

Research Article**Psychedelic Drug Use in Treatment of Mental Health: A Dream or Reality****¹Sadaf Inayat, ²Adeel Islam, ³Nabeel Aslam,****⁴Anas Ahmed Khan and ⁵Muhammad Yasir Tarar**¹Fatima Jinnah Medical University²Services Institute of Medical Sciences, Services Hospital³Services Institute of Medical Sciences, Services Hospital⁴University of Health Sciences, Services Hospital⁵Services Institute of Medical Sciences, Services Hospital**ABSTRACT:**

Psychedelics are psychoactive substances that alter perception and mood and affect numerous cognitive processesⁱ. They are considered physiologically safe and do not cause dependence or addiction. Their origin predates written history, and they were employed by early cultures in many cultural and ritualistic contexts. The classical psychedelics LSD, psilocybin, mescaline is not known to cause brain damage and are regarded as non-addictive. They exert their effect by acting on serotonin receptors (5ht-2a) in the brain as agonists or partial agonists.

Drugs such as 3,4-Methylenedioxymethamphetamine (MDMA) are classed as entactogens and act similar to psychedelics by acting on serotonin receptors(5-ht) but are substantially distinct to classical psychedelicsⁱⁱ. They also act on norepinephrine, dopamine, and alpha-2 adrenoceptors.

Psychedelic plants have been used for celebratory, religious or healing purposes for thousands of years^{iii, iv, v}. In view of the widespread historical use of psychedelics as sacraments in a variety of other cultures, Jaffe's^{vi} definition for the class of psychedelics can perhaps be appreciated: "the feature that distinguishes the psychedelic agents from other classes of drug is their capacity reliably to induce states of altered perception, thought, and feeling that are not experienced otherwise except in dreams or at times of religious exaltation." All pharmacologists will recognize that this definition for a class of psychoactive drugs is indeed quite unique. Since the 1960s psychedelics have been consumed with widespread use throughout the world. Most of the consumption is due to curiosity, mystical experiences or introspection^{vii}.

Even after consumption of millions of doses over a period of 60 years, well-documented case reports of long-term mental health problems following use of these substances are rare. They are not known to cause birth defects or genetic disorders or damage to brain or other parts of the body. Their risk of addiction, withdrawal or psychological dependence has never been documented^{viii}. LSD including psilocybin are ranked in expert assessments as causing less harm to individual users and society than alcohol, tobacco, and most other common recreational drugs^{ix, x}.

In clinical research settings around the world, renewed investigations are taking place on the use of psychedelic substances for treating illnesses such as addiction, depression, anxiety and posttraumatic stress disorder (PTSD). Since the termination of a period of research from the 1950s to the early 1970s, most psychedelic substances have been classified as drugs of abuse with no recognized medical value. Recent research, although limited in scope due to strict control on these drugs (classified as Schedule 1 in UK) in many countries, has shown significant promises. The aim of this review is to study the previous literature and their results and to recommend further approaches needed in order to make these drugs more accessible for therapeutic use.

Keywords: The keywords for the literature search for this review was peer-reviewed articles following, LSD, MDMA, psychotherapy, depression, anxiety, psychedelics, ptsd, ocd 3,4-Methylenedioxymethamphetamine.

INTRODUCTION:

Among them the papers that fit the criteria were selected and full-text articles were read. The search was carried out using the data bank of the

PubMed and Medline database updated to 2018. The references found in the search were then studied in detail.

Types of Psychedelic drugs

Substance	Effects	Harm	Uses
LSD	<ul style="list-style-type: none"> Altered consciousness (vision, auditory and visual hallucinations) Altered mood (happy, sad, fearful) Distorted sense of space and time 	<ul style="list-style-type: none"> Psychosis Altered perception syndrome 	<ul style="list-style-type: none"> Addiction Anxiety-associated with terminal illness
Psilocybin (magic mushrooms)	<ul style="list-style-type: none"> Altered mood Altered consciousness Distorted sense of time and space 	<ul style="list-style-type: none"> Psychosis Hallucinogen perception disorder 	<ul style="list-style-type: none"> Addiction Anxiety-associated with terminal illness
MDMA	<ul style="list-style-type: none"> Euphoria Arousal Enhanced social empathy and bonding 	<ul style="list-style-type: none"> Short term depression Sleep disturbance 	<ul style="list-style-type: none"> PTSD

MDMA=3,4-Methylenedioxymethamphetamine

LSD = lysergic acid diethylamide

PTSD = posttraumatic stress disorder

drug-related adverse events. The drug effects lasted no later than one day after a session.

Context and Indications

Lysergic acid diethylamide

The use of LSD in anxiety disorders and anxiety due to serious life illness is well documented^{xi, xii}. A double blind, randomized, active placebo-controlled study assessed the effects of lysergic acid diethylamide (LSD) in 12 patients (seven men, four women) with anxiety associated with life-threatening diseases (cancer, or chronic motor or inflammatory diseases)^{xiii}. It was conducted in Basel, Switzerland in 2014. They were assigned randomly into either control (20 µg LSD) or treatment group (200µg LSD). They would have drug free psychotherapy supplemented with LSD-assisted sessions two to three times a week. The data was collected at baseline, 1 week, 2 months and 12-month period. Follow up 1 year later showed increased therapeutic benefit with STAI reductions and no acute or chronic

Psilocybin

A double blind, randomized, placebo-controlled study assessed the safety and potential therapeutic effects of psilocybin in the treatment of psychological distress associated with the terminal disease^{xiv}. Twelve subjects (11 women) received oral doses of psilocybin (0.2mg/kg) in treatment group and niacin (250 mg) across two sessions two weeks apart. The results revealed decreased anxiety with improved mood and no long term drug adverse effects. By the time the study was published 10 of the 12 subjects had died. All across the STAI, BDI and POMS the scores changed dramatically.

Psilocybin was also used in a study of obsessive-compulsive disorder^{xv}. The subjects received low (100 µg/kg), medium (200 µg/kg) and high (300 µg/kg) doses. They were graded according to Yale-Brown Obsessive Compulsive Scale (YBOCS). All subjects showed 23% to 100% decrease in their scores after at least one session.

MDMA

MDMA has a well-documented role in the treatment of post-traumatic stress disorder (PTSD)^{xvi}. Phase II trials have been performed and Phase III trials are wait for USFDA approval. In this study it was concluded that 83% of patients after receiving MDMA-assisted psychotherapy no longer fit the criteria of PTSD. While the rest of the placebo group after receiving MDMA treatment showed significant improvement. None of the patients showed any lasting adverse drug effects.

MDMA was also used in to study its effect on depression. In a study by De Wit^{xvii} in three sessions, healthy adult volunteers with previous MDMA experience (N=36) received capsules containing placebo, 0.75 or 1.5 mg/kg of MDMA under double-blind conditions. During expected peak drug effect, participants played two rounds of a virtual social simulation task called "Cyber ball" during which they experienced acceptance in one round and rejection in the other. The results showed that volunteers experienced decreased sense of social rejection and decreased impact of rejection

DISCUSSION

Ever since the accidental discovery of LSD in 1943^{xviii} there has been a debated going on for their potential benefits in mental health disorders. This was fueled by the discovery of serotonin in 1953^{xix}. The name psychedelics for these substances was coined by Humphrey Osmond in 1957 indicating that these substances alter brain mechanism and had beneficial or useful properties. Although this term is very popular among the public it is still frowned upon by the scientific community. This indicates that these substances have beneficial properties. This article shows that this idea is not that farfetched and recent studies, although limited in number and scope, show that there is benefit. It should be kept in mind that the relative dearth of these researches is not due to lack of scientific communities enthusiasm but due to politicization of these substances^{xx}. The use of LSD during the 60s and 70s during the antiwar era of Vietnam and mass media's exaggeration of its effects led to it being classified as a Schedule I drug. This made them difficult to

study clinically and effectively and stopped any research into the pharmacology and medical value for more than 3 decades.

The classic serotonergic psychedelics are generally considered very physiologically safe, certainly compared with opiates and psychostimulants. Jaffe^{xxi} stated, "In man, deaths attributable to direct effects of LSD are unknown," and this statement is still true. Negative sequelae induced by classic psychedelics failed to identify significant adverse events^{xxii, xxiii}. These reviews used pure form of the drugs, hence it is difficult to talk about today's drugs due to their unknown additives.

Another issue with these drugs are the negative connotations associated with them. Such as, whenever we hear the words MDMA, the first thought that comes to mind is of ecstasy, rave parties, people experiencing hallucinations, paranoia, and disinhibitions. The quality of psychedelic experience is closely linked to social setting. During the 60s the experiments were done in isolation to social setting hence producing significantly dissimilar results to recent studies.

CONCLUSION

Even with the limited number of researches with regards to psychedelics, the results have shown great promise for use in mental health treatment. The authors propose that large scale randomized double blind control studies should be done to study not just short term but long term effects. Due to the restrictions place on such drugs this is not currently possible, but not impossible at the same time. The studies show that these drugs do not require regular dosing but rather can be administered at regular intervals in the presence of a physician. The use of these drugs as rapid-onset is theoretically well-grounded, but lacks proof of concept. If further scientific evidence accumulates on the therapeutic value of psychedelic medicines, would require specialized clinical training for physicians, nurses, psychologists and other health professionals will be required to meet an increased demand for such treatments. It behooves policy-makers to be aware of and open

to new approaches to treatments emerging in the field of psychedelic medicine.

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