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Psychedelic-Assisted Therapy:

Emerging treatments in mental health disorders

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Abstract

Psychedelics are a class of psychoactive substances that were studied extensively between 1943 and 1970 as potential therapies for treating a host of mental health disorders, including addiction. Despite promising early results, U.S. psychedelic research was halted in the early 1970s with the enactment of the Controlled Substances Act. As the field of psychedelic-assisted therapy develops, nurses can decide the role they will play in the continuing clinical and scholarly research of these substances, which may soon be used in controlled settings to treat some of the most widespread mental health disorders. To prepare for this task, this article proposes that nurses

- become familiar with the history, relevant language, and scientific findings related to the field of psychedelic research.
- learn about existing psychedelic-assisted therapy and research resources.
- examine their thoughts, judgments, and opinions about therapeutic psychedelic use.
- consider the potential role of nursing in psychedelic-assisted therapies going forward.

Keywords

entheogens; hallucinogens; holistic nursing; palliative care; psychedelic-assisted therapy; psychedelics; psychiatric nursing

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In February 1964, *AJN* published an article by Kay Parley entitled, “Supporting the Patient on LSD Day.”[1] In this work, Parley discussed nursing considerations when administering therapy with lysergic acid diethylamide (LSD), a psychedelic drug, which was under research as an adjunct to traditional psychiatric treatments for patients with alcohol use disorder. Parley described the process of “sitting” with patients over the course of a daylong LSD experience on the psychiatric unit. Since LSD can cause intense emotional experiences in people who ingest it, the duties of the nurse were to bear witness, create a safe and therapeutic environment, provide reassurance during moments of fear or anxiety, serve as a grounding presence to orient the patient to the “here and now,” and encourage the patient to explore what might emerge mentally, emotionally, or spiritually on their “journey.” In fact, Parley would narrate the experience to her patients, using the following words[1]:

> You are off on a trip … with no baggage, no destination, and no compass. That’s why I’m here. I can’t go with you, but I can be your anchor. Wherever you go, you’ll always be able to see me. I’ll be the nurse who sits beside your bed, taking notes and playing your records. You’ll never lose touch with me. Seeing me, you’ll know you are really in hospital and that you’ll be back to earth about four o’clock. I will send you signals, too, to encourage your explorations. I will remind you of places you longed to revisit and events you hoped to scan.

Parley was noting what early researchers had discovered: that the psychedelic experience led patients to “scan their life” and gain new perspectives, find meaning related to past events and relationships, explore traumatic wounds, gain insights into the cause of their illness, or experience a range of emotions that often led to self-healing and self-understanding. In much the same way that nurses create conditions conducive to self-healing of the body (by keeping a wound clean and well dressed, for example), the nurse-guided psychedelic experience often allowed patients to discover their capacity for emotional healing.

An MDMA therapy session is conducted by researchers Marcela Ot'alora, MA, LPC, and Bruce Poulter, MPH, RN. Photo courtesy of the Multidisciplinary Association for Psychedelic Studies.

A 'renaissance' in psychedelic therapy.

Fifty-seven years after publication of Parley's article, psychedelic-assisted therapy is experiencing what Sessa has called a "renaissance" across the United States and internationally.[2] To clinicians trained after these compounds had been added to Schedule I of the Comprehensive Drug Abuse Prevention and Control Act of 1970, more commonly known as the Controlled Substances Act, psychedelics may be more commonly considered drugs of abuse than potential therapies. While psychedelics are not yet approved by the U.S. Food and Drug Administration (FDA) for this purpose, one such substance, 3,4-methylenedioxymethamphetamine (MDMA), is currently in a phase 3 clinical trial as an adjunct to psychotherapy for posttraumatic stress disorder (PTSD),[3] and psilocybin is currently in two phase 2 clinical trials as an adjunct to psychotherapy for major depressive disorder (MDD).[4, 5] Both substances have been granted "breakthrough therapy designation" by the FDA, meaning they may offer substantial benefits over existing treatment options.[6]

Psychedelic research centers are being established both privately and within academe,[7, 8] and psychedelic therapy training programs are certifying practitioners to meet a future projected need for psychedelic-assisted therapy.[8] The popular press has accelerated interest in the field with stories appearing in the *New York Times*,[9] in *Psychology Today*,[10] on *60 Minutes*,[11] and with the publication of Michael Pollan's bestselling book, *How to Change Your Mind*.[12]

With the growing interest in psychedelic therapy within academia, research, education, and society at large, the nursing profession is faced with an important choice: to actively participate in the developing field of psychedelic therapy or to allow other disciplines to guide the conversation. As Parley's 1964 *AJN* article suggests, nurses have a history with psychedelic-assisted therapies,[1] and there is much nurses can learn in order to prepare for the potential rescheduling of these therapies—assigning them to a schedule with fewer regulatory restrictions, for example—particularly in the areas of psychiatry, palliative care, and addiction treatment. This article discusses the history, relevant language, and scientific findings related to psychedelic-assisted therapies; the methods of self-reflection nurses can use to clarify their thoughts, judgments, and opinions about the therapeutic use of psychedelics; and the various roles nurses might play in the future of psychedelic-assisted therapy.

HISTORICAL USES OF PSYCHEDELICS

Psychedelics, also known as hallucinogens (in both the scientific and popular literature), are a class of psychoactive substances thought to "expand consciousness." These include such substances as MDMA, which is developed in a laboratory; LSD, which is synthesized in a laboratory from an ergot fungus; and plant and fungi derivatives, often called entheogens,

which include psilocybin (the active compound in “magic” mushrooms), ayahuasca, peyote, and iboga.

The entheogens psilocybin, ayahuasca, peyote, iboga, and others have been used for millennia in some cultures as traditional, sacred medicines for physical and emotional healing and as a means of making contact with the divine.[13] Psychedelics came to the attention of Western culture as early as the 1950s and remained a focus of several Western empirical studies in mental health from the 1950s through the 1970s.[14] Despite promising early results, social and political pressures halted psychedelic research in the early 1970s.[14]

In 1990, MDD was the second leading cause of years lived with disability (YLD) in the United States, remaining the second leading cause of YLD in 2016.[15] Given the lack of significant advancements in psychopharmacology for depression over this nearly 30-year period, some researchers have been seeking to revive the dormant research on psychedelic-assisted therapy.

THE WIDE-RANGING EFFECTS OF PSYCHEDELICS

Psychedelics are a diverse class of psychoactive substances that exert a wide range of neurochemical, neuromodulatory, and hemodynamic effects on the brain.

Classic psychedelics such as psilocybin and LSD activate the serotonergic system, specifically by way of serotonin 1A, 2A, 2C, and 7 receptors, as well as the dopaminergic system through D2 receptors.[16] They interact indirectly with glutamatergic and GABAergic pathways.[16] There is also evidence that psychedelics affect epigenetic expression.[17]

MDMA is considered an atypical psychedelic, or entactogen (for its empathy enhancing effects),[18] which results from the release of serotonin, enhanced dopamine,[19] prolactin,[20] and oxytocin[21] in multiple brain regions. Subjective effects of psychedelics may include open- or closed-eye imagery, acute emotional experiences, and anti-amnesic effects, which permit the retrieval of previously unconscious material.[16]

PSYCHEDELIC USE IN PSYCHOTHERAPY

The serendipitous synthesis of LSD in 1943 by Swiss chemist Albert Hofmann[22] marked the beginning of the modern Western psychedelic era. Initially, LSD was used as an adjunct to psychotherapy for the treatment of alcohol use disorder, depression, and anxiety.[2] These treatments were halted, however, when the diversion of LSD into the popular culture led to its prohibition in 1970. After that time, LSD and other psychedelics were considered potential drugs of abuse and were classified as Schedule I substances along with other illegal drugs such as marijuana and heroin.

In 1994, researchers began reexamining the potential use of psychedelics in psychiatry. Then, as now, the studies followed a similar model: the administration of a psychoactive substance, such as psilocybin, bookended by sessions of psychotherapy conducted before the dosing session to prepare participants and afterward to help them integrate their psychedelic experience. The psychedelic substance is typically given orally, and two therapists remain

with the patient in a comfortable environment for the duration of its effects, typically 12 to 24 hours. Patients may choose to talk to the therapists during the dosing session or to focus their attention inward, using eyeshades and music as aides in the process.[23]

PSILOCYBIN AS A THERAPEUTIC ADJUNCT

Psilocybin has been studied as an adjunct treatment for tobacco cessation,[24] alcohol dependence,[25] anxiety and depression related to life-limiting illness,[26-28] and demoralization experienced by long-term AIDS survivors.[29]

In a study of 29 patients with cancer-related depression and anxiety, participants experienced clinically significant reductions in measures of depression and anxiety following psilocybin-assisted therapy, with 60% to 80% of those still alive at the 4.5-year follow-up continuing to show significant improvements, which 71% to 100% attributed to the psilocybin-assisted therapy.[30]

An open-label feasibility trial of psilocybin-assisted psychotherapy, which involved six men and six women with moderate-to-severe, unipolar, treatment-resistant MDD, produced antidepressant effects after one week, improvements that were sustained for most patients three months later. The adverse effects of psilocybin were transient and mild. These included anxiety during drug onset, which could be managed with reassurance from study therapists, as well as confusion, nausea, and headache.[31] In October 2018 and November 2019, the FDA granted COMPASS Pathways and the Usona Institute, respectively, breakthrough designation to conduct phase 2 clinical trials of psilocybin as an adjunct to psychotherapy for MDD.[4, 5, 32]

A subsequent study of psilocybin-assisted psychotherapy for MDD was conducted at the Johns Hopkins Center for Psychedelic and Consciousness Research and demonstrated similar antidepressant effects persisting at one and four weeks following treatment.[33]

RECREATIONAL VS. CLINICAL USE OF PSILOCYBIN AND MDMA

In a survey of psilocybin use in the community, 2.6% of 1,993 respondents reported that after having consumed psilocybin mushrooms they had acted in a physically aggressive manner toward themselves or others, 2.7% reported having sought medical help, and 10.7% reported putting themselves or others at risk for physical harm.[34]

The absence of such negative consequences in the clinical setting highlights the importance of therapeutic preparation and support for the psychedelic experience. The negative psychosocial outcomes reported with recreational use have not been observed in any therapeutic study. In a study by Griffiths and colleagues that included 56 participants, there were no serious adverse events attributed to psilocybin, only transient episodes of distress or discomfort, none of which required medical intervention.[26] Similarly, in a randomized, blinded, controlled crossover study investigating the efficacy of psilocybin compared with a control (niacin) in treating clinically significant anxiety or depression in 31 patients with life-threatening cancer, there were no serious adverse events, medical or psychiatric, attributed to psilocybin or niacin that required medical treatment.[28]

Although some retrospective studies of recreational use of ecstasy (street MDMA, which is often adulterated with other substances) report cognitive decline in users, especially in the area of verbal memory,[35] neurocognitive decline has been neither observed in clinical settings nor reported by participants in long-term follow-up.[36, 37] These contradictory findings highlight the difference between clinical and recreational use of psychedelics, potentially related to the quality of the drugs as well as to the clinical monitoring and the therapeutic paradigm.

MDMA FOR PTSD

MDMA has been under study for many years as a psychotherapeutic adjunct for treating PTSD. The drug is thought to permit patients with PTSD to better tolerate the examination of traumatic material in therapy. Researchers conducting a long-term follow-up of an early phase 2 pilot study found that, when queried, participants indicated that the benefit of MDMA-assisted psychotherapy persisted on average 3.75 years after the pilot study had ended.[37, 38] Furthermore, a pooled analysis of six phase 2 randomized controlled trials revealed that 54.2% of subjects treated with MDMA-assisted psychotherapy for PTSD no longer met the PTSD diagnostic criteria, compared with 22.6% in the placebo group. The treatment was generally well tolerated, with anxiety, fatigue, headache, bruxism, and loss of appetite the most common adverse effects.[36] These findings led the FDA to grant MDMA breakthrough status, allowing the initiation of its use in a phase 3 clinical trial as an adjunct to psychotherapy for PTSD.[3, 6]

THE ROLE OF NURSING IN PSYCHEDELIC-ASSISTED THERAPY

Given the emerging data in the area of psychedelic-assisted therapy, it's impossible to know the specific roles nurses will play; however, gaining a robust understanding of psychedelic pharmacology, efficacy, and safety would enable nurses to discuss the responsible use of these therapies with patients or refer patients to appropriate clinical trials. In 2020, after conducting qualitative, semistructured interviews with an interdisciplinary, expert panel of clinicians working in the areas of oncology, psychosocial oncology, palliative care, and psychiatry, researchers created a conceptual framework for integrating psychedelic therapies into extant models of care for patients with serious illness.[39] Nurses were among the professionals providing feedback and expert guidance in refining the interview guide. These interviews with clinicians and the framework for integration they inspired suggest the need for continued testing of psychedelic-assisted therapies to better evaluate their benefits, risks, and underlying mechanisms of action, as well as the need to develop approaches for adapting treatments to therapeutic, institutional, and societal contexts as appropriate.

Nurses have called for increased interdisciplinary collaboration from researchers, clinical experts, and scholars in the nursing field in order to safely guide the integration of psychedelic-assisted therapies into models of care for serious illness, which will be essential going forward.[40]

A recent scoping review of psychedelic-assisted therapy that included literature from the past 20 years revealed that while relevant research continues to grow, the voice of

nursing is notably absent.[41] While professions, such as medicine, psychopharmacology, and psychology have published findings on advancements in the area of psychedelic-assisted therapies, nursing has lagged behind in disseminating related information.[42] The absence of nursing collaboration and nurse leaders in the field presents an opportunity to consider whether explicit or implicit biases regarding the use of psychedelics are factors in this trend.

HOW NURSES CAN PREPARE TO ENTER THIS GROWING FIELD

Nurses with an interest in psychedelic-assisted therapy should first examine any implicit or explicit biases they may have about psychedelic substances or people who use them. Keeping in mind that holistic nursing recognizes multiple ways of healing, such as symbolic language; imagery; aesthetic therapies; meditation; and spiritual practices, including indigenous traditions, which may be integrated with modern clinical paradigms, we encourage nurses to gauge their unconscious attitudes toward drug use and mental illness by taking an implicit association test (IAT). The mental illness IAT and the marijuana risk IAT are available on the Project Implicit website (see https://implicit.harvard.edu/implicit/user/pih/pih/selectatest.html). It would also be helpful to read and critically appraise studies linking psychedelic-assisted psychotherapies with improving mental health and overcoming addictive behaviors, as well as reports differentiating therapeutic psychedelic use from recreational use.[43]

Nurses hoping to become involved in this growing field can pursue the following avenues:

- Explore resources for psychedelic-assisted therapy and research (see Table 1).
- Express interest in the field to psychiatric, palliative, and holistic nursing organizations that offer further education and training on this topic.
- Participate in conferences on psychedelic-assisted therapies.
- Work in clinical trials as a therapist or researcher and add to the literature on psychedelic-assisted therapy.
- Complete training to become a psychedelic therapist in anticipation of the rescheduling of psychedelic treatments.

THE IMPORTANCE OF NURSING COMPETENCIES IN THIS AREA

The knowledge, skills, and values nurses bring to patient care are central to the therapeutic use of psychedelic-assisted psychotherapy. As Phelps has pointed out, the competencies needed to sit with a patient as a psychedelic therapist include the skills long associated with nursing's humanistic, biopsychosocial approach to care, specifically, "empathetic abiding presence, trust enhancement, spiritual intelligence, knowledge of the physical and psychological effects of psychedelics, therapist self-awareness and ethical integrity, and proficiency in complementary techniques."[8] These competencies align with a holistic philosophy of nursing and an integrative, whole person framework that prioritizes values such as a caring presence and spiritual healing.[44, 45]

Nurses are skilled in holding space as patients endure challenging events in real time and for prolonged periods, whether that be during childbirth, a sudden illness, an anxiety attack, or the time surrounding death. This skill translates well to being able to sit with a patient undergoing a therapeutic psychedelic experience, allowing space for whatever arises at physical, emotional, mental, or spiritual levels. Nurses can witness patient stories and help patients find meaning in these narratives, a crucial task in integrating the therapeutic psychedelic experience. Advanced practice nurses can play a crucial role in creating guidelines for assessing patients for psychedelic-assisted therapy and in providing a firm foundation of professional ethics on which to train other nurses, an area in which the voice and experience of nurses, a consistently trusted profession, would be an asset.

The growing field of psychedelic therapy will greatly benefit from nursing participation in the interdisciplinary effort to develop safe, effective clinical approaches to psychedelic-assisted therapies. Taking the baton from predecessors like Kay Parley, nurses can help create new solutions for the issues facing patients today. Psychedelic-assisted therapies offer great potential to alleviate suffering and cultivate healing, growth, and peace amid illness, and nurses are well prepared to contribute. ▼

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Table 1.

Research Resources for Psychedelic-Assisted Therapy

Organization	Mission/Aim/Purpose	Website
Beckley Foundation	To fund scientific investigation into the effects of neuroscience psychoactive substances on consciousness and to achieve evidence-based changes in global drug policy	https://beckleyfoundation.org
Center for Psychedelic Therapies and Research at the California Institute of Integral Studies	To train licensed health care professionals and clergy to conduct psychedelic research and therapy	www.ciis.edu/research-centers/center-for-psychedelic-therapies-and-research
Johns Hopkins Center for Psychedelic and Consciousness Research	To perform clinical research into the effects of psychedelics on brain function and psychiatric conditions	https://hopkinspsychedelic.org
Multidisciplinary Association for Psychedelic Studies	Nonprofit research and educational organization that develops medical, legal, and cultural contexts in which people can benefit from the uses of psychedelics and marijuana	https://maps.org
Organization of Psychedelic and Entheogenic Nurses	Professional organization advocating for ethical best practices and the inclusion of nurses in psychedelic-assisted psychotherapy	www.openurses.org
Usona Institute	Nonprofit medical research organization conducting phase 3 clinical trials of psilocybin for the treatment of major depression	https://usonaclinicaltrials.org