EDITORIAL

Psychedelics Road Ahead: Are We Ready?

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Abstract

Psychedelics are classed as a schedule I substance under the Controlled Substances Act of 1970 because of the potential for mind-changing effects. In vulnerable people, unsupervised use has the potential to lead to suicide. However, the management of end-of-life anxiety, severe resistant depression, resistant obsessive–compulsive disorder, and substance abuse is met with a high failure rate. The preliminary study on psychedelics has yielded promising results, prompting the Food and Drug Administration (FDA) to classify them as a breakthrough medicine. More phase 3 research, funded by pharmaceutical company, are in the works. Similar studies should be funded by national institutes and government bodies to ensure unbiased results, as the findings of such studies may need legislative changes.

Keywords: LSD, MDMA, Psilocybin, Psychedelics, Psychoactive drug.

Indian Journal of Private Psychiatry (2022): 10.5005/jp-journals-10067-0113

Introduction

Psychedelic plants extracts such as mescaline (peyote cactus) and psilocybin (magic mushrooms) had been in use for millennia in various indigenous cultures all across the globe for inducing ecstatic state of consciousness and spiritual experiences.[1,2] This was introduced to the western scientific research community in 1897 when Arthur Heffter isolated mescaline; nevertheless, Albert Hofmann's synthesis of lysergic acid diethylamide (LSD) in 1938 at Sandoz was the true breakthrough.[3]

Psychedelics refer to those molecules which have 5HT2A receptor agonistic property and LSD may be considered the prototypical drug.[4] LSD, psilocybin, mescaline, and dimethyltryptamine (DMT) are classified as classic psychedelic compounds.[5]

LSD became research chemical thanks to Hofmann's memorable bicycle journey. Thousands of clinical papers and dozens of books were written within 15 years of its inception, covering thousands of patients. Psychedelic therapy has been the subject of several international conferences. LSD piqued researchers' curiosity, and the National Institutes of Health financed over 130 grants to research it (but none since the 1967 ban).[3] To meet this demand in 1967, *Journal of Psychedelic Drugs* was started which had to be later renamed as *Journal of Psychoactive Drugs* because research diminished after categorization of drugs into schedule I.[1,4]

The Controlled Substance Act of 1970 placed LSD and other psychedelics known at the time into the most restrictive category of drugs, schedule I. The implication was virtually impossible to research into the pharmacology or medical value of psychedelics.[1]

After 1990, the interest in research of psychedelics resurged. This happened after neuroimaging and psychopharmacological studies in healthy volunteers followed by a few preliminary clinical studies. The neuroimaging investigations demonstrated that activity in the subgenual cingulated brain was suppressed, which was linked to a reduction in depressed symptoms. These neuroimaging findings were consistent with previous treatments that have been shown to be effective in the treatment of depression.[6,7] Psychopharmacological experiment by Griffiths et al. at John Hopkins University, where 36 healthy individuals were administered a single 30-mg oral dose of psilocybin in a psychotherapeutic setting and followed up for 14 months. Participants found the experience personally meaningful and spiritually significant which produced positive change in attitudes and mood.[8]

The modern psychedelic research began with Hermle et al. (1992) in Germany using mescaline, Strassman et al. (1994) in the United States using DMT, and Vollenweider et al. (1998) in Switzerland using psilocybin.[3]

In an open-label study, Moreno et al.[9] (2006) at the University of Arizona included nine people with treatment-resistant obsessive–compulsive disorder (OCD) who were given three different dosages of psilocybin. There were significant reductions in OCD symptoms, and there were no serious side effects. The trial was halted due to the high costs of dealing with a prohibited substance.[3]

What do Current Studies Say?

Gradually these small studies gave way to open-label trials followed by double-blind trial. The double-blind trial conducted at prestigious John Hopkins and New York University suggested a positive effect over depressive and anxiety symptoms in life-threatening cancer patients.[3]

With initial encouraging good results, psychedelic research was eventually broadened to major depressive disorder, treatment-resistant depression, OCD, alcohol and nicotine addiction, and post-traumatic stress disorder.[10] The possibility of its use in cluster headache and autism spectrum disorder[1] is also being explored.

Based on these positive studies, the European Medical Association (EMA) and the Food and Drug Administration (FDA) have both given their approval for a multicenter multi-country trial of psilocybin

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How to cite this article: Gowda MR. Psychedelics Road Ahead: Are We Ready? Ind J Priv Psychiatry 2022;16(1):1–2.

Source of support: Nil

Conflict of interest: None

run by the UK-based pharmaceutical company called COMPASS Pathways for its effect on treatment-resistant depression and major depressive disorder. In the USA, the company USONA is in the process of developing psilocybin as a medicine for depression management.

Adverse Effects and Addiction Potential

LSD, psilocybin, and other hallucinogens use has been associated with delusional acute reaction, exacerbation of psychotic disorders or a prolonged psychotic reaction, risk of suicide, and so initially had been a model for psychosis.[11] However, a recent review of the medical use of psilocybin by Johnson et al. in 2018 showed that the risk of psychosis is higher in susceptible patients, and proper patient screening and delivery in a supervised setting reduces the chance of acute adverse effects. A similar study by Karlsen et al. on 3,4-methylenedioxy-methamphetamine (MDMA) has suggested that long-term use of high dose may cause cognitive and psychiatric symptoms but lower dose for medical purpose is safe.

Also, roughly 1% of psilocybin users experienced what is known as post-hallucinogen perception disorder (HPPD) (Jerome, 2007),[12] which is characterized by lasting changes in perception, mostly visual perception.[11]

Psychedelics' risk for addiction has been shown to be modest, and they are not considered reinforcing (O'Brien, 2001). Because of the serotonergic mechanism of action, this is predictable. The animal model for predicting the likelihood of abuse has largely failed. Retrospective studies have found a link between recreational psychedelic usage and lower rates of criminal recidivism and intimate relationship violence.[10]

Future of Psychedelics

The number of registered clinical studies has increased dramatically as a result of the favorable preliminary findings of these medications in the treatment of psychiatric diseases, with 70 registered studies detected from a clinicaltrials.gov search on December 3, 2020.[13]

MDMA-assisted psychotherapy for post traumatic stress disorder (PTSD) and psilocybin for treatment-resistant depression have been recognized as groundbreaking therapies by FDA, meaning these are some of the most promising drugs currently in development.[14]

Argento et al. from British Columbia University argue that COVID-19 has impacted mental health with rise in depression, anxiety, addiction, and post-traumatic stress disorder which may be addressed with psychedelic-assisted psychotherapy.

According to Barnett and Greer, the FDA may approve psychedelic-assisted therapy in the near future, and liaison psychiatrists will need to educate themselves in patient selection as society's interest is also growing.[15] So After a long period at psychiatry's periphery, psychedelics are now increasingly being embraced by the field.[15]

Conclusion

Psychedelics are classed as a schedule I substance under the Controlled Substances Act of 1970 because of the potential for mind-changing effects. In vulnerable people, unsupervised use has the potential to lead to suicide. However, the management of end-of-life anxiety, severe resistant depression, resistant OCD, and substance abuse is met with a high failure rate. The preliminary study on psychedelics has yielded promising results, prompting the FDA to classify them as a breakthrough medicine. More phase 3 research, funded by pharmaceutical company, are in the works. Similar studies should be funded by national institutes and government bodies to ensure unbiased results, as the findings of such studies may need legislative changes.

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