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# The Renaissance of Psychedelic Therapy

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Psychedelics are experiencing a renaissance in psychiatry (Nichols, 2016). Recent studies of psychedelic therapy have demonstrated safety and promising results for depression (Carhart-Harris et al., 2016), substance use (Johnson et al., 2014), end-of-life distress in cancer (Grob et al., 2011), post-traumatic stress disorder (Oehen et al., 2014), and obsessive-compulsive disorder (Moreno, Weigand, Taitano, & Delgado, 2006). Furthermore, interest in applying and testing psychedelic therapy to other psychiatric illnesses is growing and funding proposals are underway (Rucker, Iliff, & Nutt, 2018). Classic serotonergic psychedelics include 5HT<sub>2A</sub> agonists psilocybin (the active ingredient in what are commonly known as magic mushrooms), lysergic acid diethylamide (LSD), mescaline, and dimethyltryptamine (DMT). Scientific interest in these treatment models including these drugs have substantially increased over the last few decades (Nichols, Johnson, & Nichols, 2017), with a particular focus on the study of psilocybin therapy. Additionally, further research is underway to understand the therapeutic impact of the more broadly defined class of hallucinogens/psychedelics which includes drugs with other mechanisms of neurotransmission including ketamine, MDMA, and Ibogaine among others.

Awareness about the therapeutic use of these drugs in both the mental health field and popular culture is rapidly increasing in large part due to media attention covering therapeutic studies and Michael Pollan's recent book, *How to Change your Mind* (Pollan, 2018). However, despite recent excitement and ongoing support and study from the scientific community, psychedelics are still outgrowing their long-fraught reputation. The collective societal associations we have unwittingly inherited of psychedelic drugs as artifacts of the 1960s countercultural movement and recreational drug usage though diminishing, remain alive in mainstream culture and even the mental health field. Though an

alluring story, the recreational use of psychedelics is a small—and arguably frivolous—aspect of a much deeper medicinal history beginning with ancient medicinal purposes amongst indigenous populations; progressing to the use and study of these drugs in Western psychiatry in the 1950s; and finally, to the revival and advancement of scientific inquiry championed by highly reputable academic and funding organizations concerning the potential of psychedelic therapy for a range of psychiatric disorders (Garcia-Romeu & Richards, 2018). Though more research is needed to prove efficacy and effectiveness, scientific studies are continuously emerging showing these drugs as safe and potentially efficacious for a range of psychiatric illnesses.

## A Brief History

Recorded usage of naturally occurring hallucinogenic plant medicines date back to ancient indigenous populations (Richards, 2015; Metzner 1998). In Western medicine, scientific inquiry concerning the medicinal uses of serotonergic psychedelics grew throughout the 1950s, primarily with the study of LSD after the drug was fortuitously synthesized by Swiss chemist Albert Hoffman. These studies, though lacking in scientific rigor by today's standards, demonstrated safety and pointed to positive outcomes for various psychiatric issues. However, research was abruptly halted as psychedelics were criminalized through the Controlled Substances Act in the mid-60s in the context of socio-political factors that characterized that era. The psychedelic movement was forced dormant and pushed underground until their study was revived in the 1990s with systematic investigation of biological and psychological effects in healthy control subjects first, followed by studies investigating their therapeutic impact in psychiatric illnesses (Garcia-Romeu & Richards, 2018).

## Applications of Psilocybin-Assisted Therapy to Psychiatric Illnesses

Clinical investigation of a variety of psychedelic treatments for psychiatric illnesses are currently underway (Clinicaltrials.gov; Multidisciplinary Association for Psychedelic Studies, 2019). Much of the contemporary research on serotonergic psychedelics has focused on psilocybin-assisted therapy. Clinical studies of psilocybin include treatments for depression, end-of-life anxiety in late-stage cancer, obsessive compulsive disorders, and alcohol and tobacco addiction. Although further research is needed to prove efficacy, preliminary results are promising and have demonstrated good safety and feasibility (Johnson & Griffiths, 2018). In a pilot study targeting distress in end-stage cancer, participants reported marked reductions in both anxiety and depression symptoms up to six months following the psilocybin session (Grob et al., 2011). Treatment included a single administration of either a medium or high dose of psi-

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locybin preceded by preparatory sessions focused on building rapport with a therapist and providing education on potential effects of the drug. In a small case series paper investigating psilocybin for OCD, Moreno et al. (2006) showed a reduction in obsessive compulsive symptoms immediately following the psilocybin session across a variety of doses ranging from low to high. These results proved to be durable, with decreased scores reported up to two weeks after the session. Further studies are ongoing, including a double-blind, placebo-controlled trial, to investigate the efficacy of psilocybin in reducing symptoms of OCD (Clinicaltrials.gov; Moreno, 2017; Kelmendi, 2017).

Psilocybin has also been tested in small trials for alcohol and tobacco addictions. One study showed a reduction in drinking behavior and cravings in alcohol dependents after a single administration (Bogenschutz et al., 2015). In a small trial in tobacco users, 80% of participants were abstinent at six month follow-up (Johnson, Garcia-Romeu, Cosimano, & Griffiths, 2014). A randomized controlled trial is currently underway investigating the effects of psilocybin treatment on drinking in alcohol dependence (Clinicaltrials.gov, Bogenschutz, 2014). Results of these open-label studies are promising, though preliminary, due to the small scale and non-randomized design of these studies.

Though the results cited above are limited by size and study design, the application of psilocybin to unipolar depression is advancing. An international, multi-site randomized controlled trial funded by Compass Pathways is currently underway to investigate safety, efficacy and therapeutic dosage of psilocybin in individuals with treatment refractory depression (BusinessWire, 2017). Compass Pathways, an organization devoted to improving access to effective treatments received a “Break-through Therapy” designation from the FDA. This designation allows for expedited reviews by the FDA which would result in a swifter timeline for expanding access to this treatment if therapeutic impact is shown. (Trials for MDMA-Assisted Therapy for PTSD led by the Multidisciplinary Association for Psychedelic Studies; MAPS, is currently advancing on the same trajectory). Preliminary results from an open label study, which helped pave the way for the current depression trial, are promising. Participants who received a low dose and a high dose of psilocybin in a supportive setting with non-directive psychological support provided before and after, demonstrated meaningful reductions in depressive symptoms up to three months following the treatment (Carhart-Harris et al., 2016).

### What Does Psilocybin Therapy Involve?

There has been no systematic study of treatment models surrounding psychedelic administration. Despite this, it is generally well-accepted that psychological support surrounding a psychedelic trip is an important element (Garcia-Romeu & Richards, 2018). The integration of psychotherapy with the administration of psychedelics represents a first move in psychiatry towards integrating “the brain” and “the mind” and a shift away from a dualistic view of psychiatric medicines and psychotherapy as separate spheres of treatment (Schenberg, 2018). Though the

mechanisms of action are not fully understood, neuroimaging data suggests that psychedelics disrupt functional connectivity producing an entropic brain state and increase neural plasticity (Carhart-Harris et al., 2017; Carhart-Harris, 2019). Phenomenologically, these brain state changes may promote new insights and learning, enhance meaning, and disrupt dysfunctional and rigid styles of thinking, all of which may lead to new beliefs and behavior change (Hartogsohn, 2018).

Psychological support varies somewhat across studies, ranging from a short-term model of nondirective psychological support to structured therapies delivered as an adjunct to psilocybin. However, all models focus on optimizing “set and setting,” referring to a patient’s mindset and the external context (Carhart-Harris et al., 2018; Johnson, Richards, & Griffiths, 2008) features that are widely believed to be imperative to ensuring a therapeutic experience. Models of treatment are typically short-term and nondirective, borrowing from models forged in the earlier decades of study. Psychological support is delivered by a provider in a three-step model which includes preparatory sessions, followed by psychological support during the psychedelic trip, and integration sessions that follow the dosing session (Garcia-Romeu, 2018).

As the swift course of study of psychedelic therapy continues, our culture and healthcare communities are undergoing an important tide shift in re-shaping the popular attitude towards psychedelics as safe psychiatric medicines with the potential for significant therapeutic impact. This work will likely impact the mental health field in providing more opportunities for treatment non-responders and for mental health professionals interested in eventually participating in this work. Psychedelic therapy represents a unique paradigm of psychiatry involving the marriage of the biological and psychological. Though mechanisms of action are not yet fully understood and the role of adjunctive therapy is not yet clear, lead Hopkins researcher Matt Johnson describe the therapeutic potential as a biological effect of the drug that results in psychological opportunities for change. This integrated model denotes an opening for mental health professionals to be trained to provide therapeutic support during a psychedelic trip and therapy focused on maximal preparation and the integration of insights and experiences post-administration. This is an exciting prospect for those of us interested in participating in new and potentially more robust treatments at a time in which our currently available behavioral treatments are proving to be limited in improving mental health outcomes (Insel, 2015). ▲

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References for this article are available on request from the LACPA office, lacpa1@gmail.com.