Stellate Ganglion Block Used to Treat Symptoms Associated With Combat-Related Post-Traumatic Stress Disorder: A Case Series of 166 Patients

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ABSTRACT Objective: Report the successful use of stellate ganglion blocks (SGBs) in 166 active duty service members with multiple combat deployments experiencing anxiety symptoms associated with post-traumatic stress disorder (PTSD). Background: Successful treatment of PTSD symptoms with SGB has been reported previously. This is the largest published case series evaluating SGB with a minimum of 3 months follow-up. Methods: Following clinical interview including administration of the PTSD Checklist (PCL), 166 service members with symptoms of PTSD elected to receive a SGB. All patients received a SGB on the right side at the level of the sixth cervical vertebrae (C6). The PCL was administered the day before treatment to establish a baseline, repeated 1 week later, and then monthly out to 3 months. A positive response was considered to be an improvement in the PCL score by 10 or greater points. Follow-up PCL scores from 3 to 6 months were obtained and analyzed for 166 patients. Results: In a military population with multiple combat deployments, over 70% of the patients treated had a clinically significant improvement in their PCL score which persisted beyond 3 to 6 months postprocedure. Conclusion: Selective blockade of the right cervical sympathetic chain at the C6 level is a safe and minimally invasive procedure that may provide durable relief from anxiety symptoms associated with PTSD.

INTRODUCTION

Background

Post-traumatic stress disorder (PTSD) is defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) as a pathologic trauma and stressor disorder that occurs in some individuals following exposure to severe trauma. Symptom clusters include intrusion, avoidance, negative alterations in cognitions and mood, and alterations in arousal and reactivity.[1] Prominent symptoms of PTSD include numbness, avoidance, hyperarousal, difficulty with sleep, irritability, and concentration resulting in clinically significant distress or functional impairment.

Continuous combat operations in the last decade in support of the Global War on Terror in Iraq and Afghanistan have contributed to the steady rise in the prevalence of PTSD among military personnel. In a 2008 Department of Defense survey, the rate of service members requiring an evaluation for PTSD was 13% for those returning from combat versus 8% for those who were not deployed.[2]

Despite the growing numbers of affected individuals, PTSD symptoms remain difficult to treat with current conventional methods. Health care providers have relied on pharmacologic modalities alone or in combination with psychotherapy to treat PTSD.[3] WHO recommendations to date include the use of cognitive behavioral therapy, eye movement desensitization and reprocessing, and stress management.[4] The VA mandates that each service member being treated for PTSD have access to either prolonged exposure therapy or cognitive processing therapy.[5] Presently, first-line pharmacotherapy for PTSD consists mostly of the use of selective serotonin reuptake inhibitors, which take 4 to 8 weeks to work, have a discontinuation rate of almost 50%, and are only effective in about half of all patients.[6,7] Other pharmacological interventions include topiramate and venlafazine, but the effectiveness varies.[7,8] Prazosin has been used to manage nightmares.[9] Interestingly, antidepressants are not recommended as a first line intervention by the WHO.[4]

The accessibility and effectiveness of traditional treatments is an area of concern. Veterans and active duty service members with combat exposure have a 30% success rate for all PTSD therapies according to recent comprehensive reviews on this topic.[10,11] Also, in 2011, Hoge[12] reported current strategies effectively treat less than 25% of PTSD patients.

One major limitation of the available PTSD literature, however, is generalizability, as presentations of PTSD are typically polysymptomatic and stem from a variety of inciting traumatic experiences.[13] Treatment options such as prolonged exposure and cognitive processing are centered on exposure and cognitive restructuring. However, less attention has been placed on the psychophysiological system.[14,15] Persistent hyperarousal symptoms have been linked to high sympathetic activity in patients with PTSD.[16] Efforts to treat PTSD symptoms must include the consideration that autonomic dysfunction can

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potentially contribute to the etiology and maintenance of PTSD, and thus may be targeted with therapies for the relief of symptoms.[14] Given the limitations of research to date and the need to address the growing population of service members suffering from symptoms of PTSD, we sought therapeutic options to help close this critical gap.

One technique that has shown promise in multiple published case series is the use of stellate ganglion block (SGB) in the treatment of PTSD.[17–20] SGB has been used in pain medicine for nearly a hundred years. The concept of sympathetic blockade for the treatment of PTSD has been reported previously. In 2003, Telaranta[21] concluded that clipping the sympathetic ganglia at the second thoracic level, via an endoscopic sympathetic block, resulted in a reduction in PTSD-associated anxiety. Lipov first introduced SGB for the treatment of PTSD in 2008. Mulvaney et al,[19] Hickey et al,[18] and Alino et al[20] have demonstrated efficacy in the use of SGB in the treatment of PTSD symptoms in active duty Navy and Army personnel. Because of the initial success in smaller published case series, we used SGB in a group of 166 active duty personnel with symptoms associated with combat-related PTSD. We utilized ultrasound-guided SGB in light of a growing body of evidence showing the safety and efficacy of this imaging modality with SGB.[22–26]

METHODS

Patient Selection

The following data was taken from clinical records during treatment and follow-up of anxiety symptoms associated with PTSD at three military clinics from February 2012 to May 2013. All procedures were done by one of two fellowship trained physicians using the same technique. This project was approved by the Womack Army Medical Center (Fort Bragg, North Carolina) Institutional Review Board.

All patients considered for treatment voluntarily presented to their health care provider. Before presentation, five patients were taking a single psychotropic medicine for their symptoms. Patients were subsequently screened with the PTSD Checklist (PCL) and interviewed by a clinical psychologist or a senior military physician experienced with PTSD diagnosis and treatment. PCL scores over 35 were considered for treatment; however, in some cases service members with marginal PCL scores (30–34) were treated if the clinical psychologist felt that the patient's report of impairment was significantly under-reflected by the PCL score.

Right C6 Cervical Sympathetic Chain Blockade

Detailed informed consent was obtained, which included patient education and treatment options including available standard-of-care treatment. The SGB was performed in a designated procedure suite equipped with advanced cardiac life support equipment and medications. An intravenous access saline lock was placed with a 22 G intravenous catheter in the left antecubital fossa. The patient was positioned in the supine position with the head turned slightly to the left. The skin over the anterior right neck was prepared with an alcohol/chlorohexidine solution and allowed to dry for 1 minute. A small amount of sterile ultrasound gel was applied to the anterior neck at the level of the cricoid membrane. A right-sided SGB was performed utilizing real-time ultrasound guidance. A high frequency broadband linear transducer (GE Logic e with L12 transducer or GE Logic e9 with ML6-15 transducer) was utilized to visualize key anatomic landmarks in the anterior neck to identify the cervical sympathetic chain. The target area was scanned with color Doppler to identify potential anatomic variations in the course of the vertebral artery and other significant vasculature. The patients were not sedated. The skin was anesthetized using a 27 gauge, 30-mm needle with 1 mL of 1% buffered lidocaine. Following this a 22 gauge 100-mm long needle was introduced into the ventral fascia of the longus coli in the area immediately adjacent to the right cervical sympathetic chain at the C6 level.[24–26] After negative aspiration, 6 cc of 0.5% ropivacaine was slowly injected over 2 minutes while closely monitoring the patient. Successful sympathetic blockade was confirmed by the presence of Horner's syndrome.

There were six cases out of 166 SGB that did not result in a Horner's syndrome within 20 minutes on the first attempt. In five cases, the right-sided SGB was repeated 1 hour later using the same technique and a successful Horner's syndrome was achieved. In one case, a successful SGB was not achieved and that patient's data was not included in this analysis.

PCL-MILITARY ASSESSMENT

Baseline

Although other instruments were considered to quantify PTSD symptoms, the PCL-Military (PCL-M) was selected as the sole instrument because it facilitated straightforward follow-up while service members were deployed. Baseline PCL testing was performed in a treatment facility by a clinical psychologist or a physician experienced with PTSD. If the PCL test was over 1 week old, the test was repeated within 1 week of the SGB to establish the baseline PCL score.

Follow-Up

As part of clinical follow-up, repeat PCL scores were obtained in the first week postprocedure, and then at monthly intervals out to 3 to 6 months. If a patient initially had a good response to the SGB (an improvement in their PCL score of 10 or greater), but their symptoms returned after 3 months, they were offered a second SGB. Data collection was constrained by ongoing military deployments and/or patient compliance with planned follow-up. A patient was considered to have complete follow-up if we had 4 PCL scores, (baseline, 1 week, 1 to 2 months, and 3 to 6 months). Among 166 patients treated with SGB, 75 (45.2%) patients had

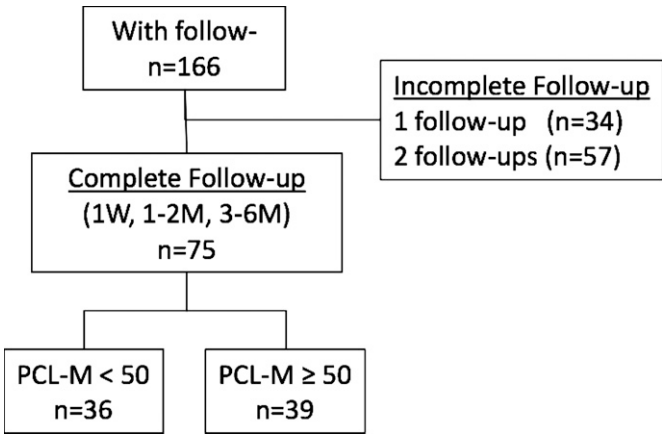


FIGURE 1. Case series population.

complete follow-up. Summary of case series population is summarized in Figure 1.

PSYCHOMETRIC TESTING

The PCL-M is a 17-item self-report one-page questionnaire endorsed by the National Center for PTSD that has been shown to have strong internal consistency, test–retest reliability, and convergent validity with other PTSD measures. The PCL has been validated for screening for PTSD, for diagnosing PTSD, and for determining response to treatment interventions.[11,27–29] For each question, respondents must indicate on a 5-point Likert scale how much they have been affected by each symptom from "Not at all" to "Extremely" and scores range from 17 (no symptoms) to 85 (severe symptoms). Although there is some debate on what exact score constitutes a positive screen, a score of 35 is generally the threshold for screening military populations.[9,27,29] For monitoring patient response, evidence suggests that a 5 to 10 point change in PCL score is not because of chance. A change of 10 to 20 points is considered to be clinically meaningful.[30] For this case series, a patient was deemed a "responder" if they exhibited a PCL score improvement (decrease) of at least 10 points.

DATA ANALYSIS

The purpose of this case series is to describe the effects of SGB on PTSD symptoms assessed by self-reported PCL scores over time. It was hypothesized that patients with higher baseline PCL scores, those more likely to have more severe PTSD symptoms, would experience greater relief of these symptoms from SGB. To address this possibility, patients were initially grouped according to their baseline PCL (≤40, 41–49, and ≥50). These groups were compared using both raw change and relative change from baseline PCL to correct for the greater potential for raw score improvement in those with a higher initial PCL score. After analysis of the three groups, we found there was not a statistically significant difference between the (PCL ≤ 40) and the (PCL 41–49) groups; these groups were subsequently combined. Comparison of the proportion of responders was analyzed using Fischer's exact test to account for low cell count in some categories. Comparison of means was accomplished using one-way analysis of variance and repeated measures analysis of variance was used to assess group differences over time. For repeated measures tests involving three or more levels, sphericity was assessed using Mauchly's test. Greenhouse–Geisser adjustments were made for violations of sphericity. All tests were performed at the 0.05 α level.

CASE SERIES

All patients considered for treatment had multiple combat deployments, and over 80% had experienced close quarters combat in the last 10 years. The average age of this patient population was 37, with an age range of 28 to 49. As high as 100% of the patients served in a combat zone and 89% of these patients were engaged in direct close combat action. Of the patients who served in direct combat operations, 81% served in five or more combat deployments. The majority of these patients reported a history of at least one occurrence of mild to moderate head trauma at some point in their lives. Only two of the self-reported "concussions" occurred within the past 12 months. Two patients reported a history of severe head trauma that resulted in a fractured skull requiring medical attention. Traumatic brain injury or repeated traumatic brain injury can produce some of the same symptoms found in PTSD, to include cognitive deficits, irritability, insomnia, depression, anxiety, and fatigue.[31,32] Over 80% of these patients were regularly exposed to closer range explosions (e.g., grenades, high explosive rounds, demolition charges) during combat operations or military training. Before receiving the SGB, five patients were taking a single psychotropic medicine for their symptoms. During the follow-up period for this review, 12 patients were initiated on selective serotonin reuptake inhibitor therapy and one patient underwent eye movement desensitization and reprocessing. Other than these 18 patients, we initiated no other specific treatments for PTSD. These 18 patients were not excluded from this case series for being already on or being started on pharmacologic therapy or other therapy.

The authors acknowledge this is a relatively large but incomplete data set. We wish to be clear that this case series is from our routine follow-up with our patients, (who are not research subjects, paid or otherwise.) Incomplete follow-up PCL scores were because of patients' military deployments, training requirements, and noncompliance with planned follow-up. To the best of our ability, we have attempted to use this data to accurately portray our clinical experience. It should be noted that over 75% of our patient population continued to deploy to combat zones and were exposed to combat after their initial treatment.

RESULTS

First SGB—Overall (n = 166)

Response

A patient was determined to be a responder if their PCL score improved (decreased) by 10 points or greater. Among patients with 1-week follow-up (n = 126), 78.6% were responders (n = 99) with an average reduction in PCL score of 22.0. Nonresponders (n = 27) had an average reduction of 4.3. Among patients with 1 to 2 month follow-up (n = 115), 81.76% were responders (n = 94) with an average reduction in PCL score of 22.0. Nonresponders (n = 21) had an average reduction of 3.7. Among patients with 3 to 6 month follow-up (n = 132), 73.5% were responders (n = 97) with an average reduction in PCL score of 21.8. Nonresponders (n = 35) had an average reduction of 2.9. Summary of responders and nonresponders among first and second SGB can be found in Table I.

Complete Follow-Up (n = 75)

Of the 166 with at least one follow-up, 75 (45.2%) had complete follow-up (1 week, 1 to 2 months, and 3 to 6 months). Potential differences between patients with complete follow-up and those with incomplete follow-up, which were subsequently excluded from analysis, were investigated. We attempted to answer two main questions: (1) was there a difference between those with complete and incomplete follow-up with respect to baseline PCL-M score and (2) if patients did not respond initially, were they less likely to provide subsequent follow-up PCL scores. There was no significant difference in mean PCL-M scores at baseline between incomplete and complete follow-up groups (47.7 and 50.3, respectively, p = 0.147). We compared the likelihood to have complete follow-up between nonresponders and responders and found no difference (p = 0.081).

In comparing mean change of follow-up PCL scores from baseline among those with baseline PCL scores 50 or greater with those less than 50, it was found that both groups demonstrated a response at all three follow-ups. It should be noted that although the 50 and greater group maintained a relatively consistent mean score at all follow-ups, among the less than 50 group, there was a significant decrease in response from 1 to 2 months and 3 to 6 months. Because this could have been as a result of the fact that those with a higher PCL score numerically have the potential for greater change, we also compared relative change from baseline in both groups and again the data supported the statement that those patients with an initial PCL score of 50 or greater had a higher percent change (improvement) from their baseline score than with an initial score of less than 50. Of the 39 patients with an initial PCL-M score 50 or greater with complete follow-up, the average improvement in the PCL-M score was 25 points out to 3 months. Summary of PCL-M <50 and more than 50 is noted in Figure 2, with the overall mean score over time presented in Figure 3. Raw change from baseline in patients with <50 and more than 50 PCL-M is presented in Figure 4. Relative change from baseline in patients with <50 and more than 50 PCL-M is presented in Figure 5.

Second SGB

Out of our 166 patients, we have partial follow-up data on 24 of those patients that elected to have a second SGB. This additional procedure was treated as a separate event for analysis. Patients were considered for a second SGB if they were a responder to their initial SGB for at least 3 months and then experienced a return of their symptoms associated with PTSD. The trends were similar to the data from the initial SGB, repeated measures ANOVA was not conducted because of the low number of patients with complete follow-up after their second SGB. PCL-M changes relative to SGB #1 and SGB #2 are compared in Figure 6.

DISCUSSION

Adverse Effects

During this case series, the only adverse effects were minor and well-known temporary adverse effects associated with SGB. No patients indicated symptoms of shortness of breath, which could indicate inadvertent block of the phrenic nerve or pneumothorax.

As mentioned in the patient selection section, there were only five patients on psychotropic medications that presented

TABLE I. Responders and Nonresponders Among First and Second SGB

	1st SGB			2nd SGB		
	1 Week	1–2 Months	3–6 Months	1 Week	1–2 Months	3–6 Months
Total *N*	126	115	132	13	17	13
Responders						
n	99	94	97	11	11	10
Percentage	78.6	81.7	73.5	84.6	64.7	76.9
Mean Change	−22.0	−22.7	−21.8	−20.2	−21.4	−16.6
Nonresponders						
n	27	21	35	2	6	3
Percentage	21.4	18.3	26.5	15.4	35.3	23.1
Mean Change	−4.3	−3.7	−2.9	−1.5	−3.2	1.0

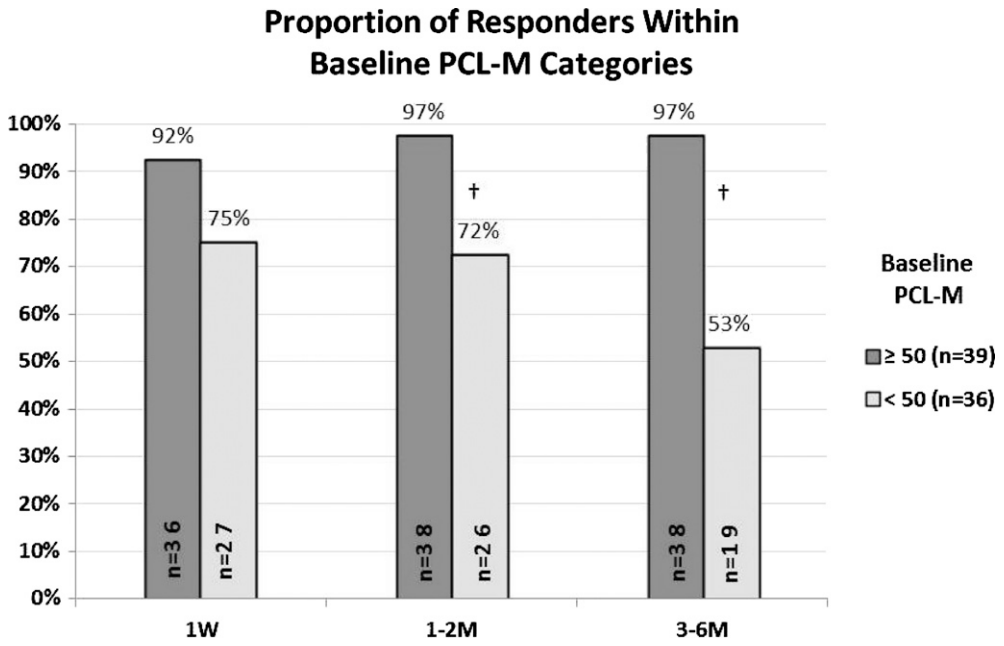


FIGURE 2. Proportion of responders among those with complete follow-up. † Indicates a significant difference in the proportion of responders among the baseline PCL 50 and greater group and less than 50 group ($p < 0.05$). Among patients with complete follow-up ($n = 75$), repeated measures ANOVA was conducted to assess PCL-M scores over time within and between the baseline PCL-M groups (50 and ≥50).

for treatment. We believe there are two reasons for this: (1) in this population, there was a low acceptance of psychotropic medications for fear that these medications would reduce combat performance and (2) most of the patients had been previously screened with the PCL and recorded inappropriately low scores because they did not want to be identified as having PTSD. Only after several patients shared their experiences with SGB did many of our patients rescreen with more accurate scores. These two opinions are based on both repeated specific comments from patients and our

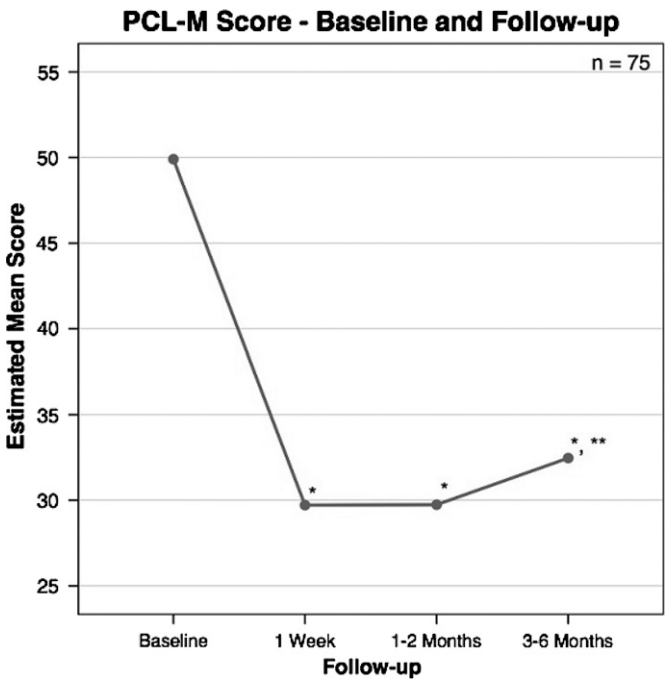


FIGURE 3. Baseline and follow-up PCL-M scores among patients with complete follow-up ($n = 75$). † Indicates a significant decrease in mean PCL-M score from baseline ($p < 0.05$). ‡ Indicates a significant increase in mean PCL-M score from 1 week and 1 to 2 month follow-up ($p < 0.01$).

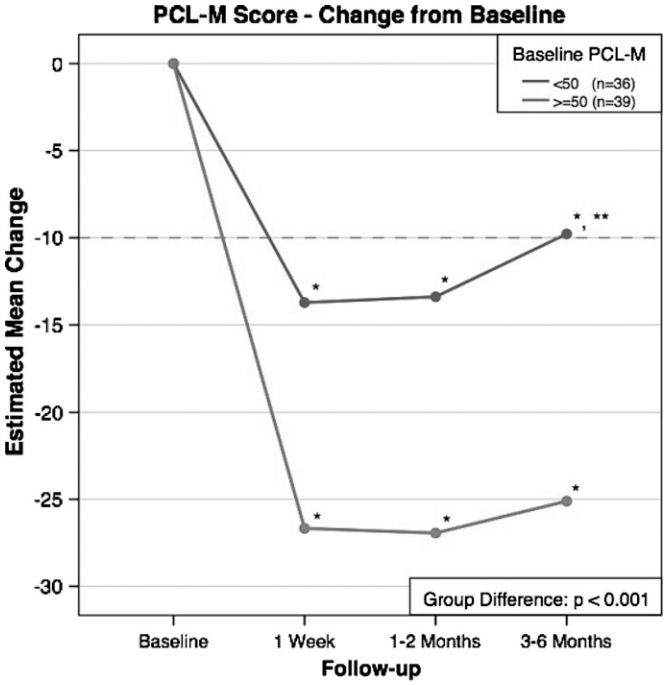


FIGURE 4. Raw change from baseline PCL-M among patients with complete follow-up ($n = 75$). † Indicates a significant decrease in reduction of PCL-M from baseline ($p < 0.001$). ‡ Indicates a significant decrease in reduction of PCL-M score from 1 to 2 months ($p < 0.05$).

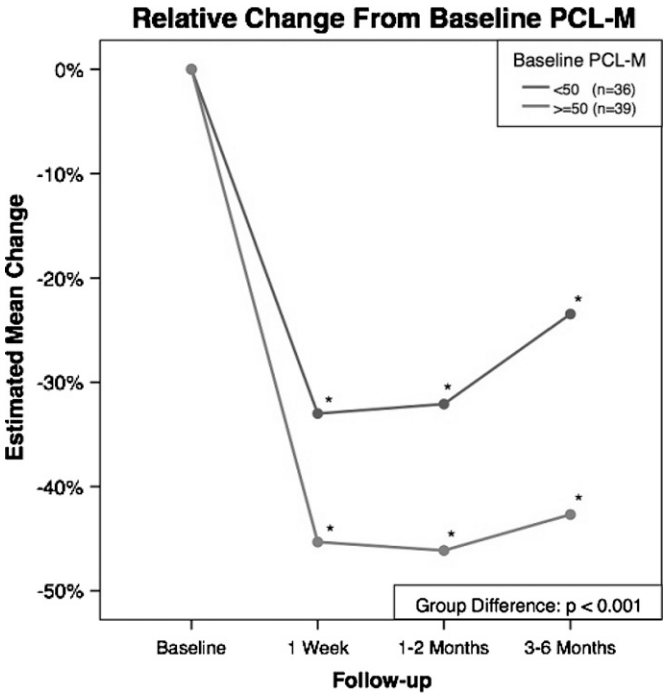


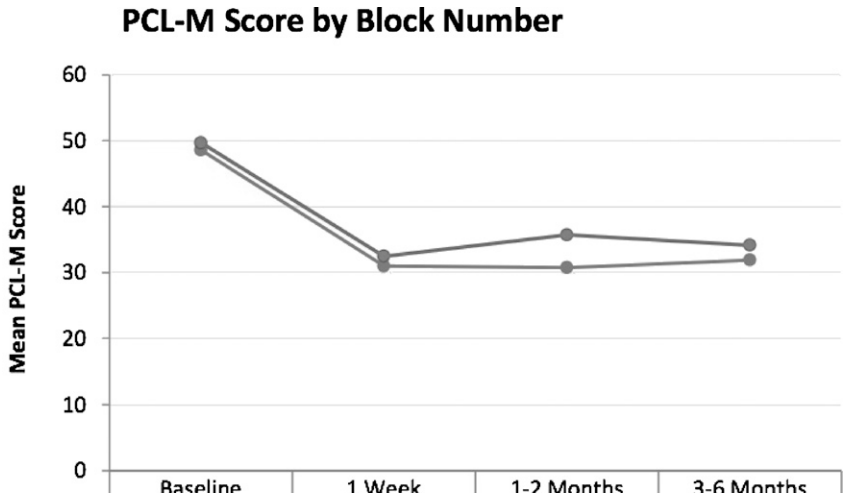
FIGURE 5. Relative change from baseline PCL-M among patients with complete follow-up ($n = 75$). † Indicates a significant decrease in reduction of PCL-M from baseline ($p < 0.001$).

experiences with one specific 31-person cohort. This cohort was a highly cohesive unit. They all had been screened with a recent postcombat deployment PCL with all scores being less than 35 points. As this cohort was preparing to redeploy to combat, a prominent member of the cohort relayed his positive experiences with the SGB, after which 20 members of the cohort rescreened with the PCL and all had scores over 35.

The hypothesis for potential mechanism of action for SGB (or cervical sympathetic chain block) has been described in multiple peer-reviewed publications.[18,19,33] The hypothesis rests on previously demonstrated evidence. The first line of evidence demonstrates a poly-synaptic neurological connection from stellate ganglion to the part of the brain associated with PTSD, mainly the amygdala.[34,35] The second set of reports focuses on nerve growth factor (NGF) increase as a physiological response to acute and chronic stress.[36,37] Brain infusion of NGF in rats leads to norepinephrine (NE) increase.[38] NGF increase leads to retrograde transport from the intracerebral site to the stellate ganglion.[39] Furthermore, a NGF increase in the stellate ganglion leads to neurite outgrowth (sprouting) and new nerve growth at the end terminals.[40] Sprouting is hypothesized to lead to increase in cerebral NE levels, thereby producing anxiety-related PTSD symptoms.[41] Finally, local anesthetic injections are known to suppress NGF leading to dying of new nerve outgrowth and sprouting which is hypothesized to reduce NE levels,[42,43] reversing the cascade of PTSD.[41] The authors emphasize that this proposed mechanism is theoretical; there remains much we do not know about the mechanism by which SGB results in apparent sustained relief of PTSD anxiety symptoms.

Successful Autonomic Dysfunction Modulation

As mentioned previously, the psychophysiological component of PTSD may serve as one valuable target in a multipronged approach to treatment of this complex disorder. SGB may provide lasting symptomatic relief for what has



	Baseline	1 Week	1-2 Months	3-6 Months
1st SGB Mean PCL	48.6	31.0	30.7	31.9
n	166	126	115	132
2nd SGB Mean PCL	49.7	32.5	35.7	34.2
n	24	13	17	13

FIGURE 6. Comparison of PCL-M score changes for 1st and 2nd SGB.

been described as autonomic nervous system dysfunction. This term or "dysfunctional sympathetic tone" describes excess sympathetic nervous system activity (i.e., hyperarousal with impaired relaxation response).[14] This may include those patients who do not meet strict criteria by DSM-V for the diagnosis of PTSD, but who may exhibit many of the same characteristics and physiologic manifestations. Often we saw patients with many of the diagnostic criteria for PTSD, but lacked one or more key features of PTSD, such as having intrusive thoughts or nightmares. Patients with dysfunctional sympathetic tone presents with a constellation of several of the following characteristics that overlap with the symptoms of PTSD: irritability, impaired articulation, concentration, memory, and/or relaxation response; feeling of inappropriate stimulation, problems with either initiating sleep or with staying asleep; and lack of feelings of closeness in relationships. Since this may include a wider population of patients suffering from a similar constellation of symptoms as PTSD, future research into SGB for this indication is warranted.

Limitations

We had incomplete data collection; of the 166 blocks performed, we have complete data on 75 and partial data collection on the remainder. Some patients had only one PCL score for follow-up, and their data were not incorporated into the final set. There was a higher percentage of incomplete data on second blocks. Although the data we do have from 24 patients support the use of a second SGB, we have limited ability to draw stronger conclusions on the potential efficacy of second blocks at this time. Despite the fact that the data we have indicate a positive response to SGB, it can only suggest an apparent trend.

CONCLUSION

Selective blockade of the right cervical sympathetic chain at the C6 level is a safe and minimally invasive procedure that may provide at least 3 months of relief from symptoms associated with combat-related PTSD. Patients with a PCL score 50 or over had a greater response to SGB than patients with a PCL score under 50, although both groups had clinically and statistically significant improvements. If the clinical improvements of a SGB lessen over time, our findings support that a second SGB appears to be as effective as the first SGB. This application of SGB to treat anxiety symptoms associated with PTSD warrants further study with a large-scale randomized clinical trial.

The authors emphasize, based on our experience in addition to the available evidence, that SGB is not a potential "cure" for PTSD. Furthermore, we the authors do not endorse SGB as a sole treatment for symptoms associated with PTSD. However, based on this large case series, SGB does have the potential to significantly reduce symptoms as part of a treatment plan for combat-related PTSD.

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