It encourages self-exploration to realise one's true self. Therapists listen actively and patients vent negative feelings, optimising their well-being, which fits what young teens and young adults are looking for: intimacy and a place to talk. This therapy is efficient at increasing young adult's recognition of their own problems (Harris& End, 2004). The reason why we encourage psilocybin development is because, according to the research by Schindler, psilocybin and relative psychedelics might be able to provide better treatment responses than existing approved therapies (Schindler et al., 2015).

We should notice that, according to Wojtas, neither psilocybin nor LSD had a significant effect on anxiety levels and both caused the decrease in immobility in the forced swim test, potentially indicating adaptive mechanisms at work. Future studies relevant to the stress models should be conducted to explore the potential antidepressant effects of psychedelics and to better understand the mechanisms underlying their therapeutic effects (Wojtas et al., 2022).

8. Conclusion

In the coming years, research will likely focus on refining dosing protocols, investigating long-term safety and efficacy, and exploring potential synergistic effects with other therapies. There is increasing evidence that psilocybin, when administered under proper medical supervision, may be an effective treatment option for people with depression. Studies have shown that psilocybin can reduce depression symptoms and functional disability in a long-term and rapid manner, and has a good safety. In addition, psilocybin appears to target the underlying causes of depression, rather than just treating symptoms, as seen in its regulation of key brain networks associated with emotion regulation and emotional processing. Neuroscience research has shown that psilocybin regulates key brain networks involved in emotion regulation, perception, and cognition. As research continues to demonstrate the therapeutic potential of psilocybin, there is growing interest in its future uses. Psilocybin's ability to aid treatment has led researchers to believe it has the potential to revolutionize the treatment of mental illness, bringing healthy lives to those suffering from depression, post-traumatic stress disorder (PTSD), addiction and other conditions. Whether these effects are good or bad is not yet known, and more research is needed to fully investigate, including the long- and short-term effects of psilocybin. However, social barriers still need to be overcome and regulation tightened before the treatment is widely accepted.

If used properly, psilocybin holds promise as a preventive intervention for depression. Studies have shown that psilocybin can make mindsets and behaviors positive and last longer, which may prevent the development of depressive symptoms. Psilocybin also has an effect on neural networks involved in emotion regulation and processing, potentially providing a more comprehensive approach to preventing depression. Although psilocybin assisted therapy has shown promising results, more research is still needed. Researchers need to fully understand its potential as a preventive intervention.

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