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TITLE: Effectiveness and Patient Acceptability of Stellate Ganglion Block (SGB) for Treatment of Posttraumatic Stress Disorder (PTSD) Symptoms among Active Duty Military Members

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14. ABSTRACT

This study seeks to evaluate the effectiveness and acceptability of stellate ganglion block (SGB) for treatment of Posttraumatic Stress Disorder (PTSD) symptoms. We will conduct two parallel studies: a randomized, controlled trial (RCT) to evaluate the effectiveness of SGB for treating PTSD, and a qualitative study to determine the degree to which the procedure is deemed acceptable by active duty service members with PTSD, their spouses, and their providers. A total of 240 individuals will be enrolled for the RCT portion of the study; qualitative study participants will be convenience sampled from among the RCT participants. For the RCT study, participants will be randomized 2:1 active (SGB) to sham across three study sites. Participants will receive the intervention (active or sham) at weeks 0 (baseline) and 2, and assessments will be conducted at weeks 0, 2, 4, 6, and 8. For the qualitative study, individuals enrolled in the RCT will be asked to participate either in a focus group or an interview with their spouse. In addition, we will conduct focus groups and key informant interviews with providers: those who refer individuals to the study, and those who provide SGB to service members.

15. SUBJECT TERMS
Stellate ganglion block, Posttraumatic Stress Disorder, randomized controlled trial, qualitative research

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1. Introduction

This study seeks to evaluate the effectiveness and acceptability of stellate ganglion block (SGB) for treatment of Posttraumatic Stress Disorder (PTSD) symptoms. We will conduct two parallel studies: a randomized, controlled trial (RCT) to evaluate the effectiveness of SGB for treating PTSD, and a qualitative study to determine the degree to which the procedure is deemed acceptable by active duty service members (SMs) with PTSD, their spouses, and their providers. A total of 240 individuals will be enrolled for the RCT portion of the study; qualitative study participants will be convenience sampled from among the RCT participants. For the RCT study, participants will be randomized 2:1 active (SGB) to sham across three study sites: Womack Army Medical Center (WAMC; Fort Bragg, NC), Tripler Army Medical Center (TAMC; Honolulu, HI), and Landstuhl Regional Medical Center (LRMC; Landstuhl, Germany). Participants will receive the study intervention (active or sham) at weeks 0 (baseline) and 2, and assessments will be conducted at weeks 0, 2, 4, 6, and 8. For the qualitative study, individuals enrolled in the RCT who have received at least one SGB within the past 3 months will be asked to participate either in a focus group or an interview with their spouse. In addition, we will conduct focus groups and key informant interviews with providers: those who refer individuals to the study, and those who provide SGB to service members.

2. Keywords

Stellate ganglion block, Posttraumatic Stress Disorder, randomized controlled trial, qualitative research

3. Accomplishments

The major goals of this project for year two focused on regulatory and enrollment activities. In sum, 10 IRB amendments/actions were submitted, and HRPO (the U.S. Army Medical Research and Materiel Command's Human Research Protection Office) approval was obtained. The amendments focused on revision of text to clarify information for participants, implementation of new means of recruitment (social media campaigns, study poster revisions, and direct marketing to service members with PTSD diagnoses), and revisions to inclusion/exclusion criteria. (Note that approval of the amendment concerning direct marketing to service members with PTSD diagnoses is pending.)

During year two, data collection began at all three study sites. Specifically, enrollment at WAMC began on May 17, 2016; enrollment began at LRMC on July 26, 2016; and enrollment began at TAMC on February 6, 2017. Significant regulatory complications and unresponsiveness resulted in the extended delay of enrollment at TAMC. 72 SMs have been prescreened (27 at WAMC, 30 at LRMC, 15 at TAMC), 46 SMs were consented (20 at WAMC, 18 at LRMC, 8 at TAMC), 29 SMs were screen-eligible (9 at WAMC, 15 at LRMC, 5 at TAMC), and 6 SMs have completed the trial (4 at WAMC,2 at LRMC, 0 at TAMC).

RCT- Task 1: Conduct Randomized Controlled Trial (Months 1-36)		
Subtask 1: Prepare Regulatory Documents and Research Protocols		
Milestone	**Complete?**	**Comments**
Finalize Clinical Protocol	Yes	
Receive Common Access Cards	No	Determined to be unnecessary
Receive all IRB and HRPO approvals	Yes	All IRB and HRPO approvals received
Subtask 2: Develop Study Infrastructure		
Milestone	**Complete?**	**Comments**
Finalized Data Platforms	Yes	
Research Coordinators in place and trained	Yes	
Subtask 3: Collect, Analyze, and Disseminate Data		
Milestone	**Complete?**	**Comments**
RCT dataset complete	No	In process
Cleaned and edited analytic dataset	No	In process
Qualitative Study- Task 1: Conduct Qualitative Study		
Subtask 1: Prepare Regulatory Documents and Research Protocols		
Milestone	**Complete?**	**Comments**
Finalized qualitative study instrumentation	Yes	
Receive all IRB and HRPO approvals	Yes	All IRB and HRPO approvals received

During year two, study staff gave a presentation at the second annual Johns Hopkins Military and Veterans Health Institute conference entitled “Service Members and Veterans: PTSD Today and Tomorrow.” Additionally, study staff presented at the 2016 Special Operations Medical Association Scientific Assembly (SOMSA) and Exhibition (“Stellate Ganglion Block for PTSD: A Randomized Controlled Trial and Qualitative Study”). Finally, study staff presented a poster entitled “Stellate Ganglion Block for Treatment of Posttraumatic Stress Disorder Symptoms: A Multi-Mode Study” at the 2016 Military Health System Research Symposium (MHSRS). We have submitted an abstract to present a poster at the 2017 MHSRS conference.

Also during year two, the study team worked with the Armed Forces Network to create a short commercial about SGB and our study. The spot began airing on 1 August 2016 and will continue running for 18 months. Study staff were interviewed for an article in Stars and Stripes, which was further disseminated by outlets including Military.com and Task and Purpose. Study staff also collaborated on articles and spots in The Paraglide (Fort Bragg paper), Time Warner Cable News, the Fayetteville Observer, and National Public Radio. These pieces and others can be found in the “Latest News” section of our study website, https://sgbstudy.rti.org.

During year two, we conducted a regulatory site visit to WAMC to ensure that all study protocols, documentation, and procedures were being implemented correctly. In addition, plans were made to conduct a regulatory site visit to LRMC and to train a new Research Coordinator.

Multiple site visits were conducted at WAMC due to its proximity to RTI. These visits focused on meeting with IRB staff, consulting with research coordinators from other studies to brainstorm enrollment activities, and meeting with clinicians and their staff (primarily Behavioral Health) to try to increase referrals to the study.

During year two, we began examining data collected to date to ensure that all data management and analytic processes are functioning appropriately. These regular reports have been, and will continue to be, run monthly. These reports do not include unblinded information, even in aggregate.

During the upcoming project year, we anticipate continuing data collection, implementing new means of participant recruitment, and expanding efforts to involve service members from installations surrounding our study sites. We also anticipate beginning data collection for the qualitative portion of the study, and conducting regulatory site visits to LRMC and TAMC. Study staff will present at the 2017 MHSRS conference. Conversations with the US Special Operations Command (SOCOM) will begin regarding the potential use of Preservation of the Force and Families (POTFF) funds to pay for service member travel costs (for those located at a distance from our study sites who wish to participate). Finally, study leadership is considering submitting a request for a no-cost extension to allow enrollment to continue beyond what was originally proposed.

4. Impact

Nothing to report.

5. Changes/Problems

Changes

Major revisions to study inclusion and exclusion criteria include discontinuation of using a score on the CAPS-5 as an inclusion criterion (although the CAPS-5 will still be administered at baseline and study conclusion), and discontinuation of concurrent psychotherapy alongside study participation as an exclusion criterion.

Problems

The study team experienced delays in initiation of recruitment and enrollment activities at LRMC and TAMC, with the most significant delay seen with TAMC. Miscommunication, lack of responsiveness, and confusion about standard processes contributed to these delays.

Study enrollment has been significantly slower than anticipated. Suspected reasons for this include the following.

- Because SGB is offered at WAMC, TAMC, and LRMC outside our study, service members are opting to receive the procedure, as opposed to participating. There is a reported belief among service members that the treatment works, so they are unwilling to take a 1 in 3 chance of being randomized to the sham condition, despite being able to receive a true SGB upon completion of their 8-week study participation. To illustrate, during the week of 2/20/17, TAMC performed 9 SGBs outside our study, and LRMC performed 2 outside the study.

- Some potential referral sources are actively dissuading their patients from participating in our study, because the provider believes SGB is effective and doesn't want the patient to run a 1 in 3 chance of randomization to the sham condition.
- Behavioral Health providers appear to not be systematically referring to the study. We have experienced particular resistance at WAMC. At WAMC, outside providers (typically non-Behavioral Health) have been the biggest source of referrals; at LRMC, self-referral (service members contacting study staff after seeing materials or hearing about the study), pain clinic referrals, and outside provider referrals are distributed approximately equally; at TAMC, outside providers are the largest source of referrals followed closely by self-referrals.
- We have experienced difficulties in visibly marketing the study in high-traffic areas. For example, two previous requests (during study year two) to allow us to post study materials (posters, flyers, business cards) in the main entrances to WAMC were denied. A recent third request, with the assistance of the WAMC Public Affairs Office (PAO) was approved. Similar difficulties persist at LRMC and TAMC; however, we are beginning to see some progress.
- Because the procedure has been performed relatively frequently over the recent past, we are encountering more individuals who have previously had an SGB procedure, making them ineligible for the study at a higher rate than anticipated when the study was conceived.
- At TAMC, many participants are being referred to the study from an intensive outpatient behavioral health program and this appears to be contributing to a higher than normal number of individuals who are ineligible due to a medication change within the last three months.

In an effort to improve enrollment, we have consulted with outside parties as well as RTI marketing experts to identify novel means of recruitment. One potential such avenue is directly contacting service members who have received a diagnosis of PTSD to inform them about the study. We continue to conduct briefings with providers who are potential referral sources. Other activities include engagement with interested community groups, renewed efforts to place study materials in high-traffic locations (hospital lobbies, restrooms, gyms, chapels, commissaries, and banks), as well as active engagement through social media channels. We also are exploring the placement of paid advertisements in local newspapers, both print and online. (Articles facilitated by WAMC and LRMC PAOs have already been run.) We have obtained a letter of support from the Commander of Medical Department Activity (MEDDAC) Bavaria which will allow us to actively engage US military sites in that region. We also have updated study posters to more clearly communicate that the purpose of the study is to examine a treatment for PTSD symptoms.

6. Products

During the course of year two, presentations at the following scientific meetings were given by study staff:

- Johns Hopkins PTSD in Service Members and Veterans Meeting (invited)
- Special Operations Medical Association Scientific Assembly
- Military Health System Research Symposium

Additional products include the news media items described above in Section 3, "Accomplishments," paragraph 4.

7. Participants and Other Collaborating Organizations

The following individuals have worked at least 160 hours on the project in total during project year two. There has been no change in support of the PIs or key personnel, and no other organizations were involved as partners.

Name	Project Role	Person months worked	Contribution to the project
Rae Olmsted, Kristine L	Co-Principal Investigator	7.6	Daily study operations; management and substantive oversight (IRB/HRPO submissions, budget, substantive materials)
Peeler, James R	Logistics Task Manager	3.4	Coordination and oversight of all study logistics (hiring and training Research Coordinators, co-designing the control system, coordination with study sites)
Croxford, Julie A	Regulatory Specialist	1.5	
Zemonek, Richard D	Computer Programming Task Leader	2.1	Oversight of all computer programming activities (web and assessment programming, co-designing the control system, quality control for all systems)
Nelson, Jessica P	Project Manager	1.5	Project management (budgeting, reporting, meeting coordination) support as well as assistance with development tasks as needed

8. Special Reporting Requirements

Not applicable.

Appendix A: Study Press

Womack Clinical Trial: Old Treatment Offers New Hope for Post-traumatic Stress (Sept. 2015)

http://m.fayobserver.com/military/womack-clinical-trial-old-treatment-offers-new-hope-for-post/article_61c8d4ae-c214-5f3f-9672-cbbfbc31726a.html?mode=jqm

WAMC part of new PTSD study (23 June, 2016):

http://www.paraglideonline.net/life/article_f96c7f82-395d-11e6-a9ed-a3b78459a627.html

New Study Helping Fort Bragg Soldiers Combat Effects of PTSD (8/29/16):

http://www.twcnews.com/nc/triangle-sandhills/news/2016/08/29/new-study-helping-fort-bragg-soldiers-combat-effects-of-ptsd.html

"Miracle" PTSD Treatment Study Needs Volunteers (10/8/16):

http://taskandpurpose.com/miracle-ptsd-treatment-study-needs-volunteers/?utm_source=newsletter&utm_medium=email&utm_campaign=tp-today

Volunteers Wanted for PTSD Study of Treatment Some Call a Miracle (10/8/16):

http://www.military.com/daily-news/2016/11/08/volunteers-wanted-for-ptsd-study-of-treatment-some-call-a-miracl.html

Volunteers Wanted for PTSD Study of Treatment Some Call a Miracle (10/8/16):

http://www.stripes.com/news/volunteers-wanted-for-ptsd-study-of-treatment-some-call-a-miracle-1.437955

PTSD Treatment Getting Scrutiny in Clinical Trials at Three Military Hospitals (12/4/16):

http://www.fayobserver.com/news/local/ptsd-treatment-getting-scrutiny-in-clinical-trials-at-thre-military/article_d6bf233f-56f4-5bab-8f00-6145b03df7ee.html

Injections Could Radically Alter PTSD for Soldiers (12/8/16):

http://wunc.org/post/injections-could-radically-alter-ptsd-soldiers

Researchers Study Injections as PTSD Treatment (12/13/16):

http://wunc.org/post/researchers-study-injections-ptsd-treatment

Effectiveness and Acceptability of Stellate Ganglion Block (SGB) for Treatment of PTSD Symptoms
Log # 13046044 - FY 13 Applied Research and Advanced Technology Development Psychological Health Award
W81XWH-15-2-0015

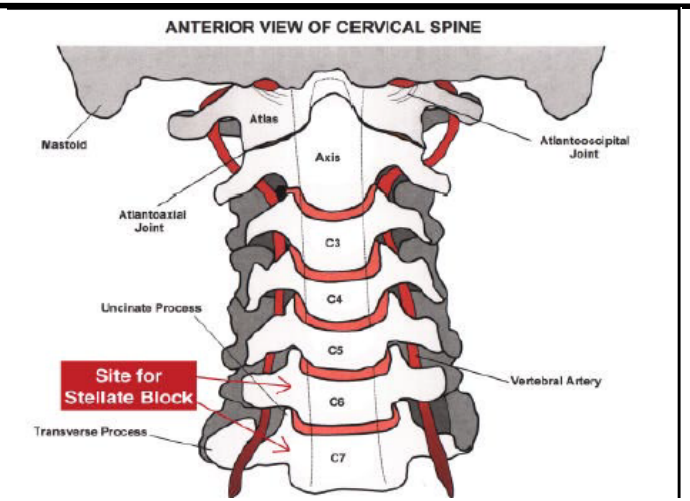
PI: Bradford Walters, MD, PhD **Org: RTI International** **Award Amount: $2,198,738.00**

Study Aims

- Determine effectiveness of SGB vs placebo in treating PTSD symptoms
- Describe the degree to which study participants are accepting of SGB

Approach

- Conduct a double-blind, sham-procedure-controlled, randomized clinical trial of 240 active duty participants with PTSD at 3 sites; primary outcome measure is CAPS-5 pre- and 8-weeks-post intervention
- Conduct focus groups and structured interviews with RCT participants (as well as spouses and clinical providers) to characterize the acceptability of the procedure



Accomplishment: Received start letter for TAMC (17-Oct-16)

Timeline and Cost

Activities / CY	15	16	17	18
Conduct Randomized Controlled Trial				
Conduct Qualitative Study				
Analyze Data				
Prepare and Submit Reports, Manuscripts and Briefings				
Estimated Budget ($K)	**$561**	**$855**	**$677**	**$106**

Updated: 2/28/17

CY 15 (funded 3/2015)
Prepare Regulatory Documents & Research Protocols
- ☑ Approved by WAMC IRB
- ☑ Submitted to HRPO

Develop Study Infrastructure
- ☑ Instrumentation programming complete
- ☑ RC identified for each site and training materials in development

CY 16
Prepare Regulatory Documents & Research Protocols
- ☑ Approved by HRPO

Develop Study Infrastructure
- ☑ In place & operational

Collect, Analyze, and Disseminate Data
- ☑ Subjects enrolling, collecting data

CY 17
Collect, Analyze, and Disseminate Data
- ☐ Enrollment complete
- ☐ Analyses Complete and data dissemination underway

Comments/Challenges/Issues/Concerns
- Enrollment is significantly lagging projections.

Budget Expenditure to Date: Projected: $1,465,825 Actual: $1,225,821