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BRIEF REPORT

Combining a stellate ganglion block with prolonged exposure therapy for posttraumatic stress disorder: A nonrandomized clinical trial

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Abstract

Prolonged exposure therapy (PE) is an efficacious treatment for active duty service members and veterans with posttraumatic stress disorder (PTSD). However, PE is sometimes associated with high dropout rates, limited tolerability, and temporary symptom exacerbation during treatment. Stellate ganglion blocks (SGBs) are an emerging treatment that has the potential to enhance outcomes for PTSD when combined with trauma-focused psychotherapy. To date, no study of which we are aware has examined the potential additive benefits of SGB injections when administered in conjunction with trauma-focused behavioral treatment for PTSD. Thus, we conducted a nonrandomized clinical trial to evaluate the use of an SGB combined with massed PE therapy for combat-related PTSD. Participants ($N = 12$) were treated with 10 daily 90-min PE sessions delivered over 2 weeks and received a single SGB injection between Sessions 1 and 2. PE sessions lasted 90 min each. Participants reported a mean posttreatment PTSD symptom reduction of 32 points on the PTSD Checklist for *DSM-5* (PCL-5), Hedges' *g*s = 1.28–2.80. Most participants (90.9%) demonstrated clinically significant change on the PCL-5 (i.e., ≥10 points) by the final treatment session and 50.0% no longer met the diagnostic criteria for PTSD per the Clinician-Administered PTSD Scale for *DSM-5* at 1-month follow-up. Adverse events for the combined treatment were consistent with those previously reported for standalone SGB and PE. This combined treatment approach provides promising results for improving the tolerability of trauma-focused therapies, reducing symptom severity, and increasing PTSD remission rates.

Over the last two decades, significant advancements have been made in the treatment of posttraumatic stress disorder (PTSD) in active duty military personnel using trauma-focused psychotherapies (Peterson, 2021; Peterson, Niles, et al., 2021). Prolonged exposure (PE) therapy is widely accepted as an evidence-based treatment for PTSD in active duty service members, often achieving 50%–70% symptom reduction (Peterson, Niles, et al., 2021). However, there is a paucity of evidence supporting similar advancements in pharmacologic approaches.

A recent medication advancement that has shown significant promise for the treatment of PTSD is the use of the stellate ganglion block (SGB), which involves the injection of a local anesthetic around the stellate ganglion at the base of the neck (Summers & Nevin, 2017). SGBs are thought to minimize PTSD symptoms by temporarily blocking sympathetic arousal and physical reactivity often associated with reminders of traumatic events. The potential treatment benefits of using SGBs for PTSD have been recognized for more than a decade, with initial case studies and series reporting impressive results (e.g., Lipov et al., 2013; Mulvaney et al., 2014). The results from randomized clinical trials (RCTs) evaluating the efficacy of SGBs as monotherapy for the treatment of PTSD among military service members have been mixed. An initial RCT studying military personnel ($N = 42$) failed to detect significant differences between the SGB (5 mL of 0.5% ropivacaine) and the sham (normal saline) conditions with regard to PTSD outcomes (Hanling et al., 2016). In a subsequent RCT ($N = 113$), Rae Olmsted et al. (2020) found that SGBs (7–10 mL of 0.5% ropivacaine) resulted in larger short-term reductions of PTSD symptoms (i.e., 12-point reduction on the PTSD Checklist for *DSM-5* [PCL-5; Weathers, Litz, et al., 2013]) over an 8-week period compared to a saline sham (i.e., 6-point PCL-5 reduction).

The greatest potential for SGB may be to pair it with an evidence-based trauma-focused psychotherapy for PTSD, such as PE (Foa et al., 2018). PE promotes the emotional processing of traumatic experiences through behavioral and experiential exposure techniques. During PE, patients are expected to deliberately and systematically approach feared trauma reminders to develop more adaptive beliefs and behaviors. As SGBs have been shown to demonstrate the most substantial impact on hyperarousal and avoidance symptoms (Lipov et al., 2013), it is reasonable to suggest that a medical blockade of the physiological activation may reduce uncomfortable physiological reactions that occur during exposure treatment and, thereby, help patients confront trauma reminders and to learn more adaptive responses.

The current study examined the safety and benefits of SGB administration combined with PE for PTSD. We hypothesized that SGB and massed PE could be safely combined and would have additive effects on the reduction of PTSD symptoms among active duty military service members and veterans. We posited that the reduced physiological arousal from the SGB might allow participants to engage with the trauma memories more fully during the imaginal exposure portion of PE and that the SGB might allow for more rapid progression up the in vivo exposure exercise hierarchy. In addition, we hypothesized that more than 50% of the participants would have clinically significant reductions in self-reported PTSD symptoms, defined as a reduction of 10 points or more on the PCL-5, and more than 50% of the participants would no longer meet the diagnostic criteria for PTSD at posttreatment, as assessed using the Clinician-Administered PTSD Scale for *DSM-5* (CAPS-5; Weathers, Blake, et al., 2013a). These thresholds were selected because they represent approximate improvements reported in previous trials of PE (Peterson, Niles, et al., 2021).

METHOD

Participants

Eligible participants were recruited through behavioral health providers at Brooke Army Medical Center and were required to be Defense Enrollment Eligibility Reporting System (DEERS)–eligible active duty or retired military service members between 18–65 years old who met the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; *DSM-5*; American Psychiatric Association, 2013) diagnostic criteria for PTSD as assessed using the CAPS-5 (Weathers, Blake, et al., 2013a). Exclusion criteria were modeled after Rae Olmsted et al. (2020) and included the following (a) current suicidal ideation, mania, or psychosis that required immediate stabilization or hospitalization; (b) psychiatric or substance use disorders severe enough to warrant designation as the primary disorder and require immediate intervention; (c) pregnancy; (d) current anticoagulant use; (e) history of a bleeding disorder; (f) an infection or mass at the injection site; (g) myocardial infarction within 6 months; (h) pathologic bradycardia or irregularities of heart rate or rhythm; (i) symptomatic hypotension; (j) phrenic or laryngeal nerve palsy; (k) history of glaucoma; (l) uncontrolled seizure disorder; and (m) history of an allergy to local anesthetics.

In total, 20 participants from Brooke Army Medical Center (San Antonio, Texas), were screened for eligibility; 12 active duty military personnel were enrolled and 11 (91.7%) completed the treatment protocol between January and July 2021. Of the individuals who were screened but not enrolled, four did not meet the criteria for PTSD, two were lost to follow-up after baseline, one was

unable to obtain military command support to participate, and one was concerned about the SGB side effects. On average, the participants were 37 years old ($SD = 6.0$); enlisted military personnel (66.7%); White, non-Hispanic (66.7%); married (66.7%), male (75.0%); serving in the U.S. Army (50.0%); and had been deployed at least once following the September 11, 2001, terrorist attacks (83.3%).

Procedure

This nonrandomized trial was conducted to evaluate the combination of massed PE with a single, right-sided block of the stellate ganglion with 6.5 mL of 0.5% ropivacaine. Massed PE involved 10 sessions of daily 90-minute PE therapy conducted over the course of 2 consecutive weeks. The SGB was given between Sessions 1 and 2 of massed PE. Session 1 included a review of the rationale for the treatment of PTSD with PE, the rationale for how SGB may benefit PTSD, and the rationale for how the combination of these two treatments might be additive or synergistic. We believed it was important to explain this prior to the administration of the SGB and the start of exposure therapy in Session 2.

The study was approved by the Institutional Review Board (IRB) at the University of Texas Health Science Center at San Antonio; Brooke Army Medical Center in San Antonio, Texas deferred their review to the university's IRB. The project was supported by the South Texas Research Organizational Network Guiding Studies on Trauma and Resilience (STRONG STAR Consortium) at the University of Texas Health Science Center at San Antonio (Peterson, Young-McCaughan et al., 2021). Before enrollment, interested retired and active duty service members were scheduled by the study project coordinator for an individual appointment, at which time a detailed explanation of the study was provided, potential risks and benefits were reviewed, and individuals were able to address any questions they might have. After obtaining written informed consent, a baseline assessment was conducted to determine eligibility. Participants who met the study criteria were then enrolled in massed PE and scheduled to receive a single SGB injection between Sessions 1 and 2. The primary outcome measures were the CAPS-5 and the PCL-5, administered 1 month following treatment completion. The CAPS-5 was administered by an independent evaluator at baseline and 1- and 3-month posttreatment follow-up assessments. The self-report PCL-5 was administered at baseline, before PE Sessions 6 and 10, and at the 1- and 3-month posttreatment follow-ups.

Massed PE

Participants received 10 daily 90-min PE sessions on weekdays over the course of 2 consecutive weeks. During the first session, an overview of the treatment course was provided, including a rationale for the combination of massed PE and an SGB; a trauma history was gathered; and a breathing exercise was introduced. Between Sessions 1 and 2, participants received a single SGB injection. In Session 2, psychoeducation about PTSD was provided and in vivo exposure was initiated, then continued daily throughout treatment. Imaginal exposure was introduced during the third session and continued throughout the remainder of treatment. As needed, participants were offered three optional booster sessions scheduled for 1-, 3-, and 7-weeks posttreatment. These booster sessions were offered because some patients who previously completed the compressed treatment program reported that suddenly discontinuing after 2 weeks of intensive, daily treatment was rather abrupt. The booster sessions focused on current functioning and allowed for a smoother transition into maintaining treatment gains and planning additional in vivo exposures. Therapists for this study included licensed psychologists, postdoctoral fellows, and interns trained in the delivery of massed PE.

SGB

The SGB was administered in accordance with established practice guidelines (Hanling et al., 2016; Mulvaney et al., 2014; Rae Olmsted et al., 2020; Summers & Nevin, 2017). Participants received the SGB between the first and second massed PE sessions. This timing ensured that the SGB was provided after the rationale for the treatment approach was reviewed with the participant but before beginning any in vivo or imaginal exposure therapy. The SGB was administered within a military interdisciplinary pain management clinic and was performed by an anesthesiologist or physical medicine and rehabilitation physician, both of whom had extensive experience in administering SGBs. Placement of the SGB was determined using either ultrasound or fluoroscopy guidance depending upon the medical providers' preference. For the SGB, 6.5 mL of 0.5% ropivacaine was injected near the right stellate ganglion nerve along the anterior or anterolateral edge of the longus colli muscle. The success of the block was confirmed by an increase in temperature of at least 1°C in the left hand and the presence of symptoms of Horner's Syndrome (i.e., ptosis, miosis, and facial anhidrosis).

Measures

STRONG STAR Common Data Elements for PTSD research were administered as part of this study (Barnes et al., 2019). Measures were selected to include those with strong psychometrics to measure the pertinent constructs.

Demographic characteristics

A brief questionnaire was administered at the baseline assessment to assess participant demographics.

Trauma exposure

General trauma exposure

Trauma exposure was measured at baseline using the Life Events Checklist-5 (LEC-5; Weathers, Blake, et al., 2013b), which includes a list of 24 potentially traumatic life events commonly associated with PTSD symptoms. Respondents are asked to indicate whether they have experienced each event as well as their level of exposure. The LEC has been shown to have good temporal stability, convergent validity with other measures, and to be significantly correlated with psychological distress and PTSD symptoms among combat veterans (Gray et al., 2004).

Deployment-specific trauma exposure

Deployment-specific trauma exposure was assessed at baseline using the 17-item Combat Experiences subscale and 13-item Postbattle Experiences subscale of the Deployment Risk and Resilience Inventory-2 (DRRI-2; Vogt et al., 2013). Respondents were asked to indicate the frequency of each listed event, rating responses on a scale of 1 (*never*) to 6 (*daily or almost every day*), with higher scores indicating higher levels of exposure. The measure has demonstrated high internal consistency reliability (Cronbach's αs = .88–.92) and criterion-related validity with PTSD symptom severity (rs = .15–.56; Vogt et al., 2013).

Primary outcomes

Clinician-rated PTSD diagnosis

PTSD diagnostic status and symptom severity were measured using the 30-item CAPS-5 (Weathers, Blake, et al., 2013a), a structured interview that is used to assess the *DSM-5* criteria for PTSD (Weathers et al., 2018). Symptom severity scores are obtained by summing scores for the 20 DSM-5 PTSD symptoms, with items scored on a scale of 0 (*absent*) to 4 (*extreme*) and higher scores indicating more severe symptom levels. Scores for each *DSM-5* symptom cluster can also be calculated by summing cluster-specific scores. The measure has demonstrated excellent psychometric properties in veteran samples, with high internal consistency (Cronbach's α = .88), good interrater reliability (κ = .78), good test–retest reliability (intraclass correlation coefficient = .78), and convergent and discriminant validity (Weathers et al., 2018). In the present study, Cronbach's alpha was .71 at baseline.

Self-reported PTSD symptoms

PTSD symptom severity was evaluated using the 20-item PCL-5 (Weathers, Litz, et al., 2013). Respondents were asked to score each item on a scale of 0 (*not at all*) to 4 (*extremely*), with higher scores reflecting more severe symptom levels. The measure has demonstrated excellent psychometric properties in civilian and military samples, with high internal consistency for the total PCL-5 score (Cronbach's αs = .91–.96), good test–retest reliability (rs = .82–.84), and convergent and discriminant validity (Blevins et al., 2015; Bovin et al., 2016; Wortman et al., 2016). In the present study, Cronbach's alpha was .81 at baseline.

Self-reported depressive symptoms

The nine-item Patient Health Questionnaire (PHQ-9; Kroenke et al., 2001) was used to measure the severity of depressive symptoms. Items reflect affective and somatic symptoms related to depression and are rated on a scale of 0 (*not at all*) to 4 (*nearly every day*). Higher scores indicate more severe depressive symptoms. The measure has demonstrated good reliability and validity, with Cronbach's alpha values ranging from .86 to .89 (Kroenke et al., 2001). In the present study Cronbach's alpha .70 at baseline.

Adverse event monitoring

Adverse event monitoring was conducted during treatment, at each interim assessment, and at each of the follow-up assessments using standardized operating procedures (Peterson et al., 2013).

Data analysis

Descriptive statistics were used to examine the prevalence and nature of adverse events reported on the adverse events monitoring logs, the proportion of participants who no longer met the *DSM-5* diagnostic criteria on the CAPS-5, and the proportion of participants who demonstrated a clinically significant change in PTSD symptoms

(i.e., reduction of 10 points or more on the PCL-5). Generalized linear mixed-effects models (GLMMs) with repeated measures were conducted to evaluate reductions in PTSD (i.e., CAPS-5, PCL-5) and depressive (i.e., PHQ-9) symptom severity following treatment. An advantage of GLMM over conventional analyses of variance (ANOVAs) includes the relaxation of equal variance assumptions and longitudinal analysis in the presence of missing data, assuming data are missing at random. Statistical models included all collected data points. The primary time points of interest were PTSD symptom reductions from baseline to 1-month follow-up and the maintenance of reductions from 1- to 3-month follow-up. Hedges' *g* effect sizes were calculated to further describe the nature of significant effects. Hedges' *g* has been recommended over Cohen's *d* for small samples but can be interpreted using Cohen's conventional recommendations of .02, .05, and .08 to indicate small, medium, and large effects, respectively (Lakens, 2013). All statistical analyses were intent-to-treat and used all data from all participants. Hypothesis tests were two-tailed. A Sidak adjustment for multiple comparisons was used for post hoc pairwise analyses when a significant main effect of time was detected. All analyses were conducted using SPSS (Version 27).

RESULTS

As seen in Table 1, 90.9% of participants demonstrated clinically significant change on the PCL-5 (i.e., a reduction of 10 or more points) at the final treatment session. At 1-month follow-up, 50.0% of participants no longer met the diagnostic criteria for PTSD based on the CAPS-5, and 80.0% of participants demonstrated clinically significant change on the PCL-5. By the 3-month follow-up, 88.9% of participants demonstrated clinically significant reductions in self-reported PTSD symptoms and 87.5% no longer met the diagnostic criteria for PTSD. Continuous outcomes yielded a significant main effect of time on the CAPS-5, $F(2, 11) = 26.22$, $p < .001$, and PCL-5, $F(4, 11) = 36.79$, $p < .001$. Participants demonstrated significant PTSD severity reductions from baseline to 1-month follow-up on the CAPS-5, $\Delta M = 14.47$, $p = .001$, and the PCL-5, $\Delta M = 24.71$, $p = .001$. PTSD symptom severity reductions were maintained at the 3-month follow-up on the CAPS-5 and further decreased on the PCL-5, $\Delta M = 7.39$, $p = .042$. PTSD severity reductions from baseline to follow-up assessments were substantial, Hedges' *g*s = 1.28–2.22. Participants also demonstrated significant reductions in depressive symptoms on the PHQ-9 from baseline to 1-month follow-up, $\Delta M = 6.19$, $p < .001$, that were maintained at the 3-month follow-up, $F(4, 11) = 27.57$, $p < .001$. Hedges' *g* effect sizes for depressive symptom severity following treatment were substantial and ranged from 1.50 to 2.80.

In total, 43 adverse events were reported during the treatment period, with every participant reporting at least one adverse event. On Study Day 2, following the SGB, 33 adverse events were reported, all of which were considered to be related to the SGB. These adverse events were mostly known manifestations of the SGB procedure, the most frequent of which were droopiness of the eyes or facial muscles; visual or eye disturbance, including Horner's Syndrome; and stiffness or soreness in the neck (see Supplementary Table S1).

DISCUSSION

This was the first study of which we are aware to examine the potential benefits of augmenting massed PE for PTSD with an SGB. The results of this nonrandomized trial provide initial support for the safety (i.e., no serious adverse events), feasibility (91.7% completion rate), and benefits (90.9% of participants demonstrated clinically significant change) of this combined treatment approach for PTSD. This dual treatment approach also appears to have large additive benefits: The previous SGB study by Rae Olmsted et al. (2020) reported a 13-point reduction on the PCL-5, and the Foa et al. (2018) massed PE study reported a 14-point reduction, whereas the combined SGB and massed PE approach used in the current study resulted in 32-point reduction (see Figure 1). These seemingly synergistic effects appear to be the result of the timing of the SGB injection, methodical integration of the SGB with massed PE, and a strong rationale for the combination of these two treatments provided to participants. It is unlikely that similar reductions would have been obtained by simply offering concurrent SGB and a trauma-focused behavioral treatment for PTSD. This supposition is supported by the rather modest reductions in PTSD symptoms reported by Rae Olmsted et al. (2020), who administered concurrent behavioral treatments to more than half of the participants in their sample.

Consistent with findings for both massed PE and SGB as monotherapies for PTSD, the combination of the two was associated with rapid reductions in self-reported PTSD symptoms over the course of treatment. Anecdotally, several participants reported immediate reductions in their hyperarousal symptoms (e.g., reduced road rage, improved sleep) after receiving the SGB. However, because the PCL-5 was not completed within 1–2 days after the SGB was administered, it is difficult to extrapolate the degree to which this rapid symptom reduction can be attributed to massed PE, SGB, or the combination of the two modalities. This limitation should be addressed in future studies.

TABLE 1 Posttraumatic stress disorder (PTSD) estimated model descriptives and treatment outcomes

Variable	*M*	*SD*	PTSD (%)[a]	≥10-point Δ (%)[b]	Δ*M*	*t*	*df*	*g*
PCL-5								
Descriptive statistics								
Baseline	53.42	9.95	—	—				
Day 6	39.79	14.05	—	—				
Day 10	28.80	12.73	—	90.9				
1 month	28.71	14.27	—	80.0				
3 months	21.41	9.94	—	88.9				
Treatment outcomes								
Baseline–Day 10					−24.62	−6.46**	12	−1.86
Baseline–1 month					−24.71	−5.18*	12	−1.49
Baseline–3 months					−32.00	−7.68***	14	−2.22
1 month–3 months					−7.39	−2.64*	10	−0.76
CAPS-5								
Descriptive statistics								
Baseline	38.83	7.51	100.0	—				
Day 6	—	—	—	—				
Day 10	—	—	—	—				
1 month	24.36	10.05	50.0	—				
3 month	19.32	10.35	12.5	—				
Treatment outcomes								
Baseline–Day 10					—	—	—	—
Baseline–1 month					−14.47	−4.44*	11	−1.28
Baseline–3 month					−19.52	−6.55***	10	−1.89
1 month–3 months					−5.05	−1.29	11	−0.37
PHQ-9								
Descriptive statistics								
Baseline	17.25	5.36	—	—				
Day 6	11.51	5.45	—	—				
Day 10	9.68	5.51	—	—				
1 month	11.06	5.65	—	—				
3 month	8.84	5.87	—	—				
Treatment outcomes								
Baseline–Day 10					−7.52	−6.37***	12	−1.84
Baseline–1 month					−6.19	−5.21***	12	−1.50
Baseline–3 month					−8.41	−9.70***	13	−2.80
1 month–3 month					−2.22	−2.52	12	−0.73

Note: Analyses were intent-to-treat. CAPS-5 = Clinician-Administered PTSD Scale for *DSM-5*; PCL-5 = PTSD Checklist for *DSM-5*.

[a]Proportion of participants who met the criteria for PTSD.

[b]Proportion of participants who had a 10-point reduction on the PCL-5.

*$p < .05$; ***$p < .001$.

With the combined SGB and massed PE treatment, both self-reported and clinician-rated PTSD symptoms continued to decrease across the 1- and 3-month follow-assessment periods. These results are consistent with larger SGB studies that have documented continued benefits with regard to PTSD symptoms at 2–6 months posttreatment (e.g., Mulvaney et al., 2014). In contrast, the enduring treatment benefits of PE as assessed 5–10 years after treatment are better documented (Resick et al., 2012). Future studies with longer follow-up assessment windows are needed to determine whether the benefits of massed PE combined with an SGB are sustained over time.

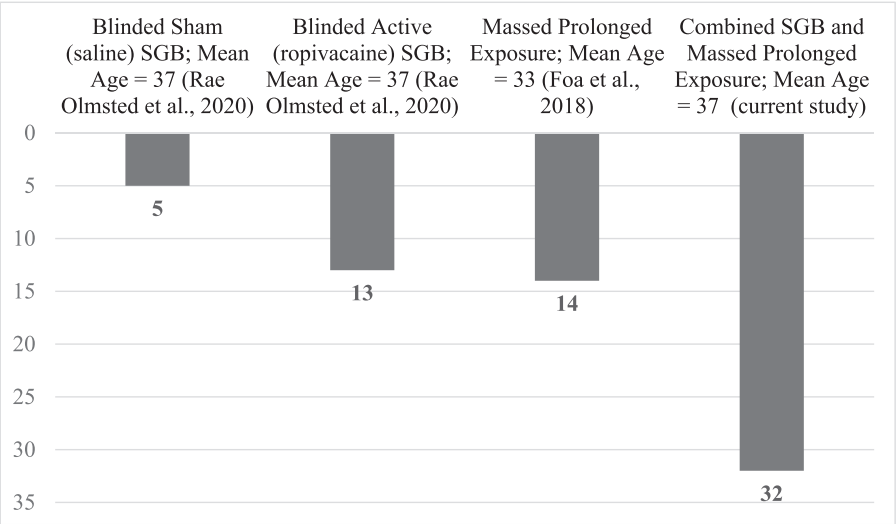

FIGURE 1 Reductions in PTSD Checklist for *DSM-5* scores after receiving a stellate ganglion block (SGB), massed prolonged exposure therapy (PE), and combined SGB and massed PE among active duty military personnel *Note*: Follow-up assessments were conducted at 8 weeks for Rae Olmsted et al. (2020) and at 12 weeks for Foa et al. (2018) and the current study. PTSD = posttraumatic stress disorder; *DSM-5* = *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.).

PTSD is maintained through behavioral and emotional avoidance as well as maladaptive thinking (Foa & Kozak, 1986). PE employs exposure strategies to reduce trauma-related avoidance by (a) facilitating emotional processing of the traumatic memories, (b) accelerating habituation to safe trauma reminders, and (c) reducing rigid and maladaptive posttraumatic cognitions. By reducing psychophysiological reactivity, the SGB may have helped participants remain in the exposures longer, engage more deeply with trauma memories, and have more opportunities for healthy learning and recovery. To test whether physiological blockade is, indeed, the mechanism for the effects of SGB, future studies should examine psychophysiological measures during exposure activities following active and sham SGB administration.

Because of national publicity and the increasing popularity of using SGBs to rapidly reduce the symptoms of PTSD, we were concerned that there might be a high dropout rate from PE after participants received the SGB. There were also concerns that the SGB might inhibit the benefits of PE. The use of medications for the reduction of arousal has been found to limit the efficacy of cognitive behavioral therapies for anxiety disorders (Otto et al., 2010). The limited improvements in outcomes with combined treatments have raised questions about whether there may be interfering effects that attenuate the magnitude of combination treatments. Researchers have also suggested that emotional activation is necessary for successful exposure-based cognitive behavioral therapy (Foa & Kozak, 1986). In contrast to these concerns, the methodological integration of SGB and massed PE and the strong rationale for the combination of these two treatments resulted in low dropout from treatment and large reductions in PTSD symptoms.

The study had several limitations common to pilot investigations. In particular, the small sample size and nonrandomized treatment study design limit the generalizability of these results as well as conclusions that can be drawn regarding treatment benefits. Additionally, as a novel treatment option producing obvious and dramatic physiological symptoms, SGB may be particularly vulnerable to positive expectations. Therefore, treatment expectancy may partially account for the large reduction in self-reported and clinician-rated PTSD scores. The use of fluoroscopy for the location of the SGB injection for some of the participants is another limitation in that it does not provide as clear guidance as ultrasound.

Future randomized clinical trials are necessary to establish the efficacy of combining an SGB with massed PE for PTSD and the potential maintenance of treatment gains as the effects of the SGB diminish over time. If the results of this study can be replicated within a well-controlled efficacy trial, the rapid reduction in PTSD symptoms over a short period associated with this dual treatment approach may prove particularly beneficial for the U.S. military, whose members have limited time available to complete PTSD treatment programs while simultaneously maintaining mission readiness. Finally, future research is needed to determine whether this treatment approach is beneficial for other trauma populations,

including veterans, first responders, and civilian trauma survivors.

OPEN PRACTICES STATEMENT

The data from this study are maintained at the University of Texas Health Science Center at San Antonio in the STRONG STAR Repository. Requests for access to the data as well as for materials and the analysis code also can be emailed to repository@strongstar.org.

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REFERENCES

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Author. https://doi.org/10.1176/appi.books.9780890425596

Barnes, J. B., Presseau, C., Jordan, A. H., Kline, N. K., Young-McCaughan, S., Keane, T. M., Peterson, A. L., Litz, B. T., & the Consortium to Alleviate PTSD. (2019). Common data elements in the assessment of military-related PTSD research applied in the Consortium to Alleviate PTSD. *Military Medicine*, *184*(5-6), e218–e226. https://doi.org/10.1093/milmed/usy226

Blevins, C. A., Weathers, F. W., Davis, M. T., Witte, T. K., & Domino, J. L. (2015). The Posttraumatic Stress Disorder Checklist for *DSM-5* (PCL-5): Development and initial psychometric evaluation. *Journal of Traumatic Stress*, *28*(6), 489–498. https://doi.org/10.1002/jts.22059

Foa, E. B., & Kozak, M. J. (1986). Emotional processing of fear: Exposure to corrective information. *Psychological Bulletin*, *99*(1), 20–35. https://doi.org/10.1037/0033-2909.99.1.20

Foa, E. B., McLean, C. P., Zang, Y., Rosenfield, D., Yadin, E., Yarvis, J. S., Mintz, J., Young-McCaughan, S., Borah, E. V., Dondanville, K. A., Fina, B. A., Hall-Clark, B. N., Lichner, T., Litz, B. T., Roache, J., Wright, E. C., & Peterson, A. L., for the STRONG STAR Consortium. (2018). Effect of prolonged exposure therapy delivered over 2 weeks vs. 8 weeks vs present-centered therapy on PTSD symptom severity in military personnel: A randomized clinical trial. *JAMA*, *319*(4), 354–364. https://doi.org/10.1001/jama.2017.21242

Gray, M. J., Litz, B. T., Hsu, J. L., & Lombardo, T. W. (2004). Psychometric properties of the Life Events Checklist. *Assessment*, *11*(4), 330–341. https://doi.org/10.1177/1073191104269954

Hanling, S. R., Hickey, A., Lesnik, I., Hackworth, R. J., Stedje-Larsen, E., Drastal, C. A., & McLay, R. N. (2016). Stellate ganglion block for the treatment of posttraumatic stress disorder: A randomized, double-blind, controlled trial. *Regional Anesthesia & Pain Medicine*, *41*(4), 494–500. https://doi.org/10.1097/AAP.0000000000000402

Kroenke, K., Spitzer, R. L., & Williams, J. B. W. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine*, *16*(9), 606–613. https://doi.org/10.1046/j.1525-1497.2001.016009606.x

Lakens, D. (2013). Calculating and reporting effect sizes to facilitate cumulative science: A practical primer for t-tests and ANOVAs. *Frontiers in Psychology*, *4*, Article 863. https://doi.org/10.3389/fpsyg.2013.00863

Lipov, E. G., Navaie, M., Brown, P. R., Hickey, A. H., Stedje-Larsen, E. T., & McLay, R. N. (2013). Stellate ganglion block improves refractory post-traumatic stress disorder and associated memory dysfunction: A case report and systematic literature review. *Military Medicine*, *178*(2), e260–e264. https://doi.org/10.7205/MILMED-D-12-00290

Mulvaney, S. W., Lynch, J. H., Hickey, M. J., Rahman-Rawlins, T., Schroeder, M., Kane, S., & Lipov, E. (2014). Stellate ganglion block used to treat symptoms associated with combat-related posttraumatic stress disorder: A case series of 166 patients. *Military Medicine*, *179*(10), 1133–1140. https://doi.org/10.7205/MILMED-D-14-00151

Otto, M. W., McHugh, R. K., & Kantak, K. M. (2010). Combined pharmacotherapy and cognitive-behavioral therapy for anxiety disorders: Medication effects, glucocorticoids, and attenuated treatment outcomes. *Clinical Psychology: Science and Practice*, *17*(2), 91–103. https://doi.org/10.1111/j.1468-2850.2010.01198.x

Peterson, A. L. (2021). General perspective on the U.S. military conflicts in Iraq and Afghanistan after 20 years. *Military Medicine*, usab496. https://doi.org/10.1093/milmed/usab496

Peterson, A. L., Roache, J. D., Raj, J., & Young-McCaughan, S., for the STRONG STAR Consortium. (2013). The need for expanded monitoring of adverse events in behavioral health clinical trials. *Contemporary Clinical Trials*, *34*(1), 152–154. https://doi.org/10.1016/j.cct.2012.10.009

Peterson, A. L., Niles, B. L., Young-McCaughan, S., & Keane, T. M. (2021). Assessment and treatment of combat-related posttraumatic stress disorder: Results from STRONG STAR and the Consortium to Alleviate PTSD. In N. Gorbunov (Ed.), *Military Medicine*. InTech Open. https://doi.org/10.5772/intechopen.96323

Peterson, A. L., Young-McCaughan, S., Roache, J. D., Mintz, J., Litz, B. T., Williamson, D. E., Resick, P. A., Foa, E. B., McGeary, D. D., Dondanville, K. A., Taylor, D. J., Wachen, J. S., Fox, P. T., Bryan, C. J., McLean, C. P., Pruiksma, K. E., Yarvis, J. S., Niles, B. L., Abdallah, C. G., … Keane, T. M., for the STRONG STAR Consortium and the Consortium to Alleviate PTSD. (2021). STRONG STAR and the Consortium to Alleviate PTSD: Shaping the future of combat PTSD and related conditions in military and veteran populations. *Contemporary Clinical Trials*, *110*, 106583. https://doi.org/10.1016/j.cct.2021.106583

Rae Olmsted, K. L., Bartoszek, M., Mulvaney, S., McLean, B., Turabi, A., Young, R., Kim, E., Vandermaas-Peeler, R., Morgan, J. K.,

Constantinescu, O., Kane, S., Nguyen, C., Hirsch, S., Munoz, B., Wallace, D., Croxford, J., Lynch, J. H., White, R., & Walters, B. B. (2020). Effect of stellate ganglion block treatment on posttraumatic stress disorder symptoms: A randomized clinical trial. *JAMA Psychiatry*, *77*(2), 130–138. https://doi.org/10.1001/jamapsychiatry.2019.3474

Resick, P. A., Williams, L. F., Suvak, M. K., Monson, C. M., & Gradus, J. L. (2012). Long-term outcomes of cognitive–behavioral treatments for posttraumatic stress disorder among female rape survivors. *Journal of Consulting and Clinical Psychology*, *80*(2), 201–210. https://doi.org/10.1037/a0026602

Summers, M. R., & Nevin, R. L. (2017). Stellate ganglion block in the treatment of posttraumatic stress disorder: A review of historical and recent literature. *Pain Practice*, *17*(4), 546–553. https://doi.org/10.1111/papr.12503

Vogt, D., Smith, B. N., King, L. A., King, D. W., Knight, J., & Vasterling, J. J. (2013). Deployment Risk and Resilience Inventory–2 (DRRI-2): An updated tool for assessing psychosocial risk and resilience factors among service members and veterans. *Journal of Traumatic Stress*, *26*(6), 710–717. https://doi.org/10.1002/jts.21868

Weathers, F. W., Blake, D. D., Schnurr, P. P., Kaloupek, D. G., Marx, B. P., & Keane, T. M. (2013a). *The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5)*. https://www.ptsd.va.gov/professional/assessment/adult-int/caps.asp

Weathers, F. W., Blake, D. D., Schnurr, P. P., Kaloupek, D. G., Marx, B. P., & Keane, T. M. (2013b). *The Life Events Checklist for DSM-5 (LEC-5)*. https://www.ptsd.va.gov/professional/assessment/te-measures/life_events_checklist.asp

Weathers, F. W., Bovin, M. J., Lee, D. J., Sloan, D. M., Schnurr, P. P., Kaloupek, D. G., Keane, T. M., & Marx, B. P. (2018). The Clinician-Administered PTSD Scale for *DSM–5* (CAPS-5): Development and initial psychometric evaluation in military veterans. *Psychological Assessment*, *30*(3), 383–395. https://doi.org/10.1037/pas0000486

Weathers, F. W., Litz, B. T., Keane, T. M., Palmieri, P. A., Marx, B. P., & Schnurr, P. P. (2013). *The PTSD Checklist for DSM-5 (PCL-5)*. https://www.ptsd.va.gov/professional/assessment/adult-sr/ptsd-checklist.asp

Wortmann, J. H., Jordan, A. H., Weathers, F. W., Resick, P. A., Dondanville, K. A., Hall-Clark, B., Foa, E. B., Young-McCaughan, S., Yarvis, J. S., Hembree, E. A., Mintz, J., Peterson, A. L., & Litz, B. T., on behalf of the STRONG STAR Consortium. (2016). Psychometric analysis of the PTSD Checklist-5 (PCL-5) among treatment-seeking military service members. *Psychological Assessment*, *28*(11), 1392–1403. https://doi.org/10.1037/pas0000260

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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