Curr Psychiatry Rep (2015) 17: 63
DOI 10.1007/s11920-015-0599-4

A Review of the Use of Stellate Ganglion Block in the Treatment of PTSD

Eugene Lipov[1] · **Elspeth Cameron Ritchie**[2]

Published online: 16 June 2015

Abstract Current treatments for PTSD are often not effective or acceptable to the patient. There are a number of emerging new treatments. One promising new one is stellate ganglion block, an anesthetic treatment for pain which relieves symptoms of severe and chronic PTSD in some patients. The focus of this chapter is to summarize clinical evidence available for the effectiveness of cervical sympathetic ganglion injection called stellate ganglion block (SGB), as well as demonstrate possible clinical applications of its use. Cervical sympathetic blockade involves injecting a local anesthetic next to a group of nerves (ganglion) in the neck. The technique has been used clinically since 1925 with very few side effects. Finally, the neurobiology of SGB is discussed. Challenges to the use of SGB include the lack of randomized clinical trials and practitioners familiar with the use of SGB for PTSD.

Keywords Post-traumatic stress disorder · PTSD · Stellate ganglion block · SGB · Anxiety · Cervical sympathetic chain · Autonomic dysfunction

This article is part of the Topical Collection on *Military Mental Health*

✉ Elspeth Cameron Ritchie
elspethcameronritchie@gmail.com

Eugene Lipov
elipovmd@aol.com

[1] Advanced Pain Centers, 2260 W Higgins Rd Ste 101, Hoffman Estates, IL 60169, USA

[2] Clinical Professor of Psychiatry, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bethesda, MD 20814, USA

Introduction

Post-traumatic stress disorder (PTSD) is a chronic anxiety disorder caused by seeing or experiencing traumatic events. The symptoms of PTSD lead to clinically significant distress, functional impairment, and potentially, to suicide. Recent wars have led to a large number of military personal having multiple and severe symptoms of psychological distress. While advances have been made in understanding and treating this syndrome, barriers to care continue to exist, especially the stigma attached to having a mental health issue and the difficulty finding a treatment regimen that works and is acceptable to the patient.

PTSD is the chronic or pathological hyperarousal that is brought on by witnessing or experiencing severe trauma. In 1980, the American Psychiatric Association (APA) added PTSD to the third edition of its Diagnostic and Statistical Manual of Mental Disorders (DSM-III) [1]. However, multiple terms describing what is currently known as PTSD preceded its use. The first modern description of PTSD emerged during the US Civil War. Dr. Mendez DaCosta described war veterans as having irritable heart or "soldiers' heart" [1]. In his 1876 research paper, Dr. DaCosta described startle responses, hypervigilance, and heart arrhythmias.

The wisdom of this report is a biological description of the nervous system overactivity. If PTSD can be recognized as a biological trauma, it may respond to an approach that reverses or treats biological alteration of the nervous system. The sympathetic nervous system seems to play a dominant role in the development and maintenance of PTSD.

The focus of this chapter is to summarize clinical evidence available for the effectiveness of cervical sympathetic ganglion injection, called stellate ganglion block (SGB), as well as demonstrate possible clinical applications of its use.

PTSD Overview

The incidence of military-related PTSD is on the rise, partly due to increased awareness and better detection. The biggest driver, however, is the continued large-scale military mobilizations in response to the sociopolitical violence of the past decade, epitomized by the wars in Afghanistan and Iraq. The prevalence and profound impact on quality of life urgently demands effective PTSD treatments [2].

Although PTSD is the most commonly diagnosed service-related mental disorder among US military personnel returning from Iraq and Afghanistan, an expert panel convened by the Institute of Medicine found little evidence for the efficacy of most currently employed PTSD treatment modalities [3]. As noted by Dr. Hoge in a JAMA 2011 editorial, current therapeutics have limited effect. He stated that veterans remain reluctant to seek care, with half of those in need not utilizing mental health services. Among veterans who begin PTSD treatment with psychotherapy or medication, there is a high percentage drop out which is commonly 20–40 % in randomized clinical trials (RCTs). "With only 50 % of veterans seeking care and a 40 % recovery rate, current strategies will effectively reach no more than 20 % of all veterans needing PTSD treatment" [4••].

The remainder of this chapter will focus on a relatively new treatment to the field of psychiatry, SGB. Essentially, SGB is an injection of a local anesthetic in the cervical spine that modulates the sympathetic nervous system. The block has a marked impact in some patients on PTSD symptoms. The impact is apparent in 30 min following the procedure and may be long lasting.

The military has been a leader in the use of SGB, especially at Walter Reed National Military Medical Center and Balboa Naval Medical Center in San Diego. With a few exceptions, it is not readily available for treatment of PTSD in the civilian world, and is not covered by insurance.

In evaluating SGB, as well as other methods, as a viable treatment option of PTSD, it is important to recall Dr. Hoge's statement, "Interventions that will have the greatest potential for improving care on a population level are those focused on enhancing the reach of treatment (e.g. engagement, adherence and acceptability" [4••].

Overview of the Sympathetic Nervous System as Related to PTSD

The focus of this section is on the manipulation of the sympathetic nervous system, which the authors believe is one of the new frontiers for treating PTSD. The sympathetic nervous system (SNS) is part of the autonomic nervous system. Its main role is to mobilize the body's resources under stress and to induce the fight-or-flight response. It is also constantly active at a basal level in order to maintain homeostasis.

In large part, the activation of the SNS is accomplished by the increase of catecholamines, mainly epinephrine and norepinephrine. The role of norepinephrine in the brain is that of a neurotransmitter leading to arousal, selective attention, and vigilance which has been demonstrated in preclinical studies [5]. Specifically, elevated urinary norepinephrine has been identified among patients with PTSD [6]. Similarly, norepinephrine concentrations in cerebrospinal fluid (CSF) are significantly higher in subjects with PTSD than among healthy controls and have been correlated with the severity of PTSD symptoms [7]. Such notable increases in noradrenergic activity among subjects with PTSD suggest that reducing CNS noradrenergic activity could be effective, especially for arousal symptoms such as nightmares and startle reactions [8].

SGB, a Cervical Sympathetic Injection

The SGB is an anesthetic injection in a group of nerves in the neck that are called the stellate ganglion. The procedure has been used to treat chronic pain since 1925 and recent studies have demonstrated great promise as a successful intervention for PTSD.

The first author reported the first successful treatment of PTSD through the use of SGB in 2008 [9]. The subject of that report was a civilian robbery victim who presented for SGB treatment due to severe anxiety related to PTSD, 2 months post being robbed at gunpoint. The patient experienced excellent response to SGB and reported significant resolution of hypervigilance and anxiety.

Proposed Mechanisms for the Clinical Effect of SGB

The hypothesis for potential mechanism of action for SGB (or cervical sympathetic chain blockade) as modulating sympathetic nervous system activity has been described in multiple peer-reviewed publications [10•, 11, 12••, 13•, 14, 15]. The hypothesis rests on previously demonstrated evidence and was originally proposed by the first author.

The first line of evidence in supporting this theory demonstrates a polysynaptic neurological connection from the stellate ganglion to the part of the brain associated with PTSD, the amygdala [16] (Fig. 1). Specifically, Dr. Liberzon demonstrated increased activation of the amygdala in PTSD patients when compared to controls [17].

The second line of evidence relies on the nerve growth factor (NGF) increase, observed as a physiological response to acute and chronic stress [18, 19]. NGF increase is known to increase perivascular norepinephrine (NE). This has been demonstrated by direct intracerebroventricular brain infusion

of NGF into adult rats [20]. Stress-induced release of NE in amygdala and related structures has been shown to facilitate a number of anxiety-like behavioral responses that are mediated in these regions [21].

Norepinephrine increase has been shown to be associated with PTSD in urine [6] and cerebrospinal fluid [7] as discussed previously. The NE increase is likely due to NGF increase in the stellate ganglion which in turn is caused by retrograde NGF transport from the intracerebral site to the stellate ganglion [22]. NGF increase is also known to promote neurite outgrowth (sprouting) at the end terminals [23]. The neurite outgrowth has been associated with NE increase [24]. Finally, local anesthetic injections are known to suppress NGF [25], leading to dying of new nerve outgrowth since maintenance of sprouting is dependent on the presence of NGF [26]. As a result, it is hypothesized that the suppression of NGF would reduce NE levels and reverse the cascade of PTSD [14, 15].

The third and final line of evidence in support of the theory is based on EEG evaluation of rats following SGB. Dr. Jeong found that SGB with bupivacaine resulted in significantly decreased EEG activities in rats. These results suggest that SGB can induce a sedative effect in rats. The proposed mechanism of the effect described above was reduction in brain norepinephrine [27•]. Similar results have been observed in a human model, where SGB with lidocaine resulted in significantly decreased EEG activities. The EEG activity, as measured by bispectral index (BIS), significantly decreased in the SGB group when compared to the values in sham group after the intervention ($P<0.05$) [28].

Method: Right-Sided C6 Cervical Sympathetic Chain Blockade

Once written consent is administered, a right-sided SGB is performed. An intravenous line is started with a 22G IV in the right hand. The patient is positioned comfortably in the supine position, prepped and draped in the sterile fashion. After radiographic confirmation of the right C6 vertebral body, the skin is anesthetized with 1 cc of 2 % lidocaine. Using an anterior paratracheal approach, a 22-gauge Quincke needle is passed under fluoroscopic guidance until it contacts the anterior lateral aspect of the C6 vertebral body, and then, it is pulled back 1 mm. Appropriate needle position is then confirmed by the injection of 2 cc of iohexol (180 mg/mL) radiopaque dye and fluoroscopy was used to monitor its spread. After negative aspiration, 7 cc of 0.5 % bupivacaine is injected slowly in order to produce a sympathetic ganglion block.

The patient is observed for facial anhidrosis (inability to sweat normally) and Horner's syndrome (i.e., enophthalmos-posterior displacement of the eye), ptosis (drooping of the upper eyelid), and miosis (constriction of the pupil). Horner's syndrome is considered demonstrative of a successful sympathetic block of the cervical sympathetic chain.

Potential Complications of SGB

Stellate ganglion blockades carry a very small risk of infection. Using prophylactic antibiotics can reduce the slight risk of infection. Although rare, severe complications following SGB do include bleeding, seizures, pneumothorax, and spinal cord trauma. A study of the incidence of severe complications was last undertaken in 1992 by German researchers Wulf and Maier, with a reported 1.7 complications per 1000 blockades based on surveys completed by patients receiving a combined total of 45,000 blocks. No fatalities or persistent complications were reported [29]. This survey was conducted prior to the use of fluoroscopic guidance where the stellate ganglion blocks were performed at the C7 level rather than C6. The current improvements in guidance technology and changing the needle location to C6 are likely to reduce the chance of complications.

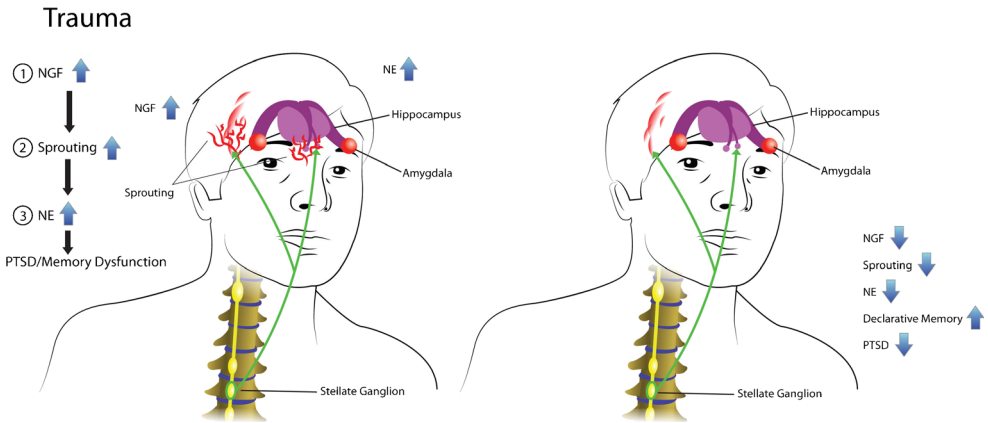

Fig. 1 Polysynaptic neurological connection from the stellate ganglion to the amygdala

Current Evidence on SGB and the Treatment of PTSD

Stellate ganglion block has been used to treat PTSD since 2008. Dr. Navaie summarized available literature published between 2008 and 2013 on the use of SGB to treat PTSD [30••]. These were primarily case reports. In her review, all patients received more than 1 year of psychotherapy and pharmacotherapy before SGB. She indicated that patients were predominantly male (n=21, 88 %) and active duty military (n=14, 58 %) or veterans (n=8, 33 %) with combat-related PTSD. The average age was 40.5 years. Seventeen patients (71 %) received one SGB, and seven (29 %) received multiple SGBs. Clinically, meaningful improvements were observed in 75 % (n=18) of patients after SGB, with significant differences in mean PTSD scores, pre- and post-treatment [30••].

In the clinical case reports reviewed above, two have specific merit. Dr. Alino reported on a patient with a 2-year history of suicidal ideation had become free of suicidal thought 2 days after SGB [10•]. Dr. Mulvaney reported on two patients with severe PTSD who were able to completely stop taking psychiatric medications after SGB [11].

Recently, further validation of SGB efficacy has been published. Dr. Mulvaney in a recent publication [12••] summarized the available data. He observed that 166 service members with symptoms of PTSD that received SGB had clinically significant reductions in PCL scores. Specifically, 70 % of those treated with SGB reported significant reductions in PCL scores and the effects were sustained 3 to 6 months post-procedure [12••]. It is important to note again that the patients were active duty service members who had extensive combat exposure.

Further validation of SGB efficacy in 2014 came from Dr. Alkire. He presented an abstract titled: "Prolonged Relief of Chronic Extreme PTSD and Depression Symptoms in Veterans Following a Stellate Ganglion Block." In this report, Dr. Alkire selected the most extreme PTSD cases in the veteran population and observed that SGB was greatly effective in helping 75 % (9/12) of the subjects [13•].

It is important to note that there are not yet published randomized control trials (RCTs) comparing SGB to placebo or to other treatments. The authors believe that RCTs are an essential next step. Arguing against a placebo effect has been the rapid remission in severe chronic PTSD discussed in the case reports.

In addition, we do not know which patients are most likely to benefit. As mentioned above much of the patient population treated have been military or veterans. However, the first author has treated many civilians with positive results. A vast majority of patients treated with SGB were receiving other treatments for PTSD such as psychotherapy and pharmaceutical interventions. The efficacy of those interventions, especially psychotherapy, seems to be significantly increased by utilization of sympathetic blockade. The exact role of SGB in the spectrum of PTSD treatments is yet to be determined; however, it seems clear at this time that it is not meant as a stand alone therapy and is usually used as a fast-acting adjuvant for other therapies, by reducing sympathetic system activation.

Challenges

There are several major challenges for the psychiatrist who is interested in offering SGB to their patients. The first challenge, as discussed above, is that there have not yet been randomized controlled studies which demonstrate efficacy, although the authors and others have been advocating for these trials.

Another major challenge is that we do not yet know which patients will benefit. The treatment has been used on relatively health service members and on veterans and civilians with severe and chronic PTSD. In a related vein, we do not know who will require more than one treatment and at what frequency.

Finally, the availability of SGB for the treatment of PTSD is very limited. It is offered on some military bases, especially Walter Reed National Military Medical Center and Balboa Naval Hospital in San Diego. The first author performs the procedure in private practice in his clinic in Chicago. Most patients pay for the procedure out of pocket as it is not yet covered by most insurance plans as a treatment for PTSD.

These challenges make it imperative that larger and randomized controlled trials be done in multiple medical centers. In our opinion, the Veteran's Health Administration would be an ideal setting to perform that urgently needed research.

Conclusion

Using the sympathetic system modulation as a new target for the treatment of psychiatric symptoms seems to have promise in the battle to resolve PTSD scourge. Although initially it seems difficult to believe that an injection in the neck may lead to such a pronounced psychiatric effect, if one considers the sympathetic activation in PTSD, this effect becomes increasingly more plausible.

At the time of writing this article, over 650 military personnel have been treated with SGB for PTSD in four military hospitals, with an over 70 % success rate. The advantages of the SGB as a PTSD therapy lie in the fact that it offers virtually immediate relief, increases compliance with the therapy, consistently maintains a high efficacy rate, reduces the use of psychiatric medications, and significantly improves the psychotherapy efficacy. As such, this innovation may not only improve the quality of life for millions of patients but also

reduce the overall socioeconomic burden of treating PTSD on the health care system. If SGB indeed lives up to its early potential, and is validated by formal studies, it may have substantial short-term and long-term benefits by alleviating suffering and hardships for PTSD patients and their loved ones.

Compliance with Ethics Guidelines

Conflict of Interest Eugene Lipov and Elspeth Cameron Ritchie declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Da Costa JM. On irritable heart; a clinical study of a form of functional cardiac disorder and its consequences. Am J Med Sci. 1871;121(1):2–52.
2. Gore AT, Richards-Reid GM. Posttraumatic stress disorder. Updated December 18, 2006. eMedicine [serial online]. Available at: http://www.emedicine.com/med/topic1900.htm. Accessed 21 Oct 2007.
3. Institute of Medicine. Treatment of posttraumatic stress disorder: an assessment of the evidence. Washington, DC: The National Academies Press; 2007.
4.•• Hoge CW. Interventions for war-related posttraumatic stress disorder: meeting veterans where they are. JAMA. 2011;306:549–51. **Dr Hoge is a military psychiatrist who is highly respected in the community and is able to give an over view of the treatment difficulty involved on military PTSD**.
5. Southwick SM, Bremner JD, Rasmusson A, et al. Role of norepinephrine in the pathophysiology and treatment of posttraumatic stress disorder. Biol Psychiatry. 1999;46:1192–204.
6. Mason JW, Giller EL, Kosten TR, et al. Elevation of urinary norepinephrine/cortisol ratio in posttraumatic stress disorder. J Nerv Ment Dis. 1988;176:498–502.
7. Geracioti TD, Baker DG, Ekhator NN, et al. CSF norepinephrine concentrations in posttraumatic stress disorder. Am J Psychiatry. 2001;158:1227–30.
8. Taylor FB, Lowe K, Thompson C, et al. Daytime prazosin reduces psychological distress to trauma specific civilian trauma post traumatic stress disorder. Biol Psychiatry. 2006;59:577–81.
9. Lipov EG, Joshi JR, Lipov SG, Sanders SE, Siroko MK. Cervical sympathetic blockade in a patient with posttraumatic stress disorder: a case report. Ann Clin Psychiatry. 2008;20:227–8.
10.• Alino J, Kosatka D, McLean B, et al. Efficacy of stellate ganglion block in the treatment of anxiety symptoms from combat-related post- traumatic stress disorder: a case series. Mil Med. 2013;178:473–7. **This is a paper on a small number of patients, n=4, however this is the first report of SGB effecting suicidal ideation**.
11. Mulvaney SW, McLean B, De Leeuw J. The use of stellate ganglion block in the treatment of panic/anxiety symptoms with combat-related post-traumatic stress disorder; preliminary results of long-term follow-up: a case series. Pain Pract. 2010;10:349–65.
12.•• Mulvaney SW, Lynch JH, Hickey MJ, et al. 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(10):1133–40. **This is the largest publication so far on the use of SGB in military PTSD**.
13.• Alkire M T, Hollifield M, Khoshsar R, et al. Prolonged relief of chronic extreme PTSD and depression symptoms in veterans following a stellate ganglion block. Presented at American Society of Anesthesiology, October 11, 2014. **This publication summarizes the results of a first prospective study in VA, as well as the most severe PTSD patients in the same VA.**
14. Lipov EG, Joshi JR, et al. A unifying theory linking the prolonged efficacy of the stellate ganglion block for the treatment of chronic regional pain syndrome (CRPS), hot flashes, and posttraumatic stress disorder (PTSD). Med Hypotheses. 2009;72(6):657–61.
15. Hickey AH, Hanling S, Pevney E, et al. Stellate ganglion block for PTSD. Am J Psychiatry. 2012;169:760.
16. Westerhaus MJ, Loewy AD. Central representation of the sympathetic nervous system in the cerebral cortex. Brain Res. 2001;903:117–27.
17. Liberzon I, Martis B. Neuroimaging studies of emotional responses in PTSD. Ann N Y Acad Sci. 2006;1071:87–109.
18. Alleva E, Petruzzi S, Cirulli F, et al. NGF regulatory role in stress and coping of rodents and humans. Pharmacol Biochem Behav. 1996;54:65–72.
19. Smith MA. Hippocampal vulnerability to stress and aging: possible role of neurotrophic factors. Behav Brain Res. 1996;78:25–36.
20. Isaacson LG, Billieu SC. Increased perivascular norepinephrine following intracerebroventricular infusion of NGF into adult rats. Exp Neurol. 1996;139(1):54–60.
21. Morilak DA, Barrera G, Echevarria DJ, et al. Role of brain norepinephrine in the behavioral response to stress. Prog Neuro-Psychopharmacol Biol Psychiatry. 2005;29(8):1214–24.
22. Johnson Jr EM, Taniuchi M, Clark HB, et al. Demonstration of the retrograde transport of nerve growth factor receptor in the peripheral and central nervous system. J Neurosci. 1987;7:923–5.
23. Chen PS, Chen LS, Cao JM, Sharifi B, Karagueuzian HS, Fishbein MC. Sympathetic nerve sprouting, electrical remodeling and the mechanisms of sudden cardiac death. Cardiovasc Res. 2001;50(2):409–16.
24. Madison R, Davis JN. Sprouting of noradrenergic fibers in hippocampus after medial septal lesions: contributions of the central and peripheral nervous systems. Exp Neurol. 1983;80(1):167–77.
25. Takatori T, Kuroda Y, Hirose M. Local anesthetics suppress nerve growth factor-mediated neurite outgrowth by inhibition of tyrosine kinase activity of TrkA. Anesth Analg. 2006;102:462–7.
26. Gatzinsky KP, Thrasivoulou C, Campioni-Noack M, Underwood C, Cowen T. The role of NGF uptake in selective vulnerability to cell death in ageing sympathetic neurons. Eur J Neurosci. 2004;20(11):2848–56.
27.• Jeong S, Jeon Y, Yeo J, Baek W. The effects of stellate ganglion block on the electroencephalogram in rats. J Anesth. 2014;28(4):601–5. **These results indicate that SGB may have a sedative effect in rats**.
28. Yeo J, Jeon Y. Effects of stellate ganglion block on sedation as assessed by bispectral index in normal healthy volunteers. Pain Physician. 2015;18:173–8.
29. Wulf H, Maier CH. Complications of stellate ganglion blockade: results of a survey. Anaesthetist. 1992;41:146–51.
30.•• Navaie M, Keefe MS, Hickey AH, et al. Use of stellate ganglion block for refractory post-traumatic stress disorder: a review of published cases. J Anesth Clin Res. 2014;5(403):2. **This is a critical paper summarizing evidence so far as reported up until August 2014**.