Key Words: post-traumatic stress disorder, PTSD, stellate ganglion block, chronic pain, anxiety

# Stellate Ganglion Blocks for Post-Traumatic Stress Disorder: A Review of Mechanisms, Efficacy, and Complications

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ABSTRACT ~ Post-traumatic stress disorder (PTSD) stands as a pervasive psychiatric condition, exerting a profound impact on millions across the globe. Despite the availability of traditional therapeutic modalities, many individuals continue to grapple with suboptimal treatment outcomes, underscoring the urgent need for novel interventions. In recent years, stellate ganglion blocks (SGBs) have garnered attention as a promising avenue in the treatment landscape for PTSD, showcasing remarkable efficacy in ameliorating symptomatology and enhancing overall quality of life. This comprehensive review seeks to delve into the current landscape of research surrounding SGBs for PTSD, including proposed mechanisms of action, clinical efficacy across diverse patient populations, safety profile, and potential avenues for further exploration and refinement. By synthesizing the latest evidence and insights, this review aims to provide clinicians and researchers with a comprehensive understanding of the role of SGBs in PTSD management, ultimately informing clinical practice and guiding future research endeavors in this area of mental health intervention. Psychopharmacology Bulletin. 2024;54(4):106–118.

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#### INTRODUCTION

Post-traumatic stress disorder (PTSD) is a multifaceted and profoundly debilitating psychiatric condition that can arise in individuals who have been exposed to or have directly experienced traumatic events. Its impact extends across a broad spectrum of psychological and physiological realms, encompassing intrusive memories that disrupt daily life, distressing flashbacks that transport individuals back to traumatic moments, hypervigilance that keeps affected individualson edge, avoidance behaviors aimed at sidestepping triggers, and notable alterations in mood and cognitive functioning. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), PTSD affects approximately 3.5% of adults in the United States alone, indicative of its significant public health burden.<sup>1</sup> This prevalence not only underscores the scale of individuals grappling with PTSD but also emphasizes the pressing need for effective interventions tailored to address its complex and pervasive effects on individuals' lives.

However, despite the growing recognition and understanding of PTSD, the journey towards finding effective treatments remains fraught with challenges. Conventional therapeutic approaches, including cognitivebehavioral therapy (CBT) and pharmacotherapy utilizing selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs), often fall short in adequately addressing the multifaceted needs of individuals afflicted by this condition. A notable subset of PTSD patients find themselves trapped in a cycle where remission remains elusive, and even those who experience some symptom relief may only achieve partial alleviation of their distress despite undergoing standard therapeutic regimens.<sup>2</sup> Moreover, the utilization of pharmacological agents introduces the risk of adverse systemic effects, which may exacerbate the already complex landscape of PTSD treatment by fostering medication noncompliance and diminishing treatment adherence.

Given the inherent limitations of established therapeutic paradigms, there has been a surge of interest in exploring alternative and adjunctive interventions for PTSD. Among these emerging modalities, stellate ganglion blocks (SGBs) have captured the attention of researchers and clinicians with their potential efficacy in mitigating PTSD-related symptomatology.

SGBs represent a minimally invasive intervention targeting the sympathetic nervous system, whose dysregulation is widely implicated in the pathophysiology of PTSD.<sup>3</sup> By modulating sympathetic activity, SGBs hold considerable promise as a novel therapeutic avenue capable of furnishing substantial relief to individuals grappling with the

burdens of PTSD, all while mitigating the reliance on traditional oral pharmacotherapy. Thus, the exploration of SGBs stands poised at the forefront of innovation in PTSD treatment, offering renewed hope for patients and clinicians navigating the complexities of this pervasive psychiatric disorder.

This review will discuss the current understanding of the mechanism of action behind SGBs, the clinical efficacy, potential complications, along with future areas for research. Ultimately, further research into the mechanisms underlying SGBs and their potential long-term effects will continue to refine our understanding and application of this promising treatment modality, ultimately paving the way for more effective and personalized interventions for individuals living with PTSD.

#### **STELLATE GANGLION: STRUCTURE AND FUNCTION**

The stellate ganglion, also known as the cervicothoracic ganglion, is a collection of sympathetic nerve cell bodies located in the cervical region and serves as a crucial hub for regulating sympathetic outflow to various organs and tissues, including the heart, lungs, and upper extremities.<sup>4</sup> This bilateral structure measures roughly 2.5 cm long, 1 cm wide, and 0.5 cm thick. It is present in 80% of the population and is formed by the fusion of the inferior cervical and first thoracic sympathetic ganglia.<sup>4,5</sup> The stellate ganglion is located along the anterior surface of the longus colli muscle and lies anterior to the first costal neck and the transverse process of C7.6 At the C6 level, the stellate ganglion is located anterior to the vertebral artery, posteromedial to the common carotid and jugular vein, and posterolateral to the trachea and esophagus. The scalene muscles and brachial plexus are located lateral to the stellate ganglion and spread of the injectate to the brachial plexus can result in a somatic block rather than sympathetic block contributing to a false positive reaction.<sup>5</sup> At the C7 level, the stellate ganglion lies posterior to the vertebral artery and above the dome of the pleura. As such, to reduce the risk of vascular puncture and pneumothorax, a SGB is commonly performed at the C6 transverse process, also known as Chassaignac's tubercle, with caudal spread of the injectate along the prevertebral fascia resulting in anesthetic blockade.<sup>7</sup>

The sympathetic nerve supply to the head and neck region is derived from preganglionic fibers with cell bodies located in the anterolateral column of the upper thoracic spinal segments.<sup>8</sup> The axons exit in the anterior root of the spinal nerve and pass via the rami communicans to the upper cervical sympathetic ganglia. The postganglionic fibers travel along the carotid and vertebral arteries to supply cranial structures or join the C7–TI nerves to supply the upper limb. As the sympathetic

input to the head, neck, upper limbs, and thoracic viscera is relayed through the stellate ganglion, injection of anesthetic near this structure can act on both pre- and post- ganglionic fibers to reversibly block these innervated areas and treat clinical conditions driven by increased sympathetic tone.<sup>9</sup> Clinical blockade of the stellate ganglion has been utilized to relieve sympathetically mediated pain in a variety of clinical conditions such as complex regional pain syndrome (CRPS), postherpetic neuralgia, phantom limb pain, and angina pectoris.<sup>10,11</sup> Reduction of vascular tone, improved vascular supply, and reduced release of vasoconstricting substances following SGB has shown to relieve pain and improve perfusion in vascular insufficiency syndromes of the upper limb.<sup>12</sup> Improved autonomic regulation of the lymphatic vasculature following SGB in patients with breast cancer related lymphedema has also been described.<sup>13</sup> SGBs have also been employed to treat refractory ventricular arrhythmias which are exacerbated by heightened sympathetic tone.<sup>14</sup> Post-menopausal vasomotor symptoms including hot flashes, and night sweats may be alleviated with SGBs via modulation of norepinephrine levels in the central thermoregulatory system.<sup>15</sup>

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#### **ULTRASOUND GUIDED TECHNIQUE**

Previously SGBs were completed by palpating landmarks for ideal needle positioning. However, this blind approach carries a high risk of injury to nearby structures such as the trachea, esophagus, thyroid gland, and carotid artery. The evolution of technique has progressed from a blind approach to fluoroscopy and now to ultrasound guided. Ultrasound is a practical, low cost, time efficient tool that is free from radiation exposure. It allows for visualization of vascular structures and soft tissue structures while also allowing for real time guidance of needle advancement to mitigate risk of injury and improve efficacy. Specifically, in SGBs, ultrasound guidance is useful in identification of the appropriate fascial plane to allow for the solution to caudally spread to the stellate ganglion at the C7-T11 level. The most common techniques are the anterior approach and the transverse approach which are typically performed at the C6 level. The anterior approach is associated with increased risk of esophageal and vascular injury.<sup>16</sup> Furthermore, the anterior technique requires displacement of the carotid artery and thyroid through applied pressure on the probe which can potentially cause vascular or visceral damage. The C6 transverse approach was refined with the goal of placing the needle at C6 beneath the prevertebral fascia over the longus colli muscle.<sup>17</sup> The patient is positioned laying supine with their head rotated to the opposite direction. The transducer is positioned in a short axis view proximal to the clavicle.

It is imperative to identify important structures such as the subclavian artery and supraclavicular plexus. By adjusting the transducer, one can visualize the anterior and middle scalene muscles, and the interscalene plexus between them. The nerve roots can be traced back to their intervertebral foramen. Commonly referred to as the "stoplight sign", the C5, C6, C7 nerve roots can be appreciated by their vertical position.<sup>17</sup> The C7 nerve root can be tracked and seen entering the foramen in front of the posterior tubercle. The transducer is adjusted cephalad and lateral to see the C6 nerve root from the interscalene plexus to the foramen flanked by the prominent anterior tubercle and short posterior tubercle. Next, the needle is used in an in-plane approach from lateral to medial depositing local anesthetic under the prevertebral fascia covering the longus colli muscle. Needle tip placement should be anterolateral to the longus colli muscle and deep to the prevertebral fascia, to avoid spread along the carotid sheath, but also superficial to the muscle fascia to prevent intramuscular injection.<sup>18</sup> When successful, the prevertebral fascia can be seen distended with injectate and an ipsilateral Horner's syndrome results.<sup>19</sup>

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## FLUOROSCOPIC GUIDED TECHNIQUE

While fluoroscopy can effectively delineate bony structures and prevent complications related to intravascular, nerve root, or neuraxial drug administration, it does not allow for direct visualization of soft tissue structures and blood vessels. Administration of contrast helps confirm needle placement and provides safety by confirming the needle is not in a vascular structure. The patient is placed in a supine position and an anteroposterior view is obtained with the C-arm to identify the C6 vertebra. A skin wheal is formed over the anterolateral aspect of the C6 vertebral body, and the needle is inserted through the skin wheal with a lateral to medical trajectory under an oblique view. The needle is advanced to the junction of the vertebral body and uncinate process of the C6 vertebra.<sup>20</sup> Anteroposterior and lateral views are obtained to confirm correct needle placement, and visualization of the needle against the periosteum confirms the needle is not located transdiscal or in the spinal canal. After negative aspiration, contrast dye is injected and a craniocaudal spread along the longus colli muscle should be noted prior to injection of the local anesthetic. A modified fluoroscopic technique targeting the junction of the vertebral body and uncinate process of the C7 vertebra has also been employed.<sup>21</sup> Guidance with computed tomography (CT) and magnetic resonance imaging (MRI) has previously been described; however, these approaches are impractical in daily clinical practice as they are time consuming and costly.

#### **MECHANISM OF ACTION**

The sympathetic nervous system (SNS) is a key component of the autonomic nervous system responsible for orchestrating the body's response to stress and threat. In individuals with PTSD, dysregulation of the SNS is commonly observed, leading to persistent hyperarousal, exaggerated startle responses, and alterations in physiological functioning.<sup>3,22</sup>

The precise mechanisms underlying the therapeutic effects of SGBs in PTSD remain the subject of ongoing investigation. However, several hypotheses have been proposed based on preclinical and clinical evidence. One theory suggests that SGBs act by interrupting the hyperactive sympathetic signaling observed in individuals with PTSD, thereby dampening physiological arousal and attenuating the exaggerated stress response.<sup>3,23</sup> By blocking sympathetic transmission at the stellate ganglion, SGBs may modulate the activity of neural circuits implicated in fear processing and emotional regulation, ultimately reducing the severity and frequency of PTSD symptoms.

Furthermore, additional studies have suggested that SGBs may exert broader effects on neurobiological systems implicated in the pathogenesis of PTSD. There is a suggestion that nerve growth factor (NGF) is involved in a signaling cascade that can contribute to stress and PTSD symptoms.<sup>24</sup> Increased levels of NGF can increase sympathetic activity along with catecholamine release.<sup>24,25</sup> SGBs can be useful in blocking the SNS pathways and decreasing these effects.<sup>25,26</sup> Additionally, SGBs may influence the function of the hypothalamicpituitary-adrenal (HPA) axis, a key neuroendocrine system involved in the regulation of stress hormone secretion. By modulating these interconnected pathways, SGBs may exert multi-dimensional effects on the neurobiology of PTSD.

**CLINICAL EFFICACY** 

Several studies have evaluated the use of SGB in PTSD patients, including recent randomized controlled trials (RCT). A sham-controlled RCT of active-duty service members found that two SGBs given two weeks apart showed improvement in Clinician Administered PTSD Scale for DSM-5 (CAPS-5) over eight weeks, with a statistically significant reduction of 12.6 points in the SGB group versus 6.1 points in the sham group.<sup>27</sup> A secondary analysis showed a significant reduction in symptom severity in the arousal and reactivity PTSD symptom cluster. While the reexperiencing cluster also exhibited a notable response to SGB in clinician-rated assessments, self-reported outcomes did not

show the same degree of improvement. Further analysis indicated that reductions in hypervigilance, concentration difficulties, and sleep disturbances predominantly drove the improvements in the arousal and reactivity cluster. In contrast, reductions in physiological and emotional reactions to trauma cues, as well as intrusions, were the primary drivers of improvements in the reexperiencing cluster as assessed by clinicians.<sup>28</sup>

The effect of SGBs on PTSD symptoms appears to decline over time. In a case series of 166 active-duty service members, 70% of the patients demonstrated a clinically significant improvement of PTSD symptoms by 10 or more points on the PTSD Checklist (PCL). At one week follow-up of 126 patients, 78.6% responded with an average decrease in PCL Score of 22.0. On one-to-two-month follow-up, 81.76% of the 115 patients were responders withan average reduction in PCL score of 22.0 points. On three-to-six-month follow-up, 73.5% of the 97 patients were responders with an average reduction in PCL score of 21.8 points.<sup>29</sup>

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In another study involving 30 patients, significant improvements in PTSD symptoms were observed following SGB treatment across various aspects, including overall symptomatology, diagnostic clusters, and 16 of 17 symptom-based questions on the PTSD Checklist-Military (PCL-M) scale. One week following the procedure, there was a notable decrease in the average PCL-M score from the initial mean of 48.69 to 32.15, signifying a substantial and statistically significant improvement in symptoms (p < 0.001). Subsequently, during the second follow-up that occurred between two and four months post-SGB procedure, subjects continued to exhibit improved PTSD symptomatology, with an average score of 31.88. In the initial week post-SGB procedure, patients experienced the most significant alleviation in symptoms such as irritability or outbursts of anger, difficulty focusing, and disruptions in sleep patterns. Subsequently, between two to four months post-procedure, patients noted the most notable improvement in feeling distant or cut off, feeling emotionally numb, irritability or angry outbursts, and difficulty concentrating.<sup>30</sup>

In a series of nine military patients treated with SGB, non-universal and transient relief of symptoms lasting one to two months was noted, suggesting use of SGB as a rapid treatment option. Five of nine (56%) of patients were noted to have a clinically significant (>30%) reduction in PTSD symptoms; two patients experienced a noticeable reduction (10–30%) in PTSD symptoms and two patients experienced no change in symptoms (<10%) on the Clinician Administered PTSD Scale (CAPS) one week after the procedure. An immediate improvement in a two-year history of suicidal ideation was reported in one patient.<sup>31</sup> Similar results were noted in a study by Alino et al. in a series of four patients.<sup>32</sup> Mulvaney et al. reported immediate, durable, and significant relief in two patients as measured by PCL score, such that both patients could discontinue antidepressant and antipsychotic medications while maintaining an improved PCL Score.<sup>33</sup>

The use of SGB along with prolonged exposure therapy has also been reported with successful outcomes. A non-randomized clinical trial studied the use of SGB combined with prolonged exposure therapy for combat-related PTSD in 12 patients. Ninety percent of the participants showed a clinically significant change on the PCL-5 while 50% of the patients no longer met PTSD diagnostic criteria at one month follow-up.<sup>34</sup>

A pilot study of the efficacy of SGB conducted in active-duty combat veterans exhibited successful outcomes in the rate and level of response, reduced stigma relative to acceptance of treatment, as well as a high perceived value of treatment by patients. As the effect peaked and plateaued with a regression to baseline at around three months, the study suggested the use of SGB as a "gateway to treatment" to increase participation and compliance of patients during the efficacy period.<sup>35</sup>

However, a double-blind RCT conducted by Hanling et al. failed to exhibit disparities in psychological or pain-related outcomes between patients with PTSD who underwent SGB compared to those subjected to sham treatment. Additionally, individuals who shifted from sham therapy to SGB did not encounter significant enhancements in their condition through SGB intervention.<sup>36</sup> Of interest, the investigation highlighted that administering a second SGB session resulted in more substantial enhancements in Clinician-Administered PTSD Scale (CAPS) scores in contrast to the initial treatment session. This suggests a potential cumulative effect or the necessity of repeated SGB administration for optimal therapeutic benefits in PTSD management.

#### SAFETY PROFILE

Recent literature consistently suggests that SGBs are generally welltolerated among patients diagnosed with PTSD. This minimally invasive procedure entails the injection of a local anesthetic near the stellate ganglion, aiming to alleviate symptoms by modulating the autonomic nervous system. Despite its documented efficacy, it is crucial to acknowledge that this procedure is not without its risks. Various studies have highlighted potential complications associated with SGB, including but not limited to vascular injury, nerve damage, local anesthetic toxicity, and rare yet severe adverse events such as pneumothorax, meningitis, osteitis, or epidural hematoma.<sup>36</sup> However, the adoption of meticulous technique, utilization of real-time ultrasound guidance,

and careful consideration of patient-specific factors can significantly mitigate these risks. Moreover, recent research underscores the notion that the potential benefits of SGB in the treatment of PTSD may outweigh its inherent risks, particularly when the procedure is performed by experienced practitioners within a controlled clinical environment.<sup>37,38</sup> This highlights the importance of ongoing research and the refinement of clinical protocols to ensure the optimal balance between therapeutic efficacy and patient safety in the context of SGB administration for PTSD management.

#### **COMMON ADVERSE EVENTS**

The most frequently documented adverse events associated with SGBs are generally mild and transient, with a notable percentage of cases reporting temporary discomfort at the injection site (20-30%), minor bruising (10–15%), and subtle alterations in voice (5–10%), attributed to the close proximity of the stellate ganglion to the recurrent laryngeal nerve.<sup>34</sup> Additionally, Horner's syndrome, characterized by ptosis, miosis, and anhidrosis, is commonly observed following SGB; however, it typically resolves spontaneously within a few hours to days. In a RCT conducted by Hanling et al., only one case of persistent Horner's syndrome was reported among 42 participants, further emphasizing the transient nature of these side effects.<sup>36</sup> Despite their occurrence, these mild adverse events are widely regarded as manageable and do not significantly compromise the overall safety profile of SGB. Furthermore, the temporary nature of these side effects underscores the attractiveness of SGB as a treatment option for many patients, particularly when compared with the potential for dependency and systemic complications associated with prolonged medication use. This highlights the importance of thorough patient education and shared decision-making in selecting the most appropriate therapeutic approach for individuals with PTSD.

## SERIOUS ADVERSE EVENTS

Serious complications associated with SGBsare rare occurrences but are not entirely absent. These infrequent yet potentially severe events encompass pneumothorax, observed in less than 1% of cases, hematoma formation, occurring in approximately 1–2% of instances, and inadvertent intravascular injection, which may precipitate systemic toxicity. However, the incidence of such complications is markedly reduced when the procedure is administered by seasoned practitioners leveraging imaging guidance modalities to ensure precise needle placement.

For instance, Goel et al., in their review encompassing 260 cases detailing all complications following SGB, reported serious adverse events in less than 1% of instances.<sup>39</sup> Within this subset, five patients developed hematoma, and one patient experienced pneumothorax, underscoring the paramount importance of adherence to proper technique and thorough training protocols. The integration of imaging technologies such as ultrasound significantly diminishes the risk of procedural complications, thereby underscoring the indispensable role of practitioner expertise in facilitating the safe execution of SGB.

Furthermore, insights gleaned from a survey study evaluating approximately 45,000 SGB procedures across various chronic syndromes unveiled a relatively low incidence of severe complications, estimated at 1.7 in 1000 blockades.<sup>40</sup> Moreover, a longitudinal investigation tracking a cohort of 250 PTSD patients over a two-year period revealed no escalation in adverse events with repeated blocks.<sup>41</sup> Impressively, 100% of surveyed patients expressed overall satisfaction with the procedure, with a noteworthy 95% indicating willingness to undergo repeat interventions owing to minimal discomfort and tolerable side effects. Collectively, these findings underscore the notion that SGB can be safely administered on multiple occasions if deemed necessary, affording sustained relief from PTSD symptomatology without incurring cumulative risk. The ability to repetitively perform the procedure over time positions SGB as a viable long-term treatment option for individuals grappling with chronic PTSD. Evidence strongly suggests that SGB stands as a low-risk therapeutic option for the enduring management of PTSD. However, continued vigilance through robust monitoring and comprehensive reporting mechanisms remains imperative to further delineate the long-term safety profile of SGB for PTSD.

#### **FUTURE DIRECTIONS**

While current research demonstrates promising results, further studies are necessary to validate the long-term efficacy and safety of SGBs in PTSD treatment. Most existing studies focus on the short-term benefits of SGBs, typically observing patients for weeks to months postprocedure. Future research should investigate the long-term efficacy of SGBs, assessing whether repeated treatments continue to provide long term symptom relief and whether the duration of effectiveness changes over time. Longitudinal studies following patients for several years would be beneficial in understanding the chronic impact of SGBs on PTSD symptoms and overall quality of life. Additionally, determining the optimal frequency and number of SGB treatments required for sustained relief is critical. Studies exploring whether booster treatments

at regular intervals could maintain symptom reduction over a long term time period are needed. Additionally, understanding the individual variability in response to SGBs could help tailor treatment protocols, ensuring that patients receive the most effective and personalized care.

The potential of SGBs as an adjunctive treatment to existing PTSD therapies, such as CBT and prolonged exposure therapy warrants further investigation. The use of SGB along with prolonged exposure therapy has also been reported with successful outcomes previously.<sup>34</sup> Combining SGB with psychological therapies may enhance treatment outcomes by simultaneously addressing the physiological and psychological aspects of PTSD. Studies should explore the synergistic effects of such combination therapies and identify the most effective integration strategies.

Future studies should include diverse patient populations, such as civilians, women, and individuals with comorbid psychiatric or medical conditions. Most current research focuses on military personnel, but broadening the study populations would enhance the generalizability of findings and ensure that SGB is effective and safe for all individuals with PTSD.

Finally, further studies to better elucidate the precise mechanisms through which SGB alleviates PTSD symptoms are needed. Research should focus on clarifying the precise neural and biochemical pathways involved, potentially leading to the identification of biomarkers that could predict treatment response. Understanding these mechanisms could also pave the way for the development of new therapeutic targets and interventions.

#### CONCLUSION

SGBs represent a promising therapeutic option for individuals suffering from PTSD, offering a minimally invasive approach that targets the SNS. Clinical evidence supports the efficacy of SGB in reducing PTSD symptoms, particularly in the short term, with a favorable safety profile. However, further research is necessary to validate its long-term benefits, optimize treatment protocols, and explore its potential as an adjunctive therapy. Continued investigation into the mechanisms of SGB's action, its combination with other therapeutic modalities, and its application across diverse patient populations will be crucial in establishing its role in PTSD treatment. With ongoing research and clinical advancements, SGBs hold the potential to significantly improve the quality of life for those affected by this challenging condition, offering hope for more effective and sustainable PTSD management. �

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