Psychedelics and Their Efficacies in Therapies when Compared to Traditional Pharmaceuticals

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Abstract

Throughout the early stages of utilizing pharmaceuticals to treat mental illnesses, psychedelics were among the most promising, albeit some of the least understood, in a clinical sense. For better or worse, the rise in the "counter-culture" movement spurred interest in psychedelics. Some preliminary studies and papers began to tout the possible benefits of using it as a treatment and others warned about the possible risks and side effects from taking psychedelics without proper guidance and vetting. Regardless of the supposed benefits, the US Congress tightened regulations on psychedelics. This led to the placing of such pharmaceuticals directly in the Schedule 1 category, and subsequently began the stigmatization of all psychedelic substances.

Psychedelics have gained a long history of stigmatization from both political and sociological outcries as being an addictive drug with potentially dangerous, or even deadly, side effects. This is generally considered the most crucial reason for the drastic decrease in, if not altogether halting, the research of the benefits or possible methods and applications of psychedelics in the treatment of mental disorders. Despite this long and bleak history, with the recent passing of legislation to ease restrictions, largely due to a slow yet meticulous research that is once again shedding light on the efficacy of psychedelics at treating mental health disorders, such as PTSD, anxiety, and depression. Psychedelics are once again gaining a more positive force in the mental health community and the public writ large. Current research, like those studies that aided in lifting of government restrictions, is starting to gain enough of a basis to allow for the comparing of the effectiveness of psychedelics to traditional drug treatment for mental health.

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Before diving into that comparison, one must first understand what constitutes a psychedelic. Psychedelics and hallucinogenics are not proxy words. Psychedelics are but a subset

of hallucinogenic drugs. Other subsets also include dissociatives, like antiglutamatergics such as nitrous oxide (laughing gas) or salvinorin A from Saliva divinorum, and deliriants, like atropine from Atropa belladonna (deadly nightshade) and diphenhydramine (Benadryl). The primary effect of psychedelics, and what makes a hallucinogen a member of the psychedelic class, is the triggered non-ordinary, or altered, state of consciousness that is commonly referred to as a "trip". It is through this modulation of cognition and sensory perception via the 5-HT2A receptor, although exact methodology is still unknown, that reduces activity in the Default Mode Network, which can be described as what makes up the standard conscious mind (Palhano-Fontes, 2015; Smigielski, 2019).

While there is still much debate on general applicability and comparative efficiency between traditional pharmaceutical treatments and more the up-and-coming treatments like psychedelic therapies, current studies and clinical trials are indicating many benefits of using psychedelics to treat mental health disorders, such as PTSD, anxiety, depression, and addiction, from a purely psychological perspective.

One of the more common psychedelic compounds, Lysergic acid diethylamide (LSD), commonly referred to as 'acid', saw a large volume of studies between the 1950s and 1970s, and the focus was to understand various behavioral phenomena, with a large portion of papers concluding with significant and positive changes to patient disposition in the short-term. Although older trials for disorders ranging from anxiety and depression, to addictions and psychosomatic diseases, would not hold up to current clinical standards, the consensus among them is that "LSD is revealed as a potential therapeutic agent in psychiatry" especially considering that "the evidence to date is strongest for the use of LSD in the treatment of alcoholism." (Fuentes, 2019). Despite the promising outlook, the ban was still put in place those

many decades ago, however the subsequent ban on psychedelics did little to suppress recreational usage in the general populace (NIDA, 2020). With the clinical trial dry-spell effectively diminished with current federal and local governments lifting restrictions, the public is now seeing a new light being cast into the beneficial properties in various psychedelics like mescaline and psilocybin (Nutt, 2019).

With the Vietnam war raging during the genesis of psychedelics as pharmaceuticals, Post-Traumatic Stress Disorder, or PTSD, was the psychological issue looming over US mental health physicians and is still a majorly untreated disorder today. One of the fundamental issues surrounding the effective treatment of PTSD is that there are only two pharmaceutical treatments approved for public use, which still show limited efficiency (Krediet, 2020). In the 1970s, when researchers were attempting using hallucinogens to treat mental disorders, PTSD was only just being discovered, which made it a solid candidate for the application of psychedelics. The increased correlation between depression and anxiety with a diagnosis of PTSD (Keane, 1997) means that the impairment of social, personal, or occupational interactions in patients with a diagnosis cause a massive disconnect between said patient and their surroundings. Enter the benefits surrounding the usage of psychedelics to treat PTSD. Many studies, like the one spearheaded by Erwin Krediet, showed psychedelic-treated patients experienced benefits ranging from increased emotional empathy and connectedness to reduced avoidance, which Erwin Krediet, et al state, “have been shown to be a key mediator in long-term psychological change in other mental disorders.”

While there is some promise to the utilization of psychedelics to treat psychological disorders, psychedelics are currently not approved for use by the average, everyday self-dose, because there is a growing but limited consensus on the physiological effects, both in the short

and long terms. The current most-sought treatment for these disorders leverages your brains natural chemistry, and specifically prevents the absorption of one or more of these neurological ingredients. One group of these pharmaceuticals is called Selective Serotonin Reuptake Inhibitors (SSRIs). While SSRIs may be one of the primary methods for treating depression and PTSD, recent studies are starting to reveal indications that SSRI treatments are less effective than psychotherapy, and only marginally more effective than older medications.

Cardiovascular issues, one of the world's largest causes of morbidity, shows an increased probability of occurrence when taking SSRIs. Although considered safe (Wessinger, 2006) SSRIs are shown to increase incidences of adverse events of the cardiovascular system, hypertension being the most common among them. "Increases in resting-state heart rate and decreases in its variability are associated with substantial morbidity and mortality" (Wang, 2018). While increased resting heart rate does not sound like a deadly side effect, the increased probability of a out-of-hospital cardiac arrest (OHCA) as assessed by Weeke, et al, can assuredly count as potential deadly side effect. "An association between cardiac arrest and antidepressant use could be documented in both the SSRI and TCA classes of drugs." (Weeke, 2012) This may raise some concerns, but there tends to be an underlying cardiovascular issue in most Adverse Cardiovascular Event (ACE) patients (Wenzel-Seifert, 2010) and are "unlikely to occur with SSRIs at therapeutic doses" (Yekehtaz, 2013).

Multimodal therapies are also becoming a common treatment plan for tackling psychological issues like depression and anxiety, but one of the core components to the foundation of the entire therapy is the intertwining of medication, as it provides the backdrop by which the other behavior modalities can be filtered. Gordon Parker, et al, state, "Although the newer and older antidepressant drugs may be of similar effectiveness in non-melancholic

depression, the newer agents appear comparatively inferior." (Parker, 2001) This seems to indicate that heterocyclic treatments, or pharmaceutical treatments that were precursors to reuptake inhibitors, are just as effective with smaller detrimental side effects (Schnieder,2018). This does not bode well for continuous use of SSRIs, especially when the growing consensus in the psychological and psychiatric community is that psychotherapy is "more strongly associated with recovery than the newer antidepressant drugs" (Parker, 2001).

Before the broad usage of SSRIs, Tricyclic and Tetracyclic antidepressants (TCAs) were once a mainstay medication to treat various disorders like depression, anxiety, and PTSD. As more longitudinal studies seem to indicate, TCAs are starting to become more detrimental to overall cardiovascular health, even more so than SSRIs.

A large volume of longitudinal studies seems to indicate that TCAs have increased in side effects over time. This may be in part due to insufficient dosages to allow for a full profiling of side effects (Ferguson, 2001). By indiscriminately inhibiting alpha-adrenergic reuptake, TCAs are effective in their treatment of depression, but the effectiveness is offset by the "significant, often intolerable adverse effects that limited their us in clinical practice" (Ferguson, 2001). Although not proscribed by a large extent, TCAs are still utilized when patients are not responding to SSRI treatments. One does not need a history of cardiovascular issues to suffer ACE from TCA treatments. "Cardiovascular complications of TCAs have been reported not only in patients with [Cardiovascular Disease] but also in people with no prior history of cardiac diseases" (Yekehtaz, 2013).

With continuous use of TCAs, sometimes commonly referred to as heterocyclic antidepressants, there is a growing number of patients that seem to exhibit signs of heterocyclic-resistant depression, and it is becoming a major clinical problem (Inoue, 1996). It could be one

of numerous potential catalysts for SSRI/SNRI development, but it is for certain “heterocyclic antidepressant compounds on the cardiovascular (CV) system shows that TCAs slow intraventricular conduction” (Glassman, 1993) and can lead to adverse CV events in patients. The continued use of TCAs where SSRIs fail is leading to finding more treatment-resistant depression. Although the pharmacology is improving, and the increased emphasis on multimodal therapy is diversifying treatment plans, there are still “about 20% of depressed patients remain resistant to treatment” (Ananth, 1998), which continues to indicate that there is still a need for treatments that do not rely on consistent pharmaceutical dosages.

Psychedelics, specifically LSD, DMT, psilocybin, and MDMA, cause a reaction with the brain’s serotonin receptors like a reaction caused by SSRIs, but also encourage the engagement of other parts of the brain which seems to be resulting in better treatments for mental health. This interaction between the Default Mode Network of the brain and other areas, like the amygdala, are what gives psychedelics a distinct advantage over other pharmaceuticals.

Both SSRIs and psychedelics like LSD, psilocybin, MDMA, and DMT, interact with the brain’s serotonin receptors, also known as 5 hydroxy-tryptamine (5-HT) receptors, but with different results. SSRIs focus on enhancing 5-HT neurotransmission, but chronic use produces a loss of 5-HT receptors. (Turcotte-Cardin, 2019). A loss of 5-HT receptors in the temporal cortex, the main complex for auditory, memory, and emotional processing, has been correlated to the rate of decline of cognitive function in Alzheimer’s Disease patients (Lai, 2004). This carries even more weight when further corroborated by a 2005 study to measure if depression symptoms could predict Alzheimer’s Disease or dementia. A high number of depression symptoms “was a significant predictor of AD and a marginally significant predictor of dementia.” (Gatz, 2005) When used in a clinical setting, psychedelics, particularly LSD, promote more production of 5-

HT receptors, as compared to the SSRI's loss of receptors after chronic use. However, LSD is not meant to be taken regularly during treatment which means the potential to lose 5-HT receptors over time is little to none compared to SSRIs (Liechti, 2017).

Along with its negligible effects on 5-HT receptors, LSD is proven to reduce fearful responses to faces by inhibiting the amygdala and increasing the use of the prefrontal cortex, or the implicit executive function system of the brain (Mueller, 2017). This is especially important when understanding the functional impact of anxiety in patients. Imaging studies of neurological functions indicate that the amygdala, a critical component of cortical and subcortical circuitry, reacts to threat-related cues like fearful faces (Whalen, 1998) and is a central tenant of anxiety-based reactions. In concert with these theories, other cognitive models used to understand anxiety predict that subjects with high levels of anxiety show a greater bias towards fearful or angry faces when orienting their gaze when compared to subjects with low levels of anxiety (Mogg, 1998). This is further refined by an fMRI study to assess cognitive control of the lateral prefrontal cortex (lateral PFC) and anterior cingulate cortex (ACC). They found that "participants with higher anxiety levels showed both less rostral ACC activity overall and reduced recruitment of lateral PFC as expectancy of threat-related distractors" (Bishop, 2004), meaning there is reduced activity in the lateral PFC and ACC and increased activity in the amygdala in subjects with higher levels of anxiety, and the opposite is true in lower-level anxiety subjects.

Aside from the benefits of increased activity in the lateral PFC and ACC when taking psychedelics, studies indicate the ability psychedelics have of generating new neural pathways and promoting both structural and functional plasticity. Stress and other stress-related factors

precipitates or exacerbates atrophy of neurological structural components in the PFC and ACC (Arnsten, 2009) and can be described as “retraction of neurites, loss of dendritic spines, and elimination of synapses” (Ly, 2018). And although there has yet to be rigorous testing of the full neuro-therapeutic potential of psychedelics (Bogenschutz, 2012), there is substantial indirect evidence that “led to the reasonable hypothesis that psychedelics promote structural and functional neural plasticity,” and growing “direct evidence for this hypothesis, demonstrating that psychedelics cause both structural and functional changes in cortical neurons” (Ly, 2018).

Although there are growing applications for the use of psychedelics in a clinical setting to treat psychological and neurological disorders, there is an already substantial headless community centered around microdosing. Microdosing as a means of self-therapy or even performance enhancement has been perpetuated for years through the analog and digital means of social distribution of each user’s anecdotal evidence, even to the point of sparking its own subreddit on the infamous social media site.

The trend is spurred from the idea that taking a subperceptable quantity of psychedelics, usually less than 20 micrograms of LSD or psylocibin (Greiner, 1958) once every 3-4 days, to gain a boost of creativity and productivity without the potential “unhealthy” effects that can come from slamming a Starbucks, Monster, or 5-Hour Energy (Glatter, 2015). The idea to increase creativity by increasing the number of concurrent interconnected neural pathways is subsumed by the increase in cognitive time dilation and perception at the suprasecond interval (Yanakieva, 2018). This means that, although there is increased cognitive activity, because psychedelics distort the perception of time, there is no apparent or measurable increase in productivity.

The other common motivation for microdosing is to alleviate various psychological symptoms like depressive mood swings or anxiety, or even physiological symptoms like chronic low-level pain. This therapeutic motivation for microdosing primarily results in positive outcomes where the user gains the intended effect, or neutral outcomes where the user effectively discontinues the microdosing regiment altogether (Johnstad, 2018). These effects are congruent with clinical therapeutic outcomes at full dosage levels for similar conditions (Carhart-Harris, 2010), but the observations in referenced microdosing studies were extremely limited, usually to one or a small handful of individuals giving anecdotal survey responses and not blind or double-blind placebo-controlled studies.

Despite the positive or neutral outlook from these studies and surveys on microdosing, there are measurable negative physiological and psychological impacts, like the development of migraine headaches or increased levels of anxiety (Johnstad, 2018). Even more critical, a study of subchronic intermittent microdoses investigated in the evidence and efficacy of such a regiment and its lasting effects yielded a conclusion that “microdosing with psychedelics for therapeutic purposes might be counter-productive” (Horsley, 2018). This is even further supported by a 2017 article of the Psychedelic Press that reports intensification, albeit anecdotal like the observations of Carhart-Harris, of the intended treated symptoms in microdose users rather than a reduction (Fadiman, 2017). Even worse, unwanted hallucinogenic effects were indicated in numerous surveyed subjects when the dosage level unintentionally exceeded that of a microdose (Fadiman, 2017; Johnstad, 2018).

Psychedelics are not a broad-sweeping wonder drug that can cure all ailments, akin to the early days of snake-oil salesmen pedaling tonics, nor are they bereft of any negative impacts to

psychological or physiological components of a potential patient. Although most clinical trails result in a positive experience, usually dependent on set and setting, there are documented cases of negative side effects.

As with the consumption of any pharmaceutical compound, there can and will be varying physiological effects, depending on the subject's biology. These can range from broad, inauspicious symptoms like nausea, dizziness, and headaches to alternating periods of shivering (feeling of coldness) and heat flushes (Ungerleider, 1967), correlated to a reduced ability to maintain regulation of one's body temperature (Clark, 1987), to a precipitation of neuroleptic malignant syndrome (NMS) but only in a single reported case where the patient, a known regular cannabis user, had consumed a large amount of alcohol in conjunction with LSD (Behan, 1991). The patient recovered fully in ten days after Dantrolene sodium therapy which is used to treat Malignant Hyperthermia (a reaction to anesthesia). There have also been eight LSD intoxication cases in Hong Kong between 2015 and 2018, after the initial establishment of the toxicological analysis lab in 2004. However, of those eight cases, five of them (62.5%) were found to also have a detectable co-ingested substance: cannabis, amphetamine, or phenibut, and only two cases were complicated by rhabdomyolysis with only one of them requiring intensive care unit admission. All patients fully recovered (Li, 2019).

Psychological effects, the main proponent of psychedelics, can also have negative results. These can range from the benign, like a man sleeping "on the floor the night he took LSD because he was sure his bed was only two inches long" to a "high school student [cutting] all the flexor tendons in her wrist when she looked in the mirror and saw her face begin to dissolve" (Ungerleider, 1967). Although these are rare and acute cases that occurred during the

metabolizing of the psychedelic, there are cases of continuous, chronic, and historic use of psychedelics that result in psychosis or psychotic episodes without in the ingestion of any psychedelic compound (Santos, 2017), but there was a limited sample size of case reports, potential conflicts of interest, and only DMT and ayahuasca were assessed. This makes it difficult to differentiate a psychedelic genesis of psychosis from a preexisting psychopathology (Garcia-Romeu, 2016).

One of the main socio-political arguments for the control and ban of psychedelic substances is the claim of its highly addictive properties. Many studies, both in historical and in recent years, still come to a similar conclusion. The consensus is that physiologically, psychedelics are considered safe for usage in clinical settings, and more research needs to be conducted in the psychological safety in long-term chronic or subchronic exposure, but the short-term has little to no negative impacts.

In no small terms, psychedelics "are generally considered physiologically safe and do not lead to dependence or addiction" (Nichols, 2016). Although there are no currently known direct causal links between psychedelics and patient morbidity or mortality, the concern many clinicians impose arises from when they are self-administered in uncontrolled and unsupervised settings. This can lead to users perceiving feelings of invulnerability, or even superhuman abilities, in the altered state of consciousness (Reynolds, 1985). This is the main driving force behind the campaign of "set and setting" in terms of psychedelic-centric clinical therapies. Clinical studies also do not suggest that serotonergic psychedelics cause long term effects on a patient's mental health, which is corroborated by the fact that psychedelic usage in the Americas has existed for thousands of years, and over 30 million people have used compounds like LSD,

psilocybin, or mescaline (Krebs, 2013). Despite the vast non-clinical usage documented throughout both North and South American cultures, there has not been a drastic uptick in psychosis-related diagnoses. There are even other studies that further define no link between psychedelic usage and suicidal behavior (Johansen, 2015). In fact, there are numerous studies that outline the therapeutic benefits of using psychedelics to treat other, and arguable worse, forms of addiction, like tobacco and alcohol (Kvam, 2018; Hamill, 2019), and it would be counter-productive to use an addictive substance to treat a preexisting addiction diagnosis.

In conclusion, the potential upside to the utilization of psychedelics to treat many of the aforementioned psychological and neurological dispositions is comparatively large to the potential downside. The benefit and effectiveness psychedelics present does not only reside in the ego-dissolving component of the altered state of consciousness, where a licensed and certified mental health practitioner could guide the patient in the dissolution and re-designing of the patient's sense of self and identity, but also in the neurological component via the chemical act of rewiring. It is in the ability of psychedelics to increase activity in other parts of the brain, like the prefrontal cortex, and its neurogenerative effects that make it a strong candidate for utilization is therapeutic settings, like in a guided therapy session. This enables the brain to generate new neural pathways and develop new methodologies of thinking in order to break current detrimental and unproductive modes of thought.

Concurrently, by chemically altering the brain's ability to reduce the "noise" of amygdala interaction in disorders like anxiety and depression, psychedelics effectively quiet the brains entrenched anxiety response and creates a double two-pronged effort in its therapeutic application. The limitation of amygdala response and the heightened prefrontal cortex

interactions have an increased efficacy in the psychological treatment of mental disorders, as well as the bolstering of neuronal activity and efficiency in the prefrontal cortex has a neuro-physiological effect. This effect, by treating both the physiological and the psychological, also coincide with other aforementioned studies in multimodal therapies, specifically that psychotherapy alone is showing the same, if not more, effectiveness than psychotherapy coupled with traditional pharmaceuticals (e.g., TCAs and SSRIs). Instead of coupling psychotherapy and TCAs/SSRIs, coupling therapy with psychedelics may have a compounding effect that could be greater than therapy alone, but further study is warranted.

Traditional depression medications, like SSRIs and TCAs, do have the same effect of reducing the amygdala response, but they do not have the same ability to bolster neurological activity within the prefrontal cortex. And worse, chronic usage of reuptake inhibitors or TCAs has the detrimental side effect of reducing 5-HT serotonin receptors in the prefrontal cortex or increasing the probability of a negative cardiovascular event, respectively. This and can lead to other, less reversible and potentially less manageable disorders like Alzheimer's Disease or Cardiovascular Disease, which drastically reduces patient prognosis. Only time and further study will prove if psychedelics are more efficient and less harmful than traditional therapies in a clinical setting, but the resurgence of clinical studies, the loosening of government restrictions, and the reduced public stigmatization are very promising.

References

Alonso, Joan Francesc, et al. (2015). “Serotonergic Psychedelics Temporarily Modify Information Transfer in Humans.” Int J Neuropsychopharmacology, 2015, 1-9. doi:10.1093/ijnp/pyv039. This is a research article discussing a study conducted in Spain on a group of 10 individuals and their brain activity while on ayahuasca. This article goes into detail about how the study was conducted and how brain activity was measured. The findings provide evidence that the prefrontal cortex becomes more active during the drug’s use which allows for more cognitive-emotional processing. This article was found on NMCI using the keywords “psychedelics” and “effects”.

Arnsten A. F. (2009). Stress signalling pathways that impair prefrontal cortex structure and function. Nature reviews. Neuroscience, 10(6), 410–422. https://doi.org/10.1038/nrn2648

Behan, W. M., Bakheit, A. M., Behan, P. O., & More, I. A. (1991). The muscle findings in the neuroleptic malignant syndrome associated with lysergic acid diethylamide. Journal of neurology, neurosurgery, and psychiatry, 54(8), 741–743. https://doi.org/10.1136/jnnp.54.8.741

Bishop, S., Duncan, J., Brett, M., & Lawrence, A. D. (2004). Prefrontal cortical function and anxiety: controlling attention to threat-related stimuli. Nature Neuroscience, 7(2), 184–188. https://doi.org/10.1038/nn1173

Bogenschutz, M. P., & Pommy, J. M. (2012). Therapeutic mechanisms of classic hallucinogens in the treatment of addictions: from indirect evidence to testable hypotheses. Drug Testing and Analysis, 4(7–8), 543–555. https://doi.org/10.1002/dta.1376

Carhart-Harris, R. L., & Nutt, D. J. (2010). User perceptions of the benefits and harms of hallucinogenic drug use: A web-based questionnaire study. Journal of Substance Use, 15(4), 283–300. https://doi.org/10.3109/14659890903271624

Clark WG. Changes in body temperature after administration of antipyretics, LSD, delta 9-THC and related agents: II. Neurosci Biobehav Rev. 1987 Spring;11(1):35-96. doi: 10.1016/s0149-7634(87)80003-9. PMID: 3033566.

Doblin, R. (2019). "The Future of Psychedelic-Assisted Psychotherapy" Ted.com. Retrieved from https://www.youtube.com/watch?v=Q9XD8yRPxc8. This video addresses how psychedelics can treat and potentially identify/correct the root causes of mental illnesses such as PTSD, depression, and anxiety. Rick Doblin briefly goes over how these drugs interact with the brain on a neurological level. This video helps explain how psychedelics, such as MDMA, increase activity in the prefrontal cortex, which is typically lower in patients diagnosed with PTSD. It simultaneously allows the amygdala and hippocampus to form new connections as well, which allows the patient to process the trauma. This video was found using a google search with the key phrase "psychedelics and treatment".

Dos Santos, R. G., Bouso, J. C., & Hallak, J. (2017). Ayahuasca, dimethyltryptamine, and psychosis: a systematic review of human studies. Therapeutic advances in psychopharmacology, 7(4), 141–157. https://doi.org/10.1177/2045125316689030

Erwin Krediet, Tijmen Bostoen, Joost Breeksema, Annette van Schagen, Torsten Passie, Eric Vermetten, Reviewing the Potential of Psychedelics for the Treatment of PTSD, International Journal of Neuropsychopharmacology, Volume 23, Issue 6, June 2020, Pages 385–

400, https://doi.org/10.1093/ijnp/pyaa018. Article discusses the recent breakthrough treatment of PTSD with the help of psychedelics. Past treatments provided little relief to those suffering with PTSD, making it a chronic condition with no cure. However, recent studies using MDMA and Ketamine have proven to be over 50 percent more effective in successfully treating PTSD patients with little to no relapses.

Ferguson J. M. (2001). SSRI Antidepressant Medications: Adverse Effects and Tolerability. Primary care companion to the Journal of clinical psychiatry, 3(1), 22–27. https://doi.org/10.4088/pcc.v03n0105. This article discusses the long-term effects of SSRIs. It delves into the benefits of SSRIs and how they are less harmful than older treatments such as TCAs, but also covers the adverse side effects such as insomnia, weight gain, and a lower production of 5HT receptors. Found using google search with the keywords “SSRI” and “effects”.

Fuentes, Juan Jose, et al. (2020). “Therapeutic Use of LSD in Psychiatry: A Systematic Review of Randomized-Controlled Clinical Trials.” Frontiers in Psychiatry Vol 10, 943. doi:10.3389/fpsyt.2019.00943. This article does an extensive review of all studies associated with LSD over the past century. It assesses the overall risks or benefits associated with LSD use in a clinical setting. This article helps emphasize the therapeutic use LSD has with alcoholism. This article was found on Google Scholar using the keywords “LSD” and “treatment”. Garcia-Romeu, A., Kersgaard, B., & Addy, P. H. (2016). Clinical applications of hallucinogens: A review. Experimental and clinical psychopharmacology, 24(4), 229–268. https://doi.org/10.1037/pha0000084

Garcia-Romeu, A., Kersgaard, B., & Addy, P. H. (2016). Clinical applications of hallucinogens: A review. Experimental and clinical psychopharmacology, 24(4), 229–268. https://doi.org/10.1037/pha0000084

Glassman, A. H., & Preud'homme, X. A. (1993). Review of the cardiovascular effects of heterocyclic antidepressants. The Journal of Clinical Psychiatry, 54(2, Suppl), 16–22. PMID: 8444830. The article discusses heart conditions that have been linked to TCA usage. It goes in depth by reviewing how the TCAs lead to heart arrhythmias by slowing it down to the point of near death. Found on PubMed with keywords “TCA” and “adverse effects”.

Glatter, R. (2015, November 30). LSD Microdosing: The New Job Enhancer In Silicon Valley And Beyond? Forbes. https://www.forbes.com/sites/robertglatter/2015/11/27/lsd-microdosing-the-new-job-enhancer-in-silicon-valley-and-beyond/?sh=38a77099188a

Godlewska, B. (2019). “Change in neural response to emotional information as an early predictor of clinical response to SSRI treatment in depression”. European Neuropsychopharmacology, Vol 29, Supp 1, p S6. https://doi.org/10.1016/j.euroneuro.2018.11.918. This article examines the increase of timeliness with treatment of SSRIs, but they were unable to do a longitudinal study due to ethical concerns. Retrieved from science direct through SVC data library.

GREINER T, BURCH NR, EDELBERG R. Psychopathology and Psychophysiology of Minimal LSD-25 Dosage: A Preliminary Dosage-Response Spectrum. AMA Arch NeurPsych. 1958;79(2):208–210. doi:10.1001/archneurpsyc.1958.02340020088016

Hamill, J., Hallak, J., Dursun, S. M., & Baker, G. (2019). Ayahuasca: Psychological and Physiologic Effects, Pharmacology and Potential Uses in Addiction and Mental Illness. Current neuropharmacology, 17(2), 108–128. https://doi.org/10.2174/1570159X16666180125095902

Heal, D., Gosden, J., & Smith, S. (2018). Evaluating the abuse potential of psychedelic drugs as part of the safety pharmacology assessment for medical use in humans. Neuropharmacology, 142, 89–115. https://doi.org/10.1016/j.neuropharm.2018.01.049. This is review of studies conducted to determine the potential abuse of psychedelics. It is summarized that while the potential to abuse any drugs is always prevalent, psychedelics do not result in a physical dependence or withdrawal phase. Found on SVC library database, ScienceDirect.

Johansen PØ, Krebs TS. Psychedelics not linked to mental health problems or suicidal behavior: a population study. J Psychopharmacol. 2015 Mar;29(3):270-9. doi: 10.1177/0269881114568039. Epub 2015 Mar 5. PMID: 25744618.

Johnson, M. W., Griffiths, R. R., Hendricks, P. S., & Henningfield, J. E. (2018). “The abuse potential of medical psilocybin according to the 8 factors of the Controlled Substances Act.” Neuropharmacology, 142, 143–166. https://doi.org/10.1016/j.neuropharm.2018.05.012. The article discusses the abuse potential of psychedelics with a focus on psilocybin. It goes over the history and recent studies that indicate these drugs could be used for medicinal only with little abuse potential. Article was found on pubmed using keywords “psychedelics”, “treatment”, and “depression”.

Johnstad, P. G. (2018). Powerful substances in tiny amounts. Nordic Studies on Alcohol and Drugs, 35(1), 39–51. https://doi.org/10.1177/1455072517753339

Krebs, T. S., & Johansen, P. Ø. (2013). Psychedelics and mental health: a population study. PloS one, 8(8), e63972. https://doi.org/10.1371/journal.pone.0063972

Kvam, T. M., Stewart, L. H., & Andreassen, O. A. (2018). Psychedelic drugs in the treatment of anxiety, depression and addiction. Psykedeliske stoffer i behandling av angst, depresjon og avhengighet. Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke, 138(18), 10.4045/tidsskr.17.1110. https://doi.org/10.4045/tidsskr.17.1110

Li, C., Tang, M. H., Chong, Y., Chan, T. Y., & Mak, T. W. (2019). Lysergic acid diethylamide–associated intoxication in Hong Kong: a case series. Hong Kong Medical Journal, 25(4), 323–325. https://doi.org/10.12809/hkmj197942 Liechti M. E. (2017). Modern Clinical Research on LSD. Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology, 42(11), 2114–2127. https://doi.org/10.1038/npp.2017.86. Article reviews modern studies on LSD and discusses findings to include immediate effects on the brain and long term effects on the patient's psyche. It goes into detail about how LSD is beneficial for psychotherapy when disbursed in a controlled clinical setting.

Ly, C., Greb, A. C., Cameron, L. P., Wong, J. M., Barragan, E. V., Wilson, P. C., Burbach, K. F., Soltanzadeh Zarandi, S., Sood, A., Paddy, M. R., Duim, W. C., Dennis, M. Y., McAllister, A. K., Ori-McKenney, K. M., Gray, J. A., & Olson, D. E. (2018). Psychedelics Promote Structural and Functional Neural Plasticity. Cell Reports, 23(11), 3170–3182. https://doi.org/10.1016/j.celrep.2018.05.022

Microdose Research: Without approvals, control groups, double-blinds, staff or funding by Dr James Fadiman. (2017, November 16). Psychedelic Press. https://psychedelicpress.co.uk/blogs/psychedelic-press-blog/microdose-research-james-fadiman

Mogg, K., & Bradley, B. P. (1998). A cognitive-motivational analysis of anxiety. Behaviour research and therapy, 36(9), 809–848. https://doi.org/10.1016/s0005-7967(98)00063-1

Mogg, K., Garner, M., & Bradley, B. P. (2007). Anxiety and orienting of gaze to angry and fearful faces. Biological psychology, 76(3), 163–169. https://doi.org/10.1016/j.biopsycho.2007.07.005

Mueller, F., Lenz, C., Dolder, P. C., Harder, S., Schmid, Y., Lang, U. E., Liechti, M. E., & Borgwardt, S. (2017). “Acute effects of LSD on amygdala activity during processing of fearful stimuli in healthy subjects”. Translational psychiatry, 7(4), e1084. https://doi.org/10.1038/tp.2017.54. This article is another study of clinical trials in Switzerland which focuses on LSD and its effects on the amygdala. It compares the use of SSRIs to LSD. This article was found on NCBI using keywords “psychedelics”, and “effects on the brain”.

National Institute on Drug Abuse (NIDA). (2020, May 04). National survey of drug use and health. Retrieved February 12, 2021, from https://www.drugabuse.gov/drug-topics/trends-statistics/national-drug-early-warning-system-ndews/national-survey-drug-use-health. Statistical data of US Citizens and reported drug use. Categorizes by type of drug, and age range. Found on CDC website under “FastStats”.

Nichols D. E. (2016). Psychedelics. Pharmacological reviews, 68(2), 264–355. https://doi.org/10.1124/pr.115.011478

Nutt D. (2019). Psychedelic drugs-a new era in psychiatry? Dialogues in clinical neuroscience, 21(2), 139–147. https://doi.org/10.31887/DCNS.2019.21.2/dnutt. This article discusses the preliminary findings of clinical trials with MDMA as a PTSD and alcoholism treatment. The current reports have led to phase three studies with the European Medicines Agency and Food and Drug Administration approval. Retrieved from NCBI.

Horsley, R. R., Páleníček, T., Kolin, J., & Valeš, K. (2018). Psilocin and ketamine microdosing: effects of subchronic intermittent microdoses in the elevated plus-maze in male Wistar rats. Behavioural pharmacology, 29(6), 530–536. https://doi.org/10.1097/FBP.0000000000000394

Palhano-Fontes F, Andrade KC, Tofoli LF, Santos AC, Crippa JAS, et al. (2015) The Psychedelic State Induced by Ayahuasca Modulates the Activity and Connectivity of the Default Mode Network. PLOS ONE 10(2): e0118143. https://doi.org/10.1371/journal.pone.0118143

Reynolds, Philip C. Jindrich, Ervin J. A Mescaline Associated Fatality, Journal of Analytical Toxicology, Volume 9, Issue 4, July-August 1985, Pages 183–184, https://doi.org/10.1093/jat/9.4.183

Schneider, C., & Wissink, T. (2018). Heterocyclic antidepressant. Integrative Medicine. https://www.sciencedirect.com/topics/neuroscience/heterocyclic-antidepressant. This article reviews several studies on typical antidepressants used for treatment, such as SSRIS and TCAs. It discusses the effects of each treatment and compares each one to highlights the

positives and negatives of each. Found on SVC Library Database, ScienceDirect. Keywords used were “Antidepressants” and “Treatment”.

Skandali, N., Rowe, J. B., Voon, V., Deakin, J. B., Cardinal, R. N., Cormack, F., Passamonti, L., Bevan-Jones, W. R., Regenthal, R., Chamberlain, S. R., Robbins, T. W., & Sahakian, B. J. (2018). Dissociable effects of acute SSRI (escitalopram) on executive, learning and emotional functions in healthy humans. Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology, 43(13), 2645–2651. https://doi.org/10.1038/s41386-018-0229-z. Found on Pubmed using keywords “SSRI”, and “effects”. This study analyzes the effects of a specific SSRI, escitalopram, on the brain and how it effects cognitive functioning. It summarized the short term positive and negative effects of the drug on volunteers. Overall, it was determined that escitalopram is good for short term use on people diagnosed with Major Depressive Disorder, but it does impair their ability to learn. This study is helpful as I discuss the negative side effects of SSRIs.

Smigielski, L. (1 august 2019). Psilocybin-assisted mindfulness training modulates self-consciousness and brain default mode network connectivity with lasting effects. NeuroImage, 196, 207-215. doi:https://doi.org/10.1016/j.neuroimage.2019.04.009

Turcotte-Cardin, V., Vahid-Ansari, F., Luckhart, C., Daigle, M., Geddes, S., Tanaka, K., Hen, R., James, J., Merali, Z., Béïque, J., & Albert, P. (2019). “Loss of Adult 5-HT1A Autoreceptors Results in a Paradoxical Anxiogenic Response to Antidepressant Treatment” The Journal of Neuroscience, 39(8), 1334–1346. https://doi.org/10.1523/JNEUROSCI.0352-18.2018. Long term use of SSRIs does not appear to improve or alter baseline anxiety or depression behaviors. This article will be used to help support my thesis that psychedelics are a better

treatment for depression and other mental health disorders. Found on Pubmed using keywords “SSRI”, and “effects”.

Ungerleider, J. T., & Fisher, D. D. (1967). The problems of LSD-25 and emotional disorder. California medicine, 106(1), 49–55.

Wang, S. M., Han, C., Bahk, W. M., Lee, S. J., Patkar, A. A., Masand, P. S., & Pae, C. U. (2018). Addressing the Side Effects of Contemporary Antidepressant Drugs: A Comprehensive Review. Chonnam medical journal, 54(2), 101–112. https://doi.org/10.4068/cmj.2018.54.2.101. Discusses the side effects of SSRIs and evaluates the safety of the drugs. Compares SSRIs to TCAs, showing the relative safety of SSRIs compared to TCAs. Found on NCBI using keywords “Side Effects” and “antidepressants”.

Whalen, P. J., Rauch, S. L., Etcoff, N. L., McInerney, S. C., Lee, M. B., & Jenike, M. A. (1998). Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. The Journal of neuroscience : the official journal of the Society for Neuroscience, 18(1), 411–418. https://doi.org/10.1523/JNEUROSCI.18-01-00411.1998

Yanakieva, S., Polychroni, N., Family, N., Williams, L. T. J., Luke, D. P., & Terhune, D. B. (2018). The effects of microdose LSD on time perception: a randomised, double-blind, placebo-controlled trial. Psychopharmacology, 236(4), 1159–1170. https://doi.org/10.1007/s00213-018-5119-x