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The Efficacy of MDMA-Assisted Therapy as a Treatment for Post-Traumatic Stress Disorder – Ava von Offenberg Ryan | Helen Sun | Jocelyn Cheung |Ksenia Grigorieva | Polina Dubakova | Sabrina Cruz | 2022

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Abstract

Several studies have shown that MDMA could be used as an effective treatment for people living with PTSD due to its properties as a stimulator of neurotransmitters. Current clinical trials have shown it to increase patient quality of life and receptiveness to therapy. The authors of this paper have found that current pharmacological treatment options for PTSD predominantly comprise SSRIs. However, due to their side effects usually requiring augmentation strategies in the form of Prazosin and Benzodiazepines, the long-term use of these drugs can cause a range of severe side effects, including worsening PTSD symptoms in the long term. With MDMA use, patients have reported having a less negative perception of traumatic memories and increasing the emergence of painful material during therapy sessions. This means that traumatic material can be worked through and managed. Despite this, it was also discovered that MDMA also has adverse side effects due to its actions as a general neurotransmitter stimulator; a small number of patients had an adverse reaction to the drug, including feelings of anxiety and a fear of loss of control. These studies show promising results as it shows a long-term improvement in PTSD

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symptoms. However, we have surmised that more clinical trials should be performed to prove these conclusions on a larger scale.

Contents

Introduction

Post-Traumatic Stress Disorder (PTSD) is the continuous recollection of intrusive thoughts related to past traumatic event(s) which can result in extreme changes in mood and attitude (Schrader and Ross, 2021). Symptoms of PTSD generally fall into four categories (Torres, 2020):

- Intrusion
- Avoidance
- Alteration in cognition and mood
- Alterations in arousal and reactivity

It is also common for people with PTSD to suffer from depression, alcoholism, drug addiction, memory loss and many other physical and mental health issues (Torres, 2020) as many of these conditions also stem from trauma.

For the most part, historically, PTSD has been considered a shameful topic of discussion and extremely taboo. It was only in the late 1800s and early 1900s that treatment was researched. 3,4-methylenedioxymethamphetamine (colloquially known as 'MDMA') is a drug that activates neurotransmitters across main neural pathways (Green et al. 2003) thereby heightening the release of norepinephrine, serotonin, oxytocin and prolactin. These neurotransmitters result in an increased feeling of energy, mood elevation, increased trust with strangers, relaxation and openness to new ideas, respectively (White, 2014; Dumont et al., 2009; Green et al., 2003; Harris et al., 2002). Moreover, the methylenedioxy- component directly stimulates the 5-HT (serotonin) 2A receptor, which is theorised to be the cause of the psychedelic effects of MDMA, where a user experiences seeing colours more vividly and has the sensation of *feeling* music (Capela et al., 2009).

When used recreationally, MDMA is rarely consumed in a pure/unadulterated state, meaning there are other substances within the sample that heighten adverse reactions (Smith et al. 2022). The strong association with recreational use (and the adverse reactions of this) led to its criminalisation in the UK in 1977 under the Misuse of Drugs Act of 1971. More recently, research into its benefits as a form of treatment for PTSD, anxiety and social anxiety (National Institute on Drug Abuse, 2020), has led to some countries opening a debate on its legalisation for limited medical use. Within this debate, some scientists highlight the possible negative long-term impacts of MDMA-assisted therapy. By analysing the available literature on PTSD, this paper will seek to provide an overview of this disorder and its current treatments, and the efficacy, safety and stability of MDMA-assisted therapy for PTSD.
Importance of PTSD Treatment Research for Our SocietyPTSD is a hidden disorder that is often forgotten about, however, its treatment is very important as it affects a myriad of people in our society; for example soldiers, women, police officers and other trauma survivors.

Having fought in wars, soldiers are prone to suffering symptoms of PTSD due to the traumas they experience. In the 20th Century alone, the world experienced several wars - World War One and Two, the Korean War, the Vietnam War, the Gulf War, the First Congo War, etc. It is estimated that 10-20% of veterans suffer from PTSD (National Centre for PTSD, 2014), meaning that there are ~200,000-415,000 veterans in the UK who have, or are still suffering from, PTSD (Support for Veterans, 2021). This statistic alone should be enough of a reason to find the most appropriate treatment for PTSD. However, veterans are not the only ones who are in serious need of treatment,

the NHS believes that PTSD affects one in every three people who are involved in traumatic experiences such as car accidents, serious health problems, severe bullying and even childbirth (NHS UK, 2021).

According to APMS (2014) and highlighted in Figure 1, 16–24-year-old women are at a much higher risk of screening positive for PTSD at 12.6% as opposed to men in the same age group at 3.6%. Although the percentages seem low, 12% of the UK population is a little less than 7,800,000 people. PTSD is a mental disorder that, despite affecting millions, is not widely discussed, nor is its treatment openly considered.

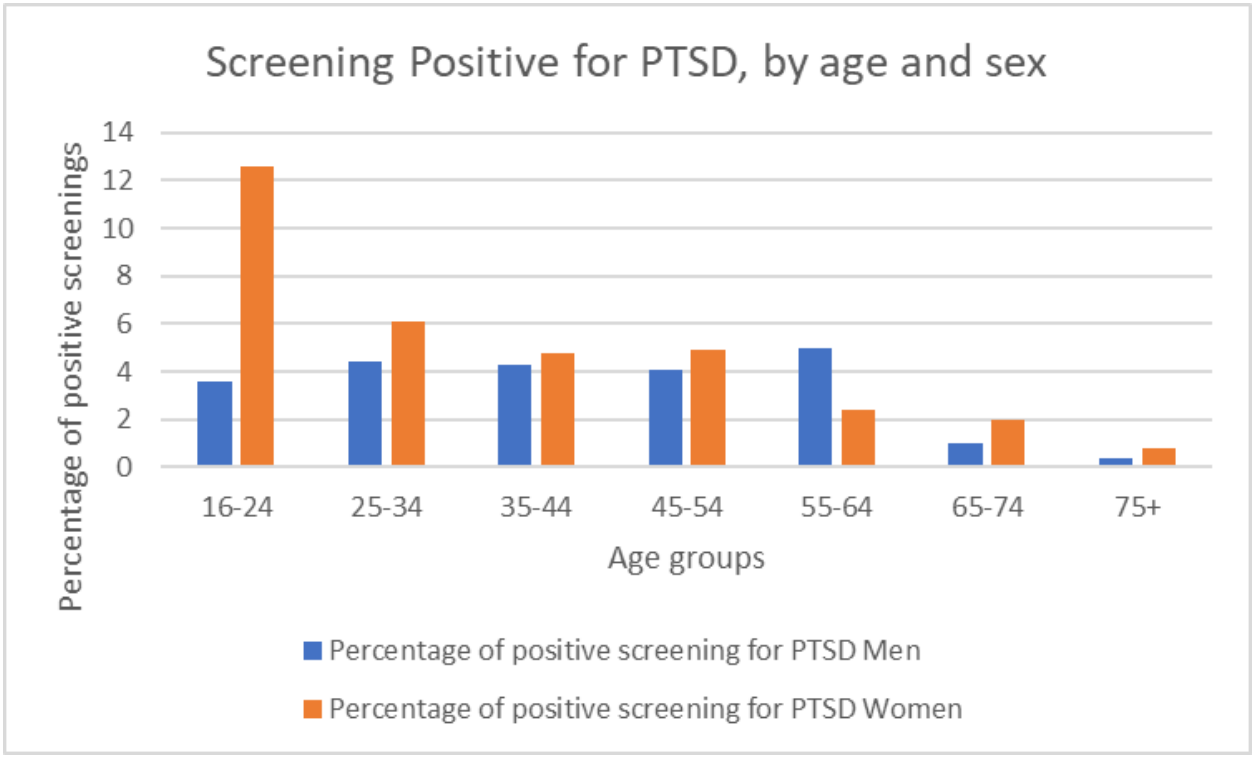

Figure 1: Screening Positive for PTSD by Age and Sex (APMS, 2014)

Hopefully, with all the attention that PTSD and its treatments are receiving currently, there will be more advancements in its treatments that will lead to millions of people in the UK and all across the world being able to have happier and healthier lives.

Current Treatment and Therapies For PTSD

Pharmacological treatment

Selective serotonin reuptake inhibitors (SSRIs) and selective norepinephrine reuptake inhibitors (SNRIs) have long-since been the primary pharmacotherapeutic treatment options for PTSD (Hoskins *et al*, 2018). Fluoxetine, Venlafaxine, Paroxetine, and Sertraline are some of the most commonly used SSRIs and SNRIs in treatments of PTSD (Ehret, 2019).

SSRIs and SNRIs increase serotonin and norepinephrine levels by blocking the reuptake of serotonin and norepinephrine respectively. As these inhibitors prevent neurotransmitters from being reabsorbed into the nerve cells in the brain after they have been released, the level of serotonin, (which is known to regulate anxiety, happiness, and mood) is kept high (Machado and Einarson, 2019). Although SSRIs and SNRIs are effective in treating depression, they may cause intolerable adverse effects that cause patients to switch or withdraw from their SSRI treatments. Gastrointestinal problems are commonly reported in patients taking an SSRI antidepressant. This is due to serotonin three and four receptors in the hypothalamus and the brainstem being stimulated by the SSRIs (de Abajo et al, 2006). The imbalance in serotonin levels increases gastrointestinal motility and cramps, leading to nausea, vomiting, and diarrhoea (Wang, 2018).

SSRIs can also affect the sexual functions of patients. A study has found that the incidence of sexual dysfunction is higher than 55% in most SSRIs and is higher than 90% when patients take Tricyclic Antidepressants (TCA) clomipramine regularly over a period of time (Cascade, 2009). A downside of SSRIs is that they increase the risk of bleeding and interfere with homeostasis – the biological self-regulation of the body in response to changing external conditions (Billman, 2020) - since they inhibit serotonin reuptake, which is responsible for platelet aggregation (de Abajo, 2011). This can be dangerous in elderly patients as blood coagulation increases with age (DeSouza, Jones and Seal, 1998). SNRIs are associated with increased heart rate and decreased heart rate variability (Nezafati, Vojdanparast and Nezafati, 2015). Furthermore, SNRI highly increases the rate of hypertension in patients, thus increasing the risk of developing cardiovascular diseases (Kemp, 2014).

Augmentation Strategies

Augmentation strategies are often utilised with the use of a primary SSRI or SNRI. Prazosin is generally used to relieve adverse side effects caused by SSRIs and SNRIs. Prazosin is an alpha-1 adrenergic receptor antagonist which works by relaxing muscles and blood vessels, thus allowing blood to pass through more easily, lowering blood pressure and reducing one's overall heart rate (Basquez and Pippin, 2022). It is generally used to relieve adverse side effects caused by SSRIs and SNRIs (Bridges et al, 2020). It also imprvoves sexual functioning as muscle relaxation leads to normal erectile function (Davis et al, 2018). Moreover, the use of prazosin leads to significant improvement in urinary flow due to the blockade of alpha adrenoceptors. (Khaw and Argo, 2019). However, side effects caused by Prazosin can be extremely dangerous or even fatal to certain patients (Paiva, Filho and Cais, 2021). Life-threatening side effects include first-dose hypotension and orthostatic hypotension. These hypotensions can cause a severe and sudden fall in blood pressure which results in a lack of blood flow to internal organs, the outcome of which is organ failure, and can be fatal (Bradley and Davis, 2003).

Benzodiazepine

Benzodiazepine is also one of the most widely used augmented strategies for PTSD, prescribed to 30-74% of patients (Guina et al., 2015), given its ability to reduce anxiety, insomnia, and irritability (Dimy et al, 2018). However, it is not well-recommended by mental health professionals due to evidence that it can be highly sedative and addictive, which can worsen symptoms of PTSD over the long-term (Guina, 2018).

A meta-analysis published in the Journal of Psychiatric Practice (2015), reviewed the results from 18 studies that, when combined, comprised a total cohort of 5236 participants with PTSD. The average age of the participants was 44 and 38% of the participants were women (Guina et al, 2015). The results of this research study revealed the high likelihood that Benzodiazepine is not only ineffective, but further endangers patients. This meta-analysis highlights that 11 out of the 13 studies which only included PTSD-specific measures (the remaining 5 were not exclusive to PTSD-specific measures), exemplified that taking benzodiazepines increased the severity of PTSD symptoms. This meant that the patients would have more symptoms of discontinuation syndrome, such as insomnia, nausea and imbalance. They would experience greater disruption of normal stress responses, and would avoid cognitive and emotional processing of their trauma (Guina et al, 2015).

With SSRIs causing a wide range of adverse side effects, augmentation strategies being potentially life-threatening, and Benzodiazepine increasing the likelihood of worsening PTSD symptoms, there is evidence to support the following statement:

Most of the current common treatments for PTSD are ineffective and unsafe. It is necessary to find an alternative that will provide better results for patients. MDMA has been proposed as the latest "safe" treatment for PTSD, however a lot of research is still required in this regard before its use can be widely supported.

Comparison of using MDMA as a treatment of PTSD to current treatments

Despite the large number of drugs available, the Veterans Administration Department of Defence guidelines for the 2017 systematic review writes that MDMA would only be used as a treatment after an unsuccessful trauma-focused psychotherapy, and before trying pharmacotherapy.

There are two most commonly used forms of psychotherapy for PTSD:

- Cognitive Behavioral Therapy
- Exposure Therapy

Both of these show a significant improvement in symptoms when compared to an absence of therapy. However, the current pharmacotherapy treatments, mentioned in the previous section, are preferable to some patients, rather than psychotherapy (Smith et al. 1995). There are a number of limitations to psychotherapy; for example, it requires multiple sessions and an experienced therapist must be present. It could also lead to an increased resistance from patients to attend sessions if they encounter difficulties when reliving their traumatic memories (Friedman 1988, Pitman et al., 1991). Prolonged exposure therapy includes ~6-19 sessions, which last ~1 hour. Due to their taxing nature, dropout rates for psychotherapy are estimated to be at 30% (Cloitre, 2009). In comparison a typical treatment for MDMA-assisted psychotherapy is 1-3 drug sessions lasting 8 hours each, including counselling, plus a number of follow-up sessions without drugs (Powers et al., 2010). In the current treatments of PTSD, there are substantial drawbacks, which are hoped to be addressed by the relatively new

treatment of MDMA. For example, only 20-30% of patients respond to the current pharmacotherapy treatments (Stein et al., 2009).

In comparison to other empathogenic substances, such as lysergic acid diethylamide (colloquially known as LSD and also a viable treatment option in psychotherapy), MDMA has been shown to induce smaller increases on the 5D-ASC scale (i.e. less intensity) and less pronounced perceptual effects (Schmid et al., 2020). The 5D-ASC scale measures a patient's altered state of consciousness on the basis of self-reporting. These perceptual changes typically appear to be more intense in female patients (Liechti et al., 2001). Overall, group psychotherapy studies conducted in Switzerland suggest that both LSD and MDMA induce altered states of consciousness and produce 'mystical experiences' (the intensity of which was measured using the Mystical Experiences Questionnaire) in patients diagnosed with various psychiatric disorders, with MDMA proving to be particularly beneficial in PTSD therapy (Amoroso and Workman, 2016; Mithoefer et al., 2010, 2018, 2019; Sessa et al., 2019).

Some difficulties arise when evaluating the benefits of MDMA as a psychotherapeutic tool, since the patient may be taking other drugs in conjunction with MDMA. In one study, patients were given MDMA after a pre-treatment of duloxetine (another treatment of PTSD). When referencing the Adjective Mood Rating Scale (60-item Likert scale evaluation), duloxetine decreased well-being, emotional excitation, and extroversion by 49.5%, 73.5% and 58.8%, respectively, in comparison to MDMA on its own (Hysek et al., 2012). Moreover, a chronic use of paroxetine and/or citalopram showed a weakening in the positive effects generated by the MDMA (Rietjens et al., 2012).

Clinical studies also suggest that there are differences in the effect of MDMA on healthy volunteers and patients diagnosed with psychiatric disorders. For example, MDMA has been shown to produce significantly greater ratings of anxiety and ego dissolution in patients than in healthy volunteers (Schmid et al., 2020). This may be due to higher levels of pre-existing anxiety in patients with psychiatric disorders. MDMA also induced greater perceptual alterations (inc. complex imagery) in patients than in healthy volunteers (Hasler et al., 2004; Hysek et al., 2011; Liechti et al., 2017; Vollenweider and Kometer, 2010; Vollenweider et al., 2007; Schmid et al., 2015a; Studerus et al., 2010). Therefore, since some clinical trials are performed on healthy volunteers, it could be more difficult to identify the precise effects of MDMA.

MDMA as a treatment of PTSD

As discussed previously, MDMA has several effects which could make it a successful psychotherapeutic tool. In one study on early substance-assisted psychotherapy (Gasser, 1994), 84% of 121 patients reported improved quality of life - with the greatest impact being on their emotional lives. Participants reported feelings of unity, spiritual experiences, and intense visions and perceptions - however, these effects are difficult to quantify and be objectively validated by clinical studies. Mood and energy elevation may be beneficial to the patient, as they could have a more positive attitude towards their session and experience less fatigue (Parrott, 2014; White, 2014). The psychedelic effects of MDMA may allow the patient to have an increased openness when talking

about their suppressed trauma, as the intense emotional experiences (such as seeing colours more vividly) allow them to perceive an environment different from their norm (White, 2014).

Research has shown that MDMA reduces the activity of the left anterior cingulate cortex, left amygdala and temporal cortex, while increasing the activity of the hippocampus (Carhart-Harris et al., 2014) - all of these are regions of the brain associated with PTSD (Bremner et al., 2005). This could be the reason why patients (who were administered MDMA) typically report a less negative perception of traumatic memories (Carhart-Harris et al., 2014), and therefore why MDMA appears to promote the emergence of painful and distressing material during a session (Bouso, 2001; Greer and Tolbert, 1986). The potential benefits of MDMA-assisted therapy are largely due to its empathogenic effects - these increase an individual's feelings of social acceptance and empathy, and have been demonstrated through clinical studies on healthy volunteers (Carhart-Harris et al., 2018). These desirable effects of MDMA, which result in a more successful therapy session, peak around 2.5 hours, when it is at a maximum concentration in the blood, and these effects are absent 6 hours after dosing, despite elevated blood concentrations (Hysek and Liechti, 2012). An increased sense of trust and reduced anxiety may allow for a stronger connection between the therapist and patient (a crucial point in PTSD therapy). More effective communication promotes introspection, which is critical to a patient's recovery (Greer and Tolber, 1998; Grinspoon & Bakalar, 1986; Greer, 1985; Bouso et al., 2008). But while such prosocial effects would be particularly beneficial to psychotherapy, there is currently no published data on the acute effects of MDMA on individuals outside controlled clinical group studies (Schmid et al., 2020).

Results Analysis

MDMA is proven to be an effective treatment for reducing the severity of PTSD symptoms. Mithoefer et al. (2011), conducted a randomised, double-blind and placebo-controlled trial, which assessed the impact of MDMA doses (125 mg) on PTSD patients. Data gathered in this study showed that MDMA was more effective at reducing mean Clinician-Administered PTSD Scale (CAPS) scores than placebo doses, since during the open-label phase of the study, all subjects averaged a significant 48% reduction in CAPS scores. A lower CAPS score correlate to a less severe case of PTSD. Mithoefer et al. also offered a supplemental MDMA or placebo dose to the patients receiving MDMA. This dosage wasn't offered in the placebo trials, which increased the chance of the therapist or patient determining who received MDMA and who received the placebo (Smith et al., 2022). Therefore we could question the adequacy of blinding in this study (Mithoefer et al., 2011).

There is also evidence to suggest that MDMA has positive long-term effects on the treatment of PTSD. 107 participants received 2-3 active sessions where a moderate to high dosage (75-125mg) of MDMA was provided. From the baseline CAPS score measurements until 1-2 months after receiving the last MDMA dose, the CAPS scores had decreased by an average of 44.8 units. 10-11 months after this final measurement the CAPS score decreased by a further mean of 5.2 units (Jerome et al., 2020).

A study by Bouso et al. (2008) examined the effects of MDMA on patients during a 6-hour experimental psychotherapy study. Despite the significant limitations of this study (most notably the

low sample size (6), caused by political pressure against this study at the time), it generated data on the impact of MDMA on the Severity of Symptoms Scale for PTSD (SSSPTSD). This study concludes that SSSPTSD scale scores were reduced by 26.8% on average, after patients were given MDMA, compared to the 10.1% decrease observed in placebo patients. SSSPTSD rates the severity of PTSD symptoms on the basis of patients' self-reporting. Although this data suggests that MDMA-assisted therapy may be particularly effective for reducing the severity of PTSD symptoms, this data is less significant due to the small sample size and the fact that the SSSPTSD scale is used less frequently in clinical studies.

When comparing a number of studies (Mithoefer et al., 2011; Oehen et al., 2013; Ot'alora et al., 2018; Mithoefer et al., 2018; Mitchell et al., 2021), statistical heterogeneity (when there is an unexpected variability in results) can be observed. This is explained by the following reasons (Smith et al., 2022):

Firstly, these studies had a variation in the baseline CAPS scores. Oehen et al. had an initial score of ~65 while Mithoefer et al. had a score of ~87 and Ot'alora et al. had a score of ~90. Oehen et al. had a less significant reduction in CAPS scores than Mithoefer et al. and Ot'alora et al.

Furthermore, there were differences in causes of PTSD. For example, the predominant trauma for Mithoefer et al., Mitchell et al. and Oehen et al. was crime, developmental and sexual assault, respectively. However there is insufficient data to determine whether these differences were the cause of statistical heterogeneity.

In order to produce more significant results, further studies should be conducted, containing a larger sample size and stronger analysis of the impact that causes of PTSD have on the efficacy of MDMA treatment. Moreover, most patients in the trials mentioned had severe PTSD, according to their CAPS scores, which were ≥50. Therefore, further analysis needs to be conducted to assess those with less severe PTSD, and see whether there is a similar impact on their CAPS scores (Smith et al., 2022). Lastly, future clinical researchers should be inclined to publish all results, irrespective of their success, as due to publication bias, there is little secondary perspective available on using MDMA as PTSD treatment (Smith et al., 2022).

Dangers of MDMA-Assisted Psychotherapy

MDMA is a drug which is documented to alter mood by increasing the concentration of serotonin in the synaptic cleft of serotonergic neurons, thereby causing it to bind in excess and creating increased nervous impulses (Parrott, 2014). Although generally less prevalent, the negative effects of MDMA have been documented in both clinical trials on those with PTSD as well as illegal MDMA users (Parrott, 2014; Jerome et al., 2020).

The drug has been used in both recreational and medical settings, and usually leads to an elevated sense of happiness or euphoria. However, even from early studies on its use, around five in 20 people reported having unpleasant drug reactions (Davidson and Parrott, 1997). The drug was reported to induce general neurochemical activation which means both positive and negative emotions are

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heightened. MDMA use has left many individuals feeling increasingly anxious, apprehensive and with a fear of losing thought control (Parrott, 2014). This sort of negative spiralling effect could be incredibly damaging for people suffering from PTSD who are already experiencing often uncontrolled episodes of fear and anxiety.

The short-term effect of MDMA could amplify and increase these uncontrollable negative emotions and plunge patients into an even more critical state. As well as short-term negative effects, there are increased longer-term side effects of long-term MDMA use (even in small doses). On a neurological basis, MDMA has been linked with serotonin neurotoxicity by depleting the brain's supply of neurotransmitters, especially serotonin and 5-HT thereby leaving long-term symptoms.

Even if the individual gains immediate positive neurological effects, these subside, and when the effect of the MDMA has worn off, the individual can be left in a state of neurochemical depletion. This leads to feelings of lethargy, depression and anger. (Parrott, 2014)

These intense psychological side effects can be dangerous for psychologically vulnerable patients who may be plunged into depressive moods after MDMA use. As well as this, Peroutka et al. (1988) described interviews with American recreational MDMA users and surmised that after prolonged use, the short-term positive effects lessened and there were more noticeable side effects.

MDMA can also have other physiological effects, such as the inhibition of CYP2D6 - an enzyme that catalyses multiple reactions involved in drug metabolism as well as the synthesis of steroids and other lipids (Papesit and Pérez-Mañá 2020). The inhibition of CYP2D6 by MDMA can reduce the efficacy of other drugs that require transformation by the enzyme and therefore make the use of MDMA and other drugs dangerous. This reduces the suitability of MDMA as a therapeutic treatment for PTSD as it will limit the other drugs available to those suffering from PTSD.

Mixing drugs has been an approach undertaken by some to reduce the effect of the drastic drop in serotonin experienced during the period after the drugs have had their “positive” effect – widely expressed as a “comedown period”. (Pilgrim et al., 2011) Taking other drugs could lead to serious consequences if they interact badly. In Pilgrim et al. (2011), the scientists looked into all closed cases reported to The National Coroners Information System in Australia between 2002 and 2008 where MDMA was detected. 106 deaths were recognised in which 43 cases involved the concomitant use of MDMA with other drugs. Though this analysis was thorough, 106 cases represent a small sample size on which to base the analysis and thus is not representative of the whole situation of the danger of concomitant use of MDMA with other drugs. It is therefore suggested (by the authors of this paper), that more data be collected from all around the world to improve the significance of the study.

In the instance of concomitant use of MDMA, an individual has a high risk of serotonin toxicity - defined by Pilgrim et al. (2011) as “a possibly lethal effect associated with ecstasy use”. Several serotonergic antidepressants can lead to serotonin toxicity, such as tramadol, fluoxetine and even “clean drugs” like moclobemide (which would not usually cause side effects) may be problematic in this instance (Pilgrim et al., 2011).

Serotonergic antidepressants are potent CYP2D6 inhibitors, therefore they increase the toxicity of MDMA. All drugs have to be metabolised in some way, and MDMA is metabolised through oxidation which is carried out by CYP2D6 and another enzyme known as CYP450. When the CYP2D6 are inhibited by the serotonergic antidepressants, MDMA are competing with other drugs for CYP450 for it to metabolise itself down for excretion; the competition for the enzyme can affect the elimination of either drug, consequently resulting in the accumulation of drugs and possible toxicity. (Pilgrim et al., 2011).

As mentioned by Pilgrim et al. (2011), women are at a higher risk for testing positive for PTSD, but unfortunately, they are also more prone to some of the unfavourable effects of MDMA (Schenk and Newcombe, 2018). In addition, older people (age 45 years and above) who are exposed to MDMA for the first time, have shown a fall in working memory that appeared additive to those experienced by normal ageing; but similar to the situation for female patients, the greatest incidence of PTSD is in those ranging from 40 to 50 years of age (Schenk and Newcombe, 2018).

In clinical trials for patients suffering from PTSD, the active dose of MDMA given has been between 25 to 125 mg of MDMA (Jerome et al., 2020). Although this is lower than that taken for illegal recreational use (~260mg of active MDMA), it is still enough to have serious negative effects.

One study that looked into the specific effects of MDMA on memory in PTSD patients found that it can have an amnestic effect on positive recollections (Doss et al., 2018). In Doss et al. (2018), the researchers gave a 1.0mg/kg dose of MDMA to six healthy participants, who were sorted into three different groups. One group was given MDMA during encoding and placebo during retrieval. The second group was given MDMA during retrieval and placebo during encoding, whilst the third group was given placebo for both events. Probabilities were calculated for each section and the statistical analysis was very thorough. However, as the sample size was so small this does provide a more limited view of the effects. To provide more significant data, more subjects should be used.

Considering that Depression and PTSD have a high comorbidity (Campbell et al., 2007), MDMA is not a suitable drug for patients who also suffer from depression, as it can reduce the recollection of positive memories. This, therefore, reduces the percentage of PTSD patients who can benefit from the drug. Additionally, there is also the risk that patients may be prescribed the drug before being diagnosed with depression.

There is certainly some evidence to suggest that there is a statistically significant number of people who could face potential long-term negative effects caused by MDMA treatments (Doss et al., 2018; Jerome et al., 2020). Therefore, because of its role as a stimulator of neurotransmitters, MDMA should be used with caution for those who are already in a compromised psychological state (Parrott, 2014).

Conclusion and Discussion

Post-Traumatic Stress Disorder (PTSD) is a prevalent psychiatric disorder in the UK and it negatively impacts the lives of people that are suffering from it, as it leads to the continuous recollection of traumatic memories, which can result in extreme changes in mood and attitude.

Suffering from depression, alcoholism, drug addiction and memory loss is common for people with PTSD, as these conditions also derive from trauma.

Numerous medications have been used in an attempt to treat PTSD, including SSRIs, SNRIs, Prazosin and Benzodiazepine, however these treatments have limited efficacy and may also cause a significant number of adverse effects. Therefore, since some patients are not willing to undertake pharmacotherapy due to potential adverse side effects, MDMA is being considered as a possible future psychotherapeutic tool.

Research indicates that MDMA significantly elevates patients' PTSD treatment, particularly in group clinical trials. After an MDMA treatment, patients may experience greater openness and transparency when talking about their emotions, potentially leading to a deeper connection between therapist and subject (which is highly beneficial to communication and success in therapy). MDMA has demonstrated the ability to lessen symptoms of PTSD in the long-term. To more accurately assess the efficacy of MDMA-assisted therapy, further large-scale studies should be conducted, particularly focusing on patients with less severe PTSD. Considering the causes of patients' PTSD may be useful in evaluating the effectiveness of MDMA in different contexts. Publication bias is a significant issue, as researchers are less inclined to publish the results of failed studies, leading to a skewed presentation of the data and preventing others from accessing all available information on clinical studies into MDMA-assisted therapy.

However, the efficacy of MDMA comes with a significant number of side effects. It could further worsen the mental state of the patient by making them experience mood swings – a patient could quickly go from experiencing euphoria to feeling incredibly anxious and apprehensive. The drug can act as an inhibitor to the drug-metabolising enzyme CYP2D6, and reduce the efficacy of other drugs. This would be a significant negative side of the drug.

In addition, as shown in the experiment by Pilgrim et al. (2011), there is a huge danger in mixing drugs with MDMA, and this act could lead to the risk of serotonin toxicity. The common antidepressants serotonergic that are commonly taken in company with MDMA would act as inhibitors to CYP2D6, which would put pressure on another enzyme that metabolises MDMA like CYP450. This would lead to serious consequences when MDMA builds up and is not metabolised. The side effects are particularly not in favour of women and elderly people who tend to be at higher risk of diagnosing PTSD. It is strongly advised by the authors of this paper that more research on drug interaction with MDMA be done to protect more patients with vulnerable minds.

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