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



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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 post-traumatic 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

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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 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-treat-

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

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