COLUMN

Psilocybin: A brief overview for psychiatric mental health nurse practitioners

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Abstract

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The use of psychedelics, such as psilocybin, has emerged in recent literature as a novel therapeutic treatment for various psychiatric disorders, including substance use, depression, and anxiety. While international and domestic trials are currently underway, there is data demonstrating both the relative safety and potential efficacy of psilocybin. Psychiatric mental health nurse practitioners are essential mental health providers that may be at the forefront of delivering these new treatment modalities. Therefore, they must be aware of the psychopharmacological and psychotherapeutic tenets of psilocybin to be prepared to treat patients.

KEYWORDS

hallucinogenic, PMHNPs, psilocybin, psilocybin in psychiatry, psychiatric care

1 | INTRODUCTION

The use of psychedelics and consciousness-altering substances, such as psilocybin, lysergic acid diethyamide (LSD), 3,4methylenedioxymethamphetamine (MDMA), ketamine, and many others, has recently been gaining a lot of media attention for relevance in treating psychiatric conditions in ongoing research trials. In fact, there are forums focused on *the third wave* of the rise of psychedelics,¹ propagating information regarding historical and current contexts of use. From a clinical and anecdotal perspective, patients are expressing interest and inquisition into such therapies secondary to a proliferation of the topic in mainstream sources. Psychiatric mental health providers must be poised to answer these questions and be aware of ongoing research trials and practice implications. It is therefore imperative that psychiatric mental health nurse practitioners (PMHNPs) be well-versed in these new and evolving treatment modalities.

Notably, PMHNPs are psychiatric providers who may be at the frontlines of providing novel therapeutic care. Some clinics are widely adopting new treatments such as ketamine and esketamine and are poised to be ready when psychedelics may inevitably join the psychotropic prescribing regimen. However, there are important tenets that PMHNPs must remember when discussing psilocybin or other psychedelics with patients. PMHNPs must be aware of both the pharmacological, psychotherapeutic, and contextual² information regarding the use of these mind-altering substances. This column will provide a brief overview of the relevant psychopharmacological attributes of psilocybin and its use in psychiatric treatment.

2 | WHAT IS PSILOCYBIN?

Psilocybin, otherwise known as 4-phospholoxy-*N*,*N*-dimethyltryptamine, is a psychedelic that originates in psilocybe mushrooms. Colloquially, psilocybin is known as magic mushrooms. It is a monoamine and indole alkaloid that functions as a serotonergic agonist³ at the 5HT_{2A} receptor.⁴ Through its serotonergic activity, the drug produces a hallucinogenic effect due to an indole ring structure on tryptamine molecules. The active ingredient of psilocybin, a pro-drug,⁵ responsible for the production of hallucinogenic effects is psilocin, otherwise known as 4-hydro xydimethyltryptamine.³ Therapeutic doses for psilocybin range from 0.045 to 0.429 mg/kg. The onset of hallucinations typically occurs

Author Note: Dina Fradkin is a recent DNPPMHNP graduate from the University of Pittsburgh awaiting to sit for board certification.

approximately one to two hours subsequent to ingestion. Duration of action ranges from three to four hours, with a half-life of two and a half hours.³

3 | POTENTIAL ADVERSE EFFECTS OF PSILOCYBIN

Interestingly, unlike most schedule I drugs, psilocybin has limited to no effect on dopaminergic activity, leading to limited dependence and addiction. In fact, psilocybin has been explored as a potential substance use treatment modality due to its antiaddictive nature.^{3,6} While there are numerous trials focused on safety and efficacy, the following negative outcomes have also been identified: increased risk of physical harm, often due to violent or aggressive behavior; endurance of psychological symptoms; rare reports of attempted suicide; disturbances in concentration and memory; acute feelings of panic, fear, or overall distress: and persistence of perceptual disturbances.⁷⁻⁹ Notably. Carbonaro et al.⁷ found that of the three reports of patients with suicide attempts, two had been diagnosed with depression before the trial and had previously attempted as well. However, this potentially fatal negative outcome is relevant for PMHNPs to consider. Conversely, a population-based study in 2013 denied any association between lifetime psychedelic use (including psilocybin) and development of mental health outcomes, consisting of overall psychological distress, panic disorder, depressive episodes, manic episodes, social phobia (social anxiety), generalized anxiety disorder, agoraphobia, posttraumatic stress disorder, or mood-incongruent psychosis.¹⁰ Therefore, while research regarding negative and adverse outcomes may be inconclusive, providers must be aware of these potential effects. Milder adverse effects include transient increases in anxiety following administration as well as transient confusion, nausea, headaches, and mild elevations in heart rate and blood pressure.^{11,12}

Continued perceptual disturbances following cessation of psilocybin use can be quite common, and a subset of this population may have distressing disturbances that will lead to seeking psychiatric care.¹³ It is critical to be aware of patients who may be at the highest risk for psychotic adverse effects, particularly those with previous mental health histories of schizophrenia or psychosis.⁶ Interestingly, those with depressive histories were also noted to be at higher risk of developing psychosis⁶ even though psilocybin has been utilized to target and treat depressive symptoms. Providers, including PMHNPs, must understand the potential risks versus benefits to advise patients accurately and safely before they trial these new modalities, either through research projects or emerging treatment options.

4 | USE OF PSYCHEDELICS IN CURRENT PSYCHIATRY

A relatively recent population-based study examined the safety and efficacy of psychedelic treatment. Opposing the aforementioned potential negative outcomes, a cross-sectional survey of over 190,000 individuals actually demonstrated an association between the use of classic psychedelics and risk reduction of past psychological distress, suicidal thinking, suicidal planning, and suicidal attempt.¹⁴ However, it is imperative to note that while this study attempted to control for use of other drugs, such as marijuana, it is nearly impossible to do so.

Notably, most studies examining psychotherapeutic use of psilocybin or other hallucinogens utilize a guided experience with a mental health professional. In fact, contextualizing the potential therapeutic use of hallucinogens is critical in evaluating their potential benefits.² Psychedelics, such as psilocybin, are used as adjuncts in drug-assisted psychotherapy¹⁵ for alternatives to traditional treatment. Modern trials utilize mental health providers as guides in preparation for and during the hallucinogenic experience,² although some population studies do outline recreational use as well.¹⁰ Moreover, psilocybin has been identified as having relevant implications in the treatment of substance use disorders and affective disorders, as well as many others.

4.1 | Substance use disorders

As mentioned previously, psilocybin has been trialed as a preliminary modality for substance use disorder treatment. Psilocybin modulates serotonergic activity, via 5HT_{2A} as well as $5 \mathrm{HT}_{1 \mathrm{A}}$ receptors. Serotonergic modulation via the $5 \mathrm{HT}_{2 \mathrm{A}}$ receptor is hypothesized to promote reversal learning through effects on compulsivity and cognitive flexibility.⁶ Additionally, psilocybin ingestion leads to a cortisol spike that is associated with the regulation of relevant brain networks implicated in substance use⁶-psilocybin modulates negative affective states and stress associated with substance use. It has demonstrable anxiolytic and affect regulation effects pertinent to substance use treatment. Amygdala hyperactivity, associated with substance abuse, may be mitigated through the use of psilocybin.⁶ Overall, psilocybin may be a relatively useful treatment for substance use disorders involving alcohol, nicotine, or other drugs.^{6,16,17} Interestingly, psilocybin has demonstrable efficacy even in its absence of any direct dopaminergic modulation.

4.2 | Depression and anxiety

Psilocybin has recently been touted as a novel option for treatment-resistant depression. As mentioned, inhibition of the amygdala by psilocybin has pertinent substance use implications.⁶ However, deactivation of the amygdala is also relevant for mood disorders, resulting in improvements in affect. Affect improvement has been measured by reductions in Hamilton Depression Rating Scale scores of up to 10 points in a period of 7 days.³ Psilocybin administration was similarly associated with reductions in depressive symptoms as well as anxiety in another small (n = 12) study targeting those with moderate-to-severe

treatment-resistant unipolar depression.¹¹ In another recent study (n = 10), the use of psilocybin in the facilitation of memory access was examined. Carhart-Harris et al.¹⁸ found that psilocybin did promote autobiographical memory activation, with more vivid sensory recollection. While the findings of these studies are quite limited due to poor generalizability, the implications promote the potential use of psilocybin as a modality for psychotherapy-perhaps in the recollection of positive memories¹⁸ in reversal of the often negative outlook and hopelessness that can be characteristic of depressive disorders. The use of psychedelics, including psilocybin, in a supportive psychotherapeutic environment,² has been cited as responsible for producing enduring anxiolytic and anti-depressant effects that remained prominent for months.¹² Notably, new and emerging research continues to propagate across the globe in light of these positive findings.

5 | PROSPECTS OF RESEARCH

Presently, psilocybin continues to be studied internationally for its use in treatment-resistant depression.¹⁹ Psychedelics are studied at research hubs across Europe, including in Switzerland, Denmark, Ireland, the Netherlands, Spain, and the United Kingdom-in fact, many are currently actively recruiting participants.²⁰

There are several domestic studies in progress as well. The Johns Hopkins Center for Psychedelic and Consciousness Research²¹ has become the research hub for psilocybin. Its research projects implicate opioid use disorder, Alzheimer's, posttraumatic stress disorder, posttreatment Lyme disease syndrome, anorexia nervosa, and alcohol use comorbid with major depressive disorder. Additionally, there are studies being performed at Yale University, University of Wisconsin, New York University, and University of Arizona utilizing psilocybin in a variety of different treatment modalities (see Table 1). Research continues to emerge implicating psilocybin as well as other psychedelics in the treatment of various psychiatric conditions.

6 | IMPLICATIONS FOR PMHNPS

Psilocybin research results thus far have been, while promising, inconclusive in nature. Adverse effects range from transient and mild symptoms to persistent and even fatal outcomes. Positive associations between psilocybin and treatment outcomes are not causal in nature. Additionally, while studies have attempted to control for other drug use, it is demonstrably difficult to accomplish this. Often, research participants have a long history blurred by previous substances, including but not limited to psychedelics, stimulants, tranquilizers, marijuana, and inhalants.¹⁴ Currently, it remains unknown whether or not psychedelic use can increase the use of other substances, as current trials demonstrate the difficulties of teasing out previous and current polysubstance use¹⁴-participants using psychedelics were far more likely to have used cocaine, opiates, marijuana, sedatives, and other recreational drugs in the past. Many research studies are also limited by self-report for control variables.^{10,14}

As of now, although psilocybin is a schedule I drug, it actually has a better safety profile than many lower scheduled drugs, which includes stimulants, opiates, and benzodiazepines. Presently, there are no documented deaths directly from psychedelic overdose in humans, but patients using hallucinogenic or dissociative drugs are at increased risk for harm due to acute perceptual and mood disturbances-users may be at increased risk of taking actions that may endanger their lives.^{7,22} Examples include jumping from high elevations, putting themselves or others at risk of physical harm, behaving aggressively or violently, or even attempting suicide.^{7,22} Moreover, recreational psilocybin may not be in its purest form, as compared to psilocybin utilized in research studies-this is an important note for patient education. Drugs obtained for recreation can be mixed with contaminants or other substances that can be dangerous; additionally, on the quest for psilocybin, patients can put themselves at risk of consuming poisonous mushrooms, which can be fatal.²² While psychedelics may likely make their way into standard psychiatric treatment in the future, these aforementioned key points are critical for nurse practitioners and other health care providers to be made aware of to best inform and take care of patients.

Use of psilocybin in	Specifier	Location
Somatic symptoms	1. Posttraumatic headaches	1. Yale University
	2. Cluster headaches	2. Yale University
Substance use	1. Adjunct treatment to buprenorphine	1. University of Wisconsin
	2. Alcohol dependence	2. New York University
Depressive disorders	1. Neuroplasticity in MDD	1. Yale University
OCD	None	1. Yale University
		+
		2. University of Arizona

TABLE 1 Select domestic research trials involving psilocybin across research institutions

Abbreviations: MDD, major depressive disorder; OCD, obsessive-compulsive disorder.

7 | CONCLUSIONS

PMHNPs and other providers must be aware of the current research regarding new modalities of care to best provide evidencebased treatment to patients. While psychedelics such as psilocybin may not yet be on the market, there is promising research in its use for depression, anxiety, and substance use disorders. Pending psilocybin advancement to market in the future, providers must consider serious adverse effects and evaluate which patients may be at increased risk for prolonged perceptual disturbances or other persisting symptoms following drug cessation. While hallucinogenic and psychedelic treatment may appear to be far from reality, the recent adoption of ketamine and other substances supports that such novel drug treatments may reach patients sooner than once expected.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no data sets were generated or analyzed during the current study.

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