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Psychedelic Research Resurgence

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Introduction

In the 1960s, more than 1,000 peer-reviewed research articles detailed the therapeutic use of psychedelic compounds. Passage of the Controlled Substance Act of 1970 classified psychedelic substances such as LSD, MDMA and Psilocybin as Schedule 1 drugs with no medical value, interrupting research into the application of psychedelic compounds for well-being. New studies from institutions such as New York University, Purdue University, Harvard University, and Johns Hopkins University are producing evidence that use of these drugs in combination with psychotherapy may have potential value for treating mental illnesses such as addiction, mood, affective, and psychotic disorders. This study explores the relationship between the effects of these drugs on well-being and the FDA scheduling of these drugs at the highest level. Analyses of six open-ended interviews with a snowball sample of college students about their recreational experiences with LSD, MDMA and Psilocybin found that college students use these drugs as a tool for spiritual and emotional development. They reported positive transformative experiences and improved relationships with family and friends. These findings support the continued expansion of research on psychedelic assisted psychotherapy for treatment of mental illness and the rescheduling of medically beneficial psychedelics by the FDA.

Hallucinogens

"Hallucinogens are substances that cause powerful changes in sensory perception, from strengthening a person's normal perceptions to inducing illusions and hallucinations" (Comer 2010, p. 389). These substances, also known as psychedelic drugs, include LSD (Lysergic Acid Diethylamide), Psilocybin (4-phosphoryloxy-N,N-dimethyltryptamine), and MDMA (3,4-methylenedioxymethamphetamine). Many people use different definitions for hallucinogens and include different types of drugs into those definitions. For the purpose of this paper, the hallucinogens being discussed will be the substances which affect serotonin (5-HT) type receptors. Many hallucinogens are found naturally in plants and animals. Evolution of tools in chemistry and the scientific method in the 1900s supported the process of synthesizing new hallucinogens.

With the enactment of the Controlled Substances Act of 1970, hallucinogens, among them LSD and Psilocybin, were classified as schedule I drugs by the United States congress (U.S. Drug Enforcement Agency 2010). In 1984, MDMA was added by the Drug Enforcement Agency (Baum 1997, p. 213).The schedule of the drugs, I being the highest and V being the lowest, determines the regulatory measures enforced by the United States DEA. The higher the drug scheduling, the stricter the policies are regarding manufacturing, importation, possession, distribution, and research for that particular drug. Placing LSD, Psilocybin and MDMA in the schedule I classification disrupted research on the application of hallucinogens to well-being and mental health. This also fostered the strictest judicial consequences for possession and distribution. Both using and distributing LSD are felonies. Anyone caught distributing LSD can get up to forty years in a federal penitentiary and a two million dollar fine (National Geographic 2009).

Three criteria the United States DEA and FDA use for determining if a substance should be classified as schedule I are: 1) the drug has no accepted medical use in the United States; 2) there is a lack of safety for use of the drug under medical supervision; 3) the substance has a high "potential for abuse" (Nichols 2003, p. 133). "Potential for abuse," an ambiguous criterion, is typically interpreted by the United States DEA and FDA as the potential for addiction.

The FDA system of scheduling has been heavily criticized due to the influence of politics. President Nixon in the early 1970's took responsibility for drug scheduling away from the Surgeon General and his team of medical experts. The responsibility was delegated instead to the office of the attorney general and his team of law enforcement experts. Since then, "cops and lawyers instead of doctors were judging the toxicity of drugs" (Baum 1997, p. 25-26). Decisions made by the U.S. attorney general's office regarding the

scheduling of drugs were more heavily influenced by the politics of the war on drugs than scientific data presented by doctors. For example, in the hearings held by the DEA in 1986 regarding the scheduling of MDMA, thirty-four witnesses, including experts in the field of psychology and psychiatry, gave testimony and a ten volume report outlining the potential medical benefits of MDMA, asking for its rank to be lowered to schedule III. DEA Administrative Law Judge Francis Young wrote a ninety page opinion paper highlighting the witness' findings and agreed that MDMA should be dropped to schedule III, IV or V because of its potential medical value in mental health. Despite the overwhelming evidence and the agreement by Judge Young that the law should be changed, Judge Young reinstated his original ban on MDMA, leading to the permanent placement of MDMA in Schedule I of the Controlled Substances Act in 1986 (Stafford 1992, p. III-63).

There is also evidence that the government was aware of this inaccurate evaluation of LSD's danger because the CIA had conducted multiple experiments on American and British military personnel. From 1947 to 1977 the CIA had conducted operations coded MKSEARCH, MKOFTEN, MKCHICKWIT, MKULTRA, MKDELTA, and MK NAOMI (General Council of the Department of Defense 1977). Their goal was to use LSD as a covert weapon to cause brain damage or permanent insanity to the enemy. Their other goal was to use LSD as a mind control agent or torture device for prisoners in order to obtain information (Greenberg 2010, p. 164) (National Geographic Documentary 2009). It would have been the perfect weapon because a 25 microgram drop (the size of two salt grains) of this colorless and odorless fluid anywhere on the skin could cause the effects. One ounce is enough to dose 300 thousand people. The CIA was unable to achieve their goals of weaponizing LSD. They were unable to control minds or cause permanent insanity by dosing personnel. Instead of being controlled or damaged, the men had fits of laughter and an enjoyment for the nature environments they were in (National Geographic Documentary 2009).

Historical Uses of Psychedelics

Psychedelics occur naturally in both animals and plants. They have played a significant role in the development of philosophy and religious thought in earlier cultures. Well documented examples of psychedelic use include the soma of ancient India, peyote used by Native American tribes, rituals by Aztec shamans, ritual use by peoples throughout Mexican history, ceremonies of the ancient Greeks, and use of ayahuasca in modern Brazil (Nichols 2003, p. 133). Psychedelics were popular for philosophy development and religious use because of their ability to induce states of altered perception. These substances were not considered "drugs" in these cultures. To find references to use in literature, it is important to look at key words such as "fruit of the gods," "divine fruit," or "flesh of the gods."

The science of psychedelics became popular after new scientific methods for synthesizing psychoactive substances became available and new techniques for studying them. MDMA was first synthesized in 1912 by Merck chemist Anton Kollisch (Ecstasy Rising 2004).
MDMA hadn't been ingested at that point, so there was no indication of its potential effects. Soon after Albert Hoffman synthesized LSD at the Sandoz pharmaceutical laboratory in 1938, scientific interest began to peak in psychedelics. Hoffman had accidentally ingested a small amount and experienced the world's first LSD trip (National Institute on Drug Abuse 2001). By the 1965 more than a thousand peer-reviewed research articles detailed the use of psychedelic compounds for medical purposes. Promising therapeutic effects were reported in over 40,000 subjects who had each used LSD in multiple sessions (Vollenweider and Kometer 2010, p. 1) (Nichols 2003, p 162) (Stafford 1992, p. 40-44). At the same time, recreational use was rampant, having been made popular by Leary and his associates (Stafford 1992, p. 51). The suicide of Diane Linkletter, daughter of the entertainer Art Linkletter, after taking LSD was one of the major sparks that allowed the passing of the Controlled Substance Act of 1970 which put all psychedelics on the schedule I list. The media had argued that Diane had no personal problems, and it was the drug that caused the suicide. While alive she was portrayed as a well-educated, Christian, white woman with no prior drug use or symptoms of depression (Baum 1997, p. 25) (Greenberg 2010, p. 256). Rampant use of ecstasy in the 1980s lead to the adding of MDMA to schedule I in 1985. The Controlled Substance Act and the war on drugs interrupted all research until the 1990s, where research began to make a slow comeback.

A recent resurgence of research on these substances questions the validity of their schedule I classification. Media outlets such as *World Report* and the *New York Times* have expressed excitement

about the psychedelic assisted psychotherapies for the treatment of anxiety, depression, post-traumatic stress disorder, obsessive compulsive disorder, addiction, and more. Tom Roberts, professor of educational psychology at Northern Illinois University, notes that "What we see now is the [US] FDA making decisions based on data rather than politics" (Morris 2008, p. 1491). Universities, among them Johns Hopkins, Purdue University, University of Arizona, Harvard, New York University, and U.C.L.A, are obtaining federal permission to study these substances, leading the way in the United States. Non-profit groups such as the Heffter Research Institute and the Multidisciplinary Association for Psychedelic Studies (MAPS) are also contributing (Tierney 2010).

Research Supporting Lowering LSD, Psilocybin, and MDMA from Schedule I

Since the 1960s, public service announcements have been making false claims about LSD and Psilocybin that had not been confirmed by ethical scientific research, frightening drug effects ranging from schizophrenia, chromosome damage, birth defects, and murder to suicide (National Geographic Documentary 2009). False claims about MDMA have included irreversible brain damage, Parkinson's after one pill, and holes in the brain (Ecstasy Rising 2004). Current leaders in this field, who have performed ethical clinical trials with animals and humans, disagree with these claims. Their research also shows that these hallucinogens meet none of the criteria required for schedule I designation.

1) The drug has a high potential for abuse.

Hallucinogens do not engender drug dependence or addiction and are not considered reinforcing substances. They don't produce drug-seeking behavior or physical withdrawal symptoms (Nichols 2003, p. 134) (Studerus et al. 2010 p. 2). The scientific community argues that dependence liability in a drug stems from the ability to affect dopaminergic (DA) transmission. "Nearly all hallucinogens lack the affinity either for DA receptors or for the DA uptake transporter and therefore do not directly affect DA neurotransmission (Nichols 2003, p 134)." There are no literature reports of successful attempts to train animals to self-administer hallucinogens, indicating that these drugs do not possess the necessary pharmacology to initiate or maintain dependence (Nichols 2003 p. 134) (Studerus et al. 2010 p. 14). Results of a clinical study involving 227 psilocybin sessions with 110 subjects conducted between 1999 and 2008, indicate that "carefully monitored administration of psilocybin to healthy volunteers within an experimental setting does not increase the risk of subsequent abuse of psilocybin or other illicit drugs (Studerus et al. 2010, p. 14)." These results are in line with another long term study involving LSD. In a ten year follow up of 247 subjects who received LSD in an experimental or therapeutic setting, most subjects reported discontinuing or reducing their hallucinogen drug use. Use of hallucinogens tends to be less frequent or discontinued over time. Regular use is unlikely for several reasons. Tolerance develops at a rapid rate (Studerus et al 2010, p. 14). Hallucinogens, when taken for a second consecutive day, do not give the user the normal effects. Subjects in the psilocybin study reported the effects as being tired. They were glad to regain their normal state of consciousness and needed time to recharge. Furthermore, hallucinogens do not produce the pleasurable effects of addictive drugs such as escape, euphoria, anxiety relief, increase of self-esteem, etc (Studerus et al. 2010, p. 14).

2) There is a lack of safety for use of the drug under medical supervision.

"Hallucinogens are generally considered to be physiologically safe molecules whose principle effects are on consciousness (Nichols 2003, p. 134)." They do not have harmful physiological effects. Hallucinogens are not toxic to any mammalian organ systems and there is no evidence to suggest that they damage any human organs. "Hallucinogens do not cause life-threatening changes in cardiovascular, renal, or hepatic function because they have little or no affinity for the biological receptors and targets that mediate vital vegetative functions (Nichols 2003, p. 134)." Dr. James Gill, Deputy Chief Medical Examiner in New York City, conducted a three year study in the early 2000s to see how many deaths in New York City were related to MDMA toxicity. He looked at all the autopsies that were not related to any natural causes of death. Out of 19,000 autopsies, only 22 subjects had MDMA in their system. Of these 22 subjects, only two of the deaths could be attributed to ecstasy alone. This study was conducted at a time when statistics from

the DEA reported New Yorkers using approximately 110 million doses of ecstasy (Ecstasy Rising 2004).

The primary effect of administering hallucinogens to subjects is psychological. LSD and psilocybin can induce disturbing experiences. They can also catalyze an onset of psychosis or depression, which has led (in some cases) to suicide. However, these drugs do not appear to produce illness in people who are not predisposed to those illnesses (Nichols 2003, p. 135). Psychosis and depression were catalyzed only in people having a genetic predisposition. The actual numbers of occurrences for recreational users are also low. A search of Medline in 2003 by Dr. Nichols for cases of LSD-induced psychosis yielded three reports in the previous 20 years (Nichols 2003, p. 135). According to the 2006 National Study on Drug Use and Health, approximately 23 million people (9.5 percent of the population) over the age of twelve had used LSD in their lifetime.

Risks can be avoided in ethical and responsible medical settings. Bad trips can be treated with "talk-down" therapy and administration of benzodiazepines (Nichols 2003, p. 135). Data from the psilocybin study demonstrate safety and tolerability in both the short term and long term with 227 psilocybin administrations. There is no indication of persisting perception disorders, prolonged psychosis, or other long-term impairments of functioning. A small proportion of "bad trips," were resolved by providing interpersonal support. The team concluded "that psilocybin administration to healthy, high functioning, and well-prepared subjects in a responsible clinical or research setting is generally well tolerated and that future studies using this important research tool are justified (Studerus et al. 2010, p. 16)." The administrations were well tolerated, producing positive outcomes. The team concluded that hallucinogenic drugs used under controlled and supportive conditions can lead to,

> "Sustained positive changes in personality, attitudes and values, particularly in those subjects who have experienced profound personal insights and transcendent or mystical experiences. Among the most often reported are more self-understanding, more tolerance of others, less egocentricity, a less materialistic and aggressive orientation, and more appreciation of music, art, and literature (Studerus et al. 2010, p. 14)."

Much contradictory research that emerged during the war on drugs neglected two very important concepts regarding hallucinogens. The first is that hallucinogens are not predictable like other central nervous system drugs. They do not have the same effects every time because primary determinants of subject experience are expectations ("set") and environment ("setting") (Nichols 2003, p. 137) (Greenberg 2010, p. 164). Hallucinogens do not directly cause any behaviors or feelings. They amplify the thoughts and emotions of the user and are completely vulnerable the user's "set" and "setting." A negative "set" and "setting" can result in a "bad trip" or a disturbing experience. If a clinical or research setting creates a positive "set" and "setting," the experience of the user can be sublime. Early research supporting the current scheduling of hallucinogens used a very negative "set" and "setting" for the subjects. Subjects were administered the drugs in very rigid, mechanical, and frightening settings. They were strapped down to a bed to be poked and prodded with tools (National Geographic Documentary 2009). The CIA also conducted unethical experiments by dosing military soldiers without their knowledge or consent. This led to a very small percent of soldiers committing suicide via jumping out of windows because they falsely believed they became permanently insane (Greenberg 2010, p. 164). It was the situation which elicited negative reactions from the patients, not the drug itself. These situations can be controlled. Secondly, different doses produce different qualitative effects (Nichols 2003, p. 137).

Increasing or decreasing dosage does not simply change the amplification of the effects. There are different thresholds for different tiered effects. For example, there is a certain dose required for people to hallucinate on LSD and psilocybin. If the dose is lower than that threshold, the subject will not have hallucinations. This is valuable because the patient can be given a dose that can provoke the emotional and perceptive effects without causing uncomfortable hallucinations. This concept was neglected in research aimed to see if hallucinogens could be safely administrated.

3) The drug has no currently accepted medical use in the United States.

LSD, Psilocybin, and MDMA each have their own unique medical applications. They have a cross tolerance and several shared effects, but their

subtle differences in chemical structure cause them to have unique effects, and thus a diversity of medical applications. LSD and psilocybin are known as Classical Hallucinogens. Classical Hallucinogens have a high affinity for serotonin (5-HT2A) receptors. MDMA does not have the same affinity and is not considered a Classical Hallucinogen. There are several potential medical applications for administration of these three hallucinogens to patients in order treat illness. The illnesses which might be effectively treated with hallucinogens currently have few highly effective treatments available which also include harmful side effects, thus necessitating this new innovative research. There is also valuable information that can be obtained about cognitive neuroscience by studying the chemical interactions in the brains of healthy subjects under the influence of Classical Hallucinogens.

Clinical Applications of Psychedelics

Psychedelic Assisted Psychotherapy

The concept for the technique of psychedelic assisted psychotherapies is completely new. Psychedelic assisted psychotherapy involves using hallucinogens to put patients in an altered mental and emotional state which would make a therapy session more effective. Dr Roland Griffiths of the School of Medicine at Johns Hopkins University describes it as,

> "Not about taking psilocybin or other compounds multiple times. It's about orchestrating, if you can, a single profound transformative experience; that then results in an unfolding of behavioral change over time (National Geographic Documentary)."

These sessions are only meant to happen once or very few times and yield results of positive long term behavioral change. The whole process has several phases. First, the subject must be fully diagnosed by a licensed professional. A review of the subject's background and diagnoses will need to be analyzed to see if the subject has the necessary prerequisites to safely take the drugs (Multidisciplinary Association for Psychedelic Studies 2005, p. 7). The subjects must then have intense preparation before the psychedelic assisted session (Vollenweider and Kometer 2010, p. 4). The therapist must form a strong therapeutic alliance, create a safe psychological and physiological space, and prepare the participant mentally for the experience. These can be accomplished in approximately two ninety minute sessions (Multidisciplinary Association for Psychedelic Studies 2005, p. 9). The drug assisted session will be longer than a typical session. It will be multiple hours; depending on which drugs are used and how long the effects from the dosage is. After the session, it is beneficial for there to be drug-free follow up sessions. All three drugs of interest, along with other hallucinogens, have special qualities for assisting therapy.

MDMA Assisted Psychotherapy

Preliminary trials with MDMA assisted psychotherapy have had very high rates of success with treating posttraumatic stress disorder. "Posttraumatic stress disorder (PTSD) is a debilitating anxiety disorder characterized by re-experiencing, hyperarousal and avoidance symptoms, and is a major worldwide public health problem (Mithoefer et al. 2010, p. 1)." "Patients with PTSD are prone to extremes of emotional numbing or overwhelming anxiety, and often have a narrow window between thresholds of under and over-arousal (Mithoefer et al. 2010, p. 1)." According to the 2005 Multidisciplinary Association for Psychedelic Studies (MAPS) handbook,

> "MDMA can attenuate the fear response and decrease defensiveness without blocking access to memories or preventing a deep and genuine experience of emotion. Participants are able to experience and express fear, anger, and grief with less likelihood of feeling overwhelmed by these emotions. MDMA seems to engender awareness that such feelings arise as an important part of the therapeutic process. In addition, feelings of empathy, love, and deep appreciation often emerge, along with a clearer perspective of the trauma as a past event and a heightened awareness of the support and safety that exists in the present. Hence, the goal of MDMA-assisted therapy in treating PTSD is to enable the participant to restructure his/her intrapsychic realities and develop a wider behavioral and emotional repertoire with which to respond to anxiogenic stimuli."

Many therapists who have experience performing MDMA assisted psychotherapy claim that it could accomplish what would take years of therapy in one session (Baum 1997, p. 212) (Greenberg 2010, p. 154). An example of feedback from a patient is that the drug helped her

confront memories of a rape she suffered, which helped her end periods of depression in panic. She told *Newsweek*, "not only did MDMA enable me to recover my sanity, it enabled me to recover my soul" (Baum 1997, p. 212). MDMA assisted psychotherapy is primarily being used for PTSD, however it has also shown promise in couple's therapy and mood and anxiety disorders. MDMA, while classified as a hallucinogen and psychedelic, does not cause psychotic-like states or hallucinations like LSD or psilocybin.

Possible theories about the chemical mechanism for MDMA are that MDMA releases serotonin, stimulates the serotonin (5-HT2) receptor, and increases the neurohormones oxytocin, prolactin and cortisol. The mood and perception lifts are caused by the serotonin release (Mithoefer et al. 2010, pg. 3). "Findings suggest that oxytocin is involved in affiliation, trust, and accurate perception of emotion, so elevated oxytocin might help participants form a therapeutic alliance and revisit traumatic experiences in an emotionally engaged state (Mithoefer et al. 2010, p. 3)." It was also found that oxytocin reduced activation of the amygdale in humans, which is responsible for fear emotions. A recent study also found that elevation of oxytocin was associated with greater sociability and gregariousness (Mithoefer et al. 2010, p. 3).

LSD and Psilocybin Assisted Psychotherapies

LSD and psilocybin have different effects than MDMA because they agonize different serotonin receptors. They both primarily agonize the serotonin (5-HT2A) receptor which plays a major role in their medical applications. Researchers believe LSD and psilocybin may be useful in treating depression, anxiety, and Obsessive Compulsive Disorder (OCD) as an adjunct to therapy. Several universities, including New York University, Johns Hopkins University, and University of California have had a lot of success with treating anxiety and depression in terminally ill cancer patients (Vollenweider and Kometer 2010, p. 3). Studies from the 1960s concluded that LSD treatment resulted in improved psychological adjustment in dying patients, made them more responsive to their families and environments, and enhanced their ability to enjoy every-day life. Later studies at Spring Grove State Hospital in Maryland showed improvement in about two-thirds of the cancer patients who had received LSD. Some of these reported improvements were improved mood, reduced fear of death, and reduction in the amount of pain-relieving medication required. Half of patients reported dramatic improvement and profound experiences (Nichols 2003, p. 163). Dr. Charles Grob and his assistant Alicia Danforth conducted an end of life study at Harbor UCLA Medical Center which involved giving psilocybin assisted psychotherapy to twelve terminally ill patients. Terminally ill patients can be overwhelmed with anxiety and fear about their upcoming death. They also are typically on a lot of pain medication and are in medical environments which restrict them from appreciating life. Before dying, the patients reported positive mood shifts and increased acceptance of death. They had mended relationships and were able to spend quality time with their families (National Geographic Documentary 2009).

There are several theories for possible mechanisms to explain how classic hallucinogens improve therapy. Scientists estimate that the brain takes in eleven million bits of information per second; however, the brain can only process about two hundred bits at a time. To handle that amount of information, the brain must filter out information that is not critical. It does this by connecting new information to preconceived concepts so that it does not have to analyze all of it (National Geographic 2009). Dr. Torsten Passie's "Hollow Mask Study" at the Hannover Medical School in Germany concluded that schizophrenics and subjects intoxicated by LSD do not process information in that same way. The filters are lifted and the ability to connect new information to preconceived concepts is temporarily suspended. This means psychedelics temporarily de-condition the mind, resulting in the ability to take in more information, more sensory impression, more emotional impression, more visual impression, and more access to parts of the mind (National Geographic Documentary 2009). This allows the LSD user to approach problems in a more genuine and open minded way that neglects socially conditioned behaviors or roles. The increased mind power and stimulation comes from the increased activity of the serotonin (5-HT2A) receptor.

Activation of serotonin (5-HT2A) receptors initiates complex chemical reactions in the pre-frontal cortex. LSD and psilocybin have such a similar shape to serotonin molecules that they are able to fit in the receptor like a lock and key. Serotonin (5-HT2A) receptors are located on the

large glutamatergic pyramidal cells in the deep cortical layers. The chemical reactions from binding with the serotonin (5-HT2A) receptors releases glutamate across the synapse, which then activates the AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid) and NMDA (*N*-methyl-d-aspartate) receptors on the cortical pyramidal neurons. In addition, LSD and psilocybin directly activate the serotonin (5-HT2A) receptors located on cortical pyramidal neurons. The synergy of activating the serotonin (5-HT2A), AMPA, and NMDA receptors on the cortical pyramidal neuron results in the increased expression of brain-derived neurotrophic factor (BDNF) (Gonzalez-Maeso and Sealfon 2009, p. 227) (Vollenweider and Kometer 2010, p. 5). BDNF is a chemical that promotes the growth and survival of neurons. A deficiency in BDNF may impair the health of neurons and lead to depression (Comer 2010, p. 250). Since serotonin (5-HT2A) receptors are linked to the prefrontal cortex, this means Classical Hallucinogens lead to increased neuron strength in the prefrontal cortex from the BDNF. Areas in the prefrontal cortex are responsible for complex mental functions such as cognition, mood, perception, self control, and somatic awareness (Nichols 2003, p. 162). The increased effectiveness of therapy may be derived from a boost of brain metabolism and strength in these mental functions.

Administration to Patients: LSD and Psilocybin for Treatment of Cluster Headaches

John Halpern's research, at the McLean Hospital at Harvard Medical School, illustrates that LSD and psilocybin may have a high success rate for reliably treating cluster headaches. Cluster headaches are severely painful and debilitating headaches that reoccur. Scientists do not fully understand what causes cluster headaches, but they know it is related to blood vessels, nerves and neurochemistry. There is no cure and few treatments. The available treatments, including oxygen and/or medication, are minimally effective. The mechanism is unknown, but LSD and psilocybin seem to be highly effective in relieving or eliminating cluster headaches. A survey by Halpern indicated that for 53 subjects, psychedelics prevented or stopped cluster headaches more reliably than medication. Halpern and his colleagues at the Hannover Medical School in Germany launched a clinical trial on six subjects with cluster headaches. The team developed a non-psychedelic form of LSD, LSD-BROMO, and administered it three times over a fifteen day period. For five of the six participants the headaches were gone. All of the participants reported that their quality of life had totally changed (National Geographic Documentary2009).

The addition of a BROMO molecule to LSD creates a molecule that is too big to fit in the receptors that would normally trigger intoxication. LSD-BROMO successfully relieves cluster headaches in the same way other LSD molecules do, except it has no hallucinogenic properties. Despite displaying no hallucinogenic properties, LSD-BROMO was added to schedule I and is illegal in the United States; thus restricting research and clinical trials. Since This trial, no further clinical trials have been funded to administer LSD, psilocybin, or non-hallucinogenic LSD-BROMO to treat cluster headaches (National Geographic Documentary 2009).

Understanding Cognitive Neuroscience through LSD-Like Intoxication in Healthy Subjects

LSD-like hallucinogens, including psilocybin but not MDMA, are psychotomimetic at high doses; meaning they induces psychotic like episodes (Gonzalez-Maeso and Sealfon 2009, p. 2) (Nichols 2003, p. 162). There are a wide variety of hallucinogens that mimic different types of psychotic symptoms and disorders. The effects are contingent on how the molecules are shaped and by what receptors they either agonize or antagonize. LSD in particular mimics the positive symptoms of schizophrenia (hallucinations and thought disorder). Psychotomimetic hallucinogens can be used as tools for understanding neuronal basis of psychiatric disorders, understanding a psychotic experience, and finding a cure for those psychiatric disorders (Vollenweider and Kometer 2010, p.1). Franz Vollenweider uses neuroimaging technology at the University Hospital of Psychiatry in Zurich to map brains on psychedelics. His data shows that a brain on hallucinogens looks the same every time (National Geographic Documentary 2009). This means clinical trials with psychotomimetics are reliable to be analyzed and compared for conclusions.

Schizophrenia is very difficult to treat and learn about because some of the symptoms make fruitful communication between the patient and doctor impossible. Formal thought disorders, loose associations, derailment, poverty of speech, avolition, and social withdrawal make verbal communication very difficult (Comer 2010, p.

462). LSD-like hallucinogens can help researchers and doctors learn more about the schizophrenic experience by taking it themselves or performing clinical trials. Once the subject is sober, they will have their previous mental capacity and intelligence restored and be able to articulate their experience in a more accurate way than a patient with a permanent psychopathology. Dr. Charles Nichols, Geneticist from the LSU Health Sciences Center, also believes "by understanding how LSD produces its effect at the molecular and genetic level, we could potentially understand mechanisms underlying diseases like psychosis that have very similar overlapping behaviors (National Geographic Documentary 2009)." By understanding the neurochemical and genetic causes of psychosis, psychopharmacologists could potentially be able to create drugs that negate those causes in order to treat psychosis more effectively.

One possible problem with finding treatments for certain psychotic disorders, such as schizophrenia, is that they are uniquely human disorders (Gonzalez-Maeso and Sealfon 2009, p. 1). This means there are no animal models to do tests on. Animal test subjects are crucial because scientists can perform tests on them that would be unethical for human subjects. They can be bred to control for variables and provide a larger supply of test subjects. Hallucinogens fix this problem because they give opportunities to test schizophrenic-like mice. According to Dr. Nichols, LSD induced mice display human symptoms of schizophrenia. This gives him the ability to study brains of schizophrenic mice and test potential treatments on them (National Geographic 2009). They can induce mice with schizophrenic episodes and test anti-psychotics to see if they bring the mice back to a normal state of health.

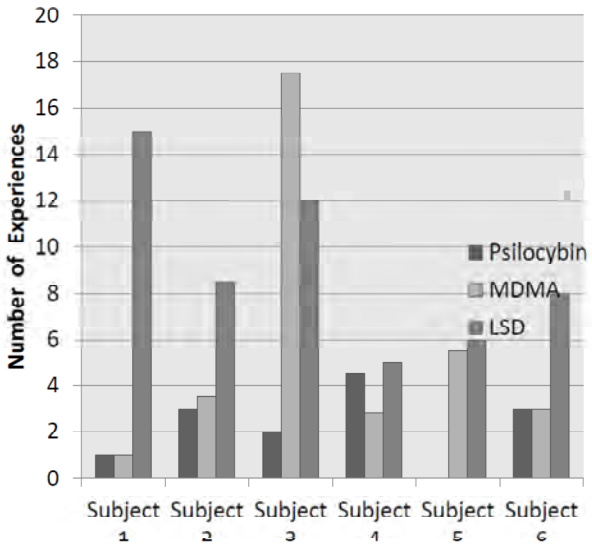
Hallucinogens agonize and antagonize various serotonin receptors, among other neurotransmitters. The serotonin receptors in particular that hallucinogens interact with affect complex parts of the human brain, including much activity in the prefrontal cortex and interconnecting pathways between the cerebral cortex and limbic systems (brain regions implicated in pathophysiology of many mental disorders) (Gonzalez-Maeso and Sealfon 2009. p 228). Pathology relating to mood and anxiety is associated with an imbalance or abnormal functioning of serotonin chemical reactions. Thus, testing and understanding the mechanisms of hallucinogens may lead to important clues for the basis of psychosis. The results obtained from the mechanism of Classical Hallucinogens may provide efficient approaches for the rational design and testing for new types of antipsychotic drugs (Gonzalez-Maeso and Sealfon 2009, p. 225). This also means experimental use with hallucinogens can be a great aid for mapping out the brain and further understanding the prefrontal cortex, pyramidal cells, serotonin, glutamate NMDA, AMPA, and BDNF interactions.

Methodology

Semi-structured interviews were conducted with a snowball sample of subjects to learn about their experiences with MDMA, LSD and psilocybin. The subjects were recruited privately through networking within the drug using community. Six public liberal arts College students were selected because of their high level of experience with the substances of interest. Five of the subjects were male and one was female. The goal of the interviews was to evaluate if the effects of MDMA, LSD, and psilocybin were recreational or entheogenic. The operational definition for "recreational experience" is experiences that cause altered physical and mental effects during intoxication. However, after the substance has been processed and excreted from the body, the subject retreats to their previous physical and mental states prior to intoxication. The operational definition of "entheogenic experience" is long term transformative effects on personality, spirituality, cognitive state, emotional state, and perception of one's self after intoxication.

The interviews ranged from twenty minutes to an hour in length. The interviews were conducted at each subject's home for comfort and privacy. To prevent coding bias, the interviews were recorded on a handheld recorder and later transcribed. The subjects gave verbal consent on the recorder. The recordings were deleted after transcription to protect the subject's from being identified by their voice. No names or information that could be used to identify the subjects were used. The interviews had a pre-set list of questions; however, the subjects had freedom to discuss details beyond the scope of the pre-set questions. The subjects were asked questions about three different phases related to their drug use. They were asked questions about their experiences leading up to their first time uses with these drugs. They were asked questions about the experiences and feelings while intoxicated by these drugs. Finally they were asked about their experiences and reflections after their intoxication had ceased.

The subjects had varying levels of experience with each drug.



Bar Chart: Subject's estimate of experiences using Psilocybin (left bars), MDMA (middle bars) and LSD (right bars). Each subject had at least twelve combined experiences with the drugs of interest.

All of the subjects reported doing some type of research before having their first experience with these hallucinogens. They approached these drugs with skepticism and caution because of the negative stigma associated with them. Each subject used sources such as books, encyclopedias, friends who had experience, and online sites for information about what to expect and how to approach the experience. All of the subjects mentioned using erowid.com for anecdotes, information about appropriate doses, and advice for activities to do while intoxicated.

Subject 5 (female) appeared to have recreational experiences while the rest of the subjects appeared to have, for the most part, entheogenic experiences. This can be explained by their different habits of use. Subject 5 typically took lower than average drug doses, which since hallucinogens have different qualitative affects at different dose levels, gave her less intense effects compared to the other users. She used the drugs to make regular recreational activities, such as dancing to music, more enjoyable.

Subjects 1,2,3,4, and 6 used hallucinogens differently than subject 5. They took higher doses and created their own private ritual-like experiences. They tended to avoid large social situations; instead, they spent their experiences in small groups and in environments where they felt safe and comfortable.

Effects and Experiences While Intoxicated

Subject 5 used MDMA and LSD as party drugs. She used them to enhance social experiences. It enables her to connect with people more easily and with more depth. "On ecstasy I just love everyone." The euphoria also amplifies the pleasure of music, colors and dancing. She also reported a greater connection with nature on LSD and psilocybin. The effects of the hallucinations were not as intense due to the relatively low doses she used. She described her environment as being "wavy" and "breathing." Since the effects were not too intense, they were always very manageable. She claimed to feel very safe and confident in her drug use.

Subjects 1,2,3,4, and 6 had different experiences than subject 5. Their experiences were more intense and more varied. They reported having few negative moments in their experiences, but they were always able to calm themselves or each other down during those unfavorable intense moments. Aside from those few moments, they report overwhelmingly positive transformative experiences. They were very introspective. According to subject 4,

> "Whatever your feeling becomes dramatic and exaggerated and richer than you've ever experienced before. You kind of see your dark side and light side. You see your persona for what it is; for all its sincerity and bulls***. You see your shadow for what it is. You see your entire personality almost from an outside perspective and I think part of being on acid is losing that sense of judgment of positive and negative and ultimately coming to the conclusion that this is who you are. And as far as today goes, you're not going to change it. So you might as well embrace it."

Subject 4 also reported the "[he] dance[s] across the entire emotional spectrum, but [he] does it with the volume turned all the way up." He later said that he has experienced a range from ecstatic bliss to depressive nihilism.

> Subject 1, when talking about LSD reported, "The way I experience the world is that everything is more beautiful. I'll just see something like a leaf with a dew drop on it and just love the natural beauty of it. Everything around just seems more vivid and I'm

generally pretty happy. I've never had a bad trip."

Subject 1 takes SSRIs, however, he reported a better mood lift with acid. "If I could take acid once a month, I could be content with the whole month."

The enthogenic subjects not only experienced introspective self-analyses, but also examined their relationships with family and friends. They reported that hallucinogens have been important aids in repairing or strengthening relationships. Four out of the five entheogenic users had specific anecdotes on how hallucinogens played a positive role in their relationships. Subject 1 reported,

> "A couple of years ago I was having a fight with my girlfriend and I just took a couple of tabs of acid, probably not the best idea to do in that situation. I just went alone and did acid with a friend. It made me feel like, why am I fighting with my girlfriend? I should just go and make amends because it's stupid. I kind of felt love for everybody."

Subject 2 had an elaborate intimate experience with his significant other which he attributed to MDMA. They both took MDMA at his house.

> "She was nervous at first. As we were coming up I comforted her and she became more comfortable with the sensation. From that point until we came down it was just heaven. We laid around in my room in our underwear and we just talked. We talked about each other and who are some people important in our lives. The whole experience centered around her and I and we really connected. And there are things that people say to each other, or don't say to each other rather. Like when you say very emotionally charged things to somebody you care about; sometimes you're apprehensive about overstating your appreciation for them to avoid maybe cheapening the relationship or feeling that you have for them. I think MDMA really let us say these things to each other and really mean it and understand that the other meant it. Like I said, sometimes you avoid saying these things to avoid cheapening what they mean and other times you simply don't get around to saying it them due to circumstances or timing or whatever. It let everything out that needed to come out. It was really instrumental in us two making that connection."

Subjects 3 and 6 talked about psilocybin experiences that elicited strong positive emotional feelings about family members. Subject 3 reported,

> "One of my first experiences with psilocybin was at a concert and I remember enjoying the music very much. But at one point in the concert, I had just stopped and found my mind wondering and daydreaming. I was thinking about the relationship I had with my mother at the time. I didn't particularly like the way the relationship was going and so in the calm state I was in I wondered, Why isn't that better? Why don't I better that relationship?"

Subject 6 detailed one of his psilocybin hallucinations and emotions associated with it.

> "My next journey was with my girlfriend. We were dressed like Adam and Eve in a forest. We held each other and spiraled into the green and blue corners of space and time. It wasn't erotic. It was a spiritual connection. I felt close to her. I felt one with her. I thought about my family. I connected with their spirits. Our energies became one. There was no more sadness. All problems ceased to exist. I met my father and we were free."

Post Experience Reflections

There were several common reflections among the subjects. All of the subjects feel safe, secure and confident with these drug experiences. They are all open-minded to using these substances again in the future. They are so confident in their experience and understanding of the drugs that they would feel comfortable recommending use to a friend or loved one. All of the users also reported having no regretted experiences on these substances. They felt the negative moments had value to their development and character.

The entheogenic users also had some common sentiments. They felt that their experiences with these drugs had a very positive impact on their relationships, mood, outlook on life, and creativity. They use these drugs primarily for spiritual and emotional development. They did not use frequently; rather, they decided to use at key moments in their life where they were struggling, had big decisions to make, or wanted to bond with friends.

Conclusion

Hallucinogens have a long history of being used by humans for spirituality and well-being. The act of moving hallucinogens to schedule I with the Controlled Substance Act was hasty and poorly thought out. This decision interrupted much needed

research into mental health and well-being. Current projects offer data that supports the lowering of hallucinogens from schedule I to a level that would continue to prohibit recreational use, while permitting research and medical use. There is overwhelming evidence that hallucinogens do not meet the criteria set by the Controlled Substance Act to be ranked as schedule I. Hallucinogens have a very low potential for abuse. They are one of the least addictive drugs that exist. They can be safely used in a medical situation because of a lack of toxicity and addiction. With the appropriate dose, set and setting, a licensed professional can create a safe and controlled environment for patients to use in a medical situation. The literature also shows that there are many potential medical uses in the United States from psychedelic assisted psychotherapy for the treatment of mood and anxiety disorder and Classical Hallucinogens for the treatment of cluster headaches, to clinical trials to aid in the creation of more efficient medications.

The research is in its preliminary stages and has not had many large trials. Much work needs to be done on understanding the mechanisms for how the drugs affect the brain and behavior at the molecular level. Success of preliminary studies justifies larger scale double blind trials. Results justify increased access to funding and permission for research institutions to use these substances in clinical trials.

The interviews support the literature and illustrate that it may be possible to orchestrate possible healthy and positive experiences with these drugs. Recreational users may not always give accurate insight or judgment about these drugs because street drugs are un-regulated. The drug's purity is unknown to the recreational user. Despite this flaw, the subjects interviewed did display characteristics predicted by the literature. Subject 5's description of how she feels on LSD is in line with Dr. Passie's conclusions from the "Hallow Mask Studies." It supported the mechanism by which LSD takes off the filters and allows a person to evaluate themselves or a situation in a new way. This account also illustrated the significance of "set" and "setting" because subject described how he feels a whole range of emotions instead of the same ones every time. All of the subjects displayed how hallucinogens can be a positive influence on mood. The anecdotes from Subjects 1, 2, 3, and 6 illustrated how hallucinogen helped them in their relationships. This supports the hypothesis that psychedelic assisted psychotherapy may be effective in couples therapy or family therapy.

Research into techniques for psychedelic assisted psychotherapy is imperative because they may be faster, safer and more effective than alternative methods used today; such as anti-depressants and other medications. According to Greenberg, anti-depressants fail to outperform placeboes in clinical trials nearly half the time. They appear to make a positive difference in approximately 60 percent of the people who take them, while having serious side effects such as suicide (Greenberg 2010, p. 8). Mental health patients need newer treatments that are more effective, just as fast and without the serious potential side effects that exist with current medications.

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