Journal of Psychiatric Research 103 (2018) 69–74

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/jpsychires

Effects of prolonged exposure and virtual reality exposure on suicidal ideation in active duty soldiers: An examination of potential mechanisms

Aaron M. Norr[a,b], Derek J. Smolenski[c], Greg M. Reger[a,b,*]

[a] VA Puget Sound Health Care System, Tacoma/Seattle, WA, USA
[b] University of Washington School of Medicine, Seattle, WA, USA
[c] Defense Health Agency, Psychological Health Center of Excellence, Tacoma, WA, USA

ARTICLE INFO

Keywords:
Suicide
Suicidal ideation
Prolonged exposure
Virtual reality
Posttraumatic stress disorder

ABSTRACT

Objective: The current study sought to investigate the effects of exposure therapy on suicidal ideation (SI), as well as potential mechanistic pathways of SI reduction among active duty military personnel.
Methods: Active duty army soldiers (N = 162) were recruited from a military base in the U.S. and were enrolled in a randomized clinical trial comparing Prolonged Exposure (PE), Virtual Reality Exposure (VRE), and a wait-list control for the treatment of posttraumatic stress disorder (PTSD) stemming from deployments to Iraq or Afghanistan. PTSD diagnosis followed DSM-IV-TR criteria. Outcome measures were assessed via self-report and clinician interview. PTSD symptoms, depressive symptoms, and SI were included in an autoregressive cross-lagged panel model to examine mechanistic pathways.
Results: Analyses revealed that PE/VRE had a lower probability of post-treatment suicidal ideation (OR = 0.23, 95% CI [0.06, 0.86]) compared to the waitlist control. Mediation analyses revealed a significant indirect effect from treatment condition to post-treatment PTSD symptoms through mid-treatment SI (Estimate = −1.420, 95% CI -3.559, −0.223]). Baseline suicidal ideation did not interact with treatment condition to predict PTSD symptom change at mid-treatment (p = .231) or post-treatment (p = .672).
Conclusion: PE/VRE successfully reduced SI, and the presence of SI at baseline did not affect PTSD symptom reduction, promoting the utility of using PE/VRE to address suicidality among individuals with PTSD. Mediation analyses suggest that reductions in SI were achieved early in treatment.

Despite unprecedented suicide prevention efforts undertaken in the last decade (Department of Veterans Affairs, 2017b), suicide rates among veterans and military service members remain elevated relative to the pre-9/11 era. Active duty military personnel, with historically lower suicide risk than civilians during peacetime (Eaton et al., 2006), have matched U.S. civilian rates after controlling for demographic differences (Pruitt et al., 2016). Furthermore, there have been no significant reductions in the suicide rates of active duty military personnel from 2012 to the most recent Department of Defense report summarizing 2015 (Pruitt et al., 2016). Among veterans, the risk of suicide is 22% higher than civilians after controlling for differences in age and gender (Department of Veterans Affairs, 2017a). These findings underscore a continued need to improve our understanding of factors contributing to elevated suicide rates and to identify additional methods of reducing suicide risk among military personnel.

Military service members and veterans are also at risk for posttraumatic stress disorder (PTSD; Hoge et al., 2004; Milliken et al., 2007; Seal et al., 2007), which has been identified as a significant risk factor for suicidal ideation (SI) and suicide attempts (Bentley et al., 2016; Kanwar et al., 2013). Thus, reducing PTSD symptoms could reduce risk for SI and suicide attempts. Given the availability of evidence-based treatments for PTSD (Management of Posttraumatic Stress Disorder Work Group, 2017), it is important to understand whether targeting PTSD is actually an effective avenue for mitigating suicide risk among service members and veterans who undergo treatment.

One such evidence-based treatment for PTSD is prolonged exposure (PE; Foa et al., 2007). PE has been shown to be effective in U.S. veterans (Eftekhari et al., 2013) and active duty military personnel (Reger et al., 2016). The treatment involves the confrontation of the patient's trauma memory during imaginal exposure and confrontation of distressing situations, places, or circumstances during in vivo exposure. Though it is logical that using PE to decrease PTSD symptoms would in turn reduce suicide risk among individuals with PTSD, there is limited research on the effects of PE among individuals with suicidal ideation (Rauch et al., 2012; van Minnen et al., 2015). Early work demonstrated that exposure therapy can be safely implemented in individuals with active suicidal

* Corresponding author. VA Puget Sound – American Lake Division, Building 61, Room 222, MS A-116, 9600 Veterans Drive, Tacoma, WA, 98493, USA.
E-mail address: Greg.Reger@va.gov (G.M. Reger).

https://doi.org/10.1016/j.jpsychires.2018.05.009
Received 16 February 2018; Received in revised form 19 April 2018; Accepted 11 May 2018
0022-3956/ Published by Elsevier Ltd.

ideation (Harned et al., 2012; Harned and Linehan, 2008). A lone study found that presence of elevated suicide risk predicted poorer PTSD symptom, though this study combined PE and cognitive therapy, did not account for the potential effects of comorbid depression, and did not have a control condition (Tarrier et al., 2000). Thus, it is currently unclear whether the presence of suicidal ideation affects PTSD treatment outcomes during PE.

Fortunately, more recent work suggests that PE may actually reduce suicide risk among civilians with PTSD. Female patients with sexual-assault-related PTSD who underwent PE saw significant decreases in suicidal ideation compared to a waitlist condition (Gradus et al., 2013). Harned et al. (2014) conducted a clinical trial of dialectical behavior therapy (DBT) compared to DBT + PE among women with PTSD and borderline personality disorder. They found that compared to DBT alone, participants who received DBT + PE had less severe urges to die by suicide and fewer incidents of non-suicidal self-injury. Regarding veterans, one study demonstrated reductions in SI during PE (Cox et al., 2016); however, this study lacked a control group and therefore a causal relationship between PTSD treatment and SI reduction was not established. We are not aware of any studies to date that have directly examined the effects of PE on SI among active-duty service members.

While PE has demonstrated an effect on both PTSD symptoms and SI, the mechanism of change is not clearly established. One study of civilian patients with PTSD found that decreases in PTSD symptoms were associated with decreases in SI for those who were treated with cognitive processing therapy (CPT), but this association was not found for those treated with PE (Gradus et al., 2013). In contrast, reductions in PTSD symptoms have been associated directly with future reductions in suicidal ideation among veterans completing PE (Cox et al., 2016), and indirectly associated via reductions in depressive symptoms among active duty military personnel completing group CPT (Bryan et al., 2016). Finally, a recent study found an association between PTSD symptom reduction and reductions in suicidal ideation due to a computerized treatment. This association was attributed to indirect effects of changes in depression and hopelessness (Boffa et al., 2018). Thus, results in the literature are inconsistent regarding the presence of an association between PTSD symptom reduction and reductions in suicidal ideation during PTSD treatment, with some studies suggesting that this relationship may exist via reductions in depressive symptoms rather than PTSD symptoms. Therefore, change in SI could be attributed to changes in PTSD symptoms, depression, symptoms, or both. It is also possible that changes in SI precede changes in other symptoms, or that these changes all co-occur.

The current study sought to investigate the association between PE (with and without virtual reality exposure; VRE) and suicidal ideation among active-duty U.S. soldiers with combat-related PTSD. First, it was hypothesized that baseline presence of suicidal ideation would not significantly impact the efficacy of exposure therapy on PTSD symptom reduction. Second, it was hypothesized that PE/VRE would significantly reduce SI compared to a waitlist control. Third, given the inconsistent findings in the literature regarding mechanisms of the reduction in suicidal ideation in PTSD treatment, the current study sought to determine whether reductions in suicidal ideation due to PE/VRE were mediated by reductions in PTSD symptoms, depressive symptoms, or both, and what was the most probable temporal sequence.

1. Materials and methods

1.1. Participants

Active-duty U.S. army soldiers ($N = 162$) were recruited from a military base and were enrolled in a randomized clinical trial comparing PE, VRE, and a wait-list condition in the treatment of PTSD stemming from deployments to Iraq or Afghanistan. Participants were largely male (96%, $n = 156$). The majority were Caucasian (60%, $n = 97$) and had some college education (66%, $n = 107$). Psychiatric medication use included antidepressants (44%, $n = 71$), benzodiazepines (24%, $n = 39$), and other (46%, $n = 75$). Participants were all diagnosed with PTSD based on the Clinician Administered PTSD Scale (CAPS; Blake et al., 1995), which follows the diagnostic criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition-Text Revision (DSM-IV-TR; American Psychiatric Association, 2000). See Reger et al. (2016) for full demographics.

Inclusion criteria required the index trauma be a non-sexual assault trauma that occurred at least 3-months prior to the baseline assessment in an environment similar to those available in the Virtual Iraq/Virtual Afghanistan software. Participants agreed to not initiate other psychotherapy for PTSD or new psychotropic medications during the treatment phase. Exclusion criteria included: a) change in psychotropic medications in the last 30 days; b) history of organic mental disorder, 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) history of seizures; g) prior PE treatment; h) other ongoing psychotherapy for PTSD; i) physical condition interfering with the ability to use a virtual reality head-mounted display or VR peripherals; j) history of a loss of consciousness for a duration of greater than 15 min since entering active duty military service.

1.2. Procedure

Assessments were conducted at baseline, at mid-treatment (after 5 treatment sessions), and at post-treatment. CAPS assessors were blind to treatment condition. Treatment was delivered consistent with the published treatment manual for PE (Foa et al., 2007), which included ten, 90–120 min individual psychotherapy sessions. VRE treatment was identical to PE other than the use of virtual reality during imaginal exposure. In the current study, the PE and VRE conditions were collapsed to compare active exposure treatment to the wait-list control. The active treatments were collapsed due to results from the main effect paper demonstrating a lack of significant differences in treatment outcomes at post-treatment (Reger et al., 2016). Data were collected from 06/2009 to 11/2013. For a more detailed description of the full study procedures see Reger et al. (2016). The study was approved by the local institutional review board, written informed consent was obtained, and the study was registered at ClinicalTrials.gov (identifier: NCT01193725).

1.3. Measures

Beck Depression Inventory-II (BDI-II; Beck et al., 1996***)***. The BDI-II is a 21-item self-report measure of the severity of depression. Responses reflect symptoms from the prior two weeks and items are rated from 0 (*least severe*) to 3 (*most severe*). In the current study BDI-II item 9 was used to assess the presence/absence of suicidal ideation (0 = “I don't have any thoughts of killing myself”; 1 = “I have thoughts of killing myself, but I would not carry them out”; 2 = “I would like to kill myself”; 3 = “I would kill myself if I had the chance”). Only one participant at one time point (baseline) had a score greater than 1 on BDI-II item 9 which was recoded to 1 to create a dichotomous variable. The BDI-II total score was created using the remaining 20 items to measure depressive symptoms independent of suicidal ideation. Higher scores represent greater depressive symptoms. In prior studies, the BDI-II has demonstrated good reliability and validity (Foa et al., 1993). In the current study, internal consistency for the BDI-II was good at baseline ($\alpha = 0.89$) and excellent at mid-treatment ($\alpha = 0.93$) and post-treatment ($\alpha = 0.96$).

Clinician Administered PTSD Scale (CAPS; Blake et al., 1995***)***. The CAPS assess the severity of PTSD symptoms (DSM-IV-TR criteria) using a structured clinical interview. Symptom frequency and intensity is coded on a scale ranging from 0 to 4. Higher scores indicate greater PTSD symptoms. The current study examined CAPS ratings for

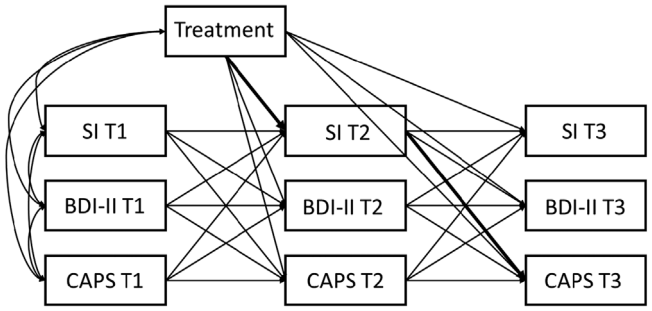

Fig. 1. Diagram of Autoregressive Cross-lagged Panel Model. T1 = Baseline; T2 = Mid-Treatment; T3 = Post-Treatment; BDI-II = Beck Depression Inventory – II without suicide item (item 9); CAPS = Clinician Administered PTSD Scale; SI = suicidal ideation, presence/absence. Significant indirect pathway from treatment to SI (time 2) to CAPS (time 3) is bolded.

symptoms from the prior week. Internal consistency for the CAPS was good at baseline (α = 0.81) and excellent at mid-treatment (α = 0.93) and post-treatment (α = 0.93).

1.4. Data analytic plan

The test for moderation used a mixed effects regression model to estimate change in PTSD symptoms from baseline to post treatment. A multiplicative interaction term between treatment group assignment (PE/VRE or waitlist) and baseline SI was used to test for a deviation in the amount of change attributed to treatment assignment as a function of baseline SI level. The growth curve model included a random intercept variance, a categorical indicator for measurement occasion. The residual variance matrix was specified as exchangeable.

For the mediation model, an autoregressive, cross-lagged panel model (Cole and Maxwell, 2003) was estimated. Fig. 1 displays the regression paths estimated in the model. CAPS scores, BDI-II scores, and the SI measure at mid and post treatment were specified as a function of scores at the pre and mid treatment time points, respectively. In addition, treatment assignment was an antecedent of all measures at mid and post treatment. This allowed for the estimation of direct effects of treatment. In addition to treatment assignment and scores on a particular measure at the preceding time point, each measure at mid and post treatment was regressed on the scores of the other measures at the preceding time point. This model allowed us to simultaneously consider four indirect associations of interest: change in the CAPS as antecedent to change in SI; change in the BDI-II as antecedent to change in SI; and change in SI as antecedent to change in the CAPS or BDI-II. Indirect effects were defined as the product of the component pathway coefficients. Percentile bias-corrected bootstrapped confidence intervals (CIs) with 5000 resamples were used to assess statistical significance and precision given the asymmetric nature of the indirect effects (Hayes and Scharkow, 2013; Preacher and Hayes, 2008).

All models were estimated in Mplus version 7.3 (Muthén and Muthén, 1996–2012) using full information maximum likelihood to account for missing data. Data were missing for 35 participants at mid-treatment and 54 at post-treatment. Prior analyses suggest that data were missing at random (Reger et al., 2016). Treatment was coded as 0 = wait-list control 1 = PE/VRE. All analyses using BDI-II item 9 as an endogenous variable were modeled using a logit link function. Preliminarily analyses comparing the PE and the VRE groups revealed no significant differences across all analyses, providing statistical support for collapsing these groups.

2. Results

The observed scores on the outcome measures, by assigned treatment condition, are provided in Table 1. These estimates represent the total effect of treatment assignment on each of the outcome measures. Consistent with the randomized design of the study, there were no significant differences at baseline between conditions on any of the variables. CAPS scores decreased more by mid treatment for those in the PE/VRE groups relative to the wait-list control group. By post treatment, there was a pronounced difference between the treatment groups in the CAPS score. Similarly, participants assigned to the PE/VRE groups had a greater decrease in the BDI-II score over time. In terms of suicidal ideation, the PE/VRE groups had a strong reduction in SI by the mid-treatment assessment; this persisted at post treatment. In contrast, the waitlist group exhibited a slight increase in the prevalence of SI. The test for moderation of the treatment effect on the CAPS did not identify a statistically significant interaction at either mid or post treatment (p = .231 and p = .672, respectively).

Table 1
Sample descriptives by treatment condition.

Variable	PE/VRE (n = 108)		Wait-list Control (n = 54)		
	M	*SD*	*M*	*SD*	*b* [95% CI]
Baseline CAPS	79.36	16.25	78.89	16.87	0.47 [-7.04, 7.99]
Mid-Treatment CAPS	67.99	26.52	74.73	21.78	−7.42 [-14.85, 0.00]
Post-Treatment CAPS	50.47	33.41	68.06	24.27	−18.02 [-25.82, −10.21]
Baseline BDI-II	27.82	10.08	27.51	9.97	0.29 [-3.46, 4.04]
Mid-Treatment BDI-II	21.91	12.15	24.46	10.58	−2.68 [-5.55, 0.18]
Post-Treatment BDI-II	17.71	14.45	25.37	12.57	−8.06 [-11.09, −5.03]
	%		%		*OR* [95% CI]
Baseline SI	10.2		13.0		0.76 [0.28, 2.09]
Mid-Treatment SI	1.9		16.7		0.19 [0.05, 0.77]
Post-Treatment SI	2.8		18.5		0.23 [0.06, 0.86]

Note. SI = suicidal ideation, presence/absence (presence of SI is indicated); BDI-II = Beck Depression Inventory – II without suicide item (item 9); CAPS = Clinician Administered PTSD Scale.

Estimates from the cross-lagged panel model are presented in Table 2. There was a significant direct effect of treatment condition on mid-treatment CAPS, BDI-II, and SI, as well as post-treatment CAPS and BDI-II scores, such that those in PE/VRE had lower symptom scores. The direct effect of treatment condition on post-treatment SI was not significant. As expected, several of the lag effects were also statistically significant in the model. Only one of the compound path coefficients involving SI was statistically significant as an indirect effect (Table 2). This path involved the change in SI observed at mid treatment and the subsequent change in the CAPS at post treatment. Given the magnitude of the treatment assignment on the CAPS from Table 1 (18.02 point reduction), the compound path through SI predicted 7.88% of the change in the CAPS.

3. Discussion

The current study sought to investigate the effect of treatment with PE/VRE on SI among active duty U.S. soldiers with combat-related PTSD. Consistent with initial hypotheses, the results demonstrated significant reductions in the presence of SI among soldiers in the PE/VRE group compared to the waitlist control. These results are consistent with prior work showing reductions in SI due to PE (Cox et al., 2016; Gradus et al., 2013; Harned et al., 2014), as well as individual and group CPT among active duty personnel (Bryan et al., 2016; Resick et al., 2017). Thus, the current study is the first to support the use of PE/VRE to reduce SI among active duty personnel, and adds to a limited body of literature supporting the targeting of PTSD symptoms as an

Table 2
Autoregressive cross-lagged panel model of direct and indirect effects of treatment on PTSD symptom and depressive symptom and SI change.

	Standardized Estimate	Unstandardized Estimate	95% CI			
			SE	LL	UL	R^2
Covariance						
Tx ↔ CAPS T1	0.014	0.105	0.609	−1.055	1.302	
Tx ↔ BDI-II T1	0.009	0.042	0.363	−0.659	0.769	
Tx ↔ SI T1	−0.042	−0.006	0.012	−0.031	0.016	
BDI-II T1 ↔ CAPS T1	**0.550**	**89.515**	**13.270**	**64.777**	**117.212**	
BDI-II T1 ↔ SI T1	**0.381**	**1.191**	**0.331**	**0.586**	**1.877**	
CAPS T1 ↔ SI T1	**0.211**	**1.082**	**0.419**	**0.314**	**1.961**	
Regression Weights						
BDI-II T2						**.571**
Tx	**−0.113**	**−2.754**	**1.340**	**−5.422**	**−0.165**	
CAPS T1	0.106	0.075	0.053	−0.028	0.185	
SI T1	−0.093	−3.399	2.362	−8.214	1.054	
BDI-II T1	**0.716**	**0.829**	**0.088**	**0.654**	**1.001**	
CAPS T2						**.411**
Tx	**−0.146**	**−7.535**	**3.243**	**−13.832**	**−0.928**	
BDI-II T1	**0.349**	**0.855**	**0.234**	**0.399**	**1.313**	
SI T1	−0.032	−2.453	6.370	−15.938	9.144	
CAPS T1	**0.375**	**0.559**	**0.117**	**0.308**	**0.767**	
SI T2						**.234**
Tx	**−0.221**	**−0.131**	**0.049**	**−0.239**	**−0.046**	
CAPS T1	−0.092	−0.002	0.002	−0.005	0.001	
BDI-II T1	0.034	0.001	0.003	−0.006	0.007	
SI T1	**0.419**	**0.373**	**0.129**	**0.121**	**0.629**	
BDI-II T3						**.746**
Tx	**−0.159**	**−4.473**	**1.260**	**−6.882**	**−1.957**	
CAPS T2	**0.230**	**0.125**	**0.040**	**0.047**	**0.203**	
SI T2	0.061	2.877	2.192	−1.420	7.236	
BDI-II T2	**0.691**	**0.796**	**0.089**	**0.610**	**0.961**	
CAPS T3						**.657**
Tx	**−0.154**	**−9.688**	**3.641**	**−17.037**	**−2.794**	
BDI-II T2	0.092	0.235	0.260	−0.286	0.732	
SI T2	0.102	10.819	5.890	−0.869	21.768	
CAPS T2	**0.709**	**0.859**	**0.106**	**0.645**	**1.056**	
SI T3						**.700**
Tx	−0.244	−1.714	25.299	−43.528	11.148	
CAPS T2	0.101	0.014	1.516	−0.321	4.321	
BDI-II T2	0.424	0.122	2.992	−0.211	2.150	
SI T2	0.526	6.226	106.435	−2.746	18.189	
Indirect Effects						
Tx → CAPS T2 → SI T3		−0.103	10.251	−33.467	1.855	
Tx → BDI-II T2 → SI T3		−0.336	8.465	−19.083	0.200	
Tx → SI T2 → CAPS T3		**−1.420**	**0.785**	**−3.559**	**−0.223**	
Tx → SI T2 → BDI-II T3		−0.378	0.302	−1.190	0.067	
Tx → BDI-II T2 → CAPS T3		−0.648	0.827	−3.031	0.486	
Tx → CAPS T2 → BDI-II T3		**−0.943**	**0.461**	**−2.087**	**−0.231**	

Note. SE = Standardized Error; CI = Confidence Interval; LL = Lower Limit; UL = Upper Limit; T1 = Baseline; T2 = Mid-Treatment; T3 = Post-Treatment; Tx = Treatment Condition; SI = suicidal ideation, presence/absence; BDI-II = Beck Depression Inventory – II without suicide item (item 9); CAPS = Clinician Administered PTSD Scale. All significant results are in bold.

avenue to achieve suicide risk reduction among individuals with comorbid PTSD and SI.

Mediation analyses revealed a significant indirect effect of treatment condition on post-treatment PTSD symptoms via mid-treatment SI. However, all other indirect pathways involving SI were not significant. These results suggest that reductions in SI were achieved prior to mid-treatment, and that SI reduction between baseline and mid-treatment is predictive of increased PTSD symptom reduction between mid-treatment and post-treatment. Unfortunately, based on our measurement frequency it is impossible to determine the true temporal sequence of reductions in PTSD symptoms or depressive symptoms and SI reduction prior to the mid-treatment assessment. This issue could account for the discrepancy between the current study and prior work finding prior session PTSD symptoms predicted changes in SI (Cox et al., 2016; Gradus et al., 2013), but that prior session SI did not predict changes in PTSD symptoms (Cox et al., 2016). The current study was also not consistent with prior work suggesting the importance of depressive symptom change to achieve SI reduction in PTSD treatment (Boffa et al., 2018; Bryan et al., 2016).

The finding that reductions in SI due to PE/VRE occurred prior to mid-treatment is surprising given that the purported active mechanisms of PE (Cooper et al., 2017) might require additional time. It may not be expected that these gains would be solidified so early on in treatment. However, cases of rapid symptom resolution during PE (Keller et al., 2014) have been observed and it is possible these cases represent such an outcome. Alternatively, it is possible that other factors associated with engaging in care could better account for SI reductions seen in the current study. For example, work has demonstrated that therapeutic alliance established in the first therapy session is predictive of suicidal ideation a year later (Gysin-Maillart et al., 2017). Similarly, cognitive behavioral therapy has been suggested to increase hope through increased agency and planning to meet treatment goals (Snyder et al., 2000), and the presence of hope mitigates risk of SI (Tucker et al., 2013). Future research should investigate other potential mechanisms that could account for the reductions in SI seen early in treatment.

Relevant to clinical decision making, the current study found that

the presence of SI at baseline had no effect on the efficacy of PE/VRE regarding PTSD symptom amelioration. These results are important given survey work suggesting approximately 85% of clinicians believe exposure therapy would be contraindicated in individuals with comorbid suicidality (Becker et al., 2004). It should be noted that one prior study did find the presence of suicidal ideation predicted poorer PTSD symptom reduction in a sample of civilians treated with PE or cognitive therapy (Tarrier et al., 2000), though they did not account for the potential effects of depression and did not have a comparison control condition.

The results of the current study should be considered in the context of several limitations. First, more than a third of the sample dropped out prior to the post-treatment assessment. This is consistent with studies examining dropout during PE among veterans (Eftekhari et al., 2013; Kehle-Forbes et al., 2016) as well as documented challenges with research and treatment among active duty personnel (Bush et al., 2013; Hoge et al., 2014). At post treatment the dropout rate for VRE/PE was 43%, while the dropout rate for the waitlist condition was 15%. Missing data were handled with maximum likelihood estimation per recommended best practices (Graham, 2009). However, despite utilizing best statistical practices for handling missing data it is still possible that the elevated dropout rate in the treatment condition could affect results compared to if the full sample had completed the study. Second, the current study utilized a single item measure of suicidal ideation, which is consistent with prior studies examining SI among individuals with PTSD (Cox et al., 2016; Gradus et al., 2013). Though a more comprehensive measure of suicide risk may provide a more nuanced perspective, research in a large sample (N = 447,245; Louzon et al., 2016) of veterans found that a single item measure of SI significantly predicted suicide mortality (HR = 1.47), supporting the utility of measuring SI in this fashion. Similarly, given the low overall frequency and severity of SI found in the current sample, these results should be interpreted with caution until future research can replicate these findings in a sample with greater frequency and severity of SI. Third, as is an issue with the clear majority of studies investigating treatment mechanisms, we attempted to model what is thought to be a continuous change process based on discrete measurements at baseline, mid-treatment, and post-treatment. It is possible that measuring symptoms at shorter intervals would reveal a more nuanced temporal pattern of symptom change.

Despite these limitations, the current study is a significant step forward as it is the first study to examine the effects of PE/VRE for PTSD on SI among active duty military personnel. PE/VRE successfully reduced SI, and the presence of SI at baseline did not affect PTSD symptom reduction, promoting the utility of using PE/VRE as one method to address suicidality among individuals with PTSD. Future work needs to further clarify mechanistic pathways associated with SI reduction to potentially maximize the effectiveness of PE/VRE regarding suicidality as findings appear to be inconsistent across studies.

Conflicts of interest

The authors have no conflicts of interest to disclose.

Author note

This research was supported by Grant W81XWH-08-2–0015 from the U.S. Army Medical Research and Materiel Command Military Operational Medicine Research Program. The views, opinions, and/or findings contained in this document are those of the authors' and should not be construed as an official Department of Defense or Department of Veteran Affairs position, policy or decision unless so designated by other official documentation. This research is also supported by the Department of Veterans Affairs Office of Academic Affiliations Advanced Fellowship Program in Mental Illness Research and Treatment, the Medical Research Service of the Veterans Affairs Puget Sound Health Care System, and the Department of Veterans Affairs Northwest Mental Illness Research, Education, and Clinical Center (MIRECC). Role of the sponsors: The supporters had no role in the design, analysis, interpretation, or publication of this study. Declarations of interest: None.

References

American Psychiatric Association, 2000. Diagnostic and Statistical Manual of Mental Disorders. American Psychiatric Publishing, Inc., Washington, DC 4th, text rev. ed.

Beck, A.T., Steer, R., Brown, G.K., 1996. Beck Depression Inventory - II. The Psychological Corporation, San Antonio, TX.

Becker, C.B., Zayfert, C., Anderson, E., 2004. A survey of psychologists' attitudes towards and utilization of exposure therapy for PTSD. Behav. Res. Ther. 42 (3), 277–292.

Bentley, K.H., Franklin, J.C., Ribeiro, J.D., Kleiman, E.M., Fox, K.R., Nock, M.K., 2016. Anxiety and its disorders as risk factors for suicidal thoughts and behaviors: a meta-analytic review. Clin. Psychol. Rev. 43, 30–46.

Blake, D.D., Weathers, F.W., Nagy, L.M., Kaloupek, D.G., Gusman, F.D., Charney, D.S., Keane, T.M., 1995. The development of a clinician-administered PTSD scale. J. Trauma Stress 8 (1), 75–90.

Boffa, J.W., King, S.L., Turecki, G., Schmidt, N.B., 2018. Investigating the role of hopelessness in the relationship between PTSD symptom change and suicidality. J. Affect. Disord. 225, 298–301.

Bryan, C.J., Clemans, T.A., Hernandez, A.M., Mintz, J., Peterson, A.L., Yarvis, J.S., Resick, P.A., 2016. Evaluating potential iatrogenic suicide risk in trauma-focused group cognitive behavioral therapy for the treatment of PTSD in active duty military personnel. Depress. Anxiety 33 (6), 549–557.

Bush, N.E., Sheppard, S.C., Fantelli, E., Bell, K.R., Reger, M.A., 2013. Recruitment and attrition issues in military clinical trials and health research studies. Mil. Med. 178 (11), 1157–1163.

Cole, D.A., Maxwell, S.E., 2003. Testing mediational models with longitudinal data: questions and tips in the use of structural equation modeling. J. Abnorm. Psychol. 112 (4), 558.

Cooper, A.A., Clifton, E.G., Feeny, N.C., 2017. An empirical review of potential mediators and mechanisms of prolonged exposure therapy. Clin. Psychol. Rev. 56, 106–121.

Cox, K.S., Mouilso, E.R., Venners, M.R., Defever, M.E., Duvivier, L., Rauch, S.A., Strom, T.Q., Joiner, T.E., Tuerk, P.W., 2016. Reducing suicidal ideation through evidence-based treatment for posttraumatic stress disorder. J. Psychiatr. Res. 80, 59–63.

Department of Veterans Affairs, 2017a. Suicide among veterans and other americans 2001-2014. updated august 2017. https://www.mentalhealth.va.gov/docs/2016suicidedatareport.pdf, Accessed date: 26 September 2017.

Department of Veterans Affairs, 2017b. Veteran outreach toolkit: preventing veteran suicide is Everyone's business - a community call to action. https://www.healthquality.va.gov/guidelines/MH/ptsd/VADoDPTSDCPGFinal082917.pdf, Accessed date: 26 September 2017.

Eaton, K.M., Messer, S.C., Garvey Wilson, A.L., Hoge, C.W., 2006. Strengthening the validity of population-based suicide rate comparisons: an illustration using US military and civilian data. Suicide Life-Threatening Behav. 36 (2), 182–191.

Eftekhari, A., Ruzek, J.I., Crowley, J.J., Rosen, C.S., Greenbaum, M.A., Karlin, B.E., 2013. Effectiveness of national implementation of prolonged exposure therapy in Veterans Affairs care. JAMA psychiatry 70 (9), 949–955.

Foa, E.B., Hembree, E.A., Rothbaum, B.O., 2007. Prolonged Exposure Therapy for PTSD: Emotional Processing of Traumatic Experiences: Therapist Guide. Oxford Universtiy Press, USA.

Foa, E.B., Riggs, D.S., Dancu, C.V., Rothbaum, B.O., 1993. Reliability and validity of a brief instrument for assessing post-traumatic stress disorder. J. Trauma Stress 6 (4), 459–473.

Gradus, J.L., Suvak, M.K., Wisco, B.E., Marx, B.P., Resick, P.A., 2013. Treatment of posttraumatic stress disorder reduces suicidal ideation. Depress. Anxiety 30 (10), 1046–1053.

Graham, J.W., 2009. Missing data analysis: making it work in the real world. Annu. Rev. Psychol. 60 (1), 549–576.

Gysin-Maillart, A.C., Soravia, L.M., Gemperli, A., Michel, K., 2017. Suicide ideation is related to therapeutic alliance in a brief therapy for attempted suicide. Arch. Suicide Res. 21 (1), 113–126.

Harned, M.S., Korslund, K.E., Foa, E.B., Linehan, M.M., 2012. Treating PTSD in suicidal and self-injuring women with borderline personality disorder: development and preliminary evaluation of a dialectical behavior therapy prolonged exposure protocol. Behav. Res. Ther. 50, 381–386.

Harned, M.S., Korslund, K.E., Linehan, M.M., 2014. A pilot randomized controlled trial of Dialectical Behavior Therapy with and without the Dialectical Behavior Therapy Prolonged Exposure protocol for suicidal and self-injuring women with borderline personality disorder and PTSD. Behav. Res. Ther. 55, 7–17.

Harned, M.S., Linehan, M.M., 2008. Integrating dialectical behavior therapy and prolonged exposure to treat co-occurring borderline personality disorder and PTSD: two case studies. Cognit. Behav. Pract. 15, 263–276.

Hayes, A.F., Scharkow, M., 2013. The relative trustworthiness of inferential tests of the indirect effect in statistical mediation analysis: does method really matter? Psychol. Sci. 24 (10), 1918–1927.

Hoge, C.W., Castro, C.A., Messer, S.C., McGurk, D., Cotting, D.I., Koffman, R.L., 2004. Combat duty in Iraq and Afghanistan, mental health problems and barriers to care. N. Engl. J. Med. 351, 13–22.

Hoge, C.W., Grossman, Sasha H., Auchterlonie, Jennifer L., Riviere, Lyndon A., Milliken, Charles S., Wilk, Joshua E., 2014. PTSD treatment for soldiers after combat deployment: low utilization of mental health care and reasons for dropout. Psychiatr. Serv.

65 (8), 997–1004.
Kanwar, A., Malik, S., Prokop, L.J., Sim, L.A., Feldstein, D., Wang, Z., Murad, M.H., 2013. The association between anxiety disorders and suicidal behaviors: a systematic review and meta-analysis. Depress. Anxiety 30 (10), 917–929.
Kehle-Forbes, S.M., Meis, L.A., Spoont, M.R., Polusny, M.A., 2016. Treatment initiation and dropout from prolonged exposure and cognitive processing therapy in a VA outpatient clinic. Psychol. Trauma. : Theor. Res. Prac. Pol. 8 (1), 107.
Keller, S.M., Feeny, N.C., Zoellner, L.A., 2014. Depression sudden gains and transient depression spikes during treatment for PTSD. J. Consult. Clin. Psychol. 82 (1), 102–111.
Louzon, S.A., Bossarte, R., McCarthy, J.F., Katz, I.R., 2016. Does suicidal ideation as measured by the PHQ-9 predict suicide among VA patients? Psychiatr. Serv. 67 (5), 517–522.
Management of Posttraumatic Stress Disorder Work Group, 2017. VA/DOD Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Actue Stress Disorder (Version 3.0). Department of Veterans Affairs and Department of Defense. https://www.healthquality.va.gov/guidelines/MH/ptsd/, Accessed date: 26 September 2017.
Milliken, C.S., Auchterlonie, J.L., Hoge, C.W., 2007. Longitudinal assessment of mental health problems among active and reserve component soldiers returning from the Iraq war. Jama 298 (18), 2141–2148.
Muthén, L.K., Muthén, B.O., 1996-2012. Mplus User's Guide, seventh ed. Muthén & Muthén, Los Angeles, CA.
Preacher, K.J., Hayes, A.F., 2008. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. Behav. Res. Meth. 40 (3), 879–891.
Pruitt, L.D., Smolenski, D.J., Bush, N.E., Skopp, N.A., Hoyt, T.V., Grady, B.J., 2016. Department of Defense Suicide Event Report: Calendar Year 2015 Annual Report.
Rauch, M., Sheila, A., Eftekhari, A., Ruzek, J.I., 2012. Review of exposure therapy: a gold standard for PTSD treatment. J. Rehabil. Res. Dev. 49 (5).
Reger, G.M., Koenen-Woods, P., Zetocha, K., Smolenski, D.J., Holloway, K.M., Rothbaum, B.O., Difede, J., Rizzo, A.A., Edwards-Stewart, A., Skopp, N.A., 2016. Randomized controlled trial of prolonged exposure using imaginal exposure vs. virtual reality exposure in active duty soldiers with deployment-related posttraumatic stress disorder (PTSD). J. Consult. Clin. Psychol. 84 (11), 946.
Resick, P.A., Wachen, J.S., Dondanville, K.A., Pruiksma, K.E., Yarvis, J.S., Peterson, A.L., Mintz, J., Borah, E.V., Brundige, A., Hembree, E.A., 2017. Effect of group vs individual cognitive processing therapy in active-duty military seeking treatment for posttraumatic stress disorder: a randomized clinical trial. JAMA psychiatry 74 (1), 28–36.
Seal, K.H., Bertenthal, D., Miner, C.R., Sen, S., Marmar, C., 2007. Bringing the war back home: mental health disorders among 103 788 US veterans returning from Iraq and Afghanistan seen at Department of Veterans Affairs Facilities. Arch. Intern. Med. 167 (5), 476–482.
Snyder, C.R., Ilardi, S.S., Cheavens, J., Michael, S.T., Yamhure, L., Sympson, S., 2000. The role of hope in cognitive-behavior therapies. Cognit. Ther. Res. 24 (6), 747–762.
Tarrier, N., Sommerfield, C., Pilgrim, H., Faragher, B., 2000. Factors associated with outcome of cognitive-behavioural treatment of chronic post-traumatic stress disorder. Behav. Res. Ther. 38 (2), 191–202.
Tucker, R.P., Wingate, L.R., O'Keefe, V.M., Mills, A.C., Rasmussen, K., Davidson, C.L., Grant, D.M., 2013. Rumination and suicidal ideation: the moderating roles of hope and optimism. Pers. Indiv. Differ. 55 (5), 606–611.
van Minnen, A., Zoellner, L.A., Harned, M.S., Mills, K., 2015. Changes in comorbid conditions after prolonged exposure for PTSD: a literature review. Curr. Psychiatr. Rep. 17 (3), 17.