REVIEW ARTICLE

Stellate Ganglion Block in the Treatment of Post-traumatic Stress Disorder: A Review of Historical and Recent Literature

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■ **Abstract:** Concerns over the rising prevalence of post-traumatic stress disorder (PTSD), particularly among military service members returning from combat, and over barriers that hinder individuals from seeking out or adhering to standard therapies have contributed to interest in alternative therapies for the disorder. A novel alternative therapy for PTSD—stellate ganglion block (SGB)—may be considered lacking in formal evidence of efficacy despite having shown considerable promise. This review of the recent and historical literature related to SGB finds evidence of substantial beneficial psychiatric effects and substantiates that this fast-acting, somatic treatment may provide positive results for patients with PTSD and may reduce barriers to therapy, particularly among military populations. ■

Key Words: post-traumatic stress, anxiety, stellate ganglion block, military, veterans, review

INTRODUCTION

Post-traumatic stress disorder (PTSD)—characterized by the experience of a life-threatening trauma resulting in symptoms such as hyperarousal, hypervigilance, re-experiencing, and avoidance[1]—has caused increasing concern as a public health problem. The disorder is highly prevalent among military service members returning from combat. Studies of service members returning from Iraq and Afghanistan have estimated PTSD prevalence ranging between 4.7% and 21.8%.[2–4] Historically, studies among service members returning since the Vietnam War have estimated PTSD prevalence ranging between 2% and 17%.[5] When compared against the current approximate 6% to 8% lifetime population prevalence of PTSD, and against that in earlier eras,[6,7] the prevalence of the disorder among military populations today is alarmingly high. Estimates of PTSD prevalence among military populations may even be underestimated due to the stigma surrounding the disorder.[8]

The current standard of care for PTSD in both civilian and military populations involves pharmacological therapies, psychotherapies such as cognitive processing therapy (CPT) and prolonged exposure (PE), or a combination of both.[9] Many pharmacological therapies are considered evidence-based; however, studies of their effectiveness suggest mixed results at best, and adverse effects associated with the use of pharmaceuticals such as monoamine oxidase inhibitors and selective serotonin reuptake inhibitors (SSRIs) in the treatment of PTSD may serve as barriers to treatment.[10] Studies of the use of CPT or PE in the treatment of PTSD among service members show dropout rates between 3% and

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50%.[11,12] The long duration of time required to obtain beneficial results from psychotherapy and the stigma that surrounds mental health care in general are also major barriers that hinder treatment-seeking behavior, especially among military populations.[8,13,14]

Due to barriers associated with current treatment options, various alternative therapies have been evaluated as treatment options for PTSD. Many of these therapies, considered outside the conventional standard of care, are often used as adjuncts in treatment. They include mindfulness techniques, yoga, virtual reality, dietary supplements, as well as some invasive procedures such as acupuncture.[15] Many of these have been attempted for use among military personnel and veterans,[16,17] with variable success.

Another invasive procedure, stellate ganglion block (SGB)—which has been used successfully for a variety of complex neurological disorders such as chronic regional pain syndrome and hot flashes[18,19]—has also recently shown promising results for the relief of certain symptoms of PTSD, particularly among military populations. This procedure involves the injection of a local anesthetic, typically under ultrasound or fluoroscopic guidance, into a nerve bundle called the stellate ganglion located between the C6 and C7 vertebrae.[20,21]

Interest in this procedure has increased considerably over the past decade as it is reported to offer rapid relief. Due to the somatic nature of the technique, this procedure may also be perceived as less stigmatizing than conventional therapies, particularly among military populations. However, despite the high level of interest and promise demonstrated by recent peer-reviewed research and publications, SGB may still be considered lacking in formal evidence of a quality on par with that of conventional therapies to support further widespread utilization of the technique in the treatment of PTSD.

The purpose of this systematic review was to build upon existing studies of the literature surrounding SGB as a treatment option for PTSD by considering evidence from new case series and recent reports discussing the first randomized controlled trial (RCT) of the procedure. Additionally, this review seeks to better contextualize the use of this novel technique in the treatment of PTSD through a review of the historical literature of the effects of SGB on psychiatric symptoms.

METHODS

The Published International Literature On Traumatic Stress (PILOTS), PubMed, and the PsycINFO databases were searched using the concepts "stellate ganglion block," "post-traumatic stress disorder," and "mental illness." The abstract of each matching publication was reviewed, or when an abstract was not available, the complete publication was retrieved and reviewed. Publications excluded from further review were those written in languages other than English, duplicate publications, and publications that were found irrelevant because they contained neither direct nor indirect discussion of the effects of SGB on psychiatric symptoms.

An extensive secondary literature search was employed to identify additional relevant historical literature and nonindexed publications. The publications were then categorized by type (case reports and case series; systematic case reviews; publications related to RCTs; and all other publications including nonsystematic reviews and opinions, guidelines, commentaries, correspondence, books, and book chapters), and key findings and results from the literature were described and summarized chronologically.

RESULTS

The database search identified 78 publications, of which 53 were subsequently excluded. The secondary literature search identified an additional 7 publications resulting in 32 publications included in the review. These comprised 15 case reports and case series,[12,20,22–34] 1 systematic case review,[35] 2 publications related to a single published RCT,[36,37] and 14 nonsystematic reviews, opinions, guidelines, commentaries, books, and book chapters.[21,38–50] The systematic search results are shown in Figure 1. One case report which included an analysis described as a systematic review was considered a case report for these purposes.[32] Arranged chronologically as shown in Figure 2, the search identified publications dating from 1947 to 2016. Described chronologically according to historical time period, the key findings from these publications are summarized below.

1940s to 1950s

The systematic search identified 4 relevant publications dating from the period 1947 to 1955. During this period, cervical sympathectomy and SGB were thought to produce beneficial effects in the treatment of a wide range of neurological and neurovascular conditions, including epilepsy, migraines, cerebral hemorrhage, embolisms, and thrombosis, and the procedures were widely used for these indications.

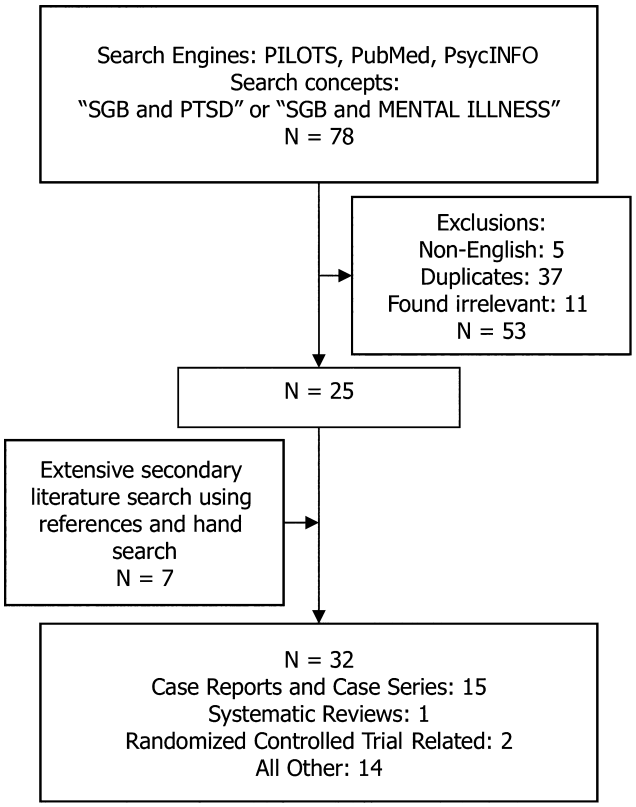

Figure 1. Systematic literature search results.

It was in the treatment of these disorders that psychiatric effects of SGB were first reported by Karnoush and Gardner in 1947.[22] In describing a large series of patients treated with SGB for neurological indications, Karnosh and Gardner[22] noted their surprise that the procedure was found to produce alterations in mood, including occasionally a feeling of euphoria, particularly in patients with "a definite pre-existing mental depression." The authors described 3 cases in detail in which the procedure was prospectively performed for psychiatric indications, consisting of 1 case of psychosis and 2 cases of depression, in which each patient experienced euphoria for at least 2 days following the procedure.[22] In a subsequent publication the following year, reviewing their experiences with "[s]omething like five hundred patients,"[23] the authors claimed that patients who reported benefits from an initial SGB, and who subsequently underwent ganglionectomy (a complete removal of the stellate ganglion that permanently mimics the effects of SGB), frequently experienced increased feelings of "self-security and elation," and additional beneficial psychiatric effects including improved sleep quality and reductions in anxiety. The authors noted that patients in whom a heightened mood was experienced were typically those whose "organic defect…was associated with a definite, prolonged anxiety, fear, or an actual pre-existing mental depression."[23] These results were discussed briefly in a 1954 book that described the techniques, indications, and uses for SGB, including in the treatment of psychiatric symptoms of "mental depression."[38]

Haber subsequently noted similar positive results using SGB for treatment of a series of patients suffering from symptoms of "psychoses of late life." As reported, the procedure appeared modestly beneficial in improving mood and affect in patients with earlier stages of dementia and psychosis.[24]

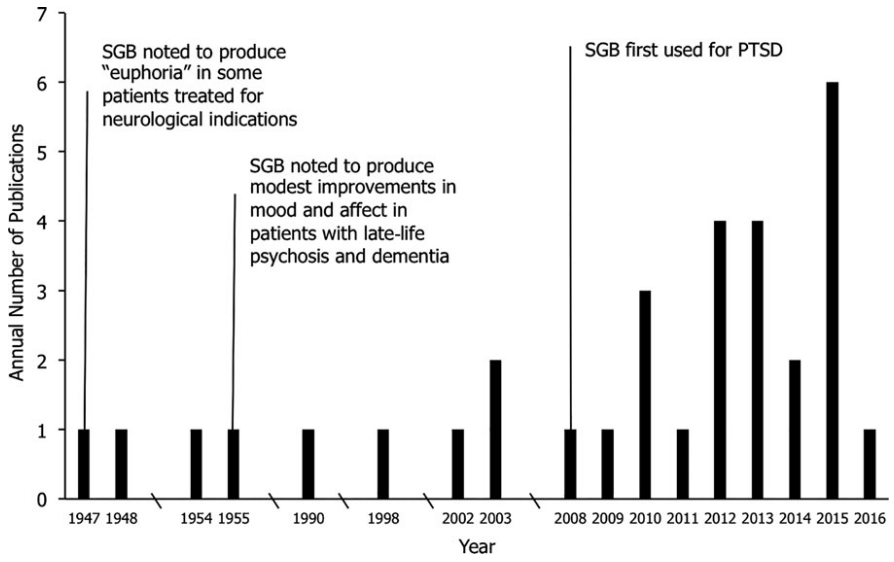

Figure 2. Publications ($N = 32$) related to the psychiatric effects of stellate ganglion block, by year.

1990s to Early 2000s

Following a prolonged absence of relevant publications in the literature from the mid-1950s to 1989, a total of 5 publications were identified dating between 1990 and 2007, beginning with a case report by Lebovitz describing the use of SGB for treatment of pain in a patient suffering physical and psychological distress as the result of gunshot wounds.[25] The patient was diagnosed with upper extremity pain for which she underwent physical therapy and received multiple SGB injections. The SGB was credited in enabling the patient to overcome "initial hesitance in seeing the psychologist" for her concomitant symptoms of PTSD.[25] However, no direct results of SGB on psychiatric symptoms were reported.

In 1998, a technique more invasive yet similar in function to SGB—endoscopic transthoracic sympathectomy (ETS), involving the destruction of the sympathetic trunk in the thoracic region through clamping the T2 to T4 ganglia—was investigated as a treatment for social phobia.[26,39,40] ETS had been used previously to treat "bodily symptoms" of social phobia, and Telaranta and colleagues[26,39,40] postulated that removal of the sympathetic chain would alleviate sympathetic arousal symptoms associated with social phobia and anxiety. Results from studies by Telaranta and colleagues[26,39,40] showed that patients receiving ETS for social phobia had statistically significant reductions in both physical and psychological symptoms.

During this period, a case report was published describing a schizophrenic patient receiving SGB for pain symptoms who also experienced "unexpected beneficial results" of decreased hallucinatory symptoms after the block was performed.[27]

2008 to 2016

The systematic search identified 23 relevant publications from 2008 through 2016, all associated with the use of SGB in treating symptoms of PTSD. The first report of SGB being used as a therapy specifically for PTSD symptoms was published in 2008 by Lipov and colleagues. A 48-year-old victim of armed robbery suffered from PTSD and was unresponsive to pharmacological treatment and psychotherapies. After receiving a right-sided SGB, the patient's feeling of anxiety disappeared and the patient's symptoms remained in remission for 32 days. Ultimately, the patient received an additional treatment—pulsed radiofrequency—targeted at the stellate ganglion, and a second SGB. The patient experienced marked improvements that remained evident 3 months postprocedures.[20,28] Lipov had previously used SGB in his practice to treat hot flashes of menopause, and, building on theories of Karnoush, Telaranta, and others, hypothesized that "neurological connections from the sympathetic ganglion to the brain structures" not only exist but also are activated in disorders such as PTSD, hot flashes, and chronic pain.[41] Lipov et al.[41] further postulated that this activation leads to a change in nerve growth factor levels with the subsequent increase in norepinephrine levels leading to pathologic states and that SGB might thus be able to alleviate symptoms of combat-related PTSD.[42]

These developments prompted Mulvaney et al.[29] to perform SGB treatment for 2 cases of PTSD in military veterans. Each patient showed promising results. Despite some disagreement in the literature related to the postulated beneficial neurophysiological mechanism of the procedure,[43] in 2012 and 2013, 3 case series[12,30,31] and a case report[32] totaling 22 patients—many of which were current or former military service members—added further evidence to the literature of clinical efficacy of SGB for treatment of PTSD, including occasionally marked reductions in standard PTSD symptom scores.[12] Multiple supporting publications authored by a core group of investigators during the period expanded on the proposed beneficial mechanism,[44–46] and additional reviews added to the evidence of beneficial results from the use of SGB for treatment of PTSD.[21,32] In 2014, Navaie et al.[35] published the first formal systematic review of previous case reports and case series, providing a synthesis of existing clinical experience to date.

Following publication of the review by Navaie and colleagues, the largest case series to date was published by Mulvaney et al.,[33] examining active-duty military patients. This study reported patient follow-up on a cohort of 166 patients for a period up to 6 months and found that administration of a second SGB could improve efficacy.[33]

In 2015, proposed clinical guidelines and additional reports on safety and patient acceptability added to the literature on the use of SGB as a PTSD treatment.[47,48] These reports considered the safety of the procedure and its improvement under ultrasound guidance. These reports also addressed theoretical considerations for how medicalization of the disorder through its treatment with SGB might increase patient acceptance, specifically among military populations.[47,48] A further case series in 2015 among military service members

diagnosed with PTSD evaluated effects of SGB on measures of neurocognitive performance, including memory and reaction time, and found no impairment in these functional categories with treatment. The authors concluded these findings constituted a potential advantage of SGB, particularly for military service members who might return to combat.[34] Bringing further synthesis to the expanding literature base, Lipov and Ritchie[49] published a new review, and Lipov published an extensive book chapter discussing the potential for SGB to serve as an alternative treatment option for combat-related PTSD.[50]

Also in 2015, results of the first RCT, conducted among military service members, of SGB as a potential treatment option for PTSD were presented as a poster at a major conference (McLay et al., "A Randomized, Double-Blind, Placebo-Controlled Trial of Stellate Ganglion Block in the Treatment of Post-Traumatic Stress Disorder," Poster 126, presented the 31st annual meeting of the American Academy of Pain Medicine, March 19, 2015). As described in a subsequent 2016 publication,[36] this small trial randomized 42 subjects: 27 to receive SGB and 15 to receive a sham procedure. Although PTSD symptoms improved significantly in both groups after treatment, there was no statistically significant difference in improvement detectable between groups.[36] The methodology of this study had been previously critiqued in a commentary anticipating its publication.[37]

DISCUSSION

Historically, SGB has been successfully used to treat a variety of physiological disorders as well as the psychological symptoms that accompany them. For example, when used in the treatment of hot flashes, SGB has demonstrated a trend toward reductions in accompanying depressive symptoms.[19] However, over the past 7 decades, case reports have also provided convincing evidence that SGB may have a beneficial effect in primary psychiatric disorders as well.

This procedure—although invasive—has proven to have an acceptable level of safety,[51] particularly when aided through the use of ultrasound or fluoroscopic guidance, which further decreases any risk of complication or adverse effects.[48,52–54] If proven satisfactorily effective for PTSD, particularly in select populations, SGB would provide a safe, fast-acting, and less stigmatizing option for treating this debilitating disorder.

The physiological mechanism or mechanisms responsible for the observed psychiatric benefits of SGB for PTSD have not been confirmed, although previously proposed mechanisms have been built upon to inform current plausible hypotheses.[44–46]

Despite biological plausibility and a large and growing body of anecdotal efficacy and safety data from clinical experience with the procedure, a remaining challenge to gaining acceptance for the use of SGB for PTSD has been the absence of formal evidence of its efficacy through RCTs. The first RCT examining the use of SGB failed to identify statistically significant differences in outcomes between the placebo and the SGB treatment arms,[36] but these negative results should be interpreted with caution. The use of a small sample of subjects who may have been influenced by secondary gains, the use of an inappropriate placebo, and a randomization ratio that overweighted the placebo group have all been reasonably suggested as some of the possible reasons for a lack of positive results in this small trial.[37]

Particularly important in this regard are differences in patient selection between this RCT and previous case series and reports. In the RCT, many of the subjects with PTSD were transitioning out of military service and undergoing medical board review to determine the extent of their disability and their subsequent level of monetary compensation for PTSD symptoms.[36,37] It appears highly plausible that subjects in such a setting might be inclined to underreport any beneficial effects from treatment out of concern that documented improvements during the study might reduce monetary compensation for their disability. In contrast to this military population in which secondary gain was a reasonable consideration, the much larger populations of military personnel and veterans studied by other investigators comprise a diverse patient base, including currently serving active-duty military—a sizeable proportion of whom continued to deploy following treatment.[33]

A second multicenter RCT, which begins data collection in 2016 and is being conducted by Olmsted and colleagues, aims to address some of these previous methodological concerns using a sham injection placed 1 to 2 cm away from the location of the stellate ganglion in order to minimize the potential for a physiological placebo effect from the sham injection. This multicenter RCT will also enroll a larger and more diverse subject base by recruiting from multiple locations and settings. To address concerns of potential underreporting, service members undergoing medical board review will be specifically excluded (Rae Olmsted, personal communication, 2016).

Through accumulated experience with the procedure, side effects from SGB have been identified, safe and therapeutic anesthetic dosages have been determined, and clinical guidelines have been developed that enable SGB—as a potential therapeutic modality for PTSD—to be considered comparable to a pharmaceutical which has successfully completed Phase I and Phase II trials. With hundreds of patients having thus far received SGB for PTSD, the procedure may be considered to have an evidence base of efficacy for this indication comparable to that of SSRIs when these were first being investigated and employed off-label as treatment for the disorder,[55] particularly among military personnel and veterans in the decade prior to the start of the major wars in Afghanistan and Iraq.[56,57] Subsequent blinded RCTs of SSRIs, which cumulatively enrolled first hundreds,[58,59] and then thousands of patients,[60,61] only some years later provided the modest but sufficient evidence of efficacy to warrant first, a formal indication of these drugs for PTSD, and then their broader acceptance as a standard of care for the disorder.

In the opinion of the authors, the quantity and quality of evidence for the use of SGB for PTSD is approximately on par with the evidence base for use of SSRIs at the time of their initial use for the disorder. Similarly, the evidence for use of SGB for PTSD is of comparable quality and quantity to that used to justify the procedure for most other indications. According to a reasonable interpretation of standard criteria for quality of clinical evidence, SGB for PTSD-related anxiety may be considered level 2C,[47] and for most existing indications such as upper limb pain may be considered level 1C.[62]

While SGB may not ultimately prove to be a viable stand-alone treatment for PTSD, if combined with techniques such as CBT or pharmacological therapies, SGB may, at the least, provide initial reductions in the PTSD symptoms that often inhibit treatment success. Regardless, the procedure deserves proper investigation into its possible utility and should be considered a high-priority area for further research. The present evidence base for SGB for this indication not only provides tantalizing suggestions of potential utility, but is also insufficient to rule out potentially clinically significant efficacy.

CONCLUSION

The possibility of a fast-acting, medically based treatment for PTSD is of potentially great significance for those suffering from the disorder, including those who have failed conventional therapies. The rapid response and destigmatization the procedure offers may enable this technique to be beneficial for particularly difficult-to-treat patient populations, including military service members and veterans. Further well-designed and adequately powered research is needed to conclusively address questions of efficacy, to identify which patient groups may receive the most benefit from this treatment, and to establish the likely neurophysiological mechanism underlying its purported beneficial effects.

DISCLOSURES

Dr. Nevin has served as consultant and expert witness in legal cases involving claims of antimalarial drug toxicity.

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