

# Treatment of Acute Stress Disorder

## A Randomized Controlled Trial

Richard A. Bryant, PhD; Julie Mastrodomenico, MPPsychol; Kim L. Felmingham, PhD; Sally Hopwood, MPPsychol; Lucy Kenny, PhD; Eva Kandris, MPPsychol; Catherine Cahill, MPPsychol; Mark Creamer, PhD

**Context:** Recent trauma survivors with acute stress disorder (ASD) are likely to subsequently develop chronic posttraumatic stress disorder (PTSD). Cognitive behavioral therapy for ASD may prevent PTSD, but trauma survivors may not tolerate exposure-based therapy in the acute phase. There is a need to compare nonexposure therapy techniques with prolonged exposure for ASD.

**Objective:** To determine the efficacy of exposure therapy or trauma-focused cognitive restructuring in preventing chronic PTSD relative to a wait-list control group.

**Design, Setting, and Participants:** A randomized controlled trial of civilians who experienced trauma and who met the diagnostic criteria for ASD (N=90) seen at an outpatient clinic between March 1, 2002, and June 30, 2006.

**Intervention:** Patients were randomly assigned to receive 5 weekly 90-minute sessions of either imaginal and in vivo exposure (n=30) or cognitive restructuring (n=30), or assessment at baseline and after 6 weeks (wait-list group; n=30).

**Main Outcome Measures:** Measures of PTSD at the 6-month follow-up visit by clinical interview and self-

report assessments of PTSD, depression, anxiety, and trauma-related cognition.

**Results:** Intent-to-treat analyses indicated that at post-treatment, fewer patients in the exposure group had PTSD than those in the cognitive restructuring or wait-list groups (33% vs 63% vs 77%;  $P=.002$ ). At follow-up, patients who underwent exposure therapy were more likely to not meet diagnostic criteria for PTSD than those who underwent cognitive restructuring (37% vs 63%; odds ratio, 2.10; 95% confidence interval, 1.12-3.94;  $P=.05$ ) and to achieve full remission (47% vs 13%; odds ratio, 2.78; 95% confidence interval, 1.14-6.83;  $P=.005$ ). On assessments of PTSD, depression, and anxiety, exposure resulted in markedly larger effect sizes at posttreatment and follow-up than cognitive restructuring.

**Conclusions:** Exposure-based therapy leads to greater reduction in subsequent PTSD symptoms in patients with ASD when compared with cognitive restructuring. Exposure should be used in early intervention for people who are at high risk for developing PTSD.

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**Author Affiliations:** School of Psychology, University of New South Wales (Drs Bryant, Felmingham, and Kenny and Mss Mastrodomenico, Hopwood, Kandris, and Cahill), Sydney; and Department of Psychiatry, University of Melbourne, Melbourne (Dr Creamer), Australia.

**P**OSTTRAUMATIC STRESS DISORDER (PTSD) is a potentially debilitating anxiety disorder that affects at least 10% of people who experience traumatic events.<sup>1</sup> The disorder is associated with mental and physical comorbid conditions,<sup>2</sup> reductions in quality of life,<sup>3</sup> and economic burden.<sup>4</sup> In recent years, there has been much attention paid to possible early intervention strategies to prevent PTSD. There is convergent evidence that trauma-focused cognitive behavioral therapy is an efficacious treatment for PTSD.<sup>5,6</sup> Cognitive behavioral therapy has been adapted to prevent PTSD by providing brief forms of treatment in the initial month after trauma exposure. Studies that have provided abridged cognitive behav-

ioral therapy to people with acute symptoms have found that it can accelerate recovery.<sup>7-9</sup> Other articles have focused on patients with acute stress disorder (ASD) because prospective studies demonstrate that these individuals are most likely to develop chronic PTSD.<sup>10</sup> A series of studies has found that 5 therapy sessions comprising prolonged exposure (PE) and cognitive restructuring (CR) are efficacious in preventing PTSD in patients with ASD in the initial month after trauma exposure,<sup>11-14</sup> and these treatment gains are maintained as long as 4 years after treatment.<sup>15,16</sup>

An outstanding issue for the field of early intervention is the type of key therapeutic intervention that should be provided. All previous early interventions have

**Table 1. Participant Characteristics**

Characteristic	Prolonged Exposure Group	Cognitive Restructuring Group	Wait-list Group	Test	P Value
Age, mean (SD), y	37.9 (15.6)	33.7 (15.1)	34.7 (11.4)	$F_{99} = 0.68$	.51
Days since trauma, mean (SD)	19.4 (8.9)	20.8 (7.4)	22.4 (7.4)	$F_{99} = 1.07$	.35
NART Score, mean (SD)	25.3 (8.4)	28.2 (5.7)	28.1 (7.0)	$F_{99} = 0.43$	.41
Ethnicity, No. (%)					
White	27 (90)	26 (87)	25 (83)	$\chi^2 = .059$	.75
Asian	3 (10)	4 (13)	5 (17)		
Sex, No. (%)					
Men	11 (37)	12 (40)	15 (50)	$\chi^2 = 1.18$	.55
Women	19 (63)	18 (60)	15 (50)		
Single, No. (%)	18 (60)	16 (53)	11 (37)	$\chi^2 = 1.10$	.67
Employed, No. (%)	23 (77)	24 (80)	24 (82)	$\chi^2 = 0.64$	.79
Trauma type, No. (%)					
MVC	8 (27)	10 (33)	15 (50)	$\chi^2 = 1.20$	.57
Assault	22 (73)	20 (67)	15 (50)		
Comorbid MDD, No. (%)	15 (50)	13 (43)	14 (47)	$\chi^2 = 0.78$	.42
Comorbid anxiety disorder, No. (%)	2 (6)	1 (3)	1 (3)	$\chi^2 = 0.78$	.52
Comorbid substance use disorder, No. (%)	0	1 (3)	1 (3)	$\chi^2 = 0.88$	.82
Logic of treatment rating, mean (SD) <sup>a</sup>	7.5 (1.4)	7.8 (1.4)	NA	$F_{99} = 0.56$	.46
Expectancy (confidence) rating, mean (SD) <sup>b</sup>	7.2 (1.7)	7.1 (1.8)	NA	$F_{99} = 0.07$	.86

Abbreviations: MDD, major depressive disorder; MVC, motor vehicle crash; NA, not applicable; NART, National Adult Reading Test.

<sup>a</sup>Logic of treatment was rated on a 10-point scale: 1, not at all logical; 10, extremely logical.

<sup>b</sup>From credibility/expectancy questionnaire.

included PE and CR. Some commentators have suggested that PE may not be the optimal strategy because of the distress that it elicits.<sup>17</sup> Furthermore, there is evidence that many mental health care providers do not use exposure therapy for trauma survivors because it causes distress.<sup>18</sup> These factors point to the need for study of the relative efficacy of exposure-based and non-exposure-based therapy for patients with ASD. The major alternative to PE is CR, which involves identification and modification of maladaptive appraisals of the traumatic event, one's response to the experience, and the future. There is much evidence that maladaptive appraisals are characteristic of ASD<sup>19,20</sup> and are strongly predictive of subsequent PTSD.<sup>21</sup> Moreover, CR can be effective in treating chronic PTSD.<sup>22</sup> Accordingly, it is logical to expect that CR could be beneficial in treating ASD.

The goal of this randomized controlled trial was to conduct the first evaluation of PE vs CR in the treatment of ASD. These 2 treatment conditions were compared with a wait-list control group, in which patients were assessed at baseline and again 6 weeks later, to determine the efficacy of PE and CR relative to no treatment. Patients in the wait-list group were then offered active treatment, and patients in the PE and CR groups were subsequently assessed 6 months after treatment. We focused on patients with ASD because, although this diagnosis fails to identify many people who will develop chronic PTSD,<sup>23</sup> most studies indicate that people who do meet criteria for ASD are likely to develop persistent PTSD.<sup>24-28</sup>

## METHODS

### PATIENTS

Participants were consecutive civilian trauma survivors who were referred to the Westmead Hospital Traumatic Stress Clinic fol-

lowing a nonsexual assault or motor vehicle crash between March 1, 2002, and June 30, 2006. Patients who were involved in a motor vehicle crash or nonsexual assault in the previous month and had a primary diagnosis of ASD were included in the study. Exclusion criteria included history of psychosis, organic brain syndrome, current substance dependence, borderline personality disorder, suicidal risk, inability to converse in English, or age younger than 17 or older than 70 years. Participants were initially screened by telephone, and full assessments were conducted only for participants who did not report any exclusion criteria during the telephone screening. All participants provided written informed consent approved by the Westmead Hospital Human Research Ethics Committee. The characteristics of the sample are presented in **Table 1**.

## MEASURES

### Diagnostic Interview

Clinical psychologists diagnosed ASD using the Acute Stress Disorder Interview.<sup>29</sup> This structured clinical interview is based on DSM-IV criteria for ASD and contains 19 dichotomously scored items that relate to ASD symptoms. The Acute Stress Disorder Interview has high test-retest reliability ( $r = 0.95$ ), sensitivity (92%), and specificity (93%).<sup>29</sup> To ensure initial ASD assessments were conducted reliably, 25 of 145 (17%) assessments were conducted by 2 independent master's-degree-level clinical psychologists (J.M., K.L.F., S.H., L.K., E.K., and C.C.). The interrater reliability of the 2 assessments in terms of diagnostic decision was 100%. Symptoms of PTSD were assessed using the Clinician-Administered PTSD Scale 2 (CAPS-2).<sup>30</sup> The CAPS-2 is a structured clinical interview that assesses the 17 symptoms described in the DSM-IV PTSD criteria. The severity and frequency of each symptom during the past week are rated on a 5-point scale. The CAPS-2 was used at the baseline assessment to provide consistency with posttreatment and follow-up assessments of PTSD. Comorbid Axis I disorders were assessed by the Structured Clinical Interview for DSM-IV.<sup>31</sup>

## Self-Report Assessments

Additional psychopathological assessments included the Beck Anxiety Inventory (BAI),<sup>32</sup> the Beck Depression Inventory 2 (BDI-2),<sup>33</sup> the Impact of Event Scale (IES),<sup>34</sup> and the Posttraumatic Cognitions Inventory (PTCI)<sup>35</sup> to quantify cognitive responses to trauma. The PTCI is a 36-item self-report scale that yields 3 factors: negative cognitions about self (PTCI-Self), negative cognitions about the world (PTCI-World), and self-blame (PTCI-Self-Blame).<sup>35</sup> At the completion of session 1 and after the rationale had been explained, patients completed the Credibility/Expectancy Questionnaire.<sup>36</sup> Specifically, patients in the PE or CR groups rated their confidence in the treatment (1, not at all confident; 10, extremely confident) and the logic of the treatment (1, not at all logical; 10, extremely logical). To obtain an estimate of verbal intelligence, participants were also administered the National Adult Reading Test before treatment.<sup>37</sup> All assessments were administered at each session, except for the Acute Stress Disorder Interview, therapy confidence and logic ratings, and the National Adult Reading Test, which were only administered at baseline. In addition, at the completion of each therapy session, participants in the PE and CR groups were required to rate their subjective level of distress on a 100-point scale (1, not at all distressed; 100, extremely distressed).

## PROCEDURE

Participants were informed that they would be randomly allocated to 1 of 3 treatment conditions. Randomization was conducted by a process of minimization stratified by sex, trauma type, and Acute Stress Disorder Interview score. Participants were assigned to groups using a random numbers system administered by an individual who worked at a site that was distant from the treatment center and was not otherwise involved with the study. Every 6 months, allocation was amended by the independent assigner to ensure that sex, trauma type, and ASD severity were balanced across conditions. If patients began taking medication after commencing treatment, they were dropped from the study to ensure that observed changes could not be attributed to medication. A total of 90 patients were randomized into the study and were allocated to either the PE (n=30), CR (n=30), or wait-list control (n=30) groups (**Figure 1**); 69 participants (77%) completed treatment, and 42 of 60 patients in the PE and CR groups (70%) completed the 6-month follow-up assessment.

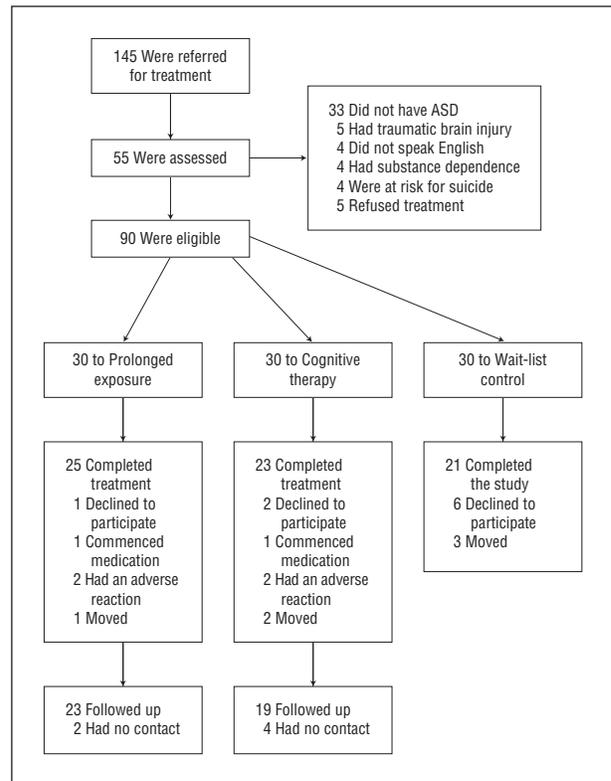
Initial assessments were conducted at the pretreatment session, before randomization. Posttreatment and 6-month follow-up assessments were conducted by independent clinical psychologists (J.M., K.L.F., S.H., L.K., E.K., and C.C.) who were unaware of the participants' treatment groups. Blindness was maintained by ensuring that clinicians who conducted assessments did not have access to participants' medical records or group allocation.

## TREATMENT CONDITIONS

Individual therapy was conducted by 1 of 6 experienced master's-degree-level clinical psychologists (J.M., K.L.F., S.H., L.K., E.K., or C.C.) who were trained to use treatment manuals and who received weekly supervision (R.A.B.). All therapists provided each type of treatment. Treatment comprised 5 once-weekly 90-minute sessions with structured daily homework activities.

### Prolonged Exposure

Session 1 focused on psychoeducation, training in breathing control, the rationale of exposure, and conducting the initial imaginal exposure. The exposure exercise occurred for 50 min-



**Figure 1.** Patient enrollment, randomization, and treatment. ASD indicates acute stress disorder.

utes, and patients were instructed to verbalize reliving the trauma experience in a vivid manner that involved all perceptual and emotional details. Imaginal exposure was not audiotaped, but participants were given explicit instructions on how to complete the exercise. Participants engaged in imaginal exposure on a daily basis for homework. Session 2 included review of homework, introduction of in vivo exposure, and a 50-minute session of imaginal exposure. Session 3 included review of homework and completion of hierarchy for in vivo exposure. Following this session, participants completed imaginal exposure and in vivo exposure for daily homework. Session 4 included review of homework, imaginal exposure, and review of in vivo exposure. Session 5 was identical to Session 4, with the addition of relapse prevention strategies that instructed participants to rehearse the strategies learned during therapy whenever they perceived increases in PTSD symptoms.

### Cognitive Restructuring

Session 1 focused on psychoeducation and the introduction of CR. Session 2 comprised identification of maladaptive thoughts about the traumatic event and the person's responses to the event and to issues occurring in the posttrauma environment; at this point, patients began monitoring automatic thoughts as daily homework. Session 3 included review of homework and CR. Cognitive restructuring involved daily monitoring of thoughts and affective states, modifying thoughts by Socratic questioning, probabilistic reasoning, and evidence-based thinking.<sup>38</sup> The common themes of CR involved addressing catastrophic appraisals of future harm, guilt about one's behavior during the trauma, and excessive appraisals about one's capacity to cope with the stress reactions. Following this session, patients engaged in CR as daily homework. Session 4 included review of homework and more CR. Session 5 was identical to session 4, with the addition of relapse prevention strategies.

Following initial assessment, patients were informed that they would be reassessed after 6 weeks and then offered active treatment. The second assessment for this group was timed to coincide with the posttreatment assessment of the PE and CR groups.

### TREATMENT FIDELITY

Of 264 therapy sessions, audiotapes of 45 (17%) were randomly selected and rated by 3 clinical psychologists experienced in cognitive behavioral therapy who were not otherwise involved with the study. Raters listened to audiotapes and determined the presence or absence of each of 34 treatment components, without regard to treatment group or session number. Raters also indicated the quality of the therapy provided on a 7-point scale (1, unacceptable; 7, very good). No PE session included CR, and no CR session included PE. The mean (SD) quality rating for treatment components in all groups was 5.8 (1.8).

### DATA ANALYSIS

To determine the relative effects of the 3 treatment conditions, we performed multivariate analyses of covariance (MANCOVAs) for each of the 2 sets of continuous assessments (PTSD symptoms and associated symptoms) using the pretreatment scores as covariates. If multivariate effects of condition were significant, we conducted univariate ANCOVAs and tested differences between groups using Tukey comparisons. We report completer analyses and intent-to-treat analyses, in which we used the last observation carried forward procedure. Treatment effect sizes were between treatment conditions at posttreatment and follow-up. We derived Cohen *d* effect size by calculating the mean difference between assessments of each treatment condition and dividing this by the pooled standard deviation.<sup>39</sup> We used Hedges *g* effect sizes to correct for variations caused by small sample sizes.<sup>40</sup> Finally, we calculated high end-state adjustment as being below specific cutoff scores for PTSD, depression, and anxiety scales at the follow-up assessment. We adopted a conservative estimate of good end-state adjustment for PTSD by following an established cutoff score of 19 on the CAPS-2 (combining frequency and intensity scores) to indicate the absence of PTSD,<sup>41</sup> a cutoff of 10 on the BDI-2,<sup>42</sup> and a cutoff of 12 on the BAI.<sup>43</sup> To estimate the number of patients required in the PE group for 1 patient to achieve a response outcome that would not have been achieved with CR, we calculated the number of patients needed to treat as 1 divided by the proportion responding to PE. Efficacious treatments typically have a number needed to treat between 2 and 4.<sup>44</sup>

## RESULTS

### PRELIMINARY ANALYSES

Planned comparisons of treatment completers and treatment dropouts indicated no differences between those who did and did not drop out of treatment on any pretreatment psychopathological or demographic variables. There were 5 reported adverse effects; 3 patients became overly distressed during exposure therapy and 2 dropped out of treatment. In addition, 2 patients dropped out of CR because they became distressed during CR sessions.

**Table 2** presents the mean psychopathological assessment scores for the completer sample. The MANCOVA for posttreatment scores of PTSD symptoms indicated a significant main effect ( $F_{6,122}=6.00$ ;  $P<.001$ ). Follow-up ANCOVAs indicated main effects for CAPS-2 ( $F_{2,62}=12.58$ ;  $P<.001$ ), IES-Intrusions ( $F_{2,62}=13.54$ ;  $P<.001$ ), and IES-Avoidance ( $F_{2,62}=10.29$ ;  $P<.001$ ). Post hoc Tukey comparisons indicated that patients in the PE group scored lower than patients in the wait-list group on CAPS-2 ( $P<.001$ ), IES-Intrusions ( $P=.002$ ), and IES-avoidance ( $P<.001$ ). Furthermore, patients in the PE group scored lower than patients in the CR group on IES-Intrusions ( $P=.03$ ). Patients in the CR group did not differ from the wait-list group on any variable. The MANCOVA for posttreatment scores of associated symptoms indicated a significant main effect ( $F_{10,116}=2.76$ ;  $P=.003$ ). Follow-up ANCOVAs indicated main effects for the BDI-2 ( $F_{2,61}=4.68$ ;  $P=.02$ ), BAI ( $F_{2,61}=5.59$ ;  $P=.003$ ), PTCI-Self ( $F_{2,61}=5.79$ ;  $P=.002$ ), PTCI-World ( $F_{2,61}=3.53$ ;  $P=.04$ ), and PTCI-Self-Blame ( $F_{2,61}=3.82$ ;  $P=.04$ ). Post hoc Tukey comparisons indicated that patients in the PE group scored lower than patients in the wait-list group on the BDI-2 ( $P=.03$ ), BAI ( $P=.03$ ), PTCI-Self ( $P=.008$ ), and PTCI-Self-Blame ( $P=.03$ ). Furthermore, patients in the PE group scored lower than patients in the CR group on the BDI-2 ( $P=.03$ ) and BAI ( $P=.007$ ). Patients in the CR group did not differ from those in the wait-list group on any variable. In follow-up analyses, the MANCOVA for PTSD symptoms indicated a significant main effect ( $F_{3,34}=2.88$ ;  $P=.04$ ). Follow-up ANCOVAs indicated main effects for CAPS-2 ( $F_{1,36}=8.42$ ;  $P=.006$ ), IES-Intrusions ( $F_{1,36}=6.56$ ;  $P=.02$ ), and IES-Avoidance ( $F_{1,36}=6.51$ ;  $P=.008$ ). Post hoc Tukey comparisons indicated that patients in the PE group scored lower than patients in the CR group on CAPS-2 ( $P=.007$ ), IES-Intrusions ( $P=.007$ ), and IES-Avoidance ( $P=.009$ ). The MANCOVA for follow-up scores of associated symptoms indicated a non-significant main effect ( $F_{5,49}=1.22$ ;  $P=.31$ ).

At posttreatment, fewer patients in the PE group (3 [12%]) met criteria for PTSD than patients in the CR (12 [52%]) ( $\chi^2_4=9.00$ ; odds ratio [OR], 8.00; 95% confidence interval [CI], 1.86-34.36;  $P=.003$ ) or wait-list (15 [71%]) ( $\chi^2_5=15.90$ ; OR, 17.11; 95% CI, 3.67-76.76;  $P<.001$ ) group. At follow-up, fewer participants in the PE group (3 [14%]) met criteria for PTSD than in the CR group (9 [47%]) ( $\chi^2_4=5.60$ ; OR, 5.70; 95% CI, 1.25-25.91;  $P=.02$ ). In terms of follow-up status, the number needed to treat was 2.96.

**Table 3** shows effect sizes for PTSD and other psychopathological assessment scores between treatment groups. According to Cohen's descriptors of effect sizes, effect sizes where *d* is greater than 0.80 are large.<sup>39</sup> Among completers, PE achieved large effect sizes and CR achieved moderate effect sizes relative to the wait-list group at posttreatment on most assessments. At follow-up, the PE group achieved large effect sizes relative to the CR group for PTSD symptoms. In addition, nearly 3 times as many participants in the PE group (14 [61%]) as in the CR group (4 [21%]) achieved high end-state functioning at follow-up ( $\chi^2_3=5.04$ ; OR, 5.76; 95% CI, 1.17-8.25;  $P=.05$ ).

**Table 2. Psychopathological Assessments for Intent-to-Treat and Completer Analyses<sup>a</sup>**

Assessment	Intent-to-Treat			Completer		
	Prolonged Exposure Group (n = 30)	Cognitive Restructuring Group (n = 30)	Wait-list Group (n = 30)	Prolonged Exposure Group (n = 25)	Cognitive Restructuring Group (n = 23)	Wait-list Group (n = 21)
<b>Pretreatment Score</b>						
CAPS-2 Total	70.6 (17.7)	66.8 (19.0)	63.6 (18.3)	71.4 (18.0)	66.9 (17.8)	61.3 (18.2)
IES-Intrusions	26.9 (8.5)	26.3 (8.2)	23.5 (9.1)	26.2 (9.0)	26.8 (8.0)	22.7 (9.8)
IES-Avoidance	26.9 (9.3)	23.6 (9.9)	24.0 (8.7)	26.6 (10.1)	23.4 (10.6)	23.2 (10.1)
BAI	23.1 (12.6)	27.5 (12.3)	22.2 (11.2)	21.6 (11.6)	27.3 (12.6)	20.0 (11.1)
BDI-2	22.1 (11.0)	24.2 (8.2)	23.8 (12.0)	22.3 (11.3)	24.6 (8.9)	21.5 (12.2)
PTCI-Self	3.5 (1.2)	3.2 (1.1)	3.3 (1.6)	3.5 (1.3)	3.1 (1.1)	2.9 (1.6)
PTCI-World	5.3 (1.2)	5.0 (1.2)	4.6 (1.7)	5.2 (1.6)	4.9 (1.2)	4.4 (1.9)
PTCI-Self-Blame	2.5 (1.4)	2.8 (1.7)	2.7 (1.5)	2.7 (1.4)	2.7 (1.5)	2.5 (1.6)
<b>Posttreatment Score</b>						
CAPS-2 Total	31.5 (27.3)	43.0 (27.6)	55.9 (23.1)	24.4 (23.1)	35.8 (24.7)	50.1 (22.9)
IES-Intrusions	12.4 (12.5)	17.7 (11.3)	22.1 (9.8)	8.8 (10.3)	15.2 (10.8)	20.7 (10.6)
IES-Avoidance	11.7 (12.4)	17.1 (12.4)	22.6 (10.8)	8.4 (10.5)	14.6 (12.6)	21.0 (12.4)
BAI	13.4 (15.3)	23.4 (14.2)	19.6 (13.7)	9.5 (11.4)	21.0 (13.9)	15.9 (13.1)
BDI-2	12.1 (11.8)	18.9 (13.3)	21.9 (13.8)	10.4 (11.5)	17.0 (14.1)	18.6 (13.9)
PTCI-Self	2.4 (1.3)	2.7 (1.5)	3.4 (1.6)	2.2 (1.4)	2.7 (1.5)	3.1 (1.7)
PTCI-World	4.4 (2.0)	4.6 (1.7)	4.8 (1.6)	4.1 (2.0)	4.2 (1.7)	4.7 (1.8)
PTCI-Self-Blame	2.0 (1.2)	2.3 (1.6)	2.8 (1.6)	1.9 (1.2)	1.9 (1.0)	2.6 (1.7)
<b>Follow-up Score</b>						
CAPS-2 Total	32.1 (29.1)	49.8 (29.4)	NA	21.4 (24.1)	44.3 (28.5)	NA
IES-Intrusions	11.4 (11.2)	18.6 (11.4)	NA	6.9 (7.4)	15.0 (10.7)	NA
IES-Avoidance	12.8 (13.5)	19.2 (12.0)	NA	7.6 (7.7)	16.3 (10.8)	NA
BAI	12.8 (16.1)	23.3 (16.7)	NA	8.6 (11.7)	17.6 (16.7)	NA
BDI-2	12.4 (13.1)	20.4 (13.1)	NA	10.1 (12.9)	15.3 (12.9)	NA
PTCI-Self	2.4 (1.4)	3.1 (1.6)	NA	2.3 (1.5)	2.6 (1.6)	NA
PTCI-World	4.4 (2.0)	4.8 (1.7)	NA	3.9 (2.0)	4.4 (1.9)	NA
PTCI-Self-Blame	2.0 (1.2)	2.4 (1.5)	NA	1.9 (1.1)	2.0 (1.2)	NA

Abbreviations: BAI, Beck Anxiety Inventory; BDI-2, Beck Depression Inventory 2; CAPS-2, Clinician-Administered PTSD Scale 2; IES, Impact of Event Scale; NA, not applicable; PTCI, Posttraumatic Cognitions Inventory; PTSD, posttraumatic stress disorder.

<sup>a</sup>Data are given as mean (SD).

## DISTRESS RATINGS

**Figure 2** presents the mean distress ratings reported by participants in the PE and CR groups at the beginning of each therapy session. A 2 (treatment condition) × 5 (session) repeated-measures analysis of variance indicated significant main effects for treatment condition ( $F_{1,46} = 14.52$ ;  $P < .001$ ), session ( $F_{4,43} = 16.62$ ;  $P < .001$ ), and a significant interaction effect ( $F_{4,43} = 3.72$ ;  $P = .04$ ). Specifically, patients in the PE group reported lower distress ratings than patients in the CR group at the completion of session 3 ( $P = .002$ ), session 4 ( $P < .001$ ), and session 5 ( $P = .003$ ).

## INTENT-TO-TREAT ANALYSES

Table 2 and **Figure 3** also present the mean psychopathological scores for the intent-to-treat sample. The MANCOVA for posttreatment scores of PTSD symptoms indicated a significant main effect ( $F_{6,164} = 4.29$ ;  $P < .001$ ). Follow-up analyses of covariance indicated main effects for CAPS-2 ( $F_{2,83} = 12.62$ ;  $P < .001$ ), IES-Intrusions ( $F_{2,83} = 11.34$ ;  $P < .001$ ), and IES-Avoidance ( $F_{2,83} = 10.02$ ;  $P < .001$ ). Post hoc Tukey comparisons indicated that patients in the PE group scored lower than

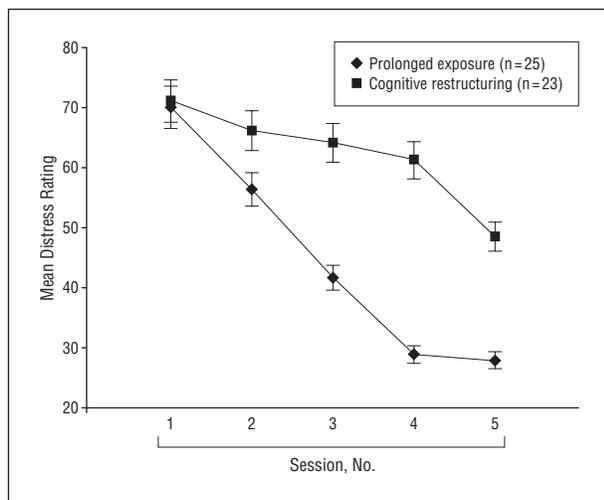
those in the wait-list group on CAPS-2 ( $P < .001$ ), IES-Intrusions ( $P = .001$ ), and IES-Avoidance ( $P < .001$ ). Patients in the CR group did not differ from patients in the wait-list group on any variable. The MANCOVA for posttreatment scores of associated symptoms indicated a significant main effect ( $F_{10,158} = 2.53$ ;  $P = .009$ ). Follow-up ANCOVAs indicated main effects for the BDI-2 ( $F_{2,82} = 7.21$ ;  $P < .001$ ), BAI ( $F_{2,82} = 5.85$ ;  $P = .003$ ), PTCI-Self ( $F_{2,82} = 8.56$ ;  $P < .001$ ), PTCI-World ( $F_{2,82} = 4.09$ ;  $P = .03$ ), and PTCI-Self-Blame ( $F_{2,82} = 3.15$ ;  $P = .04$ ). Post hoc Tukey comparisons indicated that patients in the PE group scored lower than those in the wait-list group on the BDI-2 ( $P = .003$ ), BAI ( $P = .004$ ), PTCI-Self ( $P = .009$ ), and PTCI-Self-Blame ( $P = .03$ ). Furthermore, patients in the PE group scored lower than patients in the CR group on the BAI ( $P = .008$ ). Patients in the CR group did not differ from patients in the wait-list group on any variable.

In terms of follow-up analyses, the MANCOVA for PTSD symptoms indicated a significant main effect ( $F_{3,34} = 2.88$ ;  $P = .04$ ). Follow-up ANCOVAs indicated main effects for CAPS-2 ( $F_{1,36} = 8.42$ ;  $P = .006$ ), IES-Intrusions ( $F_{1,36} = 6.56$ ;  $P = .008$ ), and IES-Avoidance ( $F_{1,36} = 6.51$ ;  $P = .0081$ ). Post hoc Tukey comparisons indicated that patients in the PE group scored lower than patients in the

**Table 3. Effect Sizes on Outcome Measures for Intent-to-Treat and Completer Analyses**

Characteristic	Effect Size (95% Confidence Interval)			
	Posttreatment			Follow-up
	PE vs WL	CR vs WL	PE vs CR	PE vs CR
Intent-to-treat				
CAPS-2	0.95 (0.42-1.49)	0.50 (-0.01 to 1.10)	0.42 (-0.09 to 0.92)	0.60 (0.08-1.11)
IES-Intrusions	0.85 (0.32-1.38)	0.41 (-0.10 to 0.92)	0.44 (-0.07 to 0.95)	0.63 (0.11-1.15)
IES-Avoidance	0.93 (0.39-1.46)	0.47 (-0.04 to 0.98)	0.43 (-0.08 to 0.94)	0.44 (-0.02 to 1.01)
BAI	0.42 (0.09-0.93)	0.27 (-0.24 to 0.78)	0.67 (0.15-1.19)	0.63 (0.11-1.15)
BDI-2	0.75 (0.23-1.27)	0.22 (-0.29 to 0.73)	0.54 (0.01-1.05)	0.60 (0.09-1.12)
Completer				
CAPS-2	1.10 (0.48-1.72)	0.59 (-0.01 to 1.93)	0.47 (-0.10 to 1.04)	0.86 (0.27-1.45)
IES-Intrusions	1.12 (0.50-1.74)	0.50 (-0.10 to 1.11)	0.59 (0.02-1.76)	0.87 (0.28-1.47)
IES-Avoidance	1.10 (0.46-1.71)	0.54 (-0.09 to 1.10)	0.53 (-0.05 to 1.10)	0.92 (0.52-1.51)
BAI	0.52 (-0.07 to 1.11)	0.27 (-0.23 to 0.97)	0.89 (0.29-1.50)	0.62 (0.04-1.20)
BDI-2	0.63 (0.04-1.23)	0.11 (-0.48 to 0.70)	0.51 (-0.07 to 1.08)	0.37 (0.18-0.97)

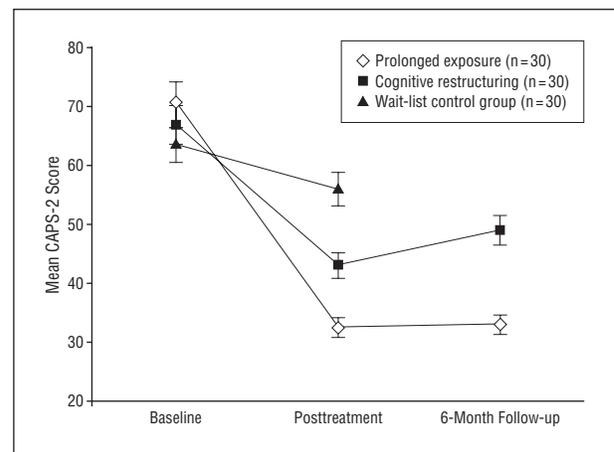
Abbreviations: BAI, Beck Anxiety Inventory; BDI-2, Beck Depression Inventory 2; CAPS-2, Clinician-Administered PTSD Scale 2; CR, cognitive restructuring; IES, Impact of Event Scale; PE, prolonged exposure; PTSD, posttraumatic stress disorder; WL, wait-list.



**Figure 2.** Changes in total scores on the Clinician-Administered Posttraumatic Stress Disorder Scale 2 (CAPS-2) for intent-to-treat analysis. Standard errors are displayed in error bars.

CR group on CAPS-2 ( $P=.03$ ), IES-Intrusions ( $P=.02$ ), and IES-Avoidance ( $P=.03$ ). The MANCOVA for follow-up scores of associated symptoms indicated a nonsignificant main effect ( $F_{5,49} = 1.22$ ;  $P = .31$ ).

The last observation carried forward method presumes that participants who drop out remain unchanged and that their pretreatment values are relevant indicators of posttreatment symptom levels. This approach is potentially problematic with ASD because of the documented tendency for symptoms to abate over time.<sup>10</sup> The tendency for more patients in the wait-list group to drop out vs other participants may provide an overestimation of the efficacy of the active treatments at posttreatment using the last observation carried forward method. Accordingly, we conducted an additional analysis that presumed all noncompleters in all groups improved as much as completers in the wait-list group and repeated the analyses in this subsection on CAPS-2 and IES scores. On the basis that wait-list



**Figure 3.** Mean distress ratings for each session as a function of treatment group for treatment completers. Standard errors are displayed in error bars.

completers improved 0.6 SD of their initial CAPS-2 scores and 0.09 SD of their initial IES scores, we calculated these rates of recovery for all noncompleters. The ANCOVAs for posttreatment scores indicated significant effects for CAPS-2 ( $F_{2,82} = 12.92$ ;  $P < .001$ ), IES-Intrusions ( $F_{2,86} = 11.84$ ;  $P < .001$ ), and IES-Avoidance ( $F_{2,86} = 17.06$ ;  $P < .001$ ). Post hoc Tukey comparisons indicated that patients in the PE group scored lower than patients in the wait-list group on CAPS-2 ( $P < .001$ ), IES-Intrusions ( $P < .002$ ), and IES-Avoidance ( $P < .001$ ). Patients in the CR group scored lower than patients in the wait-list group on CAPS-2 ( $P = .03$ ). These results confirm the finding that PE, and to a lesser extent CR, resulted in greater symptom reduction than in the wait-list group.

Intent-to-treat analyses indicated that at posttreatment fewer patients in the PE group (10 [33%]) met criteria for PTSD than patients in the CR (19 [63%]) ( $\chi^2_{60} = 9.78$ ;  $P = .002$ ; OR, 2.52; 95% CI, 1.28-4.93] or wait

list (23 [77%]) ( $\chi^2_{60}=18.49$ ; OR, 3.40; 95% CI, 1.73-6.67;  $P<.001$ ) group. At follow-up, fewer patients in the PE group (11 [37%]) met criteria for PTSD than patients in the CR group (19 [63%]) ( $\chi^2_{60}=6.78$ ; OR, 2.10; 95% CI, 1.12-3.94);  $P=.007$ . In terms of follow-up status, the number needed to treat was 3.75.

Table 3 demonstrates that PE led to larger effect sizes than CR for intent-to-treat and analyses at posttreatment. It should be noted that CR achieved a moderate effect size for most assessments relative to the wait-list group. At follow-up, PE resulted in moderate effect sizes relative to CR on all measures for intent-to-treat analyses. Nearly 4 times as many participants in the PE group (14 [47%]) as in the CR group (4 [13%]) achieved high end-state functioning at follow-up ( $\chi^2_{60}=7.94$ ; OR, 2.78; 95% CI, 1.14-6.83;  $P=.005$ ).

#### COMMENT

This study demonstrates that PE is a more efficacious intervention to prevent chronic PTSD than CR in patients with ASD. Six months after treatment, PE led to greater reductions than CR across PTSD symptoms as measured by independent clinical interviews, as well as self-report assessments of intrusive and avoidance symptoms. Moreover, at follow-up, nearly 4 times as many patients who received PE achieved high end-state functioning compared with those who received CR. Effect sizes for the PE group typically were double those of the CR group relative to the wait-list group. The pattern persisted at follow-up, when PE resulted in moderate effect sizes relative to CR. This suggests that PE probably accounted for many of the therapy gains in previous studies of cognitive behavioral therapy for patients with ASD. We note, however, that the present study compared PE with CR and did not allow for a comparison against the additive effects of PE and CR.

Despite some concerns that patients may not be able to manage the distress elicited by PE,<sup>19</sup> there was no difference in drop-out rates for the PE and CR groups (17% vs 23%). The average drop-out rate for PE in PTSD studies was 20.5%, compared with 22.1% for CR.<sup>45</sup> Therefore, the drop-out rates in the present study were comparable to drop-out rates across chronic PTSD treatment studies.

Why would PE result in better outcomes than CR? It has been suggested that PE includes habituations of anxiety triggered by the memory, correction of the belief that anxiety only reduces through avoidance, integration of corrective information into the trauma memory, and self-mastery through management of the exposure exercise,<sup>46,47</sup> whereas CR involves correction of maladaptive appraisals about the trauma and its aftermath, and it is proposed that adapting more appropriate interpretations about the traumatic experience will enhance recovery.<sup>48</sup> The current findings suggest that direct activation of trauma memories is particularly useful for prevention of PTSD symptoms in patients with ASD. This interpretation is in accordance with network models of PTSD that posit that adaptation occurs when the individual repeatedly engages with trauma reminders and learns that there is no aversive outcome.<sup>49</sup>

The finding that distress ratings were more reduced in the PE group vs the CR group after session 3 supports the hypothesis that patients experienced a marked reduction in distress after PE began. Exposure exercises began in session 2, which is also when patients were first assigned homework exercises. It appears that this resulted in reduced distress at the following session; in contrast, patients in the CR group continued to experience significant distress. This pattern underscores the conclusion posited by network models of PTSD that successful treatment of PTSD requires activation of fear memories and that treatment response is reflected in between-session habituation of distress.<sup>50</sup>

We note several limitations to this study. First, our sample was limited to survivors of motor vehicle crashes and nonsexual assaults, and it is questionable whether the findings are generalizable to other traumatized populations. Second, we note that traumatic events can lead to a broad range of psychiatric disorders.<sup>51</sup> We did not assess for Axis I disorders at post-treatment or follow-up assessments, and accordingly we did not examine the influence of therapy on other psychiatric disorders; we also did not record medication use in the period after treatment. Third, we note that using the last observation carried forward method for managing missing data at follow-up is problematic because it may bias the data in unpredictable ways.<sup>52</sup> We note, however, that completer analysis replicated the findings observed in the intent-to-treat analyses. Fourth, we did not require participants to record time spent on homework, and it is difficult to determine whether differential amounts of homework time contributed to outcomes. Finally, we did not assess functioning, and so we were not able to test the influence of treatment of functional levels.

We also note that our use of PE and CR was specific to the current research study, and there are differences in how PE and CR are used in different centers. To maintain the integrity of the research design, we did not permit the CR condition to include any exposure-based activities. It is worth noting that although this approach is consistent with traditional CR,<sup>37</sup> more recent adaptations of cognitive therapy for PTSD have explicitly integrated reliving of trauma memories into the cognitive therapy programs.<sup>53</sup> We note that although our completion rate of 77% is comparable to numerous studies, it is lower than that reported by one previous study; this study used briefer exposure periods integrated with CR, which may have resulted in greater treatment adherence.<sup>53</sup> Similarly, PE protocols often stipulate that exposure should be followed by a discussion of the thoughts that arose during the exposure.<sup>54</sup> Although the present study dictated that the therapist should discuss the patient's reactions to the exposure exercises, the PE manual precluded therapists from explicitly discussing the relationship of thoughts to feelings because this would have diluted the distinction between PE and CR. This adherence to each strategy may have resulted in the treatment gains made by patients being reduced relative to other treatment programs that have included components of both PE and CR in the therapy program. In this context, it is worth noting that cognitive change

as measured by the PTCI was no greater following CR than PE.

It should also be noted that CR was efficacious at posttreatment and follow-up assessments. This finding is expected because of evidence that CR does reduce chronic PTSD symptoms.<sup>24</sup> Although CR was a less effective intervention than PE, we recognize that it does provide an alternate early intervention for patients who are unsuitable for PE or unwilling to participate. Considering that maladaptive appraisals in the acute phase have been shown to be pivotal in the development of ASD,<sup>19,20</sup> and to maintaining chronic PTSD,<sup>21</sup> it may be useful to provide CR to patients in the acute phase to prevent subsequent PTSD.

In summary, these data provide the first evidence that PE is the more efficacious intervention for ASD shortly after trauma. The present study suggests that although CR is a useful early intervention for preventing PTSD, exposure-based therapy is likely to lead to better outcomes. Surveys highlight that many mental health care providers do not use PE for patients who have experienced trauma, apparently because of concerns that they may elicit aversive reactions.<sup>18</sup> This study demonstrates that PE does not lead to greater drop-out rates or aversive responses than CR. Accordingly, there is a need to better educate mental health care providers about the use of PE as a frontline intervention for ASD.

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**Correspondence:** Richard A. Bryant, PhD, School of Psychology, University of New South Wales, Sydney, New South Wales 2052, Australia (R.Bryant@unsw.edu.au).

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