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REVIEW

Perioperative Sympathetic Blockade: Mechanisms and Clinical Advances in Sensory Processing Modulation – A Narrative Review

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Abstract: Surgical trauma can trigger abnormal sensory processing, which plays a central role in driving pathophysiological changes during the perioperative period. In this review, we re-examine the mechanism of sympathetic nerve blockade and suggest that its essential function may involve actively resetting the maladaptive sensory signaling pathways through multi-system interactions. We explore how the sympathetic nervous system regulates sensory input through multiple layered processes—such as sympathetic-sensory coupling, neuro-immune-endocrine interactions, and microcirculatory metabolic adjustments. The analysis further describes how nerve block techniques, including stellate ganglion block and lumbar sympathetic block, interact within these networks to produce broad therapeutic outcomes—from pain relief and stress modulation to organ protection. Finally, we highlight potential future advances in precision-oriented sympathetic intervention, guided by neural circuit mapping, biomarker monitoring, and artificial intelligence.

Keywords: sympathetic nerve block, sympathetic-sensory coupling, perioperative period, sensory processing, neural circuits

Introduction

Worldwide, an estimated 300 million or more surgical procedures are performed annually, making perioperative pain and stress-related complications major public health concerns.[1] Although perioperative care has improved substantially, moderate to severe acute postoperative pain remains common, affecting a considerable proportion of surgical patients.[2] Inadequate analgesia is associated with impaired recovery, delayed mobilization, greater opioid exposure, and an increased likelihood of persistent postsurgical pain.[3] At the same time, the neuroendocrine stress response to surgery, which is closely intertwined with sympathetic activation, may contribute to cardiovascular instability, immune dysregulation, metabolic disturbance, and postoperative neurocognitive morbidity.[4] Together, these clinical and epidemiological observations support closer examination of sympathetic mechanisms in perioperative sensory processing.

During surgery, noxious stimuli travel from peripheral receptors through dorsal root ganglia (DRG) to the spinal cord's dorsal horn. This process also engages descending pain modulation pathways, which activate both the autonomic nervous system and the endocrine axis.[5] If sensory signaling becomes excessively amplified or prolonged—as occurs in peripheral or central sensitization—it can induce abnormal sympathetic activation and dysregulation of the SAM/HPA axis. These changes, in turn, initiate a cascade of metabolic, immune, and cardiovascular disturbances, marking a critical origin of perioperative pathophysiological alterations.[6,7] This maladaptive sympathetic-sensory coupling may be particularly pronounced in patients undergoing major trauma or emergency surgery, where extensive tissue injury, inflammation, ischemia, and psychological stress can amplify nociceptive input and sympathetic outflow. By contrast, although elective procedures are generally performed under more controlled conditions, substantial sympathetic-sensory dysregulation may still arise in highly invasive operations or in patients with pre-existing pain vulnerability. Although sympathetic blockade has traditionally been regarded mainly as an analgesic or vasoregulatory tool, its potential influence on higher-level neural integration has often been overlooked. In this review, we argue from a multi-level

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perspective that sympathetic blockade not only relieves pain but also helps modulate maladaptive sensory processing. By interacting with neural, immune, endocrine, and vascular components across multiple levels, it enables broader control over pathological sensory input. Compared with previous reviews that have predominantly focused on disease-specific or technique-based indications for sympathetic nerve blocks, the present article emphasizes a unifying sensory-processing–centered framework, grounded in the concept of sympathetic-sensory coupling and its multi-system consequences to interpret perioperative applications and guide future precision strategies.

Neural Circuitry Basis of Sensory Processing and Sympathetic Modulation

The process of sensory processing involves the transmission, filtering, and integration of information across widespread brain networks, from peripheral receptors to the cerebral cortex. Within this framework, the sympathetic nervous system acts not only as a stress-response effector but also as a key modulator embedded within sensory processing circuits. Its main central center is located in the intermediolateral nucleus (IML) of the spinal cord's T1-L2 segments. From there, fibers extend widely throughout the body via sympathetic chains, establishing the structural basis for information exchange between the central nervous system and peripheral organs.

In the classical somatosensory pathway, signals originate in nociceptors within the skin, muscles, and viscera. These signals are then relayed via DRG through the central terminals of primary sensory neurons into the dorsal horn of the spinal cord—mainly laminae I, II, and V. After initial integration at this site, the information travels upward along pathways such as the spinothalamic tract to the thalamus, finally reaching the somatosensory cortex where conscious pain perception emerges. It is important to note that the spinal dorsal horn functions not merely as a relay station but as a critical integration hub. Its intricate local circuits, including inhibitory interneurons, perform a "gating" function on incoming sensory information.[8] Another key circuit involves a spinal cord–brainstem–spinal cord loop: dorsal horn neurons project to brainstem regions like the parabrachial nucleus and the rostral ventromedial medulla. These areas, in turn, send descending fibers (for example, serotonergic and noradrenergic) back to the spinal cord, exerting powerful excitatory or inhibitory control over dorsal horn sensory transmission, collectively forming the descending pain modulation system.[9]

The sympathetic nervous system serves as a sophisticated regulator integrated into the pathways described above. The cell bodies of its preganglionic neurons lie within the IML of the T1–L2 spinal cord. This anatomical placement situates it close to the dorsal horn—the primary gateway for sensory input—enabling "sympathetic-sensory coupling" at the spinal level. Under normal physiological conditions, the sympathetic system exerts continuous, indirect influence over peripheral receptor sensitivity and signal-to-noise ratio by modulating local blood flow, immune cell activity, and the metabolic milieu of tissues. However, under pathological states such as tissue injury or nerve damage, this modulatory role becomes abnormally amplified, turning into a strong driving force for sensitization. A core mechanism behind this shift is the pathological "sympathetic-sensory coupling" that develops between the DRG and sites of injury,[10] leading to dysfunctional sensory processing. As a result, a normally protective neural response can escalate into persistent chronic pain. Therefore, interventions targeting the sympathetic nervous system can be seen as resetting a critical "gain control" within the overall sensory processing circuitry.

The Core Regulatory Mechanism of the Sympathetic Nervous System in Sensory Processing

The sympathetic nervous system regulates sensory processing through a complex, multi-mechanism pathway. Figure 1 provides a schematic overview of this integrated regulatory network, illustrating the key anatomical and functional components detailed in the following subsections.

Anatomical and Pathway Fundamentals: Intersection of Sympathetic and Sensory Pathways

The lower center of the sympathetic nerve (preganglionic neuron cluster) is located in the intermediolateral nucleus of the lateral horn gray matter within the T1-L2 spinal cord segments. Preganglionic fibers originating here traverse the white

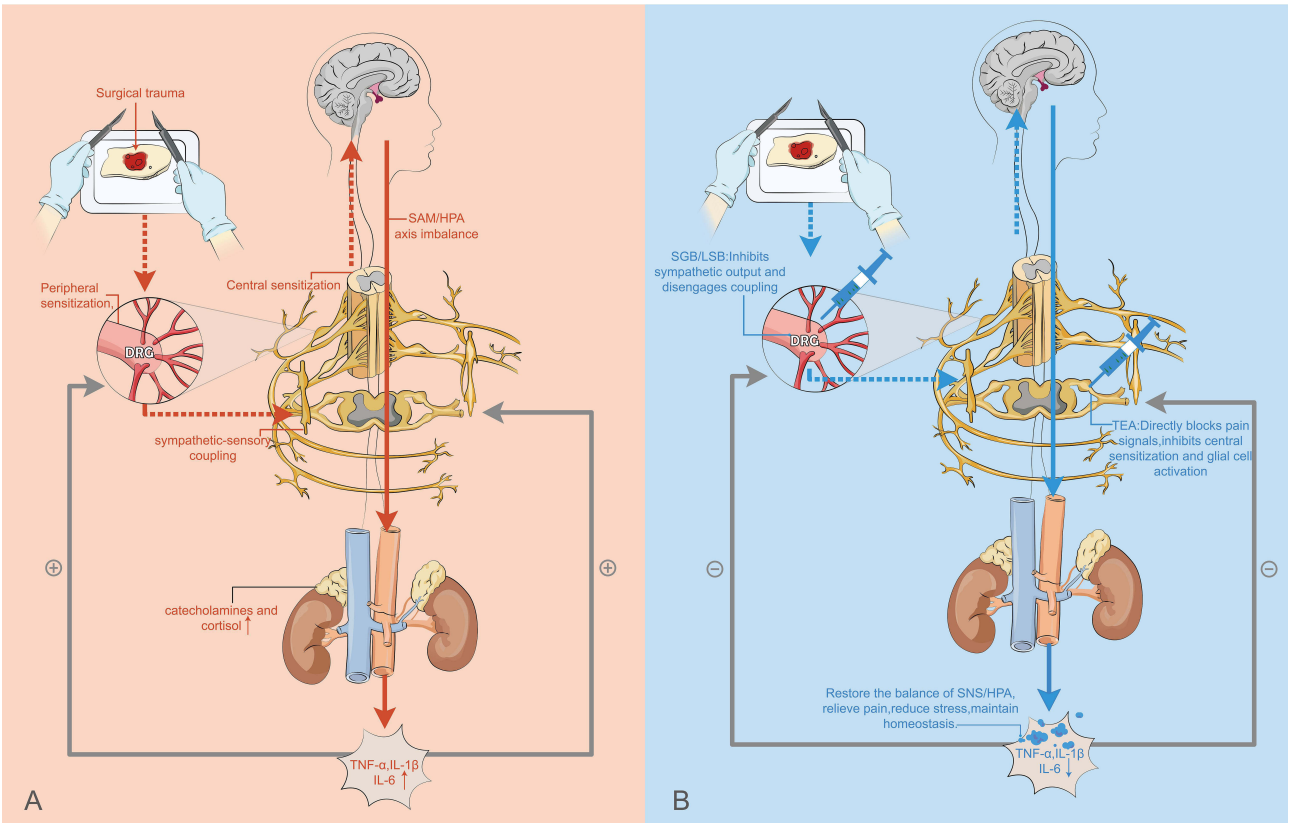

Figure 1 Systemic mechanisms of perioperative sympathetic blockade in resetting aberrant sensory processing.
Notes: Surgical trauma (**A**) promotes sympathetic overactivation and abnormal sensory processing via sympathetic–sensory coupling (SSC), resulting in peripheral and central sensitization, SAM/HPA axis imbalance, neuroinflammation, and increased stress mediators. Perioperative sympathetic blockade (**B**) including SGB, LSB, and thoracic epidural/paravertebral techniques, may attenuate these responses through desympathetization, neuroimmune–endocrine modulation, inhibition of central sensitization and glial activation, and improved microcirculation. In this schematic, dashed arrows represent afferent neural input/signaling, while solid arrows represent efferent neural output/signaling. Upward arrows (↑) denote increased levels of mediators or enhanced pathway activity, whereas downward arrows (↓) denote decreased levels of mediators or suppressed/reduced pathway activity. Plus signs (+) indicate positive-feedback or facilitative interactions, while minus signs (−) indicate inhibitory, suppressive, or negative-feedback interactions.
Abbreviations: DRG, dorsal root ganglion; SSC, sympathetic–sensory coupling; SAM, sympathetic–adrenal medullary; HPA, hypothalamic–pituitary–adrenal; SGB, stellate ganglion block; LSB, lumbar sympathetic block; TEA, thoracic epidural analgesia; SNS, sympathetic nervous system; TNF-α, tumor necrosis factor-α; IL, interleukin.

commissure to enter the paravertebral sympathetic chains (cervical, thoracic, lumbar, sacral) and connect with the prevertebral ganglia (visceral, superior/inferior mesenteric). Sympathetic nerve block (SNB) involves blocking sympathetic nerve impulse transmission through pharmacological or physical means. The earliest techniques date back to the late 19th and early 20th centuries. In 1889, Alexander first described sympathectomy, primarily used at the time to treat conditions such as epilepsy and glaucoma.[11] In 1946, the first use of sympathectomy to treat neuropathic burning pain laid the theoretical foundation for subsequent sympathetic nerve block techniques.[12] By 1949, stellate ganglion block was applied to manage head and neck pain and vascular disorders,[13] with its successful outcomes informing the development of sympathetic nerve block. Common clinical targets for sympathetic blockade include: the stellate ganglion (cervicothoracic ganglion, C7–T1), thoracic sympathetic chain, lumbar sympathetic chain, and celiac/hypogastric plexus. These respectively influence sympathetic output to the head, neck, upper limbs; thoracic organs; lower limbs/pelvis; and visceral organs. Modern ultrasound/fluoroscopy/CT guidance has enhanced localization and safety.[14]

Inhibit the Sympathetic-Sensory Coupling and Downregulate Peripheral Sensitization

Surgical procedures and tissue injury can induce abnormal sprouting of sympathetic fibers within DRG, forming pathological sympathetic-sensory coupling with primary sensory neurons. Sympathetic terminals co-release norepinephrine (NE) and chemokines (such as, CXCL16), synergistically sustaining hyperalgesia and spontaneous firing,[15] thereby driving sympathetic-dependent pain phenotypes.[16] SGB and LSB can functionally de-sympathetize this upstream driver, directly reducing

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peripheral neuronal excitability and ectopic discharge at the source, thereby optimizing the initial encoding of sensory input. Animal and translational studies have clearly identified the NE+CXCL16 synergy as a key mechanism sustaining neuropathic pain, providing direct evidence for the analgesic biological basis of sympathetic blockade.[17]

Deamplifying the Stress-Inflammation-Immune Axis to Improve the Sensory Internal Environment

Sympathetic blockade effectively reduces peak levels of stress hormones such as catecholamines and cortisol in patients by inhibiting peripheral sympathetic output, thereby alleviating sterile inflammation and immune imbalance within the body.[18,19] The massive release of inflammatory mediators like IL-1 β and TNF-α constitutes potent pathological sensory input itself. Thus, suppressing inflammation through sympathetic blockade effectively eliminates persistent abnormal sensory input, directly optimizing the body's sensory processing environment. Perioperative injury-sympathetic monitoring studies further indicate that improved sensory input control coupled with lower sympathetic tone is associated with reduced opioid consumption and more stable postoperative physiological parameters.[7]

Segmental Denervation and Microcirculatory Improvement: Optimizing Systemic Sensory Load

As a representative of sympathetic blockade and enhanced analgesia, thoracic epidural anesthesia (TEA) efficiently blocks abnormal signal transmission from nociceptive afferent fibers in the surgical field during thoracic/upper abdominal procedures by directly blocking thoracic spinal dorsal root ganglia. This controls pathological sensory input at its source. Simultaneously, selective thoracic sympathetic denervation effectively relieves visceral vasospasm and cardiac sympathetic hyperactivity, thereby optimizing visceral perfusion and improving visceral sensation.[20] This synchronous load reduction at both sensory afferent and sympathetic efferent levels forms the integrated neuroscientific basis for its exceptional performance in improving myocardial oxygen supply-demand balance and anti-ischemic effects. In randomized trials of coronary artery bypass grafting, high-level TEA improves regional left ventricular motion, reduces postoperative myocardial troponin and BNP/ANP levels, and optimizes myocardial oxygen supply-demand ratios.[21] Concurrently, TEA directly dilates stenotic coronary segments and lowers arrhythmia susceptibility, demonstrating comprehensive anti-ischemic effects.[20,22]

Application of Sympathetic Nerve Blockade in Perioperative Sensory Processing Regulation

Currently, combined nerve blocks—such as brachial plexus and sciatic nerve blocks—predominate in perioperative nerve blockade. Among isolated sympathetic nerve blocks, SGB and LSB are most widely applied.

SGB

SGB achieves reversible chemical resection of sympathetic function in the head, face, neck, and upper extremities by interrupting the cervical-thoracic sympathetic chain. The therapeutic benefits of SGB in modulating sensory processing operate through several distinct yet interconnected mechanisms. Firstly, the procedure directly counteracts regional vasoconstriction driven by sympathetic overactivity, leading to marked improvements in tissue perfusion and oxygenation.[23,24] This restoration of blood flow creates a more favorable metabolic milieu for peripheral receptors, thereby enhancing the quality of sensory input at the most fundamental, supply-side level. Secondly, as outlined in previous sections, SGB potently suppresses sympathetic-sensory coupling within the DRG, which in turn curtails the local release of norepinephrine and various pro-inflammatory mediators.[25] This action reduces both the abnormal excitability and spontaneous firing of peripheral nociceptors, effectively limiting the production of pathological sensory signals at their origin. Further reinforcing these effects, clinical evidence indicates that SGB can significantly lower circulating levels of pro-inflammatory cytokines, including TNF-α and IL-6, in surgical patients, while simultaneously promoting beneficial immunomodulation.[26,27] By resolving the inflammatory drive that persistently activates sensory neurons, SGB helps disrupt the cycle of inflammatory signaling. Given this multi-modal mechanism, it is understandable

that SGB is not only a cornerstone therapy for complex regional pain syndrome (CRPS) affecting the upper body but is also gaining recognition for its perioperative utility. Its potential applications include mitigating acute postoperative pain,[28] enhancing the recovery of cognitive function after surgery,[29] and facilitating overall recovery.[27] These diverse benefits collectively underscore the capacity of a localized sympathetic block to induce a systemic reset of the integrated sensory processing unit for the head, neck, and upper extremities.

Lumbar Sympathetic Blockade

LSB targets the sympathetic chain at the L2-L4 levels, which provides primary innervation to the pelvis and lower limbs. Its capacity to modulate abnormal sensory processing is particularly evident in managing CRPS and ischemic pain of the lower extremities. Both conditions are defined by severe peripheral sensitization, spontaneous pain, and hyperalgesia—clinical signs indicative of a profoundly disrupted sensory processing system. The therapeutic action of LSB operates through complementary pathways. It rapidly alleviates tissue ischemia by reversing pathological vasoconstriction and enhancing local blood flow. Although this microcirculatory benefit is typically immediate and may be transient after a single block, improved perfusion and enhanced clearance of algogenic substances may, particularly with repeated or sustained sympathetic interruption, help establish a local environment more conducive to tissue recovery and neural repair.[30,31] Crucially, LSB directly disrupts the pathological drive from postganglionic sympathetic fibers to sensory nerves in the lower limbs, an mechanism analogous to that of SGB in the upper extremities. This intervention promotes the normalization of highly sensitized sensory processing circuits. In the context of major lower-limb operations, such as joint replacement or vascular surgery, LSB compared to conventional opioid-based intravenous analgesia, LSB provides superior pain control, accelerates functional mobilization, and significantly reduces the need for systemic opioids, thereby minimizing opioid-related adverse effects such as PONV. The fundamental mechanism involves its active correction of the imbalance between surgically-induced peripheral sensitization and the body's inherent descending modulatory systems, thereby helping to preserve the functional stability of sensory processing throughout the perioperative period.

Thoracic Epidural and Paravertebral Blockade

TEA offers a unique model of concurrent sensory afferent and sympathetic efferent blockade.[32] In thoracic and upper abdominal surgeries, the diffusion of local anesthetics in the epidural space enables TEA to effectively block both the thoracic dorsal roots (carrying sensory input) and the ventral roots (which contain sympathetic outflow). From the afferent perspective, it physically prevents the transmission of high-intensity, high-frequency noxious signals from the surgical site to the central nervous system, effectively intercepting pathological sensory input at the source. On the efferent side, it induces a selective thoracic sympathectomy, which alleviates visceral vasospasm and counteracts excessive cardiac sympathetic tone. The benefits of this "dual afferent-efferent blockade" are twofold. By attenuating nociceptive afferent input, TEA may limit central sensitization, thereby improving postoperative pain control and reducing opioid consumption. In randomized trials and meta-analyses, compared with systemic opioid-based analgesia, TEA has shown superior dynamic pain relief—particularly during coughing and mobilization—and has been associated with a reduced incidence of postoperative pulmonary complications after major thoracic and upper abdominal surgery.[33,34] Simultaneously, by decreasing thoracic sympathetic outflow, TEA may improve visceral perfusion, reduce myocardial oxygen demand and cardiac workload, and alleviate ischemia-related visceral discomfort, thereby contributing to favorable cardiopulmonary effects. For surgeries involving the unilateral thoracic wall, paravertebral block provides a segmental sensory and sympathetic blockade comparable to TEA, establishing itself as another pivotal technique for the integrative management of truncal sensory processing.[35,36]

Technology Comparison and Objective Monitoring

Comparison and Selection Strategies for Sympathetic Nerve Block Techniques

Different sympathetic block techniques, defined by their anatomical targets and diffusion characteristics, produce distinct regional sensory modulation profiles. SGB predominantly influences the head, neck, and upper limbs. Its primary effects center on enhancing local perfusion, suppressing sympathetic-sensory coupling in the upper torso, and imparting

significant benefits to central stress responses and immune status.[37] In contrast, LSB focuses on the pelvis and lower extremities, establishing itself as a cornerstone intervention for sensory processing disorders linked to vascular insufficiency and CRPS in the lower limbs.[38,39] For more extensive truncal and visceral involvement, TEA and thoracic paravertebral block deliver the most comprehensive and potent dual blockade, simultaneously interrupting sensory afferent traffic and sympathetic efferent outflow. These techniques are particularly relevant in major thoracic and upper abdominal procedures, where they may reduce nociceptive transmission from the surgical field while modulating stress-related autonomic responses.

To facilitate a more systematic comparison, the principal characteristics of these techniques—including their anatomical targets, typical indications, potential benefits, and major limitations—are summarized in Tables 1 and 2. Selection of the optimal technique requires a structured and individualized decision-making process. The first step is to identify the predominant anatomical region in which maladaptive sensory processing is most likely to occur, whether involving the head and neck, lower extremities, or thoracoabdominal and visceral domains. This should be followed by assessment of the patient's physiological reserve, comorbidities, and the anticipated magnitude of surgical stress. Finally, the choice of block should be guided by procedural goals, operator expertise, and the availability of appropriate monitoring and perioperative support.

Objective Monitoring Indicators

Objective measurement forms the foundation of precise regulation. Although traditional vital signs like heart rate and blood pressure offer some insight into sympathetic tone, they often lack the specificity and sensitivity required for fine-tuned management. The field has therefore turned to more advanced monitoring tools, which now provide a clearer window into the physiological effects of sympathetic blockade and the resulting improvements in sensory processing.

Table 1 Target Anatomical Levels and Typical Indications of Major Sympathetic Block Techniques

Technique	Target Anatomical Level	Typical Indications
SGB	C7–T1 (cervicothoracic)	Upper-extremity sympathetically maintained pain, vascular spasm, and selected perioperative autonomic modulation
LSB	L2–L4 (lumbar)	Lower-extremity sympathetically maintained pain, ischemic pain, CRPS, and selected pelvic pain conditions
TEA	T4–T8 (thoracic), depending on surgical site	Thoracic, upper abdominal, and major visceral surgery requiring broad segmental analgesia

Notes: Although stellate ganglion block is commonly performed at the C6 level under ultrasound guidance for safety, its principal sympathetic target corresponds to the cervicothoracic region at approximately C7–T1.
Abbreviations: SGB, stellate ganglion block; LSB, lumbar sympathetic block; TEA, thoracic epidural analgesia; CRPS, complex regional pain syndrome.

Table 2 Efficacy, Physiological Modulation, and Safety Profiles of Major Sympathetic Block Techniques

Technique	Efficacy and Physiological Modulation Profile	Safety Profile and Common complications
SGB	Effective for localized cervicothoracic sympathetic overactivity and sympathetically maintained pain; may improve regional perfusion and modulate inflammatory, immune, and stress-related responses.	Transient Horner syndrome, hoarseness, dysphagia, vascular puncture, and local anesthetic systemic toxicity; rare complications include pneumothorax and seizure after inadvertent intravascular injection.
LSB	Effective for lower-extremity sympathetically maintained and ischemic pain; may improve distal perfusion and modulate pain processing in pelvic and lower-limb sympathetic territories.	Common complications include hypotension, genitofemoral neuralgia, vascular injury, retroperitoneal bleeding, injury to adjacent structures, and local anesthetic systemic toxicity.
TEA	Provides robust segmental analgesia and broad modulation of somatic and visceral afferent input as well as sympathetic efferent outflow; may reduce opioid requirements and attenuate perioperative stress responses.	Common adverse effects and complications include hypotension, urinary retention, motor block, dural puncture, epidural hematoma, and epidural infection/abscess.

Notes: Physiological effects and complication profiles may vary according to imaging guidance, injectate volume, operator experience, and patient-specific risk factors.
Abbreviations: SGB, stellate ganglion block; LSB, lumbar sympathetic block; TEA, thoracic epidural analgesia.

Microcirculation and perfusion metrics: Perfusion index (PI)[40] and laser speckle contrast imaging (LSCI)[41] allow for non-invasive, real-time assessment of local tissue blood flow. A successful stellate ganglion or lumbar sympathetic block is often followed by a marked rise in PI values and LSCI-documented flow enhancement in the corresponding limb. These changes directly confirm the release of sympathetic vasoconstrictor tone, verifying that the metabolic milieu supporting local sensory function has been optimized.

Electrophysiological Indicators: Sympathetic Skin Response (SSR),[42] which measures stimulus-induced changes in skin conductance, reflects the activity of cholinergic sympathetic fibers. A reduction or disappearance of SSR amplitude on the blocked side objectively marks the functional interruption of the sympathetic efferent pathway.

Noxious-Antinoxious Balance Indicators: The Analgesia/Noxious Index (ANI)[43] and Noxious Level Index (NOL) represent emerging multi-parameter algorithmic indices. They quantify the balance between the intensity of noxious input and the body's antinoxious defense system by analyzing signals such as heart rate variability. During sympathetic blockade,[44] an increase in ANI or decrease in NOL indicates that the central sensory processing system remains in a more balanced, controlled state even under surgical stress, providing a basis for precise titration of sedative and analgesic medications.

Neuroendocrine and Immune Markers: Although not part of real-time bedside monitoring, perioperative dynamic assessment of plasma catecholamines, cortisol, and pro-/anti-inflammatory cytokines (eg, IL-6, IL-10, TNF-α) provides critical objective evidence at the systems biology level for the "de-stressing" and "immunomodulatory" effects of sympathetic blockade.[45]

Limitations, Potential Complications, and Contraindications

While perioperative sympathetic blockade offers unique advantages in resetting sensory processing, its clinical application must be balanced against potential limitations and complications. A major concern is excessive or widespread sympathetic denervation, which may impair the physiological compensatory mechanisms needed to maintain cardiovascular stability.[20] This is particularly relevant with high thoracic epidural analgesia, where bilateral multisegmental blockade can lead to marked vasodilation, reduced venous return, hypotension, and bradycardia. Such effects may be poorly tolerated in older adults and in patients with severe valvular heart disease, autonomic dysfunction, hypovolemia, or limited cardiovascular reserve.[46]

Important limitations also arise from the current evidence base. Compared with thoracic epidural analgesia, perioperative data supporting stellate ganglion block and lumbar sympathetic block remain relatively limited and heterogeneous, with variation in indications, procedural methods, and outcome assessment. This restricts direct comparison across techniques and reduces the generalizability of published findings.

Procedure-specific complications should likewise be recognized. Stellate ganglion block may be associated with inadvertent intravascular injection, recurrent laryngeal nerve block, dysphagia, local hematoma, and local anesthetic systemic toxicity, while transient Horner syndrome is common and usually expected.[47,48] Lumbar sympathetic block carries risks related to deep needle placement, including post-procedural neuralgia, somatic nerve injury, vascular injury, and retroperitoneal bleeding. Thoracic epidural analgesia is associated with hypotension, urinary retention, motor block, dural puncture, epidural hematoma, and epidural infection or abscess.[20]

Major contraindications include patient refusal, infection at the puncture site, uncontrolled coagulopathy, severe hypovolemia, and significant hemodynamic instability. These issues are especially important for neuraxial and deep sympathetic blocks. Accordingly, the use of sympathetic blockade in perioperative practice should be individualized, with careful attention to patient selection, procedural expertise, and hemodynamic monitoring.[49]

Discussion and Outlook

Building on the sensory processing-sympathetic coupling framework, this review argues that the principal significance of sympathetic blockade extends beyond mere passive stress reduction. Instead, we posit that its core mechanism involves the active resetting of maladaptive sensory processing pathways. By simultaneously targeting peripheral/DRG excitability, central sensitization, microcirculatory perfusion, and the local immune microenvironment, sympathetic blockade functionally unifies analgesia, stress regulation, and organ recovery into a cohesive, testable mechanistic sequence.

Looking forward, several promising directions emerge. A primary goal is to deepen our understanding of the underlying neural circuits. Techniques such as optogenetics and chemogenetics could be leveraged to dissect the precise regulatory roles of sympathetic-sensory coupling within defined cell populations and neural pathways. Secondly, there is a need to develop reliable biomarkers derived from integrated multimodal data—for instance, combining ANI/NOL indices with laser speckle contrast imaging (LSCI) and functional MRI. Such efforts could yield a quantifiable sensory processing index, facilitating closed-loop, precision-guided sympathetic blockade. Another important avenue is exploring the chronic preventive potential of this intervention. Future studies should specifically evaluate whether perioperative sympathetic blockade can confer long-term protection against persistent postoperative pain, a condition fundamentally rooted in aberrant sensory processing. Lastly, the integration of artificial intelligence presents a transformative opportunity. Machine learning models, trained on patient multi-omics profiles and real-time intraoperative physiological data, may eventually predict individual responses to sympathetic blockade and support the creation of truly personalized sensory modulation strategies.

Despite a strong mechanistic rationale for sympathetic–sensory modulation, important evidence gaps remain. Current clinical data are largely limited to small studies or specific pain conditions such as CRPS, and robust multicenter randomized trials are needed to confirm the efficacy of sympathetic blockade across surgical populations. Future studies should also clarify its effects on long-term outcomes, including chronic postsurgical pain and quality of life. In addition, procedural protocols and monitoring criteria remain insufficiently standardized, particularly for assessing sensory processing rather than hemodynamic stability alone. Further work should develop multimodal sensory–sympathetic assessment tools and define the optimal timing and duration of intervention, moving sympathetic blockade toward a more precise, individualized therapeutic strategy.

In summary, by targeting the interconnected neural, immune, and vascular pathways that underlie disordered sensory processing, perioperative sympathetic blockade has the potential to transition from a conventional anesthetic technique into a systematic therapeutic strategy. This evolution could unlock novel pathways for enhancing long-term recovery and outcomes in surgical patients.

Abbreviations

SNB, Sympathetic nerve block; DRG, dorsal root ganglia; SAM, The locus coeruleus-sympathetic-adrenal medulla system; HPA, The hypothalamic-pituitary-adrenal cortex; SGB, Stellate ganglion block; LSB, Lumbar sympathetic block; IML, intermediolateral nucleus; 5-HT:5-hydroxytryptamine; NE, norepinephrine; TEA:Thoracic epidural analgesia; BNP, brain natriuretic peptide; ANP, atrial natriuretic peptide; CRPS, complex regional pain syndrome; PI, Perfusion index; LSCI, laser speckle contrast imaging; SSR, Sympathetic Skin Response; ANI, Analgesia/Noxious Index; NOL, Noxious Level Index; LSCI, laser speckle contrast imaging; MRI, Magnetic Resonance Imaging.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work the authors used ChatGpt-4.0 in order to check spell and grammar. After using this tool, the authors reviewed and edited the content as needed and takes full responsibility for the content of the publication.

Data Sharing Statement

Data and material are available from the corresponding author on reasonable request.

Consent for Publication

The authors declare no conflict of interest.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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