Effect of Stellate Ganglion Block on Specific Symptom Clusters for Treatment of Post-Traumatic Stress Disorder

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ABSTRACT This study assessed which symptoms are most impacted following stellate ganglion block (SGB) used to treat post-traumatic stress disorder (PTSD) symptoms. 30 active military service members with combat-related PTSD self-referred to their physician and psychologist. Patients were offered a SGB as part of their treatment program. Primary outcome was the magnitude of change for the 17 items on the PTSD Checklist-Military (PCL-M), which was administered the week before SGB, 1 week after SGB, and 2 to 4 months later. Mean PCL-M score decreased from 49 at baseline to 32, 1 week after the procedure ($p < 0.001$). 2 to 4 months after SGB, patients maintained an average PCL-M of 32. Patients reported greatest improvement in the first week after SGB for the following symptoms: irritability or angry outbursts, difficulty concentrating, and sleep disturbance. 2 to 4 months later, patients reported greatest improvement in the following: feeling distant or cut off, feeling emotionally numb, irritability or angry outbursts, and difficulty concentrating. SGB is a safe procedure that may provide extended relief for all clusters of PTSD symptoms. As a result of the significant reduction in hyperarousal and avoidance symptoms observed, this study supports incorporation of SGB into PTSD treatment plans.

INTRODUCTION

Post-traumatic stress disorder (PTSD), a condition characterized by symptoms originating from a traumatic event or series of events, impedes the function of afflicted individuals with particular impact upon relationships. The hallmark symptoms of PTSD are re-experiencing of the traumatic events, avoidance of reminders, negative alteration in cognitions and mood, and hyperarousal following the exposure to trauma. PTSD has a 12-month prevalence among U.S. adults of 3.5%.[1] Among high-risk groups such as combat-deployed military service members, sexual assault victims, and survivors of motor vehicle accidents, the positive screen rates for PTSD ranges between 5 and 13%.[2–4] Given the condition's prevalence and its impact on quality of life, it is critical to identify and promote effective treatments.

Evidence-based treatments for combat-related PTSD, however, are relatively few in number and provide incomplete symptomatic relief.[5,6] Exposure-based psychotherapies, considered the gold standard treatments for PTSD, are notable for dropout rates as high as one-third.[7] Pharmacotherapy has proven to be insufficient, with less robust results and varying effect sizes.[5] A recent systematic review cites that although selective serotonin reuptake inhibitors are superior to placebo in the treatment of PTSD, the effect size is small.[6] Furthermore, long-term treatment is often required to maintain gains made through treatment with selective serotonin reuptake inhibitors.[8] Given these limitations, there is a pressing need to explore additional treatment options.

Stellate ganglion block (SGB) offers a novel approach for relief of PTSD symptoms, and may serve to augment existing treatments. This outpatient procedure utilizes local anesthetic to block the cervical sympathetic chain. Successful treatment of anxiety symptoms associated with PTSD using SGB has been reported in the peer-reviewed medical literature since 2008.[9] Since that time numerous cases series—with an aggregate sample of over 200 patients—have been published demonstrating the benefits of SGB in treating symptoms associated with PTSD.[9–17] In a series of 166 combat veterans, over 70% of patients treated with SGB had a clinically significant improvement which persisted beyond 3 months.[14] Pooled data from other smaller studies reveal a similar success rate. In a recent review of published cases of SGB for PTSD, Navaie et al reported that 75% of patients had a 30% decline in PTSD symptoms after a SGB. No complications associated with the SGB procedure were reported in any of the cases compiled in this review.[15] Likely unique among therapies for PTSD, there is evidence that SGB does not degrade neurocognitive performance and potential combat survivability.[17] A research team recently presented findings

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This research is related to data used in a previously published larger case series in *Military Medicine* which examined only total Post-Traumatic Stress Disorder Checklist-Military scores and not individual symptoms scores or clusters. Mulvaney SW, Lynch JH, Hickey M J, Rahman-Rawlins T, Schroeder M, Kane S, Lipov E: Stellate ganglion block used to treat symptoms associated with combat-related post-traumatic stress disorder: a case series of 166 patients. Mil Med 2014; 179: 1133–40.

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from a randomized controlled trial of 42 patients comparing SGB to a sham injection for the treatment of PTSD symptoms.[18] Although this small study showed no statistically significant difference in the improvement of PTSD symptoms for both groups, variations in procedure technique and patient demographics (including subject motivation) may limit the generalizability of the results.[19] Additional larger randomized controlled studies are underway to further elucidate the role of SGB in the treatment of PTSD. For those interested, we refer readers to recently published clinical guidelines intended to assist both clinicians and researchers on how to incorporate SGB into a treatment plan.[20]

Given PTSD's varied and complex presentation, it can be difficult for a provider to employ evidence-based PTSD treatments toward an individual patient.[21] Robust evidence-based treatments focus principally on exposure and cognitive restructuring versus the psychophysiological system.[22,23] Since hyperarousal symptoms are associated with high sympathetic activity in patients with PTSD, some consider addressing the physiologic conditions a critical component in a comprehensive treatment plan for PTSD.[22,24] Symptoms such as irritability, impaired concentration or memory, inability to relax, and sleep disturbances commonly seen in patients with PTSD may serve as barriers to care, especially when patients are asked to face their index traumas in exposure-based psychotherapies. In this regard, autonomic nervous system dysfunction can reinforce PTSD symptoms, and thus should be addressed to relieve symptoms.[22,25] SGB has shown promise as an effective therapy targeting "dysfunctional sympathetic tone," a term describing the excess sympathetic nervous system activity manifesting as hyperarousal with impaired relaxation response.[14]

METHODS

Participants

This study examined clinical end points from a series of patients suffering from PTSD that were treated with SGB in a military clinic from August 2012 until May 2013. We analyzed 1,462 data points from the PTSD Checklist-Military (PCL-M) of 30 patients. These patients were the first 30 consecutive patients from one clinic which was involved in a previously published analysis of 166 patients from multiple clinics.[14] There were 4 patients who did not complete a PCL-M between 2 and 4 months because of loss of follow-up, so the remaining 26 patients' data were used for that analysis.

All patients in this group had multiple combat deployments spanning several years, and a majority experienced close combat, to include receiving and returning direct fire. The patients were male, with an average age of 36 (range 29–45), and actively serving in their unit without any form of limited duty. All patients considered for treatment self-referred to their primary care physician and were screened using the PCL-M. A clinical psychologist and a primary care physician experienced with the diagnosis and treatment of PTSD interviewed each patient, which included a review of combat exposure and assessment for comorbid psychiatric illnesses. Patients whose PCL-M scores exceeded 35 were selected for treatment and inclusion in this analysis. Although there is some debate on what PCL-M score constitutes a positive screen, a score of 35 is generally the threshold for screening military populations.[4,14]

Only 3 patients in this group had any psychotherapeutic treatment before. These 3 patients were receiving pharmacotherapy for their PTSD symptoms and were enrolled in formal psychotherapy. Of the remaining patients, none had previously sought care for their symptoms. On initial screening for SGB, all patients were offered care per the recommended guidelines, and opted for regular follow-up with the embedded unit psychologist after receiving the SGB.[26] None had comorbid psychiatric illnesses. All procedures were performed by a fellowship-trained physician utilizing a standard technique for real-time ultrasound-guided SGB as described below. This project was approved by the Womack Army Medical Center Institutional Review Board.

Exposure: SGB Procedure

A brief description of the procedure follows. For more detailed information including the potential risks, adverse effects, and proposed mechanism of action, we refer readers to several contemporary review articles.[15,19,20] Informed consent was obtained, which included detailed patient education and treatment options including available standard-of-care treatment in accordance with the Veterans Administration/Department of Defense Guidelines.[26] The SGB was performed in a designated procedure suite equipped with advanced cardiac life support equipment and medications. The patients were not sedated. A saline lock was placed and the patient was positioned in a supine position. The skin over the anterior right neck was prepared with an alcohol/chlorhexidine solution. A right-sided SGB at the C6 level was performed utilizing real-time ultrasound guidance. Color Doppler was used to identify key anatomic landmarks in the anterior neck and potential vascular anatomic variations. The skin was anesthetized with 1 mL of 1% lidocaine. A 22-gauge 3.5-inch-long needle was then introduced into the ventral fascia of the longus coli in the area immediately adjacent to the right cervical sympathetic chain at the C6 level. After negative aspiration, 7 mL 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.[20,27–29]

Primary Outcome Measure

PCL-M scores were collected as part of routine clinical practice. PCL-M was administered before the procedure and at 1-week follow-up and subsequent follow-up appointments (which ranged from 2 to 4 months postprocedure). Once identifying information was stripped from the data, analysis included changes to the total PCL-M score, within major

diagnostic criterion clusters, and for each PCL-M question Table I.

Analysis

To determine whether any change in response occurred following SGB, the total PCL-M and criterion (B, C, D) clusters were analyzed using repeated measures analysis of variance. Post hoc tests using the Bonferroni correction were used and sphericity was assessed by Mauchly's test. Appropriate corrections were made when the null hypothesis of sphericity was violated.

Likert items are single statements to which the respondent is asked their level of agreement and responses are ordinal in nature. Because response frequency is more restricted when analyzing individual item responses, and therefore less likely to be an appropriate approximation of an underlying continuous characteristic, nonparametric methods were used. Related-samples Friedman two-way analysis of variance by ranks (a nonparametric analog to repeated measures analysis of variance) was used to determine if responses on individual PCL-M questions differed across the 3 different time points. Wilcoxon pairwise post hoc analysis was conducted following a significant Friedman test. All tests used an a priori α level of 0.05 and appropriate adjustments were made for multiple comparisons.

RESULTS

Overall PTSD Symptom Severity Scores

Consistent with previously published results, the participants' overall level of PTSD symptoms, as measured by the PCL-M total score, improved significantly following SGB. One week after the procedure, the average PCL-M score decreased from a baseline PCL-M mean of 48.69 to 32.15. This 16-point change represents meaningful and significant symptomatic improvement ($p < 0.001$). At the second follow-up (between 2 and 4 months following SGB procedure) the subjects continued to experience improved PTSD symptoms, as evidenced by an average rating of 31.88 (Fig. 1). Although scores significantly improved from baseline, they did not significantly change from one follow-up to the next (mean difference 0.269, Bonferroni adjustment $p = 1.000$).

Scoring of Clustered Criterion Questions

The PCL-M's 17 questions are closely based on *Diagnostic and Statistical Manual for Mental Disorders-IV* (*DSM-IV*) PTSD diagnostic criteria.[30] As each question represents a symptom within a criteria cluster, averaging responses within each of the criterion clusters provides an effective heuristic for measuring overall symptomatology within a diagnostic cluster.

Figure 1 displays the mean score of each diagnostic criterion at baseline, and for subsequent encounters. As displayed in Figure 1, at baseline, patients were most distressed by Criterion D symptoms (hyperarousal). Criterion C's (persistent avoidance of stimuli associated with the traumatizing event and generalized numbing of responsiveness) baseline scores were higher than those of Criterion B (re-experiencing the trauma).

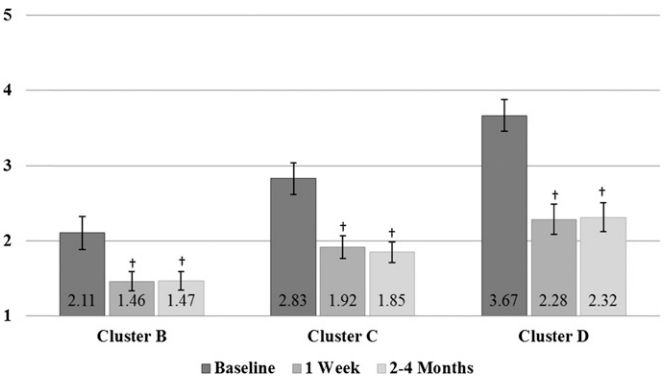

FIGURE 1. Mean cluster response with 95% CI. Response axis corresponds to agreement on PCL-M cluster questions; 1 = "Not at all," 2 = "A little bit," 3 = "Moderately," 4 = "Quite a bit," 5 = "Extremely."

Following SGB, all 3 mean Criterion scores improved by the first week's follow-up. Criterion D's baseline mean score improved from 3.67 to 2.29 ($p < 0.001$). Criterion C's mean baseline rating fell from 2.83 to 1.92 ($p < 0.001$). Finally, for Criterion B the mean baseline score 2.11 improved to 1.46 ($p < 0.001$).

At the second follow-up appointment (2–4 months following SGB administration), our patient pool continued to experience significant relief within each of the diagnostic criteria in comparison to baseline ratings. Ratings did not change significantly following the first follow-up. As depicted in Figure 1, Criterion B mean score increased slightly from 1.46 to 1.467 (mean difference 0.008, $p = 1.00$). The Criterion D mean score increased from 2.29 to 2.32 (mean difference 0.031, $p = 1.00$). Criterion C's mean response decreased from 1.92 to 1.85 (mean difference 0.066, $p = 1.000$).

Individual Symptoms

Figure 2 displays the distribution of patient responses (ranging from "not at all to" to "extremely") across each of the PCL-M's 17 questions. As each question is linked to a specified *DSM-IV* PTSD symptom, this graph effectively conveys the degree of distress for each symptom at baseline and across each follow-up encounter. To analyze the ordinal data from the PCL-M questions and test for significant change at the item level, a related-samples Friedman's two-way analysis of variance by ranks test was conducted with subsequent pairwise Wilcoxon tests.

Table II displays results from the Friedman test, identifying the median rating and mean rank for each item at baseline and follow-up appointments. Each of the PTSD symptom-derived questions, with the exception of Question 7 ("Avoiding activities or situations because they reminded you of a stressful

TABLE I. PTSD Checklist—Military Version

Patient's Name: _____

Instruction to Patient: Below is a list of problems and complaints that veterans sometimes have in response to stressful life experiences. Please read each one carefully, and put an "X" in the box to indicate how much you have been bothered by that problem *in the last month*

No.	Response	Not at All (1)	A Little Bit (2)	Moderately (3)	Quite a Bit (4)	Extremely (5)
1.	Repeated, disturbing *memories, thoughts, or images* of a stressful military experience from the past?					
2.	Repeated, disturbing *dreams* of a stressful military experience from the past?					
3.	Suddenly *acting* or *feeling* as if a stressful military experience *were happening* again (as if you were reliving it)?					
4.	Feeling *very upset* when *something reminded* you of a stressful military experience from the past?					
5.	Having *physical reactions* (e.g., heart pounding, trouble breathing, or sweating) when *something reminded* you of a stressful military experience from the past?					
6.	Avoid *thinking about* or *talking about* a stressful military experience from the past or avoid *having feelings* related to it?					
7.	Avoid *activities* or *situations* because they *remind you* of a stressful military experience from the past?					
8.	Trouble *remembering important parts* of a stressful military experience from the past?					
9.	Loss of *interest in things that you used to enjoy?*					
10.	Feeling *distant* or *cut* off from other people?					
11.	Feeling *emotionally numb* or being unable to have loving feelings for those close to you?					
12.	Feeling as if your *future* will somehow be *cut short*?					
13.	Trouble *falling* or *staying asleep*?					
14.	Feeling *irritable* or having *angry outbursts*?					
15.	Having *difficulty concentrating*?					
16.	Being *super alert* or watchful on guard?					
17.	Feeling *jumpy* or easily startled?					

PCL-M for *DSM-IV* (11/1/94) Weathers, Litz, Huska, & Keane National Center for PTSD–Behavioral Science Division.

military experience") significantly improved in the week following SGB administration.

Figure 3 ranks each of the PCL-M items according to greatest improvement from baseline to 1 week (mean rank difference). PCL-M questions 14, 15, 13, 10, 11, and 9 constituted the top third of the PCL-M's 17 items as ranked by mean rank difference. Similarly, questions 8, 5, 4, 3, 12, and 7 changed the least, with question 7 being the only one which did not significantly improve following SGB. At the second follow-up appointment (2–4 months after the procedure) significant gains persisted in each of the symptoms, with little change from 1-week follow-up.

DISCUSSION

The American Psychiatric Association published its revised diagnostic criteria for PTSD in the *DSM-5* in May 2013.[1] Following the publication of the *DSM-5*, the National Center for PTSD released the PTSD Checklist-5, to reflect *DSM-5* criteria. As the data for this study were collected before the PTSD Checklist-5's publication, it used the older PTSD diagnostic criteria. Despite this limitation, the present study found that patients experienced significant improvement in 16 of the 17 *DSM-IV* PTSD symptoms within a week of treatment, which was maintained at their second follow-up appointment (2–4 months later).

It is important to note that the sample was comprised of fit, male active duty military participants, suffering from combat-related PTSD, and not seeking any form of disability. Because of their mission, they also had a much higher level of health and fitness than most active military members, which may explain the lack of psychiatric comorbidities. Further study might clarify if females, or patients with non-combat PTSD, might respond differently to SGB. As the current study's design did not incorporate a control group, the possibility that symptoms would have improved without treatment cannot be ruled out. Randomized controlled trials are required to fully elucidate the benefit SGB may have over sham or treatment as usual, as well as to examine the role of many modifying variables (e.g., age, gender, and duration of symptoms).[31–33]

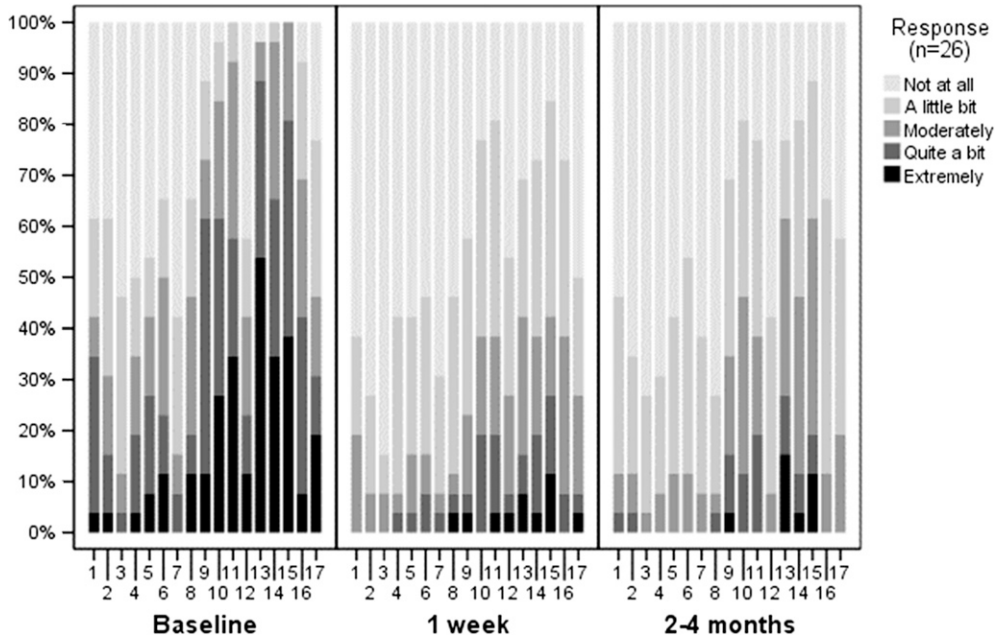

FIGURE 2. Response frequency for individual PCL-M questions (1–17) at baseline (pre-SGB), 1 week post-SGB, and 2 to 4 months post-SGB. Indicates symptomatic shift over time.

The original intent of the study was to determine which PTSD clusters and symptoms were most impacted by a SGB. The findings that all of the clusters were positively impacted following SGB, and that 16 of 17 PTSD symptoms improved significantly, was an unexpected positive finding. The magnitude of improvement in overall symptom scores and duration of effect were largely consistent with previously published studies on this topic.[9–17] At the individual symptom level, mean rank analysis would suggest the symptoms of irritability, difficulty concentrating, trouble sleeping, feeling cut off from others, emotional numbness, and anhedonia were most positively impacted. These questions, which demonstrated the

TABLE II. PCL-M Item Scores and Clusters Over Time

	Median (Mean Rank)							
Cluster and Item	Baseline (1)	1 Week (2)	2–4 Months (3)	χ^2	*df*	*n*	Asymptotic Significance	Wilcoxon Post Hoc
B								
1	2 (2.52)	1 (1.69)	1 (1.79)	22.120	2	26	0.000	2, 3 < 1
2	2 (2.56)	1 (1.69)	1 (1.75)	25.320	2	26	0.000	2, 3 < 1
3	1 (2.27)	1 (1.81)	1 (1.92)	7.610	2	26	0.022	2, 3 < 1
4	1.5 (2.37)	1 (1.90)	1 (1.73)	11.412	2	26	0.003	2, 3 < 1
5	2 (2.38)	1 (1.85)	1 (1.77)	11.259	2	26	0.004	2, 3 < 1
C								
6	2.5 (2.50)	1 (1.77)	2 (1.73)	18.815	2	26	0.000	2, 3 < 1
7	1 (2.12)	1 (1.90)	1 (1.98)	1.409	2	26	0.494	1 = 2 = 3
8	2 (2.48)	1 (1.90)	1 (1.62)	17.500	2	26	0.000	2, 3 < 1
9	4 (2.69)	2 (1.56)	2 (1.75)	25.564	2	26	0.000	2, 3 < 1
10	4 (2.81)	2 (1.60)	2 (1.60)	32.268	2	26	0.000	2, 3 < 1
11	4 (2.77)	2 (1.63)	2 (1.60)	30.795	2	26	0.000	2, 3 < 1
12	2 (2.35)	2 (2.00)	1 (1.65)	12.462	2	26	0.002	2, 3 < 1
D								
13	5 (2.77)	2 (1.50)	3 (1.73)	30.519	2	26	0.000	2, 3 < 1
14	4 (2.83)	2 (1.50)	2 (1.67)	32.345	2	26	0.000	2, 3 < 1
15	4 (2.83)	2 (1.50)	3 (1.67)	33.904	2	26	0.000	2, 3 < 1
16	3 (2.62)	2 (1.87)	2 (1.52)	27.387	2	26	0.000	2, 3 < 1
17	2 (2.46)	1.5 (1.75)	2 (1.79)	12.551	2	26	0.002	2, 3 < 1

Related-samples Friedman two-way analysis of variance by ranks. All pairwise post hoc comparisons with baseline were significant at $p < 0.001$, with the exception of item 7.

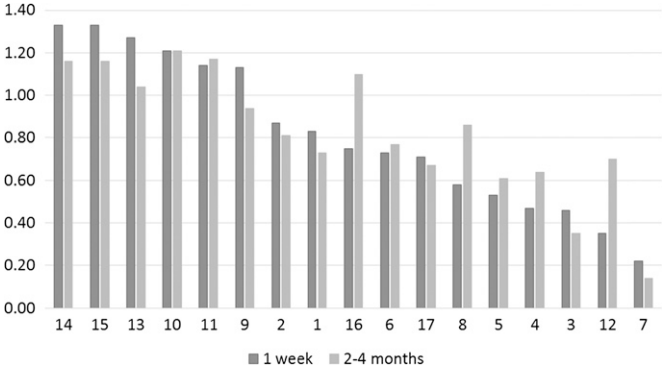

FIGURE 3. Magnitude of Change per PCL-M item number compared to baseline.

most improvement, were derived from symptoms within Criterion D (Increased Arousal) and Criterion C (Avoidance and Numbing), potentially suggesting items from Criterion B (Re-experiencing) may not respond as favorably as the other criterion symptoms. Importantly, these individual cluster effects are consistent with those reported in an earlier pilot study of SGB for PTSD.[34]

As exposure-based therapies lose as much as one-third of those who initiate treatment, SGB may improve retention and increase participation in exposure-based therapies. Another area deserving further exploration is to determine whether SGB can facilitate or potentiate gains made in exposure-based therapies. To be clear, combination of SGB and other mainstays of current PTSD treatment have yet to be fully studied, but certainly provide directions for future exploration.

CONCLUSION

In this sample of 30 patients, PTSD symptomatology improved significantly following SGB. This was evidenced by positive impacts in overall symptoms, in each of the diagnostic clusters, and for 16 of the 17 symptom-based questions of the PCL-M. Mean-rank analysis indicates that within these positive findings, hyperarousal and avoidance clusters improved to the greatest degree. This may be the result of improvement in one key symptom or symptoms, such as sleep improvement, positively impacting other symptoms, or it may be a function of an overall reduction in (chronic and dysfunctional) sympathetic tone. The authors recognize SGB is not a "cure" for PTSD, and do not endorse SGB as a sole treatment for symptoms associated with PTSD. However, on the basis of existing data including the present case series, SGB demonstrates potential to reduce symptoms as part of a treatment plan for combat-related PTSD.

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