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Mediation of suicide ideation in prolonged exposure therapy for posttraumatic stress disorder

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ABSTRACT

Background: Evidence-based treatments for posttraumatic stress disorder (PTSD) are associated with reduction in suicidal ideation (SI), yet the mechanisms underlying this reduction are unclear. The current study investigated improvements in PTSD, depression, and social support as potential mediators of the change in SI over time.
Method: Participants ($N = 200$) were active duty military personnel with PTSD randomized to prolonged exposure therapy (PE) or present-centered therapy (PCT). Using parallel mediation and serial mediation models, we examined the relative influence of the mediators on suicidal ideation over time.
Results: Consistent with our hypotheses, lagged mediation analyses revealed that depression was the strongest mediator of improvements in SI over time in PE and PCT. Reductions in PTSD were associated with subsequent reductions in depression, which was associated with reductions in SI. Treatment condition did not moderate this relationship, and social support was not a significant mediator.
Conclusions: In active duty military personnel, reduction in depression was the strongest mediator of reduction in suicidal ideation in PE and PCT for PTSD. These results were not altered by treatment condition.
Trial registration: Clinicaltrials. gov identifier: NCT01049516. http://www.clinicaltrials.gov/show/NCT01049516.

Abbreviations: BDI-II, Beck Depression Inventory; II, BSSI; Beck Scale for Suicide Ideation, CI; confidence interval, CPT; cognitive processing therapy, E-1 to E-3; junior enlisted, E-4 to E-6; junior noncommissioned officers, E-7 to E-9; senior noncommissioned officers, ISEL-12; Interpersonal Support Evaluation List, 12; MCC, minimal contact control; M-PE, massed prolonged exposure; PCL, Posttraumatic Checklist; PCT, present-centered therapy; PE, prolonged exposure; PTSD, posttraumatic stress disorder; SI, suicidal ideation; S-PE, spaced prolonged exposure

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Trauma-focused treatments are associated with significant reductions in suicidal ideation in civilians, veterans, and active duty military personnel. In civilians, both prolonged exposure therapy (PE) and cognitive processing therapy (CPT) for posttraumatic stress disorder (PTSD) result in comparable and significant reductions in suicidal ideation over time, particularly during the active treatment phase (Gradus, Suvak, Wisco, Marx, & Resick, 2013). Furthermore, decreased PTSD symptoms correlated with reductions in suicidal ideation even after controlling for baseline depression or decreased hopelessness (Gradus et al., 2013).

Similar results emerged in a naturalistic sample of veterans receiving PE for PTSD in the Veterans Health Administration, in which significant but small reductions in suicidal ideation were detected (d = .27, Cox et al., 2016). Time-lagged models indicated that PTSD symptom reduction was associated with suicidal ideation reduction and accounted for 3% of the variance in suicidal ideation, whereas suicidal ideation reduction was not associated with a reduction in PTSD symptoms (Cox et al., 2016). In active duty military personnel, CPT and present-centered therapy (PCT) resulted in comparable and significant reductions in suicidal ideation over time; reductions in depression, but not PTSD symptoms, were associated with reductions in suicidal ideation (Bryan et al., 2016). A randomized controlled trial comparing massed-PE (M-PE; daily sessions for 2 weeks) to a minimal contact control (MCC) condition found that M-PE led to significantly faster reductions (i.e., steeper slope) in suicidal ideation (Brown et al., 2019) although spaced-PE (S-PE; twice weekly sessions for 8 weeks) was associated with comparable and significant reductions in suicidal ideation compared to PCT in treatment (Brown et al., 2019). As with prior research, reductions in PTSD symptoms were significantly associated with reductions in suicidal ideation.

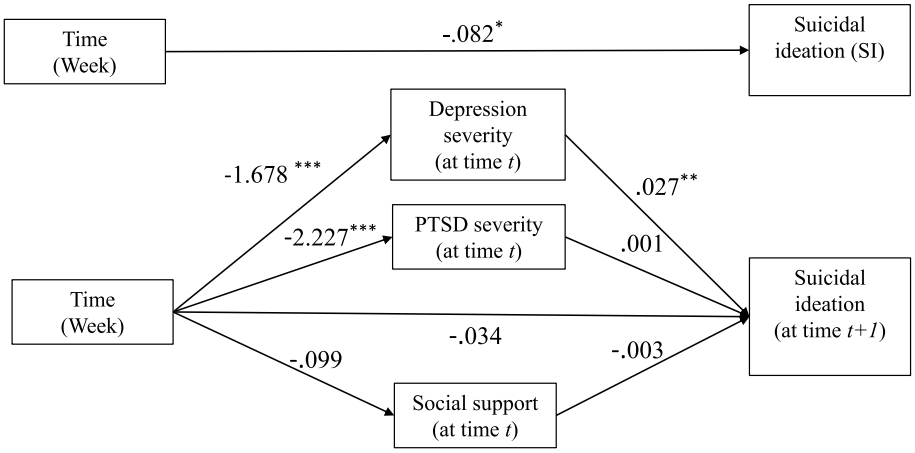
While there is growing evidence that trauma-focused treatments are associated with significant reductions in suicidal ideation, the mechanisms underlying suicidal ideation improvement remain unclear. Cross-sectional and prospective research suggest that PTSD symptom severity is indirectly related to suicidal ideation severity through depression in active duty military personnel (Bryan et al., 2015; McLean et al., 2017). Similarly, a randomized control trial of CPT and PCT in active duty personnel found that PTSD improvement was indirectly correlated with subsequent suicidal ideation severity through depression but was not associated with the change in suicidal ideation over time either directly or indirectly (Bryan et al., 2016). There is no prior research examining whether change in PTSD remains a significant predictor of suicidal ideation above and beyond change in depression for active duty service members receiving PE for PTSD. Prior research suggests that the change in PTSD and depression in PE is reciprocal in nature (Brown, Contractor, et al., 2018), but the complex associations among PTSD, depression, and suicidal ideation have not been explored in response to PE. Based on the prior research in other PTSD treatments, it is foreseeable that PTSD change would also be indirectly associated with suicidal ideation through depression change in service members receiving PE or PCT for PTSD.

Beyond depression, prior research has implicated the importance of social relationships in both PTSD and suicidal ideation. Interpersonal disconnection is a critical risk factor for suicidal ideation and suicide attempts (Joiner, 2005; Winterrowd, Canetto, & Chavez, 2010) and is also a core feature of PTSD (American Psychiatric Association, 2013). In fact, of all PTSD symptoms, interpersonal detachment was found to be the most strongly associated with suicidal ideation (Davis, Witte, & Weathers, 2014). Joiner (2005) suggested that thwarted belongingness (i.e., feeling that one does not belong socially) and perceived burdensomeness (i.e., feeling that one is a burden on social connections) are risk factors for suicidal ideation. Indeed, both thwarted belongingness and perceived burdensomeness are elevated in combat veterans (Lusk et al., 2015) and active duty service members with PTSD (Bryan & Anestis, 2011). It is unclear whether improvements in perceived social support are associated with improvements in suicidal ideation in active duty service members with PTSD.

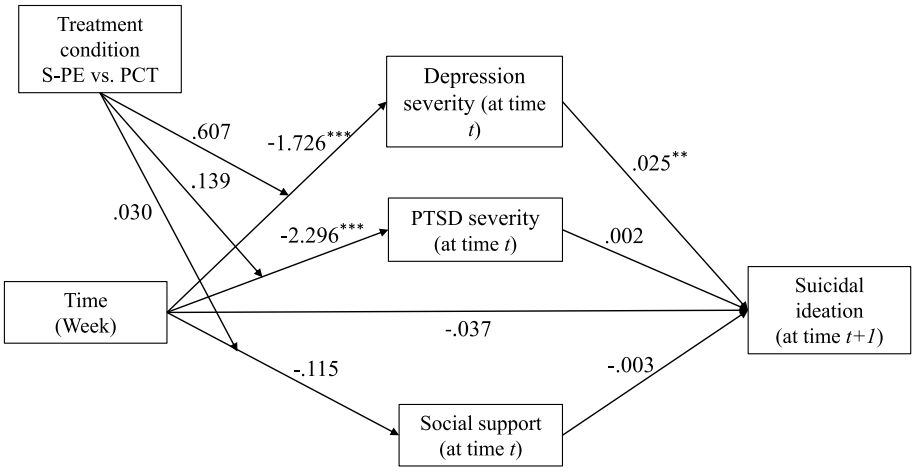
Beyond understanding how social support, PTSD, and depression changes are associated with suicidal ideation, it may be equally important to determine the potential moderation of these mediational relationships. PCT, a common comparator to PE in randomized controlled trials, is guided by the provision of social and emotional support on behalf of the therapist through the use of empathy and active listening, which may enhance the perception of social connection and reduce suicide risk. The provision of social support is not an explicit goal of PE, though it may often occur inadvertently through the use of reinforcement and cheerleading of adaptive behaviors. Some studies have found that PE was associated with significantly greater improvements in PTSD (Rauch et al., 2015; Schnurr & Lunney, 2015) and depression (de Bont et al., 2016; Nacasch et al., 2011) compared to PCT. However, a recent study in active duty military personnel found that PE and PCT were equally effective in reducing PTSD symptoms (Foa et al., 2018). In addition, an earlier study in veterans found that whereas PE was associated with lower PTSD severity at post-treatment and 3-month follow-up compared to PCT, the treatments were equally effective at 6-month follow-up (Schnurr et al., 2007). No studies to our knowledge have explored the extent to which PE and PCT may differentially affect social support or other key mediators of the reduction of suicidal ideation over time in individuals with PTSD.

The purpose of this study was to conduct secondary analyses of data from a randomized controlled trial comparing massed-PE (M-PE; 10 sessions delivered over 2 weeks), spaced-PE (S-PE; 10 sessions delivered over 8 weeks), present-centered therapy (PCT; an active control condition including 10 sessions delivered over 8 weeks), and minimal contact control group (MCC; an inactive control condition including a 10-to-15-min therapist phone call once weekly for 4 weeks). In the current study, only S-PE and PCT conditions were included because midtreatment assessments, which are necessary for mediational analyses, were collected for these conditions, but not for M-PE and MCC. The first aim of this study was to determine whether PTSD symptom reduction, depression symptom reduction, and improvements in interpersonal disconnection mediated the relationship of time and suicidal ideation. We hypothesized that reductions in PTSD, depression, and interpersonal disconnection would mediate reductions in suicide ideation over time in S-PE and PCT. The second aim was to determine the relative strength of mediation for each of these three potential mediators to inform whether one of the proposed mediators had a stronger mediational effect. We hypothesized that reductions in depression would be the most powerful mediator of the association between time and suicidal ideation. Based on prior literature (Bryan et al., 2016, 2015; McLean et al., 2017), we hypothesized that PTSD would be indirectly associated with reductions in suicidal ideation through depression. Further, we hypothesized that interpersonal disconnection would be directly associated with suicidal ideation, with greater reductions in interpersonal disconnection associated with greater reductions in suicidal ideation over time.

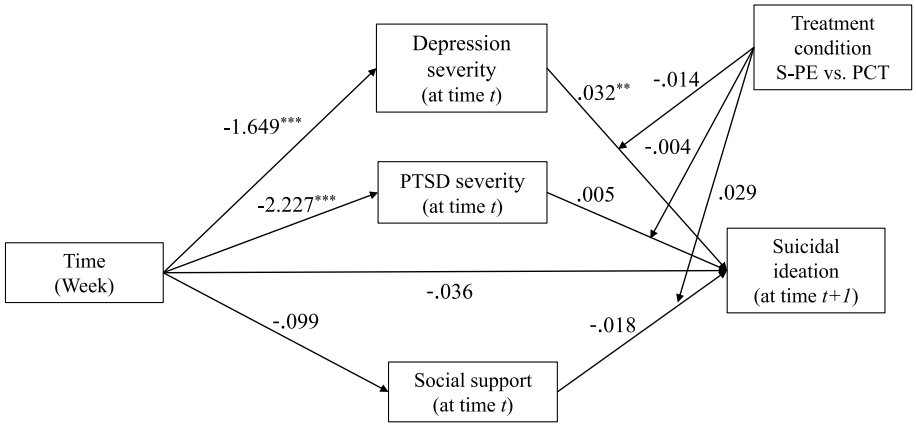
Because our main suicide outcome paper (Brown et al., 2019) found that reductions in suicidal ideation were more pronounced during treatment, we focused only on change in suicidal ideation during the course of treatment. Finally, we aimed to determine whether the mediational relationships found in this study were moderated by treatment condition. Given that PE is generally associated with more significant reductions in both PTSD and depression relative to PCT (with the exception of 2 studies, as described above), we hypothesized that the mediational relationship between: 1) PTSD and suicidal ideation, and 2) depression and suicidal ideation would be stronger in PE relative to PCT. Because PCT directly targeted interpersonal relationships as a core treatment objective, we hypothesized that the mediational relationship between interpersonal disconnection and suicidal ideation would be stronger in PCT compared to PE.



Model 1. Parallel Multiple Mediation Model



Model 2a. Moderated Parallel Multiple Mediation Model A



Model 2b. Moderated Parallel Multiple Mediation Model A

Fig. 1. Parallel mediation model. PTSD = posttraumatic stress disorder; S-PE = spaced prolonged exposure; PCT = present-centered therapy.

1. Method

1.1. Participants

Participants (N = 200) met criteria for current PTSD according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition – Text Revision* (*DSM-IV-TR;* American Psychiatric Association, 2000), were military personnel at Fort Hood, Texas, and were exposed to a combat-related trauma. Average age was 33.0 years old (SD = 7.2), and participants were primarily male (88%) and white (60%).

1.2. Procedure

All study procedures were approved by the Institutional Review Boards at Brooke Army Medical Center, The University of Texas Health Science Center at San Antonio, and the University of Pennsylvania. Informed consent was obtained from all participants. Participants in the parent study were randomized to either MCC (n = 40; weekly therapist phone calls for 4 weeks), massed-PE (M-PE; n = 75; 10 sessions over 2 weeks), spaced-PE (S-PE; n = 101; 10 sessions over 8 weeks), or PCT (n = 99; 10 sessions over 8 weeks). As described above, only participants randomized to receive S-PE and PCT were included in the current study because these conditions included a midtreatment assessment. There were no demographic or clinical differences between groups at baseline. No participants reported imminent suicidal ideation or plans to warrant exclusion from the study, though this was technically an exclusion criterion. For more information on the procedure, see Foa et al. (2018).

1.3. Treatments

1.3.1. Spaced prolonged exposure (S-PE)

S-PE is a manualized cognitive-behavioral therapy program consisting of two primary components: imaginal exposure (repeated recounting and processing of the traumatic memory) and in-vivo exposure (intentionally approaching distressing stimuli). Sessions were 90 min long and were audio-recorded and reviewed for homework. Participants completed 10 sessions over 8 weeks. Sessions 1 and 2 occurred during Week 1, followed by one treatment session per week during Weeks 2–7, and the final two treatment sessions in Week 8.

1.3.2. Present-centered therapy (PCT)

PCT is a manualized treatment focused on current life problems that provides a credible comparison therapy to control for nonspecific therapeutic factors. Sessions were 90 min long and were provided at the same frequency as S-PE. The therapist's role was to listen actively, help identify daily stressors, and discuss stressors and provide problem-solving in a supportive and nondirective manner.

1.4. Measures

All study measures for the current study were administered at baseline, 3 weeks into treatment, 5 weeks into treatment, and again at posttreatment.

1.4.1. Beck Scale for Suicide Ideation (BSSI; Beck, Kovacs, & Weissman, 1979)

The BSSI is a 21-item, self-report measure of suicidal ideation and suicide behavior. Each item has three statements to describe past-week thoughts/feelings, scored from 0 to 2. If participants denied active or passive suicidal desire (by scoring a "0" on items 4 and 5), then they did not complete items 6–21. Similarly, if an individual denies a history of suicide attempts, then they did not complete item 21. The possible range of scores on the full measure is 1–42. The BSSI has excellent internal consistency (α = .96) and strong convergent and divergent validity (Beck, Steer, & Ranieri, 1988). Similarly, the current study had strong internal consistency (α = .91). One prior report indicated that when participants were asked to reflect on their current suicidal thoughts and behaviors on the measure, as in the current study, scores of 0 or 1 were considered lower risk, whereas scores of 2 or higher were considered higher risk (Beck, Brown, Steer, Dahlsgaard, & Grisham, 1999).

1.4.2. PTSD Check List (PCL; Weathers, Litz, Herman, Huska, & Keane, 1993)

The PCL is a 17-item, self-report measure to assess PTSD severity. Scores range from 17 to 85, and the measure has strong psychometric properties (Weathers et al., 1993). The current study had strong internal consistency (α = .88) and altered the assessment timeline to reflect the PTSD severity "since the last time we saw you."

1.4.3. Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996)

The BDI-II is a 21-item, self-report measure of depression severity rated on a 0- to 3-point Likert scale. Higher scores reflect greater depression severity. As with the PCL, the assessment timeline was altered to reflect depression severity "since the last time we saw you." The measure has strong psychometric properties (Beck et al., 1996) including in the current study (α = 0.89).

1.4.4. Interpersonal Support Evaluation List - 12 (ISEL-12; Cohen & Hoberman, 1983)

The ISEL-12 is a 12-item short form of the original ISEL measure of perceived social support. Items are rated on a 4-point Likert scale ranging from 1 (*definitely false*) to 4 (*definitely true*). In addition to the total score, the measure includes three subscales reflecting appraisal (e.g., "When I need suggestions on how to deal with a personal problem, I know someone I can turn to"), belonging (e.g., "If I decide one afternoon that I would like to go to a movie that evening, I could easily find someone to go with me"), and tangible social support (e.g., "If I were sick, I could easily find someone to help me with my daily chores"). Higher total scores indicate more perceived social support. The measure has good internal consistency in the literature (α = 0.88 to 0.90; Cohen, Mermelstein, Kamarck, & Hoberman, 1985) and in the current study (α = 0.87). To reduce analyses, the current study reports only the total score.

1.5. Data analysis

Analyses were conducted using SPSS, version 24 by applying the PROCESS macro, which is a modeling program to test for both direct and indirect effects in nested data (Preacher & Hayes, 2004, 2008). Lagged mediational analyses were conducted to evaluate the relationship between putative mediators (depressive symptoms, PTSD symptoms and social support) and suicidal ideation (SI) from baseline to posttreatment. The mediator at time point t (baseline, midtreatment 1, midtreatment 2) was tested to predict the SI at next time point $t+1$ (midtreatment 1, midtreatment 2, posttreatment). This approach can control for the temporal precedence of mediator versus outcome variables in a longitudinal design. First, parallel multiple mediator models were applied to examine the most influential mediator over and above the other mediators (Preacher & Hayes, 2008). Next, moderated mediation analyses were conducted to examine whether the mediating relationship was moderated by treatment condition. Condition (S-PE vs. PCT) was added into models to test moderation of individual paths (see Fig. 1, Model 2a & 2b). Finally, serial multiple mediator analyses were conducted to examine paths between mediators. This analytic approach allows for examination of two mediators, in sequential fashion, while simultaneously testing the indirect effects of each mediator independently. For all analyses, a bootstrapping method (with 5000 bootstrap samples) was employed to estimate bias-corrected 95% confidence interval (CI) to verify indirect (mediating) effects. Bootstrapping computes more accurate confidence intervals of indirect

effects than the more commonly used methods (Preacher & Hayes, 2008), such as the causal steps strategy (Baron & Kenny, 1986), and provides more power while maintaining control over the Type I error rate (Preacher & Hayes, 2004). If the bias-corrected (BC) 95% CI for the parameter estimate did not contain zero, then the indirect effect was statistically significant and mediation was demonstrated (Mallinckrodt, Abraham, Wei, & Russell, 2006; Preacher & Hayes, 2008). Age, gender, mental and physical functioning were controlled for in all analyses to be consistent with the parent trial outcome paper (Foa et al., 2018).

2. Results

Participants' demographic characteristics and descriptive results on study variables are presented in Table 1. There were no group differences in BSSI at baseline ($p = .576$).

2.1. Mediation analysis

The parameter estimates for the total, direct and specific indirect effects with bias-corrected 95% CI are reported in Table 2. The total effect of Time on SI was significant ($B = -0.082$, $SE = 0.040$, $p = .039$), and the model significantly explained 4.2% (R^2, $p = .001$) of variance in SI. After adding a set of mediators, the direct effect of Time on SI was not significant ($B = -0.034$, $SE = 0.042$, $p = .421$), indicating that *depression severity*, *PTSD severity* and *social support*, taken as a set, fully mediated the relationship between Time and SI and the total indirect effect of Time on SI was significant (95% CI = −0.083 to −0.018). *Depression severity* was the only mediator of the Time-SI relationship ($B = 0.027$, $SE = 0.009$, $p = .002$, see Fig. 1), with the presence of the other two mediators. The model significantly explained 6.5% (R^2, $p < .001$) of variance in SI. In terms of the magnitude of the indirect effect, pairwise contrasts between the three mediators indicated that *depression severity* had a significantly greater mediating effect on SI than *social support,* but no differences were found for *depression severity* versus *PTSD severity,* or *PTSD severity* versus *social support* (Table 2). Furthermore, to avoid the confound of the suicidal ideation item on the BDI, we re-ran this analysis with this BDI suicidal ideation item removed; the results were replicated in that the effect of time on SI was mediated by depression severity ($B = 0.025$, $SE = 0.009$, $p = .006$).

2.2. Moderated mediation

Dummy-coded condition (S-PE = 1, PCT = 0) was added to the model to examine whether individual paths of the mediation model were moderated by condition. We ran two models to test condition as a moderator (Fig. 1 Models 2a and 2b). The interaction results of different paths are presented in Table 3. Depression was the only significant mediator (all $ps < .01$) in both models, and none of the individual interaction paths (see Fig. 1 Models 2a and 2b) significantly differed by condition, indicating that the mediating association between depression severity and SI over time was not moderated by condition.

2.3. Serial mediation

Serial multiple mediator models were conducted to examine whether reduction in PTSD severity accounted for the reduction in depression severity, which then accounted for the relation between Time and SI. In the alternative model, we switched depression and PTSD to test the mediation model in which the effect of time on PTSD severity was mediated by depression severity. The coefficients and significance of each path are presented in Fig. 2 Model 3a and 3b, and the bootstrap results for the indirect effect are reported in Table 4. The indirect effect path (Time→PTSD severity→Depressive severity→SI) of the mediation model was significant (95% CI = −0.036 to −0.008), but the alternative indirect effect path (Time→Depressive severity→PTSD severity→SI) was not significant (95% CI = −0.016 to 0.013), indicating that reduction in PTSD accounted for the reduction in depression, which subsequently accounted for the reduction in SI. However, the sequential model included a path from PTSD symptoms at time point *t* to predict depression symptoms at time point *t*. To further confirm this path with the temporal precedence taken into account

Table 1
Demographic and Clinical Characteristics of All Participants (N = 200).

	No. (%)	
	S-PE ($n = 101$)	PCT ($n = 99$)
Demographic Characteristics		
Age, mean (SD)	32.9 (7.2)	33.1 (7.4)
Sex		
Men	91 (90.1)	85 (85.9)
Women	10 (9.9)	14 (14.1)
Marital Status		
Not married	27 (26.8)	28 (28.3)
Married or cohabiting	74 (73.2)	71 (71.7)
Education		
High school	35 (34.7)	25 (25.3)
College experience	64 (63.3)	71 (71.7)
Postgraduate	2 (2.0)	3 (3.0)
Ethnicity		
Hispanic	20 (19.8)	24 (24.2)
Non-Hispanic	81 (80.2)	75 (75.8)
Race		
Asian	2 (2.0)	0 (0.0)
Black	25 (24.8)	21 (21.2)
White	59 (58.4)	61 (61.6)
Other	15 (15.9)	16 (16.3)
Missing	0 (0)	1 (0.01)
Military Grade		
Enlisted		
E-1 to E-3	2 (2.0)	2 (2.0)
E-4 to E-6	79 (78.2)	78 (78.8)
E-7 to E-9	17 (16.8)	17 (17.2)
Warrant officer	1 (1.0)	1 (1.0)
Officer	2 (2.0)	1 (1.0)
No. of times deployed		
1 or 2	60 (59.4)	58 (58.6)
≥3	41 (40.6)	41 (41.4)
Time in military (y), mean (SD)	10.90 (6.44)	11.22 (6.11)
Clinical Characteristics, Mean (*SD*)		
Depression Symptoms (BDI-II)		
Pretreatment	28.91 (9.47)	27.84 (9.54)
Midtreatment 1	23.77 (11.62)	21.81 (10.58)
Midtreatment 2	23.47 (12.81)	21.14 (11.66)
Posttreatment	-	-
Social Support (ISEL-12)		
Pretreatment	34.24 (7.57)	34.44 (7.99)
Midtreatment 1	33.02 (8.33)	34.66 (7.90)
Midtreatment 2	33.27 (8.02)	34.01 (7.93)
Posttreatment	-	-
PTSD Symptoms (PCL)		
Pretreatment	56.34 (10.64)	56.17 (10.98)
Midtreatment 1	52.83 (15.45)	51.21 (12.99)
Midtreatment 2	48.47 (15.45)	47.78 (14.88)
Posttreatment	-	-
Suicidal Ideation (BSSI)		
Pretreatment	.88 (2.23)	1.11 (3.45)
Midtreatment 1	.28 (1.44)	.61 (2.49)
Midtreatment 2	.31 (1.41)	.19 (1.17)
Posttreatment	.17 (1.07)	.10 (0.49)

Note. S-PE = Spaced Prolonged Exposure; PCT = Present-Centered Therapy; E-1 to E-3, junior enlisted; E-4 to E-6, junior noncommissioned officers; E-7 to E-9, senior noncommissioned officers; BDI-II = Beck Depression Inventory - II; ISEL-12 = Interpersonal Support Evaluation List - 12; PTSD = posttraumatic stress disorder; PCL = PTSD Check List; BSSI = Beck Scale for Suicide Ideation. For mediator and outcome variables, values are included for the time-points that were included in models (for mediators, this includes baseline, Midtreatment 1 and Midtreatment 2; for outcome, this includes Midtreatment 1, Midtreatment 2, and posttreatment).

Table 2
Total, direct and indirect effect of time on suicidal ideation through PTSD symptoms, depressive symptoms and social support.

Effects on SI	Variables	Point estimate	*SE*	*p*	Bias-corrected 95% CI	
					Lower	Upper
Total effect (c)	Time	−0.082	0.040	.039	−0.159	−0.004
Direct effect (c')	Time	−0.034	0.042	.421	−0.117	0.049
Indirect effect	Depressive symptoms	0.027	0.009	.624	−0.022	0.036
	PTSD symptoms	0.001	0.006	.869	−0.011	0.014
	Social support	−0.003	0.009	.772	−0.020	0.015
	Total indirect effect	−0.048	0.016	-	−0.083	−0.018
Contrasts						
Depressive symptoms vs. PTSD symptoms		−0.043	0.026	-	−0.100	0.004
Depressive symptoms vs. Social support		−0.046	0.016	-	−0.082	−0.018
PTSD symptoms vs. Social support		−0.003	0.015	-	−0.033	0.028

Note. SI = suicidal ideation; PTSD = posttraumatic stress disorder.

between these two variables, an additional mediation model was conducted to test whether PTSD symptoms (mediator) at time *t* could predict depressive symptoms (outcome) at time *t+1*. The result showed that PTSD severity mediated the relationship between Time and depressive severity and the total indirect (mediating) effect of Time on depression was significant ($B = 0.387$, $SE = 0.031$, 95% CI = −1.16 to −0.61).

3. Discussion

In active duty military personnel, reduction in depression was the strongest mediator of reduction in suicidal ideation in PE and PCT for PTSD. When considering the mediation model as a whole, depression, PTSD, and social support fully mediated the relationship between time and suicidal ideation, yet depression was the most powerful individual mediator of the three. Furthermore, depression was the only significant independent mediator of the change over time in suicidal ideation and remained significant over and above the mediational effect of PTSD and social support. These findings are consistent both with our first hypothesis and with prior research on the association between depression and suicidal ideation (Nock et al., 2008; Oquendo et al., 2004).

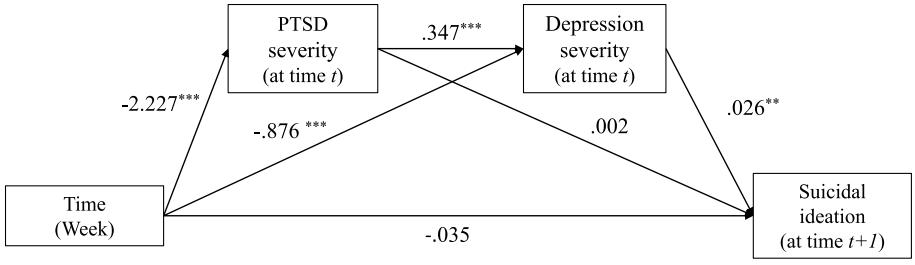
Reductions in PTSD symptoms were indirectly associated with reductions in suicidal ideation through depression. It is not surprising that some of the variance in suicidal ideation is attributed to PTSD, as PTSD is also linked to suicidal ideation (Brown, Fernandez, Kohn, Saldivia, & Vicente, 2018; Sareen, Houlahan, Cox, & Asmundson, 2005). That PTSD is indirectly associated with suicidal ideation through depression has been demonstrated in prior cross-sectional (McLean et al., 2017) and longitudinal studies (Bryan et al., 2015, 2016) in active duty military service members. Across two prior samples, alteration in arousal and reactivity and negative changes in mood in cognitions (which includes negative affect and anhedonia) were the two PTSD symptoms clusters that were most strongly associated with suicidal ideation (Brown, Contractor, & Benhamou, 2018). Therefore, perhaps underlying mechanism of the associations among PTSD, depression, and suicidal ideation may be arousal, negative affect, or anhedonia. This should be explored in future research. Furthermore, a robust body of evidence suggests PTSD may play a causal role in the development of depression (Stander, Thomsen, & Highfill-McRoy, 2014). For example, many more studies suggest that preexisting PTSD predicts the development of depression among veterans than the opposite (for a review, see Stander et al., 2014). Therefore, it is not surprising that the resolution of PTSD symptoms may lead to the resolution of depression, and ultimately to reduced suicidal ideation. The current study supports these findings and uniquely contributes to the literature in that this was a longitudinal study of active duty service members presenting for PTSD treatment who received PE or PCT. This suggests that change in PTSD was a significant predictor of reductions in suicidal ideation through depression in service members receiving PE or PCT for PTSD. The third potential mediator included in the analyses, social support, was not supported. Specifically, social support did not change significantly over the course of the intervention, and changes in social support were not associated with changes in suicidal ideation. These findings are surprising given theoretical conceptualizations of understanding suicidal ideation (Davis et al., 2014), including Joiner's Interpersonal Theory of Suicide (2005), which suggest that interpersonal disconnection (the reciprocal of social support) is a risk factor for suicidal ideation. These results converge with previous research (Bryan et al., 2017) that similarly failed to support thwarted belongingness as a mediator of suicide risk reduction among active duty military personnel receiving brief cognitive-behavioral therapy for suicide prevention (Bryan, Peterson, & Rudd, 2018), an empirically supported treatment that reduces the likelihood of suicide attempts. However, the results in the current study conflict with prior studies in which there was a significant association between interpersonal social support and suicidal ideation in active duty military personnel (McLean et al., 2017). One possible reason for this discrepancy is the nature of the interventions delivered in the current study. PE does not specifically target social support; in contrast PCT theoretically targets social support, but we are not aware of any studies that show an effect of PCT on social support. Therefore, perhaps social support did not mediate changes in PTSD and suicidal ideation because PE and PCT did not change social support in the sample.

Contrary to our third hypothesis, mediation was not altered by treatment condition. There were no significant moderating effects of treatment condition on any of the proposed mediation models. This is not wholly surprising, given that in the parent trial (Foa et al., 2018) there were not significant differences in PTSD severity reduction between PE and PCT.

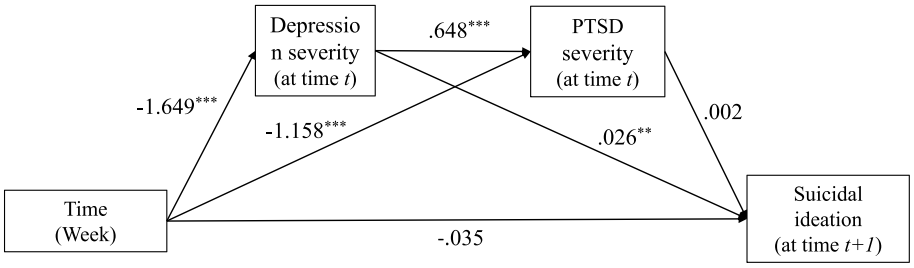
Table 3
Interaction results in moderated multiple parallel mediator analyses.

Path	Interaction	Point estimate	*SE*	*p*	Bias-corrected 95% CI	
					Lower	Upper
Model 2a						
Time → Depression severity	Time × Condition	0.162	0.440	.713	−0.701	1.025
Time → PTSD severity	Time × Condition	0.139	0.602	.987	−2.879	2.925
Time → social support	Time × Condition	0.030	0.390	.938	−0.737	0.797
Model 2b						
Depression severity → Time	BDI-II × Condition	−0.575	0.885	.393	−0.046	0.018
PTSD severity → Time	PCL × Condition	−0.004	0.012	.774	−0.028	0.021
Social support → Time	ISEL-12 × Condition	0.029	0.018	.104	−0.006	0.064

Note. PTSD = posttraumatic stress disorder; BDI-II = Beck Depression Inventory – II; PCL = Posttraumatic Checklist; ISEL-12 = Interpersonal Support Evaluation List – 12.



Model 3a. Serial Multiple Mediation Model A



Model 3b. Serial Multiple Mediation Model B

Fig. 2. Serial multiple mediation. PTSD = posttraumatic stress disorder.

Table 4
Estimates and bootstrap of the SEs and 95% CIs for the indirect effects in serial mediation models.

Indirect effect key	Point estimate	*SE*	95% CI Lower	Upper
Model				
Time→ PTSD severity →SI	−0.004	0.015	−0.033	0.025
Time→ Depression severity →SI	−0.023	0.009	−0.044	−0.008
Time→ PTSD severity → Depression severity →SI	−0.020	0.007	−0.036	−0.008
Model				
Time→ Depression severity →SI	−0.043	0.015	−0.076	−0.017
Time→ PTSD severity →SI	−0.002	0.008	−0.018	0.013
Time→ Depression severity → PTSD severity →SI	−0.002	0.007	−0.016	0.013

Note. PTSD = posttraumatic stress disorder; SI = suicidal ideation.

Several limitations of the current study are worthy of mention. First, the BSSI is a self-report measure that might introduce response bias in the sample, including potential discomfort in reporting suicidal ideation. Future research might employ an objective measure of suicidal ideation, including a clinician-administered assessment or an implicit measure of suicidal thoughts, such as the Death/Suicide Implicit Association Task (Nock et al., 2010) to obviate this concern. Second, participants were exclusively active duty military service members with PTSD; therefore, these results may not generalize to civilians or veterans or to those without a principal diagnosis of PTSD. Third, patients requiring imminent action to reduce suicide risk were not enrolled in the study, reducing the variability in suicidal ideation. Future studies might include participants with greater variation in suicidal ideation, provided that proper support and consideration for suicide risk is provided. Finally, the amount of variance in suicidal ideation attributed to the proposed mediation models is small (4.2% and 6.5%). A larger proportion of explained variance would further bolster confidence in the association of these mediators with suicidal ideation. In general, predicting suicidal ideation is extremely complex (Chan et al., 2016; Ribeiro et al., 2016), and therefore the low proportion of variance in suicidal ideation is not entirely surprising. Furthermore, several other PTSD trials have also demonstrated relatively small contributions of PTSD or depression to suicidal ideation (Bryan et al., 2016; Cox et al., 2016; Gradus et al., 2013).

When working with active duty military personnel with a principal diagnosis of PTSD, some clinicians question whether to delay evidence-based treatments until suicidal ideation is resolved. The current findings suggest that offering PE or PCT for PTSD results in significant reductions in PTSD, which result in significant reductions in depression, which ultimately lead to reductions in suicidal ideation. Therefore, unless the service member is actively suicidal, which would have resulted in exclusion from the current trial, clinicians should proceed with offering PTSD treatment when PTSD is the principal diagnosis. These findings also indicate the importance of frequently measuring PTSD symptoms, depression, and suicidal ideation in treatment. These assessments are essential to gauge treatment progress, especially in service members with PTSD and suicidal ideation.

In summary, this is the first study to demonstrate that reductions in depressive symptoms drive improvements in suicidal ideation in active duty military service members receiving PE or PCT for PTSD. Furthermore, the current study suggests that improvements in PTSD symptoms lead to reductions in depression, which in turn, lead to improvements in suicidal ideation. This study expands the extant literature implicating improvements in depression and PTSD as underlying mechanisms for positive change in suicidal ideation. In an active duty military sample with relatively mild to moderate suicidal ideation, PE and PCT may effectively reduce suicidal ideation through reductions in PTSD and depression.

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