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Treating Post Traumatic Stress Disorder (PTSD): A Critical Evaluation of Pharmacological and Psychotherapy Efficacy

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ABSTRACT

Post traumatic stress disorder (PTSD) is a psychiatric disorder that develops after an individual experience or is exposed to a traumatic event and is not equipped to handle it now. This condition is globally prevalent and can happen in any individual. The symptoms of post-traumatic stress disorders include re-experiencing traumatic memories, negative and emotional cognitions, and hyperarousal. PTSD is associated with impaired function in several brain regions, including the amygdala, hippocampus, and prefrontal cortex. This review will consider the different aspects of treatment approaches to PTSD and will examine the effectiveness and mechanisms of promising pharmacological medicines and established psychotherapies. This paper aims to help identify and discuss the most reliable and cost-effective integrated strategies for both the prevention and ongoing management of PTSD, along with exploring emerging therapies.

Keywords: *PTSD, Trauma, Treatment, Pharmacological, Therapy, Flashbacks, Amygdala, Nightmares*

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INTRODUCTION

Post-traumatic stress disorder (PTSD) is a serious psychiatric disorder that occurs because of experiencing a traumatic event. These traumatic events may include war, physical or sexual violence, natural disasters, the death of a loved one, accidents, or any situation where one feels extremely threatened and endangered (Kessler et al., 2017). Certain structures of the brain, like the amygdala, prefrontal cortex, and hippocampus, are closely related to some of the symptoms of PTSD. The amygdala plays a crucial role in diverse processes, such as emotional responding, memory formation, fear conditioning, and fear extinction, which is also known as fight or flight response. The hippocampus is essential for declarative or episodic memory, while the prefrontal cortex plays a crucial role in higher-level cognitive functions' is associated with hypoactivation of the prefrontal cortex, hyperactivation of the amygdala, and volume reductions in the hippocampus (Manthey et al., 2021).

The PTSD prevalence is much higher among veterans compared to civilian populations and women suffer from PTSD more than men. Another study states that in the civilian population the lifetime PTSD prevalence for men is 3.6% and for women is 7.9% compared to the veteran population, it is 6.2% for men and 13.2% for women (Lehavot et al., 2017). Constant symptoms and chronic nature of PTSD make it necessary to have efficient, cost-effective and reliable treatments.

This paper provides an in-depth understanding and comprehensive probe of the studies and evaluations of the most trending and established pharmacological, psychotherapeutic treatments. Comparative outcomes help assess the efficacy and cost-effectiveness of these approaches in reducing the symptoms and impairments associated with PTSD.

PHARMACOLOGICAL TREATMENTS: NEUROCHEMICAL APPROACHES

Pharmacological treatments are often used as the primary line of treatment or paired with psychotherapy methods. These modifications are considered as instant relief to relieve PTSD symptoms. For some individuals with PTSD, psychotherapeutic treatment may be ineffective for people with ongoing trauma or insecure social situations (Corrigan & Hull, 2015).

SSRIs and SNRIs: Primary pharmacological interventions

Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are the most widely studied and frequently prescribed medications since the 1980s. These medications are often primary treatments due to their efficacy in improving the core symptoms of PTSD, such as re-experiencing, avoidance, and hyperarousal. Some of the most used SSRIs include sertraline (Zoloft), fluoxetine (Prozac), and paroxetine (Paxil). A commonly used SNRI is venlafaxine (Effexor). Both sertraline and paroxetine are FDA-approved for PTSD, while fluoxetine and venlafaxine aren't FDA-approved for PTSD. A

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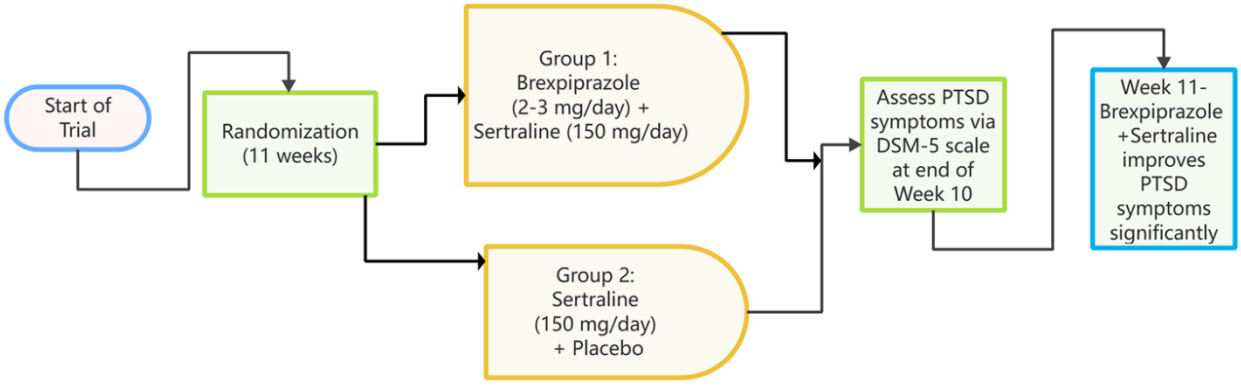
study shows that sertraline and venlafaxine outperformed many other medications for PTSD treatment, while another study says that fluoxetine, paroxetine, and venlafaxine reduced the severity of PTSD symptoms in diagnosed individuals (Hoskins et al., 2021).

Brexpiprazole: A promising adjunctive treatment for PTSD

While SSRIs have been known for their effectiveness in treating PTSD, studies say that only 60% saw a noticeable difference with the treatment (Berger et al., 2008). Therefore, brexpiprazole has been gaining popularity for PTSD treatment. Brexpiprazole is a typical antipsychotic with broad pharmacological activity across noradrenergic, serotonergic, and dopaminergic neurotransmitter systems implicated in psychiatric disorders, including PTSD. A trial (as shown in Figure 1) was conducted over 4 years with 416 participants (310 female and 106 male) who are randomized for 11 weeks. Among 214 participants, oral brexpiprazole was administered at 2 to 3 mg per day (flexible dose), along with sertraline 150 mg. In contrast, 202 participants received sertraline 150 mg per day, along with a placebo (1:1 ratio). At the end of 10 weeks, the PTSD scale for DSM-5 total score, which measures the severity of 20 PTSD symptoms, was assessed from randomization (week 1) to week 10 for the brexpiprazole and sertraline groups. The combination treatment of brexpiprazole and sertraline significantly improved PTSD symptoms, indicating its potential as a new effective treatment for PTSD (Davis et al., 2024).

Figure 1

Brexpiprazole and sertraline combination treatment in PTSD visual abstract.



Prazosin: Targeting nightmares and hyperarousal in PTSD

Sleep disturbances in PTSD remain a major clinical challenge. This is due to nightmares and internal issues. Prazosin is an alpha-1 adrenergic antagonist medication primarily used to treat high blood pressure, but it is also prescribed off-label to reduce nightmares and sleep disturbances associated with PTSD. Its efficacy has been questioned after the largest trial was negative. Randomized clinical trials were conducted comparing prazosin to placebo in samples of patients with PTSD. Analysis revealed that prazosin significantly improved

insomnia and nightmares, but not overall PTSD symptoms (Mendes et al., 2025). While prazosin has demonstrated efficacy in treating trauma-related nightmares and insomnia in PTSD, some patients remain non-respondent. There is significant uncertainty about prazosin's efficacy; higher doses of prazosin could subject patients to side risks for primarily non-pharmacological benefits.

Ketamine: An emerging treatment in PTSD care

A new emerging medication, ketamine, is a compound structurally related to phencyclidine. It is favorable in medical contexts because of its notably improved safety profile. This medication is another antidepressant, and has the potential to regulate specific molecular pathways related to PTSD symptoms. Ketamine's lipid-soluble nature and low protein binding enable it to quickly pass through the blood-brain barrier (Wellington et al., 2025). This makes it possible to use a variety of administration techniques, which speed up distribution and enhance brain effects. Ketamine administration methods include sublingual/buccal/oral, subcutaneous (SC), intramuscular (IM), intravenous (IV), and intranasal (IN) routes. According to preliminary studies, ketamine can improve extinction and prolonged exposure therapies for PTSD, particularly in patients who are not responding well to conventional therapies (Glavonic et al., 2024). According to preliminary small-scale research, ketamine may improve the efficacy of prolonged exposure therapy, which would be an advantage for individuals suffering from PTSD who don't respond to conventional therapies, and have the potential to improve fear extinction therapy. By directly targeting and reducing the activity of traumatic memory-encoding cells in brain regions such as the basolateral amygdala, when administered during a memory re-exposure timeframe, research suggests it may lessen PTSD symptoms (Glavonic et al., 2024; Li et al., 2022).

PSYCHOTHERAPEUTIC TREATMENTS: COGNITIVE AND BEHAVIORAL PATHWAYS

Comprehensive PTSD treatment requires psychotherapeutic interventions in addition to medication. These treatments help people process their experiences and build coping mechanisms by directly addressing the cognitive, emotional, and behavioral effects of trauma. These therapies are essential to recovery because they enable people to regain control and enhance their everyday functioning by actively addressing the traumatic content and related beliefs. Even though all trauma-focused psychotherapies are thought to involve a meaningful processing of the trauma memory in some respect, the proposed underlying mechanisms of trauma-focused approaches, and indeed, the specific approaches of each respective intervention, nonetheless vary (Jericho et al., 2021).

Prolonged Exposure Therapy

PE is a highly effective type of cognitive-behavioral therapy (CBT) or trauma-focused psychotherapy. It is one of the most common therapies that people with PTSD use alone or with pharmacological treatment. It focuses on helping individuals process traumatic memories and reduce fear symptoms in PTSD by confronting an individual about avoided thoughts, feelings, and situations related to the trauma. This type of therapy acts as

a fear of extinction for trauma. However, based on many studies, patients who took PE started dropping out of treatment because of worsening symptoms. In a study of post-9/11 veterans over 3 years who received individual CPT or PE as part of routine VHA practice, we found that 22.9 % of veterans experienced reliable PTSD symptom worsening. Reliable worsening was defined as a 10-point increase from pre-treatment to any point in the treatment course as measured by the PCL-5. While there are concerns about symptom worsening, regardless, PE is in use as one of the most common therapies that people with PTSD use alone or with a pharmacological treatment (Holder et al., 2025).

Cognitive Processing Therapy

Cognitive Processing Therapy (CPT) has been widely studied and is considered one of the most effective PTSD treatments. It is also a trauma-focused therapy like prolonged exposure. Cognitive Processing Therapy typically involves 12 sessions lasting about 60 to 90 minutes. There are four steps involved in Cognitive Processing Therapy. The first step is to educate the person about PTSD; the next step is processing trauma where the person writes down their trauma which helps accept the emotions and reduce the power of traumatic memory. The third step is to identify and challenge unhelpful thoughts, where CPT helps to identify stuck points, thoughts and beliefs that may be distorted or unhelpful. The last step is to learn new skills, where the patient learns new skills to cope with trauma-related thoughts and feelings during the progression of therapy.

A dismantling study was conducted over six weeks for 12 hours of treatment, and one-hour sessions that focused on identifying and exploring trauma-related beliefs. During this, women participants with PTSD related to interpersonal violence who were randomized to the full CPT protocol (CPT-C) were compared to women who were randomized to receive CPT with the written accounts portion (WA). Participants randomized in both studies demonstrated significant reductions in PTSD symptoms. Based on the meta-analyses, it's reported that CPT has a strong effect on PTSD symptoms, with rank analyses suggesting that CPT may be more effective than other treatments (Sager et al. 2025). The last few decades have seen an explosion of research on CPT, and there is strong evidence that CPT is robust across a wide range of populations and settings and in various formats. Implementation efforts are ongoing to ensure the availability of this first-line, recommended treatment on the frontlines of healthcare.

Mindfulness-Based Cognitive Therapy (MBCT)

Mindfulness Based Cognitive Therapy (MBCT) emphasizes accepting the present moment without passing judgement by combining features of Cognitive Therapy with mindfulness exercises. MBCT was created in 2002 by Zindel Segal, Mark Williams and John Teasdale, attempts to alter one's relationship with thoughts by studying mindfulness practices for a more inclusive route to favorable mental health results. Though they take different approaches, both MBCT and conventional Cognitive Behavioral Therapy (CBT) are useful for treating mental health issues. To stop relapses in conditions like depression, MBCT places a strong emphasis on mindfulness and the nonjudgmental acceptance of thoughts. Traditional CBT, on the other hand, focusses specifically on changing unfavorable thought patterns and behaviors. For instance, a CBT therapist may utilize

cognitive restructuring to treat depression, while an MBCT therapist may utilize acceptance to treat anxiety. Both approaches are based on patient symptoms. Totals of 87 studies were included in the review to assess the effects of MBCT on the brain structure changes, cognitive processes and emotional regulation (Gkintoni et al., 2025). The types of studies involve clinical trials, cohort studies and systematic reviews that comprise a comprehensive synthesis of available data. The findings point out the robust efficacy of MBCT in enhancing subjective well-being through improved neuropsychological outcomes and its potential to induce physiological and neurobiological changes, leading to lasting improvements. MBCT consistently reduces symptoms related to depression, anxiety and stress while increasing cognitive functions and emotional regulation in several populations (Gkintoni et al., 2025).

Transcendental Meditation (TM):

Transcendental Meditation (TM), which emphasizes a state of relaxed awareness, provides a unique method of treating PTSD. This method entails sitting comfortably with your eyes closed for 20 minutes, twice a day. The goal of TM is to calm distracting thoughts so that the body and mind can rest deeply. After just a few minutes, practitioners usually feel more rested, focused, and ready for everyday tasks because of this process, which is thought to relieve nervous system stress and improve brain function.

In a well-known study, 203 PTSD-afflicted veterans were randomized to receive 12 sessions of TM, PE, or PTSD health education (HE) over 12 weeks (Groessl and Rutledge, 2025). The findings showed that both TM and PE outperformed HE and that TM was not less effective than PE at enhancing PTSD outcomes. Moreover, of the three treatment approaches, TM proved to be the most economical. TM was substantially less expensive than PE ($2,822), with an estimated cost of $1504 for 12 sessions, while showing better health outcomes than both PE and HE (Groessl and Rutledge, 2025). This implies that TM, a mind-body intervention, has great potential as a non-trauma-focused PTSD treatment that offers significant advantages in terms of symptom alleviation and cost-effectiveness.

CONCLUSION

This comprehensive review emphasizes the cost-effectiveness of psychotherapeutic treatment approaches, such as Transcendental Meditation and mindfulness-based Cognitive Processing Therapy. It presents evidence from studies demonstrating sustained, long-term, consistent improvement of PTSD symptoms through therapeutic treatments. Although studies on pharmacological drugs like ketamine indicate promising results, particularly due to the fastest pass through the blood-brain barrier and providing quick relief to PTSD, there are still significant gaps in the research regarding the uncertainty and limitations of the long-term relief, as well as the potential side effects of these drugs. Further research is needed to address these uncertainties. Bridging the gap between research and clinical practice is crucial to advancing PTSD treatment, enabling more effective personalized interventions. Patients with severe symptoms can start on a medication treatment plan for the short term, but for long-term treatment, therapy-based approaches are generally used when the patient is more clinically stable.

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This insight carries real-world relevance. In a time defined by uncertainty, institutional distrust, and philosophical unease, these films encourage a deeper kind of freedom: one grounded in responsibility, presence, and care. They suggest that meaning is not a discovery waiting outside of us but a construction we must engage in—deliberately, ethically, and often in the company of others. The existential question remains unresolved, but the answer, as both films show, begins with the courage to respond.

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