Treatments Available for PTSD with an emphasis on combat-related PTSD

Bailey King

Wofford College

Abstract

PTSD has lifetime prevalence between 7% and 12% in the United States, is typically chronic with a mean duration of 20 years and is associated with a high degree of psychosocial and occupational impairment. More than 80% of those with PTSD will develop at least one other psychiatric disorder during their lifetime and are at an increased risk for developing major depression, alcoholism or substance abuse, panic disorder, generalized anxiety disorder, suicide and co-occurring medical illness. There have been several studies conducted to investigate the effectiveness of pharmacological treatments, cognitive behavioral treatments as well as a combination of the two treatment types. A vast majority of these studies have found that monotherapies consisting of either psychotropic treatment or psychotherapy are effective in treating not only symptoms of PTSD but depressive and anxiety symptoms as well. Furthermore, it has been found that, because monotherapies are limited in the extent to which a patient’s PTSD symptoms are reduced, research has suggested for a combination of psychotropic medications and psychotherapies to maximize the potential efficacy of treatment. It is important to continue research in the field of combat-related PTSD because, as of December 2009, over two million Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) troops have been deployed over seas. Of these troops, as many as 20% of those who have returned suffer from mental health difficulties including combat-related PTSD with only about half of that 20% of veterans meeting criteria for PTSD or depression actually seeking healthcare.
Introduction

Historically, posttraumatic stress disorder (PTSD) has been strongly associated with war-related situations. Over the years the elements of PTSD have been described in various ways. For example, after World War II, the symptoms were described as “traumatic war neurosis” or “combat neurosis” while the Korean and Vietnam wars focused more on the combat-related gross stress reaction as found in the first edition of the Diagnostic and Statistical Manual of Mental Health Disorders (DSM) (Martenyi & Soldatenkova, 2006). In later editions of the DSM, the symptoms of PTSD evolved to be described as Vietnam syndrome and transient situational disturbance as the term “PTSD” was not introduced until the third edition of the DSM (Martenyi & Soldatenkova, 2006). According to the fourth edition of the DSM (DSM-IV), PTSD is a disorder that occurs after exposure to an “extreme traumatic stressor” to oneself or someone close, accompanied by a response of “fear, helplessness, or horror”. It is characterized by persistent re-experiencing of intrusive and distressing recollections of the event (re-experiencing/intrusion), avoidance of cues associated with the event and numbing of general responsiveness (avoidance/numbing) and increased arousal (hyperarousal). The full symptom complex must be present for at least one month and must cause significant distress or impairment of social, occupational or other areas of functioning to fulfill the criteria for diagnosis (DSM-IV; Davidson et al., 2006a). It has been suggested in previous functional neuroimaging studies that PTSD patients show abnormal increased regional functioning in such areas as the amygdala and visual cortex while decreased regional functioning has been found in the prefrontal cortex and hippocampus. Unfortunately, it is still unclear whether these imaging deficits could change in association with clinical improvement, as there is a vast dearth in research within this area of study (Hongru et al., 2015).
PTSD TREATMENTS

PTSD has lifetime prevalence between 7% and 12% in the United States, is typically chronic with a mean duration of 20 years and is associated with a high degree of psychosocial and occupational impairment (Friedman et al., 2007). The median recovery time is between three and five years (Davidson et al., 2001b). More than 80% of those with PTSD will develop at least one other psychiatric disorder during their lifetime and are at an increased risk for developing major depression, alcoholism or substance abuse, panic disorder, generalized anxiety disorder, suicide and co-occurring medical illness (Davidson et al., 2006a). Sixty percent of people in the general population of the United States will experience at least one traumatic event in their lifetime with about 8% to 10% developing PTSD (Hertzberg et al., 2000). At-risk individuals, such as victims of criminal violence, survivors of civilian disasters and combat veterans, show prevalence rates from 4% to 30% (Tucker et al., 2001). About 10% to 15% of the severe trauma survivors will develop chronic PTSD, which can often persist for years if untreated. It is estimated that between 13% and 17% of Vietnam veterans suffer from current PTSD with an additional 11% experiencing many of the symptoms of PTSD but not meeting full DSM criteria (Hertzberg et al., 2000).

Davidson and colleagues (2001a) suggested that a potential therapy for PTSD should effectively treat the core symptoms of the disorder consisting of re-experiencing (i.e. intrusive thoughts, nightmares, flashbacks, images or memories); phobic avoidance of trauma-related situation; emotional numbing (flattened affect or detachment/loss of interest and motivation); and hyperarousal (startle reactions, poor concentration, irritability, jumpiness, insomnia and hypervigilance). While a potential therapy should treat all symptoms of the disorder, it should also insure that individuals successfully respond to the therapy and maintain remission when therapy is completed to allow an individual to sustain an improved quality of life. This review
PTSD TREATMENTS

focuses on three different types of therapy: pharmacological treatments, cognitive behavioral therapy with an emphasis on prolonged exposure therapy, and how these treatments can be compared and combined to effectively treat patients with PTSD.

Pharmacological Treatments

Originally, PTSD treatment studies focused on the efficacy and safety of various antidepressants such as selective serotonin reuptake inhibitors (SSRIs), selective serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs). More recently, there has been an increase in research attempting to define the underlying biological dysfunctions responsible for PTSD. Therefore, treatment studies have refocused to broaden the scope of other therapeutic agents that could work using alternate mechanisms that enable improvement as well as other agents that can be used as either a replacement or adjunct to antidepressants (Ravindran & Stein, 2009).

Due to the high comorbidity between PTSD and major depression, as well as the established efficacy of SSRIs for depressive and anxiety disorders, there has been considerable focus on using these antidepressants in treating PTSD patients. Three commonly used SSRIs are sertraline, paroxetine and fluoxetine, of which, the first two (sertraline and paroxetine) have FDA approval specifically for PTSD treatment in the United States. Davidson and colleagues (2001a) conducted a multicenter, double blind study to test the efficacy of sertraline in the treatment of PTSD. In their 12-week randomized, placebo-controlled study, patients who were administered up to 200 mg of sertraline a day saw significantly greater improvement on all efficacy measures tested as compared to the patients receiving the placebo. Treatment with sertraline produced a significant range of 45% to 50% average improvement from baseline scores on the primary measures of overall PTSD symptom severity. The severity of the three core symptom clusters
PTSD TREATMENTS

(re-experiencing/intrusion, avoidance/numbing, hyperarousal) also improved with the sertraline treatment as compared to the placebo treatment. In addition to improvements of PTSD symptoms, Davidson and colleagues (2001a) found that patients who received sertraline showed rapid and significant improvement on global measures of social functioning and occupational functioning.

In a follow-up study done by Davidson and colleagues (2001b), a 28-week double blind study was conducted to evaluate the efficacy of sertraline for relapse prevention in patients with PTSD. Patients were only eligible to enter the current study if they had previously completed a 12-week acute (short-term) treatment that randomly assigned sertraline or placebo and 6 months of open-label continuation (long-term) treatment in which all patients in the sample knowingly received sertraline. The study found that patients who received sertraline treatment maintained the gains achieved during the 24-week open-label treatment, while patients who received placebo significantly worsened. Not only did sertraline show a significant advantage over placebo in preventing relapse, but was also associated with a four to six-fold reduction in the possibility of a recurrence of PTSD.

Friedman and colleagues (2007) also conducted a randomized, double blind study to evaluate the efficacy of sertraline but specifically focused on patients with predominantly combat-related PTSD in a VA clinic setting. In their 12-week, flexible dose study, patients also received up to 200 mg of sertraline or placebo a day but did not find sertraline to be efficacious on any of the outcome measures used. There was no significant difference in total severity scores or in the rate of change over the course of the 12-week treatment period between the sertraline and placebo groups. Because these findings significantly conflict with previous studies, Friedman and colleagues (2007) suggest that the Vietnam veterans receiving treatment for PTSD
within the VA settings are not necessarily representative of military veterans with combat-related PTSD, which may be due to the fact that these veterans are being treated decades after their initial combat trauma. Another reason why the treatment was not effective could be because this population of veterans may represent the most severely impaired, chronic and treatment resistant sample of patients with PTSD and therefore, may not respond to sertraline treatment as positively as patients have in previous studies.

In a more recent study, Panahi and colleagues (2011) conducted a randomized, double blind study to evaluate the efficacy of sertraline in Iranian veterans with combat-related PTSD. In this 10-week, placebo-controlled study, patients who received up to 200 mg of sertraline a day showed a mean reduction in overall frequency and intensity of symptoms as well as in the three core symptoms (re-experiencing/intrusion, avoidance/numbing, hyperarousal) when compared to the placebo group. Researchers suggest that, in the sample of Iranian Iraq-Iran war veterans with combat PTSD included in the study, sertraline therapy can be associated with improved control and decreased severity of symptoms.

There seem to be some discrepancies between studies evaluating the use of sertraline in treating combat-related PTSD. One discrepancy that can be seen is the differences in traumatic conditions of war due to the time period, such as the environment of Vietnam versus Iran/Iraq, as well as the how far removed the particular conflict has become in terms of time period. Another discrepancy is the baseline clinical presentations of participants’ symptoms of PTSD as it seems that different war experiences are related to varying levels of symptom frequency and severity. Some studies have found Vietnam veterans to be most resistant to pharmacological treatment (Friedman et al., 2007; Hertzberg et al., 2000; Davidson et al., 1990). Other discrepancies that
PTSD TREATMENTS

could affect patients’ response to treatment include accompanying comorbidities and the psychosocial, racial and religious differences found between cultures (Panahi et al., 2011).

In addition to sertraline, paroxetine is another SSRI that is commonly used and FDA approved to treat PTSD. Paroxetine was initially studied for the treatment of PTSD because previous depression studies suggested that it had antianxiety effects as well. Marshall and colleagues (2001) conducted a double blind, fixed-dose multicenter study to test the efficacy of paroxetine in treating PTSD. In this 12-week placebo controlled study, nonmilitary patients were randomly assigned to three treatment groups: placebo, paroxetine at 20 mg a day and paroxetine at 40 mg a day. Researchers found that there was significant improvement for both paroxetine groups as compared to the placebo group. Patients treated with paroxetine had response rates of 62% (20 mg/day) and 54% (40 mg/day) as compared to 37% of patients treated with placebo. Marshall and colleagues (2001) also note that even though approximately one-half of the patients had comorbid major depressive disorder, it did not seem to influence treatment response as patients with and without comorbid major depressive disorder experience significant improvement while taking paroxetine as compared to placebo.

In a more recent study, Naylor and colleagues (2013) investigated the efficacy of paroxetine in a small sample of veterans from the Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) era who had already developed subthreshold PTSD and who had been symptomatic for several months or longer. Generally, subthreshold PTSD includes individuals who have experienced a traumatic event and subsequently report some but not all three core symptoms that are consistent with PTSD. In this 12-week randomized, double blind study patients who were administered up to 40 mg of paroxetine showed no significant difference in total severity scores from baseline to end point as compared to placebo. Researchers mention that
even though changes in PTSD symptoms were not significantly different, veterans receiving paroxetine tended to demonstrate a 30% greater reduction in anxiety and depression symptoms compared to the placebo group. It is understood that the degree of an individual’s impairment increases as the number of PTSD symptoms increase, which can cause subthreshold PTSD symptoms to progress to full PTSD. Therefore, early intervention treatments could a potential option to reduce commonly co-occurring mood and anxiety symptoms, minimizing an individual’s overall impairment.

Yet another SSRI commonly used to treat PTSD is fluoxetine, even though it is not FDA approved. Martenyi and colleagues (2002) conducted an initial study to evaluate the efficacy of fluoxetine in patients with PTSD from a sample of predominately men who had been exposed to combat related trauma. This 12-week double blind study found that fluoxetine was associated with a greater improvement across most assessments used as compared to the placebo with significant differences starting week six through 12.

In a follow-up study, Martenyi and Soldatenkova (2006) explored the efficacy of fluoxetine in a male sub-population of the previous study who was traumatized during the Yugoslavian civil war (1992-1996) and who suffered from combat-related PTSD. In this 12-week double blind study, patients were randomized to receive either a daily maximum of 80 mg of fluoxetine or placebo. The patients who responded to the acute treatment were then re-randomized in a 24-week relapse prevention phase. In the acute treatment phase, patients who received fluoxetine had significantly greater improvement that was detectable after only 6 weeks on treatment outcome assessments than patients who received placebo. Patients who received fluoxetine also showed significant improvements compared to the placebo group on all three core symptoms (re-experiencing/intrusion, avoidance/numbing, hyperarousal). In the relapse
prevention phase, patients who were re-randomized to a placebo treatment after receiving fluoxetine were a little over three times more likely to experience relapse than patients who continued receiving fluoxetine treatment. Researchers were able to estimate the average time it took for patients to experience relapse in the fluoxetine to placebo group at 174 days but no corresponding estimate could be made for the fluoxetine to fluoxetine group. Martenyi and colleagues (2006) suggest, in light of their findings, that the optimal periods of SSRI treatment for combat-related PTSD could be considerably longer than the recommended 12 weeks generally found in trials including civilian PTSD. They also suggest that because combat-related PTSD could be more severe and chronic than what is normally found with civilians, higher doses of SSRI treatment are needed to effectively treat veterans.

Another 12-week double blind study comparing fluoxetine to placebo, done by Hertzberg and colleagues (2000), found that fluoxetine patients did not have a greater response than placebo patients. Researchers report findings from previous research indicating that females and patients with civilian trauma respond better to serotonergic drugs. Therefore researchers suggest that no significant difference between fluoxetine and placebo was found because their population was a small sample of male Vietnam veterans. These findings are similar to those of Friedman and colleagues (2007), which suggests that the condition of Vietnam veterans may be too complex to be treated with a pharmacological monotherapy due to the elevated severity and frequency of symptoms commonly found in this sample.

Even though SSRIs have been shown to ameliorate PTSD symptoms, there has been a varied pattern of results in treatment studies that shows inconsistencies across patient types (combat veterans versus civilians), core symptoms (re-experiencing/intrusion, avoidance/numbing, and hyperarousal), and gender, including in studies with FDA approved
drugs. There was a lack of efficacy of SSRIs in treating PTSD with some studies finding response rates to SSRIs rarely exceeding 60% with even fewer patients (20% to 30%) experiencing improvement that could be categorized as remission (Stein, Kline & Matloff, 2002). These findings suggest that there is evidence for the involvement of neurotransmitters other than serotonin, such as norepinephrine, in the pathophysiology of PTSD.

Even though some PTSD components are considered as related to stress-induced increases in noradrenergic activity, the exact role of noradrenergic pathways in the pathophysiology of PTSD is still unclear (Davidson et al., 2006b). One selective serotonin norepinephrine reuptake inhibitor (SNRI), venlafaxine extended release (XR), inhibits presynaptic reuptake of both serotonin and norepinephrine (Ravindran & Stein, 2009). Venlafaxine XR is has demonstrated efficacy in producing remission and is currently approved in the US to use as treatment in patients with disorders such as generalized anxiety disorder, depression, panic disorder and social anxiety disorder.

Davidson and colleagues (2006a) conducted a randomized, double blind study to evaluate the efficacy of venlafaxine XR in treating PTSD as compared to sertraline and placebo. In this 12-week study, patients received a maximum dose of 300 mg of venlafaxine XR a day and a maximum dose of 200 mg of sertraline a day. The patients receiving venlafaxine XR showed significantly greater improvement in overall symptom severity than patients receiving the placebo. Venlafaxine XR patients also showed significantly greater improvement in avoidance/numbing and hyperarousal core symptoms but not in the re-experiencing core symptom. Researchers found that the magnitude of the differences in symptom improvement between patients who received venlafaxine XR and sertraline on outcome measures was small and insignificant. This finding suggests that, even though the two drugs may manipulate slightly
different pathways in the brain, they are broadly similar and are equally efficacious and safety to use in treating PTSD patients (Davidson et al., 2006a). When comparing pharmacological treatments, clinicians should consider the treatment that is the most effective with the least dosage as well as lowest cost. In previous studies, sertraline alone has been found to be efficacious in decreasing all three core symptoms using a lower dose than was used by Davidson and colleagues (2006a) in testing venlafaxine XR. Therefore, it seems that patients would benefit more from receiving sertraline than venlafaxine XR.

In a follow-up study, Davidson and colleagues (2006b) conducted a 6 month randomized trial using venlafaxine XR to evaluate the efficacy of venlafaxine XR in treating moderate to chronic PTSD symptoms. In this 24-week double blind study, patients receiving venlafaxine XR displayed significantly greater improvement at the endpoint than placebo on most of the outcomes measures and showed significantly greater improvement in the core symptoms of re-experiencing/intrusion and avoidance/numbing but not for hyperarousal. Researchers found that remission rates were around 60% for venlafaxine and 37% for placebo. Davidson and colleagues (2006b) mention that due to high risk of relapse in patients with chronic PTSD, continuation of medication for at least one year is considered standard clinical practice in treating PTSD symptoms. Unfortunately, there is a deficit in research studies that extend the acute test phase beyond 12 weeks. Davidson and colleagues (2006b) point out that there is a failure in their research as well as in previous studies in finding consistent results across all three core symptoms. They suggest that this failure could represent an inability of SSRIs and SNRIs to adequately control the full range of PTSD symptoms, implying that further research is needed in the efficacy of medications other than SSRIs and SNRIs.
Another class of antidepressant commonly used in treating PTSD includes tricyclic antidepressants, which have a primary mechanism of action involving varying degrees of serotonin and norepinephrine reuptake inhibition but are generally less selective in their actions on specific neurotransmitters (Ravindran & Stein, 2009). This class of medication is usually reserved for second or third line treatment for anxiety and depressive disorders due to patients experiencing a high rate of adverse events while receiving treatment.

Davidson and colleagues (1990) conducted a randomized, double blind study using a small sample of male veterans who served in World War II, Korea or Vietnam to examine the efficacy of amitriptyline in treating PTSD. In this 8-week placebo controlled study, patients receiving amitriptyline showed significantly greater recovery rates for symptom improvement than placebo. Furthermore, amitriptyline patients showed significant treatment effects on both depression and anxiety scales. Researchers suggest that the overall response indicated a modest benefit for amitriptyline in selective ways. Amitriptyline patients also significantly improved in the core symptom of avoidance/numbing but only marginally improved on the core symptom of re-experiencing/intrusion. Researchers suggest that amitriptyline could assist patients to become more comfortable in facing the painful affects associated with the trauma, rather than avoiding those affects. Unfortunately, 64% of amitriptyline patients and 72% of placebo patients still met diagnostic criteria for PTSD. Researchers note that the patients included in the study, in most cases, had been symptomatic for an extended period of time without clear remission and may represent the more severely disabled section of the veteran population who have been exposed to combat, which has been a reoccurring argument in research studies focused on Vietnam veterans with combat-related PTSD.
In addition to studies that have focused on reducing the core symptoms of PTSD, there has also been research in the alleviation of secondary symptoms such as sleep disturbance. Arguing that alpha₁ receptor stimulation is linked to sleep disruption, stress-induced disruptions in PFC cognitive processing and increased release of CRH, which are all commonly experienced in PTSD patients (Ravindran & Stein, 2006). Other clinical studies have suggested that enhanced postsynaptic adrenergic receptor responsiveness to the central nervous system norepinephrine contributes to the pathophysiology of PTSD particularly at night (Raskind et al., 2007). Trauma nightmares and sleep disturbance are among the most treatment-resistant and distressing symptoms of PTSD. The physiology of PTSD trauma nightmares differ from normal dreams such that trauma nightmares are largely expressed during light sleep and disrupted REM sleep, which can often be accompanied by motor activity (Raskind et al., 2007). These nighttime PTSD symptoms likely contribute to self-medication through alcohol and drug abuse as well as suicide ideation.

One medication commonly used as an adjunctive agent in addition to other treatments of PTSD is prazosin, which is an alpha₁ receptor antagonist that most easily enters the brain and has been demonstrated active at alpha₁ adrenergic receptors (Raskind et al., 2007). Prazosin has been used safely for many years in general medicine for hypertension and urinary outflow obstruction. Raskind and colleagues (2003) conducted to evaluate the efficacy of prazosin for treating nightmares, sleep disturbance and overall PTSD in combat veterans. Each of the 10 Vietnam combat veterans participated in a 20-week, two period, two-treatment crossover study. Patients were randomly assigned to either prazosin first or placebo first and then completed three weeks of dose titration followed by six weeks of maintenance treatment at the maximum achieved dose. At the first endpoint (week nine), the patients entered a two week washout where they took no
study drugs. At the end of week 11, the patients were crossed over to the other treatment condition. The second drug was then titrated upward for three weeks, which was then followed by a six-week maintenance treatment period that terminated at week 20. Researchers found that the participants had greater improvement when taking prazosin as compared to placebo on the primary outcome measures of nightmares, sleep disturbance and change in PTSD severity and functionality. They also found that prazosin was more effective for the core symptoms of re-experiencing/intrusion, avoidance/numbing and hyperarousal than placebo. In light of the current results, researchers concluded that as PTSD nightmares appear to come from light sleep and disrupted REM sleep, prazosin is an effective treatment to reduce light sleep and normalize REM sleep (Raskind et al., 2003).

In a follow-up study, Raskind and colleagues (2007) attempted to evaluate, overall, if prazosin would be more effective than a placebo for reducing trauma nightmares, improving sleep quality and improving global clinical status in a larger sample of combat veterans with chronic PTSD. In their previous study (Raskind et al., 2003), patients reported that “normal” dreams returned when trauma nightmares were reduced or eliminated in response to prazosin treatment. Therefore, researchers (Raskind et al., 2007) also hypothesized that the characteristics of recalled dreams in the prazosin condition would shift from those typical of trauma nightmares toward those typically found in normal dreams. In this study, most participants had been receiving group or individual psychotherapy for at least two months prior to entering the trial and maintained ongoing psychotherapy unaltered throughout the study. Twenty of the 40 participants had also been receiving one or more maintenance psychotropic medications at study entry, with the most commonly prescribed medication being SSRIs, and these medications were continued unchanged during the trial (Raskind et al., 2007). Participants were randomly assigned to receive
either prazosin or placebo for eight weeks with a maximum daily dose of 15 mg. Researchers found that prazosin produced significantly and substantially greater improvement than placebo in each of the three primary outcome measures addressing frequency and intensity of trauma-related nightmares, sleep quality and global clinical status. At the eight-week assessment, recurrent distressing dreams in prazosin decreased over 50% compared to a decrease of only 15% for placebo. There were no significant differences between patients on psychotropics versus patients not on psychotropics in change in rate of symptom or reductions in severity of recurrent distressing dreams. Raskind and colleagues (2007) concluded that taking prazosin just before bedtime substantially reduces distressing nighttime PTSD symptoms in veterans with chronic PTSD as well as reverses the effects of stimulation of the central nervous system alpha1 adrenergic receptor by decreasing light sleep and normalizing REM sleep. The findings also suggest that if prazosin is given in addition to another psychotropic medication, such as an SSRI, as an adjunctive agent there will most likely be no adverse effects. This implies that, while SSRIs may not improve the entire range of PTSD symptoms a patient could experience, adjunctive agents such as prazosin taken as a secondary treatment could ameliorate more selective symptoms like recurrent distressing dreams and sleep disturbance.

Another adjunctive medication that is becoming more common in clinical trials are atypical antipsychotics, such as olanzapine. This class of drugs is different from typical antipsychotics because of their actions on various neurotransmitter systems other than dopamine (Ravindran & Stein, 2009). Dopaminergic dysfunction has been suggested in the presence of psychotic symptoms sometimes exhibited by PTSD patients, but it has also been suggested to play a role in hyperarousal symptoms such as irritability, hypervigilance and exaggerated startle. Similar to prazosin, olanzapine is one type of drug that is an atypical antipsychotic with
prominent sedating properties and has a potential to be used in PTSD treatment but not as the primary mode of medication.

Stein, Kline and Matloff (2002) conducted a randomized, double blind study to test the efficacy of an adjunctive pharmacological treatment for SSRI-resistant PTSD. All patients PTSD symptoms were prospectively judged to be minimally responsive to 12 or more weeks of treatment with an SSRI before entry into the current study. Patients continued to take their maximally tolerated stable dose of SSRI (sertraline, paroxetine or fluoxetine) and were randomly assigned to take either olanzapine or a placebo at bedtime for the first two weeks of the 8-week trial. Researchers found that patients receiving olanzapine were associated with a significantly greater reduction in PTSD symptoms than patients receiving a placebo. Olanzapine patients also showed a greater reduction in sleep disturbance and depressive symptoms. The treatment outcomes suggested that enhanced sleep accounted for much of the patient’s reported improvement. Researchers suggested that olanzapine is significantly better than a placebo as an adjunct in the treatment of SSRI-resistant PTSD patients and atypical antipsychotic medications may have a wide therapeutic spectrum that could go beyond the treatment of psychosis.

It is important to consider pharmacological treatments especially for patients who suffer from extremely severe and chronic PTSD, as they are generally able to reduce many of the distressing symptoms and allow patients to resume normal functioning. As symptom impairment decreases, the quality of life and functionality of patients increase to where they are more inclined to engage in other therapies without experiencing the adverse symptoms of re-experiencing, avoidance and hyperarousal. It is also important to consider which medications are the most beneficial for patients in terms of cost, dosage and side effects. It seems as if, in terms of previous studies, certain tricyclic antidepressants such as paroxetine have a lower maximum
dose than SSRIs such as sertraline. Unfortunately, due to the less selective nature of tricyclic antidepressants there is a possibility that patients could experience more severe side effects and interactions with comorbid diagnoses as compared to patients who receive sertraline. Overall, these pharmacological studies have three types of durations: acute, continuation and maintenance. While some studies found that acute treatment produced significant decreases in symptom severity and intensity, it seems that the studies with continuation and maintenance treatments produced higher remission rates that were stable over time. Unfortunately, depending on the types of benefits a veteran is receiving from the VA, long-term treatments may be too expensive. These pharmacological studies show that certain antidepressants as well as adjunctive agents are efficacious in treating the symptoms of PTSD but it is important to also consider the efficacy of cognitive behavioral therapy by itself as a treatment as well as the efficacy of combining cognitive behavioral therapy and pharmacological treatment.

**Cognitive Behavioral Therapy**

Cognitive behavioral therapy (CBT) is predominately used to reduce the discomfort and improve quality of life for patients suffering from PTSD (Shubina, 2015). It is assumed that the patient’s emotional involvement in traumatic memories makes distorted cognitive content accessible and creates a base for its modification by using a combination of cognitive and behavioral techniques to help patients identify and modify distorted beliefs connected with PTSD (Shubina, 2015). CBT includes a variety of exposure techniques, cognitive restructuring anxiety control training and methods that combine those elements. Gilboa-Schechtman and Foa (2001) suggest that there are three factors of effective processing of traumatic events: (1) emotional commitment to the memory of the traumatic event, (2) organization of traumatic narratives and (3) correction of dysfunction cognitive content that occurs immediately after the traumatic event.
The general components that comprise CBT for PTSD treatment include psychoeducation, cognitive restructuring, anxiety management and exposure.

Psychoeducation includes the dissemination of information about common symptoms following a traumatic event given during initial treatment sessions. This component highlights the hallmark symptoms of posttraumatic response and discusses, with the patient, the way in which the core symptoms will be treated during course of therapy. The aim of psychoeducation is to legitimize the trauma reaction, to help the patient develop a formulation of their symptoms and to establish a rational for treatment (Harvey, Bryant & Tarrier, 2003).

Cognitive restructuring consists of network models that suggest the resolution of PTSD requires the integration of corrective information that is incompatible with the existing fear structures. This component involves teaching patients to identify and evaluate the evidence for negative automatic thoughts, as well as helping patients to evaluate their beliefs about the trauma, the self, the world and the future (Harvey et al., 2003).

Anxiety management training is another component that aims to provide patients with coping skills to assist them to gain a sense of mastery over their fear, to reduce arousal levels and to assist the patient when engaging in exposure to the traumatic memories. Approaches with this component often include stress inoculation training that follows programs of psychoeducation, relaxation skills, thought stopping and self-talk (Harvey et al., 2003).

Another component of CBT includes exposure, which requires patients to vividly imagine the trauma for prolonged periods. Therapists assist patients in providing a narrative of their traumatic experience with a heavy emphasis on the inclusion of all relevant details such as sensory cues and affective responses. In an attempt to maximize the sense of reliving the experience, the individual may be asked to provide the narrative in the present tense or speak in
the first person. Variants of the exposure component involve requiring patients to repeatedly write down detailed descriptions of their traumatic experience, listen to an audiotape of stimulus cues and implementing virtual reality paradigms via computer-generated imagery. Most exposure treatments supplement imaginal exposure with in vivo exposure that involves live graded exposure to the feared trauma-related stimuli. There are multiple benefits to CBT treatments specifically using exposure including promoting habituation and reduction of anxiety, promoting a correction of the belief that anxiety remains unless avoidance occurs, impeding the negative reinforcement associated with fear reduction, promoting the incorporation of corrective information into the trauma memory, establishing trauma as a discrete event that is not indicative of the world being globally threatening and enhancing self-mastery through the management of exposure exercises (Harvey et al., 2003).

Generally, trauma-focused psychological treatments are recommended as first-line treatments for PTSD but clinicians may be concerned that the positive outcomes observed in randomized control trials may not generalize to the wide range of traumas and presentations seen in clinical practice (Ehlers et al., 2013). There are also many factors that could potentially limit the extent that treatment effects in randomized control trials can be applied to patients seen in routine clinical practice. One such factor is that randomized control trials apply certain inclusion and exclusion criteria that may influence the outcome by increasing the average size of improvement because these criteria require a minimum severity or exclude difficult to treat patients (Ehlers et al., 2013). Another factor is that many randomized control trials select patients who suffer from discrete traumas but, in clinical practice, patients may require treatment for a wider range of traumas including prolonged and multiple traumatic events (Ehlers et al., 2013). A third factor suggests that there have been concerns about a possible risk of symptom
exacerbation found in patients with routine clinical care but it uncommon to be seen in
randomized control trials (Ehlers et al., 2013). Lastly, therapists who receive specialized training
and supervision generally administer randomized control trials, while clinicians with less training
or supervision may find it difficult to replicate their results in a clinical setting (Ehlers et al.,
2013). Ehlers and colleagues (2013) conducted a study to assess the effectiveness of cognitive
therapy in patients referred to a National Health Service outpatient clinic. Three hundred and
thirty patients received about 10 weekly treatment sessions and two booster sessions. Patients
showed a large improvement in PTSD symptom severity with an average percent change of
50.4% in PTSD symptoms. Researchers concluded that their results supported the effectiveness
of cognitive therapy in routine clinical practice and in a wide range of traumas with the majority
of patients showing clinically significant change of 57.3% in PTSD symptoms.

Another study, conducted by Bryant, Moulds and Nixon (2003), attempted to test the
long-term benefits of early provision of CBT to civilian trauma survivors with acute stress
disorder as compared to supportive counseling. Acute stress disorder (ASD) describes the
posttraumatic stress reactions that occur between two days and four weeks following a trauma.
Prospective studies indicate that 80% of people with ASD suffer from PTSD six months after the
initial trauma and between 63% and 80% suffer from PTSD two years after the initial trauma
(Bryant et al., 2003). CBT involved education about trauma reactions, breathing retraining,
progressive muscle relaxation training, learning self-talk exercises to manage anxiety-producing
situations, prolonged imaginal and in vivo exposure and cognitive therapy. CBT was compared
to supportive counseling, which involved education about trauma, general problem-solving skills
and provision of an unconditionally supportive role but specifically avoided exposure, cognitive
restructuring or anxiety management techniques. Patients were assessed at pre- and post-
treatment as well as at a six-month follow-up with therapy consisting of five weekly one and a half hours of individually administered sessions. Researchers found that patients who received CBT in the initial month after their trauma presented less intense PTSD symptoms than those who received supportive counseling. The two groups differed in symptom intensity but not in frequency of PTSD symptoms, which is consistent with the evidence that PTSD severity is associated with the distress of a symptom rather than frequency of occurrence (Bryant et al., 2003).

In a two-part study, Ehlers and colleagues (2005) attempted to develop a cognitive therapy program that aimed to modify excessively negative appraisals, correct the autobiographical memory disturbance and remove the problematic behavior and cognitive strategies. The first part of the study included a consecutive case series that identified patients suffering from moderately severe PTSD symptoms during study registration period with no control group who completed cognitive therapy and a number of outcome measures. From this study, researchers found that cognitive therapy was highly effective in reducing PTSD symptoms as well as symptoms of anxiety and depression with treatment gains were maintained during follow-up. At post-treatment, 90% of patients no longer met DSM-IV criteria for PTSD with 95% of patients classified as treatment responders and 84% of patients achieving high end-state functioning. PTSD symptom severity, anxiety and depression remained much reduced compared to initial assessments at both the three and six month follow-ups (Ehlers et al., 2005). In the second part of the study, 28 patients were randomly assigned to either immediate cognitive therapy or a 13-week waitlist condition. Cognitive therapy was found to be superior to a 3-month waitlist condition on measures of PTSD symptoms, disability and associated symptoms of anxiety and depression as 71.4% of cognitive therapy patients did not meet the diagnostic criteria
for PTSD at the three month assessment and 78.6% of cognitive therapy patients met criteria for treatment response. Subsequently, treatment gains in the cognitive therapy group were well maintained at the six-month follow-up assessment (Ehlers et al., 2005).

As previously mentioned, exposure therapy is one component of cognitive behavioral therapy used to treat PTSD. Exposure therapy has come to be the most studied, the most supported and the most frequently used treatment technique (Tarrier et al., 1990). Exposure based treatments include exposures in the imagination, which helps process the trauma emotionally by imagining and out-loud describing, and exposure in natural conditions, which assists processing actions that cause anxiety through the confrontation with particular situations (Shubina, 2015). In imaginal exposure, patients relive traumatic memories while relating these memories using the first person and present tense as well as giving rich detail about the circumstances, their responses and their feelings at the time of the traumatic event. Patients are sometimes allowed to make hierarchical lists of the elements of their traumatic memories with less distressing elements relived first as therapists ask patients to concentrate on the worst aspects of the memory. Patients relay these memories repetitively, while simultaneously engaging in anxiety management techniques, until anxiety is reduced (Richard, Lovell & Marks, 1994). Live, or in vivo, exposure requires patients to re-enter trauma related situations that they have been avoiding. These situations are not always exactly the same situations as the trauma since many traumatized patients avoid a wide range of situation they have come to associate with the traumatic experience. Therapists accompany patients during the exposure to encourage the patient to remain in the feared situation, while using anxiety management techniques, until anxiety is reduced considerably (Richards et al., 1994). It seems that the most effective CBT programs are those that rely on repeated exposure to the trauma memory and in vivo exposure to
situations avoided since the event as well as on cognitive restructuring of the meaning of the trauma of a combination of these components.

Goodson and colleagues (2013) conducted a study to investigate the effectiveness of prolonged exposure (PE) in a diverse veteran sample. They hypothesized that veterans who completed PE would show significant improvements on self-report measures of PTSD, depression and quality of life. The 115 veterans enrolled in the program attended nine to twelve weekly or twice weekly 90 minute session that included psychoeducation, breathing retraining, in vivo exposure and imaginal exposure. Researchers found the effectiveness of PE in their veteran sample to be robust and not affected by many patient characteristics. Veterans experienced a significant decrease in PTSD symptoms, depression and improvement in quality of life following PE treatment with a 41% average reduction rate in symptoms. Researchers also suggest that, because there was no significant effect of patient characteristics, PE can be effective to use as treatment for veterans with physical and mental health comorbidities.

Similarly, Boudewyns and Hyer (1990) conducted a study to compare the physiological and self-report outcome responses of inpatient Vietnam veterans who suffer from PTSD and were treated with exposure therapy to similar patients treated with a more conventional approach. Both treatment conditions had their physiological responses to imaginal exposure scenes of stressful memories of combat were recorded prior to treatment and immediately after treatment with three physiological responses evaluated (heart rate, frontalis electromyography and skin conductance). Researchers found that subjects in both groups evidenced substantial and significant physiological responding to exposure scenes of combat memory. The results suggested that exposure therapy patients did not show significant reduction in physiological responsivity when compared to the conventional therapy patients. The results also supported the
idea that subjects who did show decreased physiological responding to imaginal scenes immediately following treatment also improve physiologically at three-month follow-up when compared to patients who did not have a reduced physiological response, regardless of treatment received (Boudewyns & Hyer, 1990). In a follow-up study, Boudewyns and colleagues (1990) attempted to evaluate the outcome for treatment of chronic PTSD veterans at a three-month follow-up by comparing exposure therapy to conventional therapy. In this study, researchers were aiming to evaluate the outcomes of patients who receive exposure therapy as compared to patients who are given conventional therapy. The study sample comprised of 58 patients who had been treated on a PTSD special treatment unit and who had responded to a three-month follow-up evaluation. Researchers found that exposure therapy was more effective with patients as compared to conventional therapy with 10 out of 15 successes attributed to exposure therapy and only three of 15 failures attributed to exposure therapy.

In a study conducted by Thorp and colleagues (2012), 11 male veterans ages 55 years or older were included in a prospective, pre-post designed treatment that aimed to test the feasibility of recruitment and treatment in this particular population and to compare the outcomes between patients who received PE and patients who received treatment as usual in a Veterans Affairs (VA) PTSD clinic. After a baseline assessment, eight participants completed prolonged exposure therapy and their results were compared with a nonrandomized treatment as usual (TAU) group. TAU consisted of one appointment each week for six weeks that went over medication or case management with a physician to monitor ongoing treatment and offer general support. Researchers found that, despite this population’s chronic nature of PTSD symptoms, veterans who completed six weeks of PE showed significant reduction in clinician-rated and self-reported
PTSD symptoms. Veterans receiving PE also showed a clinically significant decline in severity of PTSD symptoms as compared to veterans who received TAU (40%).

Speckens and colleagues (2006) conducted a study to investigate possible changes in intrusive memories using imaginal reliving, which includes prolonged imaginal exposure as well as using other cognitive methods to change the meaning of problematic moments experienced during reliving. Over 12 sessions of cognitive therapy, 44 patients were treated using imaginal reliving. Researchers found that the pattern of change in intrusive memories seemed gradual rather than abrupt for the majority of patients with vividness, distress and nowness of intrusions also gradually decreased. The results showed that the frequency of the majority of patients’ main intrusive memory did not change until after the second session, where it declined significantly and remained significantly decreased for all of the following sessions. A number of factors could predict greater decreases in intrusion frequency: low anger, low negative interpretations of PTSD, low nowness of intrusive memory, and low initial PTSD symptom severity.

Richards, Lovell and Marks (1994) conducted a study to test whether giving imaginal or in vivo exposure first would affect outcome in PTSD patients who had undergone a range of traumatic events. Patients were separated into two groups: one group had four weekly, one hour sessions of imaginal exposure followed by four weekly, one hour sessions of in vivo exposure while group two had four weekly, one hour sessions of in vivo exposure followed by four weekly, one hour sessions of imaginal exposure. Researchers found that both treatments markedly improved intrusive, avoidant and hyperarousal PTSD symptoms with no patients meeting DSM-III criteria for PTSD at post-treatment and no relapses through the one-year follow-up. Improvement ranged from 75% to 80% across PTSD specific measures and 65% to 75% across depression, fear, general health and social adjustment measures. On almost all
measures, improvement was similar over the four weeks of imaginal and of live exposure whether delivered first or second but the results also suggest that the addition of in vivo exposure improved trauma-related phobic avoidance significantly more than imaginal exposure while also improving other PTSD symptoms.

As of December 2009, over two million Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) troops have been deployed over seas with as many as 20% of those who have returned suffering from mental health difficulties including combat-related PTSD with only about half of that 20% of veterans meeting criteria for PTSD or depression actually seeking healthcare (Tuerk et al., 2011). A study conducted by Tuerk and colleagues (2011) aimed to present outcome data on 65 OEF/OIF veterans treated with manualized PE intervention for PTSD by Veterans Affair clinicians. Researchers used a post-hoc analysis including archival data from patients treated by a PTSD clinical team in a VA medical center to determine the effectiveness of PTSD treatment. Researchers found that PE is an effective treatment for combat-related PTSD by showing that PE can be effectively implemented in a VA clinic setting. Rauch and colleagues (2009) aimed to present clinical treatment data on a case series of veterans with chronic PTSD treated with PE in a Veterans Affairs clinic. They expected that PTSD and depressive symptoms would be reduced between pre-treatment and post-treatment. Researchers found PE to be effective with veterans demonstrating significant reductions in total PTSD symptoms from pre-treatment to post-treatment. As such, 50% of veterans had Posttraumatic Diagnostic Scale scores lower than 15, which suggests that they no longer met criteria for PTSD. Veterans also demonstrated significant reductions in re-experiencing symptoms, avoidance symptoms and hyperarousal symptoms from pre-treatment to post-treatment as well as significant reductions in total depressive symptoms. This suggests that
veterans receiving PE treatment in a VA clinic have a very good chance of experiencing a reduction of symptoms across all three core symptom clusters.

A study conducted by van Minnen, Arntz and Keijsers (2002) aimed to investigate the predictors of treatment outcome and dropout by analyzing two separate samples of PTSD patients with mixed trauma treated with PE. Predictors analyzed included demographic variables, substance use, severity of symptoms, personality, trauma characteristics, feelings of anger, guilt and shame, and nonspecific variables regarding therapy (such as treatment motivation, treatment expectations and quality of patient-therapist relationship). Researchers found significant improvements in the two different samples but few consistent predictions of treatment success. The only stable finding across the two groups was that patients who showed more PTSD symptoms at pre-treatment also showed more symptoms at post-treatment and follow-up, suggesting that these patients might need additional sessions. Researchers suggest that it is difficult to use pre-treatment variables as a powerful and reliable tool for predicting treatment outcome or dropout because significant predictors were found to be highly sample specific, which makes the generalizability of the results questionable.

Furthermore, Tarrier and colleagues (2000) conducted another study to examine the predictors of clinical outcome for the total patient sample from a clinical trial with the specific purpose of identifying factors that can be associated with good and poor response to CBT. Tarrier and colleagues (2000) note that, in previous studies, certain factors have been identified that may or may not influence the development of chronic PTSD after traumatic experience. These factors may include past history of psychiatric illness, neuroticism as a personality trait and availability of social support. Researchers suggest that, since these factors may affect development of PTSD, it could be possible that they may also affect the response to treatment
once PTSD is established. Tarrier and colleagues (2000) conducted a randomized controlled trial where patients were assigned through a process that took into account trauma category, duration of PTSD, gender and whether they received psychotropic medication. Patients were then assigned to either the cognitive therapy treatment group or the imaginal exposure treatment group. Patients completed 16 one hour sessions followed by post-treatment assessment and follow-up assessment at six months. The results of the study showed that, even though clinical improvements were obtained after treatment and at the six-month follow-up, neither treatment was superior to the other. Duration of therapy, gender and suicide risk were the three variables significantly associated with the pre-treatment to post-treatment change in severity scores, accounting for 36.5% of the outcome variance. The best predictor of outcome was a patient’s inconsistent attendance of therapy. Researchers suggest that these results can inform clinicians of ways to improve treatment effectiveness. For example, patients should be made aware of the strong association between irregular attendance of sessions and poor outcome.

In response to the growing need for effective, reliable and safe PTSD treatments, the Department of Veterans Affairs (VA) has rolled out training initiatives and created infrastructure aimed at making evidence-based psychotherapies such as CBT and PE available at every VA facility. This implementation represents one of the largest system changes in initiatives attempted within a nationwide health care system (Finley et al., 2015). Unfortunately, these initiatives will not accomplish much if therapists and clinicians refuse to implement CBT and PE therapies in treating patients with PTSD. Exposure therapies have been a clinical option for treatment for a significant period of time and it seems that just telling therapists that such treatment exists and that they should use these treatments does not lead to widespread utilization. PE is not often accessible to veterans seeking PTSD treatment in the VA system because less
than 10% of PTSD therapists routinely use it with their clients (Rauch et al., 2009). It is commonly suggested that there is a lack of therapists that are capable of providing PE as well as certain misconceptions about PE that could also drive the deficit in usage among VA clinicians. As such, it seems that therapist factors play an equally important role in determining whether or not exposure therapy for PTSD is widely used. Dissemination of exposure therapy depends on therapist factors such as ease, understanding, cost and availability of training, willingness to receive training, availability of supervision, general clinical myths about exposure as a whole, and personal beliefs about the specific conditions and contexts for its use. Therapist variables such as knowledge and comfort could interact with a variety of patient variables such as avoidance or initial worsening of symptoms (Becker, Zayfert & Anderson, 2004).

In a study conducted by Becker and colleagues (2004), an initial survey of licensed psychologists was undertaken regarding their use of exposure therapy for PTSD and their perceived barriers to its implementation. Researchers also sought to determine the extent to which exposure is being used in clinical practice and to identify factors that may influence psychologists’ decision to use it. Researchers found that a large majority of licensed psychologists in clinical practice are not using PE to treat PTSD. Half of the sample reported that they were somewhat familiar with PE and only 17% actually used PE to treat PTSD. Furthermore, less than one third of the sample reported that they had received formal training in PE with less than half of the trained and experienced sample reported using the intervention with 50% or more of their patients. Researchers concluded that clinicians appear to perceive a significant number of barriers to implementing exposure. Therefore they avoid or refrain from using it to treat patients suffering from PTSD.
Finley and colleagues (2015) conducted a study to report the utilization of PE and cognitive processing theory (CPT) by providers within a VA specialty clinic. They hypothesized that the providers’ primary theoretical orientation would be associated with differential uptake of PE and CPT such that providers with cognitive behavioral orientation would be more likely to conduct PE and CPT than those with other theoretical orientations. They also hypothesized that providers’ perception that PE and CPT would have greater effectiveness would be positively associated with their uptake of those treatments. Lastly, researchers hypothesized that the providers’ perceptions of workplace characteristics would be associated with their uptake of PE and CPT such that positive workplace characteristics would be associated with greater adherence to or utilization of PE and CPT. The results of the study showed that providers reported conducting relatively few hours of PE and CPT per week, performing more than twice as much supportive care as PE and more than three times as much supportive care as CPT. The results supported the hypotheses that providers’ primary theoretical orientation and perception of effectiveness would be associated with their use of PE and CPT as well as adherence to treatment manuals. There was also an association between having emotional support from coworkers and increased adherence to the PE manual, which suggests that maintaining high-quality relationships among providers could have relevance not only for the VA clinic staff’s wellbeing but also for the quality of care provided. Researchers suggest that increasing staffing, enhancing the perceptions of PE and CPT treatment effectiveness and supporting positive work environments may prove to be important components of providing quality care to VA clinic patients with PTSD.

While it seems as if cognitive behavioral therapy, specifically the prolonged exposure component, has an unending list of positive outcomes from both randomized control trials and
PTSD TREATMENTS

clinical practice, there have been some treatment limitations proposed. First, it has been suggested that, while exposure therapies that include flooding (abruptly exposing patients to trauma rather than gradual exposure) may aim to reduce anxiety, it may focus on symptom change rather than modifying irrational thought. Exposure therapies may also contribute to excessive noncompliance with therapy because of its distressing nature. Also, exposure therapies do not directly teach coping strategies and, sometimes following exposure, PTDS and depressive symptoms may actually increase (Bryant, 2000). Another limitation proposed suggested that the predominance of anger may impede the activation of the fear network that usually promotes habituation because anger can reduce the level of anxiety experienced in therapy (Bryant, 2000). A third limitation suggested that the activation of the fear network might also be impeded by dissociative mechanisms such as emotional numbing as well as more effortful cognitive avoidance strategies (Bryant, 2000). Lastly, it has been suggested that therapy can be impeded by excessive anxiety such that exposure can retraumatize the patient because the experience is perceived as overwhelming. Exposure may not be successful if the patient’s memory of the trauma is characterized by mental defeat or lack of mastery of the situation. Therefore, simply activating traumatic memories in a way that heightens the individual’s sense of anxiety and helplessness may further compound the posttraumatic stress reaction.

When evaluating CBT and PE therapies in the absence of pharmacological treatments, it is important to consider the effect of therapists on treatment outcomes, duration of treatment and the efficacy of CBT in terms of reduction of symptoms and stable remission rates. Previous studies have demonstrated that a therapist can have a significant influence on the implementation of CBT as well as how much the treatment adheres to CBT manuals and treatment outcomes. If a therapist is not as familiar with CBT or has preconceived ideas about CBT, they may not be
inclined to use it in treating patients with PTSD despite the amount of supportive literature available. Similarly, if a therapist is not familiar with CBT and, therefore, does not administer CBT appropriately, the treatment outcome may not be as successful as seen in clinical trials. Furthermore, the previous studies generally implemented an increased number of CBT sessions as compared to the pharmacological studies, which could mean that CBT might be more expensive than medication, depending on insurance and VA benefits. Finally, it is extremely important to consider patient remission rates after treatment is ended. Across both pharmacological treatments and CBT, it seems as if patients maintain treatment gains equally thereby experiencing lower remission rates. If both treatment types produce equal results in remission rates, it would be beneficial to consider implementing both treatments simultaneously when treating patients with PTSD.

**Comparison Studies**

In order to address these limitations, it is important to review studies that have compared PE and CBT as well as incorporated both elements in treating patients with PTSD. Foa and colleagues (1991) conducted a study to compare the effectiveness of three treatments, prolonged exposure (PE), stress inoculation training (SIT) and supportive counseling, for reducing PTSD in rape victims to a waitlist condition. Forty five female victims were randomly assigned to four conditions with individual treatment sessions consisting of nine bi-weekly, 90 minute sessions lasting for about four and a half weeks with a follow-up interview 3.5 months after end of treatment. SIT was included in this study as seven sessions of coping skills, deep muscle relaxations and controlled breathing, thought stopping to counter ruminative or obsessive thinking, cognitive restructuring, guided self-dialogue, covert modeling and role play with no instructions for any kind of exposure therapy. Researchers found that PE appeared to be the
superior treatment as it was most effective long-term, but SIT appeared to be the most effective
treatment in short-term. Researchers suggest that SIT produced immediate relief because it was
aimed at anxiety management, while patients may not have continued to employ SIT techniques
after treatment. Alternatively, procedures utilized in PE are expected to produce temporarily high
levels of arousal but procedures are considered to lead to permanent change in memory, which
can lead to durable and lasting gains.

In a study conducted by Tarrier and colleagues (1990), two previously held, competing
hypotheses were advanced: (1) one advocated that there was an important necessity of directly
changing cognitions and beliefs resulting for the trauma and (2) one that stated only direct
exposure to memories of the trauma would result in therapeutic benefits. Tarrier and colleagues
(1990) compared the relative efficacy of cognitive therapy with no exposure to imaginal
exposure with no inclusion of thoughts or emotions. The randomized clinical trial was conducted
in two phases starting with patients going through four weeks of a baseline-monitoring period
and then patients were randomly assigned to either cognitive therapy treatment or imaginal
exposure. Both treatment types consisted of 16, one hour sessions and was followed by post-
treatment assessment and a six-month follow-up. The cognitive therapy treatment aimed to be
emotion-focused and to elicit the patient’s beliefs about the meaning of the event and the
attributions patients made following the event without discussing the trauma itself. The imaginal
exposure treatment aimed to be trauma-focused and to produce habituation of emotional
responses by instructing the patient to describe the event as if it was actually happening in the
present tense while simultaneously visualizing it. The outcome measures showed a significant
improvement over treatment that was maintained at the six-month follow-up, although there was
no indication that one treatment was superior to the other. Researchers found that all measures
used showed a significant decrease between pre-treatment and post-treatment assessments, which suggested symptom improvement. The results also suggest that neither treatment alone could produce complete symptom reduction in all cases, implying that more research should be done in combining specific treatments for PTSD patients.

Paunovic and Ost (2001) conducted a study to compare CBT to exposure therapy as treatments for refugees with PTSD. They hypothesized that both treatments would significantly reduce PTSD symptoms, but that CBT would be more effective than exposure therapy because it targets catastrophic interpretations of intrusions as well as avoidance behaviors. They also hypothesized that anxious and depressive symptoms would be significantly reduced by both treatments, but that CBT would be more effective than exposure therapy. Twenty refugee patients were randomly assigned to either CBT or exposure therapy with sessions lasting 60 to 120 minutes once a week over 16 to 20 sessions that also included pre-treatment and post-treatment assessments as well as a six-month follow-up. The results showed that exposure therapy and CBT reduced the patient’s PTSD symptoms, generalize anxiety and depression with a 43% to 60% reduction rate after treatment. Patients’ quality of life and cognitive schemas of the self, the world and meaningfulness increased significantly after treatment. Researchers found both treatments to be equally effective with no significant difference between them on any of the outcome measures.

**Discussion**

In the past, PTSD treatment studies focused on the efficacy, tolerability and safety of various antidepressants such as selective serotonin reuptake inhibitors (SSRIs), selective serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs). More recently, there has been an increase in research
PTSD TREATMENTS

attempting to define the underlying biological dysfunctions responsible for PTSD using a wide array of methods. Therefore, treatment studies have refocused to broaden the scope to investigate other therapeutic techniques that could work using alternate mechanisms, either with neurotransmitters or cognitive functioning, that may enable improvement as well as other agents that can be used as either a replacement or adjunct to these different types of treatments (Ravindran & Stein, 2009).

Multiple studies have found antidepressants, including sertraline, paroxetine and fluoxetine, to be efficacious, tolerable and safe for the use in treating PTSD patients (Davidson et al., 2001a; Davidson et al., 2001b; Marshall et al., 2001). Researchers have found these antidepressants to improve PTSD symptom, increase social functioning, and increase occupational functioning, while extended use of these medications can prevent relapse and induce a four to six-fold reduction in the possibility of a recurrence of PTSD (Davidson et al, 2001b). Additionally, it has been suggested that, with SSRI treatment, patients suffering from combat-related PTSD could have optimal treatment periods that are considerably longer than the recommended 12 weeks and require higher doses of SSRI treatment generally found in trials with patients suffering from civilian PTSD because combat-related PTSD is considered more severe and chronic than what is normally found in civilians (Martenyi et al., 2006).

Some researchers have found no significant difference in PTSD symptom severity over the course of SSRI treatments including the use of sertraline and paroxetine (Friedman et al., 2007; Panahi et al., 2011). These researchers explain potential factors that could have caused the lack of efficacy by suggested that the Vietnam veterans receiving treatment for PTSD within the VA settings of Friedman and colleagues (2011) study were not necessarily representative of military veterans with combat-related PTSD, which may be due to the fact that these veterans are
being treated decades after their initial combat trauma. Another reason suggested by Friendman and colleagues (2007) as to why the treatment was not effective could be because this population of veterans may represent the most severely impaired, chronic and treatment resistant sample of patients with PTSD and therefore, may not respond to sertraline treatment as positively as patients have in previous studies. Furthermore, Panahi and colleagues (2011) suggest that discrepancies in their study evaluating the use of sertraline in treating combat-related PTSD, including factors such as differences in traumatic conditions of war (Vietnam conflict versus Iran-Iraq war), baseline clinical presentations of participants and accompanying comorbidities and the psychosocial, racial and religious differences found between cultures. Consequently, Marshall and colleagues (2001) found significant improvement when using paroxetine to treat PTSD and suggested that even though approximately one-half of the patients had comorbid major depressive disorder, it did not seem to influence treatment response as patients with and without comorbid major depressive disorder experience significant improvement while taking paroxetine as compared to placebo.

Even though SSRIs have been commonly studied and used in treating PTSD, there has been a varied pattern of results in treatment studies showing inconsistencies across patient types (combat veterans versus civilians), core symptoms (re-experiencing/intrusion, avoidance/numbing, and hyperarousal), and gender, including in studies with FDA approved drugs. There was a lack of efficacy of SSRIs in treating PTSD with some studies finding response rates to SSRIs rarely exceeding 60% with even fewer patients (20% to 30%) experiencing improvement that could be categorized as remission (Stein, Kline & Matloff, 2002). These findings suggest that there is evidence for the involvement of neurotransmitters and pathways other than those that use serotonin. Research has been conducted to investigate the use
of SNRIs, such as venlafaxine extended release, tricyclic antidepressants, such as amitriptyline, other antidepressant agents, such as mirtazapine, and atypical antipsychotic medication, such as olanzapine, in the treatment of PTSD symptoms (Davidson et al., 2006b; Davidson et al., 2006a; Davidson et al., 1990; Davidson et al., 2003; Stein et al., 2002). A number of studies have found each of these different types of antidepressants to be efficacious when compared to a placebo but are no more efficacious than SSRIs in treating PTSD symptoms as well as anxiety and depression.

In addition to studies that have focused on medications to reduce the core symptoms of PTSD, there has also been research in the alleviation of secondary symptoms such as sleep disturbance. Trauma nightmares and sleep disturbance are among the most treatment-resistant and distressing symptoms of PTSD. The physiology of PTSD trauma nightmares differ from normal dreams such that trauma nightmares are largely expressed during light sleep and disrupted REM sleep, which can often be accompanied by motor activity (Raskind et al., 2007). These nighttime PTSD symptoms likely contribute to self-medication through alcohol and drug abuse as well as suicide ideation. A medication commonly used as an adjunctive agent in addition to other treatments of PTSD is prazosin and a number of studies have found that patients had greater improvement when taking prazosin as compared to a placebo on the primary outcomes of nightmares, sleep disturbances and PTSD symptom severity (Raskind et al., 2003; Raskind et al., 2007). Researchers have suggested that prazosin is effective and safe when given in addition to another psychotropic medication, such as an SSRI, as an adjunctive agent. This finding suggests that adjunctive agents, such as prazosin, taken as a secondary treatment could ameliorate more selective symptoms including recurrent dreams and sleep disturbance because SSRIs may not be able to improve the entire range of PTSD symptoms a patient may experience.
(Raskind et al., 2007). Due to the selective nature of SSRIs, patients may not experience as many side effects or interactions of comorbid diagnoses as compared to other antidepressants. Moreover, it seems that the best treatment would combine an SSRI, such as sertraline, to alleviate the core symptoms and severity of PTSD with an adjunctive agent, such as prazosin, to alleviate nighttime symptoms like trauma nightmares and sleep disturbances. Of course, cost of the medications, duration of prescriptions and dosage should be taken into account when treating patients.

It is important to consider pharmacological treatments especially for patients who suffer from extremely severe and chronic PTSD, as they are generally able to reduce many of the distressing symptoms and allow patients to resume normal functioning. As symptom impairment decreases, the quality of life and functionality of patients increase to where they are more inclined to engage in other therapies without experiencing the adverse symptoms of re-experiencing, avoidance and hyperarousal. Even though pharmacological treatments have shown a wide range of psychotropic agents to be effective, tolerable and safe, it is important for researchers and clinicians to use trauma-focused psychological treatments as first-line treatments for patients suffering from PTSD. This is due to the fact that trauma-focus therapies encourage the patient to face the traumatic event and its meanings as well as restructure their thoughts and emotions surrounding the trauma. These types of therapies attempt to teach patients how to take control of their treatment through methods of psychoeducation, cognitive restructuring, anxiety management and exposure to ensure the maintenance of the patient’s gains in therapy for a considerable time after therapy has ended. With cognitive behavioral therapy (CBT) and prolonged exposure therapy (PE), it is assumed that by using a combination of these techniques will help patients identify and modify distorted beliefs associated with PTSD (Shubina, 2015).
There has been considerable research to study the effectiveness of both CBT and PE, either separately or together, in treating patients with PTSD (Ehlers et al., 2013; Bryant et al., 2003; Ehlers et al., 2005; Goodson et al., 2013; Boudewyns et al., 1990; Thorp et al., 2012; Speckens et al., 2006; Richards et al., 1994; Tuerk et al., 2011; Rauch et al., 2009; Foa et al., 1991; Tarrier et al., 1990; Paunovic & Ost, 2001). In the CBT studies, researchers have found that CBT is effective in routine clinical practice, with a wide range of traumas and can reduce PTSD symptom severity, anxiety and depression. It has been found that CBT also has long-term benefits, in that surveys who have conducted follow-up assessments ranging from three months to one year have found patients who received CBT were able to maintain their gains after therapy ended. In some of these studies, patients receiving CBT were compared to control groups that either received supportive counseling or were placed on a waitlist as the control condition. CBT was consistently found to be superior to both types of control conditions in each study with a majority of the CBT patients no longer meeting the diagnostic criteria for PTSD.

Similarly, other studies have found PE to be effective in treating patients with PTSD as compared to supportive counseling or being placed on a waitlist and the outcomes are generally not affected by many patient characteristics such as age, gender, comorbidity or disability (Goodson et al., 2013). Some studies have found PE to drastically reduce the frequency of most patients’ main intrusive memory (Speckens et al., 2006) and have also found that both imaginal and in vivo exposure to equally improve intrusive, avoidant and hyperarousal PTSD symptoms (Richards et al., 1994). There have been some studies conducted that have specifically investigated the utilization and effectiveness of PE in Department of Veterans Affairs (VA) PTSD clinic as the VA has responded to the growing need for effective, reliable and safe PTSD treatments by disseminating training initiatives and creating infrastructure aimed at making
trauma-focused psychotherapies, like CBT and PE, available at every VA facility (Finley et al., 2015). Studies have shown that, generally, veterans demonstrate significant reductions in total PTSD symptoms, reductions in the three core symptoms and reductions in total depressive symptoms (Rauch et al., 2009).

Unfortunately, there seems to be some discrepancies in perspectives and beliefs dealing with exposure therapy between randomized controlled trials and clinical practice. Generally, there have been factors suggested that could potentially limit the extent that treatment effects in randomized control trials can be applied to patients seen in routine clinical practice. For example, it has been suggested that randomized control trials apply certain inclusion and exclusion criteria that may influence the outcome by increasing the average size of improvement because these criteria require a minimum severity or exclude difficult to treat patients (Ehlers et al., 2013). Similarly, it has been suggested that many randomized control trials select patients who suffer from discrete traumas but, in clinical practice, patients may require treatment for a wider range of traumas including prolonged and multiple traumatic events (Ehlers et al., 2013). Another misconception about exposure therapy that has been suggested is that there is concerns about a possible risk of symptom exacerbation found in patients with routine clinical care but it uncommon to be seen in randomized control trials (Ehlers et al., 2013). Lastly, it has been suggested that therapists who receive specialized training and supervision generally administer randomized control trials, while clinicians with less training or supervision may find it difficult to replicate their results (Ehlers et al., 2013). There have been studies conducted that attempt to determine how widely utilized exposure therapy is in VA clinics and what type of factors may influence clinicians decision to use it (Becker et al., 2004; Finley et al., 2015). These studies have found that a large majority of licensed psychologists are not using PE in clinical practice to
treat PTSD and that very few clinicians are even familiar or have received formal training with PE. These studies have also found that a clinician’s primary theoretical orientation and perception of effectiveness would be associated with their use of PE as well as CBT. From these studies, researchers conclude that there are a number of factors involved in a patient’s treatment outcome that do not necessarily come directly from treatment. Namely, researchers suggest that increasing staffing at VA clinics, enhancing the perceptions of PE and CBT treatment effectiveness and supporting positive work environments may prove to be important components of providing quality care to VA clinic patients with PTSD.

It has been found that, separately, psychotropic medications and psychotherapies are effective in reducing total PTSD symptom severity, including the three core symptoms, as well as anxiety and depressive symptoms. Consequently, these studies have found that, even though these methods were effective in most cases, in some cases they did not cover the entire spectrum of PTSD symptomology. Therefore, certain treatments that include both psychotropic and psychotherapy components may yield even better improvements across all PTSD symptoms. There have been studies conducted to compare the efficacy of augmenting PE with SSRIs such as sertraline and paroxetine (Rothbaum et al., 2006; Schneier et al., 2011). These studies have found that a combined treatment of PE and SSRI significantly reduced PTSD symptom severity, anxiety and depression. These findings suggest that medication and CBT monotherapies alone each have their own limitations but combining these treatments might maximize the efficacy of treatment (Schneier et al., 2011). Researchers suggest that these advantages must also be weighed against the potential disadvantages of greater cost for combined treatments, the risk of adverse effects of medication and the risk of eventual discontinuation of medication could be
associated with the risk of relapse, which has been shown after discontinuation of SSRI monotherapy (Schneier et al., 2011).

In considering all previously mentioned studies, it seems that there are a myriad of factors to consider when deciding on a patient’s treatment. These factors include therapists’ perspective of effectiveness, amount of previously received training or supervision and preconceived ideas pertaining to the type of treatment. This is especially important in the context of the VA broadly encouraging clinicians to utilize CBT or PE when treating veterans. Furthermore, it seems as if monotherapies of psychotropic medications or psychotherapies are appropriately effective across all trauma types but, for the best and longest lasting effects, treatments that combine elements of psychotropic medications and psychotherapies should be highly considered in treating PTSD patients.
References


treatment effectiveness for veterans of the wars in Afghanistan and Iraq. *Journal of Anxiety Disorders, 25,* 397-403.
