Missouri S&T's Peer to Peer

Volume 1 | Issue 2 Article 1

May 2017

Clinical Uses for Psychedelic Drugs

Matthew Clarkson

Matthew Clarkson
Psychology at Missouri University of Science and Technology

CLINICAL USES FOR PSYCHEDELIC DRUGS

Abstract

Throughout the last forty years, psychedelic drugs have been illegal in the United States. Stigmatized due to the potential for abuse, the use of these drugs has been relegated to simple criminal activity and research stagnated for those 40 years. Slowly, research has begun to pick up as the restrictions begin to lift incrementally. However, the current restrictions are intense, further limiting the amount of research conducted that can reveal the medical benefits of these drugs. Through multiple studies, both open-label and double-blinded to show both feasibility and efficacy, as well as the biological impact of the drugs, significant anxiolytic, antidepressant, and anti-addictive effects of hallucinogens have been demonstrated. The medical use of these drugs could have a lasting effect regarding substance abuse addictions, severe cases of anxiety, and treatment resistant depression providing alternatives to current methods of treatment.

Clinical Uses for Psychedelic Drugs

Since the late 1960s, psychedelic drugs have been outlawed in the United States. Prior to their ban, psychedelic drugs were thought to have significant medical uses, showing promise in treating a broad array of psychological disorders. Because of their proposed medical uses, psychedelic drugs were often studied prior to the ban. However, in the late 1960s, a large part of the population began to abuse psychedelic drugs and because of this, scientific research regarding psychedelics had been slowed. Although some of the barriers to the research and medical use of psychedelic drugs have been lifted, they remain heavily stigmatized and restricted, limiting the amount and the extensiveness of the research that can be conducted. As the restrictions slowly start to lift, research on psychedelics has started to proceed. This research has been conducted on lysergic acid diethylamide (LSD), psilocybin, and ayahuasca, a hallucinogen originating from the Amazon region of South America. Throughout this paper, hallucinogenic and psychedelic drugs will be used interchangeably to refer to drugs that have the potential to induce hallucinations or an altered sense of reality. Typically, the hallucinations or altered sense of reality are the goals of abuse of these drugs and cause the stigmatization of these drugs. However, despite the ban on hallucinogens, the abuse of these drugs has not significantly diminished and only serves to majorly limit the research allowed for these drugs. Current research indicates that hallucinogens have medical benefits as shown through studies and biological processes. The purported uses of psychedelics are as antidepressants, anxiolytics, meaning antianxiety, and as anti-addictive drugs.

Biology

Outside of clinical trials, hallucinogens demonstrate potential efficacy in the treatment of mood disorders. Using functional magnetic resonance imaging (fMRI) to scan the brain, psychedelic

drugs exhibited effects correlated to a decrease in mood disorders. Hyperactivity in the medial prefrontal cortex of the brain is associated with depression. With administration of psilocybin as well as non-hallucinogenic-based treatments for depression, the medial prefrontal cortex displays lessened activity and eventually leading to normalization. fMRIs also revealed that amygdala activation resulting from threat related stimuli decreased with the use of psilocybin. The amygdala plays a significant role in the creation of emotions and the hyperactivity of this section of the brain due to negative stimuli has regularly been associated with negative mood states in depressed patients. (Mahaptra, 2017, p. 55) The use of the fMRI to link the activity of hallucinogenic drugs with a decrease in brain activity related to depression shows a biological basis for clinical use of these drugs. Additionally, since both psychedelic drugs and traditional methods of depression treatment created similar responses in the brain, the medical use of these drugs is further supported.

In addition to the changes in brain activity, other biological factors also contribute to the use of hallucinogens as medication. Mahapatra (2017) writes, "Downregulation of 5-HT_{2A} receptors is purported to mediate antidepressant and antianxiety effects of antidepressants and atypical antipsychotics…Because of the high binding affinity of psilocybin to the 5-HT_{2A} receptor, its effects are thought to be mediated." (p. 54) These receptors are responsible for regulation of serotonin, a neurotransmitter. A deficit of this neurotransmitter can often lead to depression. Furthermore, the 5-HT_{2A} receptors correspond to additional factors related to depression. Idell (2017) explains that expression of 5-HT_{2A} receptors link to neuroinflammation. (pg. 50) Heightened levels of neuroinflammation can lead to depression as well and is widely regarded as a risk factor for depression. Psilocybin has the potential to regulate the expression of 5-HT_{2A} receptors and decrease inflammation in the brain. (Idell, 2017, p. 50) The potential for

hallucinogens to reduce depression in patients further supports the proposal for the clinical uses of these drugs.

Antidepressant/Anxiolytic

The proposed clinical use of psychedelic drugs revolves primarily around their use as antidepressants. In a study consisting of 22 patients with depression were treated with LSD weekly for 5-6 weeks, eighty percent of patients exhibited improvements in signs of depression within 6-18 months. (Rucker et al, 2016) The improvement of eighty percent sits well above the threshold for clinical significance and demonstrates the efficacy of the drug. Alternatively, Ayahuasca has also been studied as a treatment option for depression. Dos Santos et al. (2016) writes "Ayahuasca administration produced statistically significant reductions of up to 82% in depressive scores between baseline and 1, 7 and 21 days after drug intake, according to the Hamilton Rating Scale for Depression (HAMD), the Montgomery–Åsberg Depression Rating Scale (MADRS), and the Anxious–Depression subscale of the Brief Psychiatric Rating Scale (BPRS)" (p. 201). In this study, statistically significant numbers relating to decline in depressive scores are reached in a short time period after administration of the drug. These numbers also appear across a wide range of depression scales. The short term and long term improvement of depression with two different psychedelic drugs shows promising signs in the treatment of depression. However, these two studies were open-label, meaning these studies show potential or feasibility rather than efficacy.

Other studies have been conducted in order to test the efficacy of hallucinogens. Ross et al. (2016) conducted a study on the efficacy of psilocybin and its role as an antidepressant and anxiolytic. This study treated patients with life-threatening cancer who also underwent serious anxiety and depression. Unlike the studies mentioned above, this study was double-blinded and

tested against Niacin, a placebo. The study concluded that "Psilocybin produced immediate and enduring anxiolytic and anti-depressant response rates, as well as significant anti-depressant remission rates (measured by the HADS D and BDI)." Using the HAD A and BDI as the scale, 83% of patients administered psilocybin exhibited an antidepressant response while only 14% of those given Niacin exhibited antidepressant responses. Anxiolytic responses occurred in 58% of those given psilocybin and only in 14% of those given Niacin (pg. 1175). The chasm between antidepressant and anxiolytic effects due to psilocybin and the placebo shows that psilocybin has clinical uses. Double-blinded placebo-controlled trials have mostly been done with psilocybin although other hallucinogens are used in other studies. Another study conducted in Switzerland in 2014 treated patients with anxiety resulting from life-threatening illness with LSD. This study observed similar effects to the double-blinded placebo-controlled psilocybin study. (Cameron, 2016) The success of LSD in the treatment of these patients shows that the anxiolytic and antidepressant effects are present in hallucinogens other than psilocybin. As both of these trials were conducted against the placebo in a randomized manner and displayed large increases in efficacy of their respective hallucinogens against the placebo, these trials provide ample evidence showing that hallucinogens can significantly improve depression and anxiety.

Anti-addictive

The most prominent concerns with these drugs are safety and dependence. The use of psychedelic drugs causes great concern regarding potential for dependence. However , Psychedelics "do not induce dependence." (Rucker et al, 2016, p. 1221) In addition to being non-addictive, psychedelics are also anti-addictive, meaning they combat dependence on other substances. The two substances studied in regards to the anti-addictive effects of psychedelics are tobacco and alcohol.

Tobacco Dependence

Hallucinogens have shown potential to combat addictions to tobacco through an open-label study. In this study, the average participant smoked 19 cigarettes per day and had smoked for approximately three decades. The study measured cigarettes per day prior to and after the administration of psilocybin. 6 months after the administration of psilocybin, 80% of the participants had not smoked. Additionally, the participants reported less desire to smoke throughout the entire duration of the study as well as higher confidence in their ability to withstand the temptation to smoke. (Dos Santos, 2016, p. 199-200) Because these smokers had smoked for a great length of time, their dependence on nicotine was rather strong. Although the study was open-label and undoubtedly affected by the placebo effect, the abstinence of 80% of the sample demonstrates massive potential in aiding those who have struggled with nicotine addiction.

Alcohol Dependence

Equally as tobacco dependence, psychedelic drugs lesson one's dependence upon alcohol. An open-label trial conducted in regards to alcohol dependence administered psilocybin to the patients. These patients had been considered alcohol dependent for an average of 15.1 years with 80% of the sample experiencing withdrawal symptoms prior to the start of the trial. In addition to the psilocybin, this trial also included seven sessions of motivational enhancement therapy. Throughout the course of the trial, the days in which alcohol was consumed as well as the days the patient drank heavily, consuming 4 or more drinks consisting of more than 14 g of alcohol, substantially decreased. Throughout the 36 weeks of the trial, the decrease in alcohol dependence remained consistent. (Dos Santos, 2016, p. 200) Compared to the length of time the patients depended on alcohol before the study, their decrease in dependence marks a huge improvement.

Like the Tobacco trial, the alcohol trial was also prone to the placebo effect as it was open-label. However, this trial still shows potential relating to the anti-addictive effects of hallucinogens.

Safety

The biggest issue concerning the use of hallucinogens to treat mood disorders stems from potential adverse effects relating to both physical health and mental health. In clinical trials conducted over the safety risks of hallucinogens, most or all patients report no serious adverse effects with exceptions regarding ayahuasca and vomiting in 50% of the sample. The patients involved in the ayahuasca trial did not regard the vomiting as "causing severe discomfort" (Dos Santos et al., 2016; Ross et al, 2016). At first glance the vomiting seems rather serious especially considering its appearance in half of the sample. However, out of the three hallucinogens commonly discussed in the treatment of mood disorders, only ayahuasca caused the patients to vomit. The lack of severe adverse effects by all of the hallucinogens reported means that the use of psychedelic drugs in a controlled setting has no known major health consequences. In addition to the aforementioned vomiting, other effects have been noted as well. The effects noticed were "non-clinically significant elevations in BP [blood pressure] and HR [heart rate] (76%), headaches/migraines (28%), and nausea (14%)... transient anxiety (17%) and transient psychotic-like symptoms (7%: one case of transient paranoid ideation and one case of transient thought disorder)" (Ross et al, 2016, p. 1173). Due to the short duration of most of these effects combined with a relatively low appearance in the sample, these effects are not significant or serious. The one effect that does appear in a large majority of the sample, a rise in blood pressure and heart rate, is classified as non-clinically significant. The low incidence in serious and clinically significant symptoms in addition to the the short duration of most symptoms demonstrates the relative safety of psychedelic drugs.

Additionally, appropriate dosing and drug quality plays a role in the safety of hallucinogenic drugs. One study on hallucinogenic drugs conducted by Baumeister et al. (2014) stated that adverse effects occurred in a minority of participants, they could all be calmed down without medication, and these effects only occurred in patients who had received high doses (p. 163). The presence of adverse effects in patient who had received high doses indicates a correlation between dosage and adverse effects indicating that if lower doses were administered, the presence of adverse effects would likely drop. Drug quality is another factor connected to severe symptoms. Rucker et al. (2016) writes "The majority of studies of adverse reactions, retrospective in nature, have described a constellation of premorbid characteristics in individuals seeking treatment for these reactions where drugs of unknown purity were taken in unsupervised settings." (p. 1227) The adverse reactions reported were noticeably low with proper dosages and pharmaceutical quality drugs. Additionally, since serious conditions were only noted in those who had received high doses and drugs of questionable quality, the use of hallucinogenic drugs have limited and non-life threatening side effects when used responsibly.

Discussion

Currently, psychedelic drugs are labeled as schedule 1 drugs, meaning these drugs have no medical purposes and high potential for abuse. However, as psychedelic drugs have shown to exhibit certain clinical uses, such as antidepressant and anxiolytic effects, and have shown promise curbing dependence on other substances, to claim these drugs have no medical use would be absurd. Additionally, although these drugs could be abused, they are non-addictive. Therefore, these drugs have no potential for dependence. Lower classifications do exist for drugs that meet the criteria of non-addictive, potential for abuse, and medical purposes. Changing the classifications on these drugs would result in lessened restrictions on research of these drugs and

their uses and possibly open the door for them to be used to treat mood disorders. Furthermore, opiates are currently used in medicine. Opiates have high addiction potential and incur more danger and yet morphine is still widely used to anesthetize patients. If drugs that incur considerably more danger and have higher addiction potential are commonly used in medicine, the use of psychedelic drugs should not be so stigmatized. Since only smaller scale studies have been conducted to measure the effects of hallucinogens, more research should be conducted before they enter into mainstream clinical use. Lastly, it is important to note that these drugs will not be a magical cure for depression. Depression results from both biological and behavioral interaction. Without the proper behavioral changes, these drugs will be ineffective. Accordingly, due to the multifaceted cause of depression, multiple treatments should be used. Hollister (1969) writes "The old adage that the lack of a single effective treatment encourages multiple treatments is nowhere more evident." (p. 171) Since, depression has multiple interrelated causes, multiple treatments to combat the different interactions of its root causes becomes all the more necessary. Hallucinogenic drugs, if more research is conducted, may help curb the steadily increasing rates of depression.

References

Baumeister, D., & Barnes, G., & Giaroli, G., & Tracy, D. (2014) Classical hallucinogens as antidepressants? A review of pharmacodynamics and putative clinical roles. *Therapeutic Advances in Psychopharmacology*, Vol. 4(4) Retrieved from https://www.nlm.nih.gov/bsd/pmresources.html

Cameron, R. (2016) Look again at psychedelic drugs. *Nursingstandard.com* Vol. 30. Retrieved from https://www.nlm.nih.gov/bsd/pmresources.html

Dos Santos, R. G., & Osorio, F. L. & Crippa, J. A., & Riba, J., & Zuardi, A. W., & Hallak, J. E (2016) Antidepressive, anxiolytic, and anti-addictive effects of ayahuasca, psilocybin and lysergic acid diethylamide (LSD): a systematic review of clinical trials published in the last 25 years. *Therapeutic Advances in Psychopharmacology*, Vol. 6(3). Retrieved from https://www.nlm.nih.gov/bsd/pmresources.html

Hollister, L. E. (1969) Clinical use of psychotherapeutic drugs: Current Status. *Clinical pharmacology and therapeutics*, Vol. 10 Retrieved from https://www.nlm.nih.gov/bsd/pmresources.html

Idell, R.D., & Florova, G., & Komissarov, A. A., & Shetty, S., & Girard, R. B. S., & Idell, S. (2017) The fibrinolytic system: A new target for treatment of depression with psychedelics. *Elsevier*. Retrieved from https://www.nlm.nih.gov/bsd/pmresources.html

Mahapatra, A. & Gupta, R. (2017) Role of psilocybin in the treatment of depression. *Therapeutic Advances in Psychopharmacology*, Vol 7(1) Retrieved from https://www.nlm.nih.gov/bsd/pmresources.html

Ross, S., & Bossis, A. & Guss, J. & Gabrielle A. L., & Malone, T., & Cohen, B.,…& Corby, P., & Schmidt, B. L. (2016) Rapid and sustained symptom reduction following psilocybin

treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial. *Journal of Psychopharmacology*, Vol. 30. Retrieved from https://www.nlm.nih.gov/bsd/pmresources.html

Rucker, J. JH., & Jelen, L. A., & Flynn, S., & Frowde, K. D., & Young, A. H. (2016) Psychedelics in the treatment of unipolar mood disorders: a systematic review. *Journal of Pyschopharmacology*, Vol. 30. Retrieved from https://www.nlm.nih.gov/bsd/pmresources.html