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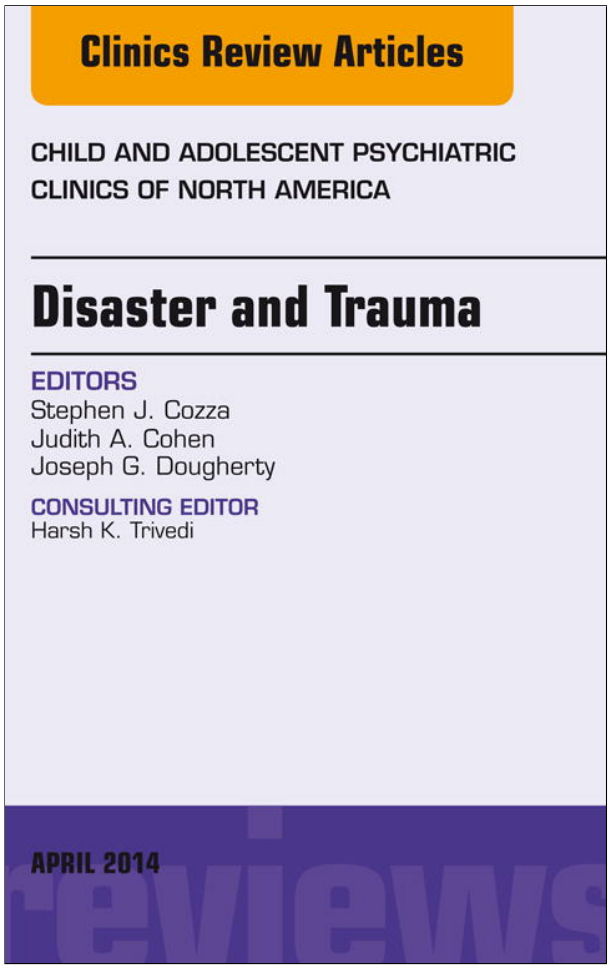

Psychological and Pharmacologic Treatment of Youth with Posttraumatic Stress Disorder

An Evidence-based Review

Brooks R. Keeshin, MD[a,b,*], Jeffrey R. Strawn, MD[b,c]

KEYWORDS

- Posttraumatic stress disorder
- Trauma-focused cognitive behavior therapy (TF-CBT)
- Selective serotonin reuptake inhibitor (SSRI, SRI) • Trauma • Prevention

KEY POINTS

- Posttraumatic stress disorder (PTSD), in children and adolescents, is a constellation of symptoms that likely represent multiple pathophysiologic responses to stress.
- Psychotherapy is the mainstay of treatment of pediatric PTSD, with the greatest evidence supporting the use of trauma-focused psychotherapies.
- Pharmacotherapy should be used in conjunction with ongoing psychotherapy when prolonged and severe symptoms (including comorbid conditions such as depression and anxiety disorders) warrant additional intervention.

EVIDENCE FOR PSYCHOTHERAPEUTIC TREATMENT OF YOUTH WITH PTSD

Children exposed to violence and abuse experience a wide range of psychological sequelae, including attention disorders, mood disorders, and anxiety disorders.[1] Many children, especially those who are exposed to child abuse and neglect, as

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Acronyms	
CAPS	Clinician-Administered PTSD Scale
CBITS	Cognitive Behavioral Interventions for Trauma in Schools
CFTSI	Child and Family Traumatic Stress Intervention
CGI	Clinical global impression scale
CPP	Child Parent Psychotherapy
DSM-5	Diagnostic Statistical Manual of Mental Disorders
EMDR	Eye Movement Desensitization and Reprocessing
PE-A	Prolonged Exposure for Adolescents
SRI	Serotonin reuptake inhibitor
SSRI	Selective serotonin reuptake inhibitor
TGCT	Trauma and grief component therapy
TSCC	Traumatic Symptom Checklist for Children

well as a variety of disasters and noninterpersonal forms of trauma, may experience stress disorders, including posttraumatic stress disorder (PTSD).[1] In the recently released *Diagnostic Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5),[2] the criteria for PTSD has been revised and new, developmentally sensitive criteria for children who experience trauma before the age of 6 years is available to guide clinicians in diagnosis of both young and older children. The revision of these criteria from the *Diagnostic Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR) criteria includes the separation of avoidance and negative alterations in mood into separate categories, as well as the categorization of dissociative experiences as a qualifier. Because PTSD has various neuroendocrine and neuroanatomic correlates that predict specific phenomenologic characteristics (reviewed by De Bellis elsewhere in this issue), it is likely that this new classification will help clinicians design treatment strategies based on specific impairing symptoms rather than on the broad, often heterogenous symptoms of PTSD.

Psychotherapeutic interventions are the mainstay of treatment of traumatized children with symptoms of traumatic stress, including those with PTSD, regardless of the cause. Although there are many permutations of these psychotherapeutic interventions, including adaptation to specific target populations (eg, individual, dyadic, group) and foundational theory (eg, cognitive behavioral, psychodynamic, and so forth), there are several core unifying concepts that characterize most evidence-based psychotherapies for traumatized youth. These include: (1) ensuring safety from continued trauma; (2) providing psychoeducation regarding the potential effects from, and responses to, trauma; (3) providing effective coping/behavior management strategies; (4) assisting children in mastering trauma avoidance, typically through trauma narration and/or exposure activities; and (5) engaging parents or other caregivers in treatment and enhancing the parent-child relationship. These concepts crosscut psychotherapeutic modalities with an emphasis on different components often depending on the specific therapy model and the child's most debilitating symptoms.[3] For example, increased focus on self-calming coping strategies are key in an adolescent with extreme hyperarrousal, whereas the parent-child relationship and behavior management are areas of focus in a young child who is reexperiencing symptoms that are born out through aggressive and assaultive play. This article reviews the primary components, target populations, and effectiveness of the most studied and commonly available evidence-based trauma treatments for children.

COGNITIVE BEHAVIOR THERAPY–BASED THERAPIES

Trauma-focused Cognitive Behavior Therapy

Trauma-focused cognitive behavior therapy (TF-CBT; www.musc.edu/tfcbt) is the most studied treatment of symptomatic children exposed to trauma,[1] with 13 randomized controlled trials showing its efficacy both in waitlist and head-to-head therapeutic trials for children aged 3 to 17 years (**Fig. 1**). Benefits of TF-CBT include reduction of PTSD symptoms and remission of PTSD, improvement of a variety of other mental health symptoms, as well as enhanced parental capacity to meet the child's emotional and behavioral needs.[1] TF-CBT has been used in a myriad of treatment settings in children exposed to a wide range of abusive and traumatic experiences, some of whom continued to experience trauma or the threat of trauma during treatment.[4] Moreover, cognitive behavior therapy (CBT)–based therapies for trauma have shown gains that continue long after treatment, with trauma symptom reduction effect sizes greater than 2 when measured at more than 6 months.[5]

The first 3 components of TF-CBT (psychoeducation, parenting skills, and relaxation skills) stabilize trauma-related physiologic and behavioral dysregulation and prepare the child and family for the therapeutic work ahead. Additional components such as affect modulation and cognitive processing give the child the capacity to better modulate dysregulated emotions and understand the interconnectedness between thoughts, feeling, and behaviors. Once the child has practiced self-regulation and has an increased capacity to modulate behavioral, cognitive, and affective states, the child and therapist begin to construct the trauma narrative. Developing the trauma narrative is a collaborative therapeutic process during which the therapist encourages the child to describe even those details about traumatic experiences that the child thinks are unspeakable, thus overcoming shame, stigma, and avoidance, and gaining mastery of the content in session. Maladaptive trauma-related cognitions are processed using cognitive processing techniques learned earlier in treatment. If the child

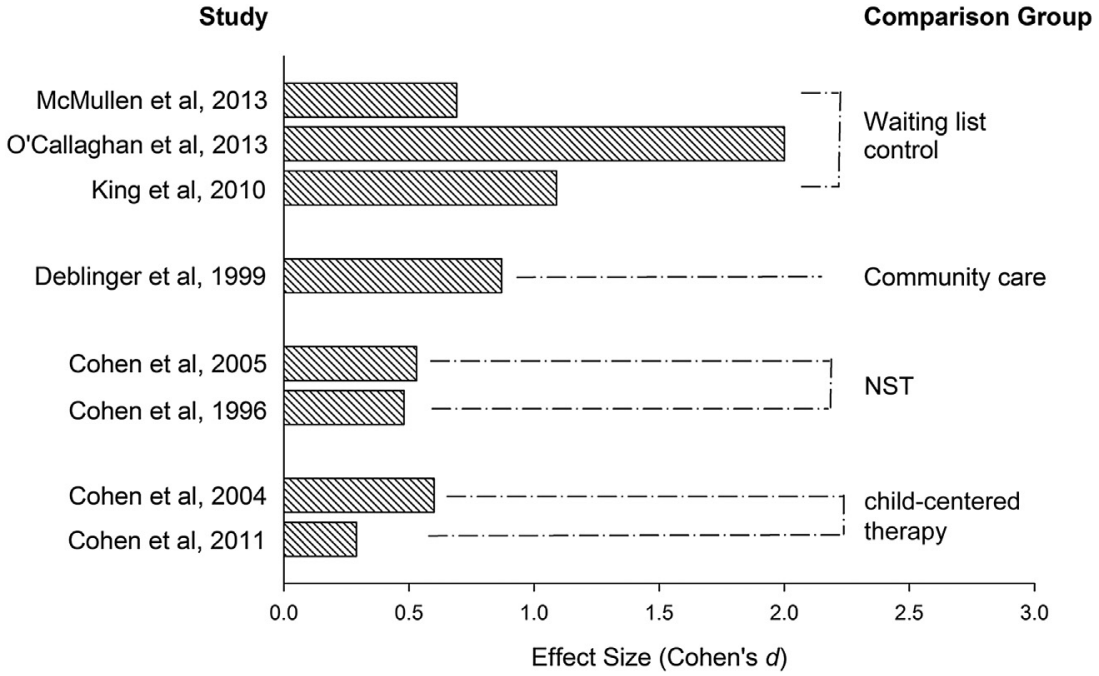

Fig. 1. Trauma-focused cognitive behavior therapy (TF-CBT) has been evaluated relative to several comparison treatments as well as waiting list comparison groups. In general, effect sizes are robust, although they depend on the comparison group, with lower effect sizes typically being observed when TF-CBT is compared with an active treatment. NST, non-directive supportive therapy.

becomes distressed while recalling aspects of the narrative, the therapist assists the child in using previously taught self-relaxation and coping techniques and then returns to the narrative, thus reinforcing mastery. Children develop mastery over generalized fears through the use of in vivo exposure hierarchies. The final TF-CBT sessions are spent in conjoint parent-child sessions. The parent typically participates with the child to share the child's narrative, to engage in safety planning, and to discuss the continued effective use of the CBT skills once TF-CBT is terminated.

Several Cognitive Behavior Therapies Have at Least One Randomized Controlled Trial Showing Efficacy with Traumatized Youth

Prolonged exposure for adolescents (PE-A) includes the development of an exposure hierarchy, practiced in vivo exposure during sessions, and assigning in vivo exposures such as listening to taped recordings by the patient recounting the trauma. Compared with a manualized, conflict-based, psychodynamic intervention, adolescents who received PE-A showed a greater reduction in symptoms of posttraumatic stress and improved rate of PTSD remission both at the end of treatment and at follow-up[6]; however, study limitations complicate a head-to-head comparison, including differences in the frequency of treatment and experience of therapists between the groups receiving psychodynamic psychotherapy and PE-A.

A 10-week CBT trial for children with single-incident traumatic exposure and PTSD maintained for a 4-week lead-in period showed significant improvement compared with a waitlist comparison group, with only 10% in the active arm meeting criteria for PTSD at the end of treatment compared with 60% in the waitlist group.[7] In contrast with TF-CBT, there was no relaxation-training component and parent-child sessions were not part of the manual but were used when deemed clinically necessary. Of primary focus was exposure to the traumatic memory through writing, talking, or drawing, with cognitive restructuring designed to modify cognitive distortions of the trauma and related symptoms.

Narrative exposure therapy (KIDNET) is an 8-week, narrative-driven individual therapy designed specifically for pediatric refugee populations.[8] During the course of therapy, a therapist uses a variety of child-friendly recall assistance techniques to enable the child to develop a coherent narrative of the child's life, with special focus given to traumatic events, both remote and recent. The development of the narrative offers the opportunity for habituation to traumatic memories. Reductions in posttraumatic symptoms were significant in the active treatment arm of the study and were maintained at both 6-month and 12-month follow-ups.[8]

NON-CBT THERAPIES

Child-Parent Psychotherapy

Child-parent psychotherapy (CPP) is a dyadic, attachment-based therapy intended for traumatized children aged 3 to 5 years. Through both joint sessions and individual sessions with the mother (or caregiver), CPP promotes affect regulation and improved behavior for the child and caregiver, and assists the dyad in producing a joint trauma narrative that resolves interdyad conflict and improves the mother-child relationship.[9] Compared with case management with community provider therapy, CPP significantly improved children's trauma-related symptoms and overall behavior problems, as well as maternal avoidance symptoms. A 6-month follow-up study with two-thirds of the original mother-child dyads observed continued improvement in children's behavior problems and maternal distress in dyads who received CPP.[10] Other attachment-based models include preschooler-parent psychotherapy, which improves maladaptive

maternal representations and mother-child relationship expectations in families with maltreated children.[11] At this time, there are few studies that have directly compared cognitive behavior and attachment/dynamic-based therapies in terms of efficacy and long-term outcomes.

Other therapies have been proposed and are often used in clinical practice to treat traumatized children, whether or not they meet criteria for PTSD. Such therapies include eye movement desensitization and reprocessing therapy (EMDR). In a meta-analysis on the use of EMDR in traumatized pediatric populations, EMDR had a medium effect size (d = .56, $P<.001$).[12] However, of the 7 pediatric studies included for analysis, only 2 had a standardized treatment comparison (CBT), and most participants completed 4 or fewer total sessions, making meaningful comparisons on the effectiveness of EMDR compared with full doses of CBT or other community treatments difficult to assess. Play therapy has also been suggested to be of value to young children exposed to traumatic events. One meta-analysis[5] showed improved social functioning with the use of play therapy techniques, whereas a later review of play therapy studies in children with and without a history of maltreatment showed improvements in both groups, suggesting that play therapy likely improves play and social skills in children, regardless of trauma history.[13]

SCHOOL-BASED/GROUP THERAPIES

The nature of large-scale disasters or widespread community violence results in increased symptoms of posttraumatic stress in children at a time of compromised resources. Therefore, using nontraditional methods of mental health care delivery, such as schools, has been investigated as a way to treat large numbers of children with available resources.

Cognitive behavioral interventions for trauma in schools (CBITS) is an example of a school-based trauma intervention.[1] CBITS includes components of psychoeducation, parent sessions, relaxation skills, affect modulation skills, cognitive coping skills, individual breakout sessions for developing and processing a trauma narrative, in vivo mastery of trauma reminders, and wrap-up sessions enhancing safety. CBITS has been shown to be effective in both natural disasters and community violence settings.[14] In addition to demonstrated efficacy, school-based programs likely improve completion rates of treatment in traumatized children. One study that compared the completion rates of CBITS with clinic-based TF-CBT in New Orleans approximately 18 months after Hurricane Katrina showed that, for every 6 children who completed CBITS, only 1 child completed TF-CBT, suggesting that school-based therapies increase access to treatment of traumatized children, especially after a disaster damages community infrastructure.[15] Trauma and grief component therapy for adolescents (TGCT) is a classroom-based group intervention, and has been evaluated in several settings in which children have been exposed to natural or man-made disasters.[16] TGCT is different than CBITS in that it includes the active promotion of beneficial grieving as a core module of the program. One randomized controlled trial showed efficacy of TGCT compared with a school-based psychoeducation program. The area of greatest improvement was grief, which was significantly better in children who received TGCT compared with the control group.[16]

PSYCHOPHARMACOLOGIC TREATMENTS

Over the last several decades, the evidence base for psychopharmacologic interventions in youth has increased, although only within the last decade have these treatments been subjected to randomized clinical trials. In general, the development of

these psychopharmacologic interventions has been largely based on data from medication trials in adults with PTSD.

ANTIDEPRESSANTS

Tricyclic Antidepressants

To date, 1 randomized, double-blind, controlled trial suggests that ultrabrief treatment with imipramine may reduce some PTSD symptoms in youth.[17] A second study of the tricyclic antidepressant imipramine and the selective serotonin reuptake inhibitor (SSRI) fluoxetine (as well as a placebo arm)[18] failed to observe differences between the treatment groups. However, this study should be interpreted cautiously given that this is a 7-day trial. The American Academy of Child and Adolescent Psychiatry recommends routine electrocardiogram monitoring in pediatric patients treated with tricyclic antidepressants.

SSRIs

There are now several studies of SSRIs in pediatric patients with PTSD. In the first study of the SSRI sertraline, Cohen and colleagues[19] compared adjunctive sertraline (mean dose 150 mg/d, range 50–200 mg/d) with placebo in pediatric patients with PTSD who were also receiving TF-CBT. No statistically significant differences were observed in the Child Global Assessment Scale scores between patients treated with sertraline compared with those receiving placebo.[19] As a caveat, it is important to recognize that, in this trial, the treatment being compared was adjunctive to a highly effective treatment (TF-CBT), which likely made the detection of any potential sertraline-related improvement difficult. A second study of sertraline in pediatric patients with PTSD evaluated flexibly dosed sertraline using similar dosing in children with PTSD (n = 131, duration 10 weeks) and did not observe differences in the University of California at Los Angeles (UCLA) PTSD-I 17-item total score between sertraline-treated patients and those receiving placebo.[20] In addition, 1 open-label trial evaluated the safety and tolerability of citalopram over the course of an 8-week treatment period. In this study, Clinician-administered PTSD Scale (CAPS) total and symptom cluster scores as well as the Clinical Global Impression Scale (CGI) score improved over the course of treatment.[21]

ANTIADRENERGIC AGENTS

Over the last several years, several reports have documented noradrenergic hyperactivity in pediatric patients with both motor vehicle accident–related PTSD[22] and in adolescents with sexual abuse–related PTSD.[23] These observations parallel similar findings in adults with sexual abuse–related PTSD and combat-related PTSD (see Strawn and Geracioti,[24] 2008, for review). Given these neuroendocrine data suggesting noradrenergic hyperactivity, antiadrenergic interventions have received increased attention over the last several years in the pediatric population.

Guanfacine and Clonidine

An open-label study recently evaluated extended-release guanfacine (1–4 mg daily) in pediatric patients with attention-deficit/hyperactivity disorder (ADHD) and co-occurring posttraumatic stress symptoms (n = 19).[25] In this 8-week open-label trial, guanfacine XR was well tolerated (mean dose, 1.2 mg ± 0.4 mg) and UCLA PTSD RI (Reaction Index) scores decreased over the course of treatment for re-experiencing, avoidant, and hyperarousal symptoms. In addition, guanfacine XR was well tolerated. To date, case series–level evidence also suggests that

immediate-release guanfacine may be effective in the treatment of nightmares associated with PTSD in youth.[26]

The nonselective alpha-2 agonist clonidine has also been shown to attenuate reenactment symptoms in children.[27,28] In addition, an interesting case report of a child with PTSD suggested that clonidine treatment may be associated with increased ratios of n-acetylaspartate to creatine in the anterior cingulate cortex, suggesting increased neuronal integrity within this region.[29]

Prazosin

Despite multiple placebo-controlled trials of the alpha-1 antagonist prazosin in adults, there are only a few reports of the use of this agent in youth. To date, case reports suggest that it may be effective as an adjunctive treatment,[30,31] as well as monotherapy in children[32] and adolescents[33,34] with PTSD. However, to date, there are no open-label trials or double-blind, placebo-controlled trials of prazosin in youth with PTSD.

Propranolol

The centrally acting β-blocker propranolol was evaluated by Famularo and colleagues[35] in 11 children with childhood abuse–related PTSD. In this study, significantly fewer symptoms were observed during the course of propranolol treatment. This agent has been also evaluated in several secondary prevention trials in traumatized youth at risk for PTSD (eg, those who have experienced burn trauma or motor vehicle accident trauma).[36,37] Additional information on these trials is given by Berkowitz elsewhere in this issue.

SECOND-GENERATION ANTIPSYCHOTICS

Several second-generation antipsychotics (SGAs) have been evaluated in adults with PTSD and these medications have been subjected to randomized controlled trials. In addition, retrospective studies suggest that exposure to trauma or abuse in pediatric patients is associated with higher rates of SGA prescribing.[38] However, the extant data for the use of PTSD are limited.

Risperidone

The SGA risperidone has been evaluated in 1 open-label trial of pediatric patients with PTSD and in several case reports. In a group of preschool-aged children (n = 3) with serious thermal burns and acute stress disorder, improvement was observed in intrusive, hyperarousal, and avoidance symptoms.[39] In addition, an open-label treatment of youth resulted in remission of PTSD symptoms in 13 of 18 youth, although many of the patients in this sample had comorbid mood disorders and thus it remains possible that some of the improvement may have been the result of improvement in symptoms that syndromically overlapped with PTSD.[40] In addition, case report–level evidence suggests that adjunctive risperidone treatment may be associated with symptomatic improvement.[41]

Quetiapine

The low-potency, SGA quetiapine has been evaluated in an open-label study of adolescents aged 15 to 17 years (n = 6). In this study, patients received flexibly dosed quetiapine (50–200 mg/d) over the course of 6 weeks and improvements were observed in Traumatic Symptom Checklist for Children posttraumatic stress t scores and in symptoms of anxiety, depression, and anger.[42] Moreover, quetiapine was well tolerated in this small study.

MOOD STABILIZERS AND OTHER MEDICATIONS

Although mood stabilizers/antiepileptic agents have been extensively evaluated in adults with PTSD, there are few data regarding these agents in traumatized youth with PTSD. To date, carbamazepine has been evaluated in pediatric patients with sexual abuse–related PTSD[43] and in this study, involving youth who were in residential treatment (n = 28), carbamazepine was titrated to achieve serum levels of 10 to 11.5 μg/mL. Most patients (79%) were asymptomatic at the end point.[43] In addition, open-label treatment with divalproex in youth with PTSD was associated with clinical improvement and good tolerability.[44] Boys (n = 12) aged 16 ± 1 years with comorbid conduct disorder and PTSD received either high-dose or low-dose divalproex. Youth who were randomized to the high-dose treatment had improvements in CGI score over the course of the trial.[44] In addition to the mood stabilizers, the serotonin and H_1 receptor antagonist cyproheptadine has been observed, in a retrospective chart review, to reduce nightmares associated with PTSD.[45]

CLINICAL PRACTICE APPLICATION

Several factors should be considered when choosing the appropriate therapeutic approach, including the experience of the practitioner and the availability of different treatment modalities in the community. Therefore advocacy and education of community providers is of the utmost importance in developing and maintaining an adequate mental health infrastructure, capable of providing evidence-based trauma therapies to address the effects of trauma in the community. In addition to availability and resources, the other factors to consider are discussed later.

Timing of Trauma

Whether or not the trauma and development of symptoms is remote or recent not only affects diagnosis, it can also direct different interventions. Recent traumatic events or recent disclosures of past traumatic events with symptoms of posttraumatic stress may benefit from a brief intervention such as Child and Family Traumatic Stress Intervention (CFTSI) (Discussed by Berkowitz elsewhere in this issue). This PTSD prevention therapy uses many of the core concepts of psychoeducation/symptom identification, enhanced parent-child relationship through improved communication, and adoption of healthy coping strategies that are advocated by other evidence-based modalities. In CFTSI, there is no exposure component such as a trauma narrative. However, in more chronic manifestations, an exposure component found in other trauma therapies such as TF-CBT, CPP, and PE-A likely assists in improving core symptoms of PTSD.

Single Versus Repeated/Multiple Traumas

One of the greatest lessons from the large body of the Adverse Childhood Experiences Study and similar research is that the effects of trauma are cumulative,[46] and that individuals with multiple exposures likely carry a greater symptom burden. Although the literature does not support the use of any particular modality for PTSD in the setting of complex or repeated trauma, it is important to recognize and prepare families for the realization that children who have experienced severe and chronic adversity may require lengthy treatment or may need to return for an additional course of treatment at subsequent developmental stages. In addition, chronic child abuse and neglect are associated with developmental and cognitive impairment,[47] and assessment, recognition, and intervention for cognitive and developmental issues (eg, individualized educational plans, 504 plans) in maltreated children may be of great clinical usefulness.

Comorbid Symptoms

Children who experience child abuse are at increased risk for both medical and psychiatric comorbidity that may affect PTSD-targeted interventions.[38,48] Clinicians, in consultation with families, are faced with the task of determining which symptoms or diagnosis results in the greatest amount of distress and functional impairment for the child, and then to develop a logical, stepwise treatment approach. For example, a 10-year-old child in foster care with a history of sexual abuse 6 months ago meets criteria for both PTSD and generalized anxiety disorder. It is possible that the anxiety disorder preceded the abuse, but there is no history or collateral information to support or refute this. As such, clinicians could proceed with a therapy such as TF-CBT and, at the end of therapy, reassess for any persistent symptoms of anxiety and treat appropriately. In contrast, if a child with PTSD also has severe, untreated ADHD that preceded the trauma, clinicians might choose to address the ADHD pharmacologically so that the patient could function better at school as well as in the trauma therapy.

Age of the Child

A child's developmental and chronologic age is of critical importance when choosing the appropriate therapy, and although some modalities (such as TF-CBT) can be performed in a wide range of ages, certain considerations need to be taken with younger or developmentally delayed children. In general, younger children are likely to benefit from dyadic approaches in which their behaviors (eg, parent-child interaction therapy) as well as relational and attachment issues (CPP) can be addressed in the therapeutic setting. Many of these families seek help for aggression or behavioral issues rather than PTSD, and require education regarding the connection of trauma and behaviors as part of a trauma-informed behavioral or dyadic intervention. In contrast, older children, especially those in foster care or those who have been emancipated, may benefit from developing a therapeutic alliance with the therapist in the individual setting, or learning from and engaging in therapy with their peers in a group setting. In addition, older children with a history of trauma are at greater risk for several sequelae such as self-harm/suicidal behaviors[38] and substance use disorders,[49] requiring escalated levels of care or specific and targeted therapies to address those symptoms (dialectical behavioral therapy, motivational enhancement therapy, and so forth) concurrent with or before trauma therapy.

Safety Concerns

Appropriate and comprehensive safety assessments are critical before and throughout treatment. For many children, especially those who experience interpersonal violence in the family, school, or community, the threat of violence continues while in treatment. In some settings, hypervigilance and avoidance are protective and adaptive rather than symptoms of PTSD. In settings in which there are persistent, ongoing threats of violence, and in which a clear understanding of the safety issues is lacking, it is impossible to make critical clinical assessments of the severity of the patient's symptoms. In addition, in settings in which some of the safety concerns are modifiable, appropriate case management to address housing, school, or legal issues that decrease the threat of continued violence may be of equal or greater benefit than evidence-based trauma treatments. Provided appropriate consent, open communication with children's services, law enforcement, and prosecutors may provide additional information and support that enhances the capacity of the system and family to provide a safe and nurturing environment for the child.

FUTURE DIRECTIONS

Accumulating data suggest that both biological and behavioral components contribute to the deleterious health effects of exposure to childhood adversity in adults[46] and children.[48] The publication of DSM-5, in conjunction with accumulating data regarding the underlying pathophysiology of stress response systems, in the face of repeated and chronic adversity,[50] provides ample opportunity for the incorporation of biomarkers into pediatric PTSD treatment studies and for investigations directed at identifying Hypothalamic Pituitary Adrenal axis (HPA) and sympathetic nervous system biomarkers of treatment response. For example, pretreatment levels of cortisol and/or norepinephrine might be useful in determining which patients may respond to specific treatments known to directly affect these stress response systems.[51] Research examining the relationship between treatment of pediatric PTSD and the resultant long-term physical and mental health is urgently needed.

SUMMARY

Strong evidence supports the efficacy of trauma-focused psychotherapies for the treatment of pediatric PTSD. In addition, a small body of literature suggests efficacy of several psychopharmacologic interventions as monotherapy for pediatric PTSD (eg, alpha-2 agonists, alpha-1 antagonists, several SGAs, and several antiepileptic agents), although double-blind, placebo-controlled trials of SSRIs do not suggest a benefit for PTSD symptoms in youth. Clinicians should tailor treatment based on the individual child's most distressing and functionally impairing symptoms in a developmentally sensitive manner.

REFERENCES

1. Cohen JA, Bukstein O, Walter H, et al. Practice parameter for the assessment and treatment of children and adolescents with posttraumatic stress disorder. J Am Acad Child Adolesc Psychiatry 2010;49(4):414–30.
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. (DSM-5). 5th edition. Washington, DC: American Psychiatric Association; 2013.
3. Plakun EM, Sudak DM, Goldberg D. The Y model: an integrated, evidence-based approach to teaching psychotherapy competencies. J Psychiatr Pract 2009;15(1):5–11.
4. Cohen JA, Mannarino AP, Murray LK. Trauma-focused CBT for youth who experience ongoing traumas. Child Abuse Negl 2011;35(8):637–46.
5. Hetzel-Riggin MD, Brausch AM, Montgomery BS. A meta-analytic investigation of therapy modality outcomes for sexually abused children and adolescents: an exploratory study. Child Abuse Negl 2007;31(2):125–41.
6. Gilboa-Schechtman E, Foa EB, Shafran N, et al. Prolonged exposure versus dynamic therapy for adolescent PTSD: a pilot randomized controlled trial. J Am Acad Child Adolesc Psychiatry 2010;49(10):1034–42.
7. Smith P, Yule W, Perrin S, et al. Cognitive-behavioral therapy for PTSD in children and adolescents: a preliminary randomized controlled trial. J Am Acad Child Adolesc Psychiatry 2007;46(8):1051–61.
8. Ruf M, Schauer M, Neurner F, et al. Narrative exposure therapy for 7 to 16 year olds: a randomized controlled trial with traumatized refugee children. J Trauma Stress 2010;23(4):437–45.

9. Lieberman AF, Van Horn P, Ippen CG. Toward evidence-based treatment: child-parent psychotherapy with preschoolers exposed to marital violence. J Am Acad Child Adolesc Psychiatry 2005;44(12):1241–8. http://dx.doi.org/10.1097/01.chi.0000181047.59702.58.
10. Lieberman AF, Ghosh Ippen C, Van Horn P. Child-parent psychotherapy: 6-month follow-up of a randomized controlled trial. J Am Acad Child Adolesc Psychiatry 2006;45(8):913–8. http://dx.doi.org/10.1097/01.chi.0000222784.03735.92.
11. Toth SL, Maughan A, Manly JT, et al. The relative efficacy of two interventions in altering maltreated preschool children's representational models: implications for attachment theory. Dev Psychopathol 2002;14(4):877–908.
12. Rodenburg R, Benjamin A, de Roos C, et al. Efficacy of EMDR in children: a meta-analysis. Clin Psychol Rev 2009;29(7):599–606. http://dx.doi.org/10.1016/j.cpr.2009.06.008.
13. Silverman WK, Ortiz CD, Viswesvaran C, et al. Evidence-based psychosocial treatments for children and adolescents exposed to traumatic events. J Clin Child Adolesc Psychol 2008;37(1):156–83. http://dx.doi.org/10.1080/15374410701818293.
14. Rolfsnes ES, Idsoe T. School-based intervention programs for PTSD symptoms: a review and meta-analysis. J Trauma Stress 2011;24(2):155–65. http://dx.doi.org/10.1002/jts.20622.
15. Jaycox LH, Cohen JA, Mannarino AP, et al. Children's mental health care following Hurricane Katrina: a field trial of trauma-focused psychotherapies. J Trauma Stress 2010;23(2):223–31. http://dx.doi.org/10.1002/jts.20518.
16. Layne CM, Saltzman WR, Poppleton L, et al. Effectiveness of a school-based group psychotherapy program for war-exposed adolescents: a randomized controlled trial. J Am Acad Child Adolesc Psychiatry 2008;47(9):1048–62.
17. Robert R, Blakeney PE, Villarreal C, et al. Imipramine treatment in pediatric burn patients with symptoms of acute stress disorder: a pilot study. J Am Acad Child Adolesc Psychiatry 1999;38(7):873–82. http://dx.doi.org/10.1097/00004583-199907000-00018.
18. Robert R, Tcheung WJ, Rosenberg L, et al. Treating thermally injured children suffering symptoms of acute stress with imipramine and fluoxetine: a randomized, double-blind study. Burns 2008;34(7):919–28. http://dx.doi.org/10.1016/j.burns.2008.04.009.
19. Cohen JA, Mannarino AP, Perel JM, et al. A pilot randomized controlled trial of combined trauma-focused CBT and sertraline for childhood PTSD symptoms. J Am Acad Child Adolesc Psychiatry 2007;46(7):811–9. http://dx.doi.org/10.1097/chi.0b013e3180547105.
20. Robb AS, Cueva JE, Sporn J, et al. Sertraline treatment of children and adolescents with posttraumatic stress disorder: a double-blind, placebo-controlled trial. J Child Adolesc Psychopharmacol 2010;20(6):463–71. http://dx.doi.org/10.1089/cap.2009.0115.
21. Seedat S, Stein DJ, Ziervogel C, et al. Comparison of response to a selective serotonin reuptake inhibitor in children, adolescents, and adults with posttraumatic stress disorder. J Child Adolesc Psychopharmacol 2002;12(1):37–46. http://dx.doi.org/10.1089/10445460252943551.
22. Pervanidou P, Kolaitis G, Charitaki S, et al. The natural history of neuroendocrine changes in pediatric posttraumatic stress disorder (PTSD) after motor vehicle accidents: progressive divergence of noradrenaline and cortisol concentrations over time. Biol Psychiatry 2007;62(10):1095–102. http://dx.doi.org/10.1016/j.biopsych.2007.02.008.

23. Keeshin BR, Strawn JR, Out D, et al. Elevations in salivary alpha amylase in acute posttraumatic stress disorder. Poster session presented at the Annual Meeting of the American Academy of Child and Adolescent Psychiatry in Orlando, October 22–27, 2013.
24. Strawn JR, Geracioti TD. Noradrenergic dysfunction and the psychopharmacology of posttraumatic stress disorder. Depress Anxiety 2008;25(3):260–71. http://dx.doi.org/10.1002/da.20292.
25. Connor DF, Grasso DJ, Slivinsky MD, et al. An open-label study of guanfacine extended release for traumatic stress related symptoms in children and adolescents. J Child Adolesc Psychopharmacol 2013;23(4):244–51. http://dx.doi.org/10.1089/cap.2012.0119.
26. Horrigan JP. Guanfacine for PTSD nightmares. J Am Acad Child Adolesc Psychiatry 1996;35(8):975–6. http://dx.doi.org/10.1097/00004583-199608000-00006.
27. Harmon RJ, Riggs PD. Clonidine for posttraumatic stress disorder in preschool children. J Am Acad Child Adolesc Psychiatry 1996;35(9):1247–9. http://dx.doi.org/10.1097/00004583-199609000-00022.
28. Porter DM, Bell CC. The use of clonidine in post-traumatic stress disorder. J Natl Med Assoc 1999;91(8):475–7.
29. De Bellis MD, Keshavan MS, Harenski KA. Anterior cingulate N-acetylaspartate/creatine ratios during clonidine treatment in a maltreated child with posttraumatic stress disorder. J Child Adolesc Psychopharmacol 2001;11(3):311–6. http://dx.doi.org/10.1089/10445460152595649.
30. Brkanac Z, Pastor JF, Storck M. Prazosin in PTSD. J Am Acad Child Adolesc Psychiatry 2003;42(4):384–5. http://dx.doi.org/10.1097/01.CHI.0000052509.98293.97.
31. Fraleigh LA, Hendratta VD, Ford JD, et al. Prazosin for the treatment of posttraumatic stress disorder-related nightmares in an adolescent male. J Child Adolesc Psychopharmacol 2009;19(4):475–6. http://dx.doi.org/10.1089/cap.2009.0002.
32. Strawn JR, Keeshin BR. Successful treatment of posttraumatic stress disorder with prazosin in a young child. Ann Pharmacother 2011;45(12):1590–1. http://dx.doi.org/10.1345/aph.1Q548.
33. Strawn JR, Delbello MP, Geracioti TD. Prazosin treatment of an adolescent with posttraumatic stress disorder. J Child Adolesc Psychopharmacol 2009;19(5):599–600. http://dx.doi.org/10.1089/cap.2009.0043.
34. Oluwabusi OO, Sedky K, Bennett DS. Prazosin treatment of nightmares and sleep disturbances associated with posttraumatic stress disorder: two adolescent cases. J Child Adolesc Psychopharmacol 2012;22(5):399–402. http://dx.doi.org/10.1089/cap.2012.0035.
35. Famularo R, Kinscherff R, Fenton T. Propranolol treatment for childhood posttraumatic stress disorder, acute type. A pilot study. Am J Dis Child 1988;142(11):1244–7.
36. Nugent NR, Christopher NC, Crow JP, et al. The efficacy of early propranolol administration at reducing PTSD symptoms in pediatric injury patients: a pilot study. J Trauma Stress 2010;23(2):282–7. http://dx.doi.org/10.1002/jts.20517.
37. Pitman RK, Delahanty DL. Conceptually driven pharmacologic approaches to acute trauma. CNS Spectr 2005;10(2):99–106.
38. Keeshin BR, Strawn JR, Luebbe AM, et al. Hospitalized youth and child abuse: a systematic examination of psychiatric morbidity and clinical severity. Child Abuse Negl 2013. http://dx.doi.org/10.1016/j.chiabu.2013.08.013.
39. Meighen KG, Hines LA, Lagges AM. Risperidone treatment of preschool children with thermal burns and acute stress disorder. J Child Adolesc Psychopharmacol 2007;17(2):223–32. http://dx.doi.org/10.1089/cap.2007.0121.

40. Horrigan JP, Barnhill LJ. Risperidone and PTSD in boys. J Neuropsychiatry Clin Neurosci 1999;11:126–7.
41. Keeshin BR, Strawn JR. Risperidone treatment of an adolescent with severe posttraumatic stress disorder. Ann Pharmacother 2009;43(7):1374. http://dx.doi.org/10.1345/aph.1M219.
42. Stathis S, Martin G, McKenna JG. A preliminary case series on the use of quetiapine for posttraumatic stress disorder in juveniles within a youth detention center. J Clin Psychopharmacol 2005;25(6):539–44.
43. Looff D, Grimley P, Kuller F, et al. Carbamazepine for PTSD. J Am Acad Child Adolesc Psychiatry 1995;34(6):703–4.
44. Steiner H, Saxena KS, Carrion V, et al. Divalproex sodium for the treatment of PTSD and conduct disordered youth: a pilot randomized controlled clinical trial. Child Psychiatry Hum Dev 2007;38(3):183–93. http://dx.doi.org/10.1007/s10578-007-0055-8.
45. Gupta S, Austin R, Cali LA, et al. Nightmares treated with cyproheptadine. J Am Acad Child Adolesc Psychiatry 1998;37(6):570–2. http://dx.doi.org/10.1097/00004583-199806000-00003.
46. Felitti VJ, Anda RF, Nordenberg D, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. Am J Prev Med 1998;14(4):245–58.
47. De Bellis MD, Woolley DP, Hooper SR. Neuropsychological findings in pediatric maltreatment: relationship of PTSD, dissociative symptoms, and abuse/neglect indices to neurocognitive outcomes. Child Maltreat 2013;18(3):171–83. http://dx.doi.org/10.1177/1077559513497420.
48. Flaherty EG, Thompson R, Litrownik AJ, et al. Adverse childhood exposures and reported child health at age 12. Acad Pediatr 2009;9(3):150–6. http://dx.doi.org/10.1016/j.acap.2008.11.003.
49. Ford JD, Elhai JD, Connor DF, et al. Poly-victimization and risk of posttraumatic, depressive, and substance use disorders and involvement in delinquency in a national sample of adolescents. J Adolesc Health 2010;46(6):545–52. http://dx.doi.org/10.1016/j.jadohealth.2009.11.212.
50. Johnson SB, Riley AW, Granger DA, et al. The science of early life toxic stress for pediatric practice and advocacy. Pediatrics 2013;131(2):319–27. http://dx.doi.org/10.1542/peds.2012-0469.
51. De Bellis MD. Developmental traumatology: the psychobiological development of maltreated children and its implications for research, treatment, and policy. Dev Psychopathol 2001;13(3):539–64.