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Development of a Psychotherapeutic Model for Psilocybin-Assisted Treatment of Alcoholism

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Abstract

Research activity on the potential clinical value of classic hallucinogens and other psychedelics has increased markedly in the past two decades, and promises to continue to expand. Experimental study of hallucinogen-assisted treatment, and any future clinical use, requires the development of psychotherapeutic models that are appropriate to the disorder being treated and effectively integrated with the pharmacologic component of the treatment. To provide a framework for thinking about possible treatment models, we provide an overview of the history of psychedelic-assisted treatment, review what is known about the therapeutic mechanisms of these treatments, and consider the various purposes of psychotherapy in the context of both research and clinical use of psychedelic-assisted treatment. We then provide a description of a therapy model we have developed and are currently using in a trial of psilocybin-assisted treatment for alcoholism. Finally, we discuss advantages and disadvantages of a range of alternative models, emphasizing the need for research to determine the most effective treatment models for any indications for which efficacy becomes established.

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Introduction

Classic hallucinogens are a class of psychedelic ("mind-manifesting") drugs defined by their action at the serotonin 2A (5HT2A) receptor. The best-known examples include lysergic acid diethylamide (LSD), psilocybin, dimethyltryptamine, and mescaline. The past two decades have seen a marked increase in interest in and research on possible clinical uses for classic hallucinogens. Procedures are well established for safely conducting sessions in which relatively high doses of classic hallucinogens such as psilocybin are administered (M. Johnson, Richards, & Griffiths, 2008). However, it is much less clear how best to integrate the psychedelic experience into treatment models designed to have specific therapeutic effects, for example, to ameliorate the symptoms of a specific disorder.

As an example of model development, in this article we will discuss the development and implementation of a treatment model for psilocybin-assisted treatment of alcohol dependence. First, we provide a brief overview of the history of psychedelic-assisted treatment of alcoholism. Next, we summarize current thinking about the possible mechanisms of treatment with classic hallucinogens, both generally and in relation to addiction. We consider the several functions of psychotherapy in the context of treatment with psychedelic medicines, and the special issues that must be considered when the therapy is provided within a research study. We then describe an integrated treatment model that has been developed, including three main components: alcohol-focused therapy incorporating elements of Motivational Enhancement Therapy (MET) and Cognitive Behavioral Therapy; therapy devoted to providing a safe and supportive therapeutic container for the use of a psychedelic, including Preparation, Support, and Integration (PSI) before, during, and after the psychedelic experience; and the psychedelic medicine itself. Finally, we consider the lessons that can be drawn from this process in relation to both addiction treatment and other possible applications of psychedelic-assisted treatment, discuss alternative approaches, and suggest directions for future research.

Historical Models

Naturally occurring psychedelics have been used by humans for at least five millennia (El-Seedi, De Smet, Beck, Possnert, & Bruhn, 2005), but they

escaped the notice of Western science until the late 1800s, when Arthur Heffter (1896, 1898) isolated mescaline and described its effects. In 1943, Albert Hofmann (1979) discovered the psychoactive effects of LSD when he accidentally ingested traces of an ergot derivative he had synthesized. He and other investigators quickly recognized the therapeutic potential of LSD (Busch & Johnson, 1950). Following Gordon Wasson's (1957) report of hallucinogenic mushroom use by the Mazatec tribe in Mexico, Hofmann et al. isolated psilocybin from samples of the mushrooms and synthesized it in the laboratory (Hofmann, Frey, Ott, Petrzilka, & Troxler, 1958; Hofmann, Heim, Brack, & Kobel, 1958).

From the 1950s through the early 1970s, there was tremendous scientific interest in these drugs and a few others such as dipropyltryptamine and 3,4-Methylene-dioxy-amphetamine. Much of the early work with these compounds explored their use as experimental models of psychopathological states such as psychosis (Rinkel, Deshon, Hyde, & Solomon, 1952). However, clinicians and clinical scientists quickly became interested in the therapeutic potential of these drugs, and began to study the use of classic hallucinogens to facilitate rapid therapeutic effects in alcohol and drug addiction, as well as anxiety and depression related to life-threating cancer, and many other conditions. Psychedelics including LSD and psilocybin were legally available for clinical use until the mid- to late 1960s. Over a 1,000 papers document the treatment of over 40,000 people with these medications during this period (Grinspoon & Balakar, 1997). The main focus of research on the use of psychedelics in the addiction field was the use of LSD for the treatment of alcoholism. Treatment of alcoholism with LSD using the psychedelic model was an accepted clinical treatment in Saskatchewan, and was subject of numerous studies (Abuzzahab & Anderson, 1971; Dyck, 2006; Grinspoon & Balakar, 1997; Halpern, 1996; Mangini, 1998). A recent meta-analysis (Krebs & Johansen, 2012) revealed consistent and clinically meaningful effects of LSD over control treatment in the six randomized trials of LSD for alcohol dependence that reported drinking outcomes, including a total of 536 participants (W. T. Bowen, Soskin, & Chotlos, 1970; Hollister, Shelton, & Krieger, 1969; Ludwig, Levine, Stark, & Lazar, 1969; Pahnke, Kurland, Unger, Savage, & Grof, 1970; Smart, Storm, Baker, & Solursh, 1966; Tomsovic & Edwards, 1970). All of the studies administered LSD in a single high-dose session, in doses ranging from about 210 to 800 mcg. LSD-treated patients were more likely to show abstinence or nonproblematic drinking at the first posttreatment follow-up (odds ratio = 1.96, 95% confidence interval [1.36, 2.84], p = .0003). The beneficial effects of LSD treatment remained significant for up to 6 months.

Although psychedelics were sometimes used as stand-alone treatment, most clinicians and researchers combined the administration of these medications with psychotherapy before, during, and/or after the drug administration sessions, believing that the subjective experience during the drug's acute effects, and the successful integration of these experiences, was crucial to achieving therapeutic benefit. Two therapeutic models widely used in the 1950s through early 1970s were psycholytic and psychedelic therapy (Grinspoon & Balakar, 1997; Grof, 2008). In the psycholytic model, clinicians administered low to moderate doses of psychedelics on multiple occasions to facilitate therapy based on traditional psychoanalytic principles, that is, helping the patient to become aware of unconscious processes and resolve intrapsychic conflicts (Buckman, 1967; Leuner, 1967). Therapy was often conducted during drug administration sessions, when the patient was experiencing the effects of the drug. In the psychedelic model, high doses of LSD were administered on one or several occasions with the goal of occasioning a "peak-psychedelic" or mystical experience. According to a classic definition (Pahnke, 1969), mystical experiences, whether drug-induced or not, include a sense of unity or oneness, transcendence of space and time, a sense of sacredness, a sense of deep truth or ultimate meaning (noetic quality), deeply felt positive mood, and ineffability (the inability to describe the experience in words). These experiences were thought to enable lasting change in habitual patterns of thought, behavior, experience of emotion, and personality (Hoffer, 1967; Sherwood, Stolaroff, & Harman, 1962). Although the psycholytic and psychedelic models are conceptually distinct and largely independent, some clinicians and investigators used both or created hybrid models (Grof, 2008; Masters & Houston, 2000).

In reaction increasing misuse of psychedelics in the context of the cultural upheaval during the mid- and late 1960s, clinical research on hallucinogens came to halt in the early 1970s, after enactment of the Controlled Substances Act placed all such compounds into the Schedule I category, reserved for drugs with high abuse potential, no accepted medical use, and a lack of accepted safety when used under medical supervision. Basic research on psychedelics continued, and many additional compounds were and continue to be discovered, few of which have been subjected to human laboratory studies or clinical trials. Illicit use for recreational, therapeutic, and/or spiritual purposes has continued.

Human research on classic hallucinogens resumed in the early 1990s with Rick Strassman's studies of the subjective and physiological effects of intravenous dimethyltryptamine on normal volunteers (Strassman & Qualls, 1994). Since the beginning of the 21st century, there has been rapid growth in research on the effects of psychedelics in humans. The safety of classic

hallucinogens (particularly psilocybin) in clinical research settings has been well documented, and procedures for safely administering these medications are well established (M. Johnson et al., 2008). There is increased recognition that the use of psychedelics in the context of organized religious activity is associated with few if any deleterious effects, and is associated with decreased rates of substance use disorder (Albaugh & Anderson, 1974; Barbosa, Mizumoto, Bogenschutz, & Strassman, 2012; Doering-Silveira et al., 2005; Fabregas et al., 2010; Garrity, 2000; Halpern, Sherwood, Hudson, Yurgelun-Todd, & Pope, 2005; Halpern, Sherwood, Passie, Blackwell, & Ruttenber, 2008; Kunitz & Levy, 1994; Lu et al., 2009; Roy, 1973). There have been major advances in the understanding of the acute effects of classic hallucinogens on physiology, cognition, emotion, and brain function. All of these factors have laid the foundation for the resumption of research into the possible clinical applications of these drugs.

In the addiction treatment field, early stage clinical research on psychedelic-assisted treatment of several substance use disorders is now underway. Proof-of-concept studies of psilocybin for nicotine dependence (M. W. Johnson, Garcia-Romeu, Cosimano, & Griffiths, 2014) and alcohol dependence (Bogenschutz et al., 2015) have recently been completed, both demonstrating substantial decreases in use of the target substance. Further trials are currently being conducted. Studies conducted in Russia in the 1990s provided evidence for the efficacy of the NMDA (N-methyl-D-aspartate) receptor antagonist psychedelic ketamine in the treatment of alcohol and heroin dependence (E. Krupitsky et al., 1992; E. Krupitsky et al., 2002; E. M. Krupitsky et al., 2007; E. M. Krupitsky & Grinenko, 1997). Ayahuasca and ibogaine (a psychedelic which a complex profile of pharmacologic effects) are being used to treat addictions in many retreat centers and treatment programs in Latin America and the Caribbean, but efficacy studies have not been done. These developments strongly suggest that therapeutic use of psychedelics in the treatment of addiction should and will continue to increase in coming years, possibly leading to approved clinical uses for these medications if they are shown to be efficacious. In this context, it will be necessary to make decisions about the role, purpose, and form of the psychosocial aspects of treatment.

Possible Therapeutic Mechanisms of Classic Hallucinogens Relevant to Psychotherapy

The hypothesized mechanisms of hallucinogen-assisted treatment have a direct bearing on development of complementary psychotherapies. As yet there are very few studies directly investigating the role of specific effects of

classic hallucinogens in subsequent change in addictive behavior or any other condition, so this section is necessarily speculative. Here, we briefly describe possible mechanisms of based on the limited existing evidence.

Basic Mechanisms of Classic Hallucinogens

Some of the most basic biological effects of classic hallucinogens have been elucidated in animal models. The primary molecular target of all classic hallucinogens is thought to be the serotonin 2A (5HT2A) receptor (Halberstadt, 2015; Nichols, 2004), which is rapidly down-regulated following hallucinogen administration. This is behaviorally relevant because fronto-limbic 5HT2A receptor density is positively correlated with increased anxiety and exaggerated stress response (Frokjaer et al., 2008). Increased 5HT2A receptor binding has been reported in people with psychiatric conditions including depression (Shelton, Sanders-Bush, Manier, & Lewis, 2009), neuroticism (Frokjaer et al., 2008), borderline personality disorder (Soloff et al., 2007), impulsive aggression (Rosell et al., 2010), and completed suicide (Anisman et al., 2008). Anxiety and stress are important triggers for relapse to substance use (Sinha & Li, 2007), so it is possible that 5HT2A receptor downregulation by classic hallucinogens could alter and diminish stress-induced relapse. Basic research in the addiction field confirms the importance of the 5HT2A receptor. Increased activity in 5HT2A-mediated pathways relative to 5HT2C pathways is associated with increased response disinhibition and cue response in rat models of cocaine addiction (Cunningham & Anastasio, 2014). The 5HT2A antagonists ritanserin and amperozide suppress alcohol consumption in animal models (B. A. Johnson, 2008), although ritanserin did not improve drinking outcomes in people with alcohol dependence in two large-scale clinical trials (B. A. Johnson et al., 1996; Wiesbeck, Weijers, Chick, Naranjo, & Boening, 1999).

There is some evidence that classic hallucinogens can induce neuroplastic changes, suggesting a possible biological basis for persisting behavioral change. Classic hallucinogens have effects on expression of brain-derived neurotrophic factor (BDNF) and glial cell line-derived neurotrophic factor (GDNF; Tsuchioka, Takebayashi, Hisaoka, Maeda, & Nakata, 2008; Vaidya, Marek, Aghajanian, & Duman, 1997). BDNF and GDNF are neurotrophic factors which are relevant to addiction and other psychiatric disorders and play critical roles in neurogenesis, synaptic plasticity, learning, and memory (Ghitza et al., 2010). BDNF and GDNF can facilitate or inhibit addictive behaviors in rats depending on the drug type and anatomical site of action, and the specific behavioral model being used (Ghitza et al., 2010). Through its action at 5HT2A receptors, the classic hallucinogen 2,5-dimethoxy-4-iodoamphetamine induces

remodeling of pyramidal cell dendrites (Jones et al., 2009). The effects of classic hallucinogens on adult neurogenesis have not been established, although a recent publication began to explore these effects (Catlow, Song, Paredes, Kirstein, & Sanchez-Ramos, 2013).

Neuroimaging Studies

Recent neuroimaging studies in humans are providing insight into the acute effects of classic hallucinogens on brain activity, and their relationships to changes in consciousness. Psilocybin appears to cause a loosening of organization in brain activity, decreasing coupling of activity within functional networks such as the default mode network, and increasing functional connectivity between networks (Carhart-Harris et al., 2012; Carhart-Harris et al., 2013; Carhart-Harris et al., 2014; Roseman, Leech, Feilding, Nutt, & Carhart-Harris, 2014; Tagliazucchi, Carhart-Harris, Leech, Nutt, & Chialvo, 2014). A recent publication reported that "ego disintegration" during psilocybin administration was associated with decreased functional connectivity of the medial temporal lobe (anterior parahippocampal cortex in particular) and decreased functional integrity of the salience network (Lebedev et al., 2015). Evidence also suggests that psilocybin acts to enhance processing of positive stimuli and decrease processing of negative stimuli (Kometer et al., 2012; Kraehenmann et al., 2014), potentially resulting in improved mood. These findings are relevant to addiction treatment because negative affect is an important predictor of relapse in addiction (Connors, Maisto, & Donovan, 1996). Although these findings provide important information about the acute effects of classic hallucinogens on brain activity, it is important to remember that all of these studies were conducted during the acute effects of psilocybin. Persisting effects would be more directly relevant to therapeutic applications. There have not yet been any published studies of persisting effects of classic hallucinogen administration on brain function in humans.

The Role of Subjective Experience

Clinical work with psychedelics has generally assumed that the patient's conscious experience during the drug's acute effects is essential for long-term clinical benefit (Grof, 2008; Hoffer, 1967; Masters & Houston, 2000; Pahnke et al., 1970; Sherwood et al., 1962). Most of the clinical studies conducted in North America using LSD in the treatment of addiction or existential anxiety in terminal cancer during the 1950s to 1970s employed the psychedelic model described above. However, past studies of addiction treatment with classic

hallucinogens have not assessed participants' experiences quantitatively. Recent pilot work with psilocybin for cigarette addiction demonstrated that patients who maintained abstinence after treatment had stronger mystical-type experiences on psilocybin than those who did not (Garcia-Romeu, Griffiths, & Johnson, 2014). In the recent pilot study of psilocybin for alcohol dependence, both mystical experience and broader measures of the intensity of subjective effects were associated with improvement in drinking (Bogenschutz et al., 2015). The idea that a "peak-psychedelic" or "mystical-type" experience can lead to lasting behavior change is consistent with the concept of "spiritual awakening" in the context of Alcoholics Anonymous (Forcehimes, 2004). Indeed, based on his own LSD experiences Bill Wilson, the founder of Alcoholics Anonymous, was supportive of the use of LSD to help alcoholics experience spiritual insight (Kurtz, 2008).

Persisting Psychological Changes

A number of persisting psychological changes have been reported following administration of classic hallucinogens (Bogenschutz & Pommy, 2012). Long-term follow-up of normal volunteers who received psilocybin has demonstrated increase in the personality dimension of openness, correlated with the intensity of mystical experience (59). Positive behavior change and improvement in well-being and life satisfaction have also been reported (60). The recently published pilot studies of psilocybin for alcohol and nicotine dependence have reported decreases in craving and increases in self-efficacy following psilocybin administration (Bogenschutz et al., 2015; M. W. Johnson et al., 2014). However, controlled trials have not yet been conducted that would allow rigorous testing of such possible mediators of therapeutic effects.

Functions of Therapy

Often, when psychotherapy is provided in the context of a pharmacological treatment, the two components of treatment may be considered to be relatively independent. In some cases, psychotherapy is used adjunctively, to provide general support and monitoring, and to encourage adherence to the pharmacologic treatment. The latter is often the case in research studies designed to test the efficacy of medications. However, the situation in hallucinogen-assisted therapy is much more complex: intentions and preparation, the psychedelic experience itself, and the meaning that is made of the experience are all thought to be very important determinants of the therapeutic outcome.

Maximizing Safety

M. Johnson et al. (2008) have published guidelines for maximizing safety and minimizing risk in the administration of classic hallucinogens. Most of the principles are integrally related to the psychosocial treatment. Careful selection of patients/subjects is important, particularly in order to avoid exposing those at elevated risk for adverse experiences due to personal or family psychiatric history or serious medical problems. Sufficient time, generally at least several hours over several sessions, should be allowed to prepare the participant for the session(s) in which the medication is administered. A critical element of this process is the establishment of rapport and trust between the therapists and the patients. Most clinical studies have used a team of two therapists, usually a female and a male, who both are present during the drug administration sessions and most if not all of the other therapy sessions. This is done primarily to increase the amount of support available to the patient during the drug administration sessions. The physical environment for the sessions should be comfortable and calm, and homelike rather than clinical to the extent possible. The therapy team should be prepared to deal with the unlikely event of any medical or psychiatric emergency that may arise. A physician should be immediately available if one of the therapists is not a physician, and emergency medications should be on hand to treat hypertension, anxiety, and psychosis, although these have rarely if ever been needed in recent trials. Finally, the therapy should include adequate time for "debriefing" and follow-up. In addition to the therapeutic role of debriefing, this allows for identification, monitoring, and if necessary treatment of any persisting adverse effects should they arise.

Optimizing Set and Setting to Maximize Therapeutic Effects

According to "set and setting" hypothesis originally elaborated by Leary, Litwin, and Metzner (1963), the mental state of the participant (including expectancies and intentions in approaching a drug administration session) and the setting of the session will affect both the experience during the session and the persisting effects after the session (M. Johnson et al., 2008). While this concept has good face validity and is generally accepted, there has been hardly any research to identify specific set and setting factors contributing to specific outcomes. One recent report identified several individual state and trait variables that affected subjective responses to psilocybin, including level of activity and emotional excitability prior to the session, and the personality trait of Absorption. (Studerus, Gamma, Kometer, & Vollenweider, 2012). In addition, participating in a positron emission study during the session was associated

with increased negative experiences. It seems reasonable to suppose that a patient is more likely to experience therapeutic benefit if his or her intention in taking the drug is therapeutic (rather than to satisfying curiosity or to get high). For example, one would not necessarily expect therapeutic effects in people with alcohol use disorders who are not interested in changing their drinking. However, there are no data to the importance of set and setting on therapeutic outcome.

If one hypothesizes that expectancies and intentions may be important predictors of outcome, this has implications for the psychosocial treatment. Positive expectancies can be systematically encouraged in the psychosocial therapy, through suggestion, affirmation, and/or reflection of positive expectancies or hopes voiced by patients. Patients' intentions for positive change could be maximized through the use of psychosocial treatment designed to heighten motivation, for example, motivational interviewing (Miller & Rollnick, 2002).

From Experience to Lasting Change

Even the most impressive psychedelic experiences are transitory, whereas the desired therapeutic effects are hoped to persist for much longer periods of time. One widely used approach to maximize the long-term positive effects of a psychedelic experience is to devote therapy time to the process of "debriefing" or "integration" of the experience. In the debriefing process, the patient provides a full account of the experience, relatively soon (hours to a few days) after the experience, in as much detail as possible, and is asked to reflect on the significance of the experience, and to describe any persisting positive or negative effects that are apparent. "Integration" includes the debriefing process but may also include additional therapy sessions over weeks to months, to further reflect on or create the meaning of the session, and to continue exploration of material that emerged during or after the session. In the context of treatment, this process would also include exploring the meaning and implications of the experience in relation to the area of desired change, possibly including (a) new understanding of the symptoms, (b) change in the symptoms or how they are experienced, (c) new intentions around management of the symptoms, (d) new insights about how the symptoms can be managed, and (e) behavioral changes made in order to better manage the symptoms.

Potential for Synergy With Medication Effects

In clinical applications, the psychosocial treatment should be compatible with the hypothesized mechanisms of drug action, and ideally designed to work

synergistically with the pharmacologic treatment to produce the effects that are thought to promote therapeutic change. Many empirically validated forms of psychosocial treatment for addictions appear to be adaptable for use in the context of hallucinogen-assisted treatment, including cognitive behavioral approaches (Magill & Ray, 2009), 12-step facilitation (Project MATCH Research Group, 1997, 1998a; Tonigan & Bogenschutz, 2008), motivational interviewing/MET (Lundhal & Burke, 2009), family/couples therapies (Powers, Vedel, & Emmelkamp, 2008; Roozen, de Waart, & van der Kroft, 2010), and mindfulness-based approaches (S. Bowen et al., 2014; Witkiewitz et al., 2014). These various forms of therapies would be expected to be synergistic with particular therapeutic mechanisms. For example, as noted above, motivational interviewing might be particularly useful to optimize therapeutic intention prior to sessions. 12-Step facilitation and mindfulness approaches might be particularly useful in enhancing change related to spiritual aspects of the psychedelic experience, whereas cognitive behavioral and behavioral approaches could be more effective if it were the case that participants were in a state of heightened neuroplastic potential after treatment with a psychedelic. Family and couples therapies might capitalize on the increased salience of relationships which is reported by many who receive treatment with psychedelics. Since the actual mechanisms of psychedelic treatment are not yet well understood, these thoughts are pure conjecture. However, formal testing of such mechanisms can be built into clinical trials by including mediational analyses in the a priori statistical analysis plan.

Are You Experienced?

It has often been argued that therapists are more effective in conducting psychedelic-assisted treatments if they have personal experience with psychedelics (Eisner & Cohen, 1958; Jensen, 1962). Personal experience could enhance understanding, particularly in working with patients to make sense of experiences very different from what most people experience normally. Personal experience could also serve as an obstacle since the therapist may tend to assume similarities between the participant's experience and the therapist's experience, when similarities may not in fact exist. It was once assumed that alcohol counselors needed to have personal experience with alcoholism to be effective, but this claim has been refuted (Culbreth, 2000; Project MATCH Research Group, 1998b). Ultimately, this is an empirical question which could be answered in the context of clinical trials in the future, if both experienced and psychedelic-naive therapists are included. In the current wave of clinical research on psychedelics, psychedelic sessions have not been provided to therapists planning to work on clinical trials with psilocybin, nor has experience with psychedelics been required.

Issues Specific to Research

For most pharmacotherapy trials, psychosocial treatment can be thought of as a "platform" on which the effects of medications can be tested. In many cases, the psychosocial treatment is intentionally kept at a low level of intensity to minimize placebo response, and treatment may be focused on medication adherence to maximize treatment exposure. Because an experimental treatment is by definition possibly ineffective, and any placebo or control medication is intended to be ineffective, for ethical reasons the psychosocial treatment should provide at least some benefit if there are known effective treatments to which the participants would otherwise have access. On the other hand, there are studies in which contrasting psychosocial treatment approaches are tested in the context of treatment with specific effective medications, for example, opioid replacement medications or antidepressants.

In any psychopharmacotherapy trial, it is desirable to standardize psychosocial treatment, even if this treatment consists only of "medical management" by the treating clinician. Treatment is usually standardized through use of a manual, with uniform procedures for training, supervision, and fidelity monitoring. As in any clinical trial employing a psychosocial treatment, therapists providing psychosocial treatment in the context of treatment with psychedelics should be trained to fidelity, and supervised and monitored appropriately.

Description of a Therapy Model

We are currently conducting a randomized, double-blind, controlled trial of psilocybin-assisted treatment for alcoholism (NCT02061293). The psychosocial treatment procedures are similar to those we used in the pilot study we have completed (Bogenschutz et al., 2015), including sessions with content directly addressing the problematic use of alcohol, other sessions focused on preparation for and debriefing of the medication sessions, and the medication sessions themselves. Figure 1 illustrates how the behavioral interventions interface each other and with the three drug administration sessions. For simplicity, the behavioral interventions that have to do with the administration of psilocybin will be referred to as PSI. The alcohol therapy component consists of MET followed by Cognitive Behavioral Therapy sessions including implementation of specific strategies for change during the later sessions. To distinguish it from more typical MET approaches, this therapy will be called Motivational Enhancement and Taking Action (META). Both components are manualized.

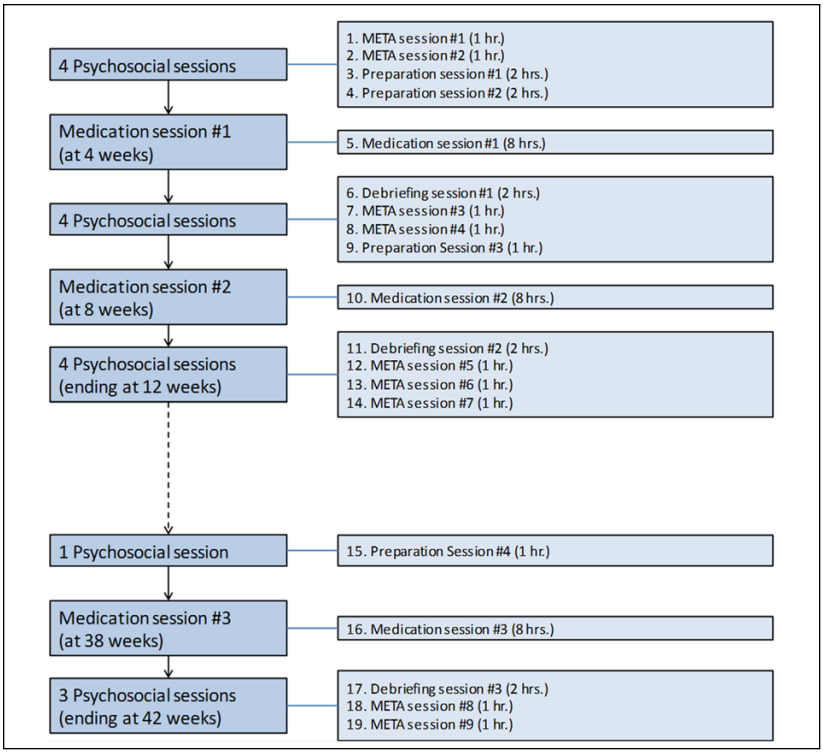

Figure 1. Overview of treatment model.
Note. META = Motivational Enhancement and Taking Action.

The therapy is conducted by a team of two therapists, one responsible for the alcohol-specific treatment (META), the other responsible for the hallucinogen-specific treatment (PSI). The two therapists forming a dyad are of opposite genders if possible, and should never both be of the gender opposite that of the patient. Both therapists attend all sessions if possible, but if necessary the META therapist may conduct the META sessions alone and the PSI therapist may conduct preparation and debriefing sessions alone. Both therapists must attend the drug administration sessions. Substitutes for drug administration sessions may be used only if they have had at least two meetings with the participant prior to the session. The separation of roles is intended to maintain clarity about the purpose of the sessions, while the attendance of the META therapist at PSI sessions allows the two components to function as an integrated whole. A practical advantage to the separation of

roles is that each therapist only needs to have a high degree of expertise in his or her respective area. This would be a practical advantage for future clinical use, where a patient might be in treatment for alcoholism and have a therapist or counselor, who could refer the patient to a psychedelic therapy center and participate in the treatment if the patient was not responding to conventional treatment.

Motivational Enhancement and Taking Action

The META content is largely based on materials used previously in multisite trials (Miller, 2004; Miller, Zweben, Diclemente, & Rychtarik, 1992; Obert & Farentinos, 2000). Because the number of sessions indicated is greater than the three to four sessions typically used in MET, and because of the relatively high motivation for change seen in many of the pilot study participants following the first psilocybin session, the META manual developed for this protocol includes greater emphasis on exploration of a patient's goals for change and the development and implementation of specific strategies to meet those change goals.

The first two META sessions occur during the month prior to the first medication session (psilocybin or control). In the first session, the therapist uses open motivational interviewing to elicit and clarify the patient's intrinsic motivation for change. During this session, therapists also offer feedback from the baseline assessment, specifically focusing on drinking percentile relative to population norms, consequences of drinking, and motivation for change. The focus of the second session is on eliciting the patient's most important values using a values card-sort and exploring the discrepancy between values and behavior as motivation for change.

The two subsequent META sessions (Sessions 3 and 4) follow up on the patient's goals for change and experiences during the first medication session in relation to the key values identified during META Session 2. During these sessions, the therapist and patient develop a specific treatment plan for the remaining sessions. These sessions use a cognitive behavioral framework which uses the acronym STORC, for Situations, Thoughts, Organic patterns (i.e., physical sensations and emotions), Responses, and Consequences. At each step in the STORC cycle there are usually a number of things that can be done to promote change. Therapists work with patients to identify specific components of STORC sequences in which the patient seems to be encountering difficulties. Patients are given a workbook that includes a menu of strategies in each of these domains. For example, the Situational Factors Menu includes modules on how to identify problem situations, monitoring urges, ways to change your environment, how to ask others for help, and how

to surround yourself with support; the Organic Patterns Menu includes modules on exercise, mindfulness practice, sleep hygiene, and nutrition. For each change goal, the therapist works with the patient to identify strategies potentially useful in facilitating change, and together they choose strategies which form the basis of an individualized change plan which provides the structure for the subsequent META sessions.

In contrast to the first four sessions which are highly structured in that all patients receive similar content on feedback, values exercise, and structuring a treatment plan, the remaining sessions are individualized to the unique needs of each patient. Specific pull-out teaching modules with worksheets—to be completed during and between sessions—offer structure for therapists in the delivery of this portion of the intervention. This allows therapists to use flexible discretion as to the content of these sessions as the needs of the patient evolve. Activities that may be used during these sessions will include 12-step or other self-help involvement, mindfulness practice, exercise, changes in social network, cognitive behavioral self-help, alternative sources of positive reinforcement that do not involve substance use, or further formal alcohol treatment. The plan for change is revisited and revised as needed during each session, and therapists will reinforce progress and revise the plan as needed in collaboration with the patient. Consistent with the motivational interviewing style, these remaining sessions are also intended to be a time to reengage the patient, continue discussions on experiences and feelings resulting from the medication sessions, support continuing efforts, and address any barriers to goal achievement.

Preparation, Support, and Integration

Preparation Sessions. There are two preparation sessions before the first drug administration session, and one before the second and third drug administration sessions. The primary goals for the first preparation session are to provide an overview of the process and rationale of the study intervention; to conduct a detailed life review including information about the participant's history, current situation, personality, relationships, goals, and so on; and to facilitate the development of rapport between the participant and the clinicians. The second session includes a review of motivation and expectations for the study; detailed information about the possible physiological and psychological effects of study medication; advice as to how to deal with dysphoric reactions to study medication, should they occur; identification of any personally meaningful items that the participant will bring to the session (e.g., images, family photographs, objects of personal, or religious significance); discussion of ground rules for the session; and addressing questions,

concerns, hopes, and fears related to the medication-assisted treatment. In the third preparation session (prior to the second and third drug administration sessions), each topic is revisited, plans are revised based on the experience in the prior drug administration sessions, and the therapists and participant decide on the dose of medication to be used in the session within the parameters of the study protocol.

Drug Administration Sessions. In our current trial, participants receive doses of psilocybin ranging from 25 mg/70 kg to 40 mg/70 kg, or control medication. The interventions employed during the drug administration sessions are intended to help the participant use the session as productively as possible, rather than to provide directive therapy. Participants wear eyeshades and listen to a standardized program of music through headphones during most of the session. Brief check-ins are used to assess the participant's mental state, and to monitor vital signs. Therapists may provide reassurance, support, grounding, and redirection as needed. Medications are available to treat dangerously elevated blood pressure, severe anxiety, or psychotic symptoms, but it has not yet been necessary to use any of these medications. Participants are encouraged to focus on their internal experience as much as possible, and to "trust, let go, and be open" to the experience rather than try to direct or control it. Once the drug effects have largely subsided (after 5-6 hours) participants may spend increasing amounts of time interacting with the therapists and discussing the content and meaning of the experience. After 8 hours, a formal mental status examination is conducted to ensure safety, and the patient is picked up by a friend or family member who has been briefed by the therapists, and has agreed to stay overnight with the patient. Participants are asked to write down an account of the experience during the evening after the experience, for discussion at subsequent debriefing sessions.

Debriefing Sessions. A debriefing session is scheduled the day after each drug administration session. The basic content of these sessions includes open-ended inquiry concerning the drug administration session and invitation to reflect on the experience. Participants are invited to consider the meaning and implications of the experience, including any changes in views of self, relationships, values, and spirituality. Using the motivational interviewing style, therapists elicit discussion of how the session has affected the participant's relationship to alcohol and desire to change drinking behavior. Safety assessment is also completed (mental status exam and follow-up on any adverse events).

Discussion

The therapy model described above was designed for use in a particular context: A clinical trial of psilocybin-assisted treatment for alcoholism, in which psilocybin is administered in relatively high doses on no more than three occasions. If psilocybin were to become an accepted treatment for alcoholism, it would initially be advisable to use the models used in the trials that showed to be efficacious. However, further work would be necessary to optimize the overall therapeutic effects of the combined pharmacologic/psychotherapeutic treatment.

Although the model presented here is similar to the model that was used historically in psychedelic treatment of addiction, other models are certainly possible, such as lower dose sessions and longer term treatment with regular drug administration sessions over time, more similar to the psycholytic model or sacramental use in religious contexts. The components of the therapy were assembled based on the constraints of this trial, historical models of psychedelic therapy, recent studies of hallucinogen administration in nonclinical populations, and existing models of psychotherapy for alcoholism. While we believe that this model has been largely successful in meeting the needs of this particular context, we have no way of knowing whether or to what extent the model is optimally suited to maximize whatever therapeutic benefits are possible with psychedelic-assisted treatment of alcoholism. Below, we provide a critique of several of the key decisions that were made, and consider the possible merits of other solutions. These decisions are all relevant to treatment of other disorders using psychedelic-assisted therapy, although the specifics of the treatment models will naturally differ depending on the purpose of the treatment.

Maximizing Synergy Between Psychedelic Medication and Disorder-Specific Therapy

Ideally, the disorder-specific therapy would be designed to mobilize or reinforce the change mechanisms activated by therapeutic administration of the psychedelic medication. However, since little is known about how psychedelic-assisted treatments actually work, we chose to use a fairly typical outpatient alcoholism therapy model which would be expected to be at least moderately effective on its own. We also made the model flexible, using a fairly wide menu of change strategies within a cognitive behavioral framework. Likewise, in the PSI preparation sessions, we did not suggest that any particular type of experience would be likely to occur or be more likely to be helpful, instead describing a broad range of possible experiences including

sensory, autobiographical, and symbolic as well as mystical-type experiences. If in the future research were to show that particular change mechanisms were critical to successful outcomes in psychedelic-assisted treatment, it might then make sense to target these mechanisms more specifically in the therapy, and possibly to be more directive with respect to the experience itself.

Therapist Roles and Format of Therapy

In constructing this therapy model, we have followed tradition and contemporary practice by using a therapist dyad to conduct therapy with an individual patient. This unusual configuration differs from the usual clinical model of a single therapist treating an individual patient, or one or two therapists conducting group therapy. There are definite advantages to this approach in terms of the amount of support that can be provided, and the presence of both male and female therapists during the medication session. It also allows the separation of roles for the therapists providing the alcohol-focused portion of the therapy and the parts of the therapy related to the administration of the psychedelic medication. However, there is a substantial cost to this arrangement in terms of therapist time. Also, there are potential advantages to group therapy related to the mutual support and understanding that patients could provide one another concerning their psychedelic experiences, which might be difficult to obtain from other people in their lives who have not had such experiences. One possible model, not yet explored in the current wave of clinical research on psychedelics, is for group therapy to supplement individual sessions.

It is also not clear at this point how much is gained by having separate individuals responsible for the two main components of the therapy rather than having a single therapist or both of two therapists take responsibility for the whole of the therapy and perhaps conducting the entire treatment in a more integrated and seamless manner. In practice, we have found that both therapists participate in both components of the therapy to some extent, and often both META and PSI sessions include some attention to the other component of the therapy. So this distinction may not be as clear-cut as it might appear on paper.

Conclusions

The administration of psychedelics can be integrated with evidence-based psychotherapy for alcoholism for use in clinical trials of psychedelic medicines. Constructing a coherent treatment model is complex, and many decisions must

be made in developing a psychedelic-assisted treatment for a specific disorder such as alcohol dependence. We have summarized our thought process in developing the specific treatment model we are currently using in a clinical trial of psilocybin-assisted treatment of alcoholism, and have described the features of this model. This model appears to be practical, and similar models appear to be feasible for clinical use should psychedelic medications become accepted as safe and effective treatments. However, we make no claims as to the superiority of this model to any other approach. Optimizing the psychotherapeutic components of psychedelic-assisted treatments will require better understanding of how these treatments actually work, and prospective trials of different treatment approaches to determine which are actually the most effective. If efficacy studies show that psychedelic-assisted treatments are clinically useful, there will be a need for considerable research on optimization of treatment models, as well as procedures for training and certification for those wishing to provide these treatments.

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References

Abuzzahab, F. S. Sr., & Anderson, B. J. (1971). A review of LSD treatment in alcoholism. *International Pharmacopsychiatry*, *6*, 223-235.

Albaugh, B. J., & Anderson, P. O. (1974). Peyote in the treatment of alcoholism among American Indians. *American Journal of Psychiatry*, *131*, 1247-1250.

Anisman, H., Du, L., Palkovits, M., Faludi, G., Kovacs, G. G., Szontagh-Kishazi, P., . . . Poulter, M. O. (2008). Serotonin receptor subtype and p11 mRNA expression in stress-relevant brain regions of suicide and control subjects. *Journal of Psychiatry & Neuroscience*, *33*, 131-141.

Barbosa, P. C., Mizumoto, S., Bogenschutz, M. P., & Strassman, R. J. (2012). Health status of ayahuasca users. *Drug Testing and Analysis*, *4*, 601-609.

Bogenschutz, M. P., Forcehimes, A. A., Pommy, J. A., Wilcox, C. E., Barbosa, P. C., & Strassman, R. J. (2015). Psilocybin-assisted treatment for alcohol dependence: A proof-of-concept study. *Journal of Psychopharmacology*, *29*, 289-299.

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*, 543-555.

Bowen, S., Witkiewitz, K., Clifasefi, S. L., Grow, J., Chawla, N., Hsu, S. H., . . . Larimer, M. E. (2014). Relative efficacy of mindfulness-based relapse prevention, standard relapse prevention, and treatment as usual for substance use disorders: A randomized clinical trial. *JAMA Psychiatry*, *71*, 547-556.

Bowen, W. T., Soskin, R. A., & Chotlos, J. W. (1970). Lysergic acid diethylamide as a variable in the hospital treatment of alcoholism: A follow-up study. *Journal of Nervous and Mental Disease*, *150*, 111-118.

Buckman, J. (1967). Theoretical aspects of LSD therapy. In H. A. Abramson (Ed.), *The use of LSD in psychotherapy and alcoholism* (pp. 83-100). Indianapolis, IN: Bobbs-Merrill.

Busch, A. K., & Johnson, W. C. (1950). L.S.D. 25 as an aid in psychotherapy: Preliminary report of a new drug. *Diseases of the Nervous System*, *11*, 241-243.

Carhart-Harris, R. L., Erritzoe, D., Williams, T., Stone, J. M., Reed, L. J., Colasanti, A., . . . Nutt, D. J. (2012). Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. *Proceedings of the National Academy of Sciences of the United States of America*, *109*, 2138-2143.

Carhart-Harris, R. L., Leech, R., Erritzoe, D., Williams, T. M., Stone, J. M., Evans, J., . . . Nutt, D. J. (2013). Functional connectivity measures after psilocybin inform a novel hypothesis of early psychosis. *Schizophrenia Bulletin*, *39*, 1343-1351.

Carhart-Harris, R. L., Leech, R., Hellyer, P. J., Shanahan, M., Feilding, A., Tagliazucchi, E., . . . Nutt, D. (2014). The entropic brain: A theory of conscious states informed by neuroimaging research with psychedelic drugs. *Frontiers in Human Neuroscience*, *8*, 20.

Catlow, B. J., Song, S., Paredes, D. A., Kirstein, C. L., & Sanchez-Ramos, J. (2013). Effects of psilocybin on hippocampal neurogenesis and extinction of trace fear conditioning. *Experimental Brain Research*, *228*, 481-491.

Connors, G. J., Maisto, S. A., & Donovan, D. M. (1996). Conceptualizations of relapse: A summary of psychological and psychobiological models. *Addiction*, *91*(Suppl. 1), S5-S14.

Culbreth, J. R. (2000). Substance abuse counselors with and without a personal history of chemical dependency: A review of the literature. *Alcoholism Treatment Quarterly*, *18*, 67-82.

Cunningham, K. A., & Anastasio, N. C. (2014). Serotonin at the nexus of impulsivity and cue reactivity in cocaine addiction. *Neuropharmacology*, *76*(Pt B), 460-478.

Doering-Silveira, E., Grob, C. S., de Rios, M. D., Lopez, E., Alonso, L. K., Tacla, C., & Da Silveira, D. X. (2005). Report on psychoactive drug use among adolescents using ayahuasca within a religious context. *Journal of Psychoactive Drugs*, *37*, 141-144.

Dyck, E. (2006). "Hitting highs at rock bottom": LSD treatment for alcoholism, 1950–1970. *Social History of Medicine*, *19*, 313-329.

Eisner, B. G., & Cohen, S. (1958). Psychotherapy with lysergic acid diethylamide. *Journal of Nervous and Mental Disease*, *127*, 528-539.

El-Seedi, H. R., De Smet, P. A., Beck, O., Possnert, G., & Bruhn, J. G. (2005). Prehistoric peyote use: Alkaloid analysis and radiocarbon dating of archaeological specimens of Lophophora from Texas. *Journal of Ethnopharmacology*, *101*, 238-242.

Fabregas, J. M., Gonzalez, D., Fondevila, S., Cutchet, M., Fernandez, X., Barbosa, P. C., . . . Bouso, J. C. (2010). Assessment of addiction severity among ritual users of ayahuasca. *Drug and Alcohol Dependence*, *111*, 257-261.

Forcehimes, A. A. (2004). *De profundis*: Spiritual transformations in Alcoholics Anonymous. *Journal of Clinical Psychology*, *60*, 503-517.

Frokjaer, V. G., Mortensen, E. L., Nielsen, F. A., Haugbol, S., Pinborg, L. H., Adams, K. H., . . . Knudsen, G. M. (2008). Frontolimbic serotonin 2A receptor binding in healthy subjects is associated with personality risk factors for affective disorder. *Biological Psychiatry*, *63*, 569-576.

Garcia-Romeu, A., Griffiths, R. R., & Johnson, M. W. (2014). Psilocybin-occasioned mystical experiences in the treatment of tobacco addiction. *Current Drug Abuse Reviews*, *7*, 157-164.

Garrity, J. F. (2000). Jesus, peyote, and the holy people: Alcohol abuse and the ethos of power in Navajo healing. *Medical Anthropology Quarterly*, *14*, 521-542.

Ghitza, U. E., Zhai, H., Wu, P., Airavaara, M., Shaham, Y., & Lu, L. (2010). Role of BDNF and GDNF in drug reward and relapse: A review. *Neuroscience & Biobehavioral Reviews*, *35*, 157-171.

Grinspoon, L., & Balakar, J. B. (1997). *Psychedelic drugs reconsidered*. New York, NY: The Lindesmith Center.

Grof, S. (2008). *LSD psychotherapy* (4th ed.). Ben Lomond, CA: Multidisciplinary Association for Psychedelic Studies.

Halberstadt, A. L. (2015). Recent advances in the neuropsychopharmacology of serotonergic hallucinogens. *Behavioural Brain Research*, *277*, 99-120.

Halpern, J. H. (1996). The use of hallucinogens in the treatment of addiction. *Addiction Research*, *4*, 177-189.

Halpern, J. H., Sherwood, A. R., Hudson, J. I., Yurgelun-Todd, D., & Pope, H. G. (2005). Psychological and cognitive effects of long-term peyote use among Native Americans. *Biological Psychiatry*, *58*, 624-631.

Halpern, J. H., Sherwood, A. R., Passie, T., Blackwell, K. C., & Ruttenber, A. J. (2008). Evidence of health and safety in American members of a religion who use a hallucinogenic sacrament. *Medical Science Monitor*, *14*(8), SR15-SR22.

Heffter, A. (1896). Ueber Cacteenalkaloïde [Concerning cactus alkaloids]. *Berichte der deutschen chemischen Gesellschaft, 29*, 216-227.

Heffter, A. (1898). Ueber Pellote: Beiträge zur chemischen und pharmakologischen Kenntniss der Cacteen Zweite Mittheilung [Concerning Peyote: Contributions to the chemical and pharmacological understanding of Cacti, second communication]. *Naunyn-Schmiedeberg's Archives of Pharmacology, 40*, 385-429.

Hoffer, A. (1967). A program for treatment of alcoholism: LSD, malvaria, and nicotinic acid. In H. A. Abramson (Ed.), *The use of LSD in psychotherapy and alcoholism* (pp. 343-406). Indianapolis, IN: Bobbs-Merrill.

Hofmann, A. (1979). How LSD originated. *Journal of Psychedelic Drugs*, *11*, 53-60.

Hofmann, A., Frey, A., Ott, H., Petrzilka, T., & Troxler, F. (1958). Konstitutionsaufklärung und Synthese von Psilocybin [Elucidation of structure and synthesis of psilocybin]. *Experientia, 14*, 397-401.

Hofmann, A., Heim, R., Brack, A., & Kobel, H. (1958). Psilocybin. ein psychotroper Wirkstoff aus dem mexikanischen Rauschpilz [Psilocybin: a psychotropic active substance from the Mexican intoxicating mushroom]. *Revue de Mycologie, 22*, 17-21.

Hollister, L. E., Shelton, J., & Krieger, G. (1969). A controlled comparison of lysergic acid diethylamide (LSD) and dextroamphetmine in alcoholics. *American Journal of Psychiatry*, *125*, 1352-1357.

Jensen, S. E. (1962). Treatment program for alcoholics in a mental hospital. *Quarterly Journal of Studies on Alcohol*, *23*, 315-320.

Johnson, B. A. (2008). Update on neuropharmacological treatments for alcoholism: Scientific basis and clinical findings. *Biochemical Pharmacology*, *75*, 34-56.

Johnson, B. A., Jasinski, D. R., Galloway, G. P., Kranzler, H., Weinreib, R., Anton, R. F., . . . Clyde, C. (1996). Ritanserin in the treatment of alcohol dependence: A multi-center clinical trial. *Psychopharmacology*, *128*, 206-215.

Johnson, M., Richards, W., & Griffiths, R. (2008). Human hallucinogen research: Guidelines for safety. *Journal of Psychopharmacology*, *22*, 603-620.

Johnson, M. W., Garcia-Romeu, A., Cosimano, M. P., & Griffiths, R. R. (2014). Pilot study of the 5-HT2AR agonist psilocybin in the treatment of tobacco addiction. *Journal of Psychopharmacology*, *28*, 983-992.

Jones, K. A., Srivastava, D. P., Allen, J. A., Strachan, R. T., Roth, B. L., & Penzes, P. (2009). Rapid modulation of spine morphology by the 5-HT2A serotonin receptor through kalirin-7 signaling. *Proceedings of the National Academy of Sciences of the United States of America*, *106*, 19575-19580.

Kometer, M., Schmidt, A., Bachmann, R., Studerus, E., Seifritz, E., & Vollenweider, F. X. (2012). Psilocybin biases facial recognition, goal-directed behavior, and mood state toward positive relative to negative emotions through different serotonergic subreceptors. *Biological Psychiatry*, *72*, 898-906.

Kraehenmann, R., Preller, K. H., Scheidegger, M., Pokorny, T., Bosch, O. G., Seifritz, E., & Vollenweider, F. X. (2014). Psilocybin-induced decrease in amygdala reactivity correlates with enhanced positive mood in healthy volunteers. *Biological Psychiatry*, *78*, 572-581.

Krebs, T. S., & Johansen, P. O. (2012). Lysergic acid diethylamide (LSD) for alcoholism: Meta-analysis of randomized controlled trials. *Journal of Psychopharmacology*, *26*, 994-1002.

Krupitsky, E., Burakov, A., Romanova, T., Dunaevsky, I., Strassman, R., & Grinenko, A. (2002). Ketamine psychotherapy for heroin addiction: Immediate effects and two-year follow-up. *Journal of Substance Abuse Treatment*, *23*, 273-283.

Krupitsky, E., Grineko, A., Berkaliev, T., Paley, A., Tetrov, U., Mushkov, K., & Borodikin, Y. (1992). The combination of psychedelic and aversive approaches in alcoholism treatment. *Alcoholism Treatment Quarterly*, *9*, 99-105.

Krupitsky, E. M., Burakov, A. M., Dunaevsky, I. V., Romanova, T. N., Slavina, T. Y., & Grinenko, A. Y. (2007). Single versus repeated sessions of ketamine-assisted psychotherapy for people with heroin dependence. *Journal of Psychoactive Drugs*, *39*, 13-19.

Krupitsky, E. M., & Grinenko, A. Y. (1997). Ketamine psychedelic therapy (KPT): A review of the results of ten years of research. *Journal of Psychoactive Drugs*, *29*, 165-183.

Kunitz, S. J., & Levy, J. E. (1994). *Drinking careers: A twenty-five year study of three Navajo populations*. New Haven, CT: Yale University Press.

Kurtz, E. (2008). Drugs and the spiritual: Bill W. takes LSD. In E. Kurtz (Ed.), *The collected Ernie Kurtz* (pp. 39-50). New York, NY: Authors Choice.

Leary, T., Litwin, G. H., & Metzner, R. (1963). Reactions to psilocybin administered in a supportive environment. *Journal of Nervous and Mental Disease*, *137*, 561-573.

Lebedev, A. V., Lovden, M., Rosenthal, G., Feilding, A., Nutt, D. J., & Carhart-Harris, R. L. (2015). Finding the self by losing the self: Neural correlates of ego-dissolution under psilocybin. *Human Brain Mapping*, *36*, 3137-3153.

Leuner, H. (1967). Present state of psycholytic therapy and its possibilities. In H. A. Abramson (Ed.), *The use of LSD in psychotherapy and alcoholism* (pp. 101-116). Indianapolis, IN: Bobbs-Merrill.

Lu, L., Liu, Y., Zhu, W., Shi, J., Liu, Y., Ling, W., & Kosten, T. (2009). Traditional medicine in the treatment of drug addiction. *American Journal of Drug and Alcohol Abuse*, *35*, 1-11.

Ludwig, A., Levine, J., Stark, L., & Lazar, R. (1969). A clinical study of LSD treatment in alcoholism. *American Journal of Psychiatry*, *126*, 59-69.

Lundhal, B., & Burke, B. L. (2009). The effectiveness and applicability of motivational interviewing: A practice-friendly review of four meta-analyses. *Journal of Clinical Psychology*, *65*, 1232-1245.

Magill, M., & Ray, L. A. (2009). Cognitive-behavioral treatment with adult alcohol and illicit drug users: A meta-analysis of randomized controlled trials. *Journal of Studies on Alcohol and Drugs*, *70*, 516-527.

Mangini, M. (1998). Treatment of alcoholism using psychedelic drugs: A review of the program of research. *Journal of Psychoactive Drugs*, *30*, 381-418.

Masters, R., & Houston, J. (2000). *The varieties of psychedelic experience: The classic guide to the effects of LSD on the human psyche*. Rochester, VT: Park Street Press.

Miller, W. R. (Ed.). (2004). *Combined behavioral intervention manual: A clinical research guide for therapists treating people with alcohol abuse and dependence* (Vol. 1). Rockville, MD: National Institute on Alcohol Abuse and Alcoholism.

Miller, W. R., & Rollnick, S. (2002). *Motivational interviewing: Preparing people for change* (2nd ed.). New York, NY: Guilford Press.

Miller, W. R., Zweben, A., Diclemente, C. C., & Rychtarik, R. G. (1992). *Motivational Enhancement Therapy manual: A clinical research guide for therapists treating individuals with alcohol abuse and dependence* (Vol. 2). Rockville, MD: National Institute on Alcohol Abuse and Alcoholism.

Nichols, D. E. (2004). Hallucinogens. *Pharmacology & Therapeutics*, *101*, 131-181.

Obert, J. L., & Farentinos, C. (2000). *A manual for Motivational Enhancement Treatment (MET) to improve treatment engagement and outcome in subjects seeking treatment for substance abuse* (Manual for Protocol 0004). Bethesda, MD: NIDA Clinical Trials Network.

Pahnke, W. N. (1969). Psychedelic drugs and mystical experience. *International Psychiatry Clinics*, *5*, 149-162.

Pahnke, W. N., Kurland, A. A., Unger, S., Savage, C., & Grof, S. (1970). The experimental use of psychedelic (LSD) psychotherapy. *Journal of the American Medical Association*, *212*, 1856-1863.

Powers, M. B., Vedel, E., & Emmelkamp, P. M. G. (2008). Behavioral couples therapy (BCT) for alcohol and drug use disorders: A meta-analysis. *Clinical Psychology Review*, *28*, 952-962.

Project MATCH Research Group. (1997). Matching alcoholism treatments to client heterogeneity: Project MATCH posttreatment drinking outcomes. *Journal of Studies on Alcohol*, *58*, 7-29.

Project MATCH Research Group. (1998a). Matching alcoholism treatments to client heterogeneity: Project MATCH three-year drinking outcomes. *Alcoholism: Clinical & Experimental Research*, *22*, 1300-1311.

Project MATCH Research Group. (1998b). Therapist effects in three treatments for alcohol problems. *Psychotherapy Research*, *8*, 455-474.

Rinkel, M., Deshon, H. J., Hyde, R. W., & Solomon, H. C. (1952). Experimental schizophrenia-like symptoms. *American Journal of Psychiatry*, *108*, 572-578.

Roozen, H. G., de Waart, R., & van der Kroft, P. (2010). Community reinforcement and family training: An effective option to engage treatment-resistant substance-abusing individuals in treatment. *Addiction*, *105*, 1729-1738.

Rosell, D. R., Thompson, J. L., Slifstein, M., Xu, X., Frankle, W. G., New, A. S., . . . Siever, L. J. (2010). Increased serotonin 2A receptor availability in the orbitofrontal cortex of physically aggressive personality disordered patients. *Biological Psychiatry*, *67*, 1154-1162.

Roseman, L., Leech, R., Feilding, A., Nutt, D. J., & Carhart-Harris, R. L. (2014). The effects of psilocybin and MDMA on between-network resting state functional connectivity in healthy volunteers. *Frontiers in Human Neuroscience*, *8*, 204.

Roy, C. (1973). Indian peyotists and alcohol. *American Journal of Psychiatry*, *130*, 329-330.

Shelton, R. C., Sanders-Bush, E., Manier, D. H., & Lewis, D. A. (2009). Elevated 5-HT 2A receptors in postmortem prefrontal cortex in major depression is associated with reduced activity of protein kinase A. *Neuroscience*, *158*, 1406-1415.

Sherwood, J. N., Stolaroff, M. J., & Harman, W. W. (1962). The psychedelic experience: A new concept in psychotherapy. *Journal of Neuropsychiatry*, *4*, 69-80.

Sinha, R., & Li, C. S. (2007). Imaging stress- and cue-induced drug and alcohol craving: Association with relapse and clinical implications. *Drug and Alcohol Review*, *26*(1), 25-31.

Smart, R. G., Storm, T., Baker, E. F., & Solursh, L. (1966). A controlled study of lysergide in the treatment of alcoholism: 1. The effects on drinking behavior. *Quarterly Journal of Studies on Alcohol*, *27*, 469-482.

Soloff, P. H., Price, J. C., Meltzer, C. C., Fabio, A., Frank, G. K., & Kaye, W. H. (2007). 5HT2A receptor binding is increased in borderline personality disorder. *Biological Psychiatry*, *62*, 580-587.

Strassman, R. J., & Qualls, C. R. (1994). Dose-response study of N,N-dimethyltryptamine in humans: I. Neuroendocrine, autonomic, and cardiovascular effects. *Archives of General Psychiatry*, *51*, 85-97.

Studerus, E., Gamma, A., Kometer, M., & Vollenweider, F. X. (2012). Prediction of psilocybin response in healthy volunteers. *PLoS ONE*, *7*(2), e30800.

Tagliazucchi, E., Carhart-Harris, R., Leech, R., Nutt, D., & Chialvo, D. R. (2014). Enhanced repertoire of brain dynamical states during the psychedelic experience. *Human Brain Mapping*, *35*, 5442-5456.

Tomsovic, M., & Edwards, R. V. (1970). Lysergide treatment of schizophrenic and nonschizophrenic alcoholics: A controlled evaluation. *Quarterly Journal of Studies on Alcohol*, *31*, 932-949.

Tonigan, J. S., & Bogenschutz, M. P. (2008). Utilization of formal treatment and AA: Relative contributions to early abstinence. *Alcoholism: Clinical & Experimental Research*, *32*(6 Suppl.), 695.

Tsuchioka, M., Takebayashi, M., Hisaoka, K., Maeda, N., & Nakata, Y. (2008). Serotonin (5-HT) induces glial cell line-derived neurotrophic factor (GDNF) mRNA expression via the transactivation of fibroblast growth factor receptor 2 (FGFR2) in rat C6 glioma cells. *Journal of Neurochemistry*, *106*, 244-257.

Vaidya, V. A., Marek, G. J., Aghajanian, G. K., & Duman, R. S. (1997). 5-HT2A receptor-mediated regulation of brain-derived neurotrophic factor mRNA in the hippocampus and the neocortex. *Journal of Neuroscience*, *17*, 2785-2795.

Wasson, R. G. (1957, May 13). Seeking the magic mushroom. *Life Magazine*, pp. 100-120.

Wiesbeck, G. A., Weijers, H. G., Chick, J., Naranjo, C. A., & Boening, J. (1999). Ritanserin in relapse prevention in abstinent alcoholics: Results from a placebo-controlled double-blind international multicenter trial. *Alcoholism Clinical & Experimental Research*, *23*, 230-235.

Witkiewitz, K., Warner, K., Sully, B., Barricks, A., Stauffer, C., Thompson, B. L., & Luoma, J. B. (2014). Randomized trial comparing mindfulness-based relapse prevention with relapse prevention for women offenders at a residential addiction treatment center. *Substance Use & Misuse*, *49*, 536-546.

Author Biographies

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Alyssa A. Forcehimes, PhD, is the executive director of Train for Change, the exclusive training partner of the Change Companies. She received her PhD in clinical psychology from the University of New Mexico in 2007. Prior to her current position, she was on the faculty of psychiatry and psychology at the University of New Mexico Health Sciences Center. She has been involved with numerous NIH funded grants examining the effectiveness of behavioral treatments for addiction, with an emphasis on developing effective methods for disseminating evidence-based behavioral treatments in real-world settings. She manages an expert team to meet the demands and opportunities of training, consultation, and evaluation services. She has an outstanding national reputation in best practices for implementation of behavioral change strategies with diverse populations and in diverse settings. With Drs. Miller and Zweben, she coauthored the book *Treating Addiction: A Guide for Professionals* (2011).