



OPINION

MAGIC MUSHROOMS

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ABSTRACT

Psilocybin is a naturally occurring compound present in numerous mushroom species characterised by its hallucinogenic and psychedelic effects. Although it has a negative reputation, psilocybin has demonstrated therapeutic potential for treating mental health disorders by allowing the brain to make new neural connections which help the neural pathways adapt and break out of certain cognitive patterns related to mental illness. In recent studies, psilocybin has shown antidepressant effects, significantly reducing depressive and anxious symptoms in affected individuals. After single or low dosage, mood disorder symptoms remained in remission for 6 to 12 months. In contrast, conventional antidepressants often require multiple doses over long treatment periods to achieve similar effects. Other findings have shown that therapeutic use of psilocybin helps combat substance abuse and addictive disorders and can be applied as a cessation tool. Despite years of controversy surrounding the benefits of psilocybin, recent scientific evidence supports psilocybin's immense potential in helping those with mental health disorders like Major Depressive Disorder (MDD), Generalised Anxiety Disorder (GAD), Post Traumatic Stress Disorder (PTSD), Obsessive-Compulsive Disorder (OCD), and addiction disorders. With such promising results, psilocybin could be incorporated into clinical use and its therapeutic effects should continue being researched.

INTRODUCTION

Known for its hallucinogenic and psychedelic effects, psilocybin is a naturally occurring compound produced in over 180 species of mushrooms worldwide.¹ The psychedelic effects of psilocybin are attributed to the similarity of its molecular structure to serotonin, which allows it to bind to the serotonin 2A receptor (5-HT_{2A}R). 5-HT_{2A}R modulates various cognitive processes, including perception, learning, mood, and imagination, meaning that it is expressed widely throughout the brain. Thus, alterations in pathways involving 5-HT_{2A}R can distort one's perception of the environment, possibly leading to hallucinations, euphoria, and intense feelings of wonder.² These effects are dose-dependent and influenced by the user's expectations of the experience of using psilocybin. Additionally, long-term changes in sensory perception and thought after the experience are not uncommon.

Ongoing research shows that psilocybin has an effect on the brain's Default Mode Network (DMN). This network allows

us to reflect on the past and plan for the future as it compiles and consolidates information in the background of everyday life. It has also been proposed that the DMN is responsible for the sense of self or individuality.³ Studies suggest that the 5-HT_{2A}R receptors are involved in and influence connections in the DMN.⁴ Psilocybin may disable some of the connections in this network, which forces new connections to form within the brain, thereby allowing one's sense of self to shift.³

Mushrooms containing psilocybin are hypothesised to have been used by humans for 5.3 million years.⁵ They have also been used in medicinal, spiritual, and ceremonial practices around the world for thousands of years.⁶ Today, however, the majority of psychedelic substances, including psilocybin, have been categorised as controlled and illegal with no recognised medical value.⁷ Before prohibitive laws ended psychedelic research programs in the 1970s, psychedelics showed initial therapeutic promise as a supplement to psychotherapy for mood disorders and

the treatment of alcohol dependence. Human psychedelic research has been slowly, but steadily, reviving since the early 1990s due to growing recognition of its clinical potential.⁸ This has led to the subject of recent controlled clinical studies exploring psilocybin's effects on the mind, and its therapeutic efficacy in aid of existing psychotherapeutic approaches.⁷ Despite years of controversy surrounding the drug, it has shown immense potential in treating various medical conditions, such as those involving mental health, and holds significant promise for continued investigation. programs in the 1970s, psychedelics showed initial therapeutic promise as a supplement to psychotherapy for mood disorders and the treatment of alcohol dependence. Human psychedelic research has been slowly but steadily reviving since the early 1990s due to growing recognition of its clinical potential.⁸ This has led to the subject of recent controlled clinical studies exploring psilocybin's effects on the mind, and its therapeutic efficacy in aid of existing psychotherapeutic approaches.⁷ Despite years of controversy surrounding the drug, it has shown immense potential in treating various medical conditions, such as those involving mental health, and holds significant promise for continued investigation.

USING PSILOCYBIN TO TREAT MOOD DISORDERS

Psilocybin was first reported to have antidepressant properties in a study carried out at Johns Hopkins University in 2016. In patients who developed anxiety disorders associated with their advanced-stage cancer diagnosis, controlled amounts of psilocybin significantly reduced anxiety and depressed mood.⁹ Additionally, Griffiths et al. demonstrated that 92% of the cancer patients who received a high dose of psilocybin showed a clinically significant decrease in depressive symptoms after the first session.⁹ Furthermore, there was a sustained symptom remission rate of 65% at the six-month follow-up assessment.⁹ By demonstrating an enhanced quality of life in these patients, the study provided a catalyst for new research aimed at replicating these findings. Psilocybin may also be effective for a larger demographic beyond cancer patients. A one-time high dose of psilocybin was shown to be associated with remission in mood disorders in patients with long-term depression at six and twelve months after treatment.¹⁰ The magnitude of the effect observed was approximately four times greater than what clinical trials have previously demonstrated for conventionally available antidepressants on the market that target the serotonergic system, similar to psilocybin.¹⁰ Given that there has been little advancement in mental health treatment over the last three decades, these findings were deemed to be remarkable by the media. This is because most other antidepressant treatments take weeks to work and require more doses that result in a high incidence of unwanted side effects.¹⁰ Further research into the therapeutic potential of psilocybin for mood disorders is, therefore, warranted.

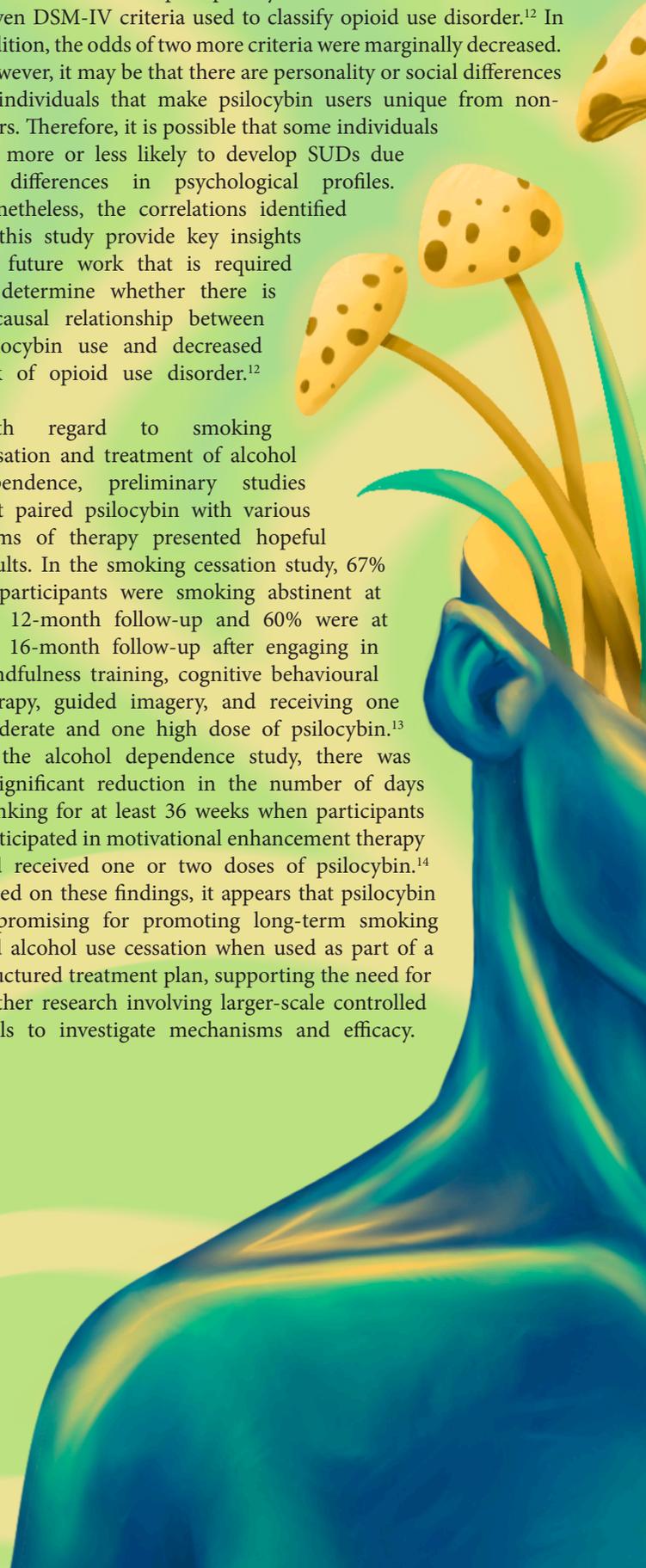
PSILOCYBIN AS A TOOL FOR ADDRESSING SUBSTANCE USE DISORDERS

Another area in which psilocybin may have a therapeutic advantage is in managing substance use disorders (SUDs). An online survey conducted in 2020 by Garcia-Romeu et al. examined self-reported instances of psychedelic use followed by a cessation or reduction in use of other substances, including cannabis, opioids, or stimulants. Results indicated that before using psychedelics, 29% of which was psilocybin, 96% of subjects met the criteria for a SUD, whereas only 27% did after use. Greater psychedelic doses were linked to lower drug consumption.

While this survey can only serve to establish a correlation between psychedelics and SUDs, the findings make a case for further clinical research on treatment with psychedelic aids.¹¹

Similarly, another study found that there was a significant negative correlation between past psilocybin use and seven out of the eleven DSM-IV criteria used to classify opioid use disorder.¹² In addition, the odds of two more criteria were marginally decreased. However, it may be that there are personality or social differences in individuals that make psilocybin users unique from non-users. Therefore, it is possible that some individuals are more or less likely to develop SUDs due to differences in psychological profiles. Nonetheless, the correlations identified in this study provide key insights for future work that is required to determine whether there is a causal relationship between psilocybin use and decreased risk of opioid use disorder.¹²

With regard to smoking cessation and treatment of alcohol dependence, preliminary studies that paired psilocybin with various forms of therapy presented hopeful results. In the smoking cessation study, 67% of participants were smoking abstinent at the 12-month follow-up and 60% were at the 16-month follow-up after engaging in mindfulness training, cognitive behavioural therapy, guided imagery, and receiving one moderate and one high dose of psilocybin.¹³ In the alcohol dependence study, there was a significant reduction in the number of days drinking for at least 36 weeks when participants participated in motivational enhancement therapy and received one or two doses of psilocybin.¹⁴ Based on these findings, it appears that psilocybin is promising for promoting long-term smoking and alcohol use cessation when used as part of a structured treatment plan, supporting the need for further research involving larger-scale controlled trials to investigate mechanisms and efficacy.



HOW PSILOCYBIN REWIRES THE BRAIN: NEUROPLASTICITY

While psilocybin has been shown to be a promising tool in addressing mental health-related conditions, serving both antidepressant and addiction recovery needs in controlled settings, some studies have tried to elucidate the underlying mechanisms. Psilocybin has been shown to increase neuroplasticity, which represents the brain's ability to adapt in response to different experiences.

Neuroplasticity is marked by the restructuring of neurons and reorganisation of their connections.¹⁵ This “rewires” the brain and allows for new functions to emerge. With regard to neuroplasticity, psilocybin has been shown to strengthen connections between various brain regions while reducing certain interactions between depression-related brain regions leading to reduced symptoms in patients diagnosed with MDD.¹⁶ Animal studies have also shown that administering psilocybin to fear-conditioned rats resulted in an increase in the number of neurons in the brain that created new connections.¹⁶ The rats were then able to break out of the conditioned response, demonstrating that psilocybin has potential as a treatment for habit-related disorders and addiction.¹⁶ These studies show how psilocybin increases the brain's ability to change and adapt in order to break out of negative habits, cognitive patterns, and harmful addictive behaviours.

CONCLUSION

Psilocybin has shown immense potential in helping those with mental health disorders, like MDD, GAD, PTSD, OCD, and addiction disorders. Many other drugs may display similar therapeutic promise if used under controlled conditions; one example is the street drug “ketamine”.¹⁷ Recent studies have exhibited interest in using specific doses of ketamine to treat MDD. Although these substances have gained notoriety in the public, they hold potential in modern medical treatment. More clinical trials are needed to further investigate the mechanisms and long-term effects of psilocybin; thus, it should be safely integrated into phase 2 and 3 trials.

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A past research scientist in pathology and molecular medicine, Dr. Katja Linher-Melville is currently a sessional instructor in the BHSc program at McMaster University (she teaches Biochem Inquiry, Cell Bio Inquiry, Symptomatology, and Research Skills & Application). Dr. Linher-Melville conducted preclinical research into cancer-induced and neuropathic pain.

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