Review

The Mechanism and Clinical Application of Transcutaneous Electrical Nerve Stimulation in The Treatment of Neuropathological Pain after Spinal Cord Injury

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Abstract: Transcutaneous electrical nerve stimulation (TENS), functioning as a prominent non-invasive neuromodulation technique, has been widely utilized as a critical adjuvant treatment for managing neuropathic pain (NP) following spinal cord injury (SCI). This article systematically reviews the underlying physiological mechanisms of TENS in alleviating NP after SCI, alongside its recent clinical application progress. Extensive studies have demonstrated that the profound analgesic effect of TENS may be intricately linked to the activation of thick myelinated Aβ fibers, which subsequently enhances the segmental inhibition of the spinal cord. Furthermore, TENS is implicated in promoting the release of endogenous opioids, regulating the descending pain inhibition pathways, significantly reducing central sensitization, and modulating complex neuroimmune responses within the central nervous system. In terms of clinical application, empirical evidence indicates that both high-frequency and low-frequency TENS modalities can substantially reduce the intensity of NP after SCI, thereby markedly improving the overall quality of life for affected patients. Despite these promising outcomes, notable individual differences in therapeutic efficacy persist, and the optimal stimulation parameters and standardized intervention protocols have yet to be universally established. The existing body of evidence firmly supports TENS as a safe, accessible, and highly effective non-pharmacological option for treating NP after SCI. Nevertheless, comprehensive, large-sample, high-quality, and long-term follow-up clinical trials are still urgently required to further optimize targeted treatment strategies and to fully elucidate the underlying neuroplasticity mechanisms driving long-term pain relief.

Keywords: neuromodulation; spinal cord injury; neuropathic pain; electrical stimulation; pain management; analgesia

Received: 31 March 2026
Revised: 21 May 2026
Accepted: 05 June 2026
Published: 12 June 2026

1. Introduction

Pain is one of the most common and challenging complications following spinal cord injury (SCI), particularly neuropathic pain (NP). This type of pain not only causes persistent physical discomfort for patients but also significantly impacts their sleep quality, emotional well-being, daily functional abilities, and participation in rehabilitation programs. Furthermore, it may elevate the likelihood of psychological challenges, such as emotional distress and mood disturbances. The mechanisms underlying NP after SCI are intricate, and effective clinical management remains a significant challenge. Currently, pharmacological therapy is the primary approach for treatment. In addition, non-pharmacological methods, including physical therapies, psychological support, and lifestyle adjustments, have increasingly become integral components of comprehensive treatment strategies. Clinical observations suggest that combining self-management techniques with both pharmacological and non-pharmacological interventions offers the most effective approach to managing NP after SCI. Transcutaneous electrical nerve stimulation (TENS) is a non-invasive physical therapy technique that delivers electrical pulses of specific frequencies, pulse widths, and intensities to peripheral nerves or pain-related areas through electrodes placed on the skin. This method aims to achieve pain relief. In recent years, research on the application of TENS for NP after SCI has grown, with some randomized controlled studies indicating its potential to reduce pain intensity and improve patients' subjective pain experiences. However, the exact mechanisms by which TENS alleviates NP after SCI remain inconclusive. This article reviews existing research on the use of TENS for NP management in SCI patients, focusing on its analgesic mechanisms, current clinical applications, optimal stimulation parameters, safety considerations, and existing challenges [1, 2]. The goal is to provide a reference for the rational application of TENS and to guide future research in the rehabilitation of NP following SCI.

2. Mechanism of Action of TENS in the Treatment of NP After SCI

The development of neuropathic pain (NP) following spinal cord injury (SCI) is a complex process involving multiple interconnected mechanisms. These include disruptions in peripheral nerve signaling, heightened excitability within the spinal cord at the segmental level, central sensitization, alterations in descending pathways responsible for pain modulation, and changes in neural plasticity. Transcutaneous electrical nerve stimulation (TENS), as a non-invasive physical therapy, achieves its analgesic effects not through a singular pathway but by engaging multiple mechanisms [3–5]. These mechanisms span peripheral, spinal, and central levels, collectively modulating the transmission and perception of pain signals in a multifaceted manner.

2.1. Gate Control Theory and Spinal Segmental Depression

The gate control theory is a foundational concept used to explain the analgesic effects of transcutaneous electrical nerve stimulation (TENS). This theory posits that pain signals can be modulated by nonnociceptive sensory inputs at the spinal dorsal horn level. When TENS is applied to stimulate sensory nerves on the skin, it preferentially activates thick myelinated Aβ fibers, which enhance nonnociceptive sensory input. Upon entering the dorsal horn of the spinal cord, these Aβ fiber impulses activate inhibitory interneurons, suppressing nociceptive signals transmitted by Aδ fibers and C fibers. This suppression reduces the transmission of pain signals to the spinothalamic tract and higher brain centers. By stimulating areas surrounding the pain site, related dermatos, or residual sensory regions, TENS may enhance the spinal cord's local inhibitory functions and decrease abnormal excitability of dorsal horn neurons, thereby alleviating pain perception. For individuals experiencing pain or partial sensory preservation near the injury level, the segmental inhibition of the spinal cord plays a significant role in the analgesic effects of TENS. This mechanism underscores the importance of targeted stimulation in managing localized pain and highlights the physiological basis for its therapeutic application.

2.2. Activation of the Endogenous Opioid System

The analgesic effect of TENS is believed to be intricately linked to the activation of the endogenous opioid system, a critical component of the body's natural pain management mechanisms. Through TENS stimulation, the release of endogenous opioids such as endorphins, enkephalins, and dynorphins may be facilitated. These substances interact with opioid receptors located in the central nervous system, effectively inhibiting the transmission of pain signals. The frequency of TENS stimulation plays a significant role in determining the specific pathways activated [6–8]. Low-frequency TENS is generally associated with the activation of mechanisms linked to μ-opioid receptors, while high-frequency TENS is thought to primarily engage δ-opioid receptor-related pathways. Both frequencies contribute to analgesia by modulating pain-inhibitory systems at the spinal cord and brainstem levels. In cases of neuropathic pain following spinal cord injury, chronic pain often results in heightened neuronal excitability and a compromised endogenous pain control system. By stimulating the endogenous opioid system, TENS may partially restore the body's natural ability to manage pain, thereby reducing the intensity of chronic pain and improving overall pain regulation.

2.3. Regulation of the Descending Pain Inhibitory Pathway

Pain perception is influenced not only by peripheral and spinal cord mechanisms but also by higher brainstem and cortical centers, which play a critical role in modulating pain signals. The descending pain modulation system encompasses key structures such as the periaqueductal gray in the midbrain, the rostral ventromedial medulla, the locus coeruleus, and the spinal dorsal horn [9, 10]. These structures interact through various neurotransmitters, including serotonin, norepinephrine, gamma-aminobutyric acid (GABA), and endogenous opioids, to regulate pain transmission. Under typical physiological conditions, this system suppresses nociceptive signals by modulating the activity of spinal dorsal horn neurons. However, after spinal cord injury (SCI), significant neuroplastic changes can occur in both ascending and descending pain pathways. These changes often result in weakened inhibitory mechanisms and heightened facilitation of pain signals, leading to persistent pain amplification and diminished modulation capacity. Interventions such as transcutaneous electrical nerve stimulation (TENS) have been shown to enhance the activity of descending pain-inhibitory pathways. This method likely improves central control over pain signals by engaging structures such as the periaqueductal gray, rostral ventromedial medulla, and spinal dorsal horn, as well as neurotransmitter systems like endogenous opioids, serotonin, and norepinephrine [11–13]. Such mechanisms underline the potential of TENS in managing chronic pain conditions effectively.

2.4. Inhibition of Central Sensitization

Central sensitization represents a pivotal mechanism contributing to the persistence of neuropathic pain following spinal cord injury. This phenomenon occurs when dorsal horn neurons in the spinal cord exhibit heightened responsiveness to both harmful and harmless stimuli. These neurons develop lowered excitation thresholds and expanded receptive fields, resulting in significant pain responses even to mild stimulation, a condition clinically observed as allodynia and hyperalgesia. The underlying processes of central sensitization involve a complex interplay of neurochemical and cellular changes, including increased release of excitatory neurotransmitters such as glutamate, activation of N-methyl-D-aspartate receptors, elevated calcium influx into neurons, diminished efficacy of inhibitory neurotransmitter systems, and intensified neuroinflammatory activity. One potential therapeutic approach to mitigate these effects is transcutaneous electrical nerve stimulation (TENS). By modulating peripheral sensory input and influencing the activity of spinal dorsal horn neurons, TENS can attenuate the exaggerated central nervous system responses to pain. When applied at appropriate intensities, TENS may enhance non-painful sensory signals, suppress abnormally amplified pain pathways, and reduce the release of excitatory neurotransmitters, thereby promoting improved inhibitory neural regulation and offering potential relief from neuropathic pain.

2.5. Regulation at the Level of Neurotransmitters and Receptors

The analgesic effect of TENS may also be associated with changes in the expression of various neurotransmitters and receptors. In a painful state, the release of excitatory neurotransmitters such as glutamate, substance P, and calcitonin gene-related peptide increases, which amplifies the transmission of pain signals. Concurrently, the dysfunction of inhibitory neurotransmitters, including γ-aminobutyric acid (GABA), glycine, serotonin, and norepinephrine, may reduce the body's natural ability to suppress pain. By influencing these neurotransmitter systems, TENS has the potential to decrease the excitability of pain pathways while simultaneously enhancing inhibitory mechanisms. Additionally, TENS may modulate the activity of specific receptors, such as opioid receptors, NMDA receptors, adrenergic receptors, and serotonin receptors, which play critical roles in pain perception and modulation. Variations in stimulation parameters, including frequency, pulse width, and intensity, can lead to distinct neurochemical responses, offering an explanation for the differing clinical outcomes observed with various TENS settings. This highlights the importance of optimizing TENS parameters to achieve maximum therapeutic efficacy [14–16].

2.6. Regulation of Glial Cell Activation and Neuroinflammatory Responses

Recent studies indicate that neuroinflammation and the activation of glial cells are critical factors in the progression and persistence of neuropathic pain (NP) following spinal cord injury (SCI). After SCI, microglia and astrocytes become activated, releasing various inflammatory mediators, including interleukins, tumor necrosis factor-α, and prostaglandins [17–19]. These mediators contribute to heightened neuronal excitability and the development of central sensitization, which are key mechanisms underlying chronic pain. Persistent inflammation can exacerbate this condition, leading to pain that is difficult to manage. Transcutaneous electrical nerve stimulation (TENS) has been shown to potentially alleviate pain by modulating neuroimmune responses, reducing the release of inflammatory mediators, and mitigating excessive glial activation. Although clinical evidence directly linking TENS to the regulation of neuroinflammation after SCI remains limited, foundational research suggests that electrical stimulation may have a broad impact on inflammatory responses, neurotransmitter dynamics, and neural network activity. These findings highlight the potential of TENS as a therapeutic approach for addressing the complex interplay of factors involved in NP.

In summary, the mechanisms through which TENS alleviates neuropathic pain (NP) following spinal cord injury (SCI) are diverse and involve multiple pathways. These include the activation of Aβ fibers, enhancement of segmental spinal inhibition, facilitation of endogenous opioid system activity, modulation of descending pain inhibitory pathways, reduction of central sensitization, adjustment of neurotransmitter and receptor functions, and improvement of neuroinflammatory responses. Given the intricate nature of NP pathophysiology after SCI, no single mechanism can fully explain the clinical effectiveness of TENS. Future research should focus on integrating objective methodologies such as neuroelectrophysiology, quantitative sensory testing, functional imaging, and analysis of inflammatory markers. This approach will help clarify the specific mechanisms of TENS under varying stimulation parameters, pain types, and injury characteristics. Such insights are essential for developing tailored clinical treatment strategies that address the unique needs of individual patients.

3. Clinical Advances in the Application of TENS for NP Following SCI

In recent years, the application of transcutaneous electrical nerve stimulation (TENS) in managing pain following spinal cord injury (SCI) has garnered increasing attention within the medical community. Neuropathic pain (NP) associated with SCI is often chronic, difficult to treat, and prone to recurrence, making it a significant challenge for both patients and healthcare providers. Pharmacological treatments, while commonly employed, frequently fail to deliver satisfactory relief due to limitations such as side effects and variable efficacy. Consequently, TENS has emerged as a promising non-invasive physical therapy that can complement traditional pharmacological approaches. Despite its potential, the clinical application of TENS remains hindered by a lack of standardized protocols, as existing studies vary widely in terms of patient demographics, stimulation parameters, treatment durations, and outcome assessment methods. Further research is essential to establish evidence-based guidelines for its optimal use.

3.1. Current Status of Clinical Research

Early studies examining transcutaneous electrical nerve stimulation (TENS) for neuropathic pain (NP) following spinal cord injury (SCI) primarily consisted of small-scale clinical trials or exploratory investigations. These studies often involved participants who were SCI patients experiencing chronic NP, with pain manifesting at the injury level, below the injury level, or across mixed distribution areas. The methodologies typically included the application of surface electrode stimulation around the painful region, over the corresponding dermatome, or on residual sensory areas. Comparisons were made against sham stimulation, conventional treatments, or pharmacological approaches. Pain intensity and subjective pain experiences were assessed using tools such as visual analog scales, numerical rating scales, or standardized pain questionnaires. Some randomized controlled trials suggested that TENS could moderately alleviate pain scores in individuals with post-SCI NP. Low-frequency TENS has been explored in several studies, indicating potential efficacy in reducing pain compared to sham stimulation and highlighting its role as a complementary option alongside medication. Additionally, longer-term TENS interventions have been employed to evaluate their effects on pain intensity, with findings showing reductions in patient-reported pain levels following treatment. Despite these promising results, the overall conclusions remain inconsistent due to limitations such as small sample sizes, variability in stimulation parameters, insufficient follow-up durations, and inadequate assessments of quality of life. Further research with larger cohorts and standardized methodologies is necessary to establish more definitive evidence regarding the clinical utility of TENS in managing post-SCI NP.

3.2. Characteristics of TENS Application in NP Following Different Types of SCI

After spinal cord injury (SCI), neuropathic pain (NP) can be categorized into three distinct types based on the spatial relationship between the pain location and the injured spinal segment: pain occurring at the injury level, pain manifesting below the injury level, and other forms of NP. These classifications are significant because the underlying mechanisms and the status of preserved neural pathways vary among these types, which may influence the effectiveness of transcutaneous electrical nerve stimulation (TENS). Pain at the injury level is typically localized near the site of nerve damage and is often associated with factors such as root injury, ectopic discharges from local neurons, heightened excitability in the spinal dorsal horn, and abnormal input from peripheral sensory afferents. Conversely, pain below the injury level generally arises in regions characterized by sensory hypoesthesia or anesthesia [20, 21]. This type of pain is more closely linked to central sensitization, maladaptive changes in the spinothalamic pathway, disruptions in descending pain modulation systems, and alterations in central nervous system plasticity. In clinical applications, the placement of electrodes for TENS should be tailored to the individual patient, taking into account the distribution of pain, corresponding dermatomes, preserved sensory areas, and regions where the patient can perceive stimulation effectively.

3.3. Clinical Applications of Stimulation Parameters

The clinical efficacy of TENS is intricately linked to various stimulation parameters, including frequency, pulse width, intensity, treatment duration, therapy course, and electrode placement. Despite its widespread use, there is currently no universally accepted protocol for TENS parameters in managing neuropathic pain following spinal cord injury. This lack of standardization contributes to inconsistencies in research findings and clinical outcomes. Frequency selection plays a pivotal role, with both low-frequency and high-frequency TENS being utilized. Low-frequency TENS typically involves lower frequencies combined with higher stimulation intensities, which may induce slight muscle contractions. In contrast, high-frequency TENS employs stimulation levels above the sensory threshold but below the motor threshold. Clinicians emphasize adjusting the intensity to achieve a sensation that is "strong but not painful" or "noticeable yet comfortable," as insufficient intensity may diminish the analgesic effects. Treatment sessions generally last around 30 minutes, with therapy courses ranging from 10 days to several weeks, although these parameters can vary significantly. Prolonged use of fixed parameters may lead to analgesic tolerance, necessitating periodic adjustments to frequency, intensity, or stimulation mode based on the patient’s therapeutic response. Electrode placement is another critical determinant of TENS effectiveness. For optimal results, electrodes should be positioned individually, taking into account the specific pain area, associated nerve pathways, dermatomal distribution, and regions where TENS sensations can be effectively elicited. This individualized approach ensures that the therapy is tailored to the unique needs of each patient, thereby enhancing its clinical efficacy [22–24].

3.4. Combined Application with Drug Therapy and Comprehensive Rehabilitation

Currently, TENS is more widely regarded as an adjunctive therapy for neuropathic pain following spinal cord injury, rather than a complete substitute for pharmacological treatment. For patients experiencing moderate to severe neuropathic pain, TENS alone may not provide sufficient pain relief. Therefore, combining it with medications, physical therapy, psychological support, sleep optimization, and health education can better address clinical needs [25–27]. Medications typically function by influencing neurotransmitter release, reducing neuronal excitability, or enhancing pain modulation, while TENS achieves its analgesic effects through mechanisms such as peripheral sensory input, segmental spinal inhibition, and central pain modulation. Due to these distinct mechanisms of action, the integration of both approaches may yield complementary benefits. For individuals who do not respond well to medications, cannot tolerate high doses, or aim to reduce dependency on drugs, TENS can serve as a valuable adjunctive strategy to alleviate pain intensity or minimize medication-related side effects. In the context of rehabilitation, effective pain management is essential for enabling functional training. Neuropathic pain following spinal cord injury can significantly impact a patient's mood, sleep quality, functional participation, and overall quality of life. Consequently, the application of TENS should extend beyond merely reducing pain scores to encompass its broader influence on functional activity, rehabilitation adherence, and overall patient well-being. This holistic approach ensures that pain management contributes meaningfully to the patient's recovery and long-term health outcomes.

4. Current Issues and Future Research Directions

Although existing research suggests that TENS holds some potential for managing neuropathic pain (NP) after spinal cord injury (SCI), the evidence remains limited [28–30]. The number of clinical studies in this field is relatively small, with generally modest sample sizes, and variations across studies in stimulation parameters, treatment duration, and outcome measures have compromised the generalizability and comparability of results [31–33]. Additionally, implementing sham stimulation controls and blinding in TENS trials presents certain challenges; establishing a credible sham device is a key methodological issue to minimize placebo effects and reduce evaluation bias [34–36]. Currently, there is no standardized protocol for TENS treatment parameters, with significant differences among studies regarding stimulation frequency, pulse width, intensity, treatment duration, session frequency, course length, and electrode placement [24, 34]. Therefore, future research should further investigate differences in efficacy among various stimulation parameters and explore dose-response relationships [8]. In terms of outcome assessment, NP following SCI is often accompanied by reduced functional participation, emotional strain, sleep-related issues, and decreased quality of life [11]. Thus, treatment evaluation should not be limited to pain intensity alone but should also consider comprehensive outcomes such as mood, function, quality of life, potential adverse effects, and treatment adherence [10]. From a clinical perspective, TENS is better suited as an adjunctive therapy within a multimodal pain management approach [2]. Future studies could further examine its effectiveness when combined with pharmacological treatments, physical therapy, psychological methods, and other neuromodulation techniques [10, 27]. Additionally, exploring innovative strategies to optimize treatment protocols and improve patient adherence could significantly enhance the clinical utility of TENS in managing NP [8, 25].

5. Conclusion

In summary, TENS, as a non-invasive, easy-to-use, and relatively safe physical therapy, demonstrates meaningful potential as an adjunctive approach for the management of neuropathic pain (NP) following spinal cord injury (SCI). Its analgesic effects may be related to several physiological mechanisms, including activation of Aβ fibers, enhancement of segmental spinal inhibition, facilitation of endogenous opioid system activity, modulation of descending pain inhibitory pathways, reduction of central sensitization, and improvement of neuroinflammatory status. Current clinical findings indicate that TENS may contribute to reductions in pain intensity in SCI patients with NP, while also improving subjective pain perception, treatment tolerance, and participation in rehabilitation programs. Nevertheless, the overall evidence base remains limited by heterogeneity in stimulation parameters, treatment duration, patient characteristics, and outcome assessment methods. Future research should prioritize rigorous study design, larger sample sizes, longer follow-up periods, and the integration of TENS with pharmacological treatments, exercise therapy, psychological approaches, and other neuromodulation methods to develop more standardized, individualized, and comprehensive pain management strategies.

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