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Classic psychedelics in the treatment of substance use disorder: Potential synergies with twelve-step programs

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ABSTRACT

Several pilot studies have provided evidence supporting the potential of classic psychedelics like psilocybin in the treatment of substance use disorders (SUDs). If larger trials confirm efficacy, classic psychedelic-assisted psychotherapy may eventually be integrated into existing addiction treatments such as cognitive behavioral therapy, contingency management, and medication-assisted therapies. Many individuals seeking treatment for SUDs also join twelve-step facilitation (TSF) programs like Alcoholics Anonymous (AA), which are among the most widely available and accessed treatments for alcohol use disorder worldwide. For such individuals, engaging in classic psychedelic-assisted psychotherapy could be seen as controversial, as members of AA/TSF programs have historically rejected medication-assisted treatments in favor of a pharmacotherapy-free approach. We argue that classic psychedelics and the subjective experiences they elicit may represent a special, more compatible case than conventional medications. In support of this claim, we describe Bill Wilson's (the founder of AA) little known experiences with psychedelics and on this basis, we argue that aspects of classic psychedelic treatments could complement AA/TSF programs. We provide a review of clinical trials evaluating psychedelics in the context of SUDs and discuss their potential large-scale impact should they be ultimately integrated into AA/TSF.

In 1934, Bill Wilson was on his fourth attempt to recover from alcohol use disorder (AUD). He was being treated in New York City's Towns Hospital, undergoing an experimental treatment using an admixture containing henbane and belladonna, plants that contain tropane alkaloids, deliriants that are sometimes classified as hallucinogens (Julien, 2001; Lattin, 2020). During this stay, an old friend of Wilson's, who had become sober, tried to convince Wilson to turn to religion for salvation from his addiction. Soon thereafter, while under the influence of the hallucinogenic admixture, Wilson experienced a bright white light and a feeling of great peace, which he interpreted as a spiritual, self-transcendent experience (Kurtz, 2008). After this moment, he reported remaining alcohol-free for the rest of his life (Miller, 2019). Bill Wilson would go on to found Alcoholics Anonymous (AA), the template for all twelve-step facilitation (TSF) programs, with a mission to heal individuals with AUD through a spiritual awakening like the one he himself had experienced.

Several years later, in 1956, Bill Wilson would take another hallucinogen, this time ingesting the classic psychedelic lysergic acid diethylamide (LSD) under the care of Dr. Sidney Cohen and the philosopher and author Gerald Heard. Wilson experienced a deep sense of peace and feelings of connection that, similar to his experience more than 20 years prior, he considered spiritual (Kurtz, 2008). In fact, Wilson later recounted in a letter to Dr. Cohen that through his experience with LSD "all of the assurances of my original experience were renewed, and more" (Lattin, 2012, p. 7). Wilson's positive experiences with LSD (he took the substance several times thereafter) and the similarity it had to his earlier self-transcendent spiritual experience during the henbane/belladonna treatment led him to believe that classic psychedelics like LSD could be used to facilitate transcendent experience and help in the treatment of substance use disorder (SUD).

That the founder of AA believed LSD could be a crucial tool in treating addiction is still often overlooked. This may in part be because Wilson's promotion of LSD was actively suppressed by AA, the very organization that he founded (Miller, 2019). According to some scholars, the board of AA likely believed that his message would be too confusing for its members, opting instead for a policy that advocated for abstinence without pharmacotherapeutic assistance of any kind in treating substance use disorders (Miller, 2019).

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While research interest on the therapeutic potential of classic psychedelics was increasing when Wilson first took LSD, investigation of the topic was subsequently stifled for many years. Although using LSD to help with SUD may have seemed radical at the time, the idea of having a spiritual experience to achieve sobriety was woven into the fabric of AA. The book of AA describes many such experiences, and states that those who have them can go on to have alcohol-free lives (e.g., Alcoholics Anonymous, 2001; pgs 56-57). The book of AA suggests everyone is capable of having a spiritual experience, though they may differ in variety (e.g., sudden vs. slowly-developing), and that these experiences allow for a connection to something greater than themselves, relieving them of the burden of self and paving the way for a drug-free life (Alcoholics Anonymous, (2001) pg 63). The book of AA was written by Bill Wilson well before his LSD experience; however, the parallels to classic psychedelic therapy inducing a mystical experience, which is correlated with better drug-use outcomes (Garcia-Romeu, Griffiths, & Johnson, 2014), are striking.

Research on classic psychedelics has reemerged in the past two decades, and has shown that these substances—LSD and psilocybin (the psychoactive substance in 'magic' mushrooms) in particular—have low toxicity and abuse potential (Johnson et al., 2018; Nichols, 2016; Nutt et al., 2010) and reliably induce experiences often described as 'self-transcendent,' 'peak,' or 'mystical,' which are characterized by a sense of unity, sacredness, ineffability, transcendence of time and space, and deeply felt positive mood (Barrett, Johnson & Griffiths, 2015; Griffiths et al., 2006; Griffiths et al., 2011, 2016, 2018; Johnson et al., 2019; Yaden, Haidt, et al., 2017; Yaden, Le Nguyen, et al., 2017). These classic psychedelic-induced experiences have been linked to lasting benefits such as improved well-being in healthy volunteers (Griffiths et al., 2008; 2018), as well as reduced anxiety in people with life-threatening illness (Grob et al., 2011; Griffiths et al., 2016; Ross et al., 2016; Gasser et al., 2014), reduced depression (Davis et al., 2020; Carhart-Harris et al., 2016; Carhart-Harris et al., 2018; Carhart-Harris et al., 2021; Osório et al., 2015; Sanches et al., 2016; Palhano-Fontes et al., 2019), and, most notably for our interests here— improvements in substance use disorders (Bogenschutz et al., 2015; Krebs & Johansen, 2012; Garcia-Romeu, Griffiths, & Johnson, 2014; Johnson et al., 2014; Savage & McCabe, 1973). This suggestive body of work comes as we face a national and global mental health crisis that necessitates improved treatment options (SAMHSA, 2019; WHO 2018) . Although contemporary published studies on classic psychedelics in the treatment of SUD have thus far constituted small, open-label trials, they have demonstrated notable therapeutic potential for additional ongoing and future research to confirm.

While the use of classic psychedelics for SUDs has shown potential, a number of established treatments have become available in medical settings since Wilson's time. These include cognitive behavioral therapy (CBT), contingency management (CM), and medication assisted treatments (MAT), none of which would preclude the integration of classic psychedelics on philosophical or other grounds, as suggested by successful adoption within classic psychedelic-assisted interventions in pilot studies (e.g., Johnson et al., 2014). However, many people experience substantial barriers to receiving SUD treatment, and dropout rates in SUD treatment average approximately 30% (Lappan et al., 2020; Priester et al., 2016). Many individuals seeking treatment for SUD therefore also engage with AA/TSF, which have shown to be at least as effective as other psychosocial treatments for AUD (Kelly, Humphreys, & Ferri, 2020). Though AA/TSF is often criticized in academic and clinical settings for its philosophical tenets, it has been widely disseminated and is highly accessible. Indeed, according to AA, there are over 120,000 AA groups across 180 countries and over 2 million members (www.aa.org). Compared to established treatments such as CBT, CM, and MAT, the peak, self-transcendent, or mystical experiences that so often result from classic psychedelic therapy seems especially compatible with AA/TSF. Yet, unlike these other treatments, AA/TSF appears unique in its opposition to pharmacotherapy in favor of a clinically controversial 'cold turkey' approach. This raises the question, could classic psychedelic treatments for SUD fit within AA/TSF programs?

In this review, we present findings to support the use of classic psychedelics as a treatment option for SUDs, and argue that despite the historic resistance from AA/TSF programs to any psychoactive drug as an adjunct to SUD treatment, classic psychedelics may represent a special, more compatible case than conventional medications. We argue that the founder of AA/TSF advocated for the use of classic psychedelics as an adjunct to AA/TSF, and that classic psychedelics may operate in part through a subjective experience (see Yaden & Griffiths, 2020) of the kind described in the AA/TSF literature , which would make classic psychedelic administration uniquely well-suited to AA/TSF treatment goals. We conclude by suggesting that classic psychedelic treatments can be seen as complementary in many ways for those who are involved in AA/TSF.

Classic Psychedelics for Substance Use Disorders

We will focus on the so-called 'classic psychedelics', or those that act primarily on the serotonin system, particularly as agonists at the serotonin 2A (5-HT_{2A}) receptor. This particular group of psychedelic substances has received the most research interest in recent years, and it includes psilocybin (the active constituent in psychedelic mushrooms), LSD, mescaline, and dimethyltryptamine (DMT), as well as the DMT containing admixture ayahuasca. These compounds have been shown to be extremely low in physiological toxicity (Strassman, 1984; Gable, 1993; Halpern et al., 1999) and non-addictive (Johnson et al., 2018; Nichols, 2016; Nutt et al., 2010) and typically induce only mild, transient physiological changes, such as modest increases in blood pressure and heart rate (Griffiths et al., 2006; Johnson, Richards, & Griffiths, 2008). Although some risks remain with recreational use—such as cardiac events in those at high cardiovascular risk, destabilization of those with psychotic disorders or predisposition, and high levels of anxiety or dangerous behavior while under the influence (Carbonaro et al., 2016)—these are strongly mitigated in a clinical setting through screening, preparation, monitoring, and follow-up care, to a risk/benefit ratio that compares favorably with many accepted practices in medicine (Johnson, Richards, & Griffiths, 2008).

As mentioned, classic psychedelic-administration studies have provided preliminary evidence suggesting they could be beneficial in treating various psychiatric disorders, including SUDs across a wide variety of substances including tobacco, alcohol, opioids, and cocaine (Krebs & Johansen, 2012; Bogenschutz et al., 2015; Johnson et al., 2014; Savage & McCabe, 1973; Thomas et al., 2013). In addition to classic psychedelic-administration studies, several studies have documented cases in which naturalistic classic psychedelic use, typically without therapeutic intent, is reported to lead to addiction recovery across a wide variety of substances including tobacco, alcohol, opioids, cocaine, methamphetamine, and cannabis (Garcia-Romeu et al., 2019; Garcia-Romeu et al., 2020; Johnson et al., 2017). While the mechanisms underlying the therapeutic efficacy of classic psychedelics are yet to be conclusively elucidated, several clinical studies have found a moderate to strong correlation between treatment outcomes and the level of 'mystical' experience a participant reports (Bogenschutz et al., 2015; Garcia-Romeu, Griffiths, & Johnson, 2014; for a review see Yaden & Griffiths, 2020). Significant relationships between mystical experience and reduction in substance use have been observed in non-clinical survey studies as well (Garcia-Romeu et al., 2019; Garcia-Romeu et al., 2020). These findings suggest an important role for these compounds' ability to reliably induce self-transcendent experiences in participants as part of their therapeutic profile (Johnson et al., 2019; Hendricks, 2018a; Yaden, Haidt, et al., 2017; Yaden, Le Nguyen, et al., 2017).

Classic psychedelics have shown preliminary evidence of efficacy across a wide range of addictions, suggesting the possibility that these substances target an underlying mechanism that is effective across drugs of addiction. Process research focused on change talk may be useful in

understanding this phenomenon (Magill et al., 2018) and some mechanisms such as awe (Hendricks, 2018a; Yaden et al., 2019) or psychological insight (Davis et al., 2021) could be operating across treatment targets. The effectiveness of classic psychedelics across substances of addiction is unusual in MAT for SUD, as most pharmacotherapies are targeted for a specific substance of addiction or pharmacological class sharing a mechanism of action. We address applications of classic psychedelics to various SUDs below.

Alcohol. As suspected by Bill Wilson 70 years ago, recent evidence has upheld classic psychedelic therapy as a possible treatment for AUD. A meta-analysis (Krebs & Johansen, 2012) reviewed six randomized controlled trials of LSD for AUD conducted between 1966 and 1970 (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). Pooled data included 536 participants with a median LSD dose of 500 mcg and showed significant declines in alcohol misuse (59% of AUD patients treated with LSD showed improvements, as compared to 38% of individuals receiving a non-LSD control treatment). More recently, a single-arm open-label pilot study was conducted assessing psilocybin in the treatment of alcohol dependence (Bogenschutz et al., 2015). The researchers followed 10 participants with AUD (with a mean 15.1 years of dependence) for 36 weeks. In that time, they went through two psilocybin administrations with Motivation Enhancement Therapy being provided outside of the psilocybin sessions. The results showed a significant decrease in the percentage of drinking and heavy drinking days (compared to baseline) at all follow up points (Bogenschutz et al., 2015). A larger, double-blind randomized clinical trial of psilocybin-assisted treatment for AUD is currently underway (clinicaltrials.gov: NCT02061293). Reports from classic psychedelic use in naturalistic settings among people reporting alcohol misuse also support these compounds' role in treating AUD. A recent survey study found that out of 343 respondents (the majority of who took a moderate or high dose of LSD [38%] or psilocybin [36%]) 83% no longer met AUD criteria after their classic psychedelic experience (Garcia-Romeu et al., 2019). Anthropological studies of religions that use classic psychedelic-containing plants as sacraments also support a role for the classic psychedelics mescaline and ayahuasca in recovery from AUD (Thomas et al., 2013; Albaugh & Anderson, 1974; Bergman, 1971; Blum, Futterman, & Pascarosa, 1977; de Rios, Grob, & Baker, 2002; Halpern et al., 2008; Fábregas et al., 2010).

Nicotine. To date there has been one single-arm open-label study of psilocybin therapy in nicotine dependent individuals, which followed 15 treatment-seeking participants through a 15-week intervention involving CBT for smoking cessation and two to three administrations of psilocybin (Johnson et al., 2014). The participants had a mean of 6 previous quit attempts, smoking on average 19 cigarettes a day for 31 years preceding the beginning of the study. The cessation protocol consisted of 2 to 3 psilocybin sessions (at weeks 5, 7, and optionally 13) in tandem with weekly CBT counseling. Results were quantified both through subjective questionnaires and confirmed via biochemical assays (exhaled carbon monoxide and urinary cotinine levels). Twelve of 15 participants (80%) showed biochemically-confirmed abstinence at the 6-month follow up. Eleven of these 12 individuals reported cessation after just the first psilocybin administration, and this was biologically verified throughout the following 10 weeks. A long-term follow-up of this study found 10 participants (67%) to be abstinent 12 months after the initial psilocybin administration (Johnson, Garcia-Romeu, & Griffiths, 2017). Furthermore, 12 participants completed a ≥16 months follow-up (mean 30 months follow-up) and 9 (60%) were confirmed as smoking abstinent (Johnson, Garcia-Romeu, & Griffiths, 2017). This preliminary study, though without a control condition, showed a substantially higher rate of cessation than existing behavioral interventions and pharmacotherapies (typically <35% at 6 months post-treatment; Cahill, Stevens, & Lancaster, 2014; Mottillo et al., 2009), suggesting psilocybin-assisted treatment as a potentially efficacious and enduring smoking cessation intervention (Hendricks, 2014). Interestingly, participants who were abstinent at 6-month follow-up had significantly higher session mystical experience scores than those who were smoking at 6-month follow-up, consistent with Wilson's observations regarding the importance of spiritual-type experiences in overcoming addiction (Garcia-Romeu, Griffiths, & Johnson, 2014). An online survey (N=358) also found reductions or complete abstinence in tobacco consumption associated with classic psychedelic use, with 38% reporting complete smoking cessation, and another 28% reporting significant enduring reductions in smoking (from a mode of 300 cigarettes/month to a mode of 1 cigarette/month) after taking a classic psychedelic in naturalistic settings (Johnson et al., 2017). A larger, randomized, comparative efficacy trial of psilocybin for smoking cessation is currently underway (clinicaltrials.gov NCT01933994).

Opioids and Cocaine. Early studies on classic psychedelic-assisted treatments have shown significant promise for opioid dependence (Savage & McCabe, 1973), which is being followed up now in contemporary studies of psilocybin for OUD. In fact, some investigators have argued that classic psychedelic therapies could be crucial in battling the opioid epidemic (see Argento, Tupper, & Socias, 2019). Savage & McCabe (1973) conducted an early controlled clinical study assessing the efficacy of LSD in treating OUD (N=78). Although the experimental group differed from the control group in that they lived in a half-way inpatient facility for the initial 6-week treatment, at the 12 month follow up 25% of the LSD group had maintained biologically-confirmed abstinence throughout the year, whereas only 5% of controls did the same (Savage & McCabe, 1973). An additional three patients in the treatment group relapsed only briefly, and maintained abstinence for a year thereafter, bringing the total percentage of those maintaining abstinence for a year to 33% in the LSD group.

An ongoing pilot study of psilocybin treatment for cocaine use disorder has also shown promising preliminary results. Among the first ten participants in a randomized controlled trial with a planned N of 40, Hendricks et al. (2018b) found that participants randomized to receive psilocybin reported significantly fewer days of cocaine use as compared to participants randomized to receive the placebo comparator diphenhydramine, with group differences maintained through the final follow-up assessment at 6 months after end-of-treatment. Furthermore, online survey and other epidemiological data indicate an association between classic psychedelic use outside of formal treatment settings and reduced substance misuse across opioids, stimulants, and cannabis. A large correlational analysis was done using data from the National Survey on Drug Use and Health looking at responses from 44,000 illicit opioid users (Pisano et al., 2017). The study found that among respondents with a history of opioid use, classic psychedelic use was associated with a 27% decline in risk of opioid dependence in the past year, and a 40% decline in the risk of opioid abuse in the past year (Pisano et al., 2017). A survey study looking particularly at naturalistic classic psychedelic use in relation to reductions in cannabis, opioid, and stimulant use found that the proportion of respondents who met SUD criteria dropped from 96% before their classic psychedelic experience to only 27% after the experience (N=444; Garcia-Romeu et al., 2020).

There is also observational evidence that classic psychedelic compounds associated with religious practices could be beneficial in combating drug addiction. Both ayahuasca (from indigenous Amazonian traditions; psychoactive component DMT) and peyote (from indigenous North American traditions;psychoactive component mescaline) contain naturally-occurring classic psychedelic compounds that have been used for centuries in indigenous rituals (Miller et al., 2019), and have recently shown promise in treating SUD. Some studies have found that populations that use these substances regularly (including religious organizations based around these substances like Santo Daime and União do Vegetal) show significantly reduced levels of SUD, AUD in particular (Fábregas et al., 2010; Lu et al., 2009). An initial observational study of an ayahuasca retreat in Canada found reductions in self-reported alcohol, tobacco, and cocaine use (but not cannabis or opiates), with all

study participants reporting positive and lasting changes from the experience (Thomas et al., 2013). Recent survey studies have also reported subjective improvements in psychiatric conditions after mescaline use (Agin-Liebes et al., 2021; Uthaug et al., 2021). Much research is left to be done in this area, but clinics adopting these traditions have shown some promising results (O'Shaughnessy et al., 2021; Berlowitz et al., 2019).

The burgeoning evidence on classic psychedelics in the context of SUD raises the question: how does this potential future treatment option fit within AA/TSF? In the following section, we describe how classic psychedelics could conceivably be integrated into AA/TSF protocols.

Twelve-step Facilitation (TSF)

Based on the model originally conceptualized and put into place in AA, TSF programs are peer-support groups with the purpose of aiding those with a SUD through regular meetings encouraging abstinence. Such programs have now been built for a variety of drugs of addiction (and behavioral addictions) but all originally stem from AA. Thus, all TSF programs follow the same format, namely the 12 Steps and 12 Traditions. They advocate an abstinence-only policy (i.e., complete abstinence from substance use is emphasized) and are grounded in regular meetings, community service, and social connection to others in the program. Importantly, in spite of evidence supporting the efficacy of MAT (e.g., Connery, 2015), TSF programs (with the exception of Narcotics Anonymous, which allows the use of MAT, though not active participation in meetings while on MAT) eschew MAT as philosophically inconsistent with their emphasis on abstinence only recovery models without pharmacotherapy. Relevant to our discussion, TSF programs have been described as "a spiritual recovery movement," with participants looking to a 'higher power' for guidance. In particular, these programs work by "engaging recruits in a social system that promotes new and transcendent meaning in their lives" (Galanter, 2007).

Although evidence has been mixed in the past, a recent Cochrane review containing 10,565 participants found AA/TSF interventions for AUD to be just as effective as other established behavioral treatments (e.g. CBT) on all outcome measures except continuous abstinence and remission, where AA/TSF programs actually outperformed active comparison treatments (Kelly, Humphreys, & Ferri, 2020). Furthermore, AA/TSF interventions were deemed more cost-effective than other AUD treatments (Kelly, Humphreys, & Ferri, 2020). While not conclusive, this evidence seems to suggest the effectiveness of AA/TSF. We understand that AA/TSF programs are not always supported in academic or clinical circles largely because of a tendency in such programs to reject solid evidence in favor of the value of MAT. Additionally, these findings do not bear on the purported theoretical underpinnings of AA/TSF. Nevertheless, AA/TSF modalities are still among the most widely used form of treatment against substance use, possibly due to their free access and global network. Therefore, it is important to investigate AA/TSF approaches and propose potential methods to enhance outcomes for AA/TSF members.

Bill Wilson's later life insight was essentially to combine classic psychedelic-assisted psychotherapy as a form of MAT with his TSF program. He did not see any contradictions between these two treatment options—on the contrary, he saw synergies. Some of the properties of classic psychedelics' subjective effects suggest mechanistic and ideological overlap with aspects of AA/TSF programs, warranting consideration of combining classic psychedelic administration with AA/TSF therapies. The most obvious connection is between the mystical or transcendent effects of classic psychedelics and the end goal of AA/TSF programs, namely connection with a higher power in order to aid the recovery process. Take, for example, this excerpt from Chapter 4 of AA's "Big Book": "If, when you honestly want to, you find you cannot quit entirely, or if when drinking, you have little control over the amount you take, you are probably alcoholic. If that be the case, you may be suffering from an illness which only a spiritual experience will conquer" (Alcoholics Anonymous, 2001). The ultimate goal of AA/TSF programs is to elicit a "spiritual" awakening that will help lift individuals out of their addiction, and classic psychedelics appear to often do just that by reliably and systematically eliciting self-transcendent experiences that participants sometimes call 'spiritual' (Griffiths et al., 2006; Griffiths et al., 2011); and potentially substantive changes in worldview and behavior as well as insights (Davis et al., 2021). Though some have dismissed such drug-induced experiences, stating that they are somehow "artificial" (Kellenberger, 1978; Zaehner, 1957), this overlooks the fact that not only are these experiences strikingly similar to "naturally-occurring" mystical experiences (Griffiths et al., 2019; Yaden et al., 2017), but also that Wilson himself had his original awakening because he was under the influence of hallucinogens. Therefore, such self-transcendent experiences with spiritual attributions should perhaps not be measured by their means of initiation, but by their power to elicit change.

The book of AA tells the story of several individuals who achieved abstinence only after a self-transcendent experience or spiritual experience/awakening. Many of these experiences came early in the journey to sobriety, for instance, in the hospital for treatment of AUD. Chapter 4 of the AA book suggests everyone has the capacity for a spiritual experience, and that having a spiritual experience is in fact vital to creating a connection with a higher power. The AA book goes on to describe the primary problem of dependence as "self-centeredness," and that only a higher power can relieve one from the burden of self. The 12th step of AA/TSF programs reads: "having had a spiritual awakening as a result of working the steps." Thus, at some point in "working the steps," one is expected to have a spiritual awakening. Therefore, as was held by Bill Wilson himself, classic psychedelics could be used to induce spiritual awakenings in AA/TSF members that are struggling to recover. While perhaps some AA/TSF advocates may balk at the prospect of skipping right to the 12th step, there is no reason in principal that classic psychedelic sessions could not be used at a time deemed appropriate by individuals in coordination perhaps with their group and/or sponsor, and in combination with medical supervision. The session could come at the end of the steps, or perhaps at the 2nd step which states "to believe that a power greater than myself could restore me to sanity." Here classic psychedelics may be useful in "surrendering" oneself to the program, a transition process during which dropout often occurs. Research has previously shown that attendance of TSF meetings is associated with improved medication adherence (Monico et al., 2015), and that medications improved meeting attendance (Klein & Seppala, 2019), suggesting that these two approaches could complement each other and mitigate important issues like dropout. Likewise, research has consistently highlighted an important role for spirituality in recovery from various SUDs, ranging from tobacco / nicotine (Gonzales et al., 2007), to other SUDs (Kelly & Eddie, 2020; Miller, 1998; Piedmont, 2004), further implicating a central place for classic psychedelics in eliciting self-transcendent experiences to promote recovery (Figure 1, Table 1).

An AA/TSF program that has openly embraced classic psychedelics in their recovery process does exist (it is the only one to our knowledge) named Psychedelics in Recovery. The program offers a space for people in AA/TSF looking to integrate classic psychedelics into their recovery (www.psychedelicsinrecovery.org). They have their own 12 steps and 12 traditions, which are essentially identical to those of AA/TSF except for the substitution of "higher power" in place of "God." There is, therefore, concrete evidence that classic psychedelics can indeed be integrated into AA/TSF programs to the apparent benefit of their members. Furthermore, even if such an integrated approach does not come to be widely accepted, there would still be value in encouraging AA/TSF circles to not bar or stigmatize individuals who do seek such approaches outside of their program—such ostracization could lead to poorer treatment outcomes through reduced meeting attendance and social exclusion in addition to other inimical interpersonal mechanisms.

Again, we reiterate that most AA/TSF programs do not currently permit its combination with MAT and would therefore likely prohibit the

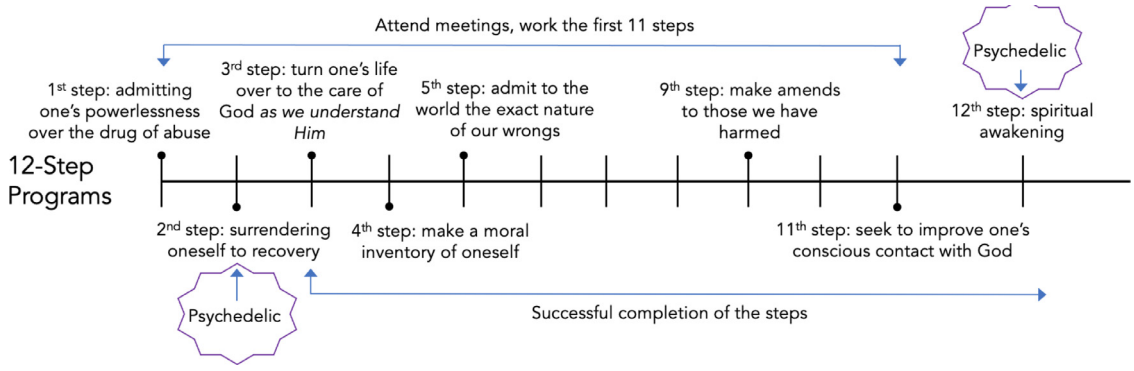

Figure 1. Incorporation of Classic Psychedelic Therapy into Twelve Step Facilitation.

Table 1
No table Classic Psychedelic Studies in SUD Treatment.

Thomas et al., 2013	Hendricks et al., (2018b)	Savage & McCabe, 1973	Garcia-Romeu et al., 2014	Johnson et al., 2014; Johnson, Garcia-Romeu, & Griffiths, 2017	Bogenschutz et al., 2015	Krebs & Johansen, 2012	Study
Various	Cocaine	Heroin	Tobacco	Tobacco	Alcohol	Alcohol	Drug of Addiction
Ayahuasca	Psilocybin	LSD	Psilocybin	Psilocybin	Psilocybin	LSD	Classic Psychedelic
Observational study	Randomized controlled clinical trial [ongoing]	Randomized controlled clinical trial	Secondary analysis	Open-label	Open-label	Meta-analysis of randomized control trials	Method
12	10 (expected 40)	78	15	15	10	536	N=
Self-reported alcohol, tobacco, and cocaine use declined, but that of cannabis and opiates did not.	The psilocybin group reported significantly fewer days of cocaine use compared to those receiving diphenhydramine, significant through the 6 month follow up	At the 12-month follow up, 25% of LSD participants were abstinent, as compared to 5% of controls	Smoking cessation outcomes were correlated with mystical experience ratings.	12 out of 15 participants (80%) showed abstinence at 6-month follow up. Long-term follow up found 67% to be abstinent at 12 months and 60% at ≥16 months	Increased abstinence, with both drinking and heavy drinking days significantly reduced.	Significant larger decline in alcohol misuse for LSD patients (59% vs. 38%).	Outcomes

use of classic psychedelic treatments. However, more awareness of Wilson's advocacy for this treatment, as well as increased understanding of the overlap between approaches, and more evidence for the efficacy of psychedelic-assisted SUD treatments may facilitate a shift towards embracing this treatment synergy, and would lend itself to better treatment outcomes, as suggested here. Such a proposal could also be empirically tested, for example by conducting quantitative surveys and qualitative interviews with individuals who have or are still engaged with AA/TSF and naturalistic use of classic psychedelics simultaneously. Such a study (say, for example, with members of Psychedelics in Recovery) could garner further insight on possible mechanisms of change and a more detailed understanding of synergies between the two approaches.

One potential challenge of integrating classic psychedelic-assisted SUD treatment with AA/TSF is the appeal to spirituality inherent in AA/TSF. Classic psychedelic-assisted SUD treatment is on track to potential approval as a regulated medical treatment. Incorporating spiritual beliefs into mainstream medical and psychological practice can be a challenge and raises various well-founded ethical issues to address, and combining classic psychedelics with AA/TSF may have potential to increase this challenge. Critical here will be how the field defines "spirituality" (see, for instance, Victor & Treschuk, 2019; Yaden et al., 2021). As has been discussed in the context of classic psychedelics (Johnson, 2020), the term can imply supernatural beliefs but also non-supernatural humanistic concepts such as connection to others and the importance of meaning in life. AA/TSF already has a long tradition of flexibility, where participants refer to, for example, "God as we understood Him." This leaves room for more inclusive interpretations of spiritual concepts. For instance, the potential atheist might conceptualize "God" as simply reality of life (Miller, 2019). The AA book states "Much to our relief, we discovered we did not need to consider another's conception of God. Our own conception, however inadequate, was sufficient to make the approach and to effect a contact with [God]… To us, the Realm of Spirit is broad, roomy, all inclusive; never exclusive or forbidding to those who earnestly seek. It is open, we believe, to all [people]." In the same way, mainstream clinicians delivering classic psychedelic-assisted therapy for SUD can let participants make their own religious, spiritual, or philosophical conclusions, if any, that result from classic psychedelic sessions (Johnson, 2020), and draw their own conclusions on the integration of such beliefs into their AA/TSF program. In sum, although there is the potential that classic psychedelics might enhance the perceived religious/spiritual aspects of AA/TSF, something that has likely dissuaded academics and empirically-informed clinicians from embracing AA/TSF (Laudet & White, 2005), we believe these concerns are navigable, and that it is possible for clinicians and participants alike to interface with these treatments from a range of spiritual or philosophical stances *including those that do not include the supernatural.*

While AA/TSF offers interesting synergies with classic psychedelic treatments, we are *not* advocating for their integration in medical settings. We agree with Johnson (2020) about the risks involved with bringing spiritual-type beliefs in treatment settings, in addition to possible risks with exploring non-standard psychotherapeutic paradigms in the context of classic psychedelic treatments in general (Yaden, Yaden, & Griffiths, 2020). We do believe, though, that as access to classic psychedelics treatments widens to patients with SUD there will inevitably be some people who avail themselves of both classic psychedelic treatments and AA/TSF. Indeed, as

stated above, this is already the case with Psychedelics in Recovery (www.psychedelicsinrecovery.org). Rather than seek to prohibit this integration, we actually see possible benefits and synergies to this approach.

Conclusion

While it might be seen as controversial in some quarters to suggest that classic psychedelic treatments for SUD are compatible with AA/TSF programs, evidence indicates that Bill Wilson, the very founder of AA/TSF, supported this view and that classic psychedelic treatments seem largely compatible with the overall philosophy of AA/TSF programs. As AA/TSF is currently the most widely used treatment of SUD, the potential impact of the combination of psychedelic treatments and AA/TSF is large in scale from the standpoint of harm reduction. We encourage future investigation in this area to objectively establish the most beneficial multi-treatment protocol.

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