Therapy of Posttraumatic Stress Disorder

Written by Brian Hoyle

Posttraumatic stress disorder (PTSD) was officially designated as a disorder in the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* in 1980, said Charles C. Engel, MD, MPH, Senior Health Scientist, RAND Corporation, Arlington, Virginia, USA, in a review of the epidemiology and psychological trauma associated with PTSD. The criteria to diagnose PTSD have been further refined, most recently in *DSM-5* in 2013 (Table 1).

PTSD comorbidities including depressive disorders, anxiety disorders (panic, generalized anxiety, phobias), substance abuse, somatic symptoms, mild traumatic brain injury, and fibromyalgia are common and affect an estimated 88% of men and 79% of women in their lifetime [Kessler RC et al. *Arch Gen Psychiatry* 2005].

Paula P. Schnurr, PhD, National Center for PTSD in the Department of Veterans Affairs and Geisel School of Medicine at Dartmouth, Hanover, New Hampshire, USA, provided an update on psychotherapy treatment for PTSD. Psychotherapy may be more effective than medication, according to a recent meta-analysis [Watts BV et al. *J Clin Psychiatry* 2013]. The delivery of treatment varies, and there are at least 7 clinical practice guidelines recommending treatment for PTSD. The Department of Veterans Affairs and Department of Defense Clinical Practice Guideline for Management of Posttraumatic Stress is used for veterans and military personnel. Using it as a framework, Dr. Schnurr recommended 5 principles to guide the choice of treatment (Table 2).

A recent randomized controlled trial with 121 patients provided evidence that an intensive 1-week regimen of cognitive therapy produced results equivalent to 12 weeks of cognitive therapy, and both were superior to 12 weeks of supportive therapy [Ehlers A et al. *Am J Psych* 2014]. A randomized, placebo-controlled trial of 67 patients with PTSD showed D-cycloserine (DCS) in addition to exposure therapy was effective only in a subgroup [de Kleine RA et al. *Biol Psychiatry* 2012]. Another randomized controlled trial (RCT) reported negative effects of DCS on exposure therapy; the authors suggested that in some cases, the compound may cause traumatic memories to be intensively reconsolidated to the detriment of the patient [Litz BT et al. *J Psych Res* 2012].

Dr. Schnurr stated that evidence-based psychotherapy works for most PTSD patients, including veterans, and the benefits can persist for years.

John H. Krystal, MD, Yale University School of Medicine, New Haven, Connecticut, USA, discussed the pharmacotherapy of PTSD. Anti-depressants have been the predominant class of drugs used in PTSD since the 1980s [Frank JB et al. *Am J Psychiatry* 1988].

Selective serotonin reuptake inhibitors (SSRIs) approved by the US Food and Drug Administration for treatment of PTSD are sertraline and paroxetine. The norepinephrine reuptake inhibitor desipramine provided benefits in a 12-week study [Petrakis IL et al. *Neuropsychopharmacology* 2012]. Norepinephrine targets adrenergic receptors, which are involved in the "fight or flight" response and learning. Antiadrenergic drugs including prazosin, clonidine, and propranolol have shown some evidence of benefit in PTSD studies, but definitive evidence of their efficacy is lacking. Other antidepressants block serotonin-2 receptors; trazodone has been the most commonly prescribed medication for PTSD in US veterans (despite the absence of placebo-controlled trials), and pilot studies of nefazodone have been positive.

Second-generation antipsychotics with prazosin-like and trazodone-like activity, as well as drugs that target the dopamine receptor D2 include risperidone, olanzepine, quetiapine, ziprasidone, clozapine, and aripiprazole. Benefits obtained with risperidone have not been compellingly different from placebo, and adverse effects including somnolence, weight gain, and decreased libido have been documented. Still, risperidone may be beneficial for paranoia and psychosis and may be warranted for those with less severe PTSD who are being treated with fewer medications. Quetiapine is the most commonly prescribed second-generation antipsychotic; preliminary data have been encouraging, with daytime sedation and weight gain being adverse concerns.

Peer-Reviewed Highlights From the

American Psychiatric Association 167th Annual Meeting

May 3-7
New York

Table 1. *DSM-5* Criteria to Diagnose PTSD

Criterion A: Trauma

Exposure to death, threatened death, actual or threatened serious injury, or actual/threatened sexual violence in one or more of the following ways:

- Direct exposure
- Witness in person
- Indirect (eg, learning of actual/threatened trauma or violent/accidental death of close relative/friend
- Repeated or extreme indirect exposure to aversive details not involving television, movies, or photographs

Criterion B: Intrusion

Traumatic event persistently reexperienced by the following:

- Recurrent, involuntary, and intrusive distressing memories
- Traumatic nightmares
- Dissociative reactions, such as flashbacks
- Intense or prolonged distress after trauma reminders
- Marked physiological reactivity after trauma reminders

Criterion C: Avoidance

Persistence, deliberate avoidance of distressing trauma-related stimuli after the event; >1 of the following:

- Trauma-related memories, thoughts, or feelings
- External reminders (eg, people, places) that arouse distressing memories, thoughts, or feelings

Criterion D: Negative Cognitions and Mood

Negatively altered cognitions or moods that begin or worsen posttrauma; ≥2 of the following:

- Inability to recall important features of trauma
- Persistent and distorted negative beliefs about self or world
- Persistent, distorted blame of self or others for trauma or consequences
- Persistent negative trauma-related emotions
- Diminished interest in significant activities
- Detachment from others
- Persistent inability to have positive feelings

Criterion E: Negative Cognitions and Mood

Trauma-related alterations in arousal and reactivity that began or worsened after the traumatic event; ≥2 or more of the following:

- Irritable or aggressive behavior
- Self-destructive or reckless behavior
- Hypervigilance
- Exaggerated startle response
- Problems in concentration
- Sleep disturbance

Benzodiazepines enhance the effects of the gamma-aminobutyric acid neurotransmitter. The resulting easing of depression-related symptoms made benzodiazepines a popular prescription for PTSD. However, use is declining because of concerns about its abuse and limited evidence-based efficacy [Hermos JA et al. *J Trauma Stress* 2007; Lund BC et al. *J Clin Psychiatry* 2012]. A GABA receptor-targeted drug that has shown more promise is S-zopiclone; a double-blind, placebo-controlled RCT demonstrated its effectiveness in improving sleep and lessening PTSD symptoms [Pollack MH et al. *J Clin Psychiatry* 2011]. Other GABA modulators being assessed for PTSD pharmacotherapy are tiagabine, valproate, and topriamate.

Table 2. Keystones to Guide the Choice of Psychotherapy for Treatment of PTSD

• Explanation of available and effective therapeutic options to patients
• Education of patients and family members about treatment
• Selection of evidence-based psychotherapy driven by patient/provider preferences as first-line treatment
• Provision of psychotherapy by trained practitioners
• Consideration of a collaborative care approach, when feasible

D-cycloserine may have potential in fear extinction through its targeted activity at the N-methyl-D-aspartate (NMDA) receptor, which is crucial in memory retention. Finally, the antidepressant action of ketamine was recently demonstrated [Berman RM et al. *Biol Psychiatry* 2000], and benefits appear to extend to PTSD treatment [Feder A et al. *JAMA Psychiatry* 2014].

David M. Benedek MD, Uniformed Services University, Bethesda, Maryland, USA, reviewed complimentary and alternatives approaches to treat PTSD. Complimentary approaches are used in conventional care. Alternative approaches are used in lieu of standard care, and can become complimentary as evidence for their efficacy accumulates. These approaches are currently the final step in a multistep hierarchy of treatment that begins with psychotherapy (cognitive-based therapy, relaxation techniques, imagery rehearsal therapy, hypnosis, group therapy, brief psychodynamic therapy) and, if necessary, progresses to include pharmacotherapy. The National Center of Complementary and Alternative Medicine (NCCAM) classification of complementary and alternative approaches are summarized in Table 3.

Table 3. NCCAM Classifications of Complementary and Alternative Approaches

Natural products: herbal remedies, diet supplements
Mind-body medicine: meditation, acupuncture, relaxation, yoga
Manipulative/body-based: massage, spinal manipulation
Whole medicine
Other: movement therapies, energy therapies

Complementary and alternative approaches, such as acupuncture, are reportedly used by about 40% of PTSD sufferers, mainly to improve mental health. The claimed benefits are currently more anecdotal than evidence-based; as of 2011, only 7 RCTs had been conducted (1 for body-oriented therapy and 6 for mind-body therapy). Evidence is relatively more solid for acupuncture, with its effect on the somatosensory cortex indicated. While relaxation therapy and yoga have health-related benefits, the evidence for their specific benefit in PTSD remains scant.