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The Use of Hallucinogens in the Treatment of Mental Health Disorders

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The Use of Hallucinogens in the Treatment of Mental Health Disorders

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Brianna Gagen

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Abstract

The percent of people with mental health disorders in the United States have skyrocketed over the past decade. With stigma surrounding the discussion of mental health and the symptoms associated with it, often those that are suffering do not receive sufficient treatment, as they might with a physical illness. The current, common treatment options for common psychological disorders, like depression, anxiety, and post-traumatic stress disorder, are sometimes not effective in patients, due to resistance or poor response outcomes. Consequently, in order to research alternative therapeutic approaches for mental health disorders, scientists are researching the effects of several hallucinogenic drugs in controlled clinical environments as options. Drugs such as MDMA, psilocybin, LSD, and ketamine are socially prohibited by law; however, some of their benefits and mechanisms of action might have positive effects on treating the disorders of the brain. This thesis provides a summary of mental illness, hallucinogenic drugs, and the ongoing research regarding the use of these drugs in mental health treatment. While the negative connotation around hallucinogenic drugs remains, researchers are proving that they might have value in medicine, but the question remains if science and society are ready to implement controlled hallucinogenic drug therapies into mental health treatment based on the present research. The exploration of this question and suggested integration strategies will be included in this thesis.

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Introduction

Mental health disorder rates have increased into a pandemic scouring the globe affecting around 350 million people (De Gregorio et al., 2021). These types of disorders manifest as impairments in a person's thoughts, emotions, and behaviors. Common examples of mental health disorders— and the ones that this thesis will be focusing on— include depression, generalized anxiety disorder, post-traumatic stress disorder, and obsessive compulsive disorder. Some of the symptoms in these disorders affect virtually every individual at some point in their life, but they are only diagnosed as a mental health disorder once they start to cause continual problems in one's daily life, career, and relationships (Gill et al., 2020). Unlike many physical diseases and disorders, mental health disorders are still not fully understood. Research has shown that mental illnesses are thought to be caused by a combination of genetic and environmental factors. While these disorders can be inherited as parents pass down their DNA to their offspring, stressful lifestyles, poverty, income, abuse, and more can have a significant correlation with the development of mental health disorders in a person (United Health Foundation, 2021). Since there are so many risk factors associated with these illnesses, it makes it difficult for researchers, physicians, and psychologists to discover the definite causes and manifestations of these disorders. Unfortunately, with the hazy understanding in this area, the problem is getting worse. Even before the pandemic, in 2017-2018, the prevalence of mental illness was increasing with 19% of adults suffering, which was an increase of 1.5 million people

since the year before (Mental Health America, 2021). There is an evident detriment affecting the minds of many United States citizens, as well as others across the world.

Treating these disorders has also become an increasing problem with varying side effects and growing resistance to the current prescriptions and therapies. Many prescriptions are available in the treatment of mental illnesses, including antidepressants, mood-stabilizers, anti-anxiety medications, and more. Oftentimes, patients do not react as hoped to these prescriptions, and are therefore considered treatment-resistant (Torres, 2020). This can be a very frustrating experience for people who already are not feeling like their normal selves, as they have to use a process of elimination with several different drugs that could give them undesirable side effects. Therapy, whether group or individual, is also a common treatment for mental health disorders, and is often used in conjunction with medication (Cuijpers et al., 2008). In these scenarios, a trained therapist is able to talk with a patient about their problems, feelings, and behaviors and suggest ways to positively react or think in varying situations (Cuijpers et al., 2008). Since there has been a trend in resistance and inadequate treatment, researchers have started looking elsewhere for alternative methods to manage mental health disorders. In particular, there is emerging evidence that using several hallucinogenic drugs in varying methods has a positive impact on mental health illnesses like major depressive disorder, post-traumatic stress disorder, generalized anxiety disorder, and obsessive compulsive disorder (De Gregorio et al.,, 2021). In this thesis, a proposal will be made on the usage, legalization, and effect these new therapeutic methods could have on science and society.

Mental Health Disorder Backgrounds

Major Depressive Disorder

Major Depressive Disorder (MDD) is considered a common, yet serious mental condition affecting one's thoughts and/or behaviors in a negative manner. Common symptoms of MDD include frequent sadness, loss of interest in activities the individual once enjoyed, abnormal sleeping habits, difficulty concentrating, suicidal thoughts, and more (Torres, 2020). Oftentimes, the presented symptoms impair a person's ability to efficiently function within their career, schoolwork, relationships, and many aspects of daily life. In order to be diagnosed with MDD, one must have experienced one or more of the symptoms for at least two weeks leading to changes in behaviors and impairments in one's life (Torres, 2020). In 2019, 19.9% of adults in the nation were reported being diagnosed with MDD (United Health Foundation, 2021). These statistics only show those that were officially diagnosed, so the actual percentage is likely much higher. In addition to this, nationally women are much more likely to suffer from depression than men, and studies have proven that one-third of women will experience a major depressive episode at least once in their lifetime (Torres, 2020). The likelihood of developing depression at some point in an individual's life is very high and provides justification that ample research should be conducted on therapeutic methods to at least ease the symptoms.

Unfortunately, we do not fully understand the risks or direct causes of depression. There is evidence that genetics plays a role in how likely it is that someone will develop MDD. For example, if a parent or sibling is diagnosed with depression, there is a 40% chance that one has inherited the gene causing the illness will progress

in them as well (Torres, 2020). In addition to this, if an identical twin has MDD, the other twin has a 70% chance of developing the illness at some point in their life (Torres, 2020). These statistics clearly show that there is some level of heritability and gene-dependence in MDD. There are also various environmental factors that are shown to have an effect on the probability of depression at some point in an individual's life. If a person has experienced a form of trauma, such as violence, abuse, or neglect at any point, they are much more at risk for moderate to severe depression affecting their life (United Health Foundation, 2021). Poverty is also considered to be a common and grave threat to the development of MDD. Income and depression are statistically shown to have an inverse relationship, meaning that as one falls into poverty or a lower income bracket, they have a higher chance of battling depression (Torres, 2020). Minor grievances like stressful careers and lifestyles also can play a role in progression of the disorder. Mental health professionals have clearly stated, however, that sadness and grief are not necessarily the same as MDD. For example, if someone enters a period of sadness and low activity while mourning the loss of a loved one, they should not be immediately diagnosed with depression, as the affliction is expected to subside eventually without medical intervention. In addition to the aforementioned risks, the symptoms of depression can result from an imbalance of neurotransmitters between nerve cells in the brain. Neurotransmitters are chemicals that are released from nerve cells to communicate with one another, so when they are not doing their job correctly, the brain is not responding as it should (Jelen & Stone, 2021). This can lead to the common symptoms of MDD.

Depression is one of the most treatable mental health disorders. In order to diagnose MDD, a psychologist or psychiatrist will interview a patient and perform a physical exam, and often a blood test to ensure depressive symptoms are not due to an alternative condition like thyroid problems or a vitamin deficiency (Torres, 2020). Medications like selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are considered first-line treatments, but 50% of MDD patients fail to respond to these prescriptions (Gill et al., 2020). Furthermore, it has been found that 42% of individuals stop antidepressant prescriptions after one month of use, and an even more staggering 72% discontinue within the first 3 months (Gill et al., 2020). Both of these drug classes work to prevent the reuptake of certain neurotransmitters in the brain. As stated before, neurotransmitters are messenger chemicals that are released from nerve cells. Once released, the neurotransmitters are commonly absorbed back into the nerve cell from which they were expelled. SSRIs and SNRIs work to stop the reabsorption process so that the neurotransmitters stay between the communicating nerve cells for a longer period of time (Newcomer et al., 2000).. In this way, antidepressants have the capability to modify an individual's chemistry of the brain without directly sedating or stimulating them.

Oftentimes, the use of psychotherapy is often applied alongside antidepressant prescription. This is often manifested as the stereotypical therapist one-on-one conversation with a patient. Cognitive behavioral therapy (CBT) is very common and can aid a person in acknowledging their negative thinking and works to alter those thoughts to respond to situations in a different, more positive way. Cuijpers et al. (2008)

defines CBT objective as “aimed at evaluating, challenging, and modifying a patient’s dysfunctional beliefs (cognitive restructuring).” In this way, the therapist focuses on teaching a patient alternative ways to cope and giving specific objectives for the patient to work on outside of their sessions. There are other forms of therapy that are also effective in relieving depressive symptoms and educating an individual how to better handle their diagnosis, including group therapy and social skills training (Cuijpers et al., 2008). If a person fails to respond to prescriptions or various forms of psychotherapy, some psychiatrists might recommend the use of Electroconvulsive Therapy (ECT). ECT can be used for depression treatment by applying electrical current to a patient's scalp to alter brain activity. The remission rate has been found to be a wide range from 20% to 80% depending on performance (Lisanby, 2007). However, this treatment can cause some severe side effects, including retrograde amnesia, meaning the individual can experience gaps in their memory from events that occurred months to years before the treatment (Lisanby, 2007). Clearly, the available treatments for depression are not perfect so further research is required to continue helping those that suffer the illness.

Post-Traumatic Stress Disorder

Post-Traumatic Stress Disorder (PTSD) is a condition resulting from the exposure to a negative life-altering or traumatic event. Oftentimes, this traumatic experience can be related to loss after a natural disaster, being a victim of sexual assault, military combat, or other life-threatening occurrences (Torres, 2020). PTSD can develop at any age, but diagnosis requires the awareness or involvement in a distressing event as explained above (Mayo Clinic, 2018). Consequently, the individual did not necessarily have to be directly exposed to the event, so someone that has been

subjected to hearing about certain personal or repeatedly upsetting events could be affected by PTSD. Depending on the event the person experienced, they might have related flashbacks or nightmares, as well as avoid other situations that have the possibility of reminding them of the trauma (Mayo Clinic, 2018). Common symptoms of PTSD fall into the categories of intrusion, alterations in cognition and mood, avoidance, or alterations in arousal and reactivity (Torres, 2020). Intrusion manifests as thoughts that bring back memories or flashbacks from the event that can be severe enough for the individual to believe they are reliving it. When an individual starts to believe misrepresentations about themselves, others, or the cause of the event, they are considered to have altered cognition. In addition to this, they can start to feel detached from people around them and the activities they used to appreciate. Avoidant behavior is similar to this and occurs when a person circumvents talking about the traumatic event or including themselves in situations that might trigger them. If an individual sometimes erupts in anger or self-destructive behavior and experiences issues focusing, their reactivity might be changing in response to the trauma (Torres, 2020). Young children that are demonstrating PTSD symptoms might have nightmares or may act out scenes of the event while playing (Mayo Clinic, 2018).

PTSD symptoms can present days to years after the individual experiences the upsetting event, and eventually causes problems in daily life. It is estimated that one in 11 people will develop PTSD over their lifetime (Torres, 2020). Treatment can help a suffering person control their symptoms and not let their illness take over their life. The most common form of treatment for PTSD patients is psychotherapy, which as previously described can involve cognitive therapy where a therapist teaches new

coping mechanisms and thought processes to handle distorted beliefs that have developed. Another form of psychotherapy that is often used for PTSD patients is exposure therapy. In this type, trained professionals introduce situations that might trigger the patient through discussions or virtual reality to find healing through direct coping (Taylor et al., 2003). Eye movement desensitization and reprocessing (EMDR) can be used through teaching external oscillatory stimulation, often by a therapist directing the patient's eye movements with their finger, to reduce distress when recalling traumatic experiences (Taylor et al., 2003). PTSD therapies can be reinforced by use of medications like antidepressants, anti-anxiety prescriptions, and the drug prazosin. The Mayo Clinic (2018) suggested that prazosin has been found to reduce PTSD-related nightmares in some studies, but has shown no benefit compared to a placebo in others. Post-traumatic stress disorder is more prevalent in our society than the movies might portray specifically in the context of military veterans. While those groups of people can still be heavily affected by PTSD, there are many other cases and situations in which someone might suffer from this disorder, lending to the idea that more research needs to be done on effective treatment options.

Generalized Anxiety Disorder

Generalized Anxiety Disorder (GAD) is often misunderstood as common stress and anxiety that people feel on a day-to-day basis; however, it is much more serious and complex. Anxiety disorders are often found in people that also suffer from MDD, with estimates as high as almost 42% (Gill et al., 2020). People suffering from GAD are overcome with feelings of nervousness and worry with often little reason behind it. This unease often leads to disruption in lifestyle and completing tasks. GAD can manifest not

only through psychological symptoms such as lack of concentration, restlessness, and constant worry, but also through physical symptoms such as excessive sweating, twitching, or stomachaches (Anxiety & Depression Association of America, 2021).. These symptoms, along with many others, often escalate in times of crisis or increased stress, including conflict within friendships or family. In order to differentiate persistent GAD from common stressors, an individual must experience this irrational anxiety for a majority of 6 months with 3 or more symptoms showing (Anxiety & Depression Association of America, 2021). Another helpful distinction is the lack of control that many with GAD feel. Often, normal anxiety can be related to stressful events in life but is limited to a short time period and can be managed by relaxation and other simple techniques that do not require medical intervention. GAD is known to develop over an individual's lifetime and may not be diagnosed until adulthood (Gill et al., 2020). In the United States, 6.8 million adults are affected by GAD each year, with women being much more likely to suffer (Anxiety & Depression Association of America, 2021). As indicated in other mental health disorders, the root cause of GAD is not fully understood but can be related to family history and inherited genes, biological factors, and environmental stressors.

Treatment for Generalized Anxiety Disorder includes many of the already discussed methods, such as cognitive behavioral therapy and prescriptions for SSRIs (Gill et al., 2020). In addition to these treatments, benzodiazepines can be prescribed for serious cases of GAD. These drugs are sedatives that can rapidly manage symptoms of anxiety disorders, but often present a long list of side effects that can be just as harsh as the disorders themselves, including depressive feelings, confusion,

dizziness, irritability, and more. Unfortunately, use of benzodiazepines can lead to heavy dependence and withdrawal symptoms if an individual suddenly stops taking the medication (Martin et al., 2007). While this prescription can be a fast-acting relief for GAD patients, the eventual outcome might outweigh the transient solace.

Obsessive Compulsive Disorder

Abnormal obsessions, compulsions, or both can be indicators of Obsessive Compulsive Disorder (OCD). Often, OCD is diagnosed while an individual is still in their teenage years, but can still be found later in life. Obsessions are thoughts that lead a person to unnatural urges or ideas, including the belief that everything must be perfect, adverse thoughts about social norms, or phobia of germs (National Institute of Mental Health, 2019). These obsessive feelings can lead to disruption in relationships or job performance. Compulsions, on the other hand, are often repeated behaviors that manifest due to the obsessions (National Institute of Mental Health, 2019). These ritualistic actions can be uncontrollable and cause distress in the individual performing them. For example, if a person has obsessive thoughts surrounding the idea of bacteria contaminating their life, they might compulsively clean their house and wash their hands excessively throughout the day. Commonly, patients that suffer OCD are also diagnosed with a tic disorder which can be motor or vocal in nature. Motor tics are physically repeated movements like jerking, blinking, or grimacing, while vocal tics can include sounds like sniffing or grunting (National Institute of Mental Health, 2019). OCD symptoms can be devastating when the patient knows their actions are not normal or healthy, but still cannot stop the behaviors.

As mentioned in the introduction of the mental health disorders above, the cause of OCD is not known, but risk factors are often associated with environmental influences, past trauma, genetics, and abnormal brain functioning (National Institute of Mental Health, 2019). In order to treat OCD effectively, a patient must also be screened for a combination of other mental health disorders. As in most cases, OCD patients can be introduced to psychotherapy to ease their symptoms. A specific type of CBT is often used in OCD cases called Exposure and Response Prevention (EX/RP). In this method, a patient is brought into an environment where they are exposed to triggering situations and then restricted from performing the related compulsive behaviors (Thordarson et al., 2004). An example of EX/RP might be walking into a room where all of the lights and appliances are turned on, then being escorted out without being allowed to turn off or unplug any items. In addition to psychotherapies, patients are often prescribed medications like SSRIs, which are usually given in higher doses to OCD individuals compared to other disorders (Pittenger & Bloch, 2014). Correspondingly to the aforementioned mental health disorders, these treatment options are not always successful or efficient in managing symptoms so researchers are studying new alternatives.

Hallucinogenic Drugs

Hallucinogenic drugs are a specific class of drugs that can modify the way an individual perceives their five senses as well as changing their thoughts and behaviors (De Gregorio et al., 2021). If a high enough dose is taken, the drugs can cause a person to hallucinate, meaning they will feel or see things that are not really present. They are generally categorized by their effects on central nervous system targets that lead to

redirection of brain communication (Sherwood & Prisinzano, 2017). There are two categories of hallucinogenic drugs: dissociative anesthetics and serotonergic classic hallucinogens, which are commonly referred to as psychedelics. Dissociatives, like ketamine, are believed to act on the glutamatergic system, while psychedelics, like psilocybin, exert agonistic effects on the 5-HT system, also known as serotonin receptors (De Gregorio et al., 2021). Serotonergic receptors are known to play a role in cognition, perception, and attention, so when increased, the effects can lead to psychedelic experiences. After taking either type of hallucinogen, the effects can start happening within minutes and could last anywhere from a few hours to days (Sherwood & Prisinzano, 2017). Hallucinogens contain a wide variety of specific drugs, each working a little differently than the next and most having an intended medical or practical use; however, as with most drugs, some individuals choose to abuse hallucinogens and use them “recreationally.”

The Drug Enforcement Administration (DEA) has listed most of the hallucinogenic drugs under a Schedule I classification in the Controlled Substances Act. This means that the drugs have no accepted medical use in the US and are considered likely to be abused (Drug Enforcement Administration, 2020). Consequently, the drugs are illegal when used in recreational settings, rather than if they have some sort of approved medical application, such as ketamine being used as an anesthetic in an operating room. Although the DEA has indicated many hallucinogens as high abuse potential, they are not necessarily considered addictive. If a person was using hallucinogenic drugs on several occasions, they will not experience withdrawal symptoms or cravings to return to use like in the disease of addiction (U.S. Department

of Justice, 2020). Nevertheless, as with many drugs, hallucinogens are widely known to lead to tolerance, meaning that with continued use, a higher dose of the drug is required to produce the same effect (National Institute on Drug Abuse, 2019). The lack of addictive quality in many hallucinogens makes them valuable for research potential in treating illnesses. The negative effects of long-term, unregulated use of psychedelics and dissociatives is not fully known, but it is expected that they are not common. Classic hallucinogens have been found to lead to Persistent Psychosis and Hallucinogen Persisting Perception Disorder, which in general lead to altered mental state and flashbacks of past drug experiences, respectively (National Institute on Drug Abuse, 2019). Most often, the concern with hallucinogenic drug usage is the indirect effects that could occur due to the modified perception and mood that do not correspond with reality (U.S. Department of Justice, 2020). For example, if an individual was under the influence of LSD, commonly referred to as “acid,” they might be more likely to indulge in risky behavior like jumping from dangerous heights because of their altered consciousness.

Although hallucinogenic drugs carry a negative connotation due to their abuse in recreational drug usage, researchers are studying the potential positive effects these types of drugs could have on mental health disorders, like the ones mentioned above. As described, both categories of hallucinogens act on systems in the brain that are closely related to the development of mental illnesses. Low levels of serotonin and glutamatergic metabolites are linked to depression symptoms, along with other mood disorder effects; by the actions of hallucinogenic drugs, there might be potential to help treat these types of disorders (Torres, 2020).

Ketamine

Ketamine falls under the dissociative category of hallucinogens and is a synthetic drug with anesthetic and analgesic properties. Due to this reason, ketamine is used as an anesthetic in operating rooms and trauma situations (Jelen & Stone, 2021). The drug is a noncompetitive NMDA receptor antagonist, meaning it can bind to a site on this receptor making it unable to activate properly (Figure 1). The NMDA receptor is a glutamate-gated ion channel that specifically plays a role in memory formation, breathing, and movement, so when ketamine prevents the activation of this receptor, it can produce psychotic symptoms that include dissociation and memory impairments (Newcomer et al., 2000). The dissociation caused by ketamine usage includes feelings described as “out-of-body” experiences, as well as hallucinations, confusion, and intense relaxation. Ketamine can be taken orally or intravenously, and the effects can become present anywhere from one to 30 minutes depending on mode of administration. Furthermore, lingering effects can occur for up to a day after delivery (Alcohol and Drug Foundation, 2021). While ketamine is illegal to be used recreationally due to its dangerous side effects that can occur when unregulated, its medicinal value is already recognized in many settings and applications.

MDMA

MDMA, which is scientifically named 3,4-methylenedioxymethamphetamine, is the active ingredient in the illicit drug ecstasy. When administered into a body, it has a very quick absorption rate and after it crosses the blood-brain barrier, its effects can be felt rapidly and include euphoria, heightened sociability, and a generally happy state (Liechti et al., 2001). This synthetic drug has the capability of distorting time and

surroundings for the user, much like other hallucinogenic drugs. Although many articles and experts explain that MDMA exhibits similar effects to both stimulants and hallucinogens, it has also been categorized as a member of another class referred to as entactogens. While many drug classes are closely intertwined in many ways, entactogens are commonly related to feelings of pleasure, empathy, and relaxation due to their properties of releasing and inhibiting reuptake of serotonin (Gouzoulis-Mayfrank, 2001; Figure 1). In addition to this, MDMA has the capability of releasing dopamine, norepinephrine, and oxytocin as well (De Gregorio et al., 2021). Before MDMA began to be sold recreationally as a "party drug," it was originally synthesized for pharmaceutical purposes. In 1912, a German scientist formulated MDMA in hopes to produce a blood-clotting agent, preceding use of the drug in many psychotherapy trials in the 1960s and 1970s, before it was officially labeled as a Schedule I drug in the Controlled Substances Act, thus requiring FDA approval for further research (Passie, 2018). The intense and popular study of MDMA because of its unique psychological properties in the mid-to-late 20th century shows great potential for its therapeutic effects; present and future research might lead to the same conclusion.

Psilocybin

Unlike ketamine and MDMA, psilocybin is a naturally-occurring substance that exhibits changes in perception, cognition, and behavior. Users can experience hallucinations, as well as distortions in time and location, increased creativity, intense emotions, and a playful euphoria, with relatively low outcomes of harm (Kargbo, 2020). Kargbo further explains that psilocybin is considered a psychedelic, or classic hallucinogen, that works by activation of the serotonin 5-HT_{2A} receptors leading to

awareness in the hallucinatory state (Figure 1). Psilocybin is found in “magic mushrooms” which can be ingested and then metabolized to the main, active ingredient psilocin, which contains psychoactive, or mind-altering properties (Al-Naggar et al., 2021). In the past, psilocybin has been popular in history during spiritual ceremonies, but was not prohibited in the United States. Psilocybin is not an addictive drug and does not lead to dependency, withdrawal symptoms, or any severe physical effects after continued use (Kargbo, 2020). Due to these findings, the drug, commonly referred to as “shrooms” in illicit, recreational use, has researchers considering positive effects in psychotherapy because of that receptor's role in anxiety and depression manifestation.

LSD

Another classic hallucinogen, LSD (lysergic acid diethylamide) is very potent in its side effects of hallucinations, distorted sense of vision and hearing, and euphoric state. Much like psilocybin, LSD acts as a serotonin 5-HT_{2A} receptor agonist, but it also has affinity for several dopamine receptors as well (De Gregorio et al., 2021; Figure 1). LSD is not generally considered high on the list of unsafe drugs since it does not lead to severe long-term effects or withdrawal symptoms after use; however, if an individual experiences a “bad trip,” meaning the drug causes disturbing hallucinations or anxiety, a person might be at higher risk of committing unsafe behavior while under the influence (U.S. Department of Justice, 2020). Synthesis of LSD occurred first in the 1930s by a Swiss chemist who absorbed part of an ergot fungus through his skin, then felt intense hallucinations and kaleidoscope-like visions from the active ingredient in LSD, lysergic acid (Dyck, 2015). Not long after, LSD found its way to raves and other party atmospheres, leading to its Schedule I listing and illegalization. Nevertheless, the

potential therapeutic properties of LSD are recognized and researched for psychotherapy methods.

The general negative reputations of hallucinogens as party drugs or illicit recreational activities hinders them from widespread research and gaining therapeutic authorization. The abuse of these drugs for non-medical purposes has led to their Schedule I classification by the DEA and criminalization. Although the recreational use of the drugs have stigmatized them for the general public, some unconventional, unsafe research has caused them to be condemned in the medical community as well. For example, psychologist Timothy Leary researched the effects of LSD and psilocybin at Harvard University. Leary was considered the Father of the Psychedelic Movement of the 1960s (NPR, 2020). At Harvard, Leary conducted investigations that did not follow research guidelines, such as being under the influence of hallucinogens during research, promoting recreational use, and administering the drugs to subjects that were not supposed to be included in the research, such as undergraduate students. Due to the violations, Leary was fired from Harvard leading to a stigma surrounding the research of hallucinogenic drugs (Harvard University, n.d.). Before the implementation of hallucinogens into medicine occurs, destigmatization will have to take place so the drugs are more widely accepted.

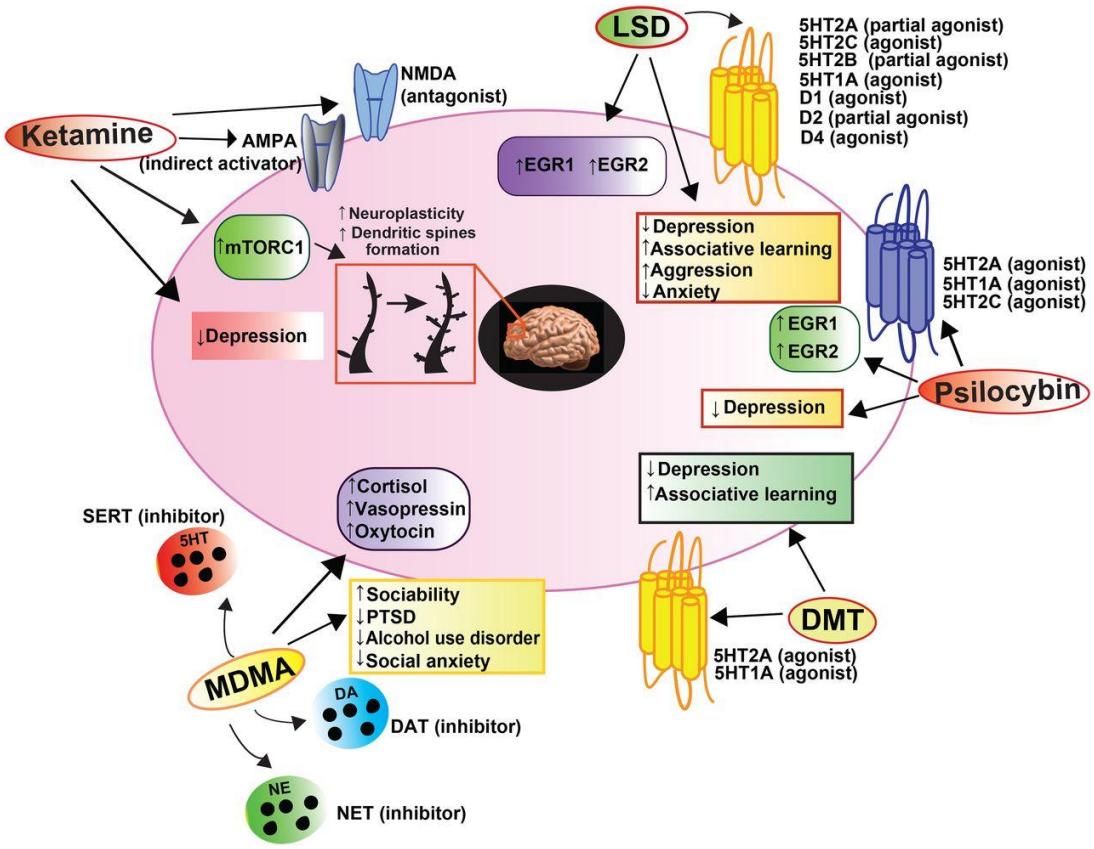

Figure 1. Targets of the hallucinogenic drugs (LSD, MDMA, Ketamine, and Psilocybin) within the body and their physiological effects. Adapted from “Hallucinogens in Mental Health: Preclinical and Clinical Studies on LSD, Psilocybin, MDMA, and Ketamine,” by De Gregorio et al., 2021, *The Journal of Neuroscience, 41*(5), 892.

Discussion of Hallucinogenic Drug Treatments

Hallucinogenic Drugs in the Treatment of Major Depressive Disorder

The use of psilocybin and ketamine have both been found to have positive potential in treating MDD in many research studies. In fact, despite its Schedule I classification in the Controlled Substances act by the DEA, psilocybin has been granted

Breakthrough Therapy status by the Food and Drug Administration for its use in the treatment of MDD, especially treatment-resistant MDD (Kargbo, 2020). This distinction signifies that psilocybin has potential and displays advantages over other current treatment options for MDD, including prescription SSRIs. Many studies have found therapeutic benefits of psilocybin to last for a significant period of time, and in some cases following only a single dose. In one study with participants suffering from treatment-resistant MDD, depressive symptoms were relieved significantly following psilocybin treatment in conjunction with psychotherapy sessions. In this trial, doses of 10 mg and 25 mg were administered 7 days apart, meaning that even after only one week with psilocybin-assisted therapy sessions, symptoms were reduced (Gill et al., 2020). Even further, the statistically significant reduction of depression was found to last for up to 4 weeks in 71% of MDD patients in another clinical trial (Barrett et al., 2021). Many other studies have found similar results in the effectiveness of psilocybin on MDD statistically significant improvements of depression symptoms quickly and for much longer than the traditional methods of medication.

The rapid onset and sustained effectiveness of ketamine infusions may be advantageous as a treatment option for MDD. A single infusion of ketamine has been found to reduce depressive symptoms over the course of just a few hours and has the capability to last from the range of days to weeks (Barrett et al., 2021). These efficacy statistics put it above common treatments of MDD, like SSRI medications and simple psychotherapy which take many administrations and much longer time periods before significant improvements emerge. Due to this, intravenous ketamine infusion treatment clinics are offered across the United States; however, other methods of infusion, such

as oral medication or nasal spray, have also been found to be practical with positive effects, especially when used alongside an antidepressant (Jelen & Stone, 2021). Since ketamine is already used medically for anaesthetic purposes, the available ketamine clinics are legal, but not FDA approved for treating depression. Oftentimes, these websites fail to mention the lack of FDA certification unless an individual thoroughly investigates its content. For example, Serenity Health, located in Louisville, Kentucky, mainly refers to their business as “Anesthesia Infusion” rather than “Ketamine Infusion,” and does not mention lack of FDA approval other than after the 8th question under the FAQ tab (Serenity Health, 2018). Nevertheless, scholarly research has shown therapeutic benefits of ketamine infusions. One study with 73 treatment-resistant MDD patients found a statistically significant reduction in depressive symptoms 24 hours after intravenous ketamine administration compared to the placebo group. In this particular experiment, the placebo was the benzodiazepine, midazolam, which is considered an active placebo due to its sedative and anxiolytic effects (Jelen & Stone, 2021). Although clinical setting doses are notably less than most recreational user doses, caution should be exercised when administering ketamine. Chronic, recreational use of ketamine has been found to lead to impairments in working and episodic memory, which could negatively impact the support for its use in mental health treatment (Jelen & Stone, 2021). Altogether, with clinically safe and monitored doses of ketamine, the research and implementation of ketamine infusion therapy has been very positive and beneficial for MDD patients.

It is known that PTSD patients risk high rates of treatment drop-out, in addition to common resistance to current accepted methods of treatment for their condition (Torres, 2020). Consequently, the identification of new potential drugs and remedies is necessary for this often long-term disorder. The increased effect that MDMA has on trust and social connection, as well as its reduction of memories related to traumatic events and fear could make it a promising candidate for disrupting the symptoms of PTSD (De Gregorio et al., 2021). Many studies have focused on the correlation between MDMA-assisted psychotherapy and PTSD symptoms, leading to a wide variety of research conclusions and suggestions on its implementation. Much like psilocybin for use in MDD treatment, MDMA has been granted Breakthrough Therapy status by the FDA for research with PTSD. Consequently, there are currently Phase 3 clinical trials being conducted studying MDMA-assisted psychotherapy, meaning its legalization and use might not be far in the future (De Gregorio et al., 2021).

Current research has shown significant improvements in PTSD patients following a long-term checkup post-MDMA-assisted psychotherapy, with no associated cognitive impairments or negative side effects, such as increased blood pressure. (Gill et al., 2020). The lack of side effects and reduction of symptoms trump some of the current options and medications used in PTSD treatment that lack fundamental support and concrete effects. In the aforementioned trial, chronic PTSD patients received two active doses (100mg and 125mg) of MDMA over the course of an 8 hour psychotherapy session. This administration demonstrated significant improvements in symptoms, even at the 12-month follow-up appointment (Gill et al., 2020). The sustainability of MDMA

over a long period of time shows its efficient execution in diminishing PTSD symptoms, which is highly efficacious over the current options that are prone to resistance.

Studies against the placebo effect have also seen promising results. In one experiment by Vermetten and Yehuda, patients diagnosed with PTSD underwent three, 8 hour psychotherapy sessions each spaced a month apart (2019). The two groups were either given an active dose of MDMA or a placebo that caused similar entactogen-like effects. The MDMA patients recorded a significant reduction in PTSD symptoms over the placebo patients, and subsequent sessions found twice the MDMA patients lacking the criteria to even meet PTSD diagnosis (Vermetten & Yehuda, 2019). Overall, the effects that MDMA studies have illustrated on the disruption of PTSD symptomology is astounding and highly successful.

Hallucinogenic Drugs in the Treatment of Generalized Anxiety Disorder

Often, Generalized Anxiety Disorder is grouped together, or comorbid, with other mental health disorders, making it difficult to research by itself; however, many studies have been conducted on the effect of hallucinogens on anxiety induced by diagnosis with a life-threatening illness. One study found that cancer patients suffering from both anxiety and depression felt statistically significant relief for up to 6 months following a therapeutic single-dose of psilocybin combined with psychotherapy (Greer, 2011). In the previous study, patients were officially diagnosed with both GAD, as well as other anxiety disorders due to cancer diagnosis. These promising results show that the use of psilocybin in conjunction with other forms of therapy might have similar effects on non-cancer patients as well. Another study found comparable results, with patients with various life-threatening illnesses finding alleviation of anxiety symptoms for up to 6

months after a one-time dose of psilocybin (McCorvy et al., 2016). Between these two studies, different control compounds were employed, with psilocybin maintaining significant results over both, substantially reducing the likelihood of placebo effect. The use of psilocybin for anxiolytic effects seems to have great potential based on available data.

Along with psilocybin psychotherapy, LSD-assisted psychotherapy has been found to lead to positive improvements in patients diagnosed with life-threatening illnesses. After completing therapy in conjunction with a medical dose of LSD, 77.8% of participants were found to maintain reduced anxiety for 12 months following the treatment, along with 66.7% that reported a rise in quality of life (Gasser et al., 2014). Due to similarities between psilocybin and LSD, the potential for both seems to make sense scientifically. Further studies might be required in patients diagnosed with anxiety who are not suffering from life-threatening illnesses. Although that is the scope of the research so far, some would argue that if the use of these classic hallucinogens can relieve that significant level of anxiety-induced by life-threatening illness diagnosis, they should likely produce similar results in GAD with no associated physical illnesses.

Hallucinogenic Drugs in the Treatment of Obsessive Compulsive Disorder

The effects of hallucinogenic treatment on OCD patients has not been thoroughly researched enough to indicate there is sufficient evidence supporting its use. As explained above, OCD is believed to be caused by defects in the 5-HT (serotonergic) system, so scientists see the possibility of psilocybin's potential therapy for these patients. Of the few reported studies, a general case study was documented of a 38-year old man who had chronic anxiety and symptoms of obsessive compulsive

disorder. He outlined that he had tried several forms of psychotherapy and prescription medication that had little effect on reducing his symptoms. Once the subject consumed “magic mushrooms” and fell into the habit of taking two grams of these mushrooms every three weeks, he experienced relief from his intrusive thoughts and anxiety (Wilcox, 2014). Although this patient had no scientific testing done on the mushrooms he was consuming, it is likely they were psilocybin-type.

Further studies by professional researchers have found more positive results with the effect of psilocybin on OCD symptoms. In one small-sample experiment, nine OCD treatment-resistant subjects were given single-dose psilocybin varying in dosage. There was no psychotherapy in conjunction with the drug, although the study took place in an outpatient clinic. In every patient, OCD symptoms were significantly reduced immediately and maintained that way for around 24 hours even after the psychedelic effects diminished (Majić et al., 2015). In order to deem any sort of hallucinogenic drug safe to treat obsessive compulsive disorder, studies with larger sample sizes and multiple dose administrations need to be executed. Due to their similar mechanisms of action, LSD should be considered as a route of study for OCD treatment along with psilocybin.

Conclusion

After analyzing the available research and studies encompassing the topic, the question remains if these drugs should be widely used in mental health treatment. As in any experimental findings and new treatment approaches, extreme caution and thoroughness needs to be explored before implementation. This situation is no different.

For example, some hallucinogenic drugs are known to lead to toxic effects or physical impairments if used chronically in unrestricted doses. MDMA has the ability to cause deficits in memory and attention (Gill et al., 2020). Due to this, extensive research is necessary to determine if clinical doses of MDMA would cause damage to forebrain structures leading to these issues in the long-term. Furthermore, ketamine is associated with bladder and neurologic toxicity with persistent use, so there should be assurance that the treatment plans would not cause these problems in patients, or at least would not be used long enough to lead to possible complications (De Gregorio et al., 2021). In a medical setting, it is likely that most of these drugs would not cause damaging effects from clinical doses, in contrast to unregulated, recreational environments which might pose more risk.

Another major concern with these drugs is the likelihood that the placebo effect might be in play during trials, with no significant way to circumvent it. The described drugs cause very distinct hallucinogenic and dissociative effects, so when patients are in the control or drug group, they likely will be able to tell either way. A major factor in ensuring drug efficiency is blinding during research and ruling out the placebo effect; however, this becomes a challenge when there are other commonly known side effects of these drugs. While some trials have resorted to the typical “sugar pill” as a placebo, many others have tried to combat this obstacle by using drugs that have somewhat similar disorienting effects to the subject drug or using lower doses of the drug in question (Jelen & Stone, 2021). Much of the current research demonstrates that the drugs reduced symptoms significantly compared to placebo, but there should be a guarantee that blinding was successful before that claim is made. Finally, the negative

social connotation that hallucinogenic drugs hold makes it difficult for them to be accepted as medically-safe. Currently, these drugs are widely known by their street names, like shrooms, ecstasy, and more, which automatically leads someone to think of their illegal, recreational use. In addition to this, the Schedule I classification of psilocybin, MDMA, and LSD limits their ability to be widely accepted in medical treatments, hindering their potential benefit.

While there are obstacles that restrict LSD, psilocybin, ketamine, and MDMA to be universally welcomed in the medical community, they each have many positive attributes as well. Most notably, trials with each of these drugs has shown that one, or a few, administrations of clinically-acceptable doses can relieve symptoms quickly and for much longer when compared to current treatment options, like therapy or prescription medications. For example, in a study involving psilocybin in MDD treatment it was found that, “a single acute exposure to the hallucinogenic agent can elicit an immediate and lasting improvement in symptoms for the patient, an effect that persists long after the drug is metabolized and gone from the body” (Sherwood & Prisinzano, 2017). SSRIs and other antidepressant medications require chronic, daily dosing regimens in order to stay effective for a patient, and oftentimes individuals are resistant to many first-line treatments (Gill et al., 2020). Moreover, with fewer doses of the drugs lasting a long period of time, there will be a significant reduction in healthcare costs for a patient in the long run. The extensive positive results that have been demonstrated most remarkably for MDMA in PTSD treatment and psilocybin in MDD treatment cannot be ignored and outweigh current courses of treatment in almost every category.

In order to eventually implement these drugs into mental health disorder treatment, education and guidelines need to be widely regulated to smoothly transition these drugs in the medical community. For example, clear examples need to be shared of how the drugs would be administered and how dosing would work. Most likely, a psychotherapy session would be accompanied by drug dispensing, which would be administered by a nurse, psychologist, or psychiatrist that has attended updated training on the use of the drugs. The environment of the session would be a comfortable and familiar clinical setting, facilitated by a guide that could reduce any negative hallucinations or thoughts that appeared during drug peaks. The dosage would likely be several orders of magnitude less than unregulated recreational users, allowing for a more controlled, safe experience. Another important way to reduce the stigma regarding hallucinogens in medicine is to reclassify them under the DEA scheduling system so that the therapeutic effects can be fully investigated without restriction or negative connotation. Currently in the Controlled Substances Act, the Schedule I classification describes the drugs as having no accepted medical use; however, it has been shown in the aforementioned research and more that the drugs have beneficial potential as a mental health remedy, so that claim has been refuted. The Controlled Substances Act also becomes contradictory in its application because even with the current scheduling, the illegal drugs are permitted to be used solely for medical research purposes. There is evident inconsistency in the classification requirements and the authorization of clinical usage. Due to this, the drugs should be destigmatized as much as possible. By recognizing this medical value and classifying them under a different schedule, MDMA, psilocybin, and LSD would be more widely investigated and accepted in clinical settings.

Compassionate use is another available policy for utilization of these unauthorized drugs that might be helpful until they are approved by the FDA. In this practice, often also called expanded access, physicians would have the capability to implement investigational treatments for patients that are living with serious diseases if alternative therapies are not working (Greif & Šurkala, 2020). Since it is a physician's duty to provide the best, fulfilling care for their patients, they would be able to utilize medications, such as these hallucinogenic drugs, outside of an enrolled clinical trial. There has been published research illustrating that, at least for use of psilocybin and MDMA, implementation into treatment programs are rational and ethical in the healthcare community after examining their safety and efficacy (Greif & Šurkala, 2020). While it might sound alarming to treat someone with a drug that is not approved, for many suffering from MDD and PTSD symptoms, doing nothing could be far more harmful.

Overall, the research and ongoing clinical trials demonstrate that use of the psychedelics and dissociatives, LSD, MDMA, psilocybin, and ketamine are promising in the treatment of mental health disorders. Further policy changes and larger sample study sizes might need to be enacted before full authorization; however, in use for severe disorders with no alternative, compassionate use should be explored. The ongoing search for more efficacious treatments in mental disorders that we do not fully understand is imperative, so if hallucinogens can pave the way to better quality of life for some of these patients, their journey to legalization and medical acceptance should be of utmost priority.

References

ADAA. (2021, July 28). *Generalized Anxiety Disorder (GAD)*. Anxiety & Depression Association of America. Retrieved October 30, 2021, from https://adaa.org/understanding-anxiety/generalized-anxiety-disorder-gad.

Al-Naggar, R. A., Alshaikhli, H., & Erlam, G. (2021). Effectiveness of psilocybin on depression: A qualitative study. *Electronic Journal of General Medicine*, *18*(3). https://doi.org/10.29333/ejgm/10862

Barrett, F. S., May, D. G., Cosimano, M. P., Sepeda, N. D., Johnson, M. W., Finan, P. H., & Griffiths, R. R. (2021). Effects of psilocybin-assisted therapy on major depressive disorder. *JAMA Psychiatry*, *78*(5), 481–489. https://doi.org/10.1001/jamapsychiatry.2020.3285

Cuijpers, P., van Straten, A., Andersson, G., & van Oppen, P. (2008). Psychotherapy for depression in adults: A meta-analysis of comparative outcome studies. *Journal of Consulting and Clinical Psychology*, *76*(6), 909–922. https://doi.org/10.1176/foc.8.1.foc75

De Gregorio, D., Aguilar-Valles, A., Preller, K. H., Heifets, B. D., Hibicke, M., Mitchell, J., & Gobbi, G. (2021). Hallucinogens in mental health: Preclinical and clinical studies on LSD, Psilocybin, MDMA, and Ketamine. *The Journal of Neuroscience*, *41*(5), 891–900. https://doi.org/10.1523/jneurosci.1659-20.2020

Dyck, E. (2015). LSD: A new treatment emerging from the past. *Canadian Medical Association Journal*, *187*(14), 1079–1080. https://doi.org/10.1503/cmaj.141358

Gasser, P., Kirchner, K., & Passie, T. (2014). LSD-assisted psychotherapy for anxiety associated with a life-threatening disease: A qualitative study of acute and sustained subjective effects. *Journal of Psychopharmacology*, *29*(1). https://doi.org/10.1177/0269881114555249

Gill, H., Gill, B., Chen-Li, D., El-Halabi, S., Rodrigues, N. B., Cha, D. S., Lipsitz, O., Lee, Y., Rosenblat, J. D., Majeed, A., Mansur, R. B., Nasri, F., Ho, R., & McIntyre, R. S. (2020). The emerging role of psilocybin and MDMA in the treatment of mental illness. *Expert Review of Neurotherapeutics*, *20*(12), 1263–1273. https://doi.org/10.1080/14737175.2020.1826931

Greif, A., & Šurkala, M. (2020). Compassionate use of psychedelics. *Medicine, Health Care and Philosophy*, *23*, 485–496. https://doi.org/10.1007/s11019-020-09958-z

Grob, C. S., Danforth, A. L., Chopra, G. S., Hagerty, M., McKay, C. R., Halberstadt, A. L., & Greer, G. R. (2011). Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Archives of General Psychiatry*, *68*(1), 71–78. https://doi.org/10.1001/archgenpsychiatry.2010.116

Gouzoulis-Mayfrank, E. (2001). Differential actions of an entactogen compared to a stimulant and a hallucinogen in healthy humans. *The Heffter Review of Psychedelic Research*, *2*, 64–72.

Harvard University. (n.d.). *Timothy Leary*. Department of Psychology. Retrieved November 8, 2021, from https://psychology.fas.harvard.edu/people/timothy-leary.

Jelen, L. A., & Stone, J. M. (2021). Ketamine for depression. *International Review of Psychiatry*, *33*(3), 207–228. https://doi.org/10.1080/09540261.2020.1854194

Kargbo, R. B. (2020). Psilocybin therapeutic research: The present and future paradigm. *ACS Medicinal Chemistry Letters*, *11*(4), 399–402. https://doi.org/10.1021/acsmedchemlett.0c00048

Ketamine. Alcohol and Drug Foundation. (2021, October 6). Retrieved October 30, 2021, from https://adf.org.au/drug-facts/ketamine/.

Liechti, M. E., Gamma, A., & Vollenweider, F. X. (2001). Gender differences in the subjective effects of MDMA. *Psychopharmacology*, *154*(2), 161–168. https://doi.org/10.1007/s002130000648

Lisanby, S. H. (2007). Electroconvulsive Therapy for Depression. *New England Journal of Medicine*, *357*(19), 1939–1945. https://doi.org/10.1056/nejmct075234

Majić, T., Schmidt, T. T., & Gallinat, J. (2015). Peak experiences and the afterglow phenomenon: When and how do therapeutic effects of hallucinogens depend on psychedelic experiences? *Journal of Psychopharmacology*, *29*(3), 241–253. https://doi.org/10.1177/0269881114568040

Martin, J. L., Sainz-Pardo, M., Furukawa, T. A., Martin-Sanchez, E., Seoane, T., & Galan, C. (2007). Benzodiazepines in generalized anxiety disorder: Heterogeneity of outcomes based on a systematic review and meta-analysis of clinical trials. Journal of Psychopharmacology, 21(7), 774–782. https://doi.org/10.1177/0269881107077355

Mayo Foundation for Medical Education and Research. (2018, July 6). *Post-traumatic stress disorder (PTSD)*. Mayo Clinic. Retrieved October 30, 2021, from https://www.mayoclinic.org/diseases-conditions/post-traumatic-stress-disorder/symptoms-causes/syc-20355967.

McCorvy, J. D., Olsen, R. H. J., & Roth, B. L. (2016). Psilocybin for depression and anxiety associated with life-threatening illnesses. *Journal of Psychopharmacology*, *30*(12), 1209–1210. https://doi.org/10.1177/0269881116675771

Newcomer, J. W., Farber, N. B., & Olney, J. W. (2000). NMDA receptor function, memory, and brain aging. *Dialogues in Clinical Neuroscience*, *2*(3), 219–232. https://doi.org/10.31887/dcns.2000.2.3/jnewcomer

NPR. (2020, October 23). *Father of the Psychedelic Movement, Timothy Leary*. NPR. Retrieved November 8, 2021, from https://www.npr.org/2020/10/21/926181349/father-of-the-psychedelic-movement-timothy-leary.

Passie, T. (2018). The early use of MDMA ('ecstasy') in psychotherapy (1977–1985). *Drug Science, Policy and Law*, *4*. https://doi.org/10.1177/2050324518767442

Pittenger, C., & Bloch, M. H. (2014). Pharmacological treatment of obsessive-compulsive disorder. *Psychiatric Clinics of North America*, *37*(3), 375–391. https://doi.org/10.1016/j.psc.2014.05.006

Serenity Health. (2018). *Anesthetic IV Infusion Therapy FAQs*. Serenity Health. Retrieved October 30, 2021, from https://www.serenityhealthky.com/.

Sherwood, A. M., & Prisinzano, T. E. (2017). Novel psychotherapeutics – a cautiously optimistic focus on hallucinogens. *Expert Review of Clinical Pharmacology*, *11*(1), 1–3. https://doi.org/10.1080/17512433.2018.1415755

Taylor, S., Thordarson, D. S., Maxfield, L., Fedoroff, I. C., Lovell, K., & Ogrodniczuk, J. (2003). Comparative efficacy, speed, and adverse effects of three PTSD treatments: Exposure therapy, EMDR, and relaxation training. *Journal of Consulting and Clinical Psychology*, *71*(2), 330–338. https://doi.org/10.1037/0022-006x.71.2.330

Thordarson, D. S., & McLean, P. D. (2004). Treatment of obsessive–compulsive disorder: Cognitive behavior therapy vs. exposure and response prevention. *Behaviour Research and Therapy*, *43*, 1559–1576. https://doi.org/10.1016/j.brat.2004.11.012

Torres, F. (2020, October). *What is Depression?* American Psychiatric Association. Retrieved October 29, 2021, from https://www.psychiatry.org/patients-families/depression/what-is-depression.

Torres, F. (2020, August). *What is Posttraumatic Stress Disorder?* American Psychiatric Association. Retrieved October 29, 2021, from https://www.psychiatry.org/patients-families/ptsd/what-is-ptsd.

United Health Foundation. (2021). Public Health Impact: Depression. America's Health Rankings. Retrieved October 29, 2021, from https://www.americashealthrankings.org/explore/annual.

U.S. Department of Health and Human Services. (2019, April 22). *Hallucinogens Drug Facts*. National Institute on Drug Abuse. Retrieved October 25, 2021, from https://www.drugabuse.gov/publications/drugfacts/hallucinogens.

U.S. Department of Health and Human Services. (2019, October). *Obsessive-Compulsive Disorder*. National Institute of Mental Health. Retrieved October 30, 2021, from https://www.nimh.nih.gov/health/topics/obsessive-compulsive-disorder-ocd.

U.S. Department of Justice. (2020, June 5). *Hallucinogens - Drug Fact Sheet*. United States Drug Enforcement Administration. Retrieved October 25, 2021, from https://www.dea.gov/documents/2020/2020-06/2020-06-05/hallucinogens-drug-fact-sheet.

Vermetten, E., & Yehuda, R. (2019). MDMA-assisted psychotherapy for posttraumatic stress disorder: A promising novel approach to treatment. *Neuropsychopharmacology*, *45*(1), 231–232. https://doi.org/10.1038/s41386-019-0482-9

Wilcox, J. A. (2014). Psilocybin and obsessive compulsive disorder. *Journal of Psychoactive Drugs*, *46*(5), 393–395. https://doi.org/10.1080/02791072.2014.963754

2020 Prevalence Data. Mental Health America. (2021). Retrieved October 25, 2021, from https://mhanational.org/issues/2020/mental-health-america-prevalence-data.