A Pilot Randomized Controlled Trial of Combined Trauma-Focused CBT and Sertraline for Childhood PTSD Symptoms

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ABSTRACT

Objective: To examine the potential benefits of adding a selective serotonin reuptake inhibitor, sertraline, versus placebo, to trauma-focused cognitive-behavioral therapy (TF-CBT) for improving posttraumatic stress disorder and related psychological symptoms in children who have experienced sexual abuse. **Method:** Twenty-four 10- to 17-year-old female children and adolescents and their primary caretakers were randomly assigned to receive TF-CBT + sertraline or TF-CBT + placebo for 12 weeks. **Results:** Both groups experienced significant improvement in posttraumatic stress disorder and other clinical outcomes from pre- to posttreatment with no significant group × time differences between groups except in Child Global Assessment Scale ratings, which favored the TF-CBT + sertraline group. **Conclusions:** Only minimal evidence suggests a benefit to adding sertraline to TF-CBT. A drawback of adding sertraline was determining whether TF-CBT or sertraline caused clinical improvement for children with comorbid depression. Current evidence therefore supports an initial trial of TF-CBT or other evidence-supported psychotherapy for most children with PTSD symptoms before adding medication. *J. Am. Acad. Child Adolesc. Psychiatry,* 2007;46(7):811–819. **Key Words:** cognitive-behavioral therapy, posttraumatic stress disorder, randomized trial, sertraline.

Posttraumatic stress disorder (PTSD) is a potentially serious mental health condition that may develop following traumatic events such as childhood sexual abuse. Children who have significant PTSD symptoms without meeting full diagnostic criteria have been shown to have comparable functional impairment to those with the full disorder (Carrion et al., 2002). Left untreated, PTSD can lead to difficulties that last into adulthood, such as increased suicide attempts, hospitalizations, substance abuse, depression, and dissociation (Warshaw et al., 1993). For survivors of child abuse, these problems are associated with increased use of health care resources (Walker et al., 1999). To minimize suffering and prevent these long-term deleterious outcomes, it is important to identify and test a range of optimal treatments for childhood PTSD symptoms.

Trauma-focused cognitive-behavioral therapy (TF-CBT) is recognized as an effective treatment for childhood PTSD symptoms (Cohen et al., 2000; Saunders et al., 2004). In six randomized, controlled trials (RCTs) for sexually abused and multiply traumatized children (reviewed in Cohen et al., 2004), TF-CBT was superior to comparison or control conditions in decreasing PTSD symptoms as well as improving depression, anxiety, and externalizing behavioral problems. In the largest study of TF-CBT to date (Cohen et al., 2004), 229 sexually abused children ages 8–14 and their nonoffending parents were randomly

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assigned to receive 12 sessions of TF-CBT or child-centered therapy (CCT). Outcomes with TF-CBT were superior for almost all measures, with effect sizes ranging from medium to large between the two groups on the three PTSD clusters and total PTSD symptoms. Despite this success, 21% of the TF-CBT group continued to carry a diagnosis of PTSD. Although this compared favorably to the CCT group, these findings suggest that for a minority of children, supplementing TF-CBT with additional interventions may be necessary to achieve remission.

Several RCTs have demonstrated that pharmacological interventions alone, particularly selective serotonin reuptake inhibitors (SSRIs), can successfully lead to remission in adult PTSD diagnosis (Brady et al., 2000; Davidson et al., 1996; van der Kolk et al., 1994). Potential mechanisms for this response include that sertraline indirectly stimulates the 5-HT_{1A} receptor and thus would be expected to be anxiolytic (Schreiber et al., 1998) and that sertraline has been shown to stimulate the CNS neurosteroid/$GABA_a$ system (Griffin and Mellon, 1999). No RCTs have yet been published for pharmacological treatments of childhood PTSD.

The typical design for a pharmacological RCT is to randomly assign participants to medication or placebo in a double-blind fashion, such that some children receive only placebo intervention. Concerns could be raised about comparing a medication condition to a placebo condition when addressing a potentially serious disorder such as PTSD, particularly when an effective psychosocial treatment such as TF-CBT is available, despite compelling cases having been made for the benefits of conducting placebo-controlled trials (Leon, 2000; Quitkin and Klein, 2000). These concerns diminish if children in both conditions also receive a psychosocial treatment with proven efficacy such as TF-CBT, although this design would decrease the likelihood of detecting differences between the medication and placebo conditions (because the majority of both groups would be expected to respond to TF-CBT alone, thus in effect reducing the sample size). This project as originally designed proposed to evaluate the relative efficacy of sertraline versus TF-CBT for treating PTSD symptoms in sexually abused children by comparing TF-CBT versus sertraline versus placebo. Because the above concerns were raised, the design was revised to provide TF-CBT to all participants and to randomize children to receive either sertraline or placebo.

The study was thus reconfigured to assess the potential benefits and risks of adding an SSRI, sertraline, versus placebo to TF-CBT in a double-blind RCT design. Our primary questions were whether adding sertraline to TF-CBT could significantly improve children's PTSD symptoms or global functioning. Our second question was whether the children who received sertraline would experience more frequent and/or more severe side effects. Exploratory questions were whether the addition of sertraline produced a more favorable (i.e., faster) response in PTSD symptoms during the course of treatment, and whether the addition of sertraline produced differential beneficial responses in terms of other symptoms typically assessed in sexually abused cohorts.

METHOD

Subjects

Funding for this project was received in April 2001 with subject recruitment beginning in January 2002. The project proposed to recruit a final cohort of 80 subjects with 40 in each treatment condition (TF-CBT + sertraline versus TF-CBT + placebo). Information became available in 2003 that children may be experiencing increased suicidal ideation while taking SSRIs (Mitka, 2003). Public warnings about antidepressant medication were issued by the U.S. Food and Drug Administration in 2003, and the eventual "black box" warnings were included on SSRI medications in 2004 (U.S. Food and Drug Administration, 2004). Families we were attempting to recruit for the present study were provided with updated information as it was issued on Web sites by the U.S. Food and Drug Administration and the American Academy of Child and Adolescent Psychiatry with regard to potential side effects of sertraline. Due to families' concerns, the total number of subjects recruited for this project was far below what we originally anticipated.

Subjects were consecutively referred children ages 10–17 years who had experienced contact sexual abuse that was confirmed by Child Protective Services (CPS), law enforcement, or a professional independent forensic evaluator, who met all study criteria and agreed (along with a custodial parent or other caregiver) to participate in the study. Referral sources included CPS, police, victim advocacy centers, pediatric care providers, mental health care providers, and self-referrals. No recruitment ads were placed. Inclusion criteria were having sexual abuse–related PTSD symptoms (defined as at least five PTSD symptoms on the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version [K-SADS-PL] with at least one symptom in each of the three PTSD clusters and clinically significant impairment), having a parent or caregiver who was available to give consent and participate, and being 10–17 years of age. Exclusionary criteria were non-English speaking; schizophrenia or other active psychotic disorder; mental retardation or pervasive developmental disorder (all due to the requirement to receive TF-CBT, a cognitive-oriented psychotherapy); or taking current psychotropic medications. Youths with substance use were not excluded from the study (in an attempt to

include a representative sample of sexually abused youths with PTSD), but those with current substance dependence were not included in the study.

A CONSORT flowchart for this study is presented in Figure 1. Of the 24 participants who met the required PTSD criteria and were randomly assigned to treatment, two did not complete the study, leaving a final treatment cohort of 22 subjects. The two participants who did not complete treatment (one in each condition) left the study before the third treatment session due to residential relocation.

Demographic information is presented in Table 1. Demographic characteristics of the final cohort included in the study did not significantly differ from the 31 children who did not meet criteria for inclusion in the study.

According to consensus interview on the K-SADS-PL, 15 (68.2%) of the subjects met criteria for diagnosis other than PTSD,

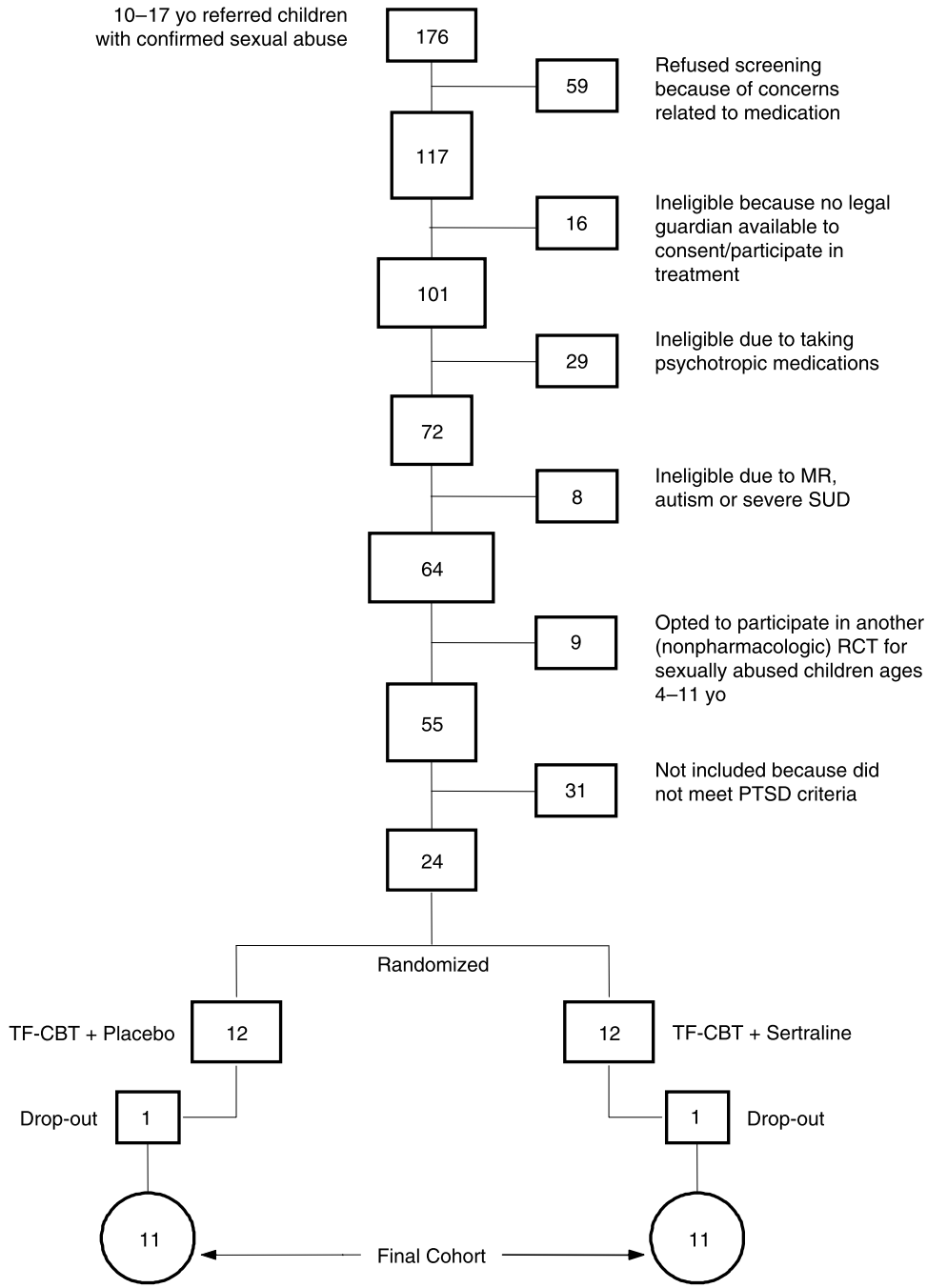

Fig. 1 Flowchart. MR = mental retardation; SUD = substance use disorder; RCT = randomized controlled trial; PTSD = posttraumatic stress disorder; TF-CBT = trauma-focused cognitive-behavioral therapy.

with seven subjects (63.5%) in the TF-CBT + sertraline condition and eight (72.7%) in the TF-CBT + placebo condition meeting criteria for at least one comorbid diagnosis. All but one of these children met criteria for major depressive disorder (MDD). Other diagnoses included general anxiety disorder, substance abuse not otherwise specified, oppositional defiant disorder, panic disorder, and anorexia nervosa.

As determined by the K-SADS-PL, this cohort had experienced a mean of 3.0 different types of previous traumas in addition to sexual abuse, including the following: 10 (45.4%) serious accidents, 2 (9%) disasters, 6 (27.2%) violent crime, 17 (77.3%) traumatic death or life-threatening illness, 4 (18.2%) domestic violence, 2 (9.1%) physical abuse, and 4 (18.2%) other PTSD-level traumas.

Procedures

Upon referral, a telephone screen was conducted and the possibility of participating in the study was discussed with parents. Those who agreed were scheduled for an initial assessment, which was conducted by an independent evaluator. This evaluator was trained in administration of the K-SADS-PL and the Children's Global Assessment Scale (CGAS). The evaluator continued to be randomly checked throughout the course of the study to ensure ongoing interrater reliability with regard to both instruments. At the initial evaluation, children and parents completed the initial assessment instruments described below and those who qualified for admission to the study read and signed informed assent/consent forms. Children were randomized according to a computerized random number sequence to the TF-CBT + placebo or TF-CBT + sertraline condition. This was a double-blind procedure whereby no one directly involved in the study (i.e., parents, children, independent evaluator, therapists, or child and adolescent psychiatrist) knew which condition the children were assigned to throughout the course of treatment.

TABLE 1
Demographic Information (N = 22)

	No. (%)
Age, y	
10–11	5 (22.7)
12–14	10 (45.5)
15–17	7 (31.8)
Gender	
Female	22 (100)
Male	0 (0)
Race	
White	17 (77.3)
African American	5 (22.7)
Identity of perpetrator	
Biological or adoptive father	5 (22.5)
Stepfather	1 (4.5)
Other adult relative	1 (4.5)
Nonrelative	5 (22.5)
Older sibling	3 (13.6)
Older peer	3 (13.6)
Multiple perpetrators	4 (18.2)
Most intrusive type of abuse	
Genital touching	3 (13.6)
Digital penetration	5 (22.2)
Simulated intercourse	1 (4.5)
Oral-genital contact	4 (18.2)
Penile penetration	9 (37.7)
Mean no. of months since most recent abuse	22.9 (SD 35.6)

Instruments

The following instruments were administered by the independent evaluator: K-SADS-PL (Kaufman et al., 1996) is a semistructured interview administered independently to child and parent to assess the presence of *DSM-IV* psychiatric disorders. For the purposes of this study only, the PTSD section was readministered posttreatment; the other sections were administered pretreatment to assess children for exclusionary criteria only. For the present sample, interrater reliability Cohen's κ for K-SADS-PL-PTSD diagnostic status (yes/no) was 0.92. The CGAS (Shaffer et al., 1983) is a 0- to 100-point scale on which an independent rater evaluates the child's global impairment. The CGAS is highly correlated with children's general functional competence and is not highly correlated with other measures of symptom severity (Green et al., 1994). For the present sample, Pearson's correlation interrater reliability of the CGAS was 0.90. The CGAS was completed pretreatment and at weeks 3, 5, 8 and 12.

Children completed the following instruments pre- and posttreatment. The Children's PTSD Symptoms Scale (CPSS; Foa et al., 2001) is a 24-item self-report measure of PTSD. Test-retest reliability for the CPSS is 0.84. The Mood and Feelings Questionnaire (MFQ; Costello and Angold, 1988) is a 33-item self-report measure of child and adolescent depression. Test-retest reliability for the MFQ is 0.85. Clinical cutoff score for this version of the MFQ is 28. (*Note:* Children additionally completed the CPSS and MFQ at weeks 3, 5, and 8.) The Screen for Children's Anxiety Related Emotional Disorders (SCARED; Birmaher et al., 1997) is a 38-item self-report measure for children's anxiety symptoms with good (0.86) test-retest reliability. Clinical cutoff score for the SCARED is 25. The Children's Attributions and Perceptions Scale (Mannarino et al., 1994) is a self-report instrument in which children report their child abuse–related attributions and perceptions related to self-blame, feeling different from peers, feelings of not being believed, and loss of interpersonal trust. Test-retest reliability for the Children's Attributions and Perceptions Scale is 0.75.

Parents completed the following instruments pre- and posttreatment. Child Behavior Checklist (Achenbach, 1991) is a 118-item parent report form for children's behaviors. Reliability is >0.90 for the broadband scales used in this study. Beck Depression Inventory II (Beck et al. 1996) is a parent self-report of depression. Test-retest reliability for the BDI-II is high (0.93). Cutoff score for a nonclinical population on the BDI is 12. The Parent's Emotional Reaction Questionnaire (Mannarino and Cohen, 1996) is a self-report measure of parental emotional distress related to the child's sexual abuse; test-retest reliability is 0.90; the Parental Support Questionnaire (Mannarino and Cohen, 1996) is a self-report questionnaire of parental support of the child and attributions about responsibility for the abuse. Test-retest reliability for the Parental Support Questionnaire is 0.82.

The child and adolescent psychiatrist assisted parents and children in completing the following form at each medication evaluation session. The Side Effects Form for Children and Adolescents (SEF-CA; Klein, 1998) is a child- and caretaker-informed form to

be completed regarding psychotropic medication side effects. Each item is completed regarding frequency and severity.

Medication

Identical pill sertraline (25 and 50 mg) and pill placebo were provided free of charge to this study by Pfizer. Pfizer had no other involvement in the study. At the initial evaluation session, a psychiatric evaluation was performed. The same child and adolescent psychiatrist performed this evaluation for all of the children in the study and conducted subsequent medication management appointments. The initial psychiatric evaluation included obtaining relevant psychiatric history, obtaining permission to receive the child's primary care provider records including the most recent physical examination; inquiring about possible pregnancy if appropriate; reviewing current medications; reviewing current and past medical conditions; and reviewing sertraline information (mechanisms of action, risks, benefits, side effects, dose, and administration). The child and parent were given written information about sertraline, and a urine sample was obtained for urine drug screen, urinalysis, and urine pregnancy test (if postmenarchal). The child and parent then were interviewed individually by the child and adolescent psychiatrist to complete the SEF-CA form.

The child and parent were seen for medication checks at sessions 1, 3, 5, 8, and 12, with sertraline/placebo dose titrated as follows. Pills were started at 25 mg/day for 3 days for all subjects, with instructions to increase the dose to 50 mg/day to be continued at a dose of 50 mg/day for the first 2 weeks. At the second appointment (week 3), subjects completed the CPSS and MFQ at the medication management session. Subjects whose CPSS indicted clinically significant improvement of symptoms from their initial score, and/or whose side effects were judged sufficiently severe to warrant holding the dose at 50 mg/day were instructed to maintain this dose. Subjects whose symptoms were not judged to be significantly improved and/or whose side effects were not judged to be severe were instructed to increase the dose to 100 mg/day for the next 2 weeks. Dose titration continued in this manner at each medication check, to a maximum of 200 mg/day. Mean maximum dose reached for the TF-CBT + sertraline group was 150 mg/day (range 50–200 mg/day). Mean maximum dose reached for the TF-CBT + placebo group was 172.73 mg/day (range 50–200 mg/day). Dose for the TF-CBT + placebo group was higher at each point in treatment from week 5 onward. This difference in dose between the two groups approached significance ($p = .078$).

TF-CBT Treatment

TF-CBT is described in detail elsewhere (Cohen et al., 2006; Deblinger and Heflin, 1996; TF-CBT Web, 2005). The primary components are summarized by the acronym PRACTICE: parenting skills, psychoeducation, relaxation, affect modulation, cognitive processing, trauma narrative, in vivo mastery of trauma reminders, conjoint child-parent session, and enhancing safety, healthy sexuality, and future development. In the present study TF-CBT was provided over the course of 12 weeks, in 12 parallel sessions for children and their parents/caretakers. TF-CBT was provided by one of two randomly assigned clinicians. Both therapists were licensed master's degree–level social workers. Treatment sessions were audiotaped for adherence to the TF-CBT model, and all sessions were required to meet >90% adherence to the model through the use of adherence checklists.

Data Analysis

Data analyses were conducted using SPSS version 14. A series of repeated-measures analyses of covariance (ANCOVAs) were conducted with the covariate in each analysis being the pretreatment score for the outcome score posttreatment under analysis. The ANCOVAs of the K-SADS-PL-PTSD were conducted separately because those were the only data collected through a semistructured interview. The CGAS is not highly correlated with measures of symptomatology (Green et al., 1994), and for this reason, a separate ANCOVA was performed for the CGAS.

Due to the large number of other overlapping child and parent self-report measures included in the study, a multivariate analysis of covariance was conducted to determine whether overall differences between the two treatment groups were present from pre- to posttreatment, before performing ANCOVAs on individual instruments. These multivariate analysis of covariances and ANCOVAs only included pre- and posttreatment data. To examine potential differences between the two groups with regard to side effects, data from the SEF-CA were compared using a two-tailed Fisher exact test. To examine suicidality, responses to "I thought about killing myself" on the MFQ were examined separately at sessions 1, 3, 5, 8, and 12. Chi-square analyses were performed to compare differences in responses between the two groups.

RESULTS

There were no significant differences between the two groups on any demographic variables at pretreatment. As shown in Table 2, on the K-SADS-PL-PTSD, although there was a highly significant effect for time, there were no significant group × time differences with regard to improvement in PTSD symptoms from pre- to posttreatment. However, effect sizes were medium in this regard ($d = -0.4$ to -0.53).

There was a significant group × time interaction with regard to the CGAS (Table 3). The largest single incremental improvement in CGAS scores in the TF-CBT + sertraline group occurred between weeks 3 and 5, a time during which the pharmacological action of sertraline could be expected to become noticeable.

The multivariate analysis of covariance showed a significant effect for time ($F = 13.59$, $p < .001$) but not for group ($F = 0.986$, $p = .51$) or group × time ($F = 1.23$, $p = .37$). However, because of the significant time effect, we examined which instruments changed significantly over time by conducting univariate ANOVAs for the entire cohort. The MFQ, SCARED, CPSS, CBCL Total, Parent's Emotional Reaction Questionnaire, BDI, and Parental Support Questionnaire showed significant (<.05) change from pre- to posttreatment.

The two groups showed no significant differences with regard to side effects at any point in the study as measured by the SEF-CA. They also showed no

TABLE 2
Repeated-Measures ANCOVA for PTSD Symptoms

PTSD Symptom	Pretreatment Mean (SD)	Posttreatment Mean (SD)	Group *F*	Time *F*	Group × Time *F*	Effect Size *d*
Re-experience						
Sertraline (n = 11)	3.91 (0.94)	1.36 (0.92)	0.497	50.81*	0.732	−0.40
Placebo (n = 11)	3.91 (0.94)	1.91 (1.70)				
Avoidance						
Sertraline	4.18 (1.33)	2.00 (1.41)	1.92	25.38*	0.133	−0.48
Placebo	4.73 (1.19)	2.82 (1.94)				
Hyperarousal						
Sertraline	3.82 (0.98)	1.45 (1.44)	3.46	39.06*	0.063	−0.53
Placebo	4.55 (0.52)	2.36 (1.96)				
Total symptoms						
Sertraline	11.09 (3.08)	4.82 (3.25)	3.82	38.82*	0.008	−0.53

Note: ANCOVA = analysis of covariance; PTSD = posttraumatic stress disorder.
* $p < .001$.

significant difference with regard to responses to the question about suicidal ideation on the MFQ at any point during the study, with equivalent proportions of children experiencing decreased suicidal ideation in both groups during the course of the study. No participant in either group developed new onset of suicidal ideation during the course of the study.

Adverse Events

Adverse events were defined as suicide attempts, reportable child abuse episodes, drug overdoses, or psychiatric hospitalizations. One participant in the TF-CBT + sertraline group was hospitalized overnight during week 12 for oppositional defiant disorder symptoms after running away from home. This child had a history of oppositional defiant disorder and running away, which preceded this treatment study. No other adverse events were reported during the study.

Clinically Meaningful Improvement

There was no significant difference between the two treatment groups with regard to clinically meaningful improvement on any instrument. The numbers of participants attaining clinically meaningful improvement follow.

PTSD Diagnosis. Two of the participants were in the no-PTSD diagnosis category at pretreatment (both in the TF-CBT + sertraline group). At posttreatment, 14 additional participants had moved into the no-PTSD diagnosis or nonclinical range in this regard (eight TF-CBT + sertraline; six TF-CBT + placebo).

Global Impairment Status. At pretreatment, all 22 participants were in the clearly impaired (CGAS <60) range on the CGAS. At posttreatment, 15 had moved into the not clearly impaired range on the CGAS (nine TF-CBT + sertraline, six TF-CBT + placebo).

Other Clinical Instruments. On the SCARED, four participants (two in each group) scored in the nonclinical range (score <25) at pretreatment; at posttreatment 13 additional participants had improved into the nonclinical range (eight TF-CBT + sertraline; five TF-CBT + placebo).

On the MFQ, nine participants scored in the nonclinical range (score <27) at pretreatment (three TF-CBT + sertraline; six TF-CBT + placebo); at

TABLE 3
Repeated-Measures ANCOVA for CGAS

Measure	Pretreatment Mean (SD)	Week 3 Mean (SD)	Week 5 Mean (SD)	Week 8 Mean (SD)	Posttreatment Mean (SD)	Group *F*	Time *F*	Group × Time *F*	*d*
CGAS-Sertraline	45.09 (5.24)	50.09 (5.36)	59.45 (6.82)	61.18 (8.62)	66.64 (10.12)	2.97	25.19**	3.63*	0.72
CGAS-Placebo	46.64 (5.03)	51.64 (4.23)	50.64 (9.12)	54.73 (8.84)	59.55 (9.70)				

Note: ANCOVA = analysis of covariance; CGAS = Children's Global Assessment Scale.
* $p < .01$; ** $p < .001$.

posttreatment, 13 additional participants had moved into the nonclinical range (eight TF-CBT + sertraline; five TF-CBT + placebo). With regard to suicidal ideation at pretreatment, five participants responded "true" to the question "I thought about killing myself" (four TF-CBT + sertraline, one TF-CBT + placebo). At posttreatment, no participants responded "true" to this question.

On the CBLC Total score, at pretreatment four participants had scores in the nonclinical range (*T* score <60; three TF-CBT + sertraline, one TF-CBT + placebo). At posttreatment eight additional participants had moved into the nonclinical range (four in each group).

On the BDI eight parents had scores in the normal range at pretreatment (four in each group); at posttreatment, six more had moved into the normal range (four TF-CBT + sertraline, two TF-CBT + placebo).

DISCUSSION

This study attempted to conduct an RCT to evaluate the benefit of adding sertraline to TF-CBT for sexually abused children with PTSD symptoms. This cohort was not representative of sexually abused children requesting clinical treatment due to the refusal of many families to consider pharmacological treatments for their children, and conclusions drawn from this study must be evaluated in this context. There were no significant group × time differences between the two groups with regard to remission of PTSD symptoms or other clinical symptomatology. The only statistically significant difference in outcome between the groups was on the CGAS, and this clinically observed improvement corresponded with the time at which clinical improvement may be expected to occur based on the pharmacological properties of sertraline. The fact that both groups improved significantly and equivalently with regard to not only PTSD but also depression, anxiety, behavior problems, and a variety of parental scores supports the idea that the treatment effect observed was due to TF-CBT interventions rather than sertraline. However, this finding must be taken in the context of the fact that the study was inadequately powered to detect significant differences between the two treatment groups.

An initial power analysis using the Sample Power 1.0 program of Borenstein et al. (1997), which allowed for the need to enter covariates, a medium effect size, and the need to conduct one-way fixed effects of covariance (ANCOVA), calculated that at least 32 treatment completers per group would be needed to achieve adequate power when comparing the TF-CBT + placebo versus and TF-CBT + sertraline groups. Clearly the final sample size of this study is too small to allow us to draw any definitive conclusions about possible benefits or lack thereof of adding sertraline to TF-CBT for this population.

The current findings are promising in that only one adverse event (likely unrelated to medication) occurred among children receiving sertraline, despite the fact that they received substantial doses of this medication (mean maximum dose of 150 mg/day). Among the 11 children and adolescents participating in this study who received sertraline, none developed significant suicidal symptoms. Although this is a small number of children on which to base any conclusions of safety, the fact that the side effects reported were also relatively low is encouraging. It is possible that the early components of TF-CBT, which provide individualized relaxation and affective modulation interventions, helped to reduce the prominence of somatic symptoms.

This study points out the substantial difficulty of recruiting a clinically representative sample with which to conduct a child psychopharmacological RCT among traumatized children. One third of the potential cohort pool (59/176) refused to consent to participate in this study, largely based on the possibility of receiving active medication. Although it is impossible to prove that this difficulty was related to parental concerns regarding the potential association between SSRIs and suicidality in children, it is interesting to note that 20 of 24 of the subjects who were randomized in this treatment trial were recruited within the first 18 months of recruitment (January 2002–July 2003), with only four additional subjects being successfully recruited from July 2003 to January 2006. If there was a systematic sampling bias in the present cohort, then one could reasonably speculate that it was more positively predisposed toward psychotropic medication use in children and adolescents.

Limitations

Limitations of this study include the small sample size, the self-selected nature of the cohort, and the lack of a representative sample with regard to gender or ethnic diversity other than African American youths.

Clinical Significance

Although children in both groups experienced equivalent improvement in all domains except CGAS scores, at the end of the study, decisions had to be made as to whether TF-CBT + sertraline participants should continue taking sertraline or taper off this medication. Because seven of these participants met criteria for MDD at the start of the study, and all of these participants responded positively to treatment with regard to improvement in depression scores, it was not possible to determine whether this response was due to TF-CBT, sertraline, or a combination of both treatments. The practice parameters in place at the time suggested that continuation treatment be maintained for at least 6 months following remission (American Academy of Child and Adolescent Psychiatry, 1998), and thus in cases in which MDD symptoms have been prominent, it was difficult to justify discontinuing the medication once it was started. This was particularly true when depressive symptoms intermittently increased after the end of the study (e.g., when legal proceedings occurred related to sexual abuse charges). In other cases, the child and adolescent psychiatrist suggested tapering medication, but the child and/or parent were reluctant to do so due to concerns about symptoms returning if medication was discontinued. Although TF-CBT treatment ended after the 12th treatment session, 4 of the 11 TF-CBT + sertraline participants continued sertraline for more than 4 months. The remaining seven tapered and discontinued sertraline within 1–4 months after the end of the study. Had these children received TF-CBT + placebo, some may have recovered without needing medication. To illustrate this, although there were seven participants in the TF-CBT + placebo group with comorbid MDD, to our knowledge, only one participant in the TF-CBT + placebo group later required ongoing SSRI treatment.

Clinical Implications

Because this study did not demonstrate a clear benefit of adding medication to TF-CBT, based on current evidence it appears that for most children with PTSD, including those with comorbid MDD, a trial of initial TF-CBT or other evidence-based trauma-focused psychotherapy alone is warranted before adding medication. Those with significant MDD or serious psychosocial stressors (e.g., subsequent legal involvement) may require medication at a later time, alone or in combination with psychotherapy. It is also important to note that in many cases, combined TF-CBT + sertraline can be provided as a short-term or time-limited treatment modality. Most participants (7/11) who received this modality were able to tolerate tapering off a relatively high dose of sertraline within 1–3 months, including three participants who had comorbid MDD.

In conclusion, this study found that for a small and self-selected group of multiply traumatized sexually abused girls, TF-CBT + sertraline was not superior to TF-CBT + placebo except with regard to CGAS outcomes. However, because the study was statistically underpowered, no definitive conclusions can be drawn about the potential benefit or lack thereof of adding sertraline to TF-CBT for this population. A potential drawback of starting combined treatment was that once a child responded positively, it was not possible to know whether the response was to psychotherapy, medication, or both, and this may have led to unnecessary prolongation of pharmacological treatment. Due to the failure of this pilot trial to demonstrate a clear benefit of adding sertraline, treatment in most cases should begin with TF psychotherapy with proven efficacy such as TF-CBT. Medication should be added only when and if an individual child's situation indicates a need to do so.

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Stress Predicts Brain Changes in Children: A Pilot Longitudinal Study on Youth Stress, Posttraumatic Stress Disorder, and the Hippocampus Victor G. Carrion, MD, Carl F. Weems, PhD, Allan L. Reiss, MD

Objective: Does stress damage the brain? Studies of adults with posttraumatic stress disorder have demonstrated smaller hippocampal volumes when compared with the volumes of adults with no posttraumatic stress disorder. Studies of children with posttraumatic stress disorder have not replicated the smaller hippocampal findings in adults, which suggests that smaller hippocampal volume may be caused by neurodevelopmental experiences with stress. Animal research has demonstrated that the glucocorticoids secreted during stress can be neurotoxic to the hippocampus, but this has not been empirically demonstrated in human samples. We hypothesized that cortisol volumes would predict hippocampal volume reduction in patients with posttraumatic symptoms. *Patients and Methods:* We report data from a pilot longitudinal study of children ($n = 15$) with history of maltreatment who underwent clinical evaluation for posttraumatic stress disorder, cortisol, and neuroimaging. *Results:* Posttraumatic stress disorder symptoms and cortisol at baseline predicted hippocampal reduction over an ensuing 12- to 18-month interval. *Conclusions:* Results from this pilot study suggest that stress is associated with hippocampal reduction in children with posttraumatic stress disorder symptoms and provide preliminary human evidence that stress may indeed damage the hippocampus. Additional studies seem to be warranted. **Pediatrics** 2007;119:e509–e516.