A Randomized Clinical Trial of Eye Movement Desensitization and Reprocessing (EMDR), Fluoxetine, and Pill Placebo in the Treatment of Posttraumatic Stress Disorder: Treatment Effects and Long-Term Maintenance

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Objective: The relative short-term efficacy and long-term benefits of pharmacologic versus psychotherapeutic interventions have not been studied for posttraumatic stress disorder (PTSD). This study compared the efficacy of a selective serotonin reuptake inhibitor (SSRI), fluoxetine, with a psychotherapeutic treatment, eye movement desensitization and reprocessing (EMDR), and pill placebo and measured maintenance of treatment gains at 6-month follow-up.

Method: Eighty-eight PTSD subjects diagnosed according to DSM-IV criteria were randomly assigned to EMDR, fluoxetine, or pill placebo. They received 8 weeks of treatment and were assessed by blind raters posttreatment and at 6-month follow-up. The primary outcome measure was the Clinician-Administered PTSD Scale, DSM-IV version, and the secondary outcome measure was the Beck Depression Inventory-II. The study ran from July 2000 through July 2003.

Results: The psychotherapy intervention was more successful than pharmacotherapy in achieving sustained reductions in PTSD and depression symptoms, but this benefit accrued primarily for adult-onset trauma survivors. At 6-month follow-up, 75.0% of adult-onset versus 33.3% of child-onset trauma subjects receiving EMDR achieved asymptomatic end-state functioning compared with none in the fluoxetine group. For most childhood-onset trauma patients, neither treatment produced complete symptom remission.

Conclusions: This study supports the efficacy of brief EMDR treatment to produce substantial and sustained reduction of PTSD and depression in most victims of adult-onset trauma. It suggests a role for SSRIs as a reliable first-line intervention to achieve moderate symptom relief for adult victims of childhood-onset trauma. Future research should assess the impact of lengthier intervention, combination treatments, and treatment sequencing on the resolution of PTSD in adults with childhood-onset trauma.

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Exposure to traumatic experiences is ubiquitous in our society: 60% of men and 51% of women in the general population report at least 1 traumatic event in their lives.[1] For men, combat and witnessing injury or death are the most frequent precipitants for developing posttraumatic stress disorder (PTSD), while for adult women, physical attacks by intimate partners is the most frequent cause. Approximately 9.8 million adult American women (10.3%) have histories of violent physical assaults, and 12.1 million (12.7%) have experienced a completed rape at some point in their lives.[2] More than twice as many women report histories of childhood sexual abuse than of adult rape,[3] which occurs in approximately 10% of the general population.[1] Childhood sexual abuse is a strong predictor of subsequent PTSD.[4,5] More than 20% of returning veterans from Iraq are currently seeking mental health services.[6]

A variety of psychotherapeutic approaches to PTSD, all involving some form of exposure and "trauma processing," have been shown to be effective (e.g., see references 7–10). Pharmacologic agents, in particular the selective serotonin reuptake inhibitors (SSRIs), have also been

shown to be effective in civilians with PTSD, but less so in veterans (e.g., see references 11–15). However, no study has directly compared the efficacy of psychotherapeutic versus pharmacologic interventions.

The relative efficacy of biological versus psychotherapeutic interventions is an issue of great clinical and economic relevance. Comparative studies have been done in panic disorder,[16–18] obsessive-compulsive disorder,[19,20] and depression.[21,22] Most studies in those disorders conclude that cognitive-behavioral therapy (CBT) and pharmacotherapy are roughly equivalent, but there continues to be considerable controversy about the interpretation of the data.[23,24]

A recent meta-analysis of a large depression sample[25] found that "among those with a history of early childhood trauma (physical or sexual abuse, neglect, or loss of parents at an early age), psychotherapy alone was superior to antidepressant monotherapy."(p14293) Treatment with psychotherapy resulted in twice the rate of remission in patients with major depression who also had histories of serious early adverse life events than did treatment with antidepressants. Surprisingly, the prevalence of PTSD was not ascertained in that sample. Given the high rate of PTSD comorbidity with depression,[1–4] the PTSD outcome literature may make an important contribution to effective treatment of this population.

Research suggests that PTSD patients are more responsive to treatments that specifically "process" traumatic memories than to either supportive counseling or stress inoculation training.[8] In 1 meta-analysis of 61 treatment outcome trials for PTSD (including drug therapies, CBT, eye movement desensitization and reprocessing [EMDR], relaxation training, hypnotherapy, and dynamic therapy), psychological therapies were more effective than drug therapies, and both were more effective than controls.[26] Psychological therapies had lower dropout rates than pharmacotherapies (14% vs. 32%). Among the psychological approaches, CBT and EMDR were the most effective, with no demonstrable differences in treatment efficacy. Among the drug therapies, the SSRIs had the greatest effect sizes. Another effect-size analysis of 14 treatment outcome studies[27] found that the drug therapies with the largest effect sizes were fluoxetine and amitriptyline.

The present study directly compared the efficacy of a psychopharmacologic agent, fluoxetine, with a psychotherapeutic, exposure-based treatment, EMDR, and a pill placebo in PTSD. EMDR is an exposure treatment in which patients perform saccadic eye movements while thinking about a traumatic experience. Rather than providing a chronological narrative of the details of the traumatic event, as is done in CBT, EMDR patients are encouraged to follow their own course, moving freely backward and forward in time, attending to inner sensations and cognitions, omitting verbal communication about content if they wish. EMDR has been declared an effective evidence-based treatment for PTSD in the professional treatment guidelines of the U.S. Department of Defense,[28] the American Psychological Association,[29] and the American Psychiatric Association.[30]

Comparing the relative effectiveness of pharmacotherapy versus exposure therapy is particularly relevant in the treatment of PTSD, since the SSRIs are widely used to treat PTSD, particularly in primary care and health maintenance organization (HMO) settings, where little attention may be paid to helping patients "process" their traumas. This is reasonable as long as the question has not been settled whether pharmacotherapy produces better or worse results than the active processing of traumatic memories (which many patients are reluctant to do because of wanting to avoid being reminded of their trauma).[31] Our study was particularly concerned with the effects of these various treatments on clinical symptomatology over time.

METHOD

Participants

Following institutional review board approval, individuals 18 to 65 years old, with current PTSD and with mixed trauma exposure at least 1 year prior to intake, were recruited via newspaper ads, the Internet, and solicitation from medical and mental health professionals. The study ran from July 2000 through July 2003. A total of 229 participants were assessed at pretreatment after giving written informed consent. Of these, 88 (38%) met study inclusion criteria and were randomly assigned to treatment. Of the remainder, 47 (21%) failed to meet DSM-IV diagnostic criteria for PTSD, 30 (13%) withdrew consent prior to randomization, and 64 (28%) met study exclusionary criteria. Baseline participant information is contained in Table 1. Trauma history was obtained by self-report. The predominant index trauma involved interpersonal victimization (71.6%); in 50% of participants, trauma onset occurred prior to age 18 (Table 2).

Exclusion criteria were unstable medical condition, contraindications to either treatment (i.e., pregnancy, glaucoma or detached retina, or history of severe allergies or multiple adverse drug reactions), inability to be weaned off current psychotropic medications, psychotic or bipolar disorder, current alcohol or substance abuse/dependence, severe dissociation, active suicidality or life-threatening mutilation, prior exposure to active study interventions, concurrent trauma-focused treatment, unstable living situation, Global Assessment of Functioning[32] score < 40, and disability compensation for PTSD or pending trauma-related lawsuit. Initial telephone screening was used to assess likely presence/absence of inclusion and exclusion criteria; potential participants were then invited for in-person assessment. Participants were not excluded for engagement in nontrauma-focused, supportive psychotherapy, provided this treatment had been ongoing for

Table 1. Baseline Analyses of Demographic Variables and Comorbid Diagnoses by Treatment Group

Variable	EMDR (N = 29)	Fluoxetine (N = 30)	Placebo (N = 29)	Total[a] (N = 88)	p Value[b]
Female, %	75.9	86.7	86.2	83.0	.46
Age, mean (SD), y	38.7 (14.3)	34.1 (12.4)	35.7 (13.4)	36.1 (13.4)	.41
White, %	69.0	63.3	69.0	67.0	.87
Unemployed, %	25.0	16.7	25.0	22.1	.67
College graduate, %	51.7	56.7	44.8	51.1	.66
Never married, %	82.8	86.7	86.2	85.2	.90
Concurrent supportive therapy, %	13.8	13.3	20.7	15.9	.69
Years since index trauma, mean (SD)	12.2 (13.7)	12.8 (11.2)	13.8 (10.9)	12.9 (11.9)	.87
CAPS total score, 1 month, mean (SD)	71.7 (11.9)	75.9 (15.6)	74.5 (12.5)	74.0 (13.4)	.48
CAPS total score, 1 week, mean (SD)	69.4 (12.7)	73.7 (13.4)	70.3 (13.0)	71.2 (13.0)	.42
BDI-II total score, mean (SD)	16.2 (9.5)	18.2 (9.2)	20.7 (9.7)	18.3 (9.6)	.20
No. of current comorbid Axis I/II diagnoses, mean (SD)[c]	3.1 (3.4)	3.2 (2.4)	3.2 (2.4)	3.2 (2.7)	.99

[a]Total of all 3 treatments combined.
[b]Used omnibus analysis of variance for continuous measures or Pearson χ^2 statistic for categorical measures.
[c]Assessed using Structured Clinical Interview for DSM-IV Disorders.[37,38]
Abbreviations: BDI-II = Beck Depression Inventory-II, CAPS = Clinician-Administered PTSD Scale, EMDR = eye movement desensitization and reprocessing, PTSD = posttraumatic stress disorder.

Table 2. Index Trauma Distribution (N = 88)

Index Trauma	N (%)
Child sexual abuse	25 (28.4)
Child physical abuse	4 (4.5)
Child sexual and physical abuse	8 (9.1)
Adult sexual assault	8 (9.1)
Adult physical assault	5 (5.7)
Domestic violence	7 (8.0)
Other adult victimization	6 (6.8)
Traumatic loss	8 (9.1)
War/terrorism/violence	3 (3.4)
Injury/accident	14 (15.9)

at least 3 months prior to study baseline and did not involve exposure to or processing of traumatic memories. A detailed report of screening attrition and exclusion data is available.[33]

Measures

Clinician-Administered PTSD Scale (CAPS), DSM-IV Version.[34] The CAPS total score was the primary continuous outcome measure as an index of PTSD symptom severity. Rating was based on a 1-week interval for immediate pretreatment and posttreatment assessment; a 1-month interval was used at baseline and 6-month follow-up. Results are also presented on PTSD diagnostic status, defined as full DSM-IV diagnostic criteria and using the following CAPS scoring rules: (1) total severity score > 50, (2) per-item frequency of at least 1 and intensity of at least 2, and (3) per-item total severity score of at least 4.[35] Asymptomatic end-state function (i.e., PTSD symptom remission), defined as CAPS score < 20, is also reported.[36]

Structured Clinical Interview for DSM-IV Axis I and Axis II Disorders (SCID I[37] and SCID II[38]). This structured interview was used for determination of PTSD and comorbid diagnoses.

Beck Depression Inventory-II (BDI-II).[39] This widely used and psychometrically sound self-report measure of depressive symptoms was used to assess secondary study hypotheses regarding the immediate and long-term efficacy of pharmacologic versus psychological interventions on amelioration of depressive symptoms in traumatized individuals with PTSD.

Procedure

Assessment. Assessments were conducted at pretreatment, posttreatment, and 6 months following treatment cessation. Assessment included interview and self-report measures, as well as psychophysiologic response to script-driven imagery. This was a modified version of the protocol adapted by Pitman and colleagues[40] for use with PTSD, consisting of a series of 30-second, audio-taped scripts in second-person, present-tense narrative, based on participants' recounting of the worst memory associated with the trauma, as well as a neutral memory from the same time period. Modifications involved use of 2 alternating sets of neutral and traumatic scripts. Physiologic responses to script-driven imagery before and after treatment will be reported elsewhere.

Evaluators were primarily postdoctoral-level clinicians who received extensive training and ongoing supervision in administration of study measures. Interrater reliability on the CAPS was established prior to the start of the study, based on coding of live and videotaped interviews, and reassessed at regular intervals to avoid rater drift. Interrater reliability for PTSD diagnosis, based on Cohen's kappa, was very good ($\kappa = 0.82$, percent agreement = 0.92). Interrater reliability for PTSD symptom severity was excellent (intraclass correlation coefficient = 0.96). All raters were blind to treatment condition and were never assigned the same participant for both pretreatment and posttreatment evaluation.

Treatment. Participants were randomly assigned to 1 of 3 treatment conditions: EMDR, fluoxetine, or pill placebo. Randomization was stratified by presence/absence of concurrent supportive psychotherapy. In order to ensure approximately equal numbers in each treatment condition, random assignment was blocked in groups of 12 consecutive participants, so that in each block, 4 participants were assigned to each condition. Participants in all 3 conditions received a total of 8 weekly treatment sessions. Following cessation of treatment, participants in the 2 active treatment conditions were asked to refrain from initiating new treatment during the 6-month follow-up period. The blind was removed from the placebo intervention following the posttreatment assessment, and, for ethical reasons, participants were offered the option of receiving either of the 2 active treatments. Consequently, placebo group data were not included in follow-up analyses.

EMDR. EMDR treatment consisted of 90-minute individual sessions. The treatment targeted memories associated with the primary trauma identified during pretreatment evaluation. Treatment was administered according to a manual developed for this study,[41] based on the standard protocol.[42] The 4 clinicians in the EMDR condition were at master's level or above, with Level II EMDR training. They were licensed in their profession and had a minimum of 3 years' experience treating patients with PTSD. Clinicians received extensive training and biweekly supervision in the manualized protocol established for the study from a certified senior EMDR instructor (D.L.K.). An average of 6 EMDR sessions were devoted to trauma processing. All EMDR sessions were videotaped, and an independent evaluator assessed treatment fidelity through videotape review from randomly sampled sessions.

Medication. Medication treatment consisted of 20- to 30-minute individual sessions. The fluoxetine and placebo interventions were administered in a double-blind, fixed-flexible-dose design according to standard protocol for double-blind pharmacologic interventions for PTSD.[12–15] This study employed a manualized pharmacotherapy protocol developed and empirically supported for intervention with fluoxetine.[11,12] The treatment manual included instructions for monitoring of adverse effects and compliance with prescribed dosage, tracking of PTSD symptom change, and ongoing assessment of mental status. Starting dosage was 10 mg/day of fluoxetine (or pill placebo equivalent). Dosage was increased in 10-mg increments per week to a maximum of 60 mg/day, or until symptom remission was achieved. Increases or decreases in dosage were based on physician judgment of clinical response and presence/absence of dose-limiting side effects. Mean fluoxetine dose across clients/sessions was 30 mg; 19 of 26 fluoxetine-condition completers received 30 mg or greater for the last 4 weeks of treatment. The modal fluoxetine dose at end of treatment was 40 mg. The drug was discontinued over a 10-day period following the 8-week intervention period. Pharmacotherapists were licensed psychiatrists (fourth-year residents and above) who received extensive training on the study protocol and received weekly supervision by the principal investigator.

Statistical Analyses

The study was designed to evaluate whether both fluoxetine and EMDR perform equally well, and better than placebo, after 8 weeks of treatment of PTSD and whether EMDR differs from fluoxetine in maintaining treatment gains over time. Secondary hypotheses addressed the impact of child- versus adult-onset trauma on treatment outcome. The impact of treatment on depressive symptoms was also assessed.

Study hypotheses were tested on both treatment completer and intent-to-treat (ITT) samples. Intent-to-treat analyses were conducted using an early termination assessment, when available, or a last-observation-carried-forward (LOCF) procedure to impute missing data. Long-term effects of active-treatment completers were assessed at 6 months posttreatment for both follow-up completer and intent-to-follow (ITF) samples. For the ITF sample, missing follow-up data were also estimated using LOCF.

Baseline group differences were assessed using analysis of variance for continuous measures and Pearson χ^2 statistic for categorical measures. To minimize bias, posttreatment continuous-measure analyses were conducted using omnibus analysis of covariance (ANCOVA) with baseline as the covariate.[43,44] These were followed by pairwise comparisons using 2-group ANCOVA. Baseline by treatment-condition interactions were tested for all primary outcome analyses. No significant interactions were found. Therefore, interaction terms were dropped from further analyses. Follow-up analyses were conducted on the 2 active treatments. Analyses of continuous variables used ANCOVA, controlling for baseline score. Posttreatment and follow-up categorical outcomes (i.e., PTSD diagnosis and end-state function) were evaluated using the Pearson χ^2 statistic. Within-group and between-group effect sizes were calculated using Cohen's d statistic on the primary outcome measure (i.e., CAPS total score) at posttreatment and at 6-month follow-up.

RESULTS

Preliminary Analyses

Baseline group differences. Participants in the 3 treatment conditions did not differ significantly on any demographic variable or on any baseline measure of psychopathology (Table 1).

Treatment dropout. Twelve people dropped out during the 8-week treatment phase, leaving 76 treatment completers. There were no significant differences in dropout rates on any baseline measure of psychopathology or

across treatment conditions. Completers in each group were 24 of 29 (83%) for EMDR, 26 of 30 (87%) for fluoxetine, and 26 of 29 (90%) for pill placebo. Dropouts were significantly younger than completers (dropout mean age = 27.1 years, completer mean age = 37.6 years; $F = 6.785$, df = 1,86; $p < .05$). In addition, dropouts were more likely to have had child- versus adult-onset trauma ($\chi^2 = 6.175$, df = 1,88; $p = .013$).

Clinician effects. Potential clinician-specific effects were examined in 3 one-way ANCOVAs on posttreatment CAPS total score for the ITT sample, controlling for baseline symptom severity. Chi-square analyses were used to compare dropout rates by clinician. Six clinicians had each treated 5 or fewer participants and were combined within treatment condition for comparison with the remaining clinicians. No significant differences were found by clinician in posttreatment scores or dropout rates.

Concurrent supportive psychotherapy. Potential impact of concurrent supportive psychotherapy at the time of randomization was examined in the same manner for both treatment completers and ITT sample. No significant main or interactive effects of concurrent treatment were found.

Treatment expectations. No group differences were found on baseline treatment expectations for participants randomly assigned to medication condition versus psychotherapy condition, nor were any significant interactions found between treatment group and expectations on study outcome. A positive main effect of baseline treatment expectations on PTSD symptom reduction at posttreatment was observed ($F = 5.8$, df = 1,84; $p = .018$).

Postintervention treatment seeking. After cessation of the study intervention, 4 participants (2 EMDR, 2 fluoxetine) initiated nonstudy treatments. To assess the potential impact on 6-month follow-up findings, a second set of analyses was run in which data from these participants were extracted (completer analyses) or carried forward from last data point preceding onset of new treatment (ITF analyses). Analyses revealed no changes in direction or significance level of findings. Thus, reported findings retain data from these participants.

Clinician treatment adherence. Videotapes of 24 EMDR sessions (over 10% of 210 total study sessions) were randomly selected for independent fidelity rating, with oversampling to ensure distribution across clinicians and session type. Fifty components across the 8 phases of treatment were included in the fidelity manual developed for this protocol. The evaluator was an experienced, independent, certified EMDR clinician who was not personally known to the study investigators. The evaluator reviewed videotapes and rated adherence according to a 4-point Likert-type scale: 0 = no adherence, 1 = some adherence, 2 = adherence acceptable, and 3 = adherence very good. The mean fidelity score across sessions was 2.57 (SD = 0.35; minimum = 1.76, maximum = 3.00). Adherence to the pharmacotherapy protocol and dosing schedule was monitored through weekly case review and supervision of study pharmacotherapists.

Primary Analyses

Means and standard deviations for all primary and secondary outcome measures are reported in Table 3. At posttreatment, the drop in total CAPS score was 59.0% for EMDR, 46.0% for fluoxetine, and 43.6% for placebo, as compared with 1-week pretreatment baseline assessment. At 6-month follow-up, the CAPS total score drop was 62.2% for EMDR and 48.3% for fluoxetine.

Notably, omnibus ANCOVA analyses (ITT and completer) of the 3-condition model failed to reveal a significant effect of treatment on the primary outcome measures. While common practice is to refrain from further analyses when the omnibus analyses reveal negative findings, because our study hypotheses emphasize 2-group outcomes over omnibus outcomes, and in light of the absence of an appropriate control group for the psychotherapy condition, pairwise comparisons of the 3 conditions were conducted and their results reported below.

EMDR versus placebo. The posttreatment ITT (LOCF) analyses revealed nonsignificant trends for greater remission of PTSD in individuals receiving EMDR versus placebo. In the completer analyses, EMDR was significantly superior to placebo on reduction of PTSD symptoms and showed a greater percentage of loss of diagnostic status compared with placebo (Table 3).

Fluoxetine versus placebo. Neither posttreatment ITT nor completer analyses revealed significant differences between fluoxetine and placebo on any outcome measure (Table 3). The majority of both fluoxetine and placebo participants demonstrated loss of PTSD diagnosis; however, few participants achieved full remission of symptoms.

EMDR versus fluoxetine. As hypothesized, at posttreatment, the 2 active treatments did not differ on measures of PTSD (Table 3). At 6-month follow-up, EMDR was superior to fluoxetine on sustained reduction of posttraumatic symptoms (Table 3) for both ITF (LOCF) and completer analyses. EMDR was superior to fluoxetine in attaining complete remission of symptoms at 6 months posttreatment: 58% of EMDR subjects were asymptomatic, compared with none in the fluoxetine group. EMDR was also superior to fluoxetine in reduction of self-reported depressive symptoms for both the ITF and completer samples.

Secondary Analyses:
Impact of Trauma Onset on Treatment Outcome

In order to account for the potential impact of index trauma onset on treatment outcome, ANCOVA analyses were rerun for continuous outcomes with a dummy-coded onset variable. Main and interactive effects for onset and

Table 3. Posttreatment and Follow-up Analyses for Primary and Secondary Outcome Measures by Sample and Treatment Condition

						2-Group Comparisons[a,b]		
Analysis	EMDR	Fluoxetine	Placebo	Total[c]	p Value[b,d,e]	EMDR vs Fluoxetine	EMDR vs Placebo	Fluoxetine vs Placebo
Completers	N = 24	N = 26	N = 26	N = 76				
CAPS total score, mean (SD)	28.37 (19.66)	38.69 (20.30)	39.81 (18.76)	35.82 (19.98)	.09*	.27	**.03***	.67
Loss of PTSD diagnosis, %	88	81	65	78	.15	.52	.07*	.21
Asymptomatic, %[f]	29	15	12	18	.24	.24	.12	.69
BDI-II total score, mean (SD)	9.21 (6.44)	12.42 (8.08)	12.38 (6.65)	11.39 (7.18)	.24	.12	.16	.72
Intent-to-treat (ITT)	N = 29	N = 30	N = 29	N = 88				
CAPS total score, mean (SD)	32.55 (22.50)	42.67 (22.11)	43.55 (22.60)	39.63 (22.70)	.16	.13	.07*	.61
Loss of PTSD diagnosis, %	76	73	59	69	.31	.82	.16	.23
Asymptomatic, %[f]	28	13	10	17	.17	.17	.09*	.72
BDI-II total score, mean (SD)	9.10 (6.02)	13.00 (8.66)	14.38 (9.74)	12.17 (8.50)	.16	.08*	.07*	.94
Follow-up completers	N = 21	N = 18		N = 39				
CAPS total score, mean (SD)	25.67 (21.17)	41.22 (15.70)	NA	32.85 (20.19)	**.05***			
Loss of PTSD diagnosis, %	91	72	NA	82	.14			
Asymptomatic, %[f]	57	0	NA	31	**< .001***			
BDI-II total score, mean (SD)	5.24 (5.37)	12.94 (7.68)	NA	8.80 (7.53)	**.002***			
Intent-to-follow (ITF)[g]	N = 24	N = 26		N = 50				
CAPS total score, mean (SD)	25.79 (21.61)	42.12 (15.83)	NA	34.28 (20.37)	**.005***			
Loss of PTSD diagnosis, %	88	73	NA	80	.20			
Asymptomatic, %[f]	58	0	NA	28	**< .001***			
BDI-II total score, mean (SD)	5.25 (5.23)	14.00 (7.71)	NA	9.80 (7.92)	**< .001***			

[a]Numbers represent p values for pairwise comparisons of continuous and categorical measures.
[b]Results at trend level or greater are indicated by an asterisk (*); p values significant at ≤ .05 are indicated with boldface.
[c]Total of all 3 treatments combined.
[d]Omnibus analysis of continuous measures used analysis of covariance with baseline as covariate; Pearson χ^2 statistic was used for categorical measures.
[e]At posttreatment, p value is for 3-group comparison; at follow-up, p value is for 2-group (active treatment) comparison.
[f]Defined as CAPS total score below 20.
[g]All active treatment completers are included in intent-to-follow analyses.
Abbreviations: BDI-II = Beck Depression Inventory-II, CAPS = Clinician-Administered PTSD Scale, EMDR = eye movement desensitization and reprocessing, NA = not applicable, PTSD = posttraumatic stress disorder.

treatment condition were entered into the model. "Child onset" was defined as onset of index trauma prior to age 18; "adult onset" was defined as index trauma onset at or after age 18. Diagnosis and asymptomatic end-state function were examined by onset and treatment condition using χ^2 analysis. Descriptives by treatment condition and trauma onset are reported in Table 4.

Baseline. Equivalent numbers of patients with child-onset (N = 45) and adult-onset (N = 43) index traumas were randomly assigned to treatment. Treatment conditions did not differ in distribution of patients by onset (child onset: EMDR, N = 15 [51.7%]; fluoxetine, N = 13 [43.3%]; placebo, N = 17 [58.6%]). At baseline, patients with child-onset trauma demonstrated significantly higher PTSD symptoms on 1-month CAPS than patients with adult-onset trauma (child onset: mean = 77.71 [SD = 13.04]; adult onset: mean = 70.26 [SD = 12.87]; F = 7.281, df = 1,86; p < .01); this dropped to a trend for 1-week CAPS (child onset: mean = 73.49 [SD = 12.99]; adult onset: mean = 68.74 [SD = 12.74]; F = 2.989, df = 1,86; p < .10).

CAPS total score. For both posttreatment and follow-up analyses, main effects for treatment as reported above were retained at similar levels of significance with the addition of the index trauma onset variable. No onset-by-treatment-condition interaction effects were observed at any time point. Onset was found to make additional contributions to outcome, as follows: immediately posttreatment, across treatment conditions, patients with adult-onset trauma showed significantly greater reduction in PTSD symptoms than those with child-onset trauma, for both ITT (p < .005) and completer (p = .02) samples. These effects were maintained at 6-month follow-up (ITT, p = .011; completer, p = .027).

The EMDR and placebo groups demonstrated larger effect sizes for adult- than for child-onset trauma, whereas fluoxetine exhibited the opposite pattern (Table 5).

PTSD diagnosis and asymptomatic end-state function. At posttreatment, differential effects were found by onset of the index trauma (Table 4). Chi-square analyses revealed that adult-onset patients were significantly more likely to both lose PTSD diagnosis (ITT, p = .052) and achieve asymptomatic end-state function (ITT, p = .037) than child-onset patients (Figure 1). When probed by treatment condition, these differential effects were found to occur only within the EMDR condition.

At 6-month follow-up, χ^2 analyses revealed that within the EMDR group, adult-onset patients were more likely to

Table 4. Posttreatment and Follow-Up Completer Descriptives by Treatment Condition and Trauma Onset

Analysis	EMDR	Fluoxetine	Placebo	Total[a]
Posttreatment				
Child-onset	N = 11	N = 10	N = 14	N = 35
CAPS total score, mean (SD)	38.36 (20.73)	40.20 (14.33)	46.57 (20.18)	42.17 (18.72)
Loss of PTSD diagnosis, %	72.7	90.0	57.1	71.4
Asymptomatic, %[b]	9.1	10.0	7.1	8.6
Adult-onset	N = 13	N = 16	N = 12	N = 41
CAPS total score, mean (SD)	19.92 (14.64)	37.75 (23.69)	31.92 (13.87)	30.39 (18.72)
Loss of PTSD diagnosis, %	100.0	75.0	75.0	82.9
Asymptomatic, %[b]	46.2	18.8	16.7	26.8
Follow-up				
Child-onset	N = 9	N = 7		N = 16
CAPS total score, mean (SD)	33.00 (22.34)	50.43 (8.24)	N/A	40.63 (19.31)
Loss of PTSD diagnosis, %	88.9	42.9	N/A	68.8
Asymptomatic, %[b]	33.3	0.0	N/A	18.8
Adult-onset	N = 12	N = 11		N = 23
CAPS total score, mean (SD)	20.17 (19.36)	35.36 (16.76)	N/A	27.43 (19.37)
Loss of PTSD diagnosis, %	91.7	90.9	N/A	91.3
Asymptomatic, %[b]	75.0	0.0	N/A	39.1

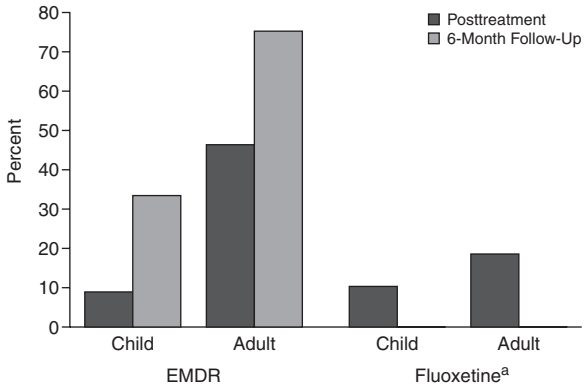
[a]Total of all 3 treatments combined.
[b]Defined as CAPS total score below 20.
Abbreviations: CAPS = Clinician-Administered PTSD Scale, EMDR = eye movement desensitization and reprocessing, NA = not applicable, PTSD = posttraumatic stress disorder.

Table 5. Effect Sizes for Primary Outcome Measure (CAPS total score) by Sample

	Between-Group Effect Size[a]		
Analysis	EMDR vs Fluoxetine	EMDR vs Placebo	Fluoxetine vs Placebo
Treatment completers			
Full group	0.35	0.58	0.18
Child-onset trauma	0.00	0.20	0.19
Adult-onset trauma	0.68	1.02	0.13
Intent-to-treat (ITT)			
Full group	0.24	0.45	0.19
Child-onset trauma	–0.01	0.24	0.25
Adult-onset trauma	0.56	0.71	0.02
Follow-up completers			
Full group	0.17	NA	NA
Child-onset trauma	0.09	NA	NA
Adult-onset trauma	0.25	NA	NA
Intent-to-follow (ITF)			
Full group	0.54	NA	NA
Child-onset trauma	0.47	NA	NA
Adult-onset trauma	0.65	NA	NA

[a]Positive between-group effect sizes favor first treatment condition over second; negative between-group effect sizes favor second treatment condition over first.
Abbreviations: CAPS = Clinician-Administered PTSD Scale, EMDR = eye movement desensitization and reprocessing, NA = not applicable, PTSD = posttraumatic stress disorder.

Figure 1. Asymptomatic End-State Function (CAPS score < 20) by Treatment Type and Index Trauma Onset



[a]At 6-month follow-up, none of the fluoxetine participants achieved asymptomatic end-state function.
Abbreviations: CAPS = Clinician-Administered PTSD Scale, EMDR = eye movement desensitization and reprocessing, PTSD = posttraumatic stress disorder.

achieve loss of PTSD diagnosis and achieve asymptomatic end state (ITF, p = .045) than those with childhood-onset trauma. None of the fluoxetine participants achieved asymptomatic end-state function, regardless of age of trauma (Figure 1). EMDR patients sustained high rates of loss of diagnosis at 6-month follow-up, regardless of age of trauma, while fluoxetine adult-onset patients were significantly more likely to lose PTSD diagnosis than fluoxetine child-onset patients (ITF, p = .036).

DISCUSSION

In this 8-week study that compared an exposure-based psychotherapeutic treatment of PTSD (EMDR) with a pharmacologic treatment (fluoxetine) and pill placebo, participants in all 3 groups sustained considerable improvement. Eighty-eight percent of EMDR, 81% of fluoxetine, and 65% of placebo completers lost their PTSD diagnosis, and 29% of EMDR, 15% of fluoxetine, and 12% of placebo completers became asymptomatic (CAPS scores under 20). Over the 6 months following the cessa-

tion of treatment, the EMDR group continued to mildly improve, while the fluoxetine group lost some of its gains: at follow-up, 57% of EMDR completers were asymptomatic, compared with none of the fluoxetine group.

In this study, every treatment group improved substantially: undergoing routine study procedures on a weekly basis seemed to have beneficial effects on most participants, regardless of treatment condition. A positive response to study participation is common in PTSD drug treatment studies: participating in a study generally accounts for more of the variance than the particular treatment received (e.g., see references 12, 14, 15). Posttraumatic stress disorder has been shown to be quite responsive to pill placebo on the order of a 35% to 40% improvement over baseline.[45] There has been considerable debate whether thorough weekly assessments themselves entail sufficient exposure therapy to make a clinically significant difference.[45–47] The magnitude of the placebo response in PTSD suggests that claims of treatment efficacy of any particular method need to be based on comparisons with a placebo or inert-treatment group rather than a wait-list control.

The effect size of the pill-placebo group in this study was larger than that of any other placebo groups in the PTSD treatment outcome literature—in fact, larger than that of several active treatments that claim efficacy compared with wait-list control groups. In order to study changes in psychophysiologic reactivity among the different treatments, all subjects in this study were exposed to 2 personalized trauma scripts that involved intense confrontation with their traumatic memories. This exposure may have played a significant role in the positive outcome across treatment conditions. Exposure to memories of one's trauma has repeatedly been identified as a critical element in effective PTSD therapy.[48,49] Exposure may also have contributed to the large effect size in the fluoxetine group, which was larger than those previously reported in pharmacologic studies.[27,46]

The effect size of the EMDR group was comparable to that of previous EMDR studies (e.g., see reference 50). The EMDR responders not only maintained their treatment gains after the study but continued to improve slightly over time: at 6-month follow-up, 57% of EMDR completers had a CAPS score below 20 (asymptomatic end-state function), compared with none of the fluoxetine group. It is not surprising that fluoxetine subjects lost some of their improvement at follow-up—pharmacologic effects cannot be expected to last over time, but the fact that the effects of EMDR were maintained, and somewhat improved, has important clinical and economic implications. Continued improvement after treatment cessation has previously been reported with prolonged exposure[8] and EMDR.[51] This suggests that, once people deal with their traumatic memories, they are likely to continue to improve without further intervention.

The clinical improvement in the EMDR group at 6-month follow-up was not confined to PTSD symptoms: EMDR completers had significantly lower BDI-II scores than fluoxetine completers. Once the trauma is resolved, other domains of psychological functioning appear to improve spontaneously. This may have significant implications for the treatment of depression in individuals with comorbid PTSD.

The issue of trauma onset has not been addressed in previous treatment outcome studies. The present study found that participants in the EMDR condition with adult-onset index traumas had a substantially better treatment response than those with childhood-onset trauma. Specifically, 100% of adult-onset participants lost diagnostic status at posttreatment, versus a significantly lower 75% of child-onset participants. This distinction became even more pronounced at 6-month follow-up. Here, trauma onset significantly predicted a large distinction in end-state functioning: 75.0% of adult-onset versus 33.3% of child-onset trauma participants receiving EMDR were asymptomatic at 6-month follow-up (see Figure 1). These findings support the efficacy of short-term treatment with EMDR in the resolution of traumatic sequelae associated with adult-onset trauma. In contrast, for most individuals with childhood-onset trauma (all of whom, in this study, were victims of chronic intrafamilial physical and/or sexual abuse), 8 weeks of therapy was not enough to resolve longstanding trauma imprints and adaptations.

In contrast to the EMDR condition, the outcome for participants in the fluoxetine condition did not vary as a function of trauma onset. Whereas participants in the fluoxetine condition exhibited a robust decrease in PTSD symptomatology, significantly fewer were entirely asymptomatic at posttreatment, and none remained asymptomatic at 6-month follow-up. This distinction is important, since recent research has revealed that patients with subthreshold PTSD have similar degrees of impairment in social and work functioning as those with full-blown PTSD.[52,53] This suggests that brief treatment with an SSRI alone is insufficient to resolve posttraumatic psychopathology for most patients with PTSD.

At 6-month follow-up, fluoxetine treatment produced a significantly larger effect size than EMDR for the subgroup of individuals with child-onset trauma. This was primarily due to the smaller standard deviation within the fluoxetine condition. Whereas EMDR participants with child-onset trauma varied markedly in PTSD symptomatology at follow-up (e.g., some were completely asymptomatic while others showed little progress or slight worsening of symptoms), child-onset PTSD participants who received fluoxetine experienced a more consistently modestly positive response to pharmacotherapy than to EMDR. This suggests that, while brief intervention with fluoxetine is unlikely to resolve PTSD for adults with

child-onset trauma, it provides moderate symptom reduction, with little risk of symptom exacerbation.

In this study, fluoxetine did not do better than placebo, not because participants receiving fluoxetine did not improve but because the placebo response in this study was so robust. Recent studies have shown that patients who receive prolonged treatment with an SSRI (beyond the customary 8- to 12-week studies) are likely to experience a gradual decrease in PTSD symptomatology.[54,55] In one study,[55] 32 weeks of treatment with sertraline achieved an end state comparable to that seen in the EMDR condition in the present study. However, that long-term study did not address the issue of whether improvement was sustained after cessation of the medication.

Clearly, more data are needed to determine which patients with chronic childhood trauma and/or multiple comorbidities will respond best to trauma processing/exposure-based therapies versus long-term pharmacologic treatment. Studies are also needed to establish whether there is a synergistic effect between pharmacotherapy and exposure therapy for PTSD, a combination that is common in clinical practice, but whose efficacy has not yet been documented.

CONCLUSIONS

Patients with trauma histories, PTSD, and depression are ubiquitous in clinical practice. This study demonstrates that the vast majority of patients with adult-onset PTSD can recover with a short period of intense, exposure-based treatment, with lasting positive results. Merely paying careful attention to the patients' symptoms, as was done here in the placebo condition, as well as treating with SSRIs, can be helpful, particularly in patients with childhood-onset trauma. However, these approaches do not lead to complete symptom remission and the benefits do not endure with time. The present study supports the empirical literature that proposes that skilled confrontation with traumatic memories within a safe therapeutic setting is the treatment of choice for PTSD with adult-onset trauma. Future research should assess the impact of lengthier interventions, combination treatments, and treatment sequencing on the resolution of PTSD in adults with childhood-onset trauma.

Drug names: fluoxetine (Prozac and others), sertraline (Zoloft and others).

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