



CENTRAL NERVOUS SYSTEM MECHANISMS OF PAIN MODULATION AND THEIR IMPLICATIONS FOR RESPONSE TO LOCAL ANESTHESIA IN DENTISTRY: A LITERATURE REVIEW

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Diterima: 03/06/2026; Direvisi: 03/10/2026; Diterbitkan: 09/10/2026

ABSTRAK

Kegagalan atau ketidakoptimalan anestesi lokal pada kondisi nyeri pulpa, khususnya *symptomatic irreversible pulpitis*, tidak hanya berkaitan dengan inflamasi perifer, tetapi juga dengan pemrosesan nyeri pada sistem saraf pusat (SSP). Literature review ini bertujuan untuk mensintesis bukti terkini mengenai mekanisme SSP dalam modulasi nyeri serta implikasinya terhadap respons terhadap anestesi lokal dalam kedokteran gigi. *Literature review* naratif dilakukan melalui pencarian pada PubMed, Google Scholar, ScienceDirect, dan Wiley Online Library. Studi yang dipublikasikan pada tahun 2021–2026 diprioritaskan, meliputi studi eksperimental, *randomized controlled trial*, studi observasional, *systematic review*, *meta-analysis*, dan *narrative review* yang relevan dengan mekanisme nyeri pada SSP, modulasi nyeri, dan anestesi lokal dalam kedokteran gigi. Literatur yang terpilih disintesis secara deskriptif ke dalam tiga tema utama, yaitu mekanisme SSP terhadap nyeri, modulasi nyeri sentral, dan respons klinis terhadap anestesi lokal. Hasil menunjukkan bahwa sensitisasi sentral, neuroplastisitas, sinyal yang dimediasi reseptor *N-methyl-D-aspartate*, jalur trigeminal, serta faktor psikologis berperan dalam amplifikasi dan persistensi nyeri orofasial. Keberhasilan anestesi lokal, terutama pada *symptomatic irreversible pulpitis*, dipengaruhi oleh berbagai faktor, termasuk inflamasi, kondisi anatomis, teknik anestesi, dan pemrosesan nyeri individu. Teknik tambahan seperti anestesi intraligamenter, intraosseous, dan *computer-controlled* dapat meningkatkan kenyamanan atau efektivitas klinis pada kondisi tertentu. Secara keseluruhan, modulasi nyeri oleh SSP berkontribusi terhadap variasi respons nyeri, tetapi belum terdapat bukti yang cukup bahwa sensitisasi sentral secara langsung menyebabkan kegagalan anestesi lokal.

Kata Kunci: anestesi lokal; kedokteran gigi; modulasi nyeri; nyeri dental; nyeri orofasial; sensitisasi sentral; sistem saraf pusat

ABSTRACT

Pain processing in patients with pulpal pain, particularly *symptomatic irreversible pulpitis*, involves not only peripheral inflammation but also pain processing within the central nervous system (CNS). This literature review aimed to synthesize recent evidence on CNS mechanisms of pain modulation and their clinical implications for the response to local anesthesia in dentistry. A narrative *literature review* was conducted using PubMed, Google Scholar, ScienceDirect, and Wiley Online Library. Studies published from 2021 to 2026 were prioritized, including experimental studies, *randomized controlled trials*, observational studies, *systematic reviews*, *meta-analyses*, and *narrative reviews* relevant to CNS pain





mechanisms, pain modulation, and local anesthesia in dentistry. The selected literature was descriptively synthesized into three themes: CNS mechanisms of pain, central pain modulation, and clinical response to local anesthesia. The findings indicate that central sensitization, neuroplasticity, *N-methyl-D-aspartate* receptor-mediated signaling, trigeminal pain pathways, and psychological factors contribute to the amplification and persistence of orofacial pain. Local anesthetic success, particularly in *symptomatic irreversible pulpitis*, is influenced by multiple factors, including inflammation, anatomical conditions, anesthetic technique, and individual pain processing. Supplemental techniques, including intraligamentary, intraosseous, and *computer-controlled* anesthesia, may improve anesthetic outcomes or procedural comfort under specific conditions. Overall, CNS pain modulation contributes to individual variability in dental pain, although current evidence does not establish central sensitization as a direct cause of local anesthetic failure. Understanding central and peripheral pain mechanisms may support individualized pain-management strategies in dentistry.

Keywords: *central nervous system; central sensitization; dentistry; dental pain; local anesthesia; orofacial pain; pain modulation*

INTRODUCTION

Pain associated with dental procedures is closely related to the interaction between peripheral nociceptive input and central nervous system (CNS) processing. In dental and orofacial tissues, nociceptive signals are transmitted through trigeminal pathways to the brainstem and higher-order brain regions, where they are processed and modulated before being perceived as pain. Consequently, differences in central pain processing may contribute to variations in the intensity and persistence of dental pain among patients. This interaction is particularly relevant in patients with persistent or intense pulpal pain, in whom peripheral nociceptive activity may interact with changes in central pain processing.

Persistent or intense nociceptive input can induce neuroplastic changes in central pain pathways, resulting in central sensitization. Increased responsiveness of central nociceptive neurons may contribute to hyperalgesia, allodynia, and persistence of pain. These processes involve, among others, *N-methyl-D-aspartate* (NMDA) receptors and glutamatergic signaling, which have been implicated in the development and maintenance of central sensitization and chronic orofacial pain (Guo et al., 2022). In parallel, descending pain-modulatory systems involving the periaqueductal gray, rostroventral medulla, and neurotransmitters such as serotonin and norepinephrine may inhibit or facilitate nociceptive transmission. Psychological factors, including anxiety and stress, may further modify pain perception and behavioral responses during dental treatment (Donertas-Ayaz & Caudle, 2023). Thus, dental pain cannot be understood solely from peripheral nociceptive mechanisms because central modulation may alter how nociceptive input is experienced.

The influence of central pain processing becomes clinically relevant when local anesthesia is used to control pain during invasive dental procedures. Local anesthetic agents primarily inhibit voltage-gated sodium channels in peripheral nerve fibers, thereby preventing the generation and propagation of action potentials. However, profound anesthesia is not always achieved, particularly in patients with *symptomatic irreversible pulpitis*. Inflammatory changes, increased peripheral nociceptive activity, anatomical conditions, and limitations of the anesthetic technique may contribute to anesthetic failure (Parirokh et al., 2022). Although central sensitization may increase pain responsiveness, the extent to which central pain processing contributes to the clinical response to local anesthesia remains uncertain. Therefore,



the presence of persistent pain during dental treatment should not be attributed solely to central sensitization, because peripheral inflammation and technical factors also have important roles.

In addition to patient- and disease-related factors, the clinical response to local anesthesia may vary according to the anesthetic technique. Computer-controlled, intraligamentary, and intraosseous techniques have been investigated as supplemental or alternative approaches to conventional injection, while photobiomodulation has been studied as an adjunct for reducing injection-related pain. These approaches indicate that clinical management of dental pain involves not only pharmacological blockade of peripheral nerve conduction but also consideration of the conditions that influence pain perception and anesthetic effectiveness. Nevertheless, findings across techniques and patient populations are not uniform, making it necessary to interpret their clinical implications in relation to both peripheral and central pain mechanisms.

Although recent literature has expanded understanding of central pain mechanisms, evidence linking central sensitization and broader CNS pain modulation specifically to the clinical response to local anesthesia in dentistry remains fragmented. Studies have addressed central sensitization, trigeminal pain processing, psychological modulation, and anesthetic techniques separately, but their implications for understanding variability in local anesthetic response have not been synthesized comprehensively. This constitutes an important gap because distinguishing the contribution of central pain modulation from peripheral inflammation, anatomical conditions, and anesthetic technique is necessary to avoid interpreting anesthetic failure from a single mechanistic perspective. The novelty of this review lies in integrating evidence on CNS pain mechanisms and central pain modulation with clinical evidence concerning local anesthesia in dentistry, particularly in the context of *symptomatic irreversible pulpitis*.

Therefore, this literature review aims to synthesize recent evidence on central nervous system mechanisms of pain and pain modulation and to examine their clinical implications for the response to local anesthesia in dentistry. The review specifically focuses on three interconnected aspects: CNS mechanisms involved in dental and orofacial pain, mechanisms of central pain modulation, and clinical responses to local anesthesia and related techniques. By integrating these aspects, the review seeks to clarify the extent to which central pain processing may contribute to variations in dental pain and anesthetic response while distinguishing this contribution from established peripheral, anatomical, and technical factors.

RESEARCH METHOD

This study employed a narrative literature review design to synthesize recent evidence on central nervous system mechanisms of pain, central pain modulation, and their clinical implications for the response to local anesthesia in dentistry. Literature searches were conducted through PubMed, Google Scholar, ScienceDirect, and Wiley Online Library, as well as other relevant scientific databases. The search strategy used combinations of keywords related to central pain mechanisms, orofacial and dental pain, local anesthesia, and anesthetic techniques. The keywords included “central sensitization,” “central pain modulation,” “descending pain modulation,” “orofacial pain,” “trigeminal pain,” “neuroinflammation,” “NMDAR and orofacial pain,” “dental pain,” “local anesthesia,” “local anesthetic failure,” “symptomatic irreversible pulpitis,” “intraosseous anesthesia,” and “photobiomodulation and dental injection pain.”

Studies published between 2021 and 2026 were prioritized to emphasize recent evidence relevant to the review objectives. The review included experimental studies, *randomized*



controlled trials, observational studies, *systematic reviews*, *meta-analyses*, and *narrative reviews* that addressed CNS pain mechanisms, central pain modulation, or local anesthesia in dentistry. Studies were excluded when they were unrelated to dental or orofacial pain or did not provide information relevant to the objectives of the review. The selection of literature was based on its relevance to the mechanisms of pain, modulation of nociceptive processing, and clinical response to local anesthesia.

The selected literature was descriptively synthesized and organized into three main themes: central nervous system mechanisms of pain, central pain modulation, and clinical response to local anesthesia in dentistry. Findings were compared according to study design, population or experimental model, mechanism or intervention investigated, and principal findings. Particular attention was given to evidence concerning central sensitization, trigeminal pain pathways, descending pain modulation, and factors associated with local anesthetic effectiveness. Because this study used a narrative review design, no quantitative meta-analysis was performed.

RESULTS DAN DISCUSION

Results

Tabel 1. Literature Study Results

No.	Author	Metode	Result
1.	Rodrigues & Bronzato (2025)	Narrative review of dental local anesthetics, vasoconstrictors, pharmacology, safety and clinical use.	Local anesthetics primarily block voltage-gated sodium channels and interrupt propagation of nociceptive impulses. Tissue condition, anesthetic properties and vasoconstrictors influence clinical effectiveness.
2.	Peron et al. (2026)	Systematic review and meta-analysis of photobiomodulation (PBMT) before local anesthesia in children.	PBMT produced a moderate reduction in injection pain versus placebo and a larger reduction versus topical anesthetic gel, although evidence remains limited and protocols are heterogeneous.
3.	AlRaddadi et al. (2025)	Split-mouth randomized controlled trial of 33 children aged 4–9 years comparing buccal infiltration and intraosseous anesthesia with QuickSleeper 5®..	Pain perception and pain-related behavior did not differ significantly between techniques, while intraosseous anesthesia was significantly faster.



4.	Dobariya et al. (2025)	Narrative review of pharmacological, non-pharmacological and integrative approaches to dental/endodontic pain.	Dental pain reflects interacting peripheral and central mechanisms. The review discusses GABAergic signaling, substance P, inflammatory mediators, local anesthetics and multimodal pain control.
5.	Korczyńska et al. (2022)	Review of the pathophysiology of post-traumatic trigeminal neuropathic pain.	Persistent orofacial neuropathic pain involves interacting peripheral and central processes after trigeminal nerve injury, with neuroplastic changes contributing to symptom persistence.
6.	Gupta et al. (2022)	Systematic review and meta-analysis of supplemental intraligamentary injection after inferior alveolar nerve block in mandibular teeth with symptomatic irreversible pulpitis.	Supplemental intraligamentary anesthesia can improve anesthetic success when conventional inferior alveolar nerve block is inadequate in symptomatic irreversible pulpitis.
7.	Vatankhah et al. (2024)	Randomized controlled trial comparing primary intraosseous injection using the QuickSleeper device with inferior alveolar nerve block using 4% articaine in mandibular first molars with symptomatic irreversible pulpitis	The study evaluated primary and supplementary anesthesia and demonstrates the clinical challenge of achieving profound anesthesia in symptomatic irreversible pulpitis.
8.	Liu et al. (2022)	Review of N-methyl-D-aspartate receptors (NMDARs) in peripheral and central sensitization associated with chronic orofacial pain.	NMDAR activation contributes to enhanced synaptic transmission and sensitization, providing a mechanistic link between persistent nociceptive input and chronic orofacial pain.
9.	Neal & Zuniga (2022)	Perspective/review of post-traumatic trigeminal	Pain severity, timing of treatment and psychological/clinical factors



	neuropathic pain and factors affecting surgical outcomes.	influence outcomes, illustrating the importance of central and patient-level modulation of pain.
10. Calixtre et al. (2024)	Cross-sectional telehealth study of central sensitization in painful temporomandibular disorders.	Central sensitization was associated with painful TMD, but the association was confounded by migraine, depressive symptoms, widespread pain and parafunctional oral habits.
11. Seweryn et al. (2024)	Prospective observational study of central sensitization and somatization in adults with TMD.	Central sensitization and somatization are relevant to the clinical presentation of TMD and chronic masticatory muscle pain, supporting altered central pain processing.
12. Gonçalves et al. (2024)	Prospective observational study of anxiety, patient characteristics and pain during oral surgery under local anesthesia.	Anxiety and patient characteristics can influence pain outcomes and complicate measurement of the relationship between psychological state and procedural pain.
13. Zhang et al. (2024)	Clinical study of dental anxiety and vital-sign responses during tooth extraction.	Dental anxiety is associated with physiological responses during extraction; management of anxiety is therefore relevant to the overall pain experience during local anesthesia and dental surgery.
14. Prol Castelo et al. (2023)	Randomized controlled split-mouth trial comparing intraligamentary and intraosseous computer-controlled anesthetic delivery with conventional inferior alveolar nerve block in 100 children.	Computer-controlled techniques provided alternative approaches to local anesthesia; pain, behavior, need for reinforcement and procedural outcomes were evaluated, supporting individualized anesthetic delivery.



15.	Smolarek et al. (2021)	Randomized clinical trial comparing distinct local dental anesthesia techniques in children aged 9–12 years.	Different anesthetic techniques produced differences in self-reported pain, with conventional anesthesia showing lower pain scores; however, no significant differences were observed in disruptive behavior, anxiety, or physiological parameters.
16.	Hamouda et al. (2024)	Randomized controlled trial evaluating laser photobiomodulation as pre-anesthetic tissue management in children.	Pre-anesthetic PBMT was investigated as a method for reducing injection pain and improving the local-anesthetic experience in pediatric dental treatment.
17.	Seraj et al. (2023)	Double-blind randomized controlled clinical trial of 810-nm diode PBMT and dental injection pain in children.	PBMT was investigated as an adjunct to topical anesthesia for infiltration and supports the potential of non-pharmacological pain modulation during injection.
18.	AmruthaVarshini et al. (2021)	Clinical study comparing pre-cooling, laser biostimulation and topical anesthetic gel for injection pain in children.	Pre-injection interventions can modify pain perception, supporting a multimodal approach to reducing discomfort associated with local anesthetic administration.

The 18 studies reviewed showed that the evidence could be grouped into three major patterns: central pain mechanisms, clinical response to local anesthesia, and interventions aimed at improving anesthetic outcomes or reducing procedural pain. Studies addressing central pain mechanisms consistently described the involvement of neuroplasticity, central sensitization, trigeminal pathways, and altered nociceptive processing in persistent orofacial pain. In contrast, studies examining local anesthesia primarily focused on the influence of tissue condition, pulpal inflammation, anesthetic technique, and patient-related factors on pain and anesthetic success. The literature therefore demonstrated that dental pain and anesthetic response were addressed from both mechanistic and clinical perspectives.

The findings concerning central pain processing showed a relatively consistent association between altered central mechanisms and persistent orofacial pain. Liu et al. (2022) reported the involvement of *N-methyl-D-aspartate* receptors in peripheral and central sensitization, while Korczeniewska et al. (2022) described interactions between peripheral and



central mechanisms in post-traumatic trigeminal neuropathic pain. Similar patterns were observed in studies of TMD, in which central sensitization and somatization were associated with painful clinical presentations (Calixtre et al., 2024; Seweryn et al., 2024). However, the findings were not entirely independent of other factors. Calixtre et al. (2024), for example, found that the relationship between central sensitization and painful TMD was influenced by migraine, depressive symptoms, widespread pain, and parafunctional oral habits. These findings indicate that central pain processing appeared repeatedly across the reviewed literature, but its clinical expression varied according to the population and accompanying factors.

Studies concerning local anesthesia showed that anesthetic response was influenced by multiple clinical factors rather than by a single mechanism. Rodrigues and Bronzato (2025) identified tissue condition, anesthetic properties, and vasoconstrictors as factors related to anesthetic effectiveness. In patients with *symptomatic irreversible pulpitis*, Gupta et al. (2022) reported improved anesthetic success with supplemental intraligamentary anesthesia when inferior alveolar nerve block was inadequate, whereas Vatankhah et al. (2024) examined intraosseous and inferior alveolar nerve block approaches in the same clinical condition and highlighted the difficulty of achieving profound anesthesia. The findings from these studies were consistent in demonstrating challenges in anesthetic management of *symptomatic irreversible pulpitis*, although the effectiveness of individual techniques differed. Psychological and patient-related factors were also identified in studies by Gonçalves et al. (2024) and Zhang et al. (2024), which reported associations between anxiety, patient characteristics, physiological responses, and procedural pain.

The studies evaluating supplemental and alternative techniques demonstrated varying outcomes. AlRaddadi et al. (2025) found no significant difference in pain perception or pain-related behavior between buccal infiltration and intraosseous anesthesia, although intraosseous anesthesia was significantly faster. Prol Castelo et al. (2023) similarly evaluated computer-controlled intraligamentary and intraosseous anesthesia as alternatives to conventional inferior alveolar nerve block, with outcomes involving pain, behavior, reinforcement requirements, and procedural variables. In studies of photobiomodulation, Peron et al. (2026) reported a reduction in injection pain compared with placebo and topical anesthetic gel, while Hamouda et al. (2024), Seraj et al. (2023), and AmruthaVarshini et al. (2021) investigated photobiomodulation, laser biostimulation, or pre-cooling as approaches for modifying injection-related pain. However, the magnitude and consistency of these effects varied across interventions and study populations.

Overall, the reviewed literature demonstrated a recurring pattern in which dental and orofacial pain involved interactions between peripheral nociceptive mechanisms, central pain processing, and patient-related factors. Evidence for central sensitization was more prominent in studies of chronic or persistent orofacial pain and TMD, whereas evidence concerning local anesthetic response was primarily associated with inflammatory or pulpal conditions, anatomical considerations, anesthetic techniques, and psychological factors. Supplemental anesthetic techniques and non-pharmacological interventions also showed potential to modify procedural pain or anesthetic outcomes, although their effects were not uniform across studies. Importantly, the reviewed studies did not provide sufficient direct evidence to establish central sensitization as an independent cause of local anesthetic failure in dentistry.

Discussion

The findings synthesized in this review indicate that dental pain is a multidimensional process involving interactions between peripheral nociceptive input and central neural





processing. Rodrigues and Bronzato (2025) describe local anesthetics as agents that primarily inhibit voltage-gated sodium channels and interrupt action-potential propagation in sensory nerves. However, this peripheral blockade does not fully explain individual differences in the experience of dental pain. Dobariya et al. (2025) emphasize that dental pain involves interactions among peripheral nociception, central pain pathways, inflammatory mediators, neurotransmitters, and patient-related factors. These findings indicate that the clinical experience of pain depends not only on whether nociceptive signals are generated at the site of stimulation but also on how those signals are processed and modulated within the nervous system.

One mechanism that may contribute to increased pain responsiveness is central sensitization. Liu et al. (2022) reported that *N-methyl-D-aspartate* receptors (NMDARs) participate in peripheral and central sensitization associated with chronic orofacial pain. Increased NMDAR-mediated excitatory transmission may facilitate synaptic plasticity within trigeminal pain pathways, thereby increasing neuronal responsiveness to subsequent nociceptive input. This mechanism provides a biological explanation for why persistent nociceptive stimulation may be accompanied by pain responses that exceed the intensity expected from the initial peripheral stimulus. Nevertheless, the presence of a central sensitization mechanism does not necessarily indicate that ongoing tissue injury is absent, because peripheral and central processes can coexist.

Evidence from trigeminal neuropathic pain and TMD further supports the involvement of altered central processing while demonstrating that this process should not be considered independently of other clinical factors. Korczeniewska et al. (2022) described post-traumatic trigeminal neuropathic pain as involving both peripheral nerve injury and subsequent neuroplastic changes, while Neal and Zuniga (2022) highlighted the influence of clinical and patient-related factors on treatment outcomes. In patients with painful TMD, Calixtre et al. (2024) found that the association between central sensitization and pain was influenced by migraine, depressive symptoms, widespread pain, and parafunctional oral habits. Seweryn et al. (2024) likewise identified central sensitization and somatization as relevant to the clinical presentation of TMD. Taken together, these findings support a multifactorial interpretation in which central sensitization represents one component of altered pain processing rather than an isolated explanation for persistent orofacial pain.

This distinction is particularly important when interpreting local-anesthetic response in *symptomatic irreversible pulpitis*. Gupta et al. (2022) reported that supplemental intraligamentary injection can improve anesthetic success after an inadequate inferior alveolar nerve block, whereas Vatankhah et al. (2024) examined alternative injection strategies in mandibular molars affected by *symptomatic irreversible pulpitis*. The difficulty in achieving profound anesthesia in this condition can be understood in relation to the interaction between inflammatory tissue changes, increased nociceptive activity, anatomical factors, and limitations of the anesthetic technique. Central pain processing may further influence the subjective intensity of pain once nociceptive input reaches the central nervous system. However, the reviewed evidence does not establish central sensitization as an independent or direct cause of local-anesthetic failure.

The pharmacological mechanism of local anesthesia provides an important basis for understanding this distinction. Rodrigues and Bronzato (2025) explain that local anesthetics inhibit voltage-gated sodium channels and consequently prevent the generation and propagation of action potentials in peripheral nerves. When this blockade is incomplete, however, residual nociceptive input may still reach the central nervous system. In patients with increased pain





responsiveness, the same peripheral input may consequently be experienced differently from that in patients without altered pain processing. Thus, persistent pain during a dental procedure should be evaluated through several possible sources, including inadequate neural blockade, tissue inflammation, anatomical variation, injection technique, and individual differences in pain processing, rather than being attributed automatically to psychological or central mechanisms.

The choice of anesthetic delivery technique also has implications for clinical pain management. AlRaddadi et al. (2025) found no significant differences in pain perception or pain-related behavior between buccal infiltration and intraosseous anesthesia in children, although intraosseous anesthesia was significantly faster. Prol Castelo et al. (2023) similarly investigated computer-controlled intraligamentary and intraosseous delivery as alternatives to conventional inferior alveolar nerve block. The findings suggest that alternative delivery systems may provide useful options when conventional approaches are insufficient or when procedural efficiency is an important consideration. However, their clinical value should be interpreted in relation to the specific patient, procedure, and outcome being considered rather than assumed to reflect superior modulation of central pain processing.

Psychological factors provide another pathway through which central processing may influence the dental pain experience. Gonçalves et al. (2024) reported that anxiety and patient characteristics influenced pain outcomes during oral surgery under local anesthesia, while Zhang et al. (2024) found an association between dental anxiety and physiological responses during tooth extraction. Smolarek et al. (2021) also observed differences in self-reported pain across anesthetic techniques in children, although behavioral and physiological outcomes did not consistently differ. These findings suggest that subjective pain intensity, behavioral responses, and physiological arousal do not necessarily represent identical dimensions of the pain experience. Accordingly, anxiety management, communication, and behavioral support may complement pharmacological anesthesia by addressing factors that influence how patients anticipate, perceive, and respond to dental procedures.

The reviewed evidence also supports the potential role of multimodal strategies for reducing injection-related pain. Peron et al. (2026) reported that *photobiomodulation therapy* (PBMT) was associated with reduced injection pain compared with placebo, although the authors identified heterogeneity and methodological limitations across the available studies. Hamouda et al. (2024) investigated PBMT as a pre-anesthetic intervention, whereas Seraj et al. (2023) examined 810-nm PBMT in combination with topical anesthesia and did not demonstrate a consistent additional benefit. AmruthaVarshini et al. (2021) similarly showed that pre-injection interventions such as cooling may influence injection-related pain. The differences among these findings indicate that the effectiveness of adjunctive interventions may depend on the protocol, comparator, patient population, and clinical setting. Therefore, PBMT and other adjunctive approaches are more appropriately considered complementary strategies for improving procedural comfort rather than replacements for adequate local anesthetic blockade.

Overall, the reviewed evidence suggests that the relationship between central pain modulation and local anesthesia is complex and cannot be reduced to a direct causal relationship between central sensitization and anesthetic failure. Central sensitization and neuroplasticity provide plausible mechanisms for increased and persistent pain responses, particularly in chronic orofacial pain conditions, but the clinical response to local anesthesia remains strongly influenced by peripheral inflammation, tissue condition, anatomical factors, anesthetic technique, and patient-related characteristics. The main implication of these findings is the need





for a multidimensional approach to dental pain management that combines effective peripheral neural blockade with appropriate supplemental techniques and consideration of individual pain-related factors. At the same time, the limited direct evidence connecting central sensitization specifically to local-anesthetic failure indicates a need for further clinical research that simultaneously evaluates central pain characteristics, pulpal or inflammatory status, anesthetic technique, and patient-reported pain outcomes.

CONCLUSION

This literature review concludes that central nervous system mechanisms, including central sensitization, neuroplasticity, trigeminal pain processing, and excitatory neurotransmission, contribute to the modulation and persistence of dental and orofacial pain. Central pain processing can influence individual variations in pain perception and may interact with peripheral factors in determining the clinical experience of dental pain. In relation to local anesthesia, however, the reviewed evidence indicates that anesthetic response is multifactorial and is influenced by peripheral inflammation, tissue conditions, anatomical factors, anesthetic technique, and individual pain characteristics. Thus, central sensitization may contribute to the amplification of pain perception but cannot currently be established as a direct cause of local anesthetic failure. These findings answer the review objective by demonstrating that CNS pain modulation is clinically relevant to variations in dental pain and anesthetic response, while its specific contribution to anesthetic failure remains insufficiently established.

Clinically, these findings support a multidimensional approach to dental pain management that combines effective peripheral neural blockade with appropriate anesthetic techniques and consideration of individual pain-related factors. Supplemental approaches such as intraosseous or computer-controlled anesthesia and photobiomodulation may be considered according to clinical needs, although their effectiveness varies across patient populations and treatment settings. Future research should directly examine the relationship between central pain sensitivity and local anesthetic success by integrating validated measures of central sensitization with clinical assessments of pulpal status, anesthetic efficacy, and patient-reported pain outcomes.

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