

MDMA-Assisted Psychotherapy for Posttraumatic Stress Disorder: An Overview

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Abstract

Posttraumatic stress disorder (PTSD) is a severe mental health condition originating from traumatic events or experiences and affects many aspects of an individual's daily functionality. Symptoms can be debilitating, devastating, and life-threatening, leading an individual suffering with PTSD to often feel overwhelmed. Currently, there are multiple accepted treatments for PTSD, including exposure therapy, cognitive behavioral therapy (CBT), and eye movement desensitization and reprocessing therapy (EMDR), and trauma-focused psychotherapy. However, many barriers exist between PTSD patients and their available treatment options. These barriers include financial difficulties, comorbidity of conditions, stigmatization of receiving mental health care, lack of insurance coverage, or difficulty finding proper treatment providers. This leads both experts and PTSD clients alike searching for alternative treatments for trauma-based, including psychedelic-assisted psychotherapy processes. This review will address MDMA as a specific adjunct to trauma-based psychotherapy, confronting topics of PTSD, MDMA as both a recreational and a therapeutic drug, MDMA's chemical workings in the brain and body, MDMA's positive and negative effects, and MDMA-assisted therapy opposed to existing PTSD therapies. This paper is written with the understanding that PTSD does not present identically in any two human beings and that psychedelic psychiatric treatment is currently a debated issue in many fields.

Posttraumatic stress disorder (PTSD) is a severe mental health condition affecting a person's daily functioning, ability to perform a job, or capability to maintain relationships ("A multi-site phase 3 study," 2018; "Post-traumatic stress disorder," 2019; Sessa, 2017). PTSD develops as a response to traumatic events such as deaths or accidents, occurrences of assaults, natural disasters, and/or war combat or first-responder situations ("A multi-site phase 3 study," 2018; U.S. Department of Veteran Affairs, 2019). The symptoms of PTSD are ongoing and can last several months to many years, including re-experiencing of trauma events, emotional instability, and avoidance (American Psychiatric Association, 2013; Amoroso & Workman, 2016; "Post-traumatic stress disorder," 2019). Currently, there are multiple treatments for PTSD including trauma-focused psychotherapy (Feduccia, Jerome, Yazar-Klosinski, Emerson, Mithoefer, & Doblin, 2019), cognitive behavioral therapy (CBT) (Thal & Lommen, 2018), eye movement desensitization and reprocessing (EMDR) (Feduccia et al., 2019; Thal & Lommen, 2018), pharmacotherapy (Feduccia et al., 2019; Thal & Lommen, 2018), and exposure therapy (Amoroso & Workman, 2016; Feduccia et al., 2019; "Post-traumatic stress disorder," 2019). A common circumstance, however, with these aforementioned psychotherapy treatments is patient dropout, occurring for reasons that include stigma attached to the seeking of psychiatric help, feelings of being overwhelmed with traumatic memories, or trauma-induced inability to trust therapy clinicians (Amoroso & Workman, 2016). Also contributing to patient psychotherapy dropout rates is difficulty in finding a proper treatment provider or the inability to meet financial obligations associated with therapy. With PTSD psychotherapy dropout rates at approximately 30% (Amoroso & Workman, 2016; Thal & Lommen, 2018) and only 20-30% of PTSD patients showing significant improvement from pharmacological

treatments (Amoroso & Workman, 2016; Thal & Lommen, 2018), there is need and incentive to discover new forms of successful PTSD treatments. Most recently, 3, 4-methylenedioxymethamphetamine, commonly known as MDMA and/or ecstasy, is currently being investigated as a psychedelic adjunct to PTSD therapy, producing both optimistic and pessimistic results for researchers. Despite its illegal federal status and potential bodily or emotional side effects, MDMA has been intensely investigated as an assistant to psychiatric therapy since the early 1960s and may soon prove to be the most suitable substance-assisted form of PTSD treatment.

Experiments with the use of psychedelic substances in psychotherapy surged after Albert Hoffman synthesized lysergic acid diethylamide (LSD) in 1938 and self-administered the drug in 1943, which led him to discover its hallucinogenic properties (Das, S., Barnwal, P., Ramasamy, A., Sen, S., & Mondhal, S., 2016). Psychedelic-assisted psychotherapy studies with LSD began in the 1950s, continuing unhindered until the drug became recreationally popular outside the research community and was subsequently made illegal in 1966 and federally scheduled under the 1970 Controlled Substances Act as a Schedule I substance (Das et al., 2016). Once LSD was federally scheduled as having no medical utility, psychotherapists and scientists began experimenting with other psychedelic substances, including methylenedioxy-amphetamine (MDA), a precursor to MDMA (Passie, 2018). Originally synthesized in 1912 by German pharmaceutical company Merck for purposes of developing a blood clotting constituent (Feduccia, Holland & Mithoefer, 2017; Freudenmann, O'xler, & Bernschneider-Reif, 2006), Alexander Shulgin again synthesized MDMA in the early 1960s (Feduccia, Holland, & Mithoefer, 2017). MDMA had slightly lower hallucinogenic properties than MDA, and Shulgin began introducing it to psychiatric practitioners such as Leo Zeff around 1977 (Passie, 2018). MDMA went on to be researched by psychotherapists and scientists until 1985 when it was federally listed as a Schedule I illegal substance with no medical utility (Passie, 2018). Most recently, throughout the 2000s, the use of psychedelic-assisted psychotherapy in cases of PTSD and/or substance abuse/addiction has been revived in MDMA-focused research studies (Feduccia, Holland, & Mithoefer, 2018; Passie, 2018), recently advancing to Phase 3 clinical trials ("A multi-site phase 3 study," 2018; Feduccia, Holland, & Mithoefer, 2018; Passie, 2018; Sessa, 2018). MDMA is being proclaimed by clinical trial researchers as the new cure-all for PTSD, addiction, and trauma-related recovery, asserted as needing only one to three substance-assisted monitored psychotherapy sessions to remove fear-trauma associations and initiate closure for PTSD sufferers (Feduccia et al., 2019; Thal & Lommen, 2018). Despite varied stances concerning MDMA use in various therapies, this report will focus specifically on its use in conjunction with PTSD psychotherapy. This review will address MDMA as a specific adjunct to trauma-based psychotherapy, confronting topics of PTSD, MDMA as both a recreational and a therapeutic drug, and MDMA's chemical workings in the human brain and body. Also, to be addressed in this paper is MDMA's alleged capacity for the elimination of PTSD-related fear responses and oppositions to MDMA-assisted therapies. This research paper looks at support for MDMA-assisted therapy as well and will report research study results as completely as possible concerning MDMA use for PTSD, allowing for the understanding that PTSD most often does not present identically in any two human beings (U.S. Department of Veteran Affairs, 2019). Inclusively, this paper will address various conflicting aspects of repeated MDMA administration during psychotherapy, revealing inconsistencies that are the reality of MDMA therapy research.

Posttraumatic Stress Disorder

PTSD is a long-lasting and life-hindering disorder characterized by re-experiencing, avoidance, arousal, and negative reactions or behaviors, and emotional instability (American Psychiatric Association, 2013; Amoroso & Workman, 2016; Feduccia et al., 2018; Feduccia & Mithoefer, 2018; Sessa, 2017; Thal & Lommen, 2018). This disorder is associated with comorbidity with other mental health disorders (Sessa, 2017), substance abuse (“A multi-site phase 3 study,” 2018; Feduccia et al., 2019; Jerome et al., 2013; Sessa, 2017), increased anxiety (Sessa, 2017), periods of depression (Feduccia et al., 2019; “A multi-site phase 3 study,” 2018; Sessa, 2017), decreased daily functionality (Feduccia et al., 2019; Feduccia, Holland, & Mithoefer, 2018; “A multi-site phase 3 study,” 2018; Sessa, 2017), diminished cognitive and emotional functioning (Feduccia et al., 2019; “A multi-site phase 3 study,” 2018; Thal & Lommen, 2018), self-harm (Sessa, 2017), and/or suicidal risk (“A multi-site phase 3 study,” 2018; Sessa, 2017). According to the U.S. Department of Veteran Affairs (2019), 7-8% of all people will have PTSD at some point in their life, with approximately 8 million adults every year suffering from PTSD. Epidemiological studies have shown that PTSD has a “high lifetime prevalence rate of 6.8% within the general population (Amoroso & Workman, 2016), with the potential to be as high as 10% (Thal & Lommen, 2018). Approximately 10% of all women develop PTSD at some point in their life, compared to only 4% of men (U.S. Department of Veterans Affairs, 2019). As mentioned earlier, PTSD can result from war combat scenarios and/or first-responder situations, and is commonly associated with veteran soldiers, policemen, firemen, and EMT’s (U.S. Department of Veteran Affairs, 2019). The occurrence of PTSD in veterans is between 8.5-24.5%, with only about 9.5% of veterans diagnosed with PTSD receiving treatment (Amoroso & Workman, 2016). Additionally, more than simply saying that people can develop PTSD from traumatic service-related events, many individuals may develop PTSD from being victims to sexual or physical assaults or witnessing the death of a loved one or close friend.

Important to mention are the dangers of untreated PTSD, including the risks of increased suicidal ideation or attempt, extended depression or anxiety, and recurring, disabling flashbacks (“A multi-site phase 3 study,” 2018; “Post-traumatic stress disorder,” 2019). Among the currently accepted treatments for PTSD are trauma-focused psychotherapy (Feduccia et al., 2019), exposure therapy (Amoroso & Workman, 2016; Feduccia et al., 2019; “Post-traumatic stress disorder,” 2019), and psychopharmacological therapies (Feduccia et al., 2019; Thal & Lommen, 2018). Most common of the pharmacological treatments are selective serotonin reuptake inhibitors (SSRIs), namely paroxetine and sertraline (Feduccia et al., 2019). However, there are reports that only about 20-30% of those diagnosed with PTSD respond to pharmacotherapy (Amoroso & Workman, 2016; Thal & Lommen, 2018). More recently, the use of psychedelic-assisted psychotherapy has been revived in trial studies, with the hope of eliminating PTSD-related fear responses and traumatic re-experiencing of trauma events more effectively than prescription antidepressants.

History of MDMA

MDMA was first synthesized in 1912 and gained popularity in the 1970s when a similar drug and mescaline derivative, MDA (methylenedioxyamphetamine), was made illegal (Passie, 2018). MDA was tested in the early 1960s as a psychotherapy adjunct by Claudio Naranjo, a Chilean psychiatrist (Passie, 2018). Naranjo and his colleague, Alexander Shulgin, continued Naranjo’s studies, eventually re-synthesizing MDMA in 1962, which was found to have “lower hallucinogenic activity than MDA” and showed promise as a psychotherapeutic drug (Passie, 2018, p. 2). Leo Zeff,

a psychologist who led the psychedelic therapy underground sector, started his experiments in psychedelic-aided therapy with LSD, continued as a promoter of MDA when LSD was outlawed in 1966, remaining underground with his psychedelic studies for most of the 1960s. After toxic occurrences with MDA in the 1970s, Zeff paired up with Shulgin in 1977 to continue Shulgin's MDMA research (Feduccia, Holland, & Mithoefer, 2018; Passie, 2018). Continuing in his "informal underground" of psychedelic studies, Zeff began conducting MDMA sessions with groups of individuals for the purposes of "personal and spiritual" development (Passie, 2018).

In time, a group called The Association for the Responsible Use of Psychedelic Agents (ARUPA) was formed and became very active between 1977-1984. During this time period, new MDMA researchers entered the scene, including Rick Doblin, an original director of the Earth Metabolic Design Laboratories, Inc. (EMDL), which is an organization founded in 1984 which coordinated and led the opposition against the proposed scheduling of MDMA; From 1978-1983, Doblin hid his research and publications which referenced the use of MDMA in psychotherapy (Passie, 2018). Rick Ingrasci, originally interested in LSD research in the early 1960s, eventually researched MDMA-assisted psychotherapy in his treatment of couples, as well as patients with life-threatening diseases (Passie, 2018). Ingrasci began using MDMA in therapy sessions for couples to break through "communication blocks" and to reduce fear responses due to patients' trauma responses that originated from experiencing possible terminal illnesses (Passie, 2018, p. 7). Ann Shulgin, wife of Alexander Shulgin, helped her friends "sort out personal problems with the use of MDMA in the early 1980s" (Passie, 2018, p. 8). Phil Wolfson treated individuals in "psychotic crisis" by administering MDMA in conjunction with psychiatric treatment (Passie, 2018, p. 8). Ralph Metzner began his psychedelic research in the 1960s and became a major influence and expert in the field of MDMA-assisted psychotherapy from 1983-1985 (Passie, 2018).

From 1970-1982, MDMA was not an FDA-approved drug and was not distributed in large quantities outside of underground psychotherapy research as an exception (Passie, 2018). MDMA in relation to psychotherapy was, in fact, largely unknown to the public since the researchers worked diligently not to attract media attention (Passie, 2018). However, when the Drug Enforcement Agency (DEA) caught wind that Michael Clegg, a theology student turned MDMA manufacturer, was widely distributing MDMA since 1983, the agency framed a moral panic around ecstasy and began proceedings for federal scheduling of the drug (Passie, 2018). In 1985, MDMA was officially banned from medical use, being emergency scheduled and listed as a Schedule I substance by the federal government, and by 1986 was considered an entirely illegal drug in the United States (Amoroso & Workman, 2016; Parrott, 2014; Passie, 2018; Thal & Lommen, 2018). At this point, psychotherapy researchers such as Rick Doblin feared losing the ability to continue their MDMA research and began applying for government approvals to continue with clinical trials (Passie, 2018). MDMA research also continued in other countries besides the United States, such as Switzerland (1988-1993) (Passie, 2018). From the 1960s to the early 1980s, there was much initial research interest concerning the psychiatric use of MDMA, followed by a period of struggle to research MDMA-assisted psychotherapy, and more recently resulting in the resurrection of MDMA-assisted psychotherapy research.

In the early 1990s, the first human trials, to be conducted by Dr. Charles Grob, the use of MDMA treatments for pain, anxiety, and depression in the terminally ill, were approved by the FDA, but delayed due to safety concerns (Multidisciplinary Association for Psychedelic Studies, 2019; "MDMA (Ecstasy) Abuse," 2019). These latter two symptoms of reaction to terminal illness

are also common to PTSD symptomology (Sessa, 2017). Phase I safety studies were approved in 1992 and completed in 1995, after which Dr. Grob was ultimately able to conduct his human trials (MAPS, 2019). In 2000, Phase 2 “randomized, placebo-controlled, double-blind study investigating MDMA-assisted psychotherapy” began (Feduccia, Holland, & Mithoefer, 2018, p. 562). In 2010, psychiatrist Michael Mithoefer published the first randomized controlled study testing MDMA-assisted psychotherapy (Sessa, 2017). In July of 2017, the FDA approved Phase 3 trials for MDMA-assisted psychotherapy (MAPS, 2019). In August of 2017, the FDA granted Breakthrough Therapy Designation for MDMA treatment of PTSD (MAPS, 2019). Breakthrough therapy designation is granted for treatments for life-threatening diseases or conditions and may show improved results over other treatments (MAPS, 2019). MDMA therapy research is now dominating the field of new psychotherapy techniques, with hopes to get MDMA pharmacologically approved for PTSD on prescription-only, therapist-monitored bases by 2021 (MAPS, 2019). With PTSD only being added to the Third Edition of the *Diagnostic and Statistical Manual of Mental Disorders* in 1980 (Friedman, M., 2019), it is reasonable to say that prior to 1980, given the above scenarios, researchers such as Ingrasci, Doblin, and Wolfson, may have unknowingly been treating symptoms of the soon-to-be defined posttraumatic stress disorder.

MDMA Characteristics and Mechanisms

MDMA, chemical name 3,4-methylenedioxymethamphetamine, is an entactogen, “a drug that can increase self-awareness and empathy” (“MDMA (Ecstasy) abuse,” 2019). MDMA, often referred to as ecstasy, is reported to have positive psychoactive effects on an individual, including a sense of euphoria or immense joy (Kalant, 2001; Parrott, 2014; Sessa, 2017; Sessa, 2018; Thal & Lommen, 2018) and enhanced visual and auditory insights (Jerome et al., 2013; Thal & Lommen, 2018). Regarding patient-therapist trust bonds and relationship establishment, MDMA is described as inducing a strengthened sense of bonding or closeness (Amoroso & Workman, 2016; Kalant, 2001; Sessa, 2017; Sessa, 2018; Thal & Lommen, 2018) and an increased sense of openness (Feduccia et al., 2019; Feduccia, Holland, & Mithoefer, 2018; Kalant, 2001; Sessa, 2017; Thal & Lommen, 2018). Concerning self-care, self-esteem, and the patient’s ability to face PTSD-related memories, MDMA-assisted therapy is said to produce heightened levels of empathy/compassion for self and others (Feduccia et al., 2019; Feduccia, Holland, & Mithoefer, 2018; Kalant, 2001; Sessa, 2017; Sessa, 2018; Thal & Lommen, 2018) and reduced feelings of fear (Feduccia et al., 2019; Feduccia, Holland, & Mithoefer, 2018; Sessa, 2018). According to a report by Monfils et al. in 2009, MDMA-assisted psychotherapy research suggests that MDMA enhances the therapeutic relationship while facilitating an easier, safer path to memory reconsolidation and fear extinction (Feduccia & Mithoefer, 2018). Individuals with PTSD are often reported to have an overactive amygdala, which can cause increases in fear response stimuli and inhibit memory processing (Jerome et al., 2013). During research studies in healthy individuals, MDMA allegedly increased the “functional connectivity” between the hippocampus and amygdala, brain regions responsible for emotional memory processing (Feduccia & Mithoefer, 2018; Feduccia, Holland, & Mithoefer, 2018), allowing for the overcoming of fear memories (Feduccia & Mithoefer, 2018; Feduccia, Holland, & Mithoefer, 2018; Sessa, 2017). Therefore, by stimulating the brain’s release of monoamines, single amine neurotransmitters, and hormones, MDMA reportedly aids in an individual’s processing of trauma memories.

Although the terms “MDMA” and “ecstasy” are often used interchangeably, when referencing the use of psychedelics in conjunction with psychotherapy it is important to stress the difference between the standardized, lab-created MDMA that is used in clinical, controlled research environments and its recreational, street-sold counterpart, ecstasy (Multidisciplinary Association for Psychedelic Studies, 2019; Sessa, 2018). When reflecting on discourses of MDMA as an adjunct to psychotherapy processes, recognize that research studies report on monitored MDMA administration in therapist-accompanied environments, and do not associate therapeutic use of the drug with self-medicating use of street level ecstasy products. MDMA, 3,4-methylenedioxymethamphetamine, is a purely synthetic, lab-made chemical substance, whereas ecstasy refers to the substance commonly distributed at rave parties and/or on the streets, is intended for recreational, non-medical use, and is often adulterated or mixed with other constituents, sometimes containing little to no MDMA at all (Feduccia et al., 2019; Kalant, 2001; Thal & Lommen, 2018). Recreational ecstasy can be dangerous because oftentimes individuals consuming street-purchased ecstasy have limited knowledge of what the ecstasy tablets truly contain (Parrott, 2014; Kalant, 2001). These unknown quantities and/or qualities of the ingredients in street ecstasy can result in accidental deaths, completed suicides, attempted suicides, exacerbated depression resulting in suicide, or overdoses of other illegal substances (Kalant, 2001). When used in a recreational setting, ecstasy often has “more serious adverse effects,” all of which can be controlled and monitored in a clinical setting using MDMA (Sessa, 2018, p. 86). Oftentimes, recreational ecstasy/MDMA users are also polydrug users, and use ecstasy in conjunction with other illegal drugs such as cocaine or alcohol; this polydrug use adds various and sometimes hard to separate confounders to research situations (Feduccia et al., 2019). In reference to medical or therapeutic use of MDMA, it should always be understood that MDMA-assisted psychotherapy cannot be directly compared to recreational, non-medical, and/or often self-administered use of street-level ecstasy (Feduccia et al., 2019; Kalant, 2001).

Increased fear responses to outside stimuli is a primary trait of PTSD (Feduccia, Holland, & Mithoefer, 2018). MDMA, however, has the potential to enable reprocessing of fear responses and trauma memories in a safe manner, allowing an individual with PTSD to reconstruct these memories in a more open, accepting, self-compassionate manner (“MDMA Therapy,” 2019). The chemicals believed to be involved in positive effects of MDMA psychotherapy include serotonin, dopamine, norepinephrine, and oxytocin (Feduccia & Mithoefer, 2018; Feduccia, Holland, & Mithoefer, 2018). Serotonin, a chemical that often contributes to positivity and happiness, is reported to “induce affective states to alter fear memories with safety information” in patients with PTSD (Feduccia & Mithoefer, 2018, p. 4). MDMA is thought to bind to and block the serotonin reuptake transports, increasing concentrations of serotonin in the synapses and resulting in improved moods to assist in fear memory processing (Kalant, 2001). When affected by MDMA, dopamine, a brain chemical responsible for behavior, emotions, cognition, and reward, may assist PTSD patients with increasing their attention (Feduccia & Mithoefer, 2018), self-confidence (Sessa, 2018), and engagement (Sessa, 2018). When dopamine is processed in the brain, it can act as a precursor in the production of norepinephrine, a chemical that helps in the processes of stress regulation, sleep, and alertness. When influenced by MDMA, norepinephrine is thought to increase emotions, enhance memory, and modulate cortisol functions (Feduccia & Mithoefer, 2018). Cortisol is a hormone that strongly regulates memory (Feduccia & Mithoefer, 2018; Thal & Lommen, 2018), especially memories of fear-related incidents or experiences (Thal & Lommen, 2018). When incited by MDMA, PTSD

patients' cortisol reportedly may "increase extinction learning by allowing for emotional engagement without interference..." enhancing patient-therapist relations and allowing improved fear memory reprocessing (Feduccia & Mithoefer, 2018, p. 8). Lastly, under the influence of MDMA, oxytocin purportedly enhances "socially reinforced learning" in PTSD related therapeutic relationships (Feduccia & Mithoefer, 2018, p. 5) by increasing levels of empathy and closeness (Jerome et al., 2013; Sessa, 2018). Considering that it is extremely difficult, and sometimes impossible, for PTSD sufferers to confront trauma memories, MDMA's influence on the abovementioned brain chemicals, therefore, may assist with increasing PTSD patients' ability to minimize fearful trauma memories.

Short and Long-Term Side effects of MDMA

Despite the seemingly positive outcomes of MDMA-assisted therapy trials thus far, there still exists some concern about the possible detrimental effects of MDMA on the human body and/or brain. Reaching its greatest concentration in the blood's plasma after two hours from oral consumption (Kalant, 2001), common side effects of MDMA include nausea (Feduccia et al., 2019; Kalant, 2001), vomiting (Thal & Lommen, 2018), jaw-clenching (Feduccia et al., 2019; Jerome et al., 2013; Kalant, 2001; Thal & Lommen, 2018), muscle aches/stiffness (Kalant, 2001; Thal & Lommen, 2018), feelings of numbness (Thal & Lommen, 2018), fatigue (Feduccia et al., 2019; Thal & Lommen, 2018), dizziness (Feduccia et al., 2019; Thal & Lommen, 2018), headache (Feduccia et al., 2019; Kalant, 2001), sweating (Thal & Lommen, 2018), decreased appetite (Feduccia et al., 2019; Jerome et al., 2013; Parrott, 2014; Thal & Lommen, 2018), teeth grinding (Kalant, 2001; Sessa, 2017), insomnia (Kalant, 2001; Parrott, 2014; Sessa, 2017), and/or restless legs (Kalant, 2001). Researchers, medical professionals, and/or patients themselves may consider these side effects to be of detriment enough to avoid MDMA treatments. Besides acute effects, MDMA is purported to have extensive and damaging long-term effects including shortfalls in cognition and memory (Thal & Lommen, 2018), depressing and confused thoughts (Thal & Lommen), anxiety (Feduccia et al., 2019; Parrott, 2014), disturbed sleep (Thal & Lommen, 2018), and the reduction of serotonin transporter levels in the cerebral cortex, which affect neurotransmissions (Kalant, 2001). Research studies by Bolla and McCann purport that MDMA may cause longstanding psychiatric problems related to permanent neurotoxic effects on the serotonin system including memory impairment (Parrott, 2014); other negative psychiatric effects are noted in studies by Parrott include difficulties with decision-making, lack of self-control, and impulsivity (Kalant, 2001). The last set of detrimental psychiatric MDMA results are panic attacks, depersonalization, paranoia, hallucinations, flashbacks, and/or severe depression (Kalant, 2001). There are also suggestions that MDMA can cause various toxicities within the body including liver, cerebral, neurological, and renal (Kalant, 2001; Parrott, 2014). There are also implications from longer-term patient check-in data suggesting that MDMA creates some level of tolerance and subsequently produces withdrawal symptoms (Sessa, 2018; Thal & Lommen, 2018). Studies by Jerome et al., 2013 suggests that the use of MDMA is associated with moderate abuse dangers, posing some risk for dependence, but stating also that this dependence has potential to be directly related to the PTSD itself rather than the characteristics of the drug (Jerome et al., 2013; Sessa, 2017). Contrarily, other studies state that there is little to no danger of dependency or problematic use/abuse associated with MDMA (Feduccia et al., 2019). Kalant (2001) cites previous studies that suggest the rewarding effects of MDMA decrease the more often the drug is administered or consumed, which may in turn defer possible MDMA users from consuming the drug repeatedly over longer periods of time (Kalant, 2001). According to reports by Liechti &

Vollenweider (2001), subjects in clinical MDMA-assisted therapy trials did not demonstrate any desires to use MDMA outside of the clinical setting (Sessa, 2018). In research by Mithoefer et al. (2013), it is indicated that illegal use of ecstasy after having clinically used MDMA is rarely observed (Sessa, 2018). Considering these conflicting reports, there is no definitive data results for whether MDMA produces tolerance, withdrawal, or the urge to continually use the drug.

MDMA Psychotherapy

MDMA-assisted therapy process

Throughout multiple research trials, the MDMA-assisted therapy format is reported similarly. Assisted psychotherapy treatments are said to effectively reduce or eliminate PTSD symptoms after only three or fewer MDMA-aided sessions, each followed by multiple non-drug sessions (Feduccia et al., 2019; Thal & Lommen, 2018). MDMA therapy sessions are often divided into three stages - a preparatory stage, the substance-assisted session, and an integration stage, with the MDMA-assisted process being repeated up to three times during the entire treatment period (Sessa, 2017; Thal & Lommen, 2018). In research trials, the preparatory stage was approximately three psychotherapy sessions preceding any administration of MDMA (Feduccia et al., 2019). This preparatory stage is utilized to record the patient's trauma history, inform the patient of risks and benefits of the MDMA treatments, assess patient physical health, and provide the patient with general MDMA information (Sessa, 2017; Thal & Lommen, 2018).

MDMA therapy sessions are described as "patient-driven" (Feduccia et al., 2019; Sessa, 2017; Thal & Lommen, 2018), with the assisting therapists responding to prompts initiated by the patient by loosely guiding clients in a safe direction regarding trauma memories (Sessa, 2017). The MDMA-assisted stage usually runs the duration of approximately eight hours, and takes place anywhere from one to three times throughout the three-stage process (Amoroso & Workman, 2016; Sessa, 2017; Thal & Lommen, 2018), sometimes even including overnight stays at a facility to ensure patient safety (Sessa, 2017). While the client is under the influence of the MDMA, therapists assist the client with confronting and reframing their trauma memories (Sessa, 2017). MDMA dosing during the therapy sessions most often involves an initial dose of 125mg (Sessa, 2017; Thal & Lommen, 2018), which can be followed up approximately two hours later with a supplemental dose of 62.5mg to prolong effects of the MDMA for psychotherapeutic purposes (Sessa, 2017). According to Sessa (2017), the supplemental dose is optional and entirely the patient's decision. The U.S. National Library of Medicine (2018) states that research trial clinicians will administer anywhere from 80-180mg of MDMA per MDMA-assisted psychotherapy session.

The Multidisciplinary Association for Psychedelic Studies (MAPS) has constructed an MDMA-assisted psychotherapy treatment manual for psychotherapists entering the field of MDMA therapy (Sessa, 2017). Clinical trial literature suggests that therapists who are interested in assisting with MDMA therapy should be trained in various trauma therapy regimens, including cognitive behavioral therapy (CBT), prolonged exposure therapy (PE), and/or eye movement desensitization and reprocessing (EMDR) (Thal & Lommen, 2018). During the MDMA therapy sessions, it would be usual to have two therapists present with the patient, with substance-assisted sessions being spaced out within the eight to sixteen-week period of total therapy sessions (Sessa, 2017). The integration stage(s) refers to the combined non-drug-assisted, maintenance therapy sessions the patient attends following each MDMA-assisted session, in which usual 90-minute psychotherapy sessions are conducted to process trauma memories from the MDMA-assisted experience(s) (Sessa,

2017; Thal & Lommen, 2018). These three stages together constitute MDMA-assisted therapy for treatment of PTSD (Amoroso & Workman, 2016; Sessa, 2017; Sessa, 2018).

Proposed benefits

Neurobiological effects of MDMA are reported to increase compassion (“A multi-site phase 3 study,” 2018; Feduccia et al., 2019; Sessa, 2017), reduce defensive responses to fear (“A multi-site phase 3 study,” 2018; Feduccia & Mithoefer, 2018; Feduccia, Holland, & Mithoefer, 2018; “MDMA Therapy,” 2019; Sessa, 2017; Sessa, 2018), decrease negativity of memories (Amoroso & Workman, 2016; Feduccia et al., 2019), improve communication (“A multi-site phase 3 study,” 2018), increase feelings of closeness (Feduccia, Holland, & Mithoefer, 2018; Sessa, 2017; Jerome et al., 2013; Thal & Lommen, 2018), heighten sensitivity (Thal & Lommen, 2018), increase empathy towards self and others (Feduccia, Holland, & Mithoefer, 2018; Jerome et al., 2013; Sessa, 2017; Sessa, 2018; Thal & Lommen, 2018), and increase openness (Feduccia, Holland, & Mithoefer, 2018; Thal & Lommen, 2018). In cases of individuals with PTSD, these neuro-effects of MDMA may be beneficial as an adjunct to psychotherapy. Research in psychedelic-assisted therapy for PTSD patients suggests that MDMA will aid patients in the accessing, reprocessing, and/or reframing of traumatic or fearful memories (Feduccia et al., 2019; Feduccia & Mithoefer, 2018; Feduccia, Holland, & Mithoefer, 2018; “MDMA Therapy,” 2019; Thal & Lommen, 2018). Additionally, studies have shown that PTSD patients have an easier time addressing and eliminating fear and/or fear responses related to prior traumatic events (“A multi-site phase 3 study,” 2018; Feduccia & Mithoefer, 2018; Feduccia, Holland, & Mithoefer, 2017; Sessa, 2017; Sessa, 2018). For sufferers of PTSD, one of the most challenging parts of the therapy process is forming a bond of comfort and/or trust with the therapist. Purportedly, MDMA assists in the forming of the patient-therapist relationship, encouraging patients to be more engaged and open with their therapists (Amoroso & Workman, 2016; Feduccia & Mithoefer, 2018; Feduccia, Holland, & Mithoefer, 2018; Sessa, 2017; Sessa, 2018). Sometimes described as an “emotional moment of grace,” MDMA experiences may allow individuals suffering from PTSD to confront themselves and share their memories with the therapist in a more honest, open, and forgiving way (“MDMA Therapy,” 2019, p. 4).

Long-term outcomes following MDMA-assisted therapy

The available literature is somewhat unclear as to the lasting duration of the therapeutic effects of MDMA-assisted therapy treatments after MDMA-assisted psychotherapy processes are completed. According to research, simple administration of MDMA to patients with PTSD will most likely not completely rid the patient of PTSD symptoms on its own but must accompany trauma therapy sessions in order to be effective in eliminating a patient’s symptoms (Jerome et al., 2013). Select studies overseen by MAPS reported that two-thirds of the MDMA-assisted participants were “cured,” considering cured as no longer meeting all the diagnostic criteria for PTSD (“MDMA Therapy,” 2019). Favorable effects of MDMA-assisted psychotherapy on PTSD symptoms reportedly last for a minimum of twelve months (Feduccia et al., 2019). Overall, however, there is a lack of extensive research on long-term success rates for MDMA-assisted therapy in PTSD patients (Thal & Lommen, 2018). This lack of long-term research is partly due to the extreme claim that three or fewer assisted sessions can essentially “cure” someone of PTSD symptoms, eliminate fear responses, remove trauma memories, and change internal self-beliefs in just a few hours of peak MDMA treatment, with an overall short treatment period for the entire proposed MDMA-assisted PTSD therapy process (Parrott, 2014). On the contrary, an article published in 2014 in *The Journal of Psychoactive Drugs*, suggests that there is only a “brief period of symptomatic relief” (Parrott, 2014).

Even if that relief lasts for a period of two or three years, this would still be considered brief in the larger context of an individual's lifetime. Considering the lack of longitudinal MDMA therapy research and some studies' loose interpretation of the terms "cured" and "eliminated" it is reasonable to say that more extensive follow-up research is needed concerning both positive and negative long-term outcomes of MDMA-assisted psychotherapy trials with PTSD patients.

MDMA vs. Other Treatment Options

Some of the controversy surrounding MDMA-assisted PTSD psychotherapy has to do with a lack of understanding concerning why MDMA-assisted therapy may be a better option compared to other psychotherapy treatment choices. Other PTSD treatment options include pharmacological prescriptions such as antidepressant selective serotonin reuptake inhibitors (SSRIs) (Feduccia et al., 2019; Thal & Lommen, 2018), trauma-based psychotherapy (Feduccia et al., 2019), cognitive behavioral therapy (CBT) (Thal & Lommen, 2018), eye movement desensitization and reprocessing (EMDR) (Thal & Lommen, 2018), and/or prolonged exposure therapy (Amoroso & Workman, 2016; Feduccia et al., 2019). For purposes of this paper, SSRI treatment of PTSD, general trauma talk therapy, and prolonged exposure therapy were considered in comparison to MDMA-assisted PTSD psychotherapy. Research claims that SSRI drugs, specifically paroxetine and sertraline, have more side effects and lower success rates in minimizing or eliminating PTSD symptoms than MDMA-assisted PTSD therapy (Feduccia et al., 2019). Several studies compare MDMA-assisted therapy to prolonged exposure therapy (PE), a type of psychotherapy specifically designed to help sufferers of PTSD confront their fears and traumatic memories or experiences (Amoroso & Workman, 2016; "Exposure therapy," 2015). Research also suggests that MDMA-assisted PTSD therapy also has lower dropout rates than other PTSD treatment options, proposing that MDMA therapy is therefore more beneficial.

SSRIs

Currently, one of the accepted treatments for PTSD is pharmacological management of symptoms. One of the most prescribed classes of drugs is SSRIs, types of antidepressant drugs that increase serotonin levels in the brain, assisting with patient positivity and happiness (Feduccia et al., 2019). However, reportedly only 20-30% of PTSD patients respond favorably to SSRIs (Amoroso & Workman, 2016; Thal & Lommen, 2018), specifically paroxetine and/or sertraline, with which participants reported only small symptom decreases (Thal & Lommen, 2018). MDMA-assisted therapy has reportedly higher success rates at alleviating fear response and negative trauma memory reaction than SSRI administration (Feduccia et al., 2019). Purportedly, adverse effects from MDMA last only hours or a few days as opposed to weeks of unpleasant effects from SSRI use (Feduccia et al., 2019), including frequent suicidal propensities noted with paroxetine, a commonly prescribed SSRI (Thal & Lommen, 2018). Another problem that often arises with SSRI prescribing in PTSD patients is compliance, which can pose many unknowns for treating professionals. Feduccia et al. (2019, p. 9) explain that "...since these drugs are take-home medications, patients are at risk of accidentally consuming contraindicated medication that could have serious adverse effects (on the patient's state of mind or SSRI dose), including death." Compared to MDMA, which purportedly has complete compliance in a supervised clinical setting, there are few ways for therapists and prescribing professionals to know if the patients have consumed prescribed SSRI drugs as instructed. Since patients self-administer prescription SSRIs, it is possible that patients may only intermittently consume the prescribed dosages, or may fail to consume the pills at all, leaving the

patient and the medical professionals with no conclusive evidence of the SSRI effects on the PTSD symptoms (Feduccia et al., 2019), while potentially simultaneously endangering the patient's life. Comparing SSRI and MDMA treatment of PTSD can be difficult, especially when considering patient physical and mental substance response variability. However, given the low rate of positive response and the high rate of lengthy adverse effect periods for SSRIs in PTSD patients, the supervised setting of MDMA-assisted psychotherapy may provide advantage rates that will never be accomplished with SSRIs.

Exposure therapy

Prolonged exposure therapy, which may include pharmacological maintenance, was designed specifically for treatment of PTSD and is intended to help people manage excessive fears but is excessively emotionally demanding on the patient (Amoroso & Workman, 2016; "Exposure therapy," 2015). The goal of exposure therapy is "to create a safe environment in which a person can reduce anxiety, decrease avoidance..., and improve one's quality of life" ("Exposure therapy," 2015, p. 1). The process of exposure therapy involves having the patient relive trauma events through a process called "flooding," suggesting that constant exposure to a traumatic memory experienced in a different environment than the threat initially occurred will produce elimination of the trauma or fear response (Amoroso & Workman, 2016, p. 596). Prolonged exposure therapy lasts about an hour per session, limited due to the emotionally demanding nature of the treatment, whereas MDMA therapy oftentimes lasts up to eight hours (Amoroso & Workman, 2016). In many studies, MDMA has been found to have comparable treatment results when compared to prolonged exposure therapy, however disadvantages are often noted, including the stress of reliving traumatic, frightful memories and exacerbation of various PTSD symptoms (Amoroso & Workman, 2016). Exposure therapy reports higher dropout rates than MDMA-assisted therapy, often attributing the patient frustration that results from lack of time to process each treatment session's re-experienced, or exposed, traumatic event (Amoroso & Workman, 2016). Due to its extreme induction of emotionality and discomfort, as well as many patients' inability to tolerate the reliving of trauma memories, PTSD exposure therapy is often frowned upon in the psychotherapy field, and other options have been sought out as treatment, including MDMA-assisted psychotherapy (Amoroso & Workman, 2016).

Conclusion

PTSD is a serious mental health condition affecting millions of individuals nationwide, bringing ideas on how these patients can be better assisted in treatment to the forefront of psychotherapy dialogues. These ideas include MDMA-assisted therapy options, citing MDMA as a beneficial, amplifying drug addition to the psychotherapy process (Feduccia et al., 2019). It can be reasonably concluded from this report that, despite its current federal Schedule I status and controversial side effects, MDMA-assisted psychotherapy may be a suitable treatment option for PTSD. MDMA has contradictory and debated positive and negative effects in patients with PTSD, often imposing the treatment decision solely on the patient, their perceived level of suffering, and perhaps even to their level of desperation for PTSD symptom alleviation. The decrease in negative feelings and fear responses resulting from MDMA-assisted therapy can be considered as either beneficial or harmful, viewed as positive in its freeing results and negative in its distressing moments and/or side effects (Parrott, 2014). Although Phase II studies to date report an overall PTSD symptom remission rate of 66.2% and low rates of adverse effects, experts agree that more studies

are needed to conclusively determine MDMA-assisted therapy as a permanent adjunct to psychotherapy; there have only been six Phase II blind trials (Thal & Lommen, 2018). Prior information considered, the MDMA-assisted therapy optimal case scenario would include minimal long-term effects, decreased fear responses, acceptance of trauma memories, high rates of PTSD symptom remission, and minimal MDMA administration occurrences.

Overall, there is a significant quantity of conflicting literature on whether repeated ecstasy and/or MDMA use is associated with long-term detrimental effects (Jerome et al., 2013), suggesting that there is not enough comparable research completed on this topic to date. Subsequently, the controversy over the use of hallucinogenic substances in therapy settings will continue, leaving such issues as “off-label” use of legalized pharmaceutical MDMA lingering and unresolved amidst the discourse of PTSD. Although not well discussed in this report, cost analysis is also in need of more attention in the field of MDMA-assisted therapy, including patient finances, Big Pharma, psychiatric providers, and insurance company aspects. All viewpoints considered, it seems logical to conclude that the safest option for a patient’s PTSD treatment options may be best determined jointly by the patient and their corresponding psychiatric professionals, leaving MDMA treatments to be further examined for definitive conclusions.

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