COVER PAGE

PROTOCOL (INCLUDES STATISTICAL ANALYSIS PLAN)

Study Title: Augmenting Massed Prolonged Exposure with a Stellate Ganglion Block to Treat Posttraumatic Stress Disorder (PTSD) in Active Duty or Retired Service Members: A Pilot Study

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HUMAN SUBJECTS RESEARCH
PROTOCOL APPLICATION – Part B

1. PROTOCOL TITLE: Augmenting Massed Prolonged Exposure with a Stellate Ganglion Block to Treat Posttraumatic Stress Disorder (PTSD) in Active Duty or Retired Service Members: A Pilot Study

2. ABSTRACT

Active duty service members and veterans with combat-related posttraumatic stress disorder (PTSD) have a lower response rate to evidence-based cognitive behavioral PTSD treatments (e.g., Prolonged Exposure) than their civilian counterparts (Steenkemp et al, 2015). Stellate ganglion blocks are an emerging treatment that may hold promise as an adjunctive treatment for PTSD when combined with an evidence-based treatment such as Prolonged Exposure. To date, no study has examined the potential benefits of a stellate ganglion block over and above cognitive behavioral treatment alone. This open-label pilot study will examine the safety and effectiveness of combining Massed Prolonged Exposure with a stellate ganglion block. The study will recruit 12 active duty or retired service members (age 18 to 60 years) who meet DSM-5 diagnostic criteria for PTSD on the Clinician-Administered Posttraumatic Stress Scale-DSM-5 at the baseline assessment. Participants will receive ten sessions of Prolonged Exposure (90-minute sessions) over the course of two consecutive weeks. The stellate ganglion block will be administered between the 1st and 2nd Prolonged Exposure sessions. Participants will be asked to complete assessment measures during treatment and one- and three-months following the completion of treatment. This study will provide valuable information about a novel intervention, stellate ganglion block, that may enhance cognitive behavioral PTSD treatment outcomes in active duty and retired service members.

3. OBJECTIVES/SPECIFIC AIMS/RESEARCH QUESTIONS.

The primary research objective is to conduct a pilot study exploring the potential treatment effectiveness and safety of a stellate ganglion block combined with Massed Prolonged Exposure in reducing PTSD symptoms in active duty and retired service members (*N* =12). The second objective of the pilot is to examine whether the combination of both treatments will reduce comorbid symptoms more than was found in a recently completed trial of Massed Prolonged Exposure in active duty service members (Foa et al, 2018).

Aim: To conduct a pilot study to evaluate the safety and effectiveness of a stellate ganglion block (with ropivacaine) combined with Massed Prolonged Exposure for the treatment of PTSD in active duty and retired military service members.

Hypothesis 1: More than 50% of the patients who receive the stellate ganglion block and Massed Prolonged Exposure will no longer meet the clinician-assessed PTSD diagnostic criteria on the CAP-5 at one-month and three-month follow-up.

Hypothesis 2: More than 50% of the patients who receive the stellate ganglion block and Massed Prolonged Exposure will have a 10 point or greater reduction in PTSD symptoms on the PCL-5 at one-month and three-month follow-up.

Hypothesis 3: The adverse events associated with the stellate ganglion block will be minimal and temporary.

4. MILITARY RELEVANCE

When left untreated, posttraumatic stress disorder (PTSD) can persist for decades and is associated with marked functional impairment including increased risk of depression, suicidality, substance abuse, relationship dysfunction, healthcare utilization, missed work days, and disability (Crum-Cianflone et al., 2016; Jacobsen et al., 2001; Lambert et al., 2012; Maynard et al., 2017; Stanley et al., 2019). Following almost two decades of combat deployments to Afghanistan, Iraq, and surrounding locations, PTSD poses a significant threat to the United States' military force strength and places additional strains on the Veterans Health Administration. Estimates of the numbers of service members and veterans returning from these deployments with PTSD are as high as 20% (range: 7-20%; Institute of Medicine, 2014; Richardson et al., 2010). Importantly, these estimates do not include service members who develop PTSD through sexual or physical assaults, motor vehicle accidents, and other non-combat related traumas. Given the costs associated with military training and the potential loss of knowledgeable and experienced service members, it is in the best interest of the military to provide opportunities for service members with PTSD to receive highly efficacious treatments that enable them to become fully fit for worldwide duty. Because those who cannot be treated into remission are at a significant risk for discharge from active duty, the provision of PTSD treatments that are both highly efficacious and accessible to active duty military personnel are urgently needed.

5. BACKGROUND AND SIGNIFICANCE.

Trauma-focused therapies such as Prolonged Exposure (PE) are effective in reducing PTSD symptoms below the diagnostic threshold in up to 80% of patients in *civilian* populations (Bisson et al., 2007; Institute of Medicine, 2008, 2014b; Resick et al., 2002), with treatment improvements lasting for years (Resick et al., 2012). However, the treatment of combat-related PTSD in active duty and veteran populations has been less successful with only 50% experiencing significant symptom reduction following treatment (Steenkamp et al., 2015).The need for treatments that produce higher response rates in active duty military is paramount.

In a seminal study, STRONG STAR (South Texas Research Organizational Network Guiding Studies on Trauma and Resilience) examined the effects of PE in 366 service members with combat-related PTSD (Foa et al., 2018). While PE is traditionally delivered in weekly sessions over the course of months, this format can pose unique obstacles to care for military patients. Therefore, in an effort to enhance treatment accessibility, the study team developed a Massed Prolonged Exposure protocol that compresses treatment into once daily treatment over a two-week period. The treatment efficacy of Massed Prolonged Exposure (ten 90-minute sessions in two weeks) was compared to spaced PE (ten 90-minute sessions in 10 weeks). Importantly, massed PE and spaced PE were equally efficacious with approximately 50% of patients experiencing reductions in their PTSD symptoms below diagnostic threshold. Additionally, massed PE had a lower drop out-rate from treatment (13.6% versus 24.8%, respectively) and fewer reported adverse effects. While the results of this study are promising, there is room for improvement.

Stellate ganglion blocks (SGBs) are an emerging treatment that may hold promise as an adjunctive treatment for PTSD when combined with an evidence-based treatment such as PE. SGBs are typically used for pain management (Gunduz & Kenis-Coskun, 2017). The use of SGB to treat PTSD was first reported by Lipov and colleagues (2008) as a means to block physiological stress response symptoms associated with PTSD. Since this report, case studies and small clinical trials have provided support for SGB's efficacy in treating PTSD in military populations. Reduction in PTSD symptoms has been reported within hours of the procedure, with researchers noting the largest reductions in symptoms of hyperarousal and avoidance (Lipov et al., 2012; Lynch et al., 2016). In a case series of 166 active duty patients, Mulvaney and colleagues (2014) found that the majority of patients experienced significant reductions in PTSD symptoms that remained 3 to 6 months following the procedure. On the other hand, a randomized clinical trial with active duty service members and veterans found no difference between those who received a SGB consisting of 5mL of 0.5% ropivacaine and those who received a sham injection in symptom reduction (Hanling et al., 2016). However, their sample size was small (*N* = 42), and the majority of participants were undergoing medical disability evaluation boards, leading researchers to suggest that larger trials with populations less susceptible to possible secondary gains need to be conducted (Hanling et al., 2016; Summers & Nevin, 2017). Furthermore, there was no control of prior or ongoing evidence-based behavioral therapy in this study. Thus, SGB may be an appropriate adjunct to increase efficacy of PTSD treatment. To date, no study has examined the potential benefits of combining SGB with an evidence-based behavioral treatment such as PE.

6. RESEARCH DESIGN

This is a small, open-label treatment study that tests the potential safety and treatment effectiveness of a stellate ganglion block combined with Massed Prolonged Exposure. Each of the 12 participants will receive ten 90-minute sessions of Massed Prolonged Exposure and an injection of a stellate ganglion block between the first and second PE sessions.

7. RESEARCH PLAN

7.1 Selection of Subjects

7.1.1. Subject Population.

The study sample will consent and screen up to 27 active duty and retired service members recruited in the community and through Brooke Army Medical Center (BAMC), JBSA-Fort Sam Houston, Texas to analyze data from at least 12.

7.1.2. Source of Research Material. All measures are being administered for research purposes. For a complete list of measures, see Section 7.3.

Source of Research Material	Clinical Purposes (Y/N)	Research Purposes (Y/N)
AHLTA Clinical Records	Yes	Yes

Clinician Rating Scales	No	Yes
Self-Report Questionnaires	No	Yes

7.1.3. Inclusion and Exclusion Criteria.

Inclusion Criteria

1. Active duty or retired military service member (age 18- 65 years) as assessed with the Demographics and Military Service Characteristics Form
2. PTSD diagnosis as assessed by Clinician-Administered Posttraumatic Stress Scale (CAPS-5)
3. Able to speak and read English (due to standardization of outcome measures)
4. Defense Enrollment Eligibility Reporting System (DEERS)-eligible to receive care at Brooke Army Medical Center for the stellate ganglion block.

Exclusion Criteria

1. Current suicidal ideation severe enough to warrant immediate intervention (as determined by the Depressive Symptoms Index – Suicidality Subscale and the Self-Injurious Thoughts and Behaviors Interview short form and corroborated by a clinical risk assessment by a credentialed provider).
2. Current manic episode or psychotic symptoms requiring immediate stabilization or hospitalization (as determined by the Mini International Neuropsychiatric Interview, 7.0 Psychosis and Mania modules and corroborated by clinical judgment).
3. Other psychiatric disorders severe enough to warrant designation as the primary disorder as determined by clinician judgment.
4. Symptoms of moderate to severe substance (to include alcohol) use warranting immediate intervention based on participant self-report on the Alcohol Use Disorders Identification Test, observation of participant behavior, and clinical judgment.
5. Pregnancy (i.e. positive pregnancy test at screening) or breastfeeding as determined by a positive urine pregnancy test or by a “yes” response on the Supplemental Health Questionnaire for SGB.
6. Current anticoagulant use as determined by a “yes” response on the Supplemental Health Questionnaire for SGB.
7. History of bleeding disorder as determined by a “yes” response on the Supplemental Health Questionnaire for SGB.
8. Infection or mass at injection site as determined by a “yes” response on the Supplemental Health Questionnaire for SGB.
9. Myocardial infarction within 6 months of procedure as determined by a “yes” response on the Supplemental Health Questionnaire for SGB.
10. Pathologic bradycardia or irregularities of heart rate or rhythm as determined by a “yes” response on the Supplemental Health Questionnaire for SGB.
11. Symptomatic hypotension as determined by a “yes” response on the Supplemental Health Questionnaire for SGB.
12. Phrenic or laryngeal nerve palsy as determined by a “yes” response on the Supplemental Health Questionnaire for SGB.
13. History of glaucoma as determined by a “yes” response on the Supplemental Health Questionnaire for SGB.
14. Uncontrolled seizure disorder as determined by a “yes” response on the Supplemental Health Questionnaire for SGB.
15. History of allergy to local anesthetics as determined by a “yes” response on the Supplemental Health Questionnaire for SGB.

7.1.4. Description of the Recruitment and Prescreening Process.

Participants will be continuously recruited through the community and Brooke Army Medical Center (BAMC), JBSA-Fort Sam Houston, Texas through provider referrals, recruitment events, flyers strategically placed at Fort Sam Houston, study information on the STRONG STAR website, and social media. Providers can give their patients contact information for the study staff so that interested individuals may contact STRONG STAR directly. Alternatively, providers can obtain consent to contact from their patients that allows the study staff to contact the potential participant directly. Medical records will not be reviewed for recruitment purposes. Instead, study participants will be provider-referred or self-identified.

Under an IRB-approved HIPAA Waiver of Authorization, study personnel will conduct a brief discussion by telephone where the basic study inclusion and exclusion criteria will be reviewed to help the individual determine if he or she meets the study criteria or has obvious exclusions from the study protocol so as to prevent individuals from making unnecessary travel for consent and more in-depth screening. This information will be entered into a secure database as a phone call to

a potential participant or a phone call from a potential participant: name, phone number, name of study the caller is interested in, referral date, referral source, potential eligibility status, reason if not eligible, and verbal permission to contact the caller in the future for other studies. We will also record the date and time of the call, outcome of the call, and any notes. Subjects who agree to study participation will sign a consent document before any further screening will take place. Any individually identifiable information and Protected Health Information (PHI) collected on individuals who do not consent to participation will not become part of the research data. If participants agree to participate in the research, the identifiable data collected will become part of the participants' research records and will be stored according to the research confidentiality plan.

Active duty or retired military service members who are not eligible or interested in other IRB-approved STRONG STAR protocols will be told about this study. If interested, a member of the research team will review eligibility with these potential participants over the phone. If the person believes they may qualify for the study, the participant will be scheduled for an appointment in which consent will be obtained, and if authorized, the first baseline assessment will be completed.

7.1.5. Consent Process.
During the consent appointment, potential participants will have the study explained to them in a private location in-person using a paper form at the UTHSCSA STRONG STAR offices located at 7550 IH10 West, Suite 1325, San Antonio, TX 78229 or online using an electronic consent (eConsent). The preferred method is to use the eConsent process. Potential participants will be provided a link to the informed consent document (ICD). The potential participant will be given a copy of the informed consent document (ICD) to read. After the potential participant has read the ICD, they will be given the opportunity to take the consent home to discuss the research with family and friends. The research team, including a research nurse, will be available to answer any questions about the research. Once the potential participant has reached a decision, a member of the study team will review the risks and benefits of the study and ensure the participant understands the research. The participant will sign the consent form either electronically or on a paper form. A copy of the signed ICD will be given to the participant. As described in the consent, participants on active duty will have the option of having their Command notified by the Research Staff to ensure active duty Service Members are afforded the time to participate in the study. Command agreement to allow for duty time to participate in this study is not a requirement for study participation. A member of the study team will document the informed consent process in the medical record of the participant. Baseline assessment will occur after consent.

7.1.6. Subject Screening Procedures.
Once the consent is signed, participants will then be asked to complete the baseline assessments. The initial consent and screening will require up to 4 hours. This will include the completion of the questionnaires and interviews outlined in the table in Section 7.3 below.

This study involves remote and/or virtual research interactions with participants by the research staff. Research activities will be audio-recorded by an independent device (separate from the conferencing platform, i.e. Zoom). Therefore, privacy and confidentiality is not guaranteed due to the nature of the electronic conferencing platforms that will be used.

A baseline assessment will then be scheduled to immediately follow consent. This may occur in-person using paper forms or the participant will be logged into the STRONG STAR eCAP online data capture system to complete self-report baseline questionnaires.

If the participant has been referred from another STRONG STAR study and already undergone baseline testing within the past 30 days, the participant will be asked as part of the consent process to use these assessments rather than repeating the assessment battery. If the participant is newly referred to this study, if it has been more than 30 days since baseline testing for another study, or the participant declines use of previously completed assessments, he or she will meet with an evaluator and complete the full baseline assessment per protocol.

7.1.7. Compensation for participation.
Participants will not be compensated for their time.

7.2 Drugs, Dietary Supplements, Biologics, or Devices.

7.2.1 Ropivacaine will be the drug used in the stellate ganglion block.

- Complete names and composition of drugs: Ropivacaine (Naropin).
- Source of the product: BAMC Pharmacy.
- Location where study product(s) will be stored: In Pyxis MedStation in the Pain Management Procedure Clinic.
- Dose range, schedule, and administration route of study product(s): 6.5cc of Ropivacaine HCl 0.5%, one time into the stellate ganglion.
- Detailed description of washout period, if used: not applicable.
- Duration of study product(s) use: For the duration of the study.
- Concomitant medications that will be allowed during the study: Only ropivacaine will be used for the stellate ganglion block and during the procedure.
- Any antidotes and treatments available for potential side effects: None.
- Plan for disposition of unused study product: Per BAMC Pharmacy and Pain Clinic SOP.
- FDA regulated studies MUST include the following information: The FDA has approved the use of ropivacaine for stellate ganglion blocks. We are not seeking a new indication with this research project.

7.2.2 Not applicable, no devices will be used in the conduct of this study.

7.3. Research Interventions/Study Procedures.

Research Interventions

Massed Prolonged Exposure. Prolonged Exposure (PE; Foa, Hembree, & Rothbaum, 2007) is a first-line, empirically supported cognitive behavioral treatment for PTSD and serves as the foundation for massed PE. Massed PE, delivered daily over two weeks, utilizes exposure-based interventions to target psychological mechanisms (i.e., experiential and behavioral avoidance; maladaptive cognitive changes) that are thought to maintain trauma-related symptoms. Ten 90-minute sessions of massed PE, which has been found to be non-inferior to ten 90-minute spaced PE delivered once or twice a week over eight weeks, helps minimize military-specific treatment barriers, and decreases treatment dropout rates (Foa et al, 2018). For the proposed study, each participant will receive ten 90-minute sessions of massed PE over the course of two weeks. Up to three weeks will be allowed to complete the ten sessions of PE and SGB to accommodate scheduling constraints. Consistent with the standard spaced PE therapy manual, massed PE includes four primary treatment components: (1) psychoeducation on common reactions to trauma; (2) relaxation training; (3) in vivo exposure; and (4) imaginal exposures. In vivo exposure involves approaching avoided situations, people, places, and/or objects that are realistically safe. With imaginal exposure, participants repeatedly and systematically revisit their trauma memory and related thoughts and feelings. Participants also will be asked to complete homework, including reviewing treatment materials, listening to recordings of their imaginal exposure, and completing in vivo exposures. Since massed PE requires considerable time and effort, the study team will work with the participant to receive a release from duty or work while participating in the treatment. The preferred method of receiving therapy is face-to-face. However, there may be circumstances when part or all of the therapy can be administered through telebehavioral/telemedicine health (i. e., phone session or using a HIPAA-compliant video calling platform). Decisions will be made case-by-case as issues arise for individuals (such as travel restricted because of a worsening of the pandemic or the need for child care) and in discussion with the treatment team. Patients who do not have internet access will need to receive treatment in person.

Post-treatment Booster Sessions. Massed PE includes three booster sessions that can last up to 1-hour, scheduled for 1 week, 3 weeks, and 7 weeks after the completion of treatment. Booster sessions will be conducted either in person-or by telebehavioral health as appropriate. Since treatment benefits are derived primarily through the 2-week treatment program, there will not be an erosion of benefit for participants who do not have the posttreatment booster sessions.

Stellate Ganglion Block (SGB). Standard procedures for sterilization of the equipment and other universal safety precautions will be followed. Peripheral intravenous access with a 20-gauge angiocatheter will be obtained as a safety precaution in the event an intravascular injection occurs during the placement of the SGB requiring intervention. Participants will be positioned supine on a table and placed into a position that allows optimal visualization of anatomic landmarks and needle placement. Noninvasive hemodynamic monitors will be used throughout the procedure. A local anesthetic will be used to numb the skin and needle track. Placement of the SGB will be determined using either ultrasound or fluoroscopy guidance, depending upon the providers' preference. For the SGB, ropivacaine will be injected on the right in the anterior or anterolateral edge of the longus colli muscle.

Study Procedures.

Interested service members will be given a brief description of the study and will be asked to participate in a brief telephone call to determine initial interest in the study. If the individual is still interested, an appointment will be scheduled to meet with research staff to review and document informed consent. This appointment will be held at the UTHSCSA STRONG STAR offices located at 7550 IH10 West, Suite 1325, San Antonio, TX 78229 or may be completed online or by phone as described in section 7.1.5. As described in the consent, participants on active duty will have the option of having their Command notified by the Research Staff to ensure active duty Service Members are afforded the time to participate in the study. Likewise, retired service members will have the option of having their work supervisor notified to secure their support for participation in the study. Command or work agreement to allow for duty time to participate in this study is not a requirement for study participation. After signing the informed consent document, participants will complete a baseline assessment to determine full eligibility. Structured interviews will be administered by a trained independent evaluator with at least a master's degree education. As all study procedures are for screening or research purposes, the item responses will be maintained in the participant's research file and not be entered into the participant's electronic medical record.

During the course of the assessment, if a participant's symptom reports indicate that he or she is at high risk for suicidality according to the "STRONG STAR Suicide_Risk_Assessment_and_Risk-Crisis_Management" SOP, risk management procedures outlined in this SOP will be followed. If the research team feels that hospitalization should be considered, the participant's primary care provider or unit will be contacted to escort the individual to the ED. If a participant reports experiencing psychotic or mania symptoms, or reports dangerous amounts of alcohol and/or substance use, additional assessment by a licensed provider for consideration of referral for clinical care and for screening participants out of the study will be conducted. If a participant is determined to be ineligible for the study for any reason, a referral back to the referring provider or the patient's primary care provider for clinical follow-up will be made.

Once it has been determined that individuals meet the inclusion and exclusion criteria, participants will work with the research staff to schedule treatment and, if requested, secure a release from duty from their command or work to participate in the two-week treatment. Massed PE will be conducted by doctoral-level therapists at the UTHSCSA STRONG STAR offices. Participants will meet with their providers for individual, 90-minute sessions. They will then be asked to complete out-of-session treatment assignments throughout the rest of the day. Between the individual therapy session and out-of-session treatment assignments, participants will engage in approximately four to six hours of treatment per day, Monday through Friday, for two weeks. The stellate ganglion block injection will be administered between the first and second massed PE session at the BAMC Pain Clinic by qualified medical personnel supervised by MAJ John P. McCallin III, MD. The BAMC SOP for the placement of a stellate ganglion block will be followed. A research nurse will be in attendance during the procedure and will recover the participant for at least 1 hour following the procedure.

During PE treatment, participants will complete interim assessments of their PTSD symptoms, mood symptoms, trauma-related cognitions, and suicidal ideation proceeding sessions 6 and 10. This abbreviated assessment battery will include the PTSD Checklist for the DSM-5, Patient Health Questionnaire-9, Depressive Symptom Index – Suicidality Subscale, and Posttraumatic Cognitions Inventory and should take less than 15 minutes to complete. The full assessment battery outlined in the measure section will be re-administered one- and three-months following the completion of treatment by an independent evaluator. These assessments may occur in person at the UTHSCSA STRONG STAR offices or online/by phone as needed to accommodate participant scheduling and circumstances.

In order to examine the safety of the stellate ganglion block in combination with massed PE for the treatment of PTSD, adverse event monitoring will be conducted throughout the treatment phase, at each interim assessment, and again at the one-month posttreatment and three-month follow-up assessments. STRONG STAR has well established standard operating procedures for adverse event monitoring. An adverse event that leads to hospitalization will be considered a serious adverse event (SAE), and adverse events that are unexpected and increase risk to participants will be considered an Unanticipated Problems Involving Risk to Subjects or Others (UPIRSO). SAEs and UPIRSOs will be promptly reported to the IRB. The categorization and relatedness of each potential adverse event will be adjudicated by the study team during weekly calls.

Study Procedures	**Base Line**	**PE Day 1**	**SGB Txt between Txt PE Days 1& 2**	**PE Days 2-5**	**Interim Assess Day 6**	**PE Days 6-9**	**Interim Assess Day 10**	**PE Day 10**	1wk Post txt	3wk Post txt	1M F/U	7wk Post txt	3M F/U
Phone Discussion													
Informed Consent	R												

Study Procedures	Base Line	PE Day 1	SGB Txt between Txt PE Days 1& 2	PE Days 2-5	Interim Assess Day 6	PE Days 6-9	Interim Assess Day 10	PE Day 10	1wk Post txt	3wk Post txt	1M F/U	7wk Post txt	3M F/U
Demographics and Military Service Characteristics Form	S,R												
Life Events Checklist for the DSM-5	S,R										R		R
Deployment Risk and Resilience Inventory-2	S,R												
Mini International Neuropsychiatric Interview (MINI 7.0) Psychosis and Mania modules	S												
Health Questionnaire	R										R		R
Health Questionnaire-Supplemental for SGB	S												
Self-Injurious Thoughts and Behaviors Interview short form	S,R										R		R
Depressive Symptom Index – Suicidality Subscale	S,R				R		R		R	R	R	R	R
Clinician-Administered PTSD Scale for the DSM-5	S,R										R		R
PTSD Checklist for the DSM-5	R				R		R		R	R	R	R	R
Patient Health Questionnaire-9	S,R				R		R		R	R	R	R	R
Generalized Anxiety Disorder-7	R										R		R
Brief Inventory of Psychosocial Functioning	R										R		R
Veterans RAND 12-Item Short Form Health Survey	R										R		R
Alcohol Use Disorders Identification Test	S,R										R		R
Insomnia Severity Index	R										R		R
Posttraumatic Cognitions Inventory	R				R		R		R	R	R	R	R
Credibility and Expectancy Questionnaire for PE			R								R		R
Credibility and Expectancy Questionnaire for SGB			R								R		R
Massed Prolonged Exposure (PE)		R		R		R		R					

Study Procedures	Base Line	PE Day 1	SGB Txt between Txt PE Days 1& 2	PE Days 2-5	Interim Assess Day 6	PE Days 6-9	Interim Assess Day 10	PE Day 10	1wk Post txt	3wk Post txt	1M F/U	7wk Post txt	3M F/U
Ultrasound or Fluoroscopy (for SGB placement guidance)			R										
Stellate Ganglion Block (SGB)			R										
Adverse Event Monitoring		R	R	R	R	R	R	R	R	R	R	R	R
Urine Pregnancy Test	S												
Booster Sessions									R	R		R	

Key: R = administered for research purposes, S = administered for screening purposes

7.3.1 Collection of Human Biological Specimens. Urine pregnancy tests will be conducted at baseline.

7.3.1.1 Laboratory evaluations and special precautions. Urine pregnancy test will be conducted at baseline and the remaining sample will be discarded. Universal precautions will be followed when collecting and testing all urine samples.

7.3.1.2 Specimen storage. Not applicable

7.3.2 Data Collection.
A comprehensive list of assessments is included in the Section 7.3 table. The data collected in the study will be coded using an assigned number. Hard copies of data collected during the study will securely stored in locked cabinets at the STRONG STAR offices. Data will be entered into the STRONG STAR database on a secure UTHSCSA server (physically located at the Advanced Data Center), by member of the research team. Electronic data will be stored, managed, and analyzed by the STRONG STAR – Data and Statistics Core staff of the STRONG STAR consortium. Every member of the Research Team will be trained and monitored about how to handle and protect both medical and research records. Furthermore, the Research Team strictly controls access to study data.

7.3.3. Human Biological Specimens/Tissue/Data Banking. Not applicable

7.4 Statistical Consideration

7.4.1 Sample Size Estimation. This study is a pilot investigation. Consequently, a power analysis was not conducted.

Estimate Required Sample Size	12
Screened Out/Excluded	12
Estimate Participant Drop Out / Withdrawal	3
Total Enrollment Requirement	27

7.4.2 Primary (i.e., primary outcome variables) and secondary endpoints.
The primary aim of this pilot is to explore the potential treatment effectiveness and safety of a stellate ganglion block combined with Massed Prolonged Exposure in reducing PTSD symptoms in active duty and retired service members. Therefore, the primary outcome variables include the CAPS-5 severity score, the PCL-5, and adverse event monitoring. Secondary endpoints include associated psychopathology (severity scores on measures of depression, general anxiety, disability, and PTSD-related cognitions).

7.4.3 Data analysis.
Prior to statistical analyses, the data will be carefully inspected to identify such problems as unusual distributions, the desirability of transformations (e.g., logarithmic is often useful), missing data, and outliers. Data are also screened to identify potentially important covariates, i.e., variables (e.g., age) that are not of primary interest in the hypotheses but that

relate to the outcome measures (including such variables as covariates increases power and reduces bias).The primary software for statistical analyses is the SAS statistical system, that is widely available and well known. Our current version is SAS 9.4. We also have specialized software, including Stata 14, Mplus 8.2, and SPSS 25.

The proposed study is in preparation for a larger clinical trial, with the primary goals of the pilot study being to demonstrate feasibility through evaluating recruitment, retention, and adverse events, and to estimate the magnitude of potential impact on selected outcomes. A total of 12 participants with PTSD to receive a combination treatment of Massed Prolonged Exposure with a stellate ganglion block will be included in the analysis. Assessments will be done at three time points (baseline, one- and three-months following the completion of treatment). Statistical analyses will be intent to treat, using all data from participants regardless of the extent of participation. We are requesting to consent up to 27 participants to include12 participants for analysis.

The primary aim of this project is to evaluate the effectiveness and safety of a stellate ganglion block combined with Massed Prolonged Exposure for the treatment of PTSD in active duty and retired military service members. Tests of the descriptive hypotheses will involve calculation of the relevant proportions with 95% confidence limits based on PTSD diagnosis, PTSD symptom severity, and adverse events over the course of therapy, and dropout.

7.7 Confidentiality.

All Prolonged Exposure sessions and interview assessments will be delivered in private offices at the STRONG STAR Clinic at the UTHSCSA. The stellate ganglion block will be administered in Pain Clinic at the Brooke Army Medical Center following standard operating procedures for patient safety and confidentiality. Data will be stored by an assigned participant code number so that data records can be viewed by password-authenticated, authorized investigators and Consortium personnel. Digital audio recordings of assessments and PE sessions will be labeled with the participant's study id number and saved on a secure password protected server. Those recordings, to be reviewed for fidelity to ensure that the treatment is being delivered in accordance with the treatment manual, will be viewed on a secure, password protected server. There is no option for the reviewers to download or otherwise save the recordings to their computers. Every member of the Research Team will be trained and monitored about how to handle and protect both medical and research records. The recording will be deleted from the recorder after it has been saved to the secure password protected server. In the circumstance that an audio recording cannot be immediately saved (e.g., network or electrical outage, computer unavailable, etc.), the recording device will be placed in a locked file cabinet in the STRONG STAR Clinic offices. Study staff will be responsible to upload the recordings as soon as possible and then deleting the recording from the recorder. Only authorized study staff, and members of the STRONG STAR Biostatistics and Data Management Core staff will have access to either the raw data or electronic study data.

7.7.1 Certificate of Confidentiality. We are not seeking a Certificate of Confidentiality.

7.7.2. Data Protection.

Data will be coded using an assigned number. Data collected during treatment will be placed into a locked filing cabinet and stored securely in a locked room by a STRONG STAR staff member. Files will be kept securely at the University of Texas Health Science Center (UTHSCSA) STRONG STAR offices in San Antonio. The STRONG STAR data server is physically located at the Advanced Data Center (ADC) has 24x7 onsite security, card key, biometric access controls and video surveillance. University of Texas Health Science Center at San Antonio (UTHSCSA) ADC facility also maintains Gen 2 firewall devices to protect and prohibit any unauthorized access to UTHSCSA data. All UTHSCSA network devices are monitored by state of the art monitoring applications that include configuration audit, management, and availability 24x7. Every member of the Research Team will be trained and monitored about how to handle and protect both medical and research records. Furthermore, the Research Team strictly controls access to study data. The local study site will maintain a list of assignment numbers for the purpose of linking subsequent research materials.

A Data Safety and Monitoring Plan (DSMP) has been developed in accordance with the National Institutes of Health Office of Human Research Protection to assure the appropriate clinical safety monitoring of study subjects participating in this study.

7.7.3. Long Term Data Storage.

A *STRONG STAR Repository* has been approved by both the UTHSCSA (HSC20100475H) IRB to enable the STRONG STAR Consortium to store specimens and data for future use. The STRONG STAR Repository will create a large comprehensive database of information, biological specimens and neuroimages related to the identification, assessment, and treatment of PTSD in our active duty and retired veterans of conflicts following 9-11. All information entered into the STRONG

STAR Repository will be extracted from primary datasets collected as part of IRB-approved studies, including this study, being conducted and /or supported by the projects of the STRONG STAR Consortium. These study databases will be established and maintained by the Biostatistics and Data Management Core of the STRONG STAR Consortium. A unique, sequential alpha-numeric STRONG STAR ID will be assigned to each participant at the time of recruitment into this study. However, all Repository data will be identified with a different code number that can be cross linked to the original study code only through records maintained by the STRONG STAR Biostatistics and Data Management Core. Data, biological specimens and images will constitute the STRONG STAR PTSD Repository. Participation in the repository will be completely voluntary and entirely optional which means that a potential participant's willingness to participate in the repository has no influence upon their eligibility to participate in the primary STRONG STAR study they have either already enrolled in or are considering enrolling in. At the conclusion of this study, participants who signed the consent to have their specimens and data placed in the STRONG STAR Repository will be maintained under the IRB-approved Repository protocol. Biological specimens and information from study participants who declined participation in the STRONG STAR Repository will be permanently de-identified (i. e., all PHI will be deleted from the study data bases) and the de-identified blood and information placed in the STRONG STAR Repository for future use.

8.0 RISKS/BENEFITS ASSESSMENT

8.1 Risks.

Likely, but Not Serious Risks

Potential risks associated with the assessments and PE can include temporary increase in relationship distress, becoming emotionally upset or experiencing an initial increase of PTSD symptoms due to the consideration of traumatic events. Studies with PE suggest that a small minority experience an increase in symptoms of PTSD after the initiation of imaginal exposure exercises and for this minority, the distress and increased symptoms are temporary, are not predictive of poor outcome, and are not associated with increased likelihood of dropout (Foa et al., 2002).

Potential risks associated with the stellate ganglion block can include a temporary change in skin temperature; temporary hoarseness, voice changes or loss of voice; or Horner's Syndrome.

Potential risks related to ropivacain used in the stellate ganglion block can include signs of an allergic reaction (hives or red skin rash; dizziness; sneezing; difficulty breathing; nausea or vomiting; sweating; swelling of your face, lips, tongue, or throat; gastrointestinal distress; pain (headache, back pain); skin (itching); numbness or tingly feeling; fever; genital-urinary (problems with urination or sexual function).

Rare, but Serious Risks

With the handling of medical and research records there is always the possibility of a breach of confidentiality. However, every effort is made to protect the privacy of participants. Every member of the Research Team is carefully trained and monitored about how to store, handle, and protect participant records.

Rare but more serious risks associated with the stellate ganglion block include bleeding from a broken blood vessel that results in a hematoma; injury to the nerves around the injection site; injury to the esophagus; pneumothorax; spinal cord trauma; infection of the tissues of the neck, nerves, bone or disc material in the area of the injection or IV placement; incomplete recovery of normal function.

Rare but more serious risks related to ropivacain used in the stellate ganglion block include feeling anxious, restless, confused, or like you might pass out; problems with speech or vision; ringing in the ears, metallic taste, numbness or tingling around the mouth, or tremors; seizure (convulsions); weak or shallow breathing; slow heart rate, weak pulse or fast heart rate, gasping, feeling unusually hot.

Rare but more serious risks if fluoroscopy is used for a prolonged time to guide the placement of the block are reddening of the skin, a very slight increase in the chance of contracting cancer, and a potential risk to an unborn embryo/fetus should a woman undergoing fluoroscopy be pregnant. Normally fluoroscopy will be used for less than one minute.

Concerns for Pregnant and Breastfeeding Women

It is not known whether ropivacaine can cause birth defects or other problems in an unborn child. Ropivacaine might be harmful to (1) an unborn child or (2) an infant who is breast-fed. Participants should not get pregnant or breastfeed while in this study.

Risks of PTSD Diagnosis regardless of Treatment

Possibility of increased suicidal risk. One of the risks of PTSD both in and out of treatment is attempted suicide, which can result in death.

Safeguards for Protecting Participants

For urgent issues, whether potentially related to the PE or to the stellate ganglion block, participants will be instructed to get help immediately by going to the Emergency Department open 24 hours at the Brooke Army Medical Center. For suicidal thoughts, participants can also be advised to call the suicide hotline, or go to a nearby civilian emergency room. Each week, the therapist will review the participant's progress and symptom levels and will provide individualized feedback to the participant as needed. Participants complete weekly self-report assessment measures that will assess PTSD severity, depressive symptoms, and suicidal ideation. This will allow therapists to closely monitor any increase in distress. Individualized safety planning will be utilized as needed by members of the treatment team. Any indication that the participant is considering suicide will be handled following the STRONG STAR Consortium SOPs in concert with the local site-specific policies and procedures. Participants can be seen at the Brooke Army Medical Center Emergency Department at any time.

The possible risks (i.e., temporary increase in distress and severity) associated with participation are reasonable in this context given the level of participant monitoring and access to research and clinical staff. We believe that the possible benefits from participating in this study outweigh the possible risks. However, if a service member decides against participation, he/she can still access mental health treatment through the Brooke Army Medical Center or Army One-Source.

Research Monitor:

Karen Nijland, BPharm will serve as the DoD Independent Research Monitor. The duties of the research monitor shall be determined on the basis of specific risks or concerns about the research. The research monitor may perform oversight functions (e.g., observe recruitment, enrollment procedures, and the consent process for individuals, groups or units; oversee study interventions and interactions; review monitoring plans and UPIRTSO reports; and oversee data matching, data collection, and analysis) and report their observations and findings to the IRB or a designated official. The research monitor may discuss the research protocol with the investigators, interview human subjects, and consult with others outside of the study about the research. The research monitor shall have authority to stop a research protocol in progress, remove individual human subjects from a research protocol, and take whatever steps are necessary to protect the safety and well-being of human subjects until the IRB can assess the monitor's report. Research monitors shall have the responsibility to promptly report their observations and findings to the IRB or other designated official.

8.2 Potential Benefits.

Potential benefits of participation in this study may include a reduction in PTSD symptoms over the course of therapy. In addition, the knowledge gained from this study will serve to inform the most effective early interventions for the prevention and treatment of PTSD in active-duty military personnel.

9.0 ADVERSE EVENTS, UNANTICIPATED PROBLEMS, AND DEVIATIONS

9.1 Adverse Events will be assessed and monitored according to the established STRONG STAR SOP and the IRB of record's policies and procedures.

9.2 Reporting Unanticipated Problems Involving Risks to Subjects or Others, Serious Adverse Events and Deaths to the IRB of Record.

All adverse events, unanticipated problems involving risk to subjects or others, and deviations will be reported to the Institutional Review Board (IRB) in accordance with current IRB policy. UPIRSOs and recurrent non-compliance with study procedures will be reported promptly to the IRB. All adverse events that do not meet the UPIRSO criteria and deviations that are not non-compliance will be summarized at Continuing Review per the IRB of record's policy.

10.0 WITHDRAWAL FROM STUDY PARTICIPATION.

Participation in the study may be discontinued by the principal investigator if continued participation is considered a danger to a participant's welfare. Reasons for discontinuation include: 1) a serious adverse event such that continued participation would be a danger to the participant; 2) clinical worsening for any reason that is deemed to necessitate non-study psychological or psychiatric treatment; 3) exacerbation of PTSD, anxiety, or depressive symptoms that the participant cannot tolerate; or 4) discontinuation would be in the participant's best interest. Participants deemed candidates for discontinuation will be discussed in the weekly conference calls with the therapist and the supervisor and will be brought to the attention of the PI for final decision.

Participants who are discontinued from the study for any reason will be scheduled for a final evaluation within one week and given appropriate treatment referrals. If participants are discontinued due to a serious adverse event, they will continue to be followed clinically by the therapist and/or member of the research staff until the adverse event is resolved or becomes stable. If participants are discontinued for a medical or psychiatric reason, they will be given the opportunity to either complete the balance of their Massed-PE sessions or to receive a full course of Massed-PE after the condition has resolved or stabilized and the endpoint assessment has been completed. The reason the participants are discontinued from the study and any referrals made will be documented. Participants will be told they will be contacted for follow-up whether or not they complete the trial.

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12.0 TIME REQUIRED TO COMPLETE THE RESEARCH (including data analysis).

The following table provides an overview of activities that the research team plans to accomplish. We anticipate recruiting and treating two eligible service members per month to meet study goals. We anticipate that the study will be completed by December 31, 2020.

Activities (Months)	1	2	3	4	5	6	7	8	9	10	11	12
IRB approvals, prepare materials; train staff on procedures	■	■	■									
Recruit, screen, and treat 12 participants				■	■	■	■	■	■			
Complete follow-up assessments										■	■	■

13.0 STUDY CLOSURE PROCEDURES

At the conclusion of the study all data will be stripped of identifiers. De-identified (anonymized) data will be maintained indefinitely in the STRONG STAR Repository. Informed consent documents will be stored securely for a minimum of three years following completion of the research; HIPAA authorizations will be stored for a minimum of six years IAW Federal regulations. A protocol completion form will be filed with the IRB.

14.0 DESCRIPTION OF ASSESSMENTS

The majority of the measures listed below is commonly used, have adequate to good psychometrics, and are part of the Consortium common data elements (CDE). As outlined in the National Research Action Plan, evidence-based CDEs and measures for STRONG STAR studies will ensure comparability of results across the consortium as well as other clinical trials and epidemiological studies of PTSD.

Demographics and Military Service Characteristics Form: The Demographics Form measures standard demographics (race, gender, age) and military service information (e.g., rank). This measure will be administered at the baseline assessment.

Life Events Checklist-5 (LEC-5). The LEC includes a list of 24 potentially traumatic life events commonly associated with PTSD symptoms. The instrument was designed to facilitate the diagnosis of PTSD (Weathers, Blake, Schnurr, Kaloupek, Marx, & Keane, 2013a).). In this study, the LEC-5 will also be used to identify the index event and focus of the PTSD treatment. For each potentially traumatic life event, respondents rate their experience of that event on a 5-point nominal scale (1 = happened to me, 2 = witnessed it, 3 = learned about it, 4 =part of my job, 5= not sure, and 6 = does not apply). Each nominal point will be scored separately, as either 0 (=not endorsed by participant) or 1 (=endorsed by participant). This measure will be administered at the baseline assessment, the one-month follow-up assessment, and the three-month follow-up assessment.

Deployment Risk and Resilience Inventory-2 (DRRI-2) Combat Experience and Post-battle -Scales: High- and low-intensity deployment stress exposure will be assessed using scales from the DRRI-2 (Vogt, Smith, King, & King, 2012). The DRRI-2 is an update of the original DRRI (King, King, Vogt, Knight, & Samper, 2006), which was developed and tested in three separate national samples of veterans of the first Gulf War. It has been revised and tested with OEF/OIF/OND returnees (Vogt et al., 2008). The DRRI-2 provides an update of the DRRI's assessment of deployment-related factors to ensure the instrument's applicability across a variety of deployment circumstances (e.g., different eras of service) and military subgroups (e.g., men and women), as well as to validate updated measures in a contemporary

Veteran cohort (Vogt, et al., 2012). High intensity stressor exposures will be assessed using the DRRI Combat Experiences and Aftermath of Battle subscales. Responses to these scales are on a 6-point Likert scale. The total score is the sum of the item scores, where higher scores signify greater exposure to combat or exposure to the consequences of combat, respectively. Both subscales have very good internal consistency (α = .90 to .92) and construct validity (Vogt et al., 2012). This measure will be administered at the baseline assessment.

Mini-International Neuropsychiatric Interview (MINI-7.0) Psychosis and Mania modules. The MINI 7.0 is a short, structured clinical diagnostic interview designed to cover the major psychiatric disorders in DSM-5 and ICD-10. It is widely used in epidemiological studies and multi-site clinical trials. Responses to the interviewer's questions are rated as either "yes" or "no." As is the case on the SCID, there are skip-outs, which saves time. However, this means that the MINI cannot be used to index the severity of a given psychiatric problem, only caseness. When there are many skip-outs, the MINI takes ~15 minutes to administer. The MINI can be used to assess the full spectrum of psychiatric problems, or specific modules can be employed (e.g., the schizophrenia module to rule out thought disorder). This measure will be administered at the baseline assessment.

Health Questionnaire. The original Health Care Utilization (HCU) is a 16-item questionnaire developed in 2000 for Dr. Patricia A. Resick's NIH grant, "Cognitive Processes in PTSD: Treatment II." The questionnaire was based on the 1999 Behavioral Risk Factor Surveillance System. The version that will be administered as part of the STRONG STAR Consortium has been modified to be of increased relevance to active-duty service personnel. The measure includes items regarding use of mental health services, current psychiatric medication, past psychiatric medication, hospitalization, and outpatient medical services, as well as items intended to assess changes in participants' military status. Tobacco/nicotine use will also be queried. This measure will be administered at the baseline assessment, the one-month follow-up assessment, and the three-month follow-up assessment.

Health Questionnaire – Supplemental for SGB. The Health Questionnaire – Supplemental for SGB is a 11-item self-report measure that assesses health conditions that would exclude individuals from receiving a stellate ganglion block. Respondents are asked to answer "yes" or "no" to each of the items. This measure was created specifically for this study and will be administered at the baseline assessment.

Self-Injurious Thoughts and Behaviors Interview (SITBI): The SITBI (Nock, Holmberg, Photos, & Michel, 2007) is a structured interview assessing the presence, frequency, and characteristics of self-injurious and suicidal thoughts and behaviors. The SITBI will be administered by an Independent Evaluator, who will instruct the participants to answer the questions based on their entire lifetime of experience. The SITBI has shown high interrater reliability, test-retest reliability, and concurrent validity (Nock et al., 2007). This measure will be administered at the baseline assessment, the one-month follow-up assessment, and the three-month follow-up assessment.

Depressive Symptoms Index-Suicidality Subscale (DSI-SS): The DSI-SS (Metalsky & Joiner, 1997) will be used to assess current suicidal ideation. The DSI-SS is a 4-item self-report measure of suicidal ideation that focuses on ideation, plans, perceived control over ideation, and impulses for suicide. It is being used as a core measure in the Military Suicide Research Consortium. Scores on each item range from 0 to 3, with higher scores reflecting greater severity of suicidal ideation. Instructions will instruct the participants to respond based on the past two weeks. A systematic review of measures of suicidal ideation and behaviors found that the DSI-SS had evidence of excellent internal consistency and concurrent validity (Batterham et al., 2014). This measure will be administered at the baseline assessment, the two interim assessments, the one-month follow-up assessment, and the three-month follow-up assessment.

The Clinician Administered PTSD Scale for DSM-5 (CAPS-5; Weathers, Blake, Schnurr, Kaloupek, Marx, & Keane, 2012): The CAPS-5 is structured interview that assesses the DSM-5 criteria for PTSD (Weathers et al., 2013). Each item is rated on a severity scale ranging from 0 (Absent) to 4 (Extreme/incapacitating) and combines information about frequency and intensity for each of the 20 symptoms. Additional items that are not included in the total score evaluate overall symptom duration, distress, impairment, dissociative symptoms, and global ratings by the interviewer. Validation studies are nearly complete to establish the psychometric properties of the CAPS-5 and findings will be reported in peer-reviewed publications. This interview is very similar to its predecessor, the CAPS for DSM-IV, which has been considered the gold standard for evaluating PTSD and demonstrated good reliability and validity (Weathers, Keane, & Davidson, 2001). In addition to reflecting diagnostic changes for PTSD in DSM-5, the CAPS-5 differs from the CAPS in that frequency and intensity ratings for each symptom are no longer scored separately, so the severity rating for each item determines whether a symptom is present or not. Subscale scores are calculated by summing severity scores for items in the following PTSD symptom clusters: re-experiencing, avoidance, negative alterations in cognitions and mood, and hyperarousal. Scores ≥ 25 indicate a probable diagnosis of PTSD. This measure will be administered at the baseline assessment, the one-month follow-up assessment, and the three-

month follow-up assessment.

PTSD CheckList-5 (PCL-5): The PCL-5 (Weathers, et al., 2010) is a 20-item self-report measure update of the PCL designed to assess PSTSD symptoms as defined by the DSM-5. The PCL-5 is currently available and has been shown to have good psychometric properties. The PCL-5 evaluates how much participants have been bothered by PTSD symptoms in the past week (for all assessments during treatment) or the past two weeks (all other assessment time points) as a result of a specific life event. Each item of the PCL-5 is scored on a five point scale ranging from 0 "not at all") to 4 ("extremely). This measure will be administered at the baseline assessment, the two interim assessments, the one-month follow-up assessment, and the three-month follow-up assessment.

Patient Health Questionnaire-9 (PHQ-9): The PHQ-9 is a widely used and well-validated instrument for measuring the severity of depressive symptoms (Kroenke, Spitzer, & Williams, 2001). It consists of 9 items that assess both affective and somatic symptoms related to depression and depressive disorders; these 9 items correspond to the diagnostic criteria for DSM MDD. Respondents rate the frequency with which they have been bothered by depressive symptoms within the past two weeks on a scale ranging from 0 ("not at all") to 3 ("nearly every day"). Scores on all items are summed to obtain a total severity score. Scores reflect no significant depressive symptoms (0-4), mild depressive symptoms (5-9), moderate depressive symptoms (10-14), moderately severe depressive symptoms (15-19), and severe depressive symptoms (>19). Respondents also indicate the degree to which their depressive symptoms have made it difficult for them to do their work, take care of things at home, or get along with other people, from "not difficult at all" to "extremely difficult." The PHQ-9 has high internal consistency (e.g., alpha ranging from .83 to .92; Cameron, Crawford, Lawton, & Reid, 2008), and correlates strongly with other measures of depression (Kroenke et al., 2001). This measure will be administered at the baseline assessment, the two interim assessments, the one-month follow-up assessment, and the three-month follow-up assessment.

Generalized Anxiety Disorder Screener (GAD-7): The GAD-7 (Spitzer, Kroenke, Williams, & Lowe, 2006) will be used to assess generalized anxiety symptomology. This is a 7-item measure that asks participants to rate the frequency with which they have been bothered by anxiety symptoms within the past two weeks on a scale ranging from 0 ("not at all") to 3 ("nearly every day"). Scores on all items are summed to obtain a total severity score. Scores reflect no significant anxiety symptoms (0-4), mild anxiety symptoms (5-9), moderate anxiety symptoms (10-14), and severe anxiety symptoms (>15). Respondents also indicate the degree to which their anxious symptoms have made it difficult for them to do their work, take care of things at home, or get along with other people, from "not difficult at all" to "extremely difficult." The GAD-7 has been shown to have high internal consistency (e.g., $\alpha = .89$; Lowe et al., 2008) and has been shown to reliably discriminate between anxious and non-anxious diagnostic groups (Kroenke, Spitzer, Williams, & Lowe, 2010).

Brief Inventory of Psychosocial Functioning: The Brief Inventory of Psychosocial Functioning (Marx et al. 2013) is a 7-item self-report instrument measuring respondents' level of functioning in seven life domains: romantic relationship, relationship with children, family relationships, friendships and socializing, work, training and education, and activities of daily living. Respondents indicate the degree to which they had trouble in the last 30 days in each area on a 7-point scale ranging from "0 = Not at all" to "6 = Very much." This measure will be administered at the baseline assessment, the one-month follow-up assessment, and the three-month follow-up assessment.

Veterans Rand 12-Item Health Survey (VR-12): Because a certain level of PTSD symptoms is an occupational hazard among service members redeployed for combat, it is critical to pay close attention to functional capacities as an important index of intervention efficacy. The Veterans SF-36 (VR-36) was adapted from the RAND SF-36 Version 1.0 questionnaire, and spans the range of health domains from physical to psychological health status. It includes two modifications. The first modification is an increase in the number of response choices for the role physical (RP) and role emotional (RE) items from a two point yes/no choice to a five-point likert scale (no, none of the time, yes, a little of the time, yes, some of the time, yes, most of the time, yes, all of the time). The second modification is the use of two items to assess health change, one focusing on physical health and one on emotional problems, in contrast to the one general change item in the RAND SF-36 (Kazis, Lee et al., 2004; Kazis, Miller, Clark et al 2004). The VR-36 has been widely used, distributed and documented in the Veterans Health Administration (VHA) with close to 2 million questionnaires administered nationally in six national surveys since 1996. The changes to the survey have increased the overall precision of the instrument and the discriminant validity of the physical and mental component summary scales (Kazis, Nethercot, et al 2006). The VR-36 is comprised of 37 items and eight scales: physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, energy/ vitality, social functioning, role limitations due to emotional problems, and mental health. Also, there are two summary scales: a physical component summary (PCS) and mental component summary (MCS). Higher scores indicate better health. Each summary is expressed as a T score, which facilitates comparisons between the VA patients and the general U.S. population. The PCS and MCS scores provide at

least 90% of the reliable variance in the eight SF-36 concepts (Kazis & Wilson, 1998; Kazis, Wilson, et al., 1999). The Veterans SF-12 was developed from the Veterans SF-36 and adapted from the MOS SF-36. It includes fewer items for seven of the eight scales and provides 90% of the reliable variance in the two component summary measures using the Veterans SF-36. Using independent results from the Veterans Health Study and the 1996 National Survey of Ambulatory Care Patients, the results for the Veterans SF-12 corresponded very closely with the results for the Veterans SF-36 (average differences of 0.06 points between them for PCS and 0.31 points for MCS; Kazis et al., 1996; Kazis & Wilson, 1998). This measure will be administered at the baseline assessment, the one-month follow-up assessment, and the three-month follow-up assessment.

Alcohol Use Disorders Identification Test (AUDIT): The AUDIT (Babor et al, 2001) will be used to identify people with hazardous or harmful patterns of alcohol consumption. The AUDIT is a 10-item screening measure, developed by the World Health Organization (WHO), with three subscales (alcohol consumption, drinking behavior, and alcohol-related problems) that are scored on a 4-point scale for a highest possible total score of 40. Among those identified as using alcohol in a harmful manner, 92% had scores of 8 or more, though determining a cutoff score should be left up to the clinician, depending upon the population being studied. The AUDIT has good internal consistency (α = .80-.93) as well as sensitivity and specificity (Saunders, Aasland, Babor, De La Fuente & Grant, 1993). This measure will be administered at the baseline assessment, the one-month follow-up assessment, and the three-month follow-up assessment.

Insomnia Severity Index (ISI). The ISI (Morin, 1993) is a 7-item self-report measure that assesses perceived severity of insomnia. Each item uses a 4-point Likert type scale from 0 (not at all satisfied) to 4 (very much satisfied). The items sum to produce a total score (range 0 – 28). The ISI has an internal consistency alpha coefficient of 0.74, and has shown convergent validity with other measures such as the Pittsburgh Sleep Quality Index (r = 0.67), the Dysfunctional Beliefs and Attitudes about Sleep (r = 0.55), and sleep diaries (r ranges from 0.32-0.91) (Bastien, Vallieres & Morin, 2001). This measure will be administered at the baseline assessment, the one-month follow-up assessment, and the three-month follow-up assessment.

Posttraumatic Cognitions Inventory (PTCI): The PTCI is a 36-item questionnaire that was developed to determine how an individual views the trauma and its sequelae in an attempt to understand both how PTSD develops and is maintained (Foa, Elhers, Clark, Tolin, & Orsillo, 1999). Using an emotional processing theory, Foa and her colleagues (1999) have suggested that PTSD is a consequence of disruptions in the normal processes of recovery when an individual has excessively rigid concepts about self and world rendering the person vulnerable if a traumatic event occurs. Thus the PTCI was developed as a measure of trauma-related thoughts and beliefs. It is comprised of three subscales (Negative Cognitions about the Self, Negative Cognitions about the World, and Self-Blame). The measure was tested in almost 600 adult volunteers recruited from two university PTSD treatment clinics as well as a university community. Approximately 65% (n=392) of individuals reported having experienced a trauma in which their own life or that of another person was perceived to be in danger and their response at the time included intense terror, horror, or helplessness (Criterion A event). The remaining 35% (n=162) denied such a traumatic experience. Of those who had experienced a trauma, 170 had PTSD symptoms of at least moderate severity while the remaining 185 reported a low symptom severity. The three subscales of the PTCI demonstrated internal consistency with alpha coefficients ranging from 0.86 to 0.97. Convergent validity was demonstrated comparing the PTCI to appropriate subscales of the World Assumptions Scale and Personal Beliefs and Reactions Scale. Significant correlations between the appropriate subscales ranged from 0.20 to 0.85. The PTCI was able to differentiate individuals with and without PTSD demonstrating discriminate validity (sensitivity = 0.78, specificity = 0.93). Test–retest reliability for each of the three subscales at a 1-week interval ranged from 0.75 to 0.89 and for a 3-week interval ranged from 0.80 to 0.86. This measure will be administered at the baseline assessment, the two interim assessments, the one-month follow-up assessment, and the three-month follow-up assessment.

Credibility/ Expectancy Questionnaire (CEQ): The CEQ is a 6-item measure that was designed to assess treatment expectancy and rationale credibility for use in clinical outcomes studies (Devilly & Borkovec, 2000). The credibility and expectancy for the PE will be assessed separately from the credibility and expectancy for the stellate ganglion block. It has been expanded from a 5-item measure designed primarily to assess credibility (Borkovec & Nau, 1972), 4-items of which have been used by both Foa and Resick (P.A. Resick, personal communication, February 22, 2010; E.A. Hembree, personal communication, February 23, 2010; E. B. Foa, personal communication, February 25, 2010) with the name Expectancy of Therapeutic Outcomes (ETO). The 6-item CEQ assesses both whether the person cognitively understands how the therapy works (credibility) as well as whether the person affectively believes that the therapy will work for them personally (expectancy). The 6-item CEQ has been tested in 217 individuals including 68 male Vietnam veterans and 58 female spouses, 69 individuals diagnosed with general anxiety disorder who had received treatment, and 22 individuals who had received either Cognitive Based Therapy (CBT) or Eye Movement Desensitization and Reprocessing (EMDR) for the treatment of PTSD. The scale demonstrated high internal consistency (alpha coefficients ranged from 0.84 to 0.85). Test-

retest reliability over a one-week period was found to be 0.82 for expectancy and 0.75 for credibility. The CEQ was able to differentiate between two treatment rationales in one study, one with and one without an encompassing theory while maintaining equivalence between three rationales in another study. Responses to four questions are scored using a 9-point Likert scale (1= not at all, 9= extremely). Responses to two of the questions are scored using an 11-point Likert Scale (0% to 100%). The combined responses are used to generate a score for credibility and another score for expectancy. This measure will be administered at the baseline assessment, the one-month follow-up assessment, and the three-month follow-up assessment.