Can MDMA Play a Role in the Treatment of Substance Abuse?

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Abstract: A wider array of treatments are needed for people with substance abuse disorders. Some psychedelic compounds have been assessed as potential substance abuse treatments with promising results. MDMA may also help treat substance abuse based on shared features with psychedelic compounds and recent reports indicating that MDMA-assisted psychotherapy can reduce symptoms of PTSD. Narrative reports and data from early investigations found that some people reduced or eliminated their substance use after receiving MDMA, especially in a therapeutic setting. MDMA is a potent monoamine releaser with sympathomimetic effects that may indirectly activate 5-HT$_{2A}$ receptors. It increases interpersonal closeness and prosocial feelings, potentially through oxytocin release. Findings suggest that ecstasy, material represented as containing MDMA, is associated with deleterious long-term effects after heavy lifetime use, including fewer serotonin transporter sites and impaired verbal memory. Animal and human studies demonstrate moderate abuse liability for MDMA, and this effect may be of most concern to those treating substance abuse disorders. However, subjects who received MDMA-assisted psychotherapy in two recent clinical studies were not motivated to seek out ecstasy, and tested negative in random drug tests during follow-up in one study. MDMA could either directly treat neuropharmacological abnormalities associated with addiction, or it could indirectly assist with the therapeutic process or reduce symptoms of comorbid psychiatric conditions, providing a greater opportunity to address problematic substance use. Studies directly testing MDMA-assisted psychotherapy in people with active substance abuse disorder may be warranted.

Keywords: 3,4-methylenedioxymethamphetamine, entactogen, MDMA, oxytocin, psychedelic, psychotherapy, addiction.

INTRODUCTION

Substance dependence and abuse clearly represent a significant problem in the U.S. According to the National Survey on Drug Use and Health [1] in 2010, an estimated 8.9% of Americans aged 12 or older reported illicit drug use at least once in the past month (approximately 22.6 million people). Substances most commonly used were marijuana, non-medical use of psychiatric medication (e.g. benzodiazepine anxiolytics), cocaine, hallucinogens, and methamphetamine. An estimated 23.1 million individuals aged 12 years or older (9.1%) were in need of treatment for a substance abuse disorder, while only approximately 11.2% of those needing treatment (approximately 1% of the general population over 12 years old) received treatment [1].

There are a number of available treatments for substance abuse with an established history of use or some evidence supporting efficacy when compared against standard treatment [2-5]. These include outpatient psychotherapy in individual or group settings that include a variety of behavioral and psychotherapeutic programs, pharmaco-logical treatment that either substitutes for a given substance (e.g. methadone), is intended to make use aversive (e.g. disulfiram), or targets the neuropharmacology of addiction (e.g. buproprion), self-help groups (e.g. Alcoholics Anonymous), detoxification, rehabilitation facilities, and therapeutic communities [6-8]. Recent systematic reviews fail to find strong support for even well recognized interventions in treating tobacco, alcohol, and opiate use [2, 3, 5, 9, 10]. A review of psychosocial treatments for opiate addiction also suggests that even effective treatments do not sustain reduced opiate use when followed up one to three months later [4]. Despite the diversity of existing treatments, they are underutilized or not very effective, suggesting a substantial portion of the population receiving treatment for substance abuse may be refractory to treatment [2, 4]. Furthermore, findings from studies supporting substance abuse treatments may not be generalizable to real world settings [11]. Interest remains in discovering new routes for helping people with problematic substance use.

One potentially useful therapy for treating substance abuse employs psychedelic (hallucinogenic) compounds, drugs that alter perception, thought and emotion, with most acting through one or more related serotonin receptor. Starting in the 1950s, psychiatric researchers examined psychedelic drugs, such as lysergic acid diethylamide (LSD), in the treatment of alcoholism [12, 13]. These drugs can radically alter consciousness in ways that can potentially lead people to view their life or behavior in new ways. A recent meta-analysis of randomized, double-blind, controlled studies suggests that people diagnosed with alcoholism reduced alcohol use after a single exposure to LSD [12]. Early investigations did not use modern research design, but some later studies were randomized and placebo-controlled. Given the encouraging history of treatment with psychedelic compounds, it is worth asking whether drugs with similar, but not identical, pharmacological profiles could also help

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people with substance abuse disorders, including the drug 3,4-methylenedioxymethamphetamine (MDMA).

MDMA AS A PSYCHOTHERAPEUTIC ADJUNCT

MDMA is a ring-substituted phenethylamine with an unusual history, traveling from obscurity to rediscovery, from use in psychotherapy to recreational use. Sustained efforts have recently revived interest in the therapeutic potential of MDMA [14]. First patented as an intermediate step in the production of a drug to stop bleeding, the next documented appearance is found in the reported synthesis and description of effects by the chemist Alexander Shulgin in 1977 [15, 16]. MDMA was used by some psychotherapists as an adjunct to psychotherapy, prior to becoming a Schedule 1 controlled substance due to extensive use in non-medical settings [15, 17-19]. In the late 1970s and early 1980s, therapists around the U.S. combined MDMA with psychotherapy to address neuroses, relationship difficulties, psychological problems, and PTSD [20, 21]. Participants in one of the first investigations of MDMA in a psychotherapeutic context reported positive changes in their attitudes, beliefs and life activities in a sample of people with psychological difficulties [22]. A subsequent investigation found MDMA-assisted psychotherapy to be safe in a small group of women with PTSD [23]. Two recent randomized, blinded, controlled clinical trials (RCTs) of MDMA-assisted psychotherapy suggest MDMA may be efficacious in reducing PTSD symptoms in men and women with PTSD from sexual assault, crime victimization or combat, with effects lasting for at least a year after the initial treatment [24-26].

Early research into the therapeutic potential of LSD and other psychedelic drugs included studies supporting use in treating alcoholism (See 13, for examples, see 27, 28). The mechanism by which psychedelic compounds treat alcoholism is unknown but may relate to their psychological impact, including the effects of undergoing a mystical experience, changes in motivation to undertake behavioral change or confidence in ability to undertake change [29]. Therapists familiar with psychedelic-assisted psychotherapy modified and applied these methods to therapy with MDMA, under the premise that similar to these compounds, MDMA could help people confront substance abuse through a psychological mechanism of action. MDMA-assisted psychotherapy included encouraging direct engagement with difficult or upsetting memories, experiences, or thoughts within the context of supportive but non-directive psychotherapy. There are no published reports of MDMA-assisted psychotherapy specifically used to address problematic substance use.

In anecdotal reports collected prior to or soon after the scheduling of MDMA, individuals reported reduced substance use or elimination of interest in continued use after at least one session of MDMA-assisted psychotherapy [22, 30]. Greer and Tolbert reported that after undergoing a session of MDMA-assisted psychotherapy, 14 of 29 participants reported a decreased desire for substances such as alcohol, cannabis, and caffeine, though two participants reported increased consumption. Reduction in substance use ranged from limited reduction in alcohol or cannabis use to continued abstinence or low use at the time of follow-up. To date, no RCTs have been specifically conducted to study MDMA-assisted psychotherapy in the treatment of substance abuse.

Recognizing the lack of studies addressing MDMA-assisted psychotherapy as an intervention for substance abuse, the authors examined literature describing MDMA-assisted psychotherapy for any information relating to substance abuse disorders. This information was considered in the light of research on the psychological and physiological effects of MDMA in humans and past reports of classic psychedelics in treating addiction.

PHARMACOLOGICAL AND SUBJECTIVE EFFECTS OF MDMA

The chemistry of MDMA does suggest that it holds promise as a pharmacological treatment for substance abuse. One model of the pharmacological basis of substance abuse disorder is that drugs of abuse cause increases or sustained presence of dopamine in specific brain regions, including the nucleus accumbens and ventral tegmental area (VTA), and that over time this can lead to changes in dopaminergic and serotonergic signaling that influences the reward system or can cause new pathways to form in the brain [31-34]. The structure and pharmacological profile of MDMA is similar to dopamine-releasing psychostimulants (e.g. d-amphetamine), and the selective norepinephrine/dopamine reuptake inhibitor buproprion, approved by the FDA to treat nicotine addiction [8, 35-37]. Buproprion is an atypical antidepressant that lacks serotonergic activity and is sometimes combined with serotonin reuptake inhibitors to optimize treatment [8, 38]. Unlike buproprion and psychostimulants, MDMA possesses primarily serotonergic effects [39-42]. However, it also releases norepinephrine and dopamine [43], and some effects may be related to norepinephrine release [44]. Like psychostimulants, MDMA produces increases in positive mood, energy, and anxiety, and like psychedelics, it induces altered perception, which can include viewing events, thoughts or feelings in a new way [22, 45]. *In vitro* binding studies suggest that MDMA differs from classic psychedelics in having little to no direct effects on the 5-HT_{2A} receptor, but findings in humans suggest that the effects of MDMA are at least partially due to 5-HT_{2A} receptor activation [46-48], perhaps through presynaptic serotonin release. Thus, MDMA has both serotonergic activity similar to psychedelic compounds, and prevents reuptake of catecholamines similar to buproprion, both of which have been used in the treatment of addiction.

In addition to its monoaminergic effects, MDMA is associated with elevated levels of oxytocin, a neuropeptide associated with affiliation and bonding in mammals [49]. Findings of an association between elevated oxytocin and detectable MDMA in peripheral blood were first reported in a naturalistic study of London nightclub attendees with and without detectable serum MDMA levels [50]. Elevated serum oxytocin is an imperfect but somewhat reliable indicator of elevated oxytocin in the central nervous system [49]. Dumont and colleagues reproduced these results in humans and found that MDMA significantly elevated peripheral plasma oxytocin levels in a placebo-controlled study in healthy volunteers [51], in addition to a positive association between elevated levels of oxytocin and

prosocial feelings. Hysek and colleagues replicated these results and reported that administering a serotonin reuptake inhibitor, but not a norepinephrine uptake inhibitor nor several adrenergic antagonists, attenuated the effects of MDMA on oxytocin levels, suggesting a serotonergic mechanism in producing elevated oxytocin [52]. Preclinical research suggests that MDMA administered in rodents increases oxytocin in the brain and is associated with prosocial effects [53, 54]. Co-administration of MDMA with a 5-HT$_{1A}$ receptor antagonist blocks oxytocin secretion as well as the prosocial effects of MDMA, suggesting that oxytocin may be responsible for the prosocial effects of MDMA in rodents [55, 56]. Oxytocin itself has been proposed as a potential treatment for PTSD [57, 58], as well as substance abuse or dependence disorders, based on its ability to decrease methamphetamine self-administration in rodents [58, 59]. Oxytocin neurons may be modulated by monoaminergic signaling and may also be associated with monoamine release through a positive feedback loop in areas of the brain associated with reward, including drug reward [60]. These monoaminergic effects, and the subjective effects they produce, are likely to differ between intranasal administration of oxytocin and oral administration of MDMA at least on the basis of route of delivery to the brain, since oxytocin is a large molecule [61]. Hence, some of the benefits of MDMA noted by psychotherapists may be the result of elevating oxytocin levels [62], leaving open the question of other contributing factors involved in producing the effects of MDMA. Future studies should focus on measuring changes in oxytocin and serotonin in blood samples as a result of MDMA administration.

In humans, MDMA reportedly produces a unique state that includes elevated mood, increased sociability or feelings of closeness to others and slight alterations in perception that include facilitated imagination and memory, changed perception of the meaning or significance of objects, and increases in anxiety related to loss of ego [63-67]. People report experiencing greater compassion, feelings of sociability, closeness and empathy for others and themselves while under the influence of MDMA [39, 52, 65, 68-70]. MDMA reduces activity in the amygdala [71], an area that deals with processing potentially threatening stimuli and that may be overactive in people with PTSD, who are also at greater risk of developing substance abuse disorder [72, 73]. People viewing happy faces after receiving MDMA exhibited greater activity in the reward pathways in the VTA in comparison to placebo. The same study reported that MDMA was associated with less activity in the left amygdala after viewing angry faces, suggesting less reactivity to anger [74]. After receiving MDMA, 48 participants in a study conducted by Hysek and colleagues showed a better ability to detect positive facial expressions, as presented in the Reading the Mind in the Eyes Task (RMET), and greater difficulty detecting negative facial expressions [52]. 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 substance abuse disorder and comorbid psychological disorders.

RISKS OF MDMA

Administering MDMA produces a number of physiological and psychological risks and discomforts. The risk of MDMA that may be of most concern to therapists treating people with substance abuse is its status as a drug of abuse. To date, trials of MDMA-assisted psychotherapy have excluded participants with active substance abuse, defined as exhibiting symptoms within 60 days of examination. While MDMA appears to be a promising treatment for at least one psychiatric disorder when combined with psychotherapy, it also possesses moderate abuse potential. Rodents and primates will self-administer MDMA [75-77]. For instance, monkeys will regularly self-administer MDMA, though they will pay a higher cost in lever presses for amphetamine or methamphetamine [78, 79]. The mood elevation produced by MDMA can be experienced as rewarding [see for instance 64, 65, 74, 80]. A national survey found that an estimated 2.5% of youths aged 12-17 and 12.4% of young adults aged 18 to 24 report using ecstasy at least once in their lives [81] and 9.1% reported use upon a second follow-up. Of those, 0.6% of this representative sample of young people, [82] and a higher percentage of polydrug users [83], report developing ecstasy dependence, though estimates vary between nations and over time, with polydrug users reporting more abuse of ecstasy. Regular and heavy users will take ecstasy once or twice a week or once every two weeks rather than on a daily basis. However, some people report problems arising from their use. Hence, like psychostimulants and unlike classic psychedelics, MDMA is associated with some abuse liability.

In contrast, administering MDMA to healthy volunteers without any previous experience with ecstasy did not instill a desire to use it outside of the laboratory [65], and only one participant in a study of MDMA-assisted psychotherapy for PTSD reported use of ecstasy subsequent to study participation [24]. In another study of MDMA-assisted psychotherapy in people with PTSD, urinary drug screens taken during follow up assessments were all negative [26]. Taken together, these findings suggest that when given in these contexts, MDMA is not likely to produce problematic use. People undergoing MDMA-assisted psychotherapy are liable to experience painful and frightening thoughts, memories, and emotions during sessions in addition to (or even instead of) euphoria. It is notable that these studies excluded people with current diagnoses of substance abuse, and that people with such comorbidities might be more vulnerable to problematic use of ecstasy after receiving MDMA in a therapeutic setting.

In a clinical setting, MDMA has cardiovascular effects such as increasing blood pressure and heart rate, and it produces a slight increase in body temperature [65, 66, 84, 85]. Commonly reported adverse events include experiencing tightness in the jaw or bruxism, loss of appetite, difficulty concentrating and impaired gait or balance acutely after MDMA in samples of healthy volunteers and people with PTSD [25, 65]. MDMA can increase anxiety over loss of ego and negatively experienced derealization in healthy controls, and healthy controls and

people with PTSD report a transient increase in anxiety [25, 42, 65, 86]. Researchers have also detected acute reduction in verbal and visual memory [87, 88], possibly as a result of less brain activity in areas relating to encoding words [89]. In contrast, people taking ecstasy in non-medical settings have experienced serious adverse events, including hyperthermia (overheating), extreme psychological distress, liver disease and hyponatremia (water intoxication or low blood sodium) [90-92]. Many of these events, though not all, occurred in the context of a dance event, night club or party and after prolonged dancing. To date, these medical emergencies have not occurred during controlled investigations of MDMA in healthy volunteers or in people with PTSD.

There is an extensive amount of conflicting literature pertaining to whether or not repeated ecstasy use is associated with long-term deleterious effects [92-94]. Many studies have reported an association between repeated use of ecstasy and other drugs and impaired cognitive function and reduction in detectable serotonin uptake sites, but other studies have failed to detect these associations [95-98]. Studies of high, repeated doses of MDMA in rodents and monkeys have found reductions in brain serotonin and some signs of damage to serotonergic axons [99-101]. More recent findings suggest that the doses of MDMA employed in these investigations greatly exceed doses used by humans, partially because methods used to calculate equivalence do not work well when pharmacokinetics are nonlinear, with higher doses producing greater plasma drug levels than expected [102, 103]. Recent studies comparing the brains of people who used ecstasy regularly to non-drug using controls showed a reduction in estimated brain serotonin transporter sites an average of a month to six months after last use [104, 105]. However, not all investigations have detected this reduction [95, 98]. It is notable that people reporting regular use of ecstasy do not use the drug exclusively, and material sold as ecstasy can vary considerably in purity, identity, and excipients [106-110]. Retrospective comparisons of regular ecstasy users detect impaired memory [92, 111-114], especially impaired verbal memory. Only a single prospective study examined cognitive function before and after participants reported their first use of ecstasy (range cumulative use of 0.5-30 tablets), reporting a small but detectable effect, a failure to improve on verbal memory tasks after retesting [115]. Impaired memory or executive functions are sometimes not detected in people reporting low to moderate use of ecstasy, on average below 50 lifetime uses [95, 111, 116]. Subjects receiving two sessions of MDMA-assisted psychotherapy for PTSD did not exhibit impaired cognitive function [25]. Nevertheless, these potential long-term risks must be weighed when considering MDMA-assisted psychotherapy in the treatment of substance abuse.

A ROLE FOR MDMA IN TREATING SUBSTANCE ABUSE?

Though narrative reports and an early investigation of MDMA-assisted psychotherapy hint at the possibility that MDMA could assist people in addressing substance abuse, these reports and studies did not systematically or objectively assess changes in substance use. Recent studies

of MDMA-assisted psychotherapy in people with PTSD did not report any signs of ecstasy abuse, but did these studies also did not directly address effects on substance abuse. Currently, there are no studies of MDMA as an intervention for substance abuse disorders.

If self-reported changes in substance use are reflective of genuine efficacy in treating problematic substance use, it is likely that these benefits are derived from its properties as a general psychotherapeutic adjunction rather than possessing properties specifically of benefit to people with substance abuse. There is some evidence that problematic drinking may be more strongly related to PTSD than it is to depression or social anxiety [117]. Individuals who are able to reduce or eliminate PTSD symptoms with MDMA-assisted psychotherapy may be more prepared to confront their substance abuse. People with PTSD and a substance abuse find it harder to remain abstinent than people without PTSD [118], and the combination of PTSD and substance abuse is associated with poorer life functioning, even when it does not affect treatment retention [119]. Response to an intervention for PTSD is more likely to translate into reduction in substance abuse symptoms, whereas response to substance abuse treatment only does not have a similarly positive outcome on PTSD response [120], and people with substance abuse treated for PTSD are less likely to relapse [121]. These findings suggest that treating PTSD with MDMA-assisted psychotherapy can increase the chances of responding to a treatment for substance abuse. PTSD is associated with comorbid substance abuse or dependence [122, 123].

An examination of early reports describing MDMA-assisted psychotherapy suggests that MDMA could ameliorate specific psychological problems that may be tied to PTSD and doing this can, in turn, make it easier for people to devote time and energy to their addressing their substance abuse. Avoiding potential trauma-related memories or thoughts is one symptom of PTSD, and it may be more generally tied to avoidant coping, a tendency to disengage from the source of distress [124]. Avoidant coping may be especially prominent in people with substance abuse, as was found in motor vehicle accident survivors assessed for PTSD symptoms, signs of alcohol abuse, and avoidant coping [125]. MDMA or psychedelic compounds given in a therapeutic setting may help people deal with emotionally intense or upsetting memories, thoughts or feelings, and can generate new insights into addiction that can be put to use, and MDMA-assisted psychotherapy might reduce avoidance, thus reducing a potential motivator for problematic substance use in people with PTSD.

Early observers of the effects of MDMA within and outside of a psychotherapeutic context noted the ability of these compounds to spark feelings of empathy and compassion for the self and others [16, 18, 21, 126]. Increasing empathy may permit people to acknowledge the impact that their substance abuse has had on themselves and others. Increased self-awareness and empathy may reduce or attenuate the individual's denial of substance abuse, removing this hurdle to treatment. Increased empathy and reduced need for denial may support a greater motivation to change behavior, a hypothesized effect of classic psychedelics [29]. In all of these cases, MDMA could

enhance and intensify the psychotherapeutic processes taking place in the treatment of substance abuse.

Taken together, the unique effects of MDMA given in a psychotherapeutic context may reduce avoidance of emotionally distressing thoughts, images or memories while increasing empathy for the self and others, and it may also address symptoms of other conditions that are frequently comorbid with PTSD, including those of substance abuse. The combination of these effects may make it easier for people to undergo treatment for substance abuse. However, simply administering MDMA is not guaranteed to produce any therapeutic benefits.

Most of the major risks of MDMA can be addressed by careful screening of participants for contraindicated medical conditions, such as cardiac or cardiovascular disease, or contraindicated psychiatric conditions, such as psychotic disorders or bipolar affective disorder – 1. However, investigations of MDMA-assisted psychotherapy have been limited to people without a diagnosis of current substance abuse. Mithoefer and colleagues excluded participants diagnosed with substance abuse within sixty days of enrollment. People experiencing problematic substance use may face greater risk of abusing MDMA. Since there have not been any trials of MDMA as an adjunct in the treatment of substance abuse disorders, the risk of using MDMA as part of a treatment program for people with substance abuse remains unclear. The similarities MDMA shares with classic psychedelics and experiences recorded in some narrative reports suggest that MDMA-assisted psychotherapy would not produce ecstasy-related substance abuse disorders. The psychotherapeutic environment differs in a number of ways from ecstasy use outside of therapy. Therapy often includes addressing one or more specific goals, the expectation of approaching emotionally difficult material, and interaction with attentive therapists. While people may be rewarded by mood elevation, they will also be very likely to experience anger, fear or grief.

In conclusion, it appears that MDMA, like classic psychedelics, may have a place in addressing substance abuse or dependence, which could be linked to its pharmacology or its psychological effects. The complex monoaminergic effects of MDMA suggest that it could influence neurobiological pathways that may underlie substance abuse disorder. By reducing symptom severity of sometimes hard-to-treat psychiatric comorbidities, MDMA may also provide people with different resources for dealing with problematic substance use. In some respects, classic psychedelics such as LSD in a psychotherapeutic setting may have a better risk to benefit ratio in treating people with substance abuse because they are associated with fewer risks and appear to have lesser abuse potential. However, MDMA produces alterations in consciousness that are less intense than classic psychedelics. Within the context of psychotherapy, MDMA may be a more appropriate choice for some individuals who would otherwise not tolerate the intense alteration in consciousness produced by psychedelics. MDMA-assisted psychotherapy may play a role in helping people with problematic substance use by alleviating other psychiatric conditions and by increasing trust and psychotherapeutic rapport, both of which may contribute to enhancing the effects of psychotherapy.

Key Learning Objectives:

- PTSD is associated with comorbid substance abuse or dependence. Several studies suggests that addiction is related to emotional and/or psychological trauma caused by having experienced or witnessed violence, atrocities or abuse.

- Despite the diversity of existing treatments for helping people with substance abuse, these treatments are underutilized or have limited durability of effectiveness. In consequence, interest remains in discovering new routes for helping people with problematic substance use.

- MDMA may be a potential candidate for treatment of addiction due to shared characteristics with mechanisms of action of existing pharmacologic treatments for addiction.

- MDMA-assisted psychotherapy can reduce symptoms of PTSD, and may help people confront substance abuse through a psychological mechanism of action.

- Individuals taking part in research on MDMA-assisted psychotherapy reported reduced substance use or elimination of interest in continued use after at least one session of MDMA-assisted psychotherapy.

- MDMA possesses a number of physiological and psychological risks, including increased abuse potential, cardiovascular effects, and potentially long-term effects on the serotonin system and cognitive function after repeated use at high doses.

- Several findings suggest that when given in psychotherapy contexts, MDMA is not likely to produce problematic use. Most research subjects report little interest in use of the drug outside of research, and only one participant in a study of MDMA-assisted psychotherapy for PTSD took "Ecstasy" (material represented as being MDMA) beyond the therapeutic setting.

Future Research Questions:

- There are no published reports of MDMA-assisted psychotherapy that specifically address problematic substance use.

- Future studies should focus on measuring the neurophysiologic and neurochemical correlates of response to MDMA-assisted psychotherapy to better understand its mechanisms of action.

- Future research should consider the risks and benefits of MDMA-assisted psychotherapy in people with PTSD and substance abuse disorders.

- Future studies should also assess the risk and potential benefit of using MDMA as part of a specific treatment program for people with substance abuse.

- Researchers should address if MDMA given in a psychotherapeutic context can reduce avoidance of distressing mental processes or increase feelings of empathy and self-confidence.

- In future, research should also investigate whether increases in trust or rapport are present during MDMA-assisted psychotherapy and, if present, whether they correlate with greater therapeutic response.

ABBREVIATIONS

DSM	=	Diagnostic and Statistical Manual of Mental Disorders
LSD	=	Lysergic acid diethylamide
MDMA	=	3,4-methylenedioxymethamphetamine
PTSD	=	Posttraumatic stress disorder
RCT	=	Randomized clinical trial
RMET	=	Reading the Mind in the Eyes Task
SERT	=	Serotonin transporter
5HT	=	5-hydroxytrypatmine, serotonin
$5HT_{2A}$	=	Serotonin 2A receptor

CONFLICT OF INTEREST

ACKNOWLEDGEMENTS

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