MDMA for Treatment of PTSD

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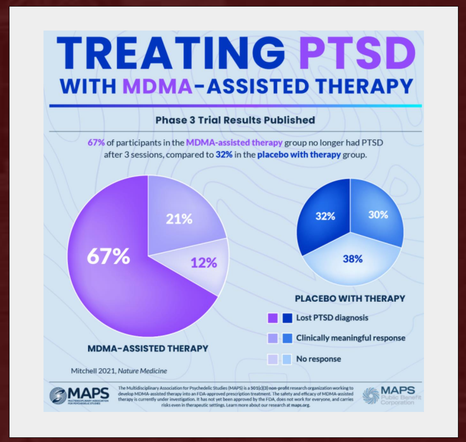
Introduction

- Post-traumatic Stress Disorder (PTSD) is a diagnosis that over 13 million people have in the United States as of 2020 (U.S. Department of Veterans Affairs, n.d.).
- Current SSRIs have an overall response rate of 60%; however, only 20—30% of people with PTSD treated with these medications achieve remission (Schrader & Ross, 2021).
- In the most recent trial, 71.2% of the participants in the MDMA and psychotherapy group no longer met the diagnostic criteria for PTSD at the end of the 18 weeks versus 47.6% of the placebo plus psychotherapy group (Mitchell et al., 2023).
- MDMA produces no serious adverse side effects (Mitchell et al., 2023).
- MDMA reduces or eliminates fear and anxiety, allowing patients access to their traumatic emotions and easing the inability to express their thoughts and fears (Mitchell et al., 2021).
- MDMA was made a Schedule 1 drug in 1985 and requires permission from the FDA for research (Hendy, 2020).



Purpose

- PTSD affects an estimated 7.7 million Americans annually (Gorman et al., 2020).
- The total economic burden was estimated at $232 billion in 2018 (Davis et al., 2022).
- The purpose of this paper is to show the current success of using MDMA and psychotherapy to treat this devastating disorder.

PICOT

- Does the administration of MDMA-assisted psychotherapy, as compared to traditional pharmacology or psychotherapy alone, result in a superior reduction of PTSD symptoms and show an overall improvement in the quality of life?

Methods

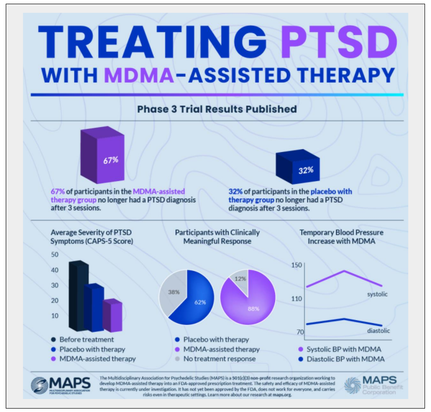
- The literature used in this review was compiled using an electronic search of databases, which included CINAHL, PubMed, and MEDLINE.
- The searches used the following keywords: "PTSD," "MDMA," "3.4-methylenedioxymethamphetamine", "MDMA-assisted psychotherapy," "post-traumatic stress disorder," and "ecstasy."
- The searches were conducted from 2018– 2023, plus a seminal study done in 2008.
- All searches included only English literature.
- Articles were excluded if they used other psychedelics with MDMA, focused on a specific type of psychotherapy, or focused more on a social issue instead of using MDMA as the focus of treatment.
- Articles were manually searched to ensure the electronic search missed no inclusion criteria.
- The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram was used to visualize the research strategy and the systematic review results.
- Each of the 23 articles was screened using the Rapid Critical Appraisal Questions for Randomized Clinical Trials (RCT) to exclude and further finalize the nine articles used in this systematic review.

Strengths

- Only RCTs were analyzed for this analysis.
- All studies were published between 2018 and 2023, except the seminal study published in 2008.
- All studies required a diagnosis of PTSD before enrollment in the study.
- There was a CAPS-IV or CAPS-V range that all participants had to be within to enroll.
- Outcomes were measured by validated measurement tools such as CAPS-IV, CAPS-V, AUDIT/DUDIT, or PQSI.

Results

- Three phased trials were reviewed, pooled, and their data analyzed (Ot'alora et al., 2018; Mithoefer et al., 2018; Mitchell et al., 2021).
- One study showed that consistent with prior research, there was a significant reduction in CAPS-IV scores in the MDMA groups (Ot'alora et al., 2018).
- The crucial part of that study is that it showed a continued reduction in the 12-month follow-up, with 76% (n= 25) of the study participants not meeting the criteria for a PTSD diagnosis (Ot'alora et al, 2018).
- Another part of this study showed a significant reduction in secondary outcome measures (sleep, depression, and dissociation) compared to their initial baseline after the administration of MDMA and psychotherapy (Ot'alora et al., 2018).
- Another study compared CAPS-IV scores at baseline and 12 months; all showed a statistically significant improvement ($p<0.0001$) (Mithoefer et al., 2018).
- This study also showed that MDMA was well tolerated with few significant side effects or adverse reactions and secondary reductions in depression, sleep quality, and dissociative symptoms with low treatment discontinuation rates (7.7%) (Mithoefer et al., 2018).
- There have been enough studies showing a potentially positive correlation between MDMA-assisted psychotherapy and the significant reduction or elimination of PTSD symptoms that this treatment modality needs to be taken seriously, and more, larger, studies need to be implemented.

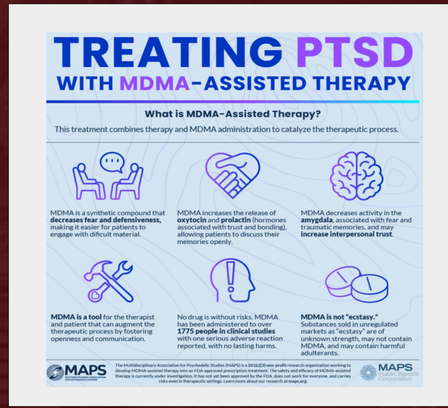


Weaknesses

- In 1985, an emergency ban was placed on MDMA by the Drug Enforcement Agency (DEA) due to its widespread availability; it was then made a Schedule 1 drug, and all research was halted (National Institute on Drug Abuse, 2017).
- To study MDMA, a special, closely regulated permit must be obtained by the FDA.
- There is a stigma attached to MDMA use that increases the difficulty of obtaining support for therapeutic studies.

Implications for Practice

- PTSD has been shown to have a high level of comorbidity, often coexisting with substance use disorders, mood disorders, anxiety disorders, and depression; MDMA with psychotherapy has been found to reduce PTSD symptoms significantly (Nicholas et al., 2022).
- Having been studied as a treatment for alcohol use disorder (AUD), MDMA was not found to have a significant impact; however, since AUD is closely associated with PTSD, it shows promise as a potentially successful treatment when approached from this direction (Nicholas et al., 2022).
- Currently, 40-60% of patients do not respond to the two FDA-approved medications for PTSD, paroxetine and sertraline; this gives them another successful option (Mitchell et al., 2021).
- When used with MDMA dosing, fear-extinction training participants achieved a marked reduction in fear-potentiated symptoms (Maples-Keller et al., 2022).



Recommendations

- Lobbying for the rescheduling of MDMA from a Schedule 1 to a Schedule 2 medication would make further research studies profoundly easier.
- Future RCTs would be designed with larger study groups to further demonstrate the potential success of this treatment.
- There are detailed instructions on the FDA website to assist in obtaining the proper permits and sponsorship for further studies.

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References available upon request