Neuroplastic Effects of Psilocybin-Assisted Psychotherapy in Alcohol Use Disorder and Depression

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In recent years, hallucinogens have been researched clinically for their optimization in mental health in the West. For about a quarter of the 20th century, hallucinogenic research persisted but was halted due to cultural repercussions and recreational drug use. Hallucinogens were labeled as Schedule I, prohibiting not only use but research as well. In 2000, Johns Hopkins (2023) gained approval to research the therapeutic benefits of hallucinogens. Research has demonstrated that psilocybin (colloquially known as “magic mushrooms”) increases neuroplasticity in the brain (Doss, 2021). Research has also demonstrated that psychedelics' neuroplastic effects promote a positive affect and variety in spiritual experiences (Crowe et al., 2022). Common conditions that are looked at through psychedelic research include depression and substance use disorders. Evidence concludes that alcoholism and depression are associated with decreased neural networks in the brain (Peregud et al., 2023). Promotion of neuroplasticity is implicated as a solution to recovery. This union of behavioral, biological, and spiritual aspects denotes that nursing participation may benefit the growing field of psychedelic treatment. Nursing is a holistic profession that requires a biopsychosocial approach to adequately assess and care for members of a population. Mental health disorders, such as major depression and alcohol abuse, often impact the healthcare system and require care from well-trained nurses. The goal of this paper is to explore nursing’s role in the treatment of co-occurring alcohol use disorder and major depression with psilocybin and psychotherapy to promote neuroplasticity and its effects.

The National Institute on Alcohol Abuse and Alcoholism (2023) estimates that over 28.6 million adults in the United States suffer from alcohol use disorder (AUD). Depression is the most common co-occurring disorder with AUD. Statistics demonstrate that those with AUD are

2.3 times more likely than the general population to suffer from depression (McHugh & Weiss, 2019). AUD is characterized by being a chronic, recurrent condition (Varcarolis & Fosbre, 2021) that yields aberrant neuroplasticity. Neuroplasticity is defined as the ability of neural networks and neurons within the brain to reroute their connections and change behaviors in response to new information, stimulation, development, dysfunction, or damage (Rugnetta, 2023). Alcohol intake has an impact on the brain at structural and molecular levels. These changes are associated with a decrease in brain-derived neurotrophic factor (BDNF). BDNF is a protein responsible for the strengthening of synapses. Ethanol impacts neuroplasticity by reducing the neurons' tendency to generate action potentials (intrinsic excitability) and preventing synaptic transmission (synaptogenesis). Recovery requires strengthening synapses. Structural changes related to excess ethanol consumption include degeneration in the ventral tegmental area (motivation), frontal cortex (decision-making), hippocampus (memory and emotion), and amygdala (stress response) (Peregud et al., 2023).

There are also macrostructural deviations in people with major depression disorder (MDD), such as hippocampal volume decrease, as well as neurotrophic and chemical differences. Depression severity negatively correlates with BDNF levels (Yang et al., 2020). Serum BDNF levels increase in those with MDD who receive antidepressants or electroconvulsive therapy. This demonstrates that relief in symptoms of depression is congruent with an increase in BDNF levels (Kishi et al., 2018). This increase can be explained by how selective serotonin reuptake inhibitors (SSRIs) bind to certain receptors in the brain. Fluoxetine, a first-line SSRI, binds to BDNF's receptor tropomyosin receptor kinase B (TrkB) resulting in allosteric regulation of BDNF, thus potentiating its effects (Cassoroto et al., 2022). Psilocin (PSI), the psychoactive component of psilocybin, was found to bind to TrkB with affinities a thousand times more

compared to SSRIs (Moliner et al., 2023). Due to the higher affinity of PSI with TrkB, the neuroplastic and behavioral effects are rapid as compared to SSRIs. This is exceptional considering that the therapeutic effects of SSRIs are not reached until around four weeks. Other studies set out to see if the neuroplastic results were sustainable, as demonstrated by long-term changes in mood and beliefs.

One study from Johns Hopkins followed 24 participants with a mean GRID-HAMD baseline score of 22.8 (severe depression) for 12 months. After completing initial preparatory therapy sessions, each participant received a dose of psilocybin during psychotherapy with a dyad of licensed mental health clinicians. After two weeks, participants received an additional psychoactive session. Then, every participant received a 1-2 hour follow-up session after 1 day, 1 week, and then 1, 3, 6, and 12 months where their GRID-HAMD scores were assessed. The scores revealed a change of over 50% from the baseline. An average score of 7.7, indicating no depression, was revealed at 12 months as compared to the baseline average of 22.8 (Davis et al., 2020). One double-blind study had two groups of participants who were diagnosed with alcohol dependence complete 12 psychotherapy sessions over 32 weeks, where they received either psilocybin or diphenhydramine during two of their sessions. Results concluded that participants who received psilocybin were more likely to have a reduction in their percentages of drinking days and mean drinks per day, as well as an increase in abstinence. Results were established through hair and fingernail samples tested for ethyl-glucuronide, self-reports, and the Short Index of Problems (SIP-2R) assessment tool (Bogenshutz et al., 2022). In this study, medications were available for the treatment of potential severe anxiety, hypertension, or psychotic symptoms. In the psilocybin group, there was an association with an increase in blood pressure and heart rate, both of which were reduced after 300-360 minutes into the session. No interventions were

needed for treatment, but the protocol for the availability of medications and required monitoring indicates that a nurse's presence may benefit treatment.

While there are physical and chemical changes occurring with psilocybin consumption, there are also emotional, mental, and metaphysical changes happening. Psychotherapy is used to help enhance a trusting alliance between the healthcare team and recipient, prepare for the psychoactive session, promote safety, and integrate new developments in the sessions following psilocybin treatment (Pots & Chakhssi, 2022). Alcohol use disorder and depression are both associated with isolation, disconnection, negative self-beliefs, and stigma. What has been found across a range of clinical conditions, is that the psychedelic experience promotes themes of connection and acceptance, which then empower a transformation process. The transformation process was described as a change in perception of self, beliefs, values, and clinical condition, as well as a relief from the past. Participants attributed these changes as being the result of the mystical experience of ego dissolution (Crowe et al., 2022). This dissolution of self is described as enhanced feelings of connection for the participant with the surrounding environment, people, self, and a power greater than themselves. This is understood to be therapeutic due to the fact that disorders such as depression and addiction are heavily centered on negative ruminations of self and the world. When the self is briefly eliminated and is instead associated as a part of the larger whole, this assists in changing the perception of self and placement in the world. Reduction in alcohol consumption was reported by participants as relating to the spiritual aspects of the psychedelic experience (Kelly et al., 2021). This finding is unsurprising considering the basis of many abstinence programs, specifically Twelve Step programs, are rooted in the development of a spiritual practice. The follow-up therapy sessions create a space for participants to talk further about insights they gained from their psychoactive session (Van der

Meer et al., 2023). Integration promotes lasting effects in enhancing the participants' understanding of their experience.

An important part of any nurse's role in the healthcare system is to implement therapeutic strategies that enhance readiness for health promotion, as well as to promote understanding and acceptance of clinical conditions (Crowe et al., 2022). This role is congruent with the transformative process that takes place during and following psilocybin treatment. Mental health nurses may benefit the treatment process due to their skills in supporting clients during hallucinations and periods of heightened anxiety. Additionally, a thorough assessment and health history are required to ensure that treatment is not contraindicated for the client. Current contraindications include a history of psychosis in the patient or a first-degree relative, as well as a diagnosis of bipolar disorder due to the risk of precipitous mania. Certain medications may also have an implication for treatment, requiring medication reconciliation. Psilocybin's action is potentiated by binding with the 5-Ht2A receptor (serotonin) which is blocked by antipsychotics such as quetiapine. SSRIs desensitize 5-Ht2A receptors, thus reducing the effects of psilocybin. This would require cessation of these drugs prior to treatment, which could put the patient at risk for withdrawal symptoms, worsening depression, and suicidal ideation. The nurse should assist in monitoring these risks (Nutt, 2019). Additionally, the potential somatic symptoms that can occur during care, such as an increase in blood pressure or heart rate, indicate frequent monitoring and potentially the administration of treatment medication. Other medications that may be indicated and administered by the nurse include benzodiazepines for anxiety relief during the altered state. Psychiatric-mental health nurse practitioners (PMHNP) are also pivotal members of the psychiatric health care team and provide a unique perspective given their holistic background. They should be expected to be competent in understanding the development of new

treatment modalities, including the therapeutic, pharmacologic, and contextual aspects and implications (Fradkin, 2020). The PMHNP can also play a role in providing therapy, medication maintenance, proper dosing, diagnosis of conditions that are indicated (or contraindicated) in treatment, as well as perform research, as designated by their state licensure guidelines.

While psilocybin is not yet in practice outside of research, it is currently in Phase III of research. Soon, research will be in Phase IV, which results in Food and Drug Administration (FDA) approval or disapproval. The FDA has created a draft for the guidance of additional clinical trials to promote safe research (Food and Drug Administration, 2023). Providers should begin to prepare for potential implementation by learning about potential treatment modalities and obtaining the required education. One contextual piece that healthcare providers should be made aware of, is that although psilocybin and other psychedelics are labeled Schedule I, research demonstrates a lower risk for reinforcing effects as compared to other (recreational) substances. Addiction disorders are associated with dysregulation of the reward system in the brain, whereas there have not been reports of similar effects in those who have ingested psilocybin (Crowe et al., 2022). Psilocybin is considered to be relatively physiologically safe. Reported emergency room visits related to psilocybin appear to be psychological, and are considered rare. Physical harm is mostly related to the risk of self-injurious behavior from a psychotic episode due to ingestion, which can be avoided with proper assessment and treatment regarding therapeutic use. There have only been three known deaths related to mushroom toxicity, which is infrequent due to the lethal dose being six grams of psilocin (10 kilograms of the physical mushroom). This is 300 fold the dose used in psychotherapy research. Overdose is rare as emesis typically occurs prior to toxic absorption levels (Kopra et al., 2022).

In conclusion, despite its complicated cultural history, psilocybin is in a research renaissance for a variety of medical conditions. This renaissance has even been recognized as a breakthrough therapy by the FDA, resulting in a draft of how to move forward with research. Mental health conditions are at the forefront of this research. Depression and alcohol use disorder specifically have been found to benefit from psilocybin-assisted psychotherapy. Research demonstrates that psilocybin promotes neuroplasticity through an increase in BDNF due to psilocin's affinity for the TrkB receptor. These neuroplastic changes have resulted in lasting affective changes; including increased openness, enhanced feelings of connection, transformation, changes in negative perceptions, and reductions in alcohol consumption. These treatments require a well-informed care team because although there are strong benefits, there are also great risks that must be carefully assessed for. The holistic background of the nursing profession is compatible with the biopsychosocial and spiritual implications of psilocybin therapy. Skills that registered nurses can offer include implementing therapeutic strategies that promote health enhancement, thorough assessments, supporting the client during hallucinatory experiences, monitoring physiologic effects, and providing necessary interventions. Healthcare is a constantly evolving field that requires being up-to-date on progressive treatments and research. It will be exciting to see how mental health treatment continues to change and grow.

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