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Can 3,4,-methylenedioxymethamphetamine therapy be used to treat alcohol use disorder?

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Treating people with alcohol use disorder has been an important target area for psychedelic research – both in the first studies of the 1950s and during the Psychedelic Renaissance of the last 10 years. To date, most studies have looked at the classical psychedelic drugs as adjuncts to psychotherapy; with attention paid to the psychospiritual aspect of the experience as a central therapeutic process in effecting abstinence from drinking. Psychotherapy assisted with 3,4,-methylenedioxymethamphetamine (MDMA) has never been explored for treating alcohol use disorder. However, MDMA has some unique pharmacological characteristics – particularly its capacity for reducing the fear response and facilitating engagement in therapy around past psychological trauma – that could make it a useful candidate for tackling the core features of alcohol use disorder. This paper briefly describes the burden of alcohol use disorders and the history of psychedelic-assisted psychotherapy in the field of addictions. It gives the theoretical and experimental justification for MDMA-assisted psychotherapy for treating people with alcohol use disorder and introduces a forthcoming study from Bristol and London, UK, exploring the role for MDMA in treating a person with this challenging condition.

Keywords: MDMA, alcohol use disorder, dependence, psychedelic, trauma, LSD

INTRODUCTION

At the turn of the 20th Century, the personal, societal, and clinical burden of alcohol misuse reached a historical peak (Wilson, 1940). There followed a move away from the moralistic "Inebriety Asylum" approach, with a reappraisal of the problem using a medical-/disease-based model (Mann, Hermann, & Heinz, 2000). Since then we have seen a plethora of different treatment approaches from the religious to the pharmaceutical. Despite our current wide range of pharmacological and psychosocial treatments for patients addicted to alcohol, the rates of relapse, a return to drinking after detoxification, remain high (Miller, Walters, & Bennett, 2001). This perennial problem for medicine and society deserves an innovative approach.

People with alcohol use disorder are often stigmatized, maligned by society and blamed. However, many of these patients have experienced adverse psychosocial circumstances. Their trajectory into alcohol use disorder has often resulted from childhood trauma into drug dependence that ties them to a lifestyle of emotional, psychosocial and financial dysfunction. Because of the complexity of etiology and the resulting psychological and physiological dependence that results, treating people with alcohol use disorders can be very challenging (Sessa & Johnson, 2014).

In the 1950s and 1960s, the treatment of people with alcohol use disorder became an important priority for some of the earliest psychedelic drug-assisted therapies with lysergic acid diethylamide (LSD). And now, after a hiatus of almost half a century, this research is being revisited with a number of contemporary studies examining the medicines psilocybin, ketamine, ibogaine, and ayahuasca as potential treatments for people with various drug dependence, all which are described later. To date, 3,4,-methylenedioxymethamphetamine (MDMA)-assisted psychotherapy research has focused primarily on post-traumatic stress disorder (PTSD). However, MDMA has never been explored as a tool to treat people with alcohol use disorder. It could be, however, that delivered in a safe setting, after thorough screening of suitable patients, careful scrutiny of physiological measures, and intensive integrative follow-up, a course of MDMA-assisted therapy can assist a patient's capacity to access, explore, and resolve ingrained negative beliefs about self and others that maintain addictive behaviors. This can provide an important opportunity for people with alcohol use disorder to maintain abstinence, reduce the harms associated with drinking, and achieve improved psychosocial functioning associated with recovery.

THE CLINICAL, SOCIAL, AND FINANCIAL BURDEN OF ALCOHOL DEPENDENCE

Although drinking alcohol is a widely socially acceptable behavior and many people consume alcohol without experiencing any problems, approximately 24% of the adult population of England consume alcohol in a way that is potentially or actually harmful (NICE, 2011). In the UK, the prevalence of alcohol use disorder is about 4%; with 6% of men and 2% of women. The disorder is characterized by withdrawal symptoms on cessation of alcohol, or drinking to avoid withdrawal symptoms, tolerance, and the persistent desire to continue drinking despite negative consequences (American Psychiatric Association, 2013). Patients with

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alcohol use disorder frequently have a past history of psychological trauma and there is an association between alcohol use disorder and PTSD (Brady, Back, & Coffey, 2004). Patients commonly present with high levels of depression, social anxiety, and social exclusion and use alcohol as a form of self-medication (McDevitt-Murphy, Murphy, Monahan, Flood, & Weathers, 2010). The impact of alcohol misuse is widespread, encompassing alcohol-related illness and injuries and significant social impacts to family, friends, and wider community. In 2012, there were around 7,000 alcohol-related deaths in the UK and the Department of Health estimates that alcohol misuse is now costing around £20 billion a year in England alone (HM Government, 2012).

A BRIEF REVIEW OF THE CURRENT TREATMENTS FOR ALCOHOL DEPENDENCE

There are many different sorts of treatments for people with alcohol use disorder; with big overlaps between treatments and large differences between patients' presentations, severity of disease, and multiple confounding psychosocial factors.

Licensed pharmacological options for treating alcohol use disorders include acamprosate, disulfiram, naltrexone, and nalmefene. Acamprosate, a glutamate antagonist, reduces N-methyl-D-aspartate activity associated with alcohol withdrawal and reduces relapse rates (Rösner et al., 2010). Disulfiram is used as an agent to deter relapse by preventing the elimination of acetaldehyde. This results in an unpleasant physical reaction if alcohol is used in combination with this medication (Krampe et al., 2006). Naltrexone, a competitive opioid antagonist, which decreases cravings from alcohol (Soyka & Rösner, 2008). Nalmefene is opioid antagonist, similar to naltrexone but with a longer half life and lower risk of toxicity than naltrexone. This can be given to patients while still drinking alcohol in order to reduce cravings (Paille & Martini, 2014). Benzodiazepines are prescribed most commonly as a time-limited course as part of alcohol detoxification program (Lingford-hughes, Welch, Peters, & Nutt, 2012).

Several large systematic reviews and prospective studies have reviewed the efficacy of both medication and psychosocial interventions. The Project MATCH was a large 3-year follow-up study that showed that 12-step facilitation (TSF), motivational enhancement therapy (MET), and cognitive-behavioral therapy (CBT) coping skills are in general equally effective. At 3 years, 36% of the TSF clients were abstinent compared with 27% of the MET and 24% of the CBT clients (Project MATCH Research Group, 1998).

A more recent review, the COMBINE Project was designed to evaluate the efficacy of two relapse prevention medications in various combinations with behavioral treatment. Results indicated that both naltrexone and acamprosate show minor positive effects in relapse prevention, but only when used in conjunction with psychosocial interventions (Anton et al., 2006).

In a similar UK-based study, "UKATT" identified that social behavior and network therapy and MET produced equal improvements in drinking and general functioning. Clients in both groups reported that total alcohol consumption had decreased by 48% at 3 months and by 45% at 12 months and that alcohol-related problems had decreased by 44% at 3 months and by 50% at 12 months. There were no significant differences in effectiveness between the groups (UKATT Research Team, 2005).

Mindfulness techniques, originally derived from Vipassana meditation, that encourage awareness and acceptance of moment-to-moment thoughts to interrupt responding to stress with alcohol, have also been increasingly explored as a potential approach for treating people with alcohol use disorder (Marcus & Zgierska, 2009). In terms of psychosocial interventions, the best approaches are those that foster good relationships and are delivered by the most experienced, highly trained therapists. The Mesa Grande systematic review looked at 361 controlled studies of treatments for alcohol use disorder in 2002 and identified 46 possible interventions (Miller & Wilbourne, 2002). Interventions were ranked according to the rates of abstinence achieved. The brief intervention approach ranked highest and MET, which is a counseling approach that helps individuals resolve their ambivalence about engaging in treatment and stopping their drug use, ranked 2nd. The MET aims to evoke rapid and internally motivated change rather than guide the patient stepwise through the recovery process. Pharmacotherapy with acamprosate and the opiate antagonist, naltrexone ranked 3rd and 4th, respectively. The lowest ranked approaches were designed to educate, confront, shock, or foster insight regarding the nature of alcoholism. From this systematic review, psychotherapy produced the best outcomes.

However, the efficacy of current available treatments is far from satisfactory, with long-term relapse rates up to 80% (Finney, Moos, & Timko, 1999).

A BRIEF HISTORY OF PSYCHEDELIC THERAPIES FOR ALCOHOL USE DISORDER AND OTHER ADDICTIONS

There are cross-cultural examples of the naturalistic use of psychedelic plants to treat people with alcohol use disorder. These include the West African use of the iboga root (containing ibogaine), the South American use of ayahuasca (containing N,N-Dimethyltryptamine), and the North American use of the peyote cactus (containing mescaline); all of which have been described to reduce the rates of alcohol use disorder within their indigenous communities (Halpern, 1996).

In the 1950s and 1960s, psychiatrists Humphry Osmond and Abram Hoffer at the Weyburn Mental Hospital, Saskatchewan, aware of the observed significant rates of sobriety in patients who had experienced Delirium Tremens ("the DTs"), used LSD to provide a clinician-induced organic psychosis to treat people with alcohol use disorder (Dyck, 2008). It was found that the mystical–spiritual experiences, not the psychotic experiences, with the drug were associated with treatment success. Combined with supportive psychotherapy, Osmond's team described abstinence rates superior to other treatments for the disorder before or since (Chwelos, Blewett, Smith, & Hoffer, 1959). However, these and other uncontrolled studies of the time also received criticism in terms of their methodologies. For example, one such study that concluded, "LSD does not enhance the psychotherapeutic treatment for alcoholism"

(Ludwig, Levine, & Stark, 1970), paid little attention to the consideration of set and setting; patients were left on their own and when they became acutely distressed by the effects of the drugs, patients were physically restrained and tied to their beds rather than talked down. Osmond, who coined the term "psychedelic," administered LSD to the founder of Alcoholics Anonymous, Bill Wilson, who recognized psychedelics as beneficial for people with alcohol use disorder by producing an intense spiritual peak experience that encourages sobriety (Hartigan, 2000). In 2012, a meta-analysis of the historical studies of LSD for alcohol treatments of the 1950s and 1960s showed a pattern of generally favorable results, with 59% of the LSD-treated participants significantly improved compared to 38% of the controls (Krebs & Johansen, 2012).

Treating people with alcohol use disorder with psychedelic-assisted psychotherapy has seen considerable research in recent years (Bogenschutz & Pommy, 2012). Contemporary placebo-controlled studies showed that ketamine-assisted psychotherapy produced total abstinence for more than 1 year in 66% of the alcoholic patients in the Ketamine group, compared to just 24% of the control group (Krupitsky & Grinenko, 1997). More recently, an open-label study with psilocybin-assisted psychotherapy for people with alcohol use disorder has shown the percent of heavy drinking days decreased following psilocybin-assisted psychotherapy relative to baseline [mean difference (SD) = 26.0 (22.4), 95% CI 8.7–43.2, $t(8) = 3.477$, $p = .008$]. Gains were largely maintained at follow-up at 36 weeks and there were no significant treatment-related adverse events (Bogenschutz et al., 2015). Psychedelic therapies have also been researched for other addiction disorders, including ayahuasca-assisted and ibogaine-assisted therapies for people with polysubstance misuse disorders (Lotsof, 1995; Thomas, Lucas, Capler, Tupper, & Martin, 2013) and psilocybin-assisted psychotherapy for people with nicotine dependence (Johnson, Garcia-Romeu, Cosimano, & Griffiths, 2014).

MDMA AS A TREATMENT FOR ALCOHOL USE DISORDER

MDMA has been used as a therapeutic agent to enhance psychotherapy since the 1970s. More recently, the main focus of research has been developing MDMA-assisted psychotherapy for people with treatment-resistant PTSD (Sessa, 2016). Long-term follow-up data from the first completed trial of MDMA-assisted psychotherapy for chronic, treatment-resistant PTSD found statistically and clinically significant gains in symptom relief with no subjects reporting harm from participation in the studies (Mithoefer, Wagner, Mithoefer, Jerome, & Doblin, 2011; Mithoefer et al., 2013). It is well known that there are significant rates of early psychological trauma among people with alcohol use disorder and similarly high rates of harmful alcohol use among sufferers of PTSD. One of the potential mechanisms by which MDMA therapy could theoretically treat people with alcohol use disorder, therefore, is its ability to reduce comorbid trauma.

To date, using MDMA therapy to treat people with any addiction disorders, including alcohol, has never been studied but the theoretical proposition has been mooted with a number of potential mechanisms put forward (Jerome, Schuster, & Yazar-Klosinski, 2013). The idea of psychedelic-induced mystical–spiritual experiences resulting in personality change was explored by Pahnke (1969) and Leary's team at Harvard (Leary & Metzner, 1968). Revisited in recent times, the peak experience induced by classical psychedelics and the subsequently sustained positive changes in attitudes and behavior could be an important clinical mechanism in reducing the rigidity of addiction behaviors (MacLean, Johnson, & Griffiths, 2011). However, not all patients are able to tolerate the classical psychedelic experience, or even the idea of a treatment involving these experiences, and compliance is a critical part of addiction therapy. While there is also a subjective mystical–spiritual experience associated with MDMA use (Sumnall, Cole, & Jerome, 2006; Watson & Beck, 1991), it is generally less perceptually disturbing and more easily tolerated than LSD and psilocybin, which could make MDMA a more accepted alternative for enhanced psychotherapy.

There are only scant animal studies on the subject of MDMA for alcohol use disorder. However, two strains of rats that had been previously conditioned to show a preference for alcohol showed an attenuation of alcohol use after administration with MDMA (Rezvani, Garges, Miller, & Gordon, 1992).

An American study showed that a small sample of users (who were not specifically from a substance misuse population) reported positive changes in their attitudes, beliefs, and life activities after MDMA-assisted psychotherapy in a clinical setting. Fourteen of the twenty-nine patients reported a decreased desire for substances including alcohol, cannabis, and caffeine, though two patients reported increased consumption (Greer & Tolbert, 1986).

Another study, in a naturalistic setting with recreational MDMA users, indicated that MDMA enhances intrapersonal prosocial attitudes, which might be especially useful for patients with pre-existing histories of trauma (Stolaroff, 2004). The capacity for MDMA to increase the feelings of empathy and compassion for the self and others may subsequently reduce the use of alcohol as a form of self-medication. Similarly, studies examining MDMA therapy for PTSD have described MDMA's capacity to "make yourself present in the moment," which is a core concept of mindfulness (Mithoefer et al., 2011, 2013).

THE PHARMACOLOGY OF MDMA

The pharmacokinetics of MDMA have been well studied in humans. Based on doses ranging 100–125 mg, the peak plasma concentration and subjective effects of MDMA are reached after 2–3 hr (Harris, Baggott, Mendelson, Mendelson, & Jones, 2002) and the elimination half-life is between 7 and 9 hr (Mas et al., 1999). MDMA is a ring-substituted phenethylamine exerting its effects primarily through promoting raised levels of monoamine neurotransmitters in the brain, in particular serotonin, but also dopamine and noradrenaline. Increased activity at 5-HT_{1A} and

5-HT_{1B} receptors reduces the feelings of depression and anxiety, reduces the amygdala fear response, and increases the levels of self-confidence (Liechti & Vollenweider, 2001). Due to alpha 2-adrenoceptor-mediated effects, MDMA makes an individual feel relaxed (Lavelle, Honner, & Docherty, 1999), which reduces hypervigilance. Furthermore, the effect of raised serotonin at 5-HT_{2A} receptors provides alterations in the perceptions of meanings and facilitates new ways of thinking about old experiences (Simmler, Rickli, Hoener, & Liechti, 2014). MDMA has also been shown to facilitate the release of oxytocin – the hormone associated with early infantile bonding and increase the levels of empathy and closeness (Kirkpatrick, Francis, Lee, de Wit, & Jacob, 2014). The associated prosocial effects (Dumont et al., 2009) give rise to its description clinically as an "empathogen" or "entactogen" (Nichols, 1986). The combined dynamic interaction of increased serotonin, dopamine, and noradrenaline in multiple brain regions modulating learning and memory, emotion, reward, attention, and sympathetic/parasympathetic activity contribute to MDMA's subjective psychological effects (Gudelsky & Yamamoto, 2008).

MDMA acutely decreases the activity in the left amygdala and increases blood flow to the prefrontal cortex (Carhart-Harris et al., 2015), produces greater compassion, feelings of sociability, closeness, and increased empathy for self and others (Hysek et al., 2013). The reduced fear response and greater activity in the reward pathways in subjects receiving MDMA is associated with a better ability to detect positive facial expressions and a greater difficulty detecting negative facial expressions (Hysek, Domes, & Liechti, 2012). Taken together, these changes in social cognition, interpersonal closeness, communication, and brain activity upon viewing facial expressions of specific emotions may influence the outcome of psychotherapeutic treatments for people with alcohol use disorder and comorbid psychological disorders (Jerome et al., 2013).

In summary, MDMA has the potential to enhance and intensify the psychotherapeutic processes in the treatment of people with alcohol use disorder. Its unique effects in a psychotherapeutic context may reduce avoidance of emotionally distressing thoughts and memories while increasing empathy for the self and others. It may also address comorbid symptoms, particularly those associated with a history of psychological trauma.

THE SAFETY OF CLINICAL MDMA

When discussing the safety of clinical MDMA, it is not relevant to describe at length the large body of literature associated with recreational ecstasy use. Understanding the former is not significantly improved by discussion of the latter. Furthermore, it is important to destigmatize the medical acceptance of clinical MDMA by separating it from ecstasy (Sessa & Nutt, 2007).

Some users of clinical MDMA may experience an increase in anxiety associated with derealization-type experiences (Mithoefer et al., 2011). Acute neurocognitive effects may include reduction in verbal and visual memory, which tend to be transient and resolve after the acute subjective psychological effects of the drug have worn off (Kuypers & Ramaekers, 2007). MDMA possesses only moderate abuse potential, as evidenced by animal and epidemiological studies of recreational ecstasy users (Degenhardt, Bruno, & Topp, 2010). However, this needs to be borne in mind when giving the drug to patients with addiction issues. In the limited studies in which MDMA has been administered clinically in a therapeutic setting to healthy volunteers or clinical patients, subjects did not generally express a wish to use it outside of the clinical setting. In Mithoefer's long-term follow-up study, only one patient reported the use of illicit ecstasy after receiving MDMA-assisted psychotherapy for PTSD (Mithoefer et al., 2013).

Acute MDMA produces cardiovascular effects, including increased blood pressure and heart rate and an increase in body temperature (Harris et al., 2002; Liechti & Vollenweider, 2001). Jaw tightness and bruxism are also common, as well as reduced appetite, poor concentration, and impaired balance (Mithoefer et al., 2011, Oehen, Traber, Widmer, & Schnyder, 2013). When recreational ecstasy is taken outside of the clinical setting, more serious adverse effects have been observed, including hyperthermia, liver disease, and hyponatremia (Rogers et al., 2009). However, safety data gathered by the multidisciplinary association of psychedelic studies (MAPS) from 482 experimental sessions with clinical MDMA administered to 153 subjects in the last 15 years, there has been only one single significant drug-induced adverse reaction to clinical MDMA, in which a participant experienced a short-lived asymptomatic abnormal cardiac arrhythmia which required an admission to hospital for observation but no formal treatment and no fatalities (MAPS, 2016).

Regarding long-term neurotoxicity or associated neurocognitive impairments, when pure MDMA is administered in a controlled clinical setting, there have been no such events observed (Doblin et al., 2014; Mithoefer et al., 2013). Research on short-term effects of MDMA in humans is contradictory. Some studies have demonstrated transient verbal memory deficits (Verheyden, Henry, & Curran, 2003), slow processing speeds (Halpern et al., 2004), and a range of executive impairments, including spatial working memory (Hanson & Luciana, 2010) and verbal fluency (Bhattachary & Powell, 2001). However, other studies have reported a lack of such deficits (Back-Madruga et al., 2003; Gouzoulis-Mayfrank, Thimm, Rezk, Hensen, & Daumann, 2003).

A BRISTOL-BASED STUDY EXPLORING THE SAFETY AND TOLERABILITY OF MDMA THERAPY FOR TREATING ALCOHOL USE DISORDER

A forthcoming study, sponsored by Imperial College London and being delivered clinically in the city of Bristol in South West England, will test the hypothesis that MDMA therapy can be delivered safely and effectively in a clinical setting to people with alcohol use disorder. Approximately 450 patients per annum present to the Bristol Specialist Drug and Alcohol Services (SDASs) for community

detoxification. Using an open-label design, our study will examine whether 20 patients between 18 and 65 years old who have been medically detoxified off alcohol can tolerate and benefit from an 8-week course of MDMA therapy.

Important exclusion criteria include a personal or family history of a primary psychotic disorder, a history of cardiac disease, hypertension and stroke, severe liver disease, or epilepsy. Patients who present a serious suicide risk, those who are regular users of other drugs of abuse (excluding cannabis) and females who are pregnant are also excluded. Patients must be willing to stop any medications inhibiting CYP 2D6, monoamine oxidase inhibitors, Ritonavir (HIV treatment), paroxetine, fluoxetine, citalopram, regular benzodiazepines, or any other medications likely to interact with MDMA during the 8-week MDMA-assisted therapy course.

Participants will complete a standard drink diary and a range of questionnaires assessing aspects of their mental health, quality of life, and the severity and impact of their drinking. They then proceed with their seven- to ten-day detoxification delivered by their local SDAS team. After detoxification, baseline data will be collected and eligible patients will receive an 8-week course of MDMA therapy, which comprises two drug-assisted sessions and eight non-drug supportive sessions. Outcome data will be collected at face-to-face interviews at 3, 6, and 9 months to assess drinking behavior, psychological well-being, and quality of life.

The assessment tools used are typical for alcohol research studies, including the Timeline Followback method to assess daily drinking and recreational drug use over time (Sobell et al., 2001), craving and obsession scales (Anton, Moak, & Latham, 1995; Flannery, Volpicelli, & Pettinati, 1999), quality of life measures (Kiluk, Dreifuss, Weiss, Morgenstern, & Carroll, 2013), and sleep measures (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989; Parrott & Hindmarch, 1980). The Mindfulness Attention Awareness Scale (Brown & Ryan, 2003), the Childhood Traumatic Events Scale (Pennebaker & Sussman, 1988), and the Altered States of Consciousness Questionnaire (Dittrich, 1998) will be used alongside measures to safely and effectively monitor the use of MDMA as an adjunct to psychotherapy.

THE STRUCTURE OF THE PROPOSED THERAPY

The therapeutic intervention itself involves participants receiving 10 therapy sessions facilitated by a male consultant addictions psychiatrist and a female addictions clinical psychologist, both of whom have received specialist MDMA therapy training in the USA supported by the MAPS. Psychotherapy sessions will employ aspects of motivational interviewing and MDMA psychotherapy, as developed by MAPS for treating PTSD. During the two MDMA-assisted sessions, participants will receive an initial dose of 125 mg MDMA followed by the option to receive a supplemental dose of 62.5 mg MDMA after 2 hr. Facilitators may gently guide the participant into discussing aspects of their history as lead by the participant but the MDMA sessions are relatively nondirective. The participant may choose to lie down wearing eye shades and headphones; music being an important aspect of the therapeutic effects of psychedelic-assisted therapies (Kaelen et al., 2015).

Heart rate, blood pressure, and temperature will be taken before the MDMA is administered and monitored throughout the drug sessions. Before discharge (minimum 5 hr after first dosing), vital signs will be checked and a psychiatric assessment will determine fitness to leave. If the participant is deemed ready and safe to leave, they will be allowed home accompanied by a previously identified significant other. In the event of adverse psychological or physiological drug-mediated events, a safety protocol, including the option of admission to hospital will be followed.

In order to assess post-MDMA mood, risk issues and sleep functioning patients will receive daily telephone calls for 5 days after each drug-assisted session.

Summary of the MDMA for alcohol use disorder study

2 weeks pre-detox	Screening, consent, and eligibility interview	
Detoxification (detox)	7–10 days, carried out by local Community Alcohol Detox Team	
	Followed by baseline assessments	
1 week post detox	Session 1	60-min therapy session
2 weeks post detox	Session 2	60-min therapy session
3 weeks post detox	**Session 3**	**MDMA-assisted therapy session 1 (~6–8 hr)**
	Session 4	Next day follow-up session (60 min) then daily phone calls for 4 days
4 weeks post detox	Session 5	60-min therapy session
5 weeks post detox	Session 6	60-min therapy session
6 weeks post detox	**Session 7**	**MDMA-assisted therapy session 1 (~6–8 hr)**
	Session 8	Next day follow-up session (60 min) then daily phone calls for 4 days
7 weeks post detox	Session 9	60-min therapy session
8 weeks post detox	Session 10	60-min therapy session
3 months post detox	Face-to-face follow-up interview	
6 months post detox	Face-to-face follow-up interview	
9 months post detox	Face-to-face follow-up interview	

Note. Bold text refers to the MDMA-assisted sessions. All the other sessions are non-drug assisted.

CHALLENGES REGARDING THIS STUDY AND SUMMARY

It has been a complex process setting up this Bristol-based study, including lengthy negotiations with the local National Health Service Trust, the sponsoring academic organization (Imperial College London), and local ethical review committees. There are extra levels of regulatory difficulties because of the schedule 1 status of MDMA (Sessa & Nutt, 2015). There have been challenging negotiations with the Home Office, local pharmacy departments, the Medicines and Healthcare products Regulatory Agency, and the UK manufacturers and encapsulators of the good medical practice-grade MDMA.

Nevertheless, the world's first clinical study to test the safety and efficacy of MDMA-assisted therapy to treat alcohol use disorder is now underway. Given that the physical, mental, and social problems associated with alcohol use disorder now affect almost a quarter of all adults in the UK, this is an area of medicine in need of an innovative approach. This study could provide an important opportunity for patients to maintain abstinence and recovery from drinking – offering a potential new approach for treating people with the chronic and relapsing condition of alcohol use disorder.

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