Analysis of the Different Potential Treatment Venues of Psychedelic Medicines

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Abstract

In the growing field of psychedelic medicine, there are a variety of avenues one may take when choosing the context in which patients are administered psychedelic medicines. After conducting a literature review to determine the current state of research regarding these avenues, it was determined that there exists a major gap in the current protocols for administering such medications. The main types of avenues discovered and analyzed were shamanistic/religious ceremonies, clinical trials, wellness retreats, and the presence of a sitter/guide. While there are some analyses of patient outcomes and their subjective experience in individual settings, there does not exist an analysis comparing the different methods of psychedelic administration. Utilizing the current literature, a preliminary comparison of the main environments of psychedelic administration was conducted, paying specific attention to the necessary psychological, ethical, and physiological considerations. Additionally, Dr. Efrem Nulman, a psychotherapist with over 45 years of relevant experience, was interviewed about his opinions on the matter, on psychedelic research in general, as well as on the future of psychedelics.

Introduction

Psychedelics, a category of substances defined by their hallucinogenic, perception-altering properties, have recently gained recognition in mainstream medicine for their benefits in treating psychiatric conditions such as addiction, Post-Traumatic Stress Disorder (PTSD), Obsessive-Compulsive Disorder (OCD), depression, and anxiety. Despite these substances having only recently been recognized for their ability to effectively treat these behavioral conditions when the current standard treatments fall short, psychedelics have been around for much longer than conventional treatments and are used in a myriad of different practices and applications worldwide.

Some naturally derived psychedelics like ayahuasca and psilocybin, commonly known as magic mushrooms, have been known for thousands of years and used for spiritual ceremonies in Eastern and indigenous cultures. Others, like LSD and MDMA, commonly known as ecstasy, were developed by Western scientists in the early 20th century for research in psychotherapy. During the 1960s, psychedelics became widely used in Western culture as recreational drugs, known for their "trip" inducing qualities, and were associated with the hippie counter-culture movement. This increased use of psychedelics led many countries, as well as the United Nations, to label psychedelic medicines as Schedule 1 controlled substances, which prevented these drugs from potentially being utilized for medical purposes.

The prohibition of these psychedelic medicines led to a halt in essentially all research on the drugs for decades. However, we are now living through what is known as the "psychedelic

renaissance," and the abundance of research on these substances that has been conducted in the recent past has resulted in an increase in their popularity. Recognition of their abilities to treat a variety of psychiatric conditions led many to be interested in experimenting with the hallucinogens for themselves, and psychedelic retreats and wellness centers have started offering them as medications for behavioral disorders. Additionally, some of the ancient spiritual ceremonies are available for the public to experience, and for those looking to try the drugs in a neutral and/or controlled environment, they can use a sitter or participate in FDA clinical trials, respectively.

Despite the deluge of research that has been published on these substances- their efficacy in treating psychiatric conditions and the outcomes of ingesting them under specific conditions- there is a major gap in the literature comparing the various avenues in which people take psychedelics. As taking psychedelics leaves the user in a vulnerable and impressionable state, the set and setting, as Timothy Leary and Richard Alpert explained, in which one takes psychedelics is of utmost importance. Whether one was alone or in a group, examined by a medical professional, or guided by a trained professional, are only some of many clinical, psychological, and ethical considerations that must be considered.

Interning in a private research group comprised of physicians, medical residents, and experts in the field of psychedelics and mental health, my role was to focus on reviewing the literature and analyzing the potential venues in which one may ingest psychedelic medicines. One goal of our

research was to determine exactly what was lacking in current research, and subsequently, to compare the ethical, clinical, and psychological standing of each option.

However, this is only the first step in the long journey of the acceptance and legalization of psychedelic medicines and their incorporation into mainstream psychiatric treatment. There is much research to be done on both the medications themselves, as well as to fill the current gap in the literature comparing the multitude of available environments in which to ingest psychedelics and to study their psychiatric, ethical, and physiological considerations.

Background

Psychedelic drugs can originate from one of two places - in nature and in the laboratory. Examples of the former are the plant-derived psychedelics ayahuasca, psilocybin, ibogaine, and peyote, and of the latter are the laboratory-synthesized drugs LSD, Ketamine, and MDMA. Some of the naturally-derived drugs have been utilized for centuries in spiritual and religious ceremonies in ancient cultures around the world.

Ayahuasca

Ayahuasca, as seen in Figure 1, is a tea-like drink whose name translates to "vine of the spirits," or "vine of the dead," in the Quechua language of South America where the plant originated. For thousands of years, ayahuasca has been used in the Amazon, including Brazil, Ecuador, Peru, and Colombia for both medicinal purposes and religious ceremonies.[i]

Figure 1. Ayahuasca[ii]

Ayahuasca is composed of the hallucinogenic compound dimethyltryptamine (DMT) and various beta-carboline alkaloids, whose structures can be seen in Figures 2 and 3, respectively. Upon ingesting, the psychedelic effects of ayahuasca start to emerge around the one-hour mark, peak at the two-hour mark, and last for as long as six hours[iii]. While under the influence, users report feeling increased euphoria, and emotional liability, as well as experiencing visual effects. These include an increased brightness and intensity of colors, and seeing imagery of nature, people, and animals. The nature of these symptoms in combination with the psychological effects of the drug led many to deem their ayahuasca trips an emotional and transformative experience.

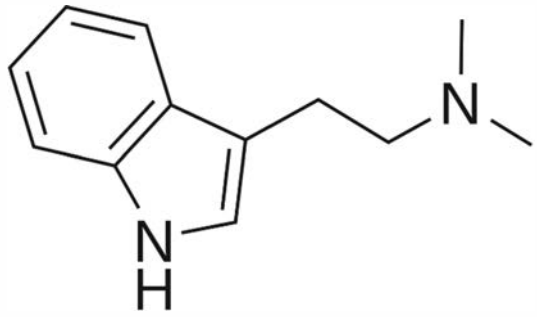

Figure 2. Structure of DMT[iv]

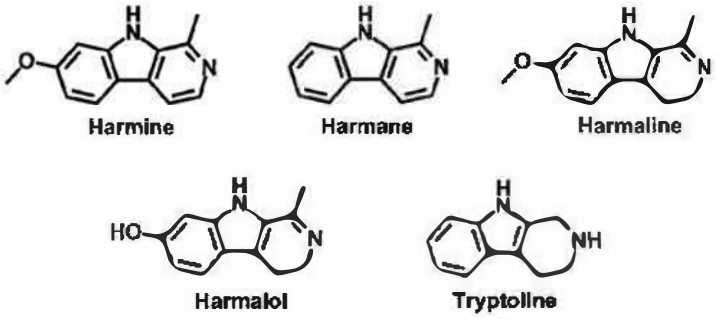

Figure 3. Structure of various beta-carboline alkaloids[v]

The most common side effects of ayahuasca administration are nausea and vomiting within the hours post-ingestion. During this window of time, other acute physiological changes occur in the immune, endocrine, and cardiovascular systems, but all typically return to baseline post-treatment. There have been a few cases of ayahuasca poisoning, but most were from intake of doses significantly higher than typically used. There have also not been any deaths directly attributed to the intake of ayahuasca. [vi] Most researchers state, however, that more studies must be done to validate this.

As with all psychedelics, there are some adverse effects, albeit rare, associated with ayahuasca. A bad trip can involve paranoia, fear, dysphoria, anxiety, frightening illusions, hyperawareness of physiological processes, and troubling thoughts of one's life or of evil forces. If these symptoms do arise, the intensified emotional experience may lead to dangerous behavior. Prolonged psychosis after the administration of psychedelics may occur for days or even months after a trip, but this is mainly seen in those with other psychological conditions and thus it is unclear as to whether this was caused by the psychedelics themselves or would have happened regardless, as a result of their impaired condition. There are cases of hallucinogen persisting perception disorder (HPPD), in which perceptual effects similar to those experienced during a trip occur after cessation of hallucinogen use. The effects are re-experienced, impair functioning, and are unexplained by another condition. HPPD was thought to have occurred in the 1960s, but even then incidence was uncommon. The current incidence of HPPD is unknown. [vii] In terms of physiological risks, many psychedelics can raise blood pressure and heart rate, and therefore those with diabetes and hypertension should be aware of the risks and consult a physician prior to usage.

Psilocybin

Commonly known as "magic mushrooms," psilocybin, seen in Figures 4 and 5, is a psychoactive compound found in over 100 species of mushrooms, many of which are a member of the genus *Psilocybe*. It is believed to have been used in a variety of Central American cultures, as well as around the world for centuries, and more recent findings of *Psilocybe* mushrooms around the world suggest their widespread usage throughout history. In the 1950s, these mushrooms were

re-discovered by an American mycologist and researcher, who studied their psychoactive properties.[viii]

Figure 4. Psilocybin[ix]

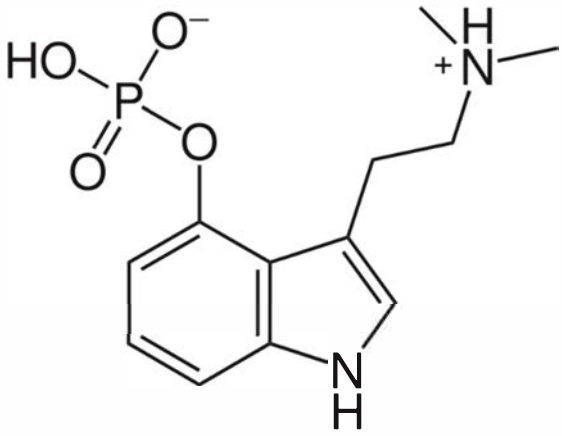

Figure 5. Structure of Psilocybin[x]

Psilocybin is a derivative of the amino acid tryptophan, similar to the neurotransmitter serotonin, and when metabolized in the body it is de-phosphorylated from its pro-drug form into its active form, known as psilocin. The hallucinogenic effects are the result of its agonistic activity at the serotonin 5-hydroxytryptamine receptors, but these interactions are not solely responsible for its effects, and its interactions with other nervous system receptors are not well understood.[xi]

A psilocybin trip can induce an altered sense of time, perception of illusions, and synesthesia, and like ayahuasca, many have deemed their trip a transcendental and transformative experience. Possible adverse effects can include raised blood pressure and interactions with other drugs, and seizures have been infrequently reported[xii]. Similar to ayahuasca and other psychedelics, there is still ongoing research to further understand its effects on users, and the same general adverse effects related to all psychedelics such as HPPD, prolonged psychosis, and a bad trip, apply to psilocybin as well.

History

Pre-Prohibition

Natural hallucinogens such as ayahuasca and psilocybin have been used for thousands of years around the world in traditional, religious, and medical contexts. Over the last few centuries, these substances have crept their way into the Western world, but not until the 20th century when synthetic psychedelics were created did their popularity arise. In 1943, researcher Albert Hoffman in partnership with Sandoz, a Swiss chemical company, discovered the psychoactive properties of lysergic acid diethylamide (LSD), which he synthesized some years prior, and this

is considered the start of psychedelic research in the West. In 1957 at a meeting of the New York Academy of Sciences, the term "psychedelic" was first proposed by Humphry Osmond to mean "mind manifested" from the Greek words for *psyche* and *delos,* which translated to "clear."[xiii] Also during the fifties, psilocybin and LSD were studied as treatments for conditions such as alcoholism.[xiv]

Global Prohibition

The 1960s was a significant decade for the history of psychedelics for a variety of reasons, one of which is the emergence of the hippie counter-culture movement. A defining characteristic of this movement was an increase in recreational drug usage, and as a response to this, the United States, along with the United Kingdom, outlawed the possession of psychedelics under the Drug Abuse Control Act. In 1970 and 1971, the United States passed the Controlled Substances Act, and the United Nations passed the Convention on Psychotropic Substances[xv], respectively, which labeled most psychedelics, including LSD, MDMA, and psilocybin, as Schedule 1 drugs. The status of various psychedelic medicines can be seen in Figure 4. According to the Drug Enforcement Administration (DEA)," Schedule I drugs, substances, or chemicals are defined as drugs with no currently accepted medical use and a high potential for abuse."[xvi] Consequently, in addition to their possession being outlawed, these drugs are unable to be prescribed by a medical professional.

	UN Status* (under the Convention on Psychotropic Substances)	US Status
Ayahuasca	Not	Not
Cannabis	Specifically Controlled	Specifically Controlled
DMT	Schedule I	Schedule I
Ibogaine	Schedule I	Schedule I
Ketamine	Uncontrolled	Schedule I
LSD	Uncontrolled	Schedule III
MDMA	Schedule I	Schedule I
Mescaline	Schedule I	Schedule I
Psilocybin	Schedule I	Schedule I

*The UN Convention has four schedules of controlled substances, ranging from Schedule I (most restrictive) to Schedule IV (least restrictive). A small number of UN member states are not party to the convention or acceded to the convention with conditions such as provisions for the right of indigenous peoples to make use of traditionally used substances. Cannabis is controlled primarily under the Single Convention on Narcotic Drugs 1961. US drug schedules are classified into five distinct categories or schedules depending upon the drug's acceptable medical use and the drug's abuse or dependency potential. The abuse rate is a determinate factor in the scheduling of the drug; for example, Schedule I drugs have a high potential for abuse and the potential to create severe psychological and/or physical dependence.

Source: Prohibition Partners

Figure 4. Status of various psychedelic drugs under UN and in US[xvii]

Timothy Leary and Richard Alpert

Another major development in the 1960s was the research on psychedelics conducted by Harvard professors Timothy Leary and Richard Alpert. Together, they developed the Harvard Psilocybin Project, in which they administered psilocybin to volunteer subjects to determine the effects of the drug on the subjects in real-time. However, this research received major backlash from Harvard faculty for its unorthodox methodology, non-randomness of participants, and

poorly controlled conditions. A couple of years later, both Leary and Alpert were fired from the university and their research ended, but both remained active in the psychedelic movement.[xviii] One of Leary and Alpert's major developments was their Set and Setting Hypothesis. This postulates that the primary determinants of a psychedelic experience are the user's internal set- intention, expectation, motivation- and the external setting or context, including the presence of a guide or therapist. The significance of this theory was that it set apart the highly variable psychedelic experiences from those of other drugs, such as narcotics, stimulants, and depressants, which are typically consistent among users, and laid the foundation for the analysis of future research on psychedelics. [xix]

Cultural Taboo

For the decades following their prohibition, the interest in or usage of psychedelics was taboo due to their illegal status, and consequently, all, except for a select few scientists around the world, research on psychedelics came to a halt. However, the usage of psychedelics during this time did not cease. Those looking for a transformative spiritual experience, a last-ditch cure for their mental illness, or just a way to get high, found other avenues to obtain the hallucinogens. These included traveling to the Amazon to take part in a traditional ayahuasca ceremony, traveling to locations where the drugs remained legal, or participating in the developing psychedelic "underground."

The Psychedelic Renaissance- Modern Day

This phenomenon has slowly gained popularity, and in recent years there has been a psychedelic renaissance. Although still illegal and labeled as Schedule 1 drugs, psychedelics are now being

provided in a variety of ways and viewed as more than just a way to "get high." From a clinical perspective, psychedelics are being evaluated for their therapeutic and medicinal qualities by doctors and therapists, and respected institutions such as Johns Hopkins University, New York University, and Yale University, among others, have opened departments dedicated to uncovering the potential uses of psychedelics. They are also being studied by the FDA, possibly foreshadowing the legalization of these substances for medical usage.

In addition to research settings, the growth in popularity of psychedelics and their potential therapeutic properties has led to a surge in the public interest and the various methods through which people obtain them. One way in which psychedelic medicines are provided is through "wellness" centers and retreats, advertised as immersive psychedelic experiences leading to growth and well-being. There are also providers known as "sitters" or "guides" who serve as impartial "supervisors," ensuring a user's safety or offering necessary guidance during an experience. The Eastern and indigenous ayahuasca and psilocybin experiences also still exist today, led by spiritual leaders or shamans who provide an ancient spiritual psychedelic experience.

Psychiatric disorders

Psychedelics have recently been gaining recognition in mainstream medicine for their benefits in treating psychiatric conditions. Unlike other medications, the same psychedelic medicines possess the ability to treat a variety of these disorders, including stress disorders, mood disorders, substance abuse disorders, and anxiety disorders- addiction, post-traumatic stress disorder (PTSD), obsessive-compulsive disorder (OCD), depression, and anxiety.

Mood Disorders

According to the Mayo Clinic, "If you have a mood disorder, your general emotional state or mood is distorted or inconsistent with your circumstances and interferes with your ability to function. You may be extremely sad, empty or irritable (depressed), or you may have periods of depression alternating with being excessively happy (mania)."[xx] Examples of mood disorders are major depressive disorder (MDD)- which affected 6% of all US adults and 17% of US adolescents in 2020[xxi]- and bipolar disorder- which affects about 3% of adults in the US[xxii]- and both have been shown to be effectively treated by psychedelic medicine, even in treatment-resistant cases. A recent study published in the New England Journal of Medicine demonstrated that a single dose of Psilocybin reduced treatment-resistant depression,[xxiii] and another study concluded that psilocybin-assisted therapy has substantial and durable antidepressant effects following acute intervention in some patients with moderate to severe Major Depressive Disorder.[xxiv] Additionally, a systematic review of data related to serotonergic hallucinogens determined that ayahuasca reduced depression symptoms in treatment-resistant depression[xxv]

As a treatment for bipolar disorder, which has the highest lifetime risk of suicide among all psychiatric disorders, and for other depressive disorders, Ketamine has been shown to be an effective treatment- studies have shown that a single administration of ketamine had rapid antidepressant effects, and multiple administrations also show promising results, although available data is scarce. This is highly significant, as the prevalence of treatment-resistant cases is even higher than for MDD. Additionally, suicidality, which accounts for 15-20% of deaths in

those with bipolar disorder and has no approved pharmacological interventions, has been shown to be reduced with ketamine treatment. Two open-label studies have shown that a single infusion of intravenous ketamine significantly decreased suicidal ideation, and a systematic review of the available literature concluded that the drug's anti-suicidal effects can occur even within hours of administration.[xxvi]

Anxiety Disorders

Anxiety disorders, such as generalized anxiety disorder, panic disorder, and obsessive-compulsive disorder, are the most common mental disorders and affect nearly 30% of adults at some point in their lives.[xxvii] Multiple case reports have demonstrated that a single dose of psilocybin can be effective at improving symptoms of OCD[xxviii], and Yale Medicine is currently conducting a study on the effects of psilocybin on OCD.[xxix] Also, a recent study concluded that a high dose of psilocybin was able to decrease anxiety and depressive symptoms in those suffering from a life-threatening cancer diagnosis with little to no adverse effects, and consequently improve their quality of life.[xxx] NYU and Johns Hopkins also published studies that showed that one-time treatment of cancer patients with psilocybin brought quick relief from distressing anxiety and depressive symptoms, and results persisted for greater than 6 months for over 80% of participants.[xxxi]

Stress Disorders

Post-traumatic stress disorder, which was recently re-classified as being a stress disorder from an anxiety disorder, affects 3.5% of US adults each year, and about 1 in 11 people with be

diagnosed with PTSD in their lifetime. Characterized by intrusive thoughts, avoidance, alterations in arousal and reactivity, and alterations in cognition and mood, PTSD can be developed after experiencing a traumatic event.[xxxii] Unfortunately, though, the FDA-recommended treatment of PTSD with selective serotonin reuptake inhibitors are not effective for 40-60% of those who take them. MDMA, however, shows promising results as an effective treatment for treatment-resistant PTSD. A recent study concluded that MDMA significantly reduced PTSD symptoms in participants without any adverse effects, and results were consistent even among those with comorbidities that are associated with treatment resistance.[xxxiii]

Substance Abuse Disorders

Substance abuse disorders (SUDs) affect over 20 million Americans ages 12 and over and include addiction to substances such as alcohol, marijuana, and opioids[xxxiv]. These disorders are also found to be comorbid with other mental disorders which affect over 1 in 5 Americans,[xxxv] and according to the National Institute of Mental Health, approximately half of those with a SUD also have a mental health condition or disorder. This relationship can occur because those with depression, anxiety, or PTSD may use drugs or alcohol as a form of self-medication, or because SUDs can cause changes in the brain that increase the likelihood of developing a mental health condition.[xxxvi] In terms of treating substance use disorders, psilocybin has been shown to significantly increase abstinence in those suffering from alcoholism, and results were maintained even at a 36-week follow-up.[xxxvii] Also, a systematic review of systematic reviews assessing psychedelics found that LSD and psilocybin reduced symptoms of alcohol and tobacco dependence.[xxxviii]

Current State of Psychedelic Research

With the increase in popularity of psychedelic medicines, their safety and efficacy must be established, as well as the outcome of the experience. Based on a review of psychedelic literature as part of a private research group, it became evident that while there have been studies conducted that analyze the safety and effectiveness of psychedelics in treating certain psychiatric conditions, as well as the outcomes experienced in different avenues of psychedelic administration, there is a lack of research comparing these different contexts in which psychedelics are taken. In addition to the safety and efficacy considerations, there are ethical issues in some of these settings that can potentially compromise the very vulnerable and impressionable person who is under the influence of psychedelics.

Set and setting are primary and crucial aspects of psychedelic treatment. It is therefore imperative that we be conscious and sensitive to our choice of psychedelic context, specifically when one ingests psychedelic medicines.

Spiritual/Religious Group Settings

When organizing psychedelic experiences, the shamanistic and religious rituals appear to be the most ethically challenged when compared to the more traditional research contexts. Shamanistic ceremonies typically contain a group of 10 people, take place over a few consecutive nights, and are led by a shaman or religious leader who has had extensive training in their tradition. During the ceremony, there may be chanting, rhythmic dancing and music, a prayer service, or silence. The ceremonies also take place in dim light to induce visions. Depending on the

medicine used - typically ayahuasca or psilocybin - there is also a purging component, as the medicine causes some users to become sick and vomit. Before and/or after the ceremony, there is usually a preparation and/or review to clarify and frame the users' experience. The specifics of how the experience is presented are dependent on the tradition of the group leader or shaman, but generally, it is framed as accessing metaphysical realms or worlds via spiritual beings and interacting with 'good" and "bad" spirits. Through purging, which is framed as the removal of spiritual toxins, interactions with these spirits, and the feeling of being separated from one's physical body in another realm, the result is that the user is left with a healthier and stronger body.[xxxix] Some of these religious retreats also contain daytime activities like tai-chi and yoga or fasting, and as their popularity has grown in recent years, more westernized, tourist-attracting versions have been created.

The religious nature of these ceremonies may be viewed as unethical by some, since it seems that the shaman is pushing religious beliefs on the ceremony participants while they are in a vulnerable and impressionable state. However, this spiritual way of framing the experience may have a positive effect, arguably replacing psychotherapy and psychopharmacology, and helping participants to work through and interpret what may be confusing experiences. The ancient traditions of these ceremonies also place emphasis on the significance of set and setting. Their rhythmic beats, which help participants minimize the chance of getting stuck in an unwanted experience, and the presence of a trained leader are both intended to ensure a meaningful and productive experience. While a study exists that analyzes many individual aspects of ayahuasca ceremonies and the experiences and outcomes of participants[xl], further research should be

conducted to determine if there are any short- or long-term consequences of these religious ceremonies attributed specifically to religious indoctrination.

An additional concern may also be due to the lack of a health screen before and after these ceremonies, ensuring that all participants were not at risk for complications during the ceremony or had adverse reactions. While some psychedelics have been shown to be among the safest recreational drugs[xli], they do, like all things, have some contraindications and risks. The psychological risks of a bad trip, the accompanying acute and chronic emotional effects, hallucinogen persisting perception disorder, and other known possible side effects are concerns, along with the physiological effects of increased heart rate and blood pressure[xlii]. Also, although the accuracy of the relationship is still unclear, those who may be suffering from premorbid mental illness may be at increased risk for prolonged psychosis and psychological difficulties post-psychedelic sessions. It has also been shown that the incidence of these conditions appears to be much lower in contexts with careful screening and preparation.[xliii]

Non-clinical Private Settings - Sitters

Seemingly on the other end of the spectrum of ethical psychedelic providers are “sitters" or “guides.” A part of the underground psychedelic movement, a sitter is anyone who is present for another’s psychedelic experience and serves as an impartial resource for them, ensuring the user’s safety and helping them through their experience when necessary. In other words, they serve to maintain a set and setting which is conducive to the user having, ideally, an uninterrupted and uninfluenced experience. A guide can be an experienced psychedelics user, a licensed therapist, or someone who has never taken these medicines at all. There are many

individuals and groups which offer their own certifications or proposed instructions to follow, however, there is no official certification or training that is technically necessary to be a sitter, and no official manual to reference. While using a guide for one's psychedelic experience may be viewed as the most unadulterated and ethically sound route, as the one-on-one experience and absence of third-party interpretations allow the user to have a completely uninfluenced experience, the lack of training of the guide, lack of health screen or follow up, and lack of supplemental therapies or activities must be considered. Additionally, due to the informal nature of sitters and their use in the underground scene, there is an absence of any data and research for the method.

In terms of available data and detailed protocols, the FDA's clinical trials on psychedelics are arguably the safest providers of psychedelics. Due to the psychedelic renaissance in recent years, the FDA has been performing clinical trials on the safety and efficacy of various psychedelics to treat different conditions. The exact nature of one's psychedelic experience in a trial, i.e., the drug being used, the number of sessions, dosage, supplemental activities, accompanying psychotherapy, *etc*. will differ from trial to trial, but common factors include the multiple, spread-out sessions taking place over a few weeks, taking place in quiet, neutral settings, with trained staff and medical personnel available if necessary. Short-term follow-ups with participants were performed at various points after the session(s) to assess the efficacy of the drug. Health screens are also performed before each trial, however not all trials test for the same criteria. While most have the exclusion criteria of certain psychological conditions like schizophrenia or bipolar disorder, not all trials perform extensive medical testing to screen for conditions such as hypertension that are possible contraindications for taking certain

psychedelics. Additionally, not all trials perform long-term follow-ups or post-session health screens to detect any adverse events. That there are trained personnel present measuring outcome data in real-time is something that does not take place in the informal settings described above.

Non-clinical group settings- Wellness Retreats

Additional psychedelic providers which have become popular are wellness retreats. Located around the United States and across the world, these retreats are marketed toward both first-time as well as experienced psychedelic users. Somewhat of a culmination of the previously mentioned psychedelic providers, they have the greatest diversity in offerings - group or solo sessions, pre- and post-session psychotherapy and integration, and supplementary activities like yoga and massages- allowing for the user to tailor the experience to his or her needs. Consequently though, depending on the nature of a specific retreat, the ethical and safety concerns of the previously mentioned distributors may apply to it well. The staff of these retreats usually have some third-party certifications in and/or experience with psychedelics, but as stated previously, there is no agreed-upon standard for what it means to be qualified in this field. Interestingly, these retreats commonly have medical staff such as psychiatrists and nurses that are very involved with participants, performing detailed health screening and therapies throughout the process to ensure a safe and productive experience.

Dr. Nulman Interview

After evaluating the various psychedelic treatment avenues, the gap in the research regarding a comparison of the various psychedelic administration avenues is clear. Even more so, there is a

lack of research on psychedelic medicines and their potential for treatment, their side effects, and all the other factors that are necessary to be determined before one can expect their Schedule 1 status to be re-evaluated. To navigate the complex world of psychedelics, it is beneficial to speak with someone who has decades of experience in the field, as well as in treating mental health disorders in general. Therefore, I interviewed Efrem Nulman, Ph.D., who is a psychotherapist and researcher with 45 years of experience, and a member of the private research group to which I belong.

Dr. Nulman's expertise is in addiction treatment and his research focused on novel approaches to treating addiction and mental health conditions. He was the director of substance use and health at Yeshiva University for 10 years. He was part of the original psychedelic research group, the first psychedelic research group at NYU Medical Center. Dr. Nulman did founding work in 30 years of work in harm reduction with drugs in general, and with psychedelics in particular, and he supervised doctoral and medical research at the Albert Einstein College of Medicine, Ferkauf Graduate School of Psychology, and Wurzweiler School of Social Work. He has also been on faculty at various medical psychology and social work schools.

What is your take on the different methods of providing psychedelic medicines to patients? Do you have any concerns and/or preferences for any specific one?

Our research is attempting to address your questions:

We look at three potential treatment venues - research settings, private nonclinical settings, and (oftentimes shaman-led) group retreats. It is currently assumed that the safest place for patients

to access psychedelic medicines is a research/medical center setting. The other settings are chosen by reputation and word of mouth.

Research studies are somewhat more cumbersome because they require many preparatory sessions and follow-ups. As a result, they can take a lot more time than in the other two settings. In the other two settings, you potentially risk in other areas, including medical, psychological, ethical, and psychiatric. One needs to consider if professionals with a public code of ethics behave more responsibly than the general population with their accompanying moral principle.

What types of people would you recommend to try psychedelics, and which approach would you recommend them to take?

People who have tried other medications and treatment approaches that weren't successful ought to consider psychedelics. Some people may benefit from psychedelics as their primary treatment. So far, as in any clinical setting, treatment is determined on a case-by-case basis- like with any other field of medicine and its treatments where you look at each individual and their specific needs. Protocols are yet to be and need to be formally considered and developed for psychedelics.

People with PTSD do extremely well with taking MDMA (MAPS), and within the next 2 years, it will most likely be legal to treat PTSD (with FDA approval) in medical settings. We also are confident that psilocybin is effective for treating depression (Professor David Nutt) and anxiety in cancer patients (Johns Hopkins, NYU, and UCLA), as well as for treating depression in general. And, psilocybin has been successful in treating alcoholism (NYU) and nicotine use disorder (Johns Hopkins). At the University of Alabama, it was found that psilocybin was effective at treating cocaine use disorder. Johns Hopkins is studying psilocybin for treating depression in Alzheimers patients and for OCD.

Ketamine is already legal, and ketamine clinics are proliferating in many states. John Crystal at Yale found that it was effective at treating bipolar disorder, major depressive disorder, and severe suicidal ideation, although the length of time of its effectiveness is still unclear.

Aspergers/autistic spectrum disorder was studied as well as ADD with MDMA treatments at UCLA and those went well. Further studies are needed.

Ibogaine for alcohol withdrawal is being studied at Hopkins, and for opiate withdrawal has been studied for many years and continues to this day.

In what way do you think the literature is lacking in terms of psychedelic research, and what studies should be done to remedy this?

There is a need to complete phase 3 studies in all areas of psychedelic research. Currently, MDMA phase 3 studies are being completed, and a number of other psychedelics are currently in phase 1 and 2 studies. Significant replication over time is necessary. Moreover, medical protocols need to be formally established. Much work is yet to be done, although it is clear that safety and efficacy have been firmly established.

What is the future of psychedelics?

It's like every other medicine in America. We're going to make it the greatest thing, and then people will abuse it and it'll blow up. It's the history of drugs in America, we get carried away. But it will also help a lot of people. What we have now, selective serotonin reuptake inhibitors, *etc*. aren't effective at treating these psychiatric conditions (Dr. Irving Kirsch, New England Journal of Medicine). The future for psychedelics is bright, and for those patients who take them in the correct way they can be extremely effective.

Conclusion

Despite their utilization for thousands of years for spiritual and medicinal purposes and being a defining factor of the hippie counter-culture movement of the 1960s, psychedelic medicines are only now, after decades of halted research and taboo, gaining widespread recognition for their abilities to treat psychiatric conditions such as addiction, PTSD, OCD, depression, and anxiety.

This resurgence in the popularity of psychedelic medicines has brought with it a new wave of research, but also a variety of avenues in which to take these medicines with no proper regulations and protocols. Additionally, there has been no comparison of these avenues with respect to their ethical, psychological, and physiological considerations. As more of these psychedelic providers are emerging, and in research settings, the safety and efficacy of these medicines have been proven time and time again, it is imperative that the contexts of these psychedelic providers are studied to ensure ethical, safe, and efficacious delivery of psychedelic medicines to those in search of a treatment for psychiatric conditions, for an introspective experience, or even are just curious about psychedelics. Factors like set and setting, pre- and post-session health screening, training of the provider (the shaman, the sitter, or the guide), supplemental therapies, religious agendas, and session follow-ups are only some of many factors which must be reviewed.

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