Review

The use of prolonged exposure therapy to help patients with post-traumatic stress disorder



Practice Points

- The burden of post-traumatic stress disorder
- Post-traumatic stress disorder (PTSD) is often a chronic, disabling condition that is frequently comorbid with other psychiatric disorders.
- **Comorbidity in PTSD**
- The presence of PTSD comorbidity challenges differential diagnosis and treatment planning.
- **Overview of evidence-based treatments for PTSD**
- Cognitive-behavior therapy, and in particular exposure therapy, has been found effective in reducing PTSD severity relative to waitlist and active control conditions.
- Description of prolonged exposure therapy for PTSD
- Prolonged exposure (PE) is a specific exposure therapy program that has been extensively researched and is considered a first-line evidence-based treatment for PTSD.
 Does PE work for comorbid populations?
- PE is efficacious for PTSD sufferers with comorbid disorders including depression, substance dependence, traumatic brain injury and borderline personality disorder.
- In addition to reducing PTSD, PE significantly ameliorates associated symptoms, such as depression, anxiety and anger.

Post-traumatic stress disorder (PTSD) is a chronic psychiatric disorder characterized by intrusive re-experiencing symptoms, avoidance behaviors, elevated arousal, and changes in cognition and mood. Nearly all individuals with PTSD suffer from at least one additional psychiatric diagnosis. Prolonged exposure is one of several evidencebased treatments for PTSD that has been efficacious for PTSD sufferers with a range of comorbid disorders. In this review, we first discuss the prevalence of PTSD comorbidity and the challenges that it presents to clinicians working with traumatized patients. We then discuss the treatment of PTSD, focusing on prolonged exposure therapy. After providing a brief overview of PE, we review evidence supporting the use of PE in reducing PTSD severity and associated symptoms in a variety of comorbid samples.

Keywords: comorbidity • evidence-based treatment • post-traumatic stress disorder • prolonged exposure therapy • trauma

The burden of PTSD

Post-traumatic stress disorder (PTSD) is a chronic and disabling disorder characterized by intrusive re-experiencing symptoms, avoidance behaviors, elevated arousal, and changes in cognition and mood. PTSD affects an estimated 3.4% of men and 8.5% of women during their lifetime [1], and certain types of traumas are more likely to lead to PTSD than others. For example, 14% of military personnel deployed to Operations Iraqi Freedom and Operation Enduring Freedom [2] and approximately 40% of women exposed to sexual assault [3] met criteria for PTSD. Because

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PTSD is comprised of a large range of symptoms, it can cause dysfunction across multiple areas. Without effective treatment, after 1 year PTSD typically becomes chronic, debilitating, and associated with significant distress and overall functional impairment [4]. Moreover, most individuals with PTSD suffer from at least one additional psychiatric diagnosis [5]. For example, major depressive disorder (MDD), anxiety disorders and substance use disorders all frequently co-occur with PTSD. This high prevalence of comorbidity greatly impacts both the clinical presentation and treatment of PTSD. Therefore, in order to help patients overcome PTSD, it is imperative that treatment addresses the high level of comorbidity seen in this population.

Comorbidity in PTSD

As noted above, comorbidity of PTSD with other psychiatric disorders is the rule rather than the exception. Epidemiological studies have found that 59% of men and 44% of women with PTSD meet criteria for at least three psychiatric disorders [5]. In a study of community outpatients, PTSD showed a more severe and diverse pattern of comorbidity than any other anxiety or mood disorder [6]. One of the most frequently comorbid disorders associated with PTSD is MDD. Between 48% and 77% of all PTSD sufferers also meet criteria for MDD [5-6]. PTSD often co-occurs with substance use disorders, with rates of PTSD estimated to be at least twice as high among individuals with alcohol dependence compared with the general population [7]. Other anxiety disorders, particularly generalized anxiety disorder (GAD), are also highly prevalent among individuals with PTSD [6]. In addition, PTSD is associated with elevated rates of physical health problems, including circulatory, digestive, musculoskeletal, nervous system and respiratory disorders [8-10]. Personality disorders such as borderline and antisocial personality disorder are more common among individuals with PTSD compared with those without PTSD [11,12].

The high level of psychiatric and medical comorbidity among individuals with PTSD presents a significant challenge to arrive at an accurate diagnosis. There are many PTSD symptoms that overlap with those of frequently co-occurring disorders. For example, diminished interest in activities may be present in both PTSD and MDD. Similarly, irritability is common to PTSD and GAD. Difficulty sleeping and concentration problems are symptoms of PTSD, MDD and GAD. Panic attacks are characteristic of panic disorder but may also be present in individuals with PTSD. This high degree of symptom overlap between PTSD and comorbid conditions is especially problematic because PTSD has a heterogeneous presentation with many different symptom constellations. This, combined with the fact that individuals are often reluctant to volunteer information about traumatic experiences, increases the risk that a PTSD diagnosis is missed. Since an accurate diagnosis of PTSD is necessary to ensure an appropriate treatment program is initiated that will help the patient overcome the disorder, it important that clinicians conduct a thorough assessment that includes screening for traumatic events.

In addition to making differential diagnosis more challenging, PTSD comorbidity may complicate treatment. PTSD comorbidity is associated with more severe clinical impairment, lower quality of life [13-15] and poorer treatment prognosis [16-18]. Although a large number of studies find that certain psychosocial treatments are efficacious in reducing PTSD severity, fewer studies have examined the effect of treatment on comorbid conditions. Clinicians should select treatments that demonstrated efficacy in ameliorating PTSD among diverse populations, including those with comorbid conditions. Ideally, clinicians would implement treatments that reduce the symptoms of PTSD as well as symptoms of commonly comorbid conditions.

Overview of evidence-based treatments for PTSD

Cognitive-behavior therapy (CBT) refers to a family of treatment approaches and includes exposure therapy, cognitive therapy and anxiety management. CBT has been deemed the treatment approach of choice in clinical practice guidelines for PTSD [19-22]. Several CBTs for PTSD have received empirical support, including prolonged exposure (PE) [23], cognitive processing therapy (CPT) [24], cognitive therapy [25] and stress-inoculation therapy (SIT) [26]. Eye movement desensitization retraining (EMDR) has also been found efficacious for PTSD [27]. PE, which was developed by the second author, has been examined in the largest number of empirical studies in independent research centers. It is for this reason that we focus our review on PE, while acknowledging that there are several other psychotherapies that have demonstrated efficacy treating PTSD.

Description of PE therapy for PTSD

PE is a manualized exposure therapy program that involves three main components:

- *In vivo* exposure to trauma reminders, typically completed as between-session assignments;
- Imaginal exposure to the memory of the traumatic event, completed during and between sessions;
- Processing of imaginal exposure.

There are two additional minor components:

- Psychoeducation about the nature of trauma and trauma reactions;
- Training in slow diaphragmic breathing.

PE typically consists of eight to 15 individual 90-min sessions delivered once or twice weekly.

Therapy begins with the clinician providing a rationale for exposure therapy. The therapist explains that PTSD symptoms are maintained by two factors: avoidance of thoughts and feelings related to the trauma and avoidance of trauma reminders; and the presence of unhelpful, distorted beliefs such as "the world is extremely dangerous" and "I am extremely incompetent". PE alters these negative, distorted perceptions by providing opportunities for experiential learning (i.e., exposure) that disconfirms them. In addition, during the first session, patients learn a diaphragmatic breathing technique that they can use to reduce daily stress.

The second session involves a discussion of common reactions to trauma, which provides patients with a framework for understanding their symptoms. Next, the clinician introduces *in vivo* exposure, which refers to confronting avoided places, people and objects that remind the patient of the trauma. The clinician and patient collaboratively construct a hierarchical list of safe or low-risk situations that the patient has been avoiding. *In vivo* exposure is conducted in a stepwise fashion, beginning with situations that provoke moderate anxiety, and gradually progressing to more challenging situations.

In session 3, the clinician provides the rationale for imaginal exposure, which is conducted from session 3 through to session 10. Imaginal exposure involves asking the patient to confront the memory of his or her trauma by revisiting it in their imagination and recounting it in detail aloud for approximately 30-45 min. Imaginal exposure is followed by 15–20 min of 'processing', in which the clinician and patient discuss thoughts and feelings about the trauma and about themselves, with the aim of helping the patient to develop a more realistic and helpful perspective on the event itself and their behaviors and emotions during the event. Processing the imaginal exposure allows patients to articulate and integrate new information and insights into their memory. Patients are instructed to listen to an audio recording of the imaginal exposure each day as homework.

The remaining sessions follow a standard agenda that begins with homework review, followed by imaginal exposure and processing, and ending with the assignment of homework exposure exercises for the coming week. The final session involves reviewing progress, discussing lessons learned, and relapse prevention.

Evidence supporting the use of PE

Numerous randomized trials indicate that PE is effective in reducing PTSD symptoms [28]. Exposure therapy has been found effective for both acute and chronic PTSD [26,29], and studies show that gains made during treatment are maintained at follow-ups of 1-5 years [30,31]. PE has been associated with rapid change and maintenance of large effect sizes over time [32,33]. Exposure therapy was identified in the joint Veterans Affairs-Department of Defense Clinical Practice Guideline for PTSD [34] as "strongly recommended" for use with veterans with PTSD. A 2008 report issued by the Institute of Medicine (IOM) concluded that exposure therapy was the sole treatment for PTSD with sufficient evidence for its efficacy. This conclusion is consistent with practice guidelines from the American Psychiatric Association [35], the Departments of Veterans Affairs and Defense (2004) and the International Society for Traumatic Stress [36].

PE has been associated with significantly greater preto post-treatment reduction in PTSD symptomatology when compared with waitlist [23,26,28,37-40], supportive counseling [41,42], relaxation [33,43-44] and treatment as usual [45-48]. A meta-analysis found that PE was associated with large effect sizes compared with control conditions at post-treatment and at follow-up [49]. Other meta-analyses that have examined the efficacy of exposure therapy in general have shown that exposure therapy was more effective than waitlist control or supportive therapy [50], and that exposure therapy is associated with a lower dropout rate than pharmacotherapy [51]. Some meta-analyses have found that exposure therapy is more effective than nontrauma-focused treatments or waitlist/control at reducing PTSD symptoms, but have not found significant differences in outcomes among specific exposure therapies [52-54]. In sum, the evidence in support of the efficacy of exposure therapy in general, and PE specifically, is extensive.

Does PE work for comorbid populations?

As noted, patients rarely present with PTSD in the absence of additional psychiatric and physical health problems. More often, PTSD sufferers face additional comorbidities such as depression and substance use, and associated symptoms such as dissociation and elevated anger. The most useful treatment for PTSD, therefore, is one that demonstrates efficacy among PTSD sufferers with and without commonly co-occurring disorders.

PE has been found effective in reducing PTSD symptoms among patients with comorbid depression. In a study examining the impact of depression on the efficacy of PE, comorbid depression was found to be unrelated to decrease in PTSD symptoms [55,56]. Those

with current major depression, past major depression and no history of major depression all benefitted equally from PE. Interestingly, patients with higher depression in baseline who received either CPT or PE showed greater improvement in PTSD symptoms from pre- to post-treatment than those with lower depression [57].

Importantly, PE has not only been found effective among those with PTSD and comorbid depression, but it has also been found to significantly reduce depressive symptoms in a number of studies [26,38,43,58]. Thus, the presence of comorbid depression is not a contraindication to PE treatment. However, in cases where major depression is the primary disorder, or when patients are at a high risk for suicide, therapists must first provide crisis management and containment.

Many treatment studies for PTSD have excluded patients with comorbid substance dependence disorders [23,24] due to concern that substance use will interfere with patients' ability to benefit from PTSD treatment and/or for fear that PTSD treatment will exacerbate substance use. However, studies examining the efficacy of PE with this population have found positive results. PE was shown to be effective in reducing PTSD symptoms among patients with PTSD and comorbid alcohol dependence [59], and among those with comorbid cocaine dependence [60]. PE was not associated with increased substance use in either of the aforementioned studies. Interestingly, Foa et al. found that patients who received PE were also less likely to increase their drinking 6 months after treatment termination [59]. Thus, PE not only reduces PTSD symptoms in this population, but can also help maintain reductions in drinking behavior.

Traumatic brain injury (TBI) is frequently comorbid among PTSD patients, especially active military personnel and veterans, because brain injuries are often sustained in traumatic experiences. A recent study of veterans with PTSD found that PE was equally effective in individuals with and without a history of TBI [61]. Regardless of TBI status, veterans with PTSD showed a significant reduction in PTSD severity posttreatment. Although there is little research on this issue at present, the results of this study provide promising evidence that PE can be helpful for individuals with PTSD and a history of mild TBI.

Patients with PTSD and borderline personality disorder (BPD) have also been excluded from some treatment studies, especially when they report recent intentional self-injury [62-67]. Personality disorders, particularly BPD, have been thought to impede the effects of treatment of PTSD [68]. However, research suggests that individuals with PTSD and comorbid BPD can also benefit from PTSD treatment. Feeny, Zoellner and Foa re-analyzed data of patients who received PE, SIT or their combination, and found that women with BPD symptoms benefited as much from treatment as those without these symptoms [64]. Indeed, patients with BPD symptoms evidenced significant improvement on PTSD symptoms, PTSD diagnostic status, depression, anxiety and social functioning.

Similar results were found in a study that examined women with comorbid BPD and PTSD with recent and/or imminent serious intentional self-injury [69] who received PE concurrently with dialectical behavior therapy (DBT). The results showed that DBT PE resulted in significant reductions in PTSD, and at post-treatment a majority of patients no longer met criteria for PTSD. Importantly, DBT PE did not exacerbate PTSD or BPD symptoms, including self-injurious behavior.

The finding that dissociative symptoms did not interfere with PE contradicts the previously held concern that dissociation would reduce the efficacy of PTSD treatment by limiting emotional engagement [70,71]. In contrast to Harned *et al.*'s hypothesis, pretreatment levels of trait dissociation, depersonalization, numbing and depressive symptoms were not related to improvement or dropout [69]. Patients with high levels of dissociative symptoms showed a similar reduction of PTSD as patients with low levels of dissociative phenomena. In sum, there is no evidence to date that dissociative phenomena predict treatment outcome.

PE has also been shown to significantly reduce symptoms that are commonly associated with PTSD. As noted above, these include depressive symptoms [26,40] and alcohol use [59]. In addition, PE has been shown to significantly reduce general anxiety [23], trauma-related guilt [40], state-anger [72], and improves social adjustment and functioning [23]. PE, with or without the addition of cognitive restructuring, has also been shown to significantly decrease reported physical health difficulties compared with waitlist, and these improvements persisted at 12 months post-treatment [73]. In sum, PE can have a broad impact on the lives of PTSD sufferers by reducing both PTSD severity and associated symptoms, and improving overall functioning.

Challenges to implementing PE

Although PE and several other evidence-based treatments have been found effective in significantly reducing symptoms of PTSD and associated problems, it is important to note that some patients drop out of treatment or do not achieve a good response. A drop-out rate of approximately 20–30% has been found for both exposure and nonexposure treatments [74], and up to 40–50% of patients do not achieve a good response [75], defined as >70% reduction in symptoms. Research on predictors of dropout and response is currently lacking. One exception is a study that examined assault-related predictors of PE, and found that the childhood trauma and trauma that results in sustained physical injury during adulthood predicted greater PTSD severity following PE [76].

Like any treatment, there are some contraindications to implementing PE. When considering using PE, clinicians should be careful to ensure that: PTSD is the primary presenting issue; there are no safety issues (i.e., imminent risk of suicide or homicide, currently known as self-harm behavior); and there are no comorbid disorders that might interfere with treatment including unmanaged bipolar disorder or psychosis. That said, as noted above, most of the commonly occurring comorbidities should not necessarily be considered contraindications to treatment. Concurrent pharmacotherapy should also not be considered a contraindication to PE, although as a general rule, it is best if medication dosage remains stable during therapy so that the patient and therapist can accurately gauge the efficacy of therapy.

Research on adjuncts to PE has found that adding stress inoculation training (for example, see [26]) and cognitive restructuring [23,43] does not improve outcome compared with PE alone. It has been hypothesized that additional efficacious treatment components fail to improve outcomes because all efficacious treatments modify the same dysfunctional cognitions underlying PTSD [77]. In other words, despite differences at the level of therapy technique, all evidence-based treatments for PTSD may share similar mechanisms of change. Ongoing research examining strategies to augment exposure therapy with medications (e.g., D-cycloserine, Methylene Blue) thought to boost extinction learning may result in even more efficient treatment programs for PTSD.

Conclusion & future perspective

Untreated PTSD is often associated with a host of additional problems, including high rates of comorbid conditions such as major depression and substance use disorders [5], as well as poor physical health [9,10] and low quality of life [15]. A number of evidence-based treatments for PTSD have been developed to date and the efficacy of PE has been supported by the greatest number of studies. PE has demonstrated efficacy with a range of trauma populations and by multiple research groups (e.g., Israel [78]; Japan [79]; Australia [80]; The Netherlands [81]). Importantly, PE has demonstrated efficacy for those with PTSD and a number of the commonly comorbid conditions. On the whole, these studies have shown that the efficacy of PE in reducing PTSD severity is unhampered by the presence of many comorbid disorders, and it has also been shown to reduce symptoms commonly associated with PTSD such as depression, anxiety and anger. Thus, there is sufficient evidence to consider PE a first line of treatment for individuals with PTSD and comorbid disorders.

In the next 5-10 years, we expect to see continued growth of clinical research that will increase our understanding of how best to treat PTSD across populations. We have already seen encouraging results from studies examining PE in comorbid samples and we expect that this research will continue to expand the indication for evidence-based exposure therapy in new patient populations. For example, little is currently known about whether modifications are necessary when treating PTSD patients on pain medication for physical health problems. Although there is some evidence that patients who are permanently disabled during trauma may require additional therapy to help them adjust to their limitations [76], the role of pain medications has not been examined. We also expect to see the target outcomes broadened to include commonly associated problems such as depression and anger, as well as quality of life and functioning. These outcomes are not consistently described in treatment outcome research yet are critical to evaluating the potential value of an intervention. Furthermore, we expect that the next decade will witness considerable progress in developing strategies to optimize the efficiency of evidence-based treatments such as PE. For example, several studies are now underway to examine the use of adjunct pharmacological agents that are thought to facilitate extinction learning during exposure therapy. Finally, we expect that there will be further development in novel treatment delivery methods that exploit technological advances. Mobile application- and internet-based treatments for PTSD have great potential to increase the cost-effectiveness of treatment and reduce barriers to accessing evidence-based treatment. Currently, most PTSD sufferers do not receive appropriate treatment [4], in part because there are far too few mental health professionals trained in evidence-based treatments for PTSD (for example, see [82,83]). We hope that the coming years will witness significant growth in our understanding of effective dissemination and implementation strategies so that we can better connect evidence-based treatments with those who stand to benefit from them.

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