

# Psychedelic Medicine: Is it a False Dawn or a Renaissance?

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**ABSTRACT:** *Aim:* There has been renewed interest in “psychedelics” in the last 10 years and their usefulness in Psychiatric treatment explored. The aim of the article is to highlight current controversies surrounding psychedelics medicinal uses and address imminent international legislation changes and the effects these will have in the face of new evidence showing their efficacy in some resistant mental health diagnoses. **Conclusion:** Possession and use of drugs that fall under the category of psychedelics is criminalized universally. They are considered to have no medical use and high potential for abuse. The dissensus about their use in treatment of mental disorders continues and there is a lack of compelling evidence proving their efficacy. Their use has far been limited to a handful of research centers, due to their criminalization, but the evidence is building and becoming very hard to ignore.

## INTRODUCTION

In April 2016 the United Nations will debate control of illicit drugs, a process that started in September 2015 by the declaration of the SDGs for 2030 (Sustainable Development Goals). The SDGs prescribe human rights-centered approaches to ensure health and wellbeing of all the people and the public health approaches concerning illicit drugs are a target for change, since they are viewed as controversial, inconsistent with human rights and have historically yielded limited effects. (Unvienna.org/2016).

The topic of illicit drugs is hot in the United Kingdom also, as the Psychoactive substances bill comes into effect, also in April 2016, and the critics are already loudly protesting the unscientific approach to the blanket ban, which is targeting the “legal highs”. It is drawing a new tribe into the mainstream discussion, those who are taking Nootropics, whether OTC Racetams or prescription medicines like Modafinil (a stimulant prescribed for treatment of narcolepsy) and Adderall (another stimulant and mixed salt amphetamine prescription medicine for ADHD). In the background cannabis in both forms natural and synthetic cannabinoids is making sure it remains at the heart of the debate. (The Guardian, 2016.)

The two contradictory approaches above are further complicated by the considerable weight of new evidence showing that there might be a big role for some of these psychoactive /illicit drugs (Hallucinogens or psychedelics) in the treatment of some intractable and refractory psychiatric conditions like PTSD and depression.

This complicates matters further and shows the wide gap between the legislative agencies both at local and international levels at one end, and the scientific community at the other. The scientific community themselves are divided and use the terms loosely. You need to be extremely disciplined to follow the definitions and not to join the chorus, which is not easy with terms like (Psychotomimetic, Enteogens, Entactogens, Psychotogens, and Empathogens, etc...).

In part 5, I will focus on the use of 4 of these drugs which are making a comeback into psychiatric treatments namely, psychedelics LSD, MDMA, Psilocybin and the dissociative, Ketamine. But, first some essential definitions:

## Hallucinogens

A Hallucinogenic substance is a psychoactive drug whose

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primary action is to alter cognition, mood and perception. The hallucinogenic or psychedelic experience is often compared to non- ordinary forms of consciousness such as trance, meditation, yoga, religious ecstasy, dreaming and even near-death experiences. They produce minimal craving or autonomic side effects. Another close term used is “*Illusinogens*” as the description fits alterations or enhancement in existing perceptions. Reality testing is generally intact and their effects vary with expectations and environment. Individuals transcend their primary identification with their bodies and experience ego-free states.

The classical hallucinogens (5HT<sub>2A</sub> agonists or partial agonists or serotonergic hallucinogens) are:

### *Indolealkylamines (5HTanalogs)*

- LSD.
- Psilocybin.
- DMT.
- Ayahuasca.

### *Phenylalkylamines (norepinephrine analogs)*

- Mescaline, Peyote.
- DOM, DOB, DMA, MDA, Nexus (2-CB). 2.1(E. Zerbo, 2015).

## Dissociatives

These are NMDA receptor antagonists. This family comprises of:

### *Arylcyclohexamines:*

- PCP.
- Ketamine.
- Dextromethorphan (DXM).
- Nitrous Oxide.

(Adapted from E. Zerbo, ASAM review course 2015).

## Designer drugs

A designer drug is a structural or functional analog of a controlled substance that has been designed to mimic the pharmacological effects of the original drug, while avoiding classification as illegal and/or detection in standard drug test.

According to many authorities these encompasses some drugs

unique to the group as well as others from the other two groups, psychedelics and Nootropics. The ASAM Principles of Addiction Medicine textbook lists the following as designer drugs:

- **Phenylisopropylamine** analogue Methamphetamine.
- **Alpha-desmethyl DOB** or 2-CB also known as Nexus.
- **Cathinone** (naturally occurring in the Khat plant) and Methcathinone.
- **MDMA**(Methylenedioxy methamphetamine) also known as Ecstasy or XTC

Their actions are unpredictable, not dose dependent and have resulted in fatalities due to overdosing. (ASAM, 2009.)

Another approach considers the following as *Psychedelics* and we will refer to it so the reader can compare with the above:

- Mescaline, PCP, LSD, Psilocybin, ketamine.

It is important to keep in mind the historical perspectives and remember that the relationship between mankind and drugs goes back thousands of years. The current debate is only new in terms of the types of drugs, the evidence for and against and the influence of times, cultural changes and emerging scientific evidence.

## Medicinal uses of psychedelics and designer drugs

Reviewing the literature, the reader comes across a range of information from sensationalism to realistic, factual and disciplined scientific writings. The list of disorders where experimental work has been done or is ongoing includes: PTSD, OCD, Depression, Addiction (especially Alcohol, Nicotine related disorders), couples counseling (some claim it has gone underground but still practiced) and psychotherapy assisted end of life anxiety in cancer patients.

In the next section we will focus on the top 4 drugs that are currently being investigated for their medicinal use in Psychiatry.

## LSD (Lysergic Acid Diethylamide)

No current medical uses and high potential for abuse. (Schedule 1) 80 Street names: Acid, CID, trips, dots, blotter (potential uses in alcohol dependence, micro dosing for creativity).

LSD is synthesized from ergot, a fungus that grows on rye and other grains. The British Newspaper the Guardian lead in 2006 with an article claiming British Psychiatrists were calling for an end to the 30-year taboo over the use of LSD as a medical treatment. The article was published on the 100<sup>th</sup> Birthday LSD, Albert Hofmann who first synthesized the drug in 1938. (The Guardian, 2016).

In the 1960s the drug was used to treat alcoholism, OCD, autistic children, schizophrenics, depressed patients, convicts, end of life anxiety and ordinary people to study creativity and spirituality. The APA held meetings centered on LSD. In 1970 LSD along with most Psychedelics became a schedule 1 drug in the United States after President Nixon signed the Controlled Substances Act, hence putting the brakes on research.

There is currently some fascinating work at imperial college in London, where researchers are scanning volunteers who are given the psychedelic to find out what happens to the brain. Contrary to expectations, they discovered psychedelics reduce brain activity in a certain area called the default-mode network. This network was discovered in 2001 and links the cerebral cortex with deeper parts of the brain like the hippocampus and the limbic system. It is active when we are in metacognitive states and holds the whole system together. What got researchers even more interested was another study finding, also using fMRIs, that the default-mode network was also dampened in experienced meditators compared to novice ones. (Brewer et al., 2011).

Micro-dosing on LSD and other psychedelics is a practice that is gaining popularity. It is known that Steve Jobs (Apple CEO) was open about his use of LSD and there are claims that many celebrities and even scientists do the same. A hoax on the internet claims Francis Crick conceived the double helix of the DNA under the influence of LSD. "Micro-dosers" are after creativity, innovation and cognitive enhancement but would be satisfied by just a better day. Many will resort to other smart drugs or Nootropics.

## Psilocybin

No current medical uses and high potential for abuse, (Schedule 1). (Potential uses in alcohol and tobacco addiction, cluster headaches, anxiety especially in cancer patients and neurobiology of mystical experience.)

Psilocybin is one of a class of compounds whose primary activity is known to be on 5-HT-2a/c serotonin receptors. Their effects include changes in perception and cognition. It is considered a "hallucinogen and an 'entheogen, meaning "spirit-facilitating". Some even nicknamed them, "God in a pill".

Its plant origin is the *Psilocybe Mexicana* & *Psilocybe Cubensis* aka magic mushrooms.

There has been renewed research interest into its potential for use in controlled medical situations. This is led by John Griffith of Johns Hopkins since 1999 and his landmark publication in 2006, "Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance"; has become a classic in the field. In psilocybin sessions volunteers who had had the most complete mystical experiences showed significant increases in their "openness," one of the five domains that psychologists look at in assessing personality traits. (The others are conscientiousness, extroversion, agreeableness, and neuroticism). Openness, which encompasses aesthetic appreciation, imagination, and tolerance of others' viewpoints, is a good predictor of creativity. (MacLean, Johnson & Griffiths, 2011).

In 2014 the same group published their work after using psilocybin to treat tobacco addiction. In an open label pilot study of a small sample of 15 subjects they found the 6 months' abstinence rate to be 80%. This is far better than the commonly reported abstinence rates of less than 35% by pharmacological and behavioral interventions. (Johnson, Garcia-Romeu, Cosimano & Griffiths, 2014).

Psilocybin effects have been compared to profound religious experiences, fasting, meditation, controlled breathing, sleep deprivation, near death experiences, infectious disease states. Due to its effects on the Serotonergic system, it is also being studied to understand the role of 5-HT in psychopathology.

## Ketamine

Ketamine is a dissociative anesthetic and a glutamate N-methyl-D-aspartate (NMDA) receptor antagonist. It has been investigated in treatment resistant depression and the following observations made:

- Rapid antidepressant effect (measured in hours, (up to 64% in 24 hours in treatment resistant depressed patients after a single intravenous dose.) (Murrough et al. 2013),
- Small sample sizes precluding conclusions.
- Support for NMDA receptor modulation as a novel mechanism for accelerated improvement in severe and chronic forms of depression.
- The efficacy of Ketamine has also been shown in bipolar depression and in depression with suicidal ideation.
- Limitations include transient nature of its antidepressant effect (days only), the need for repeated dosing and potential for abuse.

## CONCLUSION

It has been recognized as a cause of a serious complication that has become known as the "Ketamine bladder" or *K-bladder*. It results in physical damage to the bladder and many will have their bladders surgically removed, unfortunately. The drug has become a serious problem in many countries especially in China and many European countries where the powder form of the drug is snorted or injected. The usual complications of IDU like blood borne diseases; HIV and hepatitis B&C need to be kept in minds of the treating clinicians.

## MDMA

3-4 methylendioxyamphetamine. Street names; Ecstasy, XTC, love drug, Molly. No current medical uses.

**Research:** Treatment-resistant PTSD, social anxiety in autistic adults, adjunct in substance abuse treatment.

In their paper in the *British Journal of Psychiatry* "Making a medicine out of MDMA" Sessa and Nutt claim there is enough evidence now to remove MDMA from its current status on schedule 1 (no medical use) to schedule 2 (misused but useful medicine). The authors explain that since it was synthesized in 1912 it wasn't till the 1970s when it became useful in couples' psychotherapy and then banned in the mid-1980s, due to growing recreational use. They quote two studies that prove the efficacy of MDMA-assisted psychotherapy for PTSD patients the first by Mithoefer et al. (2010) and the second by Chabrol (2013). In the former study 85% of the participants on MDMA-assisted psychotherapy no longer had PTSD diagnosis compared to 15% of the placebo arm. After 3.5 years the improvement was sustained. The latter study also showed remarkable improvement in the symptoms of PTSD. The rationale for the improvement of symptoms in PTSD seems to be the effect of MDMA on the hyperactive Amygdala (fear and alertness as part of the fight flight response). It is presumed that MDMA helps the patient to stay at PFC or prefrontal cortex level and do not get dragged to the limbic system (emotional) level.

Another reason for the effects of MDMA is linked to its action on the hormonal system. It stimulates the release of oxytocin and prolactin, which are considered empathogenic and foster trust and closeness. They are secreted in abundance in nursing women and also post-orgasmic, hence called, cuddle hormones.

MDMA use in couples counseling in the 1970s (*claimed to have never gone away, just went underground*) was championed by "Sasha Shulgin", who authored PIHKAL and TIHKAL and became known as the godfather of ecstasy.

An angle that needs mentioning also is the claim that the Vietnam War helped in criminalizing psychedelics use, in fear of the counterculture and the opposition of the war by the youth. On the other hand the Iraq and Afghanistan wars are helping bringing them back to the scene to find a treatment to so many soldiers suffering from PTSD. The soldiers have a phenomenal suicide rate and depression and the currently FDA approved antidepressants for PTSD (Sertraline and Paroxetine) are not really a solution. The two SSRIs have to be taken daily, for years and are not without side effects. In STAR\*D trial the rate of remission after the first level was only a third of the patients. This shows that better interventions, not necessarily psychedelics, are needed.

Proponents of MDMA research would tell you that it is not a dangerous drug in its pure form and that street versions probably contain less than 50% of the drug or none at all. Confiscated samples show they could be anything from ketamine or heroin or just chalk. Still, as an amphetamine we need to consider the serious possibilities of malignant hyperthermia and the need to monitor hydration especially young people at night clubs where over or under-hydration can be fatal.

It is important to be aware of the turbulent history of psychedelics and the cycles of liberal use to total ban and the current ginger introduction into clinical research. The work of some great minds needs to be read and comprehended, like Humphrey Osmond who coined the phrase psychedelic meaning Mind manifesting in a letter in the late 1950s to Aldous Huxley who then suggested giving psychedelics to terminal cancer patients.

The scientific community is divided between supporting the research like Tom Insel, director of NIMH who thinks they should be looked at if they prove to be useful to people who are suffering or caution against using them outside clinical research like Nora Volkow of the NIDA. Others are against their use citing small sample sizes and adverse reaction potential warning they may not be ready for the prime time. Nora Volkow, of NIDA, wrote that "the main concern we have at NIDA in relation to this work is that the public will walk away with the message that psilocybin is a safe drug to use. In fact, its adverse effects are well known, although not completely predictable." She added, "Progress has been made in decreasing use of hallucinogens, particularly in young people. We would not want to see that trend altered." On balance one has to respect this advice. We can only support psychedelics use to treat mental disorders only after meticulous and disciplined scientific research informs us about safety, efficacy and the required medico-legal frameworks for prescribing them are in place.

Finally it remains to be seen even if the clinical trials yield positive results, as the drug industry will not find them lucrative since these drugs cannot be patented.

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