Medication and non-medication treatments of post-traumatic stress disorder

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Recent developments in the psychological and pharmacological management of post-traumatic stress disorder are reviewed. This review of controlled outcome studies indicates that: (i) cognitive behavior therapy is the psychological treatment of choice; (ii) different components of cognitive behavior therapy can be effective; (iii) eye movement desensitization and reprocessing is not as effective as cognitive behavior therapy; (iv) selective serotonin re-uptake inhibitors are the pharmacological treatment of choice; and (v) there is increasing support for nefazadone but not for cyproheptadine in reducing the symptoms of post-traumatic stress disorder. The need for increased treatment effectiveness and the integration of recent findings into clinical practice is discussed. Curr Opin Psychiatry 14:119–123. © 2001 Lippincott Williams & Wilkins.

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Abbreviations

ASD	acute stress disorder
CBT	cognitive behavior therapy
CT	cognitive therapy
EMDR	eye movement desensitization and reprocessing
FDA	US Food and Drug Administration
PE	prolonged exposure
PTSD	post-traumatic stress disorder
SC	supportive counselling
SIT	stress inoculation training
SSRI	selective serotonin re-uptake inhibitor

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Introduction

Lifetime prevalence rates of post-traumatic stress disorder (PTSD) have been reported to be approximately 30% in traumatized populations [1,2]. The prevalence of PTSD and the potentially debilitating nature of this condition points to the need for effective treatments of PTSD. In response to this need, there has been a surge of research activities in recent years in both psychological and pharmacological interventions for PTSD. This article provides a critical review of recent treatment outcome studies that have attempted to reduce PTSD symptoms through pharmacological or psychological techniques. Although many clinical reports and uncontrolled studies have been reported, this review will focus exclusively on recent adequately controlled outcome studies.

Psychological treatments

Although there is a wide array of popular psychological treatments available, many of these are not empirically validated. In this review, we focus exclusively on those that have been subjected to controlled study. Overall, there is convergent evidence that the most effective psychological treatment of PTSD is cognitive behavior therapy (CBT) [3•,4•,5].

Cognitive behavior therapy

CBT can include prolonged exposure (PE) that may be either imaginal or *in vivo*, cognitive therapy (CT), anxiety management, or stress inoculation training (SIT), or a combination of all these components. Individuals are presumed to adapt psychologically after a trauma because they: (i) emotionally engage with and habituate to their traumatic memories; (ii) organize their trauma memories in an adaptive manner; and (iii) correct dysfunctional cognitions about the traumatic experience [6•]. It is assumed that CBT is effective because it facilitates these mechanisms after trauma. The utility of CBT in reducing PTSD symptoms has recently been supported by randomized studies that have indicated the effectiveness of CBT for African American and Caucasian groups [7•] and for traumatized police officers [8•].

The major focus of recent CBT treatment studies has been on dismantling the effective components of CBT. Specifically, there has been a trend to disentangle the effects of exposure from CT or anxiety management. In a large-scale study that attempted to index relative contributions of PE and SIT, Foa and colleagues [9••] randomly allocated 96 female assault victims to nine

sessions of either PE, SIT, combined PE/SIT, or a wait-list control condition. PE included education about trauma responses, breathing control, prolonged imaginal exposure to traumatic memories, and in-vivo exposure to feared situations. SIT comprised education, breathing control and relaxation training, thought stopping, self-talk, CT, modelling, and role playing. Whereas all wait-list participants still had PTSD at the end of the wait period, at 12 month follow-up PTSD was noted in 35% of PE, 32% of SIT, and 32% of combined PE/SIT participants. Unexpectedly, PE participants made more gains on a number of treatment variables than SIT or PE/SIT participants.

Hembree and Foa [6•] also reported the results of an ongoing study in which 96 female assault victims with PTSD were randomly allocated to nine sessions of either PE, PE plus CT, or wait-list control. The study defined initial treatment success as a 70% improvement in PTSD severity by session 8. Using this criterion, the study found that more PE participants (57%) reached this mark than PE/CT participants (23%). Another recent study [10] randomly allocated 121 female sexual assault victims to 13 sessions of either cognitive processing therapy (comprised of CT plus exposure through written form), PE, or a wait-list control. After blind assessments at 9 months follow-up, both intent-to-treat analyses and those that focused on treatment completers indicated that both treatments were comparably and highly effective in reducing PTSD and depression.

Marks and colleagues [11] randomly allocated 87 civilian trauma victims to 10 sessions of either PE, CT, PE/CT, or relaxation. At 6 months post-treatment, the PE, CT, and PE/CT (but not the relaxation) groups had achieved comparable reductions in PTSD symptoms. Perusal of the PTSD severity scores of the study suggests, however, that the PE and PE/CT participants had achieved greater symptom reduction on some variables relative to the CT alone condition.

Tarrier and colleagues [12•] randomly allocated 72 civilian trauma survivors to either PE (without in-vivo exposure) or CT. Participants received 16 1 h sessions and were assessed post-treatment and at 6 months. At both post-treatment and follow-up, PE and CT were reported to be equally effective in reducing PTSD symptoms. Moreover, these comparable treatment gains were maintained at 2 years follow-up [13•]. That study found that treatment success was associated with less expressed emotion by partners [14•], missed treatment sessions, male sex, and suicidal risk [15]. Inferences from the study need to be considered cautiously, however, because the reported treatment effects were somewhat lower than previous studies, and optimal treatment fidelity checks were not conducted [16].

The finding that treatments that combine components of CBT are no more effective than those that use the components singularly is surprising. Different commentators have suggested that the failure to observe an additive benefit of combined treatments may occur because the use of combined treatments within the same amount of treatment time may result in less provision of the active treatment strategies [4•,12•]. In contrast to this pattern, however, another recent study by Bryant and colleagues (unpublished data) has compared PE, PE combined with CT, and supportive counselling (SC) in a mixed civilian trauma population. Their study carefully managed the time allocated to the treatment components by ensuring that equivalent periods of time were allocated to PE and CT across the eight sessions of therapy. At 6 months follow-up the study found that PE/CT resulted in a significantly greater reduction in PTSD symptoms than PE alone, which in turn had better outcomes than SC.

Eye movement desensitization and reprocessing

One popular variant of CBT is eye movement desensitization and reprocessing (EMDR). This therapy involves having the patient visualize trauma images while having the client rapidly move their eyes sideways by following the therapist's moving finger; this exercise is followed by a CT approach that attempts to replace negative cognitions with positive ones [17•]. Despite the many clinical reports and commentaries available on this topic, there are relatively few well-controlled studies [18•,19•,20••,21•]. To summarize the available data, there is no convincing evidence that eye movements play any therapeutic role in EMDR [18•,21•]. In terms of outcome studies, EMDR appears to be more effective than no treatment, supportive listening, and relaxation [22•].

In terms of the standing of EMDR compared with established treatments, one study has directly compared its efficacy with CBT [23••]. That well-controlled study randomly allocated civilian trauma survivors to nine sessions of either CBT or EMDR. Although the study found that both treatment groups improved at post-treatment, the gains made by CBT participants were greater than those made by participants receiving EMDR. Furthermore, whereas those in the CBT condition maintained their treatment gains over the following 3 months, those in the EMDR group tended to relapse. The evidence against considering EMDR as a treatment of choice for PTSD is further supported by a recent 5 year follow-up of patients treated with EMDR [24•]. That study found that treatment gains displayed initially after treatment were not maintained in the sample. Overall, the empirical status of EMDR is summed up in the statement that 'what is effective in EMDR (imaginal exposure) is not new, and what is new (eye movements) is not effective' [21•].

Early interventions

The recent introduction of acute stress disorder (ASD) as a precursor of PTSD has stimulated closer study of the potential benefits of early intervention to prevent PTSD [25••]. In an extension of an earlier treatment study, Bryant and colleagues [26••] randomly allocated 45 civilian trauma survivors with ASD to five sessions of either CBT (PE, CT, anxiety management), PE combined with CT, or SC [26••]. That study found that at 6 months follow-up, PTSD was observed in approximately 20% of both active treatment groups compared with 67% of those receiving SC. Interestingly, the study found that 20% of their sample dropped out of treatment, and these patients were characterized by more severe ASD. Treatment success was associated with more adaptive cognitive strategies that minimized avoidance and increased constructive reappraisal of events [27•].

In a recent study (unpublished data), Bryant and colleagues randomly allocated 60 civilian trauma survivors who met the criteria for ASD to either CBT, combined CBT plus hypnosis, or SC [28]. Therapy consisted of six 90 min sessions that commenced within one month of trauma. Hypnosis was introduced because many commentators have suggested that hypnosis is an appropriate means to overcome some of the dissociative barriers that may occur in ASD. Furthermore, a recent study demonstrates that ASD participants are characterized by high levels of hypnotizability, and for this reason they may be adept at using hypnosis [29]. In that study, the imaginal exposure was preceded by a hypnotic induction and suggestions to engage in the exposure exercise. Although both CBT and CBT/hypnosis had comparably superior reductions in PTSD compared with SC, the CBT/hypnosis group had fewer re-experiencing symptoms at post-treatment follow-up. The study suggests that although both treatments enjoyed comparable success, the addition of hypnosis hastened symptom reduction. The potential for brief early intervention is also indicated by a demonstration that video-presented information immediately after rape can reduce post-traumatic distress [30•].

Pharmacotherapy

Given space limitations, we have restricted this review of research on pharmacotherapy for PTSD primarily to the most recent reports. A more comprehensive overview and guide to the older literature can be found elsewhere [31•,32••,33•].

Most importantly, the US Food and Drug Administration (FDA) has recently approved the selective serotonin reuptake inhibitor (SSRI) sertraline as an indicated treatment for PTSD. This is the first medication so designated. FDA approval was based on two successful 12 week randomized clinical trials of sertraline versus placebo in studies with 187 and 208 male and female subjects, respectively [34••,35]. Subjects in both trials showed significant reductions in PTSD symptomatology as well as in clinical global improvement. Furthermore, all three PTSD symptom clusters (e.g. intrusion, avoidant/numbing and arousal) responded to medication.

Similar results have been presented but not published regarding a large multisite trial with the SSRI, paroxetine, in which 551 men and women were randomly assigned to either paroxetine 20 mg, 40 mg, or placebo [36]. In addition, positive results have been found in smaller studies with the SSRI, fluoxetine, with 64 and 53 subjects, respectively [37,38••], in which civilian, but not veteran, subjects had a favorable response. Citations for positive, but less well-controlled, trials with sertraline, fluoxetine, and other SSRIs can be found in the reviews mentioned above. Taken together, these reports all suggest that SSRIs are an effective class of medications for patients with PTSD.

An extremely important recent development that has been presented, but not published, is the sertraline 28 week discontinuation study, in which 96 subjects who had complete remission of PTSD symptoms after sertraline treatment were randomly assigned to either medication or placebo. At the end of 28 weeks, 82% of subjects kept on sertraline did not relapse in contrast to 50% of the placebo group who had a relapse of PTSD [39].

Three recent studies with SSRIs [40•,41•,42] suggest that therapeutic efficacy is associated with a reduction of the physiological alterations associated with PTSD, exhibited by the normalization of autonomic dysregulation, indicated by heart rate variability [40•] and by the elimination of abnormal physiological reactivity to script-driven imagery, assessed by increases in blood pressure and heart rate [41•,42].

Other medications

The only other placebo-controlled randomized clinical trial to have been published recently [43•] concerns the failure of the serotonin antagonist cyproheptadine to reduce PTSD symptoms, traumatic nightmares and sleep problems among 69 Vietnam veterans with PTSD. These findings were supported by an open-label trial [44•], in which cyproheptadine again failed to reduce nightmares or improve sleep.

Open-label trials with the antidepressant nefazadone [45•–47•] show promising results, especially with chronic or treatment-refractory patients. Other recent successful open-label trials concern the antidepressant buproprion [48•], the anticonvulsant/mood stabilizer divalproex

[49•], and the anticonvulsant/mood stabilizer lamotrigine [50•]. Reports on randomized clinical trials with these medications are eagerly awaited.

Conclusion

There is increasing recognition that all interventions for traumatized patients need to be subjected to controlled outcome studies, supported by empirical findings, and consistent with available knowledge. This trend is reflected in two recent publications that outline the critical treatments for PTSD. One is a comprehensive review of the entire empirical literature on medication and psychological trials [51••], which generates evidence-based recommendations for best practices in PTSD. This book on treatment guidelines for PTSD makes evidence-based recommendations concerning pharmacological interventions, CBT, EMDR, psychological debriefing and other PTSD treatments. The second publication is a monograph [52••] reporting the responses of an expert consensus panel of international experts to a detailed questionnaire concerning both pharmacotherapy and psychotherapy for PTSD.

In summary, recent developments indicate that there is increasing evidence for the benefits of selective psychological and pharmacological interventions for reducing PTSD symptoms. This empirical base forms a framework to guide clinical practice. Despite the advances of recent work, there is a marked need for future research to address the issues of: (i) increasing treatment effectiveness by addressing PTSD in those patients who do not complete or respond to treatment; (ii) reducing the co-morbid symptoms that occur with PTSD; and (iii) identifying those interventions that are applicable to diverse traumatized populations.

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