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The Therapeutic Effects of Psychedelics in Addiction Treatment

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Introduction:

When they were first introduced to the psychiatric research community in the 1950's, psychedelics were hailed as the tools of the future (Morris, 2008). When recreational use exploded in the 60's, however, it was met with cultural backlash that labeled the drugs as dangerous (Morris, 2008). In the past 20 years, psychedelic research has seen a resurgence, in large part due to the increasing reliance of the FDA on data in decision-making and researchers adopting more measured attitudes toward the risks and benefits of psychedelic use (Morris, 2008). Nowadays, psychedelics have been indicated as effective psychotherapeutic treatments for anxiety, PTSD, OCD, depression, addiction as well as improving the symptoms of cluster headaches and helping terminal cancer patients reach an acceptance of death (Morris, 2008). This review will focus on the past and present research on the interaction of psychedelics and addiction to elucidate common, large-scale, cognitive mechanisms of psychedelics in addiction treatment and general life-improvement.

Psychedelics and Addiction:

Before almost all LSD (a tryptamine psychedelic) treatment research stopped abruptly in the seventies, there were over 30 publications that examined the effect of LSD in treating alcoholism (Bogenschutz and Johnson, 2016). Generalized conclusions have been hard to draw from this body of work, as many suffer from internally poor methodology (of the 31 known studies, 17 were conducted without controls and only 6 were randomized) (Abuzzahab and Anderson, 1971). Methodologies also differ greatly between studies; some were single-dose while others were multiple-dose, follow-up times ranged from no follow-up to a 65-month

follow-up, and single doses ranged from 50-800 μg (~.5-8 standard recreational doses) between studies (Abuzzahab and Anderson, 1971). Recently, however, a meta-analysis of the 6 randomized studies from this body of work claims to have drawn meaningful conclusions (Krebs and Johansen, 2012). In total, these studies investigated 536 male, inpatient alcoholics, in which 325 participants were given a single high dose (210-800 μg) of LSD and 211 were given a control of either low-dose (~50 μg) LSD, placebo, amphetamine, or ephedrine (Krebs and Johansen, 2012). Though the studies varied in debriefing of subjects and conditions during sessions, inter-trial heterogeneity was quantifiably negligible ($I^2 = 0\%$) (Krebs and Johansen, 2012). The meta-analysis used Odds Ratios (ORs) to pool data and found that single-dose LSD treatment had a significant effect on alcohol misuse, with 59% of the treatment group reporting improvement at the first follow-up compared to 38% of the control group (OR=1.96, p=.0003) (Krebs and Johansen, 2012). This effect was homogeneous across the 6 studies analyzed (Krebs and Johansen, 2012).

Recent research has elucidated the potential anti-addictive properties of ayahuasca (a tryptamine psychedelic). In a human study, 18 members of a rural First Nations community in Canada with substance abuse issues were led on an addiction treatment retreat that included group counselling and two expert-led ayahuasca ceremonies (Thomas et al., 2013). At post-treatment follow-ups, all participants reported positive, lasting changes from the ayahuasca experience, and statistically significant improvements ($p < .05$) on questionnaires measuring quality of life, hopefulness, mindfulness, and empowerment were demonstrated (Thomas et al., 2013). 4WSUS substance use scores generated from self-reports at follow-up decreased significantly for alcohol, tobacco, and cocaine (which were used by 40% of participants at

baseline) but not for opiates and marijuana (Thomas et al., 2013). These results are supported by a laboratory study with mice in which ayahuasca inhibited development of alcohol dependence (Oliveira-Lima et al., 2015).

Subjective Mystical Experiences as a Potential Mechanism:

Serotonin and its receptors are thought to be the general mechanism of the therapeutic effects of psychedelics in addiction treatment due to the consistently observed low levels of serotonin in addict populations and the wide ranging roles of serotonin in modulating the activity of other neurotransmitter pathways (Winkelman, 2014). Serotonin has long been shown to be integral to the general physical, emotional, and cognitive effects of psychedelics (Winkelman, 2014). In the wake of new research, it has been suggested that the manner in which psychedelics affect conscious thought processes may play an active mediating role in the therapeutic effects of psychedelics in addiction treatment.

Within the realm of conscious thought processes, subjective mystical experiences are now thought to have an active role in addiction therapy, and psilocybin (a tryptamine psychedelic) has been repeatedly used as a window into these experiences. In one open label pilot study, 15 smoking participants were given multiple doses of psilocybin during Cognitive Behavioral Therapy (CBT) sessions for smoking cessation (Johnson et al., 2014). At a 6-month follow-up, 75% (n=12) of participants reported smoking abstinence with biological verification. The 12 abstainers differed significantly from the 3 smokers in their scores on the Mystical Experience Questionnaire (MEQ) as well as retrospective ratings of personal significance and meaning during session days, with 60% (n=9) of the 15 participants meeting the criteria for a

Complete Mystical Experience in the context of the MEQ (Johnson et al., 2014). Importantly, there was no variability in the intensity of the experience, separating the variables of intensity of experience and score on the MEQ and supporting the conclusion that subjective mystical experiences are an active mediator in the interaction between psychedelics and addiction pathways (Johnson et al., 2014).

Johnson et al. (2014) was conducted in the wake of two previous studies by largely the same cohort of researchers that established the usefulness of the MEQ in elucidating how the interaction between psychedelics and conscious thought pathways can have lasting effects on the user's life. Griffiths et al. (2006) used 36 adult participants who regularly participated in religious and spiritual activities. Some were given psilocybin, some were given methylphenidate, and some were given both during sessions. The study concluded that psilocybin increased measures of mystical experience that were similar to those that occur spontaneously (i.e. in a religious/spiritual activity setting), and at a 2-month follow-up, participants reported that the psilocybin experience held substantial personal and spiritual significance and was accompanied by positive attitude and behavior changes that were consistent with the reports of community observers (Griffiths et al., 2006). A follow-up study by the same authors examined the dose-related effects of psilocybin in a similar fashion. Participants were split into groups and received either an ascending or descending sequence of psilocybin doses (Griffiths et al., 2011). This study confirmed the results of the previous study, finding that psilocybin experiences had personal and spiritual significance, positively affected mood, attitude, and behavior, and occasioned mystical experiences in 72% of participants (Griffiths et al. 2011). The study also

found that the ascending dose sequence had greater positive effects, and that the persistent and acute effects of psilocybin increased as a function of dose (Griffiths et al., 2011).

A final study by the same cohort of authors conducted a meta-analysis of pooled data from the previous three studies and two others by the same cohort (n=184). Confirmatory factor analysis confirmed the internal validity of the MEQ, and external validity was demonstrated with equation models that showed that latent variable MEQ scores positively predicted positive mood, attitude, and behavior changes even when intensity of the psilocybin experience was controlled for (Barrett et al., 2015). Though research on the effects of psychedelic-induced mystical experiences is in its infancy, this study (along with the previous 5 from the same group) supports a causal, positive relationship between mystical experiences and the persistent benefits of psilocybin. These studies use a different substance but match the results of Thomas et al. (2015), in which ayahuasca was linked to both improvement in quality of life and a decrease in substance abuse, providing preliminary support for the generalizability of the importance of mystical experiences and conscious thought in the therapeutic effects of many psychedelics.

Conclusions:

Due to the decades-long hiatus on psychedelic research caused by the sweeping illegalizations at the end of the 60's and early 70's (Morris, 2008) psychedelic research on addiction is still in its infancy. Already, however, a wide range of preliminary results indicate a strong potential for psychedelics as effective addiction treatments (Johnson et al. 2014, Thomas et al., 2013, Oliveira-Lima et al., 2015, Krebs and Johansen, 2012) and demonstrate the ability of psychedelics to improve the lives of users through positive mood, attitude, and behavior shifts

(Thomas et al., 2013, Barrett et al., 2015, Griffiths et al., 2011, Griffiths et al., 2006). Further research is needed to resolve this three-way association between psychedelics, positive mood/behavior shifts, and positive addiction treatment results. It may be that the positive mood/behavior shifts brought on by psychedelics are directly involved in addiction treatment improvement, or it may be that psychedelics independently affect both mood/behavior and addiction treatment in separate processes that are both mediated by the effect of psychedelics on conscious thought pathways. The wide-ranging ability of psychedelics to improve the lives of their users that has been demonstrated with modern methodology in the less than 20 years since the resurgence of psychedelic research confirms the beliefs of the original psychedelic research community and has firmly established that psychedelics can be a helpful asset in psychotherapy, even if their specific benefits and mechanisms of action are still largely unknown.

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