

SUURJ: Seattle University Undergraduate Research Journal

Volume 2

Article 6

2018

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Recommended Citation

Hernandez, Xavier M. (2018) "Exploring the Therapeutic Potential of Psychedelics," *SUURJ: Seattle University Undergraduate Research Journal*: Vol. 2 , Article 6.

Available at: <https://scholarworks.seattleu.edu/suurj/vol2/iss1/6>

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Exploring the Therapeutic Potential of Psychedelics

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Introduction

Psychedelic compounds, those commonly associated with the recreational drug use of the counterculture movement of the 1960s and 1970s, have long been misunderstood. Research with psychedelic compounds dates to 1897 when mescaline, the primary psychoactive compound of the peyote cactus, was first isolated by German chemist Arthur Heffter (Bayliss, 1987). In 1943, Swiss chemist Albert Hofmann first discovered the psychedelic effects of lysergic acid diethylamide, commonly known as LSD, at Sandoz Pharmaceuticals in Basel, Switzerland (Hofmann, 1970). Hofmann went on to isolate psilocybin and psilocin, the psychoactive components of *Psilocybe mexicana*, also known as the Mexican “magic mushroom,” 15 years later in 1958 (Hofmann, 1970). Unbeknownst to the general public, close to 700 studies with psychedelic compounds took place before 1972, with research suggesting that psychedelics offer significant therapeutic benefits, including “helping recovering alcoholics abstain, soothing the anxieties of terminal cancer patients, and easing the symptoms of many difficult-to-treat psychiatric illnesses, such as obsessive-compulsive disorder” (Brown, 2007, p.67).

Research with these compounds has shown strong therapeutic promise for helping treat mental health conditions. However, multiple factors led to a strict federal regulatory environment in the absence of a compelling medical or scientific rationale (Hendricks, Thorne, Clark, Coombs, & Johnson, 2015). These factors include sensationalized media coverage of the recreational use of psychedelics in the 1960s and the administration of psychedelic compounds to an undergraduate population at Harvard University in poorly designed and controlled experiments (Russin & Weil, 1963). Unfortunately, a fuller exploration of the potential therapeutic use of these compounds was restricted in 1970 when the Controlled Substance Act was passed and established five levels of drug severity, with psychedelics being categorized as Schedule I, the strictest level (Hendricks et al., 2015). Though initial scientific exploration of the potential benefit of these compounds was halted, there has been a resurgence of interest in the field. This paper supports the idea that psychedelics can be largely beneficial in the therapeutic treatment of mental health conditions such as anxiety, depression, and addiction. The psychedelics that are explored in this paper include psilocybin, LSD, and ayahuasca, known for its isolated alkaloid, DMT. This paper will explore first a general therapeutic overview of psychedelics; second, psychedelics in the treatment of anxiety and depression; and third, psychedelics in the treatment of addiction.

Overview of Therapeutic Use

It is important to establish that psychedelics can be beneficial in therapy for serious mental health conditions. These compounds have been stigmatized since their DEA scheduling in the 1970s, limiting significant research into the treatment of disorders that are still not fully

understood in the psychiatric community. With mental health problems affecting almost half a billion people worldwide at substantial cost to society (World Health Organization, 2001), more effective treatments are needed. Psychedelics are a viable option for innovative mental health treatments for several reasons. Psychedelic compounds have naturally occurred in various plant and fungi species for millennia and cultures across the world have used them in sacramental healing contexts for over 5,000 years (El-Seedi, De Smet, Beck, Possnert, & Bruhn, 2005; Nichols, 2004). Psychedelic compounds are known to affect all mental functions, including perception, emotion, cognition, awareness of body, and sense of self (Brown, 2007). The effects of psychedelics depend heavily on the environment and the expectations of the subject (Brown, 2007), which is why combining them with psychotherapy is crucial. This also explains why the recreational use of psychedelics is vastly different than the therapeutic use of the same compounds. According to psychiatrist Rick Strassman, “psychedelics can be therapeutic to the extent that they elicit processes that are known to be useful in a therapeutic context: transference reactions and working through them; enhanced symbolism and imagery; increased suggestibility; increased contact between emotions and ideations” (as cited in Brown, 2004). This means psychedelics may enhance well-established therapy techniques. The classic psychedelic treatment method has the goal of inducing a “psychedelic,” “mystical,” or “peak” experience, which has been understood to elicit lasting change in habitual patterns of thought, emotional response, and behavior and which can be a key factor in the treatment of conditions such as addiction (Hoffer, 1967; Sherwood, Stolaroff, & Harman 1962).

Brief Psychopharmacology of Psychedelics

Psychedelics are divided into two basic chemical groups: tryptamines—such as psilocybin, LSD, and DMT—and phenethylamines—such as MDMA and mescaline (Brown, 2007). Tryptamines are a family of compounds that “selectively bind to specific serotonin (5-HT) receptors on neurons, mimicking the effects of the nerve-signaling chemical, or neurotransmitter, serotonin on these receptors,” which is responsible for stimulating parts of the brain related to important functions including mood, memory, appetite, sex, and sleep (Brown, 2007, p.67). Research with rat models has shown that tryptamines activate a specific subtype of serotonin receptors known as the 5-HT_{2A} subtype, inducing down-regulation of these receptors, effectively reducing binding at these receptors (Bogenschutz & Johnson, 2015). This is relevant to psychotherapy because increased binding at 5-HT_{2A} receptors has been reported in people with depression (Shelton, Sanders-Bush, Manier, & Lewis, 2009), impulsive aggression (Rosell et al., 2010), completed suicide (Anisman et al., 2008), and other mental health conditions. Also, 5-HT_{2A} receptor down-regulation could be effective in treating anxiety, stress, and addiction. Research has shown a positive correlation between fronto-limbic 5-HT_{2A} receptor density and increased anxiety and exaggerated stress response, both of which

are important triggers for relapse to substance abuse (Frokjaer et al., 2008; Sinha & Li, 2007). Another benefit of the use of psychedelics as therapeutic drugs is that they are noninvasive. Physiological toxicity and evidence of resulting organ damage or neurophysiological deficits are virtually nonexistent regarding the use of psychedelics, even at very high doses (Gable, 1993; Strassman, 1984). For these reasons, it is crucial to further explore the therapeutic uses of psychedelics. Because psychedelics can significantly influence habitual patterns of thought, emotional response, and behavior, considering the role of psychedelic therapy in the treatment of anxiety and depression is a logical step toward the treatment of the whole person who suffers from disorders of mental health.

Treatment of Anxiety and Depression

Anxiety and depression are serious mental health conditions that affect millions of people and often coexist and exacerbate one another (Hirschfeld, 2001). Most of the studies examined in this paper discuss anxiety and depression as related to palliative care. Several studies have explored the therapeutic use of psychedelics in the treatment of anxiety and depression in terminal cancer patients using psilocybin, including studies at New York University, Johns Hopkins University, and Harbor-UCLA Medical Center with results favoring the positive effects of psilocybin (Brown, 2007; Kelmendi, Krystal, Corlett, D'Souza, & Ranganathan, 2016). These studies have found that psilocybin can rapidly produce "large and sustained decreases in clinician- and patient-related measures of depressed mood and anxiety," improved quality of life, life meaning and optimism, as well as decreases in death-related anxiety in advanced-stage cancer patients (Kelmendi et al., 2016, p. 1212). These positive effects have also been shown to be fast-acting and long-lasting, not requiring chronic administration that most conventional medications necessitate. Follow-up studies conducted six and a half months to a year after the initial psilocybin session showed that the effects endured in over half of the individuals, while the vast majority reported the experience as increasing their life satisfaction and wellbeing (Ross et al., 2016). The fast-acting nature of psychedelics also seems promising in therapeutic treatment, considering most antidepressants on the market today take two weeks for the onset of therapeutic action (dos Santos, Osório, Crippa, & Hallak, 2016).

Psilocybin is not the only psychedelic that shows promise in the treatment of anxiety and depression. LSD has been shown to produce lasting reductions in anxiety in individuals with life-threatening diseases (Gasser et al., 2014). Additionally, ayahuasca and one of its isolated alkaloids, DMT, have shown anxiolytic and antidepressant qualities. Anxiety and depression are associated with increased rumination, which is characterized by cyclical thought. This behavioral tendency can cause individuals to spiral into a seemingly hopeless thought pattern of worthlessness and inadequacy. This is important because ayahuasca use has been shown to significantly reduce activity in areas of the brain associated with increased

rumination (dos Santos et al., 2016). Because ayahuasca dampens neural networks associated with rumination, it and other drugs targeting the serotonin system should be considered as plausible psychological treatment for conditions such as anxiety and depression. Evidence that serotonin receptor agonists regulate emotional processing, reduce anxiety and depressive symptoms, and increase positive mood supports a case for all tryptamines as effective in treatment of conditions related to these symptoms (dos Santos et al., 2016). Anxiety and depression have also been shown to be associated with inflammatory processes, and serotonin-receptor agonists have anti-inflammatory properties (dos Santos et al., 2016). This further supports a case for tryptamines such as psilocybin, LSD, and ayahuasca as effective treatments because they can potentially help reduce inflammatory processes associated with anxiety and depression.

Treatment of Addiction

Addiction is also related to anxiety and depression in the effects it has on human wellbeing. Most addiction treatments that are currently available are mildly effective at best, whereas research has demonstrated promise in the use of psychedelics for addiction treatment (Bogenschutz & Johnson, 2015). The leading preventable cause of death and disability globally is addiction to alcohol, tobacco, and other drugs (Rehm, Taylor, & Room, 2006; Volkow & Li, 2005). Several lines of research have shown psychedelics to be nonaddictive (Berglund, 2005; Bogenschutz, & Pommy, 2012) so addiction to psychedelics is not of significant concern. On the contrary, LSD has been shown to be almost twice as effective in the treatment of alcoholism as compared to standard treatments (Krebs & Johansen, 2012,). One of the tenets of Alcoholics Anonymous, or AA, is the concept of spiritual awakening, the idea that lasting behavioral change in recovery can be brought about by a mystical-type experience (Forcehimes, 2004). Bill Wilson, the founder of AA, acknowledged the efficacy of LSD use to help alcoholics experience spiritual insight and became an enthusiastic proponent of the compound based on his own LSD experiences (Kurtz, 2008).

At least six different studies conducted during the early psychedelic research era have shown results supporting the effective treatment of alcohol addiction with LSD treatment (Bowen, Soskin, & Chotlos, 1970; Hollister, Shelton, & Krieger, 1969; Ludwig, Levine, Stark, & Lazar, 1969; Pahnke, Kurland, Unger, Savage, & Grof, 1970; Smart, Storm, Baker, & Solursh, 1966; Tomsovic & Edwards, 1970). Psilocybin has also been effective in the treatment of alcohol addiction, with results “displaying improvement in drinking habits with decreases in craving and increases in abstinence self-efficacy” (Bogenschutz & Johnson, 2015, p. 5). Decreased rates of alcohol addiction have been consistently correlated with ayahuasca use (Doering-Silveira et al., 2005; Halpern, Sherwood, Passie, Blackwell, & Rutenber, 2008). It has also been frequently reported that peyote use in the context of Native American Church ceremonies

helps individuals who are recovering from alcohol addiction achieve and maintain sobriety (Albaugh & Anderson, 1974; Garrity, 2000; Kunitz & Levy, 1994; Lu et al., 2009). Another study has shown psilocybin to be highly effective in the treatment of tobacco addiction, more than doubling abstinence rates of approved tobacco addiction treatments and resulting in excellent clinical outcomes (Johnson, Garcia-Romeu, Cosimano, & Griffiths, 2014). In regards to the role of psychedelic mechanisms in addiction treatments, psychedelics are believed to induce changes in neuroplasticity, suggesting a possible biological basis for persisting behavioral change (Bogenschutz & Johnson, 2015). Other possible mechanisms include emotional catharsis (Albaugh & Anderson, 1974) and improved self-understanding and motivation for sobriety (Garrity, 2000). Psychedelics seem promising in the treatment of addiction because they lack addictive effects themselves, can provide mystical-type experiences found to support naturalistic addiction recovery and are safe when used in a proper therapeutic context. Additionally, they can induce long-lasting changes in behavior, while non-psychedelic medications for addiction treatments only provide effects as long as they are being regularly taken.

Conclusion

Therapeutic treatment with psychedelics seems especially promising considering that their healing covers a broad scope—working on a physiological, psychological, and even mystical or spiritual level. The quick onset and noninvasive, persistent effects of psychedelics are highly preferable in therapeutic treatment. Investigation of these compounds could provide new pharmacological treatments with fast-acting beneficial effects for patients with anxiety, depression, and addiction.

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