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Randomized Controlled Trial of Prolonged Exposure Using Imaginal Exposure vs. Virtual Reality Exposure in Active Duty Soldiers With Deployment-Related Posttraumatic Stress Disorder (PTSD)

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Objective: Prolonged exposure (PE) is an evidence-based psychotherapy for posttraumatic stress disorder (PTSD) but there is limited research with active-duty military populations. Virtual reality exposure (VRE) has shown promise but randomized trials are needed to evaluate efficacy relative to existing standards of care. This study evaluated the efficacy of VRE and PE for active duty soldiers with PTSD from deployments to Iraq and Afghanistan. ***Method:*** Active-duty soldiers ($N = 162$) were randomized

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Dr. Barbara Rothbaum owns equity in Virtually Better, Inc., which is developing products related to virtual reality, and Dr. Rothbaum is a consultant for Virtually Better, Inc. The terms of this arrangement have been reviewed and approved by Emory University in accordance with its conflict of interest policies. However, the virtual reality used in this study was created by Dr. Skip Rizzo and the ICT lab at USC, not Virtually Better, Inc. Dr. Rothbaum receives royalties from Oxford University Press, Guilford, APPI, and Emory University and received one advisory board payment from Genentech.

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to 10-sessions of PE, VRE, or a minimal attention waitlist (WL). Blinded assessors evaluated symptoms at baseline, halfway through treatment, at posttreatment, and at 3- and 6-month follow-ups using the Clinician Administered PTSD Scale (CAPS). ***Results:*** Intent-to-treat analyses found that both PE and VRE resulted in significant reductions in PTSD symptoms relative to those in the WL. The majority of patients demonstrated reliable change in PTSD symptoms. There was no difference between PE and VRE regarding treatment drop out before completing 10 sessions (44 and 41% for VRE and PE, respectively). Contrary to hypotheses, analyses at posttreatment did not show that VRE was superior to PE. Post hoc analyses found that PE resulted in significantly greater symptom reductions than VRE at 3- and 6-month follow-up. Both treatments significantly reduced self-reported stigma. ***Conclusions:*** PE is an efficacious treatment for active-duty Army soldiers with PTSD from deployments to Iraq or Afghanistan. Results extend previous evidence supporting the efficacy of PE to active-duty military personnel and raise important questions for future research on VRE.

What is the public health significance of this article?
Results provide convergent evidence suggesting that exposure therapy is an effective treatment for active duty U.S. Army soldiers with posttraumatic stress disorder from deployments to Iraq and Afghanistan.

Keywords: exposure therapy, virtual reality, military, posttraumatic stress disorder, Army

Military service members who deployed in support of combat operations in Iraq and Afghanistan are at risk of developing posttraumatic stress disorder (PTSD; Hoge, Auchterlonie, & Milliken, 2006; Hoge et al., 2004; Milliken, Auchterlonie, & Hoge, 2007; Smith et al., 2008). Effective treatments for PTSD have been developed (Institute of Medicine, 2008) and research provides strong evidence supporting the efficacy of exposure therapy (Bradley, Greene, Russ, Dutra, & Westen, 2005; Department of Veterans Affairs & Department of Defense, 2010; Institute of Medicine, 2008).

Prolonged exposure (PE; Foa, Hembree, & Rothbaum, 2007) is a treatment protocol that is based on emotional processing theory (Foa & Kozak, 1986). According to this theory, PTSD involves a pathological fear structure that maintains symptoms and prevents recovery. Treatment by PE requires the activation of the fear structure and incorporation of corrective information via imaginal exposure to the trauma memory and in vivo exposure to safe but feared situations, places, and circumstances. Emotional engagement during imaginal exposure is theoretically important to treatment outcome (Foa, Huppert, & Cahill, 2006; Foa, Riggs, Massie, & Yarczower, 1995; Jaycox, Foa, & Morral, 1998). PE has demonstrated efficacy with a range of trauma populations (Powers, Halpern, Ferenschak, Gillihan, & Foa, 2010) and several studies have demonstrated PEs effectiveness in the treatment of military veterans (Rauch et al., 2009; Schnurr et al., 2007; Tuerk, Yoder, Ruggiero, Gros, & Acierno, 2010), including several effectiveness trials among veterans of Operations Iraqi and Enduring Freedom (Eftekhari et al., 2013; Tuerk et al., 2011). However, only limited research exists with regard to efficacy among active-duty military personnel (e.g., Blount, Cigrang, Foa, Ford, & Peterson, 2014; Cigrang, Peterson, & Schobitz, 2005) and even less on service members with trauma from deployments to Iraq or Afghanistan.

Additionally, military members face many barriers to care including the stigma associated with seeking mental health treatment (Hoge, Auchterlonie, & Milliken, 2006; Hoge et al., 2004, 2014). A majority of soldiers and Marines report that receiving mental health services would cause them to be seen as weak or treated differently by leaders (Hoge et al., 2004). While experience with mental health treatment typically reduces stigma in general (Brown et al., 2011), it is possible that a high tech, videogame-like treatment will have added benefits for the young military population who could describe the treatment in terms more acceptable to others (and themselves). Virtual reality (VR) is an advanced form of human-computer interaction that provides the user with the psychological sense of participating in a computer-generated environment. VR has been used during exposure therapy of anxiety disorders to assist in the activation of the fear structure and increase emotional engagement during exposure (Parsons & Rizzo, 2008; Powers & Emmelkamp, 2008). Given the theoretical importance of emotional engagement during exposure (Foa, Huppert, & Cahill, 2006; Jaycox, Foa, & Morral, 1998), multisensory VR may serve as a tool to aid exposure and improve activation relative to imaginal exposure. In addition, given the treatment barrier of stigma it is possible that virtual reality exposure (VRE) offers an important advantage as a more appealing treatment option for some service members relative to traditional therapies. Some military personnel who report an unwillingness to utilize traditional counseling state that they would be willing to use a virtual reality approach to mental health care (Wilson, Onorati, Mishkind, Reger, & Gahm, 2008).

Several studies have reported reductions in PTSD symptoms using VRE, including studies of the treatment of veterans (Rothbaum, Hodges, Ready, Graap, & Alarcon, 2001; Rothbaum et al., 2014), survivors of the World Trade Center collapse (Difede et al., 2007; Difede et al., 2014), and survivors of motor vehicle accidents (Beck, Palyo, Winer, Schwagler, & Ang, 2007). Case reports (Gerardi, Rothbaum, Ressler, Heekin, & Rizzo, 2008; Reger & Gahm, 2008) and small sample effectiveness data (Reger et al., 2011; Rizzo et al., 2011) have reported reductions in PTSD symptoms for VRE in the treatment of active-duty personnel with PTSD. However, none have compared VRE to a standard of care. Although the initial data on the effectiveness of VRE to treat anxiety disorders (mostly phobias) has been promising, most randomized trials that evaluated VRE lacked key features of quality

designs, such as use of intent-to-treat analyses, blind assessment of outcome, and adequate power (McCann et al., 2014). This randomized, controlled study compared PE and VRE in a waitlist-controlled clinical trial for active-duty soldiers with PTSD resulting from deployments in support of Operation Iraqi Freedom and Operation Enduring Freedom. A noninferiority design was considered but not utilized as the existing VRE literature and the theoretical support for the importance of emotional engagement in PTSD treatment led us to hypothesize VRE superiority. Therefore, we hypothesized that VRE and PE would reduce PTSD symptoms compared with a minimal attention waitlist. Furthermore, we hypothesized that VRE would significantly reduce PTSD symptoms compared with PE. We also hypothesized that soldiers assigned to VRE would demonstrate lower dropout rates, lower stigma and higher treatment satisfaction than soldiers assigned to PE.

Method

Participants

Participants were treated in accordance with established ethical guidelines (American Psychiatric Association, 2010) and the study was approved by the local institutional review board. Participants were either referred by providers at an Army medical center or self-referred based on study advertisements located on the military installation. Recruitment occurred between May, 2009 and April 2013. Participants were eligible if they were active-duty soldiers who had a deployment-related trauma that occurred in Iraq or Afghanistan that met *Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition-Text Revision* (*DSM–IV-TR*; American Psychiatric Association, 2000) criteria for PTSD based on the Clinician-Administered PTSD Scale (CAPS; Blake et al., 1995). Inclusion criteria required that the index trauma be a nonsexual assault trauma and the trauma must have occurred at least 3-months before the baseline assessment in an environment similar to those environments available in the Virtual Iraq/Virtual Afghanistan software. Participants also had to agree not to initiate other psychotherapy for PTSD or new psychotropic medications during the treatment phase of the study. Exclusion criteria included: (a) a change in the type or strength of psychotropic medications in the last 30 days; (b) a history of organic mental disorder, schizophrenia, other psychotic disorder, or bipolar disorder; (c) hospitalization in the past 6 months for suicidal risk or self-harm; (d) an ongoing threatening situation (e.g., domestic violence); (e) current drug or alcohol dependence; (f) a history of seizures; (g) prior PE treatment; (h) other ongoing psychotherapy for PTSD; (i) a physical condition interfering with the ability to use a virtual reality head-mounted display or VR peripherals, such as a gaming joystick; and (j) a history of a loss of consciousness for a duration of greater than 15 min since entering active-duty military service. Of the 292 participants who consented and were assessed, 162 participants were enrolled and randomized. Three participants were discovered to be ineligible postrandomization and were removed from the study but are included in the intent-to-treat analyses. Two of these soldiers were withdrawn before Session 1 after discovering a history of prior PE, and one was withdrawn after Session 2 after the treating therapist learned of ongoing cognitive–behavioral therapy for PTSD. Intent-to-treat analysis for this study retained all study participants who were randomized. Mean age (*SD*) for the three treatment groups were 30.39 (6.45) for WL, 30.89 (7.09) for PE, and 29.52 (6.47) for VRE, and there was no significant difference. Table 1 describes the other characteristics of the sample. There were no statistically significant differences across the three groups in the distributions of demographic characteristics or in the baseline outcome measures.

Measures and Equipment

All measures were administered by doctoral level assessors trained in clinical psychology. Seven clinicians served as independent assessors, blind to participant treatment group assignment.

Primary outcome measure. The CAPS is a structured clinical interview that assesses the presence and severity of PTSD according to *DSM–IV* criteria. The frequency and intensity of each symptom is coded on a scale ranging from 0 to 4. The "F1/I2/TSEV65" CAPS scoring rule was used to establish the diagnosis of PTSD at enrollment (Weathers, Ruscio, & Keane, 1999). According to this rule, a diagnosis of PTSD is rendered when required symptoms in the prior month are scored at a frequency of at least 1 and an intensity of at least 2 and there is a significant overall level of symptom severity (i.e., a CAPS total severity score of 65 of greater). The CAPS was used with a "last month" reference period for screening for study eligibility and to determine the presence of the diagnosis at follow-up assessments. The CAPS was also used with a "last week" reference at all assessments to serve as the primary outcome measure given the potential for only 2.5 and 5 weeks of treatment at the mid- and posttreatment assessments, respectively.

Assessor CAPS training included training DVDs and coding of other clinicians' video-recorded CAPS, followed by video recorded practice interviews with supervision until CAPS administration reached an acceptable level of reliability ($\kappa > .80$) with a trauma expert. All assessors were kept blind to patients' treatment group assignment through the use of assessment offices located in a separate hallway or a separate building relative to treating clinicians. Assessors were excluded from all study meetings involving discussions of clinical issues. Patients were instructed not to disclose their treatment group to the assessing clinicians. Assessors recorded accidental patient disclosures of treatment group and also guessed treatment group assignment at the end of each assessment. Patients broke the treatment group blind 29 times (WL = 12, PE = 5, VRE = 12). Assessors guessed the correct treatment Group 53.8% of the time. At both the mid- and posttreatment assessments, over half of the correct guesses were WL, which likely reflects increased accuracy based on symptom presentation at the assessment. Restricting the guesses to only PE and VRE, the assessor was correct 36% of the time for the midpoint assessment, $\chi^2(2) = 2.31$, $p = .31$ and 46% of the time for the posttreatment assessment, $\chi^2(2) = 5.11$, $p = .08$.

All CAPS interviews were video recorded and 10% of the scheduled assessments were randomly selected for coding interrater reliability. Videos were rated every 2 weeks by the assessors and feedback was provided by a lead investigator to prevent drift in coding over time. The intraclass correlation for CAPS severity was 0.94 at baseline using the last month reference period and 0.96 using the last week reference period. The intraclass correlation for CAPS severity at postassessment was 0.99 using the last week reference period. The intraclass correlation for PTSD diagnosis at baseline was 0.83 using CAPS last month reference period. Inter-

Table 1
Demographic Characteristics of Subjects Randomized to the Three Study Groups

Variable	WL		PE		VRE		χ^2, *df*
	n	%	*n*	%	*n*	%	
Male	53	98.15	51	94.44	52	96.30	1.04, 2
Marital status							3.76, 6
Not married	8	14.81	5	9.26	9	16.67	
Married	31	57.41	39	72.22	34	62.96	
Separated	7	12.96	6	11.11	6	11.11	
Divorced	8	14.81	4	7.41	5	9.26	
Education							5.59, 6
High school	19	35.19	16	29.63	20	37.04	
Some college, no degree	23	42.59	25	46.30	27	50.00	
2-year degree/Technical certificate	9	16.67	6	11.11	5	9.26	
4-year degree or more	3	5.56	7	12.96	2	3.70	
Race/Ethnicity							10.02, 10[a]
White, not Hispanic	28	51.85	30	55.56	39	72.22	
Black, not Hispanic	8	14.81	5	9.26	2	3.70	
Asian/Pacific Islander, not Hispanic	3	5.56	3	5.56	4	7.41	
Alaskan Indian/American Native, not Hispanic	3	5.56	1	1.85	1	1.85	
Other, not Hispanic	3	5.56	3	5.56	1	1.85	
Hispanic, any race	9	16.67	12	22.22	7	12.96	
Military rank/Grade							3.15, 4
E-1–E-4	19	35.19	20	37.04	25	46.30	
E-5–E-9	34	62.96	31	57.41	28	51.85	
Officer	1	1.85	3	5.56	1	1.85	
Prior treatment for PTSD	21	38.89	17	31.48	15	27.78	1.57, 2
Year of enrollment							.49, 8
2009	8	14.81	8	14.81	7	12.96	
2010	18	33.33	17	31.48	18	33.33	
2011	11	20.37	12	22.22	11	20.37	
2012	13	24.07	12	22.22	14	25.93	
2013	4	7.41	5	9.26	4	7.41	

Note. WL = waitlist control; PE = prolonged exposure; VRE = virtual reality exposure therapy; PTSD = posttraumatic stress disorder.
[a] Use of Fisher's exact test did not change the result of the test.

nal consistency reliability estimates for this measure and all secondary measures used at multiple time points are presented in Table 2.

Secondary measures. The PTSD Checklist, Civilian Version (PCL-C; Weathers, Litz, Herman, Huska, & Keane, 1993, Oct) is a 17-item self-report measure of PTSD symptom intensity. Participants rated how much they had been bothered by each symptom in the past month on a 5-point scale ranging from 1 (*not at all*) to 5 (*extremely*). The PCL-C is widely used in trauma research, is a standard measure used in U.S. postdeployment assessments, and has demonstrated strong internal consistency, test–retest reliability, and convergent validity (Blanchard et al., 1996; Bliese et al., 2008).

The Beck Depression Inventory-II (Beck, Steer, & Brown, 1996) is a 21-item self-report measure of the severity of depression. Responses reflect how the individual has been feeling in the prior 2 weeks and items are rated from 0 (*least severe*) to 3 (*most severe*). Studies have previously reported high internal consistency (Beck, Steer, & Carbin, 1988), and scores correlate well with clinician ratings (Foa et al., 1993).

The Beck Anxiety Inventory (Beck & Steer, 1993) is a 21-item self-report measure that assesses for symptoms of anxiety in the prior week. Items range from 0 (*not at all*) to 3 (*severely*) and reflect subjective, somatic, or panic-related symptoms. Beck et al. (1988) examined its psychometric properties and reported an internal consistency of 0.92, and a 1 week test–retest reliability of 0.75. The measure has demonstrated adequate discriminant, concurrent, and divergent validity.

Stigma Scale for Receiving Psychological Help (SSRPH; Komiya, Good, & Sherrod, 2000) is a 5-item scale that assesses perceptions of how stigmatizing it is to receive mental health treatment with higher scores reflecting a greater perception of stigma. Each item is rated from 0 (*strongly disagree*) to 3 (*strongly agree*). We calculated a sum score of the items to use in analysis with higher scores indicating higher levels of perceived stigma. The SSRPH has demonstrated adequate internal consistency (0.72). Komiya, Good, and Sherrod (2000) found support for its construct validity.

Inventory of Attitudes Toward Seeking Mental Health Services (IASMHS; Mackenzie, Knox, Gekoski, & Macaulay, 2004) is a 24-item self-report scale. Items are rated on a scale from 0 (*disagree*) to 4 (*agree*). A sum of the items was used in analyses with higher scores indicating higher levels of perceived stigma. Previous research found a coeffficient α of 0.78 among medical patients and the IASMHS distinguished between those with and without prior mental health treatment history (Mackenzie et al., 2004).

The Client Satisfaction Questionnaire (Larsen, Attkisson, Hargreaves, & Nguyen, 1979; CSQ) is an 8-item self-report measure of general satisfaction with treatment. Items include a 4-point scale with a variety of anchor descriptions ranging from

Table 2
Means, Minima, Maxima, and Internal Consistency Reliability for Study Measures, by Treatment Group and Measurement Occasion

	WL[a]				PE				VRET			
Time	*n*	*M* (*SD*)	Min., Max.	α	*n*	*M* (*SD*)	Min., Max.	α	*n*	*M* (*SD*)	Min., Max.	α
CAPS (week)												
Baseline	54	78.89 (16.87)	45, 114	.70	54	78.28 (16.35)	54, 123	.66	54	80.44 (16.23)	51, 111	.66
Midtreatment	52	74.73 (21.78)	30, 117	.83	39	65.03 (29.19)	11, 109	.91	36	71.19 (23.27)	9, 115	.86
Posttreatment	47	68.06 (24.27)	10, 108	.86	32	44.28 (33.73)	0, 121	.94	30	57.07 (32.32)	0, 104	.93
12-week					27	36.63 (31.80)	0, 109	.93	25	56.64 (31.50)	11, 102	.92
26-week					24	38.33 (28.49)	4, 95	.90	18	53.50 (28.07)	13, 91	.88
CAPS (month)												
Baseline	54	87.61 (12.88)	66, 114	.63	54	85.44 (14.06)	66, 124	.63	54	88.70 (12.86)	65, 115	.62
12-week					27	41.74 (32.52)	0, 111	.94	24	62.71 (30.51)	9, 102	.92
26-week					24	44.92 (29.34)	7, 108	.91	18	59.61 (27.51)	18, 98	.88
PCL-C												
Baseline	54	60.30 (8.97)	33, 74	.81	54	59.74 (9.09)	38, 79	.79	54	61.85 (9.03)	41, 81	.81
Midtreatment	52	55.58 (11.95)	31, 76	.90	39	49.28 (14.85)	22, 80	.94	36	53.17 (15.08)	20, 78	.94
Posttreatment	46	53.89 (11.77)	25, 78	.88	32	40.63 (18.57)	17, 81	.97	30	45.57 (15.88)	17, 69	.95
12-week					27	38.41 (17.98)	17, 72	.95	25	46.96 (15.95)	21, 70	.95
26-week					24	40.83 (18.56)	18, 71	.92	17	42.88 (15.96)	19, 71	.95
BDI-II												
Baseline	54	27.67 (9.99)	2, 52	.89	54	28.02 (11.18)	10, 53	.90	54	27.87 (9.19)	12, 51	.86
Midtreatment	52	24.63 (10.70)	4, 50	.91	39	21.69 (13.27)	1, 55	.95	36	22.81 (11.44)	0, 45	.92
Posttreatment	46	25.63 (12.87)	2, 57	.94	32	17.06 (16.18)	0, 59	.97	30	18.50 (12.70)	1, 46	.95
12-week					27	13.70 (13.52)	0, 48	.96	25	20.04 (12.41)	1, 46	.94
26-week					24	14.42 (13.38)	0, 42	.96	17	18.59 (11.03)	1, 40	.93
BAI												
Baseline	54	23.81 (11.09)	2, 50	.90	54	22.11 (9.34)	2, 42	.86	54	24.57 (11.19)	8, 61	.90
Midtreatment	52	21.35 (12.80)	0, 48	.94	39	17.41 (9.72)	0, 40	.89	36	19.78 (11.86)	3, 46	.93
Posttreatment	47	18.83 (11.93)	0, 49	.93	32	13.28 (12.11)	0, 43	.95	30	17.17 (12.80)	0, 50	.94
12-week					27	11.44 (11.79)	0, 42	.94	25	19.28 (14.92)	0, 48	.96
26-week					24	9.83 (10.02)	0, 32	.93	17	15.24 (12.19)	0, 43	.94
SSRPH												
Baseline	54	7.48 (3.10)	0, 15	.83	54	7.04 (3.53)	0, 15	.86	54	6.83 (3.52)	0, 14	.84
Midtreatment	52	6.73 (3.35)	0, 15	.84	39	5.59 (3.54)	0, 12	.87	36	5.86 (2.94)	0, 11	.77
Posttreatment	47	6.77 (3.40)	0, 15	.85	32	5.16 (3.73)	0, 14	.89	30	5.43 (3.23)	0, 11	.87
12-week					27	4.78 (3.67)	0, 11	.89	25	4.64 (3.41)	0, 10	.89
26-week					24	5.38 (3.98)	0, 14	.94	17	5.53 (2.45)	0, 8	.75
IASMHS												
Baseline	54	43.91 (13.75)	18, 79	.84	54	41.09 (15.93)	13, 79	.89	54	43.80 (12.65)	19, 71	.81
Midtreatment	52	45.48 (16.08)	13, 76	.90	39	36.97 (16.10)	13, 76	.91	36	41.36 (12.61)	12, 69	.83
Posttreatment	47	43.49 (15.43)	14, 70	.90	32	34.56 (15.66)	9, 66	.91	29	39.21 (13.80)	10, 63	.87
12-week					27	34.00 (16.93)	9, 65	.93	25	37.08 (13.80)	15, 73	.88
26-week					24	33.04 (17.46)	9, 65	.93	17	38.06 (12.75)	13, 60	.90

Note. WL = waitlist control; PE = prolonged exposure; VRE = virtual reality exposure therapy; *M* = mean; α = Cronbach's α; CAPS = Clinician Administered PTSD Scale for DSM-IV; PCL-C = PTSD Checklist; BDI-II = Beck Depression Inventory-II; BAI = Beck Anxiety Inventory; SSRPH = Stigma Scale for Receiving Psychological Help; IASMHS = Inventory of Attitudes toward Seeking Mental Health Services; BASIS 24 = Behavior and Symptom Identification Scale; CSQ = Client Satisfaction Questionnaire.
[a] Participants in the WL group received treatment after the posttreatment assessment. They did not provide study measures after the posttreatment assessment.

1, which characterized quite dissatisfied anchors, to 4, which characterized anchors related to being very satisfied. We calculated a mean score of the items to use in analysis with higher scores indicating greater satisfaction. Psychometrics of the CSQ have been examined in psychiatric samples (Attkisson & Zwick, 1982; Larsen et al., 1979; Nguyen, Attkisson, & Stegner, 1983). It had high internal consistency and correlated well with treatment completion-termination. Scores also correlated well with change in client reported symptoms (Attkisson & Zwick, 1982). Coefficient α for this measure at posttreatment was 0.93 among participants in the PE group and 0.89 among participants in the VRE group.

The *Virtual Reality Iraq/Afghanistan System* (Rizzo, Reger, Gahm, Difede, & Rothbaum, 2009) included a Dell XPS desktop computer and an eMagin z800 head-mounted display (HMD), which is a headset with screens for each eye. An inertia cube orientation tracker was attached to the HMD, which enabled replication of the patient's head movements in the virtual environment. Patients navigated in the environment by using a Logitech joystick or a mini joystick attached to a mock M4 rifle. High audio fidelity, over-the-ear headphones were used for audio stimuli, and therapists spoke with patients via a digital microphone that could be heard in the headphones. Participants stood or sat on a platform with bass shaker speakers attached to a stereo amplifier and computer, such that low frequency sounds were experienced as vibrations. An EnviroScent Scent Palette (Biopac Systems, 2013) delivered olfactory stimuli, when relevant to the memory being revisited during imaginal exposure.

The VR Iraq/Afghanistan software has been described in detail elsewhere (Rizzo et al., 2009). Briefly, the system includes a clinician's interface that allows real time customization of a broad range of stimuli to match relevant characteristics of the patient's memory. Time of day, position in vehicle or city, type of weather, convoy location, presence or absence of civilians or other military personnel, improvised explosive devices, small arms fire, mortar attacks, vehicle borne IEDs, and rocket propelled grenades provide examples of stimuli that can be customized or included.

Procedure

After initial referral, a study team member met with the participant or contacted the participant by phone to provide a brief description of the study and an opportunity to schedule consenting and initial assessment. At the initial assessment, participants provided written informed consent and subsequently completed an initial eligibility assessment of all inclusion and exclusion criteria. Patients were informed that treatment encounters, including the diagnosis of PTSD and treatment interventions used, would be documented in their military medical record but that all research assessments (e.g., CAPS, self-report measures) would be retained only in a separate research file. A research coordinator provided their treatment group assignment based on computerized random number generation. Randomization was blocked in groups of three, such that one patient was assigned to each treatment group (PE, VRE, or WL) for every three participants enrolled.

Participants were assessed at enrollment, after five treatment sessions or 2.5 weeks into the waitlist (WL) period, and at post-treatment or after 5 weeks for WL. Participants assigned to either of the two active treatments also completed 3- and 6-month follow-up assessments. Participants who dropped out of treatment were invited to participate in future study assessments. Figure 1 illustrated the flow of participants throughout the study.

Treatments. Ten 90–120 min treatment sessions were delivered for both active treatments. Standard PE involves 90-min sessions and with additional research procedures, additional time was often needed. Treatments were delivered with a frequency of once or twice a week, although flexibility in frequency of session was allowed to accommodate soldiers' military training schedules. Sessions 1 and 2 included the same preparatory treatment components (e.g., rationale, construction of in vivo exposure hierarchy) for both active treatments. Exposure to the trauma memory began in Session 3 for both treatments. The duration of exposure to the memory was the same for both treatments (30–45 min per session).

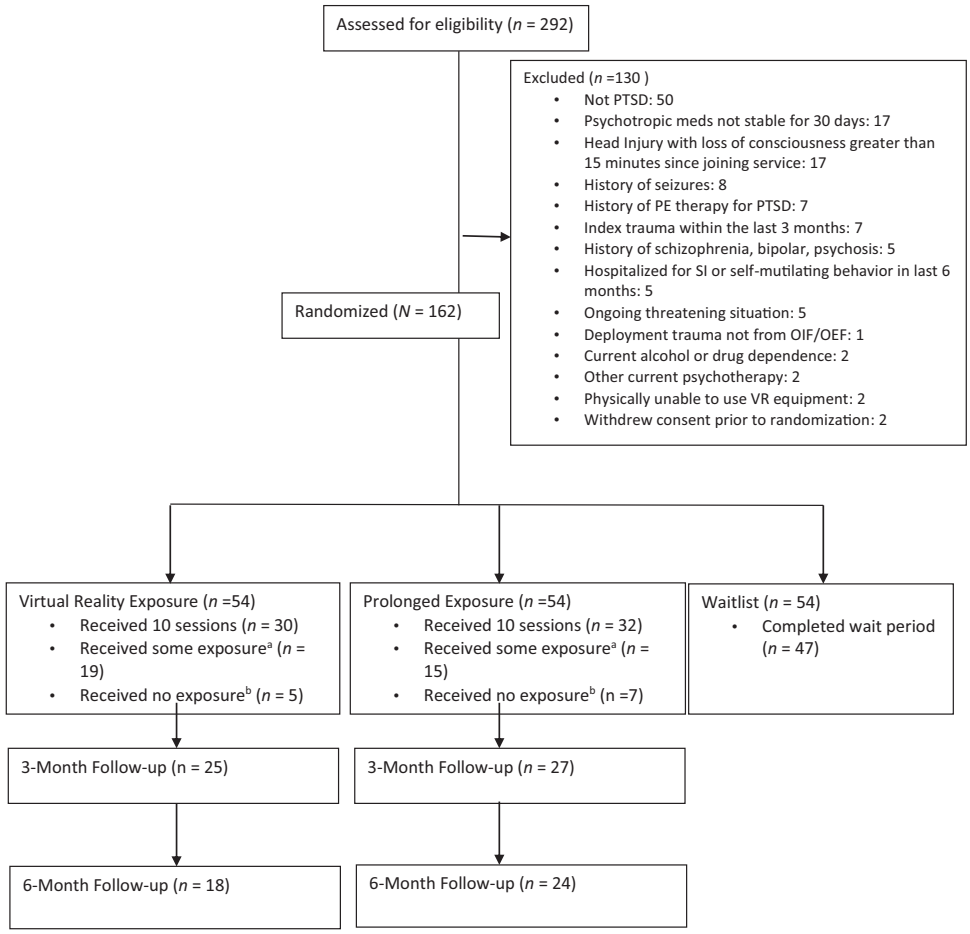

Figure 1. Flow of participants through the study. *Note:* [a] These patients completed between three and nine sessions of psychotherapy. [b] These patients dropped out of treatment before Session 3.

Prolonged exposure. PE is a manualized treatment for PTSD (Foa et al., 2007) that involves psychoeducation on PTSD and common responses to traumatic events, breathing retraining, repeated and prolonged imaginal exposure to the trauma memory, cognitive and emotional processing of traumatic material that emerged in the exposure, and in vivo exposure to safe but feared situations that are avoided.

Virtual reality exposure. In this study, VRE followed the PE treatment protocol (Foa et al., 2007) with two exceptions. First, during VRE, the therapist placed the soldier in a relevant VR environment and patients confronted their memory with their eyes open, wearing the HMD. Similar to PE, patients in VRE revisited the memory by verbally describing the events in the first person, present tense. As the patient articulated the memory, the therapist customized the scene and associated stimuli to match the memory in relevant respects. Second, in Session 2 of VRE, the patient was briefly introduced to the VR equipment and instructed in its use while immersed in a calm virtual park environment (NeuroVR; Riva et al., 2009).

Minimal attention waitlist. A minimal attention waitlist was included to control for factors such as regression to the mean, the effects of repeated assessments, and any potential benefits from nontherapeutic contact with the research team. Upon completion of the 5 week waiting period, the study team provided them with their choice of active treatment. The 5-week waiting period was selected to reflect the minimum period of time required for completion of active treatment. To expedite PTSD treatment of military personnel with deployment-related mental health problems, study participation for those in the WL ended after the posttreatment assessment. No data was collected on their treatment selection or outcomes for their poststudy treatment.

Therapist training and treatment adherence/competence. Therapists were five doctoral level clinicians trained in clinical psychology. All were trained in PE through a 2-day workshop provided by the Center for Deployment Psychology by an expert in PE. The same therapists were trained in a separate 2-day workshop in VRE techniques instructed by leading VRE researchers and clinicians. Therapists treated a minimum of two videotaped practice patients with supervision before treating study participants. All therapists treated both PE and VRE cases. Weekly supervision was provided by experienced exposure therapy clinicians.

All therapy sessions were video recorded and 15% of planned sessions were randomly selected in advance for independent rating of treatment adherence and competence. Therapists were unaware of which sessions would be sent out for adherence review. Coders were not involved in other aspects of the study and were selected for this role based on experience as investigators on previous clinical trials of PE and VRE. Treatment adherence forms used in previous clinical trials of PE (Rothbaum, Astin, & Marsteller, 2005) were used for PE and adapted for VRE. Videos were coded, reviewed, and feedback provided to therapists on an ongoing basis throughout the trial for fidelity review and adherence monitoring (Barber, Triffleman, & Marmar, 2007). In 71 treatment sessions using prolonged exposure, 97.27% (962/989) of required criteria were observed. In 50 treatment sessions using virtual reality exposure therapy, 96.87% (649/670) of required criteria were observed.

Sample Size

The initial sample size calculation for the trial was based on the omnibus F test for a group by time interaction. Assuming a Cohen's f^2 of 0.20, an α of 0.05, and a β of 0.20, the study required 33 subjects per group. When the opportunity to add a second study site became available to permit increased recruitment (90 subjects per group, accounting for anticipated dropout), a power analysis revealed that an expanded study would be able to detect a Cohen's f^2 value of 0.09, assuming 69 participants per group).

Analysis

Assessments and treatment sessions were conducted on one large Army military installation and study clinicians had adjunct clinical appointments at an Army medical center. Funding for an additional recruitment site was received midway through the trial and the protocol was amended. In accordance with the documented plan for the grant at the end of the site's period of performance, the data from the original site were analyzed. This required a protocol deviation report to the institutional review board (IRB), as the amended protocol to add the second site was not sufficiently updated to reflect this planned analysis. However, once the findings were reviewed and presented to the IRB, the decision was made in collaboration with the IRB to halt recruitment at the second site and close the study. The IRB's independent statistical reviewer concluded that the data were adequate to address the hypotheses and that additional data collection was unlikely to change the direction of the findings. The decision to halt the trial also took into consideration difficulties recruiting qualified staff to the more remote geographic location of the second site, poor treatment fidelity by one of the hired therapists at the second site, and statistical considerations with low recruitment at this site. Only nine soldiers completed study participation from the second site. Accordingly, these soldiers were excluded from analyses and this article reports on all data collected at the primary study site.

Statistical Analyses

Treatment adherence. We compared the proportion of participants completing all 10 treatment sessions in the VRE group to the PE group using a two-sample difference of proportions test of the null hypothesis that the completion proportion of the VRE group would be less than or equal to that of the PE group. We also estimated Kaplan-Meier curves for a graphical assessment of the rate of dropout or loss to follow-up as a function of the number of treatment sessions. We used a Poisson regression with the number of treatment sessions as an exposure variable to test the null hypothesis that the rate of nonadherence in the VRE group would be less than or equal to that of the PE group.

Psychological symptoms. The primary hypothesis stipulated that both the PE and the VRE groups would have improved CAPS scores as compared to the WL group. Moreover, it was hypothesized that the VRE group would improve more than the PE group. To account for attrition, we used linear mixed effects regression models (Singer & Willett, 2003) to estimate the differences in means of the behavioral outcomes. All study participants who provided data at baseline were retained in the intent-to-treat mod-

els through maximum likelihood. We estimated a random coefficient for the intercept to account for individual variability in baseline outcome scores. Measurement occasions were treated categorically with baseline as the reference value. This specification of time did not make an assumption about the shape of change in the treatment groups and allowed for a direct test of differences at the designed measurement times as opposed to model-implied differences based on the assumed shape of change. The parameter estimates of interest were the interaction terms between treatment group assignment and measurement occasion at midtreatment and posttreatment. These estimates indicated the magnitude and direction of the difference in means between the study groups at the particular measurement occasion. We report the regression coefficients (unstandardized differences), 95% confidence intervals (CIs), and one-tailed *p* values associated with the a priori specified test of superiority of the active treatments over the wait list condition and the VRE condition over the PE condition. We also report the effect sizes as the regression coefficients standardized to the baseline *SD* of each outcome in the total study sample (Feingold, 2009).

In a second analytic approach, the CAPS last week measure was also analyzed per protocol by restricting the model estimation to those study subjects who had completed all 10 treatment sessions and provided data at the posttreatment measurement occasion. A final model of the CAPS last week and last month included data from all available measurement occasions to look at differences between the VRE and PE groups at the 12- and 26-week follow-up times. All models were estimated in Stata 12.1 (StataCorp, 2011) using restricted maximum likelihood.

Conditional power. We used the methods described by Proschan, Lan, and Wittes (2006) to evaluate the probability of observing a statistically significant conclusion of superiority with additional data collection given the data observed at the time of analysis. Given the consideration of futility, we based the calculation on the assumption that additional data collected would follow the alternative hypothesis of superiority to give a conservative estimate of conditional power.

Missing data. A key assumption of the linear mixed effects regression model is that the data were generated under a missing at random (MAR) or a covariate dependent assumption. Before estimating these models, we used a generalized linear model with a logit link and a Binomial error distribution to examine the association between the likelihood of dropout and several determinants, including CAPS scores, treatment assignment, and demographic variables. The results suggested that participants with lower education and those who did not identify as non-Hispanic White were more likely to drop out of the study during the treatment phase. Dropout was not related to CAPS scores. All regression models included education and race to improve the estimation. As a sensitivity analysis, we estimated a random coefficient selection model (Enders, 2010) that is appropriate for data that are missing not at random (MNAR). We specified a linear growth curve model for the first three measurement occasions using the CAPS last week. We estimated the selection model using M*plus* 7 (Muthen & Muthen, 2012).

Treatment satisfaction. We used a two-sample student's *t* test to compare the means of the CSQ at posttreatment between participants assigned to the VRE and PE groups. For this analysis, we only included study subjects who completed all 10 sessions of the assigned treatment.

Reliable and clinically significant change. We used the methods described in Hageman and Arrindell (1999) to calculate reliable and clinically significant change for both treatment groups. For clinically significant change, we defined the cutoff as the baseline mean for the total study population less twice the reliable *SD* of the baseline measurement. Reliability values for baseline, posttreatment, and difference scores followed the formula: $(s_t^2 - S_E^2)/s_t^2$, where s_t is the time- or difference-specific *SD* and S_E is the *SEM* derived from the baseline mean and internal consistency of the CAPS last week for all study participants.

Results

By posttreatment, 44.44% of participants in the VRE group were lost to follow up or had withdrawn from the study compared to 40.74% of participants in the PE group (d = .04, 95% CI [−0.22, 0.15], $p_{d<0}$ = .651). Participants assigned to PE completed an average of 7.50 sessions (*SD* = 3.46) and VRE participants completed a mean of 7.11 sessions (*SD* 3.58). Major reasons participants dropped out during treatment included geographic relocation away from the study site (WL [n = 4], PE [n = 4], and VRE [n = 5]), time demands of military training/scheduling problems (WL [n = 0], PE [n = 1], VRE [n = 3]), increases in symptomatology (WL [n = 1], PE [n = 1], VRE [n = 3]), improvements in symptoms (VRE [n = 2]), dissatisfaction with assigned treatment (WL [n = 1], PE [n = 4], VRE [n = 2]), and losses to follow up (WL [n = 1], PE [n = 7], and VRE [n = 5]). Figure 2 displays the Kaplan-Meier curves for treatment retention of participants assigned to the VRE and PE groups. Both groups showed substantial attrition over the course of treatment with most occurring by mid treatment. The Poisson regression coefficient comparing VRE to PE was 0.05 (95% CI [−0.57, 0.67]; $p_{b<0}$ = .567). For the assessment of both proportion and rate of dropout, we observed little difference between the treatment groups and failed to reject the null hypothesis.

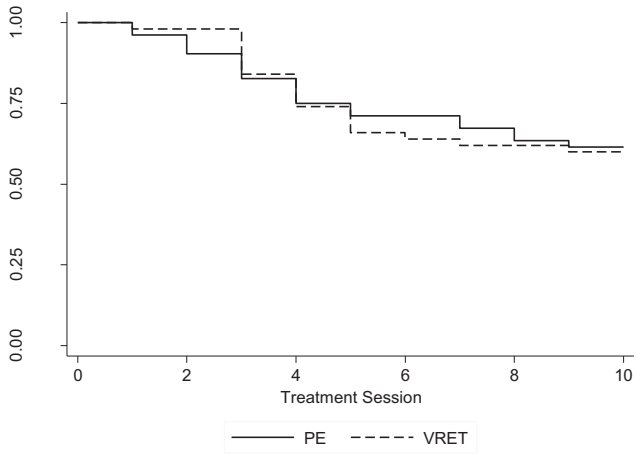

Figure 2. Kaplan-Meier curves for treatment retention of participants assigned to prolonged exposure and virtual reality exposure.

Table 2 provides descriptive data on the primary and secondary outcome measures for each treatment group at baseline, midtreatment, and posttreatment. For the CAPS last week scores, the means decreased at each measurement occasion for all three study groups. The decreases were larger for the two active treatment groups. Internal consistency was high for all three study groups at all measurement occasions with the exception of baseline that was hindered by a compressed score range given the eligibility criteria for study participation. The secondary measures all showed adequate to good internal consistency reliability across measurement occasions and treatment groups.

Table 3 presents the results of the intent-to-treat test of the hypothesis of superiority of the active treatments in reducing PTSD symptom severity over WL. Compared with participants in the WL, participants in PE had a decrease of 21.90 points on the CAPS last week and participants in VRE had a decrease of 13.23 points by posttreatment. Both of these differences were statistically significant. The post hoc power to detect these differences was 1.00 for PE and 0.95 for VRE. Participants in the PE group had statistically significantly lower scores on all secondary outcomes listed in Table 2 compared with WL. The VRE group scores on the secondary outcomes were also lower than the WL with all differences statistically significant except for the SSRPH.

In directly comparing the CAPS week and month scores between the VRE and PE groups, we observed a positive difference between the group means (see Table 4). This was consistent with the data in Table 2 that showed that the means posttreatment were higher for those in the VRE group compared to PE. We failed to reject the null hypothesis of PTSD symptoms in the VRE group greater than or equal to those in the PE group at posttreatment. The post hoc power to detect a one-tailed difference of a magnitude of 8.67 was 0.69, assuming it was in the anticipated direction of superiority. Given the direction favoring inferiority, our power was effectively 0.00. Increasing the sample size through additional randomization would not alter our ability to reject the null hypothesis of no difference or inferiority of VRE compared with PE. At the two posttreatment follow-up assessments, the differences between the VRE and the PE groups increased.

Given the unexpected differences favoring PE, we also examined the 95% CIs to get a two-tailed perspective. The 95% CIs at posttreatment showed that most of the area covered was above zero, and there was a significant difference between PE and VRE for the 12-week (b = 14.50, 95% CI [3.24, 25.76]) and 26-week (b = 13.68, 95% CI [1.45, 25.76]) follow up time points, which indicated inferiority of VRE to PE. It should be noted, however, that these a posteriori assessments of difference, not only superiority, produced results that were unexpected and the CIs were quite wide.

Figure 3 illustrates the mean changes in CAPS scores over time. Estimation of the random coefficient selection model did not change the conclusions, so there was no evidence of data missing not at random that could produce the results observed in the primary model. Finally, examination of the CAPS month assessment at the 12 and 26 week posttreatment follow up assessments both indicated inferiority of VRE relative to PE in the reduction of PTSD symptoms (see Table 4).

There were no statistically significant differences between the two active treatment groups on the secondary outcome measures (see Table 4). Specifically, we failed to reject the null hypothesis that mental health treatment stigma in the VRE group would be greater than or equal to that of the PE group. Finally, participants in both the VRE and PE groups had high treatment satisfaction at

Table 3
Intent-To-Treat Differences on Primary and Secondary Outcome Measures Between the Active Treatment Groups and the Waitlist Control Group at Mid- and Posttreatment

	PE-WL			VRE-WL		
Measure	b [95% CI]	p[a]	ES [95% CI]	b [95% CI]	p[a]	ES
CAPS (week)						
Midpoint	−9.07 [−18.12, −.03]	.025	−.55 [−1.10, .00]	−4.73 [−14.13, 4.66]	.162	−.29 [−.86, .28]
Posttreatment	−21.90 [−31.60, −12.19]	<.001	−1.33 [−1.93, −.74]	−13.23 [−23.22, −3.23]	.005	−.81 [−1.42, −.20]
PCL-C						
Midpoint	−5.18 [−9.53, −.83]	.010	−.57 [−1.06, −.09]	−4.72 [−9.24, −.20]	.020	−.52 [−1.02, −.02]
Posttreatment	−11.23 [−15.93, −6.54]	<.001	−1.25 [−1.77, −.72]	−11.33 [−16.18, −6.48]	<.001	−1.26 [−1.79, −.72]
BDI-II						
Midpoint	−3.46 [−7.07, .14]	.030	−.34 [−.70, .01]	−2.42 [−6.18, 1.33]	.103	−.24 [−.61, .13]
Posttreatment	−9.09 [−12.97, −5.20]	<.001	−.90 [−1.29, −.52]	−7.87 [−11.89, −3.85]	<.001	−.78 [−1.18, −.38]
BAI						
Midpoint	−2.50 [−6.16, 1.67]	.091	−.24 [−.58, .11]	−4.22 [−8.04, −.41]	.015	−.40 [−.76, −.04]
Posttreatment	−5.46 [−9.40, −1.52]	.003	−.52 [−.89, −.14]	−5.31 [−9.37, −1.25]	.005	−.50 [−.89, −.12]
SSRPH						
Midpoint	−.59 [−1.77, .58]	.162	−.18 [−.52, .17]	−.14 [−1.37, 1.08]	.408	−.04 [−.41, .32]
Posttreatment	−1.36 [−2.62, −.09]	.018	−.40 [−.78, −.03]	−1.02 [−2.32, .29]	.064	−.30 [−.69, .09]
IASMHS						
Midpoint	−4.92 [−9.42, −.43]	.016	−.35 [−.67, −.03]	−4.05 [−8.73, .63]	.045	−.29 [−.62, .04]
Posttreatment	−7.45 [−12.28, −2.62]	.001	−.53 [−.87, −.19]	−5.88 [−10.91, −.85]	.011	−.42 [−.77, −.06]

Note. WL = waitlist control; PE = prolonged exposure; VRE = virtual reality exposure therapy; b = unstandardized coefficient; CI = confidence interval; ES = effect size; CAPS = Clinician Administered PTSD Scale for DSM-IV; PCL-C = PTSD Checklist; BDI-II = Beck Depression Inventory-II; BAI = Beck Anxiety Inventory; SSRPH = Stigma Scale for Receiving Psychological Help; IASMHS = Inventory of Attitudes toward Seeking Mental Health Services.

[a] One-tailed p-value to test the null hypothesis of treatment differences greater than or equal to zero in comparison to WL.

Table 4
Intent-To-Treat Differences (VRE-PE) on Primary and Secondary Outcome Measures

Measure and time	*b* [95% CI]	*p*[a]	ES [95% CI]
CAPS (week)			
Midpoint	4.34 [−5.48, 14.16]	.807	.26 [−.33, .86]
Posttreatment	8.67 [−1.86, 19.20]	.947	.53 [−.11, 1.17]
12 week	14.50 [3.24, 25.76]	.994	.88 [.20, 1.57]
26 week	13.68 [1.45, 25.91]	.986	.83 [.09, 1.58]
CAPS (month)			
12 week	15.46 [4.18, 26.74]	.996	1.14 [.31, 1.98]
26 week	14.43 [2.20, 26.65]	.990	1.07 [.16, 1.97]
PCL-C			
Midpoint	.46 [−4.28, 5.20]	.575	.05 [−.47, .58]
Posttreatment	−.10 [−5.18, 4.98]	.485	−.01 [−.57, .55]
12-week	2.86 [−2.58, 8.29]	.849	.32 [−.29, .92]
26-week	−.06 [−6.02, 5.90]	.492	−.01 [−.67, .65]
BDI-II			
Midpoint	1.04 [−2.90, 4.98]	.698	.10 [−.29, .49]
Posttreatment	1.22 [−3.01, 5.44]	.714	.12 [−.30, .54]
12-week	4.46 [−.05, 8.98]	.974	.44 [−.01, .89]
26-week	4.63 [−.32, 9.58]	.967	.46 [−.03, .95]
BAI			
Midpoint	−1.73 [−5.72, 2.27]	.199	−.16 [−.54, .22]
Posttreatment	.15 [−4.14, 4.44]	.527	.01 [−.39, .42]
12-week	3.51 [−1.08, 8.09]	.933	.33 [−.10, .77]
26-week	3.01 [−2.02, 8.03]	.880	.28 [−.19, .76]
SSRPH			
Midpoint	.45 [−.83, 1.73]	.754	.13 [−.25, .51]
Posttreatment	.34 [−1.03, 1.72]	.687	.10 [−.31, .51]
12-week	.03 [−1.44, 1.50]	.515	.01 [−.43, .44]
26-week	.38 [−1.23, 1.99]	.678	.11 [−.37, .59]
IASMHS			
Midpoint	.87 [−4.04, 5.78]	.636	.06 [−.29, .41]
Posttreatment	1.57 [−3.73, 6.88]	.719	.11 [−.26, .49]
12-week	2.02 [−3.61, 7.65]	.759	.14 [−.26, .54]
26-week	3.08 [−3.09, 9.25]	.836	.22 [−.22, .65]

Note. WL = waitlist control; PE = prolonged exposure; VRE = virtual reality exposure therapy; *b* = unstandardized coefficient; CI = confidence interval; ES = effect size; CAPS = Clinician Administered PTSD Scale for DSM-IV; PCL-C = PTSD Checklist; BDI-II = Beck Depression Inventory-II; BAI = Beck Anxiety Inventory; SSRPH = Stigma Scale for Receiving Psychological Help; IASMHS = Inventory of Attitudes toward Seeking Mental Health Services.
[a] One-tailed *p*-value to test the null hypothesis of symptoms in the VRE group greater than or equal to those in the PE group.

posttreatment (VRE: $M = 3.47$, $SD = 0.47$; PE: $M = 3.52$, $SD = 0.52$). The difference in means was trivial ($d = -0.05$, 95% CI [−0.21, 0.30], $p_{d<0} = 0.650$). Consequently, we failed to reject the null hypothesis of satisfaction in the VRE group being less than or equal to that of the PE group.

Treatment Completers

The results of these models, when restricted to treatment completers, were consistent with those observed from the intent-to-treat analysis (posttreatment: PE—WL: $b = -24.22$, 95% CI [−34.49, −13.93], $p_{b<0} < .001$; VRE—WL: $b = -12.50$, 95% CI [−23.06, −1.95], $p_{b<0} = .010$; VRE—PE: $b = 11.72$, 95% CI [0.40, 23.03], $p_{b<0} = .979$). Similar to the intent-to-treat analysis, the CAPS last week differences between VRE and PE at posttreatment did not indicate that VRE was superior. We again made an a posteriori examination of the 95% CIs to get a two-tailed perspective. The 95% CIs showed that there was a significant difference between PE and VRE for the 12-week ($b = 16.50$, 95% CI [4.56, 28.44]) and 26-week ($b = 15.66$, 95% CI [2.79, 28.53]) follow-up measurement times. The CAPS last month measure, which was only given at baseline and at the two posttreatment follow-up assessments, was consistent with the CAPS last week at the follow-up measurement times (VRE—PE; 12-week: $b = 15.46$, 95% CI [4.18, 26.74] and 26-week: $b = 14.43$, 95% CI [2.20, 26.65]).

Reliable and Clinically Significant Change

A majority of participants in both the PE and VRE groups demonstrated reliable change at posttreatment (see Table 5). A total of 10 participants in the WL group (21.28%), 21 in the PE group (65.63%), and 17 in the VRE group (56.67%) demonstrated a reliable or clinically significant change at posttreatment. Only one participant demonstrated a reliable worsening of symptoms in the study; this participant was in the VRE group.

Discussion

Active-duty U.S. Army soldiers with PTSD resulting from trauma during a deployment to Iraq or Afghanistan showed significant improvement in PTSD and depression after treatment with either PE or VRE, relative to those assigned to a minimal attention waitlist. However, contrary to our hypothesis, VRE was not superior to PE. At the posttreatment assessment there were not statistically significant differences between PE and VR. Post hoc analyses indicate a greater improvement in PTSD symptoms among those assigned to PE at the 3- and 6-month follow-up. These findings build on previous research of the effectiveness of exposure therapy in general (Bisson et al., 2007; Bradley et al., 2005) and PE in particular (Powers et al., 2010). Notably, there are very few clinical trials of PTSD treatments with U.S. service members and this is the first randomized trial of PE or VRE with U.S. active-duty military personnel with deployment-related trauma.

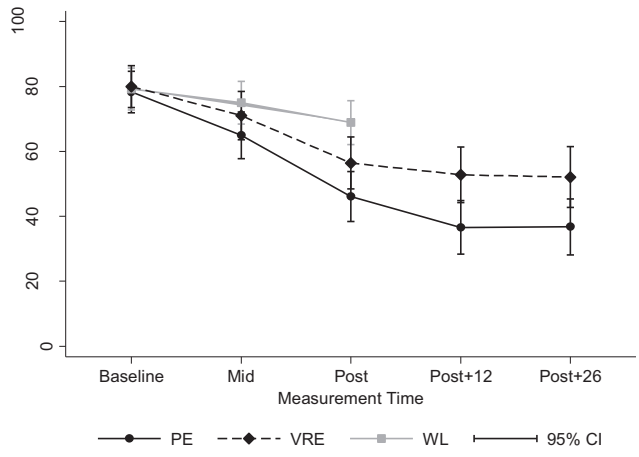

Figure 3. Clinician Administered PTSD Scale (CAPS) scores across time for soldiers assigned to prolonged exposure (PE), virtual reality exposure (VRE), or wait-list (WL).

Table 5
Individual Reliable and Clinically Significant Change at Posttreatment on the CAPS "Last Week"

Type of change	WL		PE		VRE	
	n	%	*n*	%	*n*	%
Individual change						
Deteriorated ($RC_{indiv} > 1.65$)	0	.00	0	.00	1	3.33
No reliable change ($-1.65 \leq RC_{indiv} \leq 1.65$)	37	78.72	11	34.38	12	40.00
Reliable change, not clinically significant ($RC_{indiv} < -1.65$; $CS_{indiv} > -1.65$)	5	10.64	5	15.63	7	23.33
Reliable and clinically significant change ($RC_{indiv} < -1.65$; $CS_{indiv} < -1.65$)	5	10.64	16	50.00	10	33.33

Note. PE = prolonged exposure; VRE = virtual reality exposure therapy; RC_{indiv} = individual reliable change index; CS_{indiv} = individual clinical significance index. The *SEM* was 9.73. The threshold value for a clinically significant improvement was 52.78.

This study extends previous findings of the efficacy of exposure therapy to this important population.

The rationale for VRE emerges from its presumed role in emotional processing theory (Foa & Kozak, 1986). Patients revisit traumatic events to activate the fear structure so that it can be modified. PE utilizes the techniques of imaginal exposure to accomplish this but concerns about the potential for patient underengagement to interfere with clinical outcomes for some patients have been noted (Foa et al., 1995; Jaycox et al., 1998). Multisensory virtual reality systems with customizable virtual environments have been conceptualized as a tool to increase emotional engagement and potentially, improve clinical outcomes. It is noteworthy that a previous study found that Veterans with PTSD demonstrated increased physiological reactivity to Virtual Iraq relative to controls (Webb et al., 2015). However, in the context of treatment, the effective use of VRE assumes that the virtual environment is successful at facilitating activation of the fear structure. The clinician's ability to modify the environment is limited by the constraints of the system and, in this study, by the capabilities of Virtual Iraq/Afghanistan at the time of study launch. Clinicians worked carefully and closely with soldiers to expose them to the most relevant stimuli available. However, it is possible that the environments were not activating for some, or worse, distracting from engagement. Unfortunately, this study had no measure of the soldiers' subjective experience of the environments or the degree to which they experienced the VRE to aid emotional engagement. Clearly a subgroup of soldiers experienced large magnitude improvement during VRE. Variation in the individual experience of the virtual environments as activating maybe one explanation for some of the variance. The challenge to customize VRE content may be better addressed in future research as the Virtual Iraq/Afghanistan software has been significantly updated since the start of the present study, currently including 10 additional scenarios (compared with 4 used in this study). Future studies will have a more comprehensive set of experiences to address a broader range of traumas.

Unlike soldiers assigned to PE, those in the VRE group did not continue to experience symptom recovery during the follow-up period. Continued symptom reduction during follow-up is observed in some (Foa et al., 1991; McDonagh et al., 2005), though not all (Resick et al., 2002; Schnurr et al., 2007) trials of exposure therapy. When it occurs, it is often thought to reflect the benefit of continued utilization of learned skills after treatment has formally ended (e.g., continued confrontation of anxiety provoking situations). Other studies suggest that the symptom reduction evident at posttreatment simply persists over time. It is unclear why soldiers who received VRE did not continue to improve whereas soldiers who received PE did. Previous studies of VRE have found mixed results regarding continued symptom recovery during follow-up (Difede et al., 2014; Rizzo et al., 2011; Rothbaum et al., 2014). Future clinical trials involving VRE may continue to clarify the pattern of symptom reduction posttreatment.

The treatment protocol in this study compared manualized PE to the same PE protocol with one difference—the use of VRE as a replacement for imaginal exposure. A strength of this design is that it allowed for a controlled evaluation of the role of VRE relative to imaginal exposure. However, results may not generalize to other VRE treatment protocols. The literature on VRE for combat-related PTSD represents a range of treatment protocols, including approaches incorporating Zen meditation techniques (McLay et al., 2011), the initial use of imaginal exposure in the first two sessions followed by VRE (Rothbaum, Difede, & Rizzo, 2008) and brief treatments combined with medication and no homework (Rothbaum et al., 2014). Future research should evaluate the differences between treatment protocols and how they fare relative to PTSD standards of care.

Regarding treatment stigma, our hypothesis that soldiers assigned to VRE would demonstrate significant reductions in treatment stigma relative to those receiving PE was not supported. It is encouraging that soldiers who received PE and VRE reported significant decreases in stigma at posttreatment relative to soldiers assigned to the waitlist. Notwithstanding the high dropout rates, participating in either type of exposure therapy appears to have reduced perceptions of stigma. Our findings are consistent with a prior study of deployed soldiers who reported no significant differences in their stigma-related reactions to descriptions of PE and VRE (Reger et al., 2013). The present study did not address the important question of whether the availability of VRE as a treatment choice increased rates of psychotherapy utilization among soldiers. This question will have to be answered in future research.

Contrary to our hypothesis, soldiers assigned to VRE did not drop out at a significantly lower rate than soldiers assigned to PE. When drop out was defined as failure to complete 10 sessions of psychotherapy, 44% of soldiers assigned to VRE and 41% of those

assigned to PE dropped out. This rate is higher than many studies of civilian trauma populations (Hembree et al., 2003) but only slightly higher than studies of veterans, which found dropout rates of 28% when completion required only eight sessions (Eftekhari et al., 2013) and 38% (Schnurr et al., 2007) when female veterans were asked to complete 10 sessions. A recent review of the routine clinical care of 195 Veterans who initiated PE found that 44.9% dropped out of treatment (Kehle-Forbes et al., 2016). In the present study, neither initial PTSD symptom severity nor the slope of change in symptoms during treatment predicted drop out. Military service related issues may be a primary concern. At least 17 individuals dropped out during the treatment phase of the study because of military service-related reasons. Unique barriers and challenges to retaining participants in military RCTs have been previously described (Bush, Sheppard, Fantelli, Bell, & Reger, 2013). Prior deployments to Iraq and Afghanistan are associated with decreased completion of evidence-based treatments for PTSD among veterans (Mott et al., 2014). Soldiers have long work hours with team-based training schedules and work interference is a frequent reason for drop out (Hoge et al., 2014). Treatment can also be interrupted by changes in geographic locations because of changes in duty stations, medical retirement, deployment, or extended training exercises at remote locations. It should be noted that our structured clinical trial included research coordinators who called soldiers and sent follow-up letters to disengaged soldiers. Our high drop out rate despite these efforts is noteworthy, and may suggest that rates could be higher in routine clinical practice with active duty military personnel.

Our study only recruited soldiers with PTSD resulting from deployments in support of Operations Iraqi and Enduring Freedom and it is not known how findings would generalize to soldiers who experienced traumatic events during other conflicts. Another limitation is the predominantly male sample. Additional research is needed to evaluate the efficacy of PE and VRE with female soldiers. We should note that the waitlist period was 5-weeks though treatment typically took longer. We chose not to ask soldiers with PTSD to wait longer for treatment. Although there was no significant difference in the time of the treatment period for the two active treatments (PE and VRE), the time difference is a limitation in the comparisons with soldiers assigned to the waitlist. It is also noteworthy that the different military services have different missions and cultures and it is not known how well the current findings with Army personnel would generalize to service members from the other military services.

Exposure therapy in general, and prolonged exposure in particular, are first line treatments for PTSD (Bradley et al., 2005; Powers et al., 2010; Cahill, Rothbaum, Resick, & Follette, 2009). This study bolsters the evidence for exposure-based trauma therapy and demonstrates its efficacy among active-duty soldiers. However, evidence-based treatments like PE are utilized by soldiers at low rates (Hoge et al., 2014). The dropout rate in this study further underscores the pressing need to develop additional means of enhancing treatment engagement among soldiers and supporting systems improvements to reduce attrition among those who would likely benefit from evidence-based treatments (Institute of Medicine, 2008).

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