

REVIEW ARTICLE

Mechanisms, Clinical Applications, and Future Directions of Transcutaneous Spinal Cord Stimulation on Spinal Cord Injury Recovery: A Narrative Review.

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DOI: <https://doi.org/10.70672/54a5fs17>

Received: 09/12/2025. Revised: 20/03/2026. Accepted: 01/04/2026. Published online: 01/06/2026.

Abstract

Transcutaneous spinal cord stimulation (TSCS) is an emerging non-invasive approach for spinal cord injury (SCI) rehabilitation. This narrative review synthesizes current evidence on its neurophysiological mechanisms and clinical applications while identifying limitations to its clinical integration. A comprehensive literature search reveals that TSCS can transiently modulate spinal excitability, facilitating improvements in motor control, autonomic regulation, and neuropathic pain. When paired with task-specific physiotherapy, TSCS appears to enhance neuroplasticity and functional recovery. However, the field is hampered by heterogeneity in patient populations, stimulation protocols, and outcome measures, leading to inconsistent therapeutic outcomes. The absence of standardized protocols and robust longitudinal data remains a major barrier. To accelerate clinical adoption, future efforts should focus on multicenter randomized controlled trials, protocol harmonization, and the development of accessible, portable TSCS systems suitable for home and community-based rehabilitation.

Keywords: *Cardiovascular regulation, motor recovery, neuropathic pain, transcutaneous spinal cord stimulation, spinal cord injury (SCI).*



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Introduction

Spinal cord injury (SCI) is a devastating condition that disrupts motor, sensory, and autonomic functions, leading to profound physical, psychological, and socioeconomic consequences for affected individuals and their caregivers [1, 2]. Globally, the incidence of SCI is estimated at 250,000 to 500,000 new cases annually, contributing to substantial long-term burdens on healthcare systems and society [3, 4]. Beyond motor impairments, individuals often experience complications such as spasticity, neuropathic pain, bladder and bowel dysfunction, cardiovascular instability, and respiratory issues. These multifaceted challenges underscore the urgent need for rehabilitation strategies that go beyond symptomatic management to restore neural function and improve quality of life [5-8].

Despite incremental advances in rehabilitative care, conventional interventions such as physical therapy, robotic-assisted training, and task-specific exercise have shown limited efficacy in eliciting meaningful functional recovery, particularly among individuals with chronic or motor-complete SCI [1,9,10]. This therapeutic gap has driven the exploration of neuromodulatory interventions that can re-engage dormant spinal circuits and facilitate neuroplasticity below the level of injury. Among these, transcutaneous spinal cord stimulation (TSCS) has emerged as a non-invasive and cost-effective alternative to epidural spinal cord stimulation (ESCS), with promising applications across motor, autonomic, and sensory domains [11-13].

Nevertheless, critical challenges continue to limit the translation of TSCS from experimental trials to mainstream clinical practice. Patient responses vary considerably, influenced by factors such as injury severity, chronicity, and pre-existing neurological conditions [14,15]. Evidence regarding its effectiveness in individuals with complete SCI remains inconclusive, with some studies reporting minimal functional improvements and others showing no meaningful changes even after prolonged intervention. These inconsistencies highlight the variability of TSCS

outcomes across different patient populations and raise important concerns regarding its universal applicability in SCI rehabilitation.

Furthermore, the lack of standardized stimulation parameters, including frequency, intensity, electrode placement, and duration, complicates comparisons across studies and contributes to inconsistent findings [16]. Most research has focused on short-term outcomes, leaving uncertainty about the durability of neuroplastic changes and long-term functional benefits [17]. In addition, the precise mechanisms by which TSCS modulates central pattern generators (CPGs), propriospinal pathways, and motor circuits remain insufficiently understood, further limiting its clinical translation [18].

Although preliminary studies indicate improvements in motor, autonomic, genitourinary, and respiratory functions, the heterogeneity of methodologies and lack of large-scale randomized controlled trials severely limit the generalizability of current findings [19]. TSCS appears to modulate spinal excitability by activating posterior root afferents and influencing propriospinal networks, yet the overlapping roles of descending pathways and CPGs recruitment require further elucidation [20]. Moreover, while TSCS shares sub-threshold neuromodulatory principles with other non-invasive brain stimulation methods, such as transcranial direct current stimulation (tDCS), clearer biomarkers and dose response models are essential to improve individual responsiveness and minimize variability [21]. Thus, a more unified approach to protocol design, combined with computational modelling and mechanistic research, is necessary for TSCS to evolve into a widely adopted clinical modality.

TSCS has been investigated not only for motor recovery but also for its potential to regulate cardiovascular function and alleviate neuropathic pain. Cardiovascular instability remains a major complication following SCI, especially in high-thoracic and cervical injuries. Emerging evidence suggests that TSCS can influence autonomic pathways, stabilize blood pressure, and modulate

sympathetic activity, offering a promising non-pharmacological approach to managing dysautonomia in this population [22,23]. However, findings are mixed, while several studies support the use of TSCS for autonomic regulation, others caution that stimulation, particularly in individuals with high-thoracic injuries, may exacerbate episodes of autonomic dysreflexia.

This paradoxical response highlights the importance of careful patient selection, individualized stimulation protocols, and close monitoring during intervention [23], whereas others report beneficial effects on cardiovascular regulation, particularly when stimulation is applied at lumbosacral spinal segments [24]. Similarly, the role of TSCS in managing neuropathic pain remains inconclusive, with some studies reporting temporary reductions in pain intensity and spasticity [25], whereas others found no significant differences between active and sham stimulation [26]. Taken together, these findings illustrate a dynamic yet inconclusive landscape of TSCS research, where potential clinical benefits are frequently offset by variability in protocols, unclear mechanisms, and small sample sizes. Given the rapid evolution of TSCS research and its emerging role in neurorehabilitation, a critical synthesis of existing evidence is warranted. Therefore, this narrative review aims to:

- Synthesize current evidence on the neurophysiological mechanisms underlying TSCS in individuals with SCI;
- Review the clinical applications and therapeutic effects of TSCS on motor recovery, cardiovascular or autonomic function, and neuropathic pain;
- Discuss the integration of TSCS with physiotherapy and activity-based rehabilitation approaches in SCI;
- Discuss current limitations, knowledge gaps, and future directions for optimizing the clinical implementation of TSCS.

Methods

A narrative review approach was adopted to synthesize current evidence on the mechanisms, clinical applications, and therapeutic potential of TSCS in individuals with SCI. A comprehensive literature search was conducted exclusively in the Web of Science (WoS) Core Collection, selected for its high-quality indexing of peer-reviewed and high-impact scientific publications. The search was limited to studies published between 2010 and 2025 to capture the most relevant and recent developments in TSCS research. A structured search strategy was applied using combinations of keywords and Boolean operators, including “transcutaneous spinal cord stimulation,” “TSCS,” “spinal cord injury,” “neuromodulation,” “motor recovery,” “autonomic function,” “cardiovascular regulation,” “neuropathic pain,” and “neuroplasticity.”

Studies were included if they (1) investigated the neurophysiological mechanisms of TSCS, (2) reported clinical outcomes such as motor, sensory, autonomic, or pain-related effects, or (3) explored rehabilitation applications of TSCS in individuals with SCI. Both experimental and clinical study designs, including randomized controlled trials, cohort studies, case series, and mechanistic studies, were considered to provide a comprehensive overview of the field. Studies were excluded if they were (1) not published in English, (2) conference abstracts without full-text availability, (3) unrelated to SCI populations, or (4) focused exclusively on invasive neuromodulation techniques (e.g., epidural spinal cord stimulation) without relevance to TSCS.

Given the narrative nature of this review, no formal risk-of-bias assessment or meta-analysis was conducted. Instead, the selected studies were critically analyzed and synthesized to identify key mechanisms, clinical outcomes, and research gaps. This approach allows for an integrative interpretation of findings while accommodating heterogeneity in study designs, stimulation protocols, and outcome measures.

Transcutaneous Spinal Cord Stimulation (TSCS)

Mechanism of TSCS

Neuromodulation techniques have emerged as promising interventions to enhance motor, sensory, and autonomic functions in individuals with SCI [13, 27]. TSCS has gained considerable attention due to its non-invasive nature and its potential to reactivate dormant spinal networks below the level of injury [13]. This section discusses the fundamental principles of TSCS's mechanism of action, its neurophysiological effects, its interaction with spinal neural circuits, and how it differs from ESCS.

TSCS shows promise in modulating spinal networks but faces translation barriers due to inconsistent protocols and unclear mechanisms [19]. Compared to transcranial methods like transcranial tDCS and repetitive transcranial magnetic stimulation (rTMS), which are more standardized and clinically accepted [21], TSCS lacks uniformity. TSCS influences CPGs and propriospinal pathways, yet its physiological mechanisms remain underexplored [20]. Focused ultrasound (FUS) offers deeper precision but is still investigational [28]. While TSCS holds functional potential, rigorous standardization and mechanistic clarity are essential before it can match the reliability of cortical-based neuromodulation.

TSCS operates through the application of surface electrodes over the vertebral column, inducing electrical fields that modulate spinal neuronal excitability. Milosevic et al. [29] demonstrated that cervical TSCS can activate sensory afferents in the dorsal roots and modulate spinal excitability through presynaptic and transsynaptic mechanisms, enhancing upper limb motor output. Their findings highlight the potential of cervical TSCS to engage spinal sensory pathways relevant to neurorehabilitation in SCI patients. Unlike epidural stimulation, which requires surgically implanted electrodes [27,30,31]. TSCS leverages non-invasive electrical fields to engage residual

neural pathways. This stimulation enhances spinal network activation [31], modulates propriospinal pathways [18], and influences segmental [33] and descending reflex circuits [18].

TSCS functions primarily through sub-threshold electrical stimulation, which does not directly trigger action potentials but modulates intraneuronal circuits, facilitating motor recovery [34] and cardiovascular function restoration [22]. One of the key mechanisms of TSCS is its interaction with CPGs, a network of neurons located in the spinal cord responsible for rhythmic movement patterns such as walking [35]. In patients with chronic SCI, TSCS has been shown to enhance locomotor activity, improve walking ability [36], reduce neuropathic pain [26], and increase voluntary muscle activation [37], particularly when combined with activity-based therapy [38,39].

Despite the increasing use of TSCS, the optimal “dosing” strategy remains a subject of ongoing debate. Most studies employ stimulation frequencies between 20 and 50 Hz; however, different stimulation paradigms may produce distinct neurophysiological effects. Continuous stimulation is commonly used to maintain spinal excitability, whereas burst-pattern stimulation and the use of high-frequency carrier waves (e.g., 5–10 kHz) are being explored to improve patient comfort and enable deeper neural engagement [13,14]. For locomotor recovery, lumbosacral stimulation within the 30–50 Hz range has been associated with improved stepping and gait coordination, likely through activation of CPGs [60, 51]. In contrast, cervical TSCS for upper limb function typically incorporates task-specific training with repeated stimulation sessions, although optimal parameter configurations remain less clearly defined (12,11). These variations highlight the need for systematic dose response studies to establish standardized, domain-specific stimulation protocols.

The activation of CPGs in the lumbosacral spinal cord plays a crucial role in locomotion, even in the absence of direct cortical input. Studies using

robot-assisted gait analysis demonstrated that TSCS applied at the lumbosacral level significantly enhanced gait performance and motor control in SCI patients [40]. This suggests that TSCS facilitates coordinated stepping movements by reactivating pre-existing spinal circuits, highlighting its potential as an effective neuromodulator intervention.

Comparison of TSCS with ESCS

A primary distinction between TSCS and ESCS lies in their electrode placement and mode of neuromodulation. ESCS involves the surgical implantation of electrodes over the dorsal aspect of the spinal cord at targeted vertebral levels, providing continuous electrical stimulation to facilitate motor, sensory, and autonomic function [22]. Conversely, TSCS delivers electrical stimulation through surface electrodes placed over the skin, eliminating the need for invasive procedures. This non-invasive approach makes TSCS a safer, more cost-effective, and accessible alternative for a broader range of individuals with SCI [15].

While ESCS provides direct stimulation to the spinal circuits, enabling volitional movement in some patients, TSCS primarily modulates sub-threshold excitability, engaging residual pathways over time [17]. TSCS, while less targeted, modulates subthreshold excitability [41], engages dormant neural pathways [17], and enhances residual function over time. The ability of TSCS to engage dormant neural pathways is particularly important in chronic SCI cases, where spontaneous recovery is limited. Despite these differences, both techniques have been shown to promote neuroplasticity and functional improvements, albeit through distinct mechanisms.

TSCS has also demonstrated the ability to attenuate spasticity temporarily, with effects similar to ESCS, reinforcing its potential as a non-invasive alternative [14,42]. This reduction in spasticity is believed to be mediated by the modulation of inhibitory and excitatory spinal

circuits, which regulate motor function and autonomic responses [32,41]. Furthermore, TSCS has been shown to enhance residual spinal network activity [32], modulate propriospinal pathways [41], and influence segmental reflex circuits [18], ultimately leading to improvements in motor recovery [12], autonomic function improvement [23], and sensory restoration in SCI patients [11].

However, while TSCS offers promising advantages, its effects remain less localized and targeted compared to ESCS. The latter has been shown to facilitate standing and stepping ability in individuals with complete SCI by providing more precise neural engagement [17]. In contrast, TSCS engages broader neuromodulatory effects, which, while beneficial in many cases, may lead to less precise control over motor activation compared to ESCS. To fully realize its therapeutic potential, further research is needed to optimize stimulation parameters, tailor interventions to individual patient profiles, and establish standardized clinical protocols. Table 1 shows the comparison between TSCS and ESCS.

Table 1 presents a comparative synthesis of TSCS and ESCS, highlighting key differences in mechanisms, clinical applications, and practical implementation in SCI rehabilitation. A fundamental distinction lies in electrode placement and invasiveness: TSCS uses surface electrodes applied over the vertebral column, offering a non-invasive and safer alternative, whereas ESCS requires surgical implantation within the epidural space [47]. This difference significantly influences clinical accessibility, as TSCS is more feasible for widespread use, including outpatient and home-based settings, while ESCS is restricted to specialized centers due to surgical and economic constraints [12].

From a mechanistic perspective, TSCS operates primarily through sub-threshold neuromodulation, enhancing spinal excitability and facilitating the activation of residual neural circuits, including CPGs and propriospinal pathways (14, 29). However, this indirect mode of activation may

contribute to variability in patient responses and reduced stimulation specificity. In contrast, ESCS delivers direct electrical stimulation to targeted spinal segments, enabling more precise neural engagement and facilitating volitional motor output [33]. This targeted activation is likely responsible for the more robust functional outcomes observed in ESCS, particularly in individuals with motor-complete SCI.

In terms of motor recovery, TSCS has been shown to enhance residual voluntary movement, modulate spinal reflexes, and improve motor control, particularly when combined with task-specific rehabilitation [12, 66]. However, these improvements are often modest and highly dependent on individual factors such as injury level and chronicity. Conversely, ESCS has demonstrated the ability to restore standing and stepping functions in selected individuals with complete SCI, although these outcomes typically require intensive training and precise parameter optimization [33]. Both TSCS and ESCS exhibit potential in autonomic regulation, particularly in modulating cardiovascular and bladder functions. TSCS has been associated with improvements in blood pressure stabilization and bladder control through modulation of sympathetic pathways [47, 23]. However, findings remain inconsistent, and in some cases, TSCS may exacerbate autonomic dysreflexia, particularly in individuals with high-level injuries [23]. ESCS, due to its direct neural targeting, appears to produce more consistent autonomic effects, although its application is limited by invasiveness.

Regarding spasticity management, both modalities demonstrate inhibitory effects on hyperexcitable spinal circuits. TSCS has been shown to produce temporary reductions in spasticity, likely mediated through modulation of inhibitory interneurons and reflex pathways [25]. In contrast, ESCS may offer more sustained spasticity control due to continuous and targeted stimulation, although long-term data remain limited. From a clinical implementation perspective, TSCS represents a cost-effective, scalable, and low-risk intervention, making it

highly suitable for integration into conventional physiotherapy and community-based rehabilitation programs [42]. In contrast, ESCS is associated with high costs, surgical risks, and the need for specialized programming, limiting its widespread adoption despite its superior precision and efficacy in selected cases.

Despite these advantages, TSCS is limited by reduced spatial specificity, lack of standardized stimulation protocols, and high inter-individual variability in outcomes [29]. ESCS, while offering greater precision, is constrained by invasiveness, economic burden, and limited accessibility, which restrict its clinical use to highly controlled settings. Overall, this comparison highlights a critical trade-off between accessibility and precision. TSCS offers a promising non-invasive neuromodulatory approach with broad applicability, whereas ESCS provides more targeted and potent effects at the expense of invasiveness and scalability. Future research should focus on optimizing TSCS stimulation parameters and integrating advanced technologies, such as computational modelling and real-time feedback systems, to enhance its specificity and reduce variability, thereby narrowing the gap between these two neuromodulation strategies.

TSCS for Motor Recovery in SCI Rehabilitation

TSCS has emerged as a promising neuromodulation strategy for motor recovery in individuals with SCI by enhancing spinal excitability, reorganizing neural pathways, and engaging residual neural networks [14,43,44]. Studies suggest that TSCS can improve gait function, hand dexterity, and overall neuromuscular coordination, particularly when combined with rehabilitation interventions such as physical therapy and functional electrical stimulation [11,45,46]. Despite these advancements, challenges related to patient variability, optimal stimulation parameters, and long-term efficacy remain unresolved.

TSCS facilitates motor recovery by modulating spinal reflex pathways, including both excitatory and inhibitory circuits, which are essential for motor function and autonomic regulation [15,17,37,47]. By influencing spinal excitability, TSCS enhances the CPGs in the lumbosacral spinal cord, which are crucial for generating rhythmic locomotion patterns such as walking [35]. This is particularly beneficial for patients with chronic SCI, where TSCS has been shown to improve walking ability [36], reduce neuropathic pain [26], and increase voluntary muscle activation [37]. The ability of TSCS to reorganize segmental reflex circuits contributes to improved muscle activation and coordination, leading to enhanced functional outcomes in both upper- and lower-limb rehabilitation [33,48].

A key mechanism of TSCS is sub-threshold stimulation, in which electrical pulses are applied below the threshold required to trigger an action potential. These pulses modulate the interneuronal circuits' excitability, enhancing the neural pathways' responsiveness to subsequent stimuli [41]. This modulation facilitates neuroplasticity and improves motor coordination without causing discomfort or adverse effects associated with higher-intensity stimulation. Studies have demonstrated that sub-threshold TSCS enhances stepping ability [49]. Increases walking endurance [50] and improves balance control in individuals with motor-incomplete SCI [51,52].

Beyond lower limb rehabilitation, TSCS has also been explored for upper limb recovery, particularly in individuals with cervical SCI. Cervical TSCS has been shown to enhance hand grip strength, improve dexterity, and facilitate sensorimotor recovery. A case study by Chandrasekaran et al. [11] reported a 47% increase in hand strength and a three-point improvement in tactile sensation following six weeks of TSCS therapy, suggesting its potential for upper limb rehabilitation. Multi-site TSCS stimulation has also been shown to enhance upper limb motor activation, though functional improvements remain variable, indicating the

need for individualized protocols and optimized stimulation parameters [48].

Despite promising findings, several challenges and limitations hinder the clinical application of TSCS for motor recovery. Patient responses vary widely, with some individuals showing marked improvements while others exhibit minimal effects [53]. This inconsistency is likely due to differences in injury level, lesion completeness, and baseline neuromuscular function [23]. Additionally, the absence of standardized TSCS protocols represents a major barrier to its widespread clinical implementation. Key stimulation parameters - such as frequency, intensity, duration, and electrode placement - vary considerably across studies, making it difficult to establish optimal treatment guidelines.

TSCS for Cardiovascular Function

While motor recovery has been the primary focus of TSCS research, its influence extends beyond locomotor control. Autonomic dysfunction is a major challenge in SCI rehabilitation, affecting cardiovascular, respiratory, bladder, bowel, and sexual functions [54]. TSCS has emerged as a potential neuromodulation strategy to regulate autonomic nervous system activity, yet its effectiveness remains under investigation. Recent studies suggest that TSCS may improve blood pressure regulation [22], respiratory function [55], and autonomic control [23] in individuals with SCI. However, challenges such as individual variability in responses and the lack of large-scale clinical trials limit its widespread adoption.

TSCS has been investigated for its effects on cardiovascular function in individuals with SCI, with mixed findings highlighting both potential benefits and risks. A case series by Engel-Haber et al. [24] examined TSCS's impact on blood pressure in individuals with chronic cervical SCI, revealing that stimulation at the lumbosacral levels significantly increased blood pressure, whereas cervical stimulation had no observable effect. These findings suggest that the site of

stimulation is crucial in modulating cardiovascular outcomes. Conversely, Solinsky et al. [23] conducted a comparative study assessing cardiovascular autonomic function and found that TSCS worsened autonomic dysreflexia and increased blood pressure instability in individuals with high-thoracic SCI. This raises important concerns regarding the safety of TSCS in certain populations, particularly individuals susceptible to autonomic dysreflexia. The variability in blood pressure responses among patients further complicates its clinical application, underscoring the need for carefully tailored stimulation protocols to minimize the risk of adverse cardiovascular events. Despite its potential, TSCS remains a developing field, and several limitations must be addressed before widespread clinical adoption, although short-term studies have demonstrated promising outcomes in blood pressure regulation [23], respiratory function [55], and bladder control [27].

TSCS for Neuropathic Pain Management.

In addition to motor and autonomic domains, neuropathic pain remains a significant clinical concern among individuals with SCI. TSCS has gained attention for its possible role in sensory modulation and pain reduction, although current findings remain inconclusive and variable. Neuropathic pain is a debilitating condition affecting 40–70% of individuals with SCI, often resulting from maladaptive reorganization of spinal and supraspinal circuits [56]. Conventional pain management strategies, including opioid medications [57], anticonvulsants [58], and non-invasive neurostimulation techniques, have shown limited effectiveness, prompting researchers to explore TSCS as an alternative approach.

TSCS has been investigated for its potential to enhance sensory recovery, particularly when combined with activity-based training. Inanici et al. [12] have demonstrated that cervical TSCS combined with motor rehabilitation leads to

significant improvement in motor and sensory functions in individuals with motor-complete SCI. Participants exhibit up to a two-point increase in clinical assessments of tactile sensation, with gains persisting even one month after discontinuation of stimulation, suggesting potential long-term benefits [39]. These findings align with the hypothesis that TSCS activates afferent pathways, promoting cortical reorganization and sensory restoration [59,60]. Despite these promising results, the current body of evidence is limited by small sample sizes, lack of control groups, and variability in SCI severity among study participants [26,50,61]. Differences in stimulation parameters, such as frequency, intensity, and duration, further complicate the determination of optimal protocols for sensory recovery [62]. Additionally, few studies have conducted long-term follow-ups to assess the durability of sensory improvements, highlighting the need for large-scale randomized controlled trials (RCTs) with standardized protocols and extended monitoring periods.

While TSCS has been widely studied for its effects on motor and sensory recovery [17], its efficacy in NP modulation remains inconclusive. Choi et al. [23] conducted a single-blind crossover trial involving individuals with cervical SCI and found no significant reduction in neuropathic pain compared to sham stimulation. These findings suggest that TSCS alone may not be sufficient for pain relief or that its effectiveness may depend on individual factors such as injury level, chronicity, and baseline pain severity.

Contrasting evidence from Sandler et al. [25] suggests that TSCS may provide temporary relief in individuals with severe baseline spasticity. Their findings indicate that TSCS reduced spasticity-associated pain for up to 45 minutes post-stimulation, potentially by modulating spinal excitability and inhibitory interneurons. Although these effects were short-lived, they highlight the possibility of TSCS as an adjunct therapy for pain management. The discrepancy in findings between Choi et al. [26] and Sandler et al. [25]

underscores the need for further investigation into the optimal stimulation parameters for pain relief. Several factors may contribute to the inconsistencies in TSCS-induced pain relief, including variations in electrode placement, frequency, and intensity. Studies suggest that individuals with incomplete versus complete SCI may exhibit different pain modulation pathways, influencing TSCS outcomes [55]. While short-term studies show modest effects on pain [63], longitudinal research is required to determine whether repeated TSCS exposure leads to sustained pain relief. Studies by Chandrasekaran et al. [11] and Lin et al. [64] support TSCS's role in afferent pathway activation, while Choi et al. [26] suggest limited effectiveness in pain modulation. These contrasting findings highlight the complexity of sensory and pain modulation mechanisms in SCI and reinforce the necessity for further research to optimize TSCS parameters for individualized treatment.

A key challenge in TSCS research is the absence of standardized stimulation protocols, particularly for pain relief applications. Studies such as Finn et al. [65] have demonstrated that electrode placement significantly influences TSCS effects, indicating that protocol optimization is crucial for achieving consistent outcomes. Additionally, while Sandler et al. [25] reported short-term reductions in spasticity-associated pain, the long-term effects of TSCS on neuropathic pain remain unclear. As research on TSCS continues to evolve, its translation into clinical practice remains a key objective in SCI rehabilitation. The growing body of evidence supports TSCS as a potential neuromodulator for motor recovery, autonomic regulation, and sensory restoration. However, widespread clinical implementation is still limited by variability in patient response, lack of standardized stimulation protocols, and the need for long-term studies.

To bridge this gap, ongoing clinical trials and future research efforts must focus on personalized rehabilitation approaches that tailor TSCS parameters to individual patient needs, large-scale efficacy trials with standardized stimulation

protocols, and the development of wearable TSCS devices for broader accessibility in clinical and home-based rehabilitation settings. With continued advancements, TSCS holds promise as an effective tool for improving sensory function and pain management in individuals with SCI. However, rigorous clinical validation and optimization of stimulation parameters are essential for its integration into mainstream rehabilitation strategies.

Table 2 synthesizes key studies examining the effects of TSCS across three major domains in SCI rehabilitation, such as motor recovery, cardiovascular function, and neuropathic pain. Overall, the findings demonstrate promising yet heterogeneous outcomes, reflecting variability in injury characteristics, stimulation parameters, and study designs. In the domain of motor recovery, the evidence consistently supports the role of TSCS in enhancing residual motor function through modulation of spinal reflexes and activation of CPGs [42, 48]. These mechanisms appear particularly effective at the lumbosacral level, where stimulation facilitates stepping, gait performance, and voluntary muscle activation. Studies incorporating multisite stimulation and task-specific training further highlight the importance of combining TSCS with rehabilitation to induce cortical reorganization and sustain functional improvements [12, 66]. However, outcomes vary depending on injury completeness, with individuals with motor-incomplete SCI generally demonstrating greater improvements compared to those with complete injuries. Additionally, while case studies and experimental designs report substantial gains, the lack of large-scale randomized controlled trials limits the generalizability of these findings.

Cervical TSCS targeting upper limb function has also shown encouraging results, particularly in enhancing hand strength and tactile sensation through increased corticospinal drive [11]. Nevertheless, these findings are primarily derived from small-scale or case-based studies, emphasizing the need for more rigorous trials to

confirm efficacy. Furthermore, studies exploring sub-threshold stimulation and neuroplasticity mechanisms suggest that repeated activation of residual pathways can improve coordination and long-term neuromuscular control, although optimal stimulation parameters remain unclear [41].

In the cardiovascular domain, TSCS demonstrates a complex and site-dependent influence on autonomic regulation. Cervical stimulation has been associated with improvements in respiratory function through activation of phrenic and accessory muscles, leading to enhanced inspiratory and expiratory performance [47]. In contrast, stimulation at lumbosacral or thoracic levels appears to modulate sympathetic pathways and blood pressure regulation [24]. However, findings are not consistently beneficial. Evidence from Solinsky et al. [23] indicates that TSCS may exacerbate autonomic dysreflexia and blood pressure instability in individuals with high-thoracic injuries. This variability underscores the importance of stimulation site selection and highlights the potential risks associated with inappropriate parameter settings, particularly in patients with severe autonomic impairment.

The effects of TSCS on neuropathic pain remain inconclusive. Some studies suggest that TSCS can enhance sensory processing and induce cortical plasticity through activation of dorsal column pathways, resulting in improved tactile discrimination and potential secondary reductions in pain perception [12; 39]. Additionally, stimulation of inhibitory interneurons may temporarily reduce spasticity-related discomfort [25]. However, randomized controlled evidence indicates that TSCS may not produce significant pain relief compared to sham stimulation in individuals with chronic neuropathic pain [26]. These conflicting findings suggest that the analgesic effects of TSCS are likely indirect, transient, and highly dependent on individual neurophysiological profiles.

Across all domains, a critical limitation is the substantial heterogeneity in stimulation

parameters, including frequency, intensity, electrode placement, and duration. Most studies employ frequencies ranging from 20 to 50 Hz and utilize sub-threshold stimulation, yet there is no consensus on optimal dosing strategies. Additionally, the predominance of small sample sizes, case studies, and pilot trials reduces the strength of evidence and limits clinical translation. Another important consideration is the influence of injury characteristics on outcomes. Individuals with chronic, incomplete SCI and preserved descending pathways appear to benefit more consistently from TSCS, whereas responses in motor-complete or high-thoracic injuries are less predictable and, in some cases, potentially adverse. This highlights the necessity for individualized treatment protocols based on injury level, completeness, and autonomic status. Overall, Table 2 illustrates that TSCS holds significant potential as a neuromodulatory intervention across multiple functional domains in SCI rehabilitation. However, its clinical effectiveness is constrained by variability in patient response, lack of standardized protocols, and limited high-quality evidence. Future research should prioritize large-scale randomized controlled trials, parameter optimization, and the integration of TSCS with task-specific rehabilitation to enhance functional outcomes and improve the consistency of therapeutic effects.

Integration of TSCS with Other Rehabilitation Interventions

TSCS is particularly effective when integrated with other rehabilitation interventions, such as physical therapy and activity-based training. By combining TSCS with traditional rehabilitation techniques, synergistic effects can be achieved, leading to enhanced motor recovery and functional outcomes [62]. Research indicates that this combination can improve movement control and coordination, aiding in the recovery of walking abilities in individuals with SCI [46]. A recent case study by Tharu et al. [63] demonstrated that combining TSCS with activity-

based therapy significantly increased walking distance from 3.5m to 10m, indicating that TSCS may enhance motor output when paired with rehabilitation exercises.

In robotic-assisted stepping, TSCS has been shown to modulate lower limb muscle activation, supporting its role in gait rehabilitation protocols [9]. Anodal TSCS has also been found to enhance dynamic balance control by increasing hip muscle activity, reinforcing its potential as an adjunct intervention in locomotor training. Beyond motor recovery, TSCS has also been linked to enhancements in autonomic functions, such as bladder and bowel control, further supporting its integration into multidisciplinary rehabilitation programs [27].

TSCS has shown enhanced therapeutic potential when integrated with established rehabilitation interventions. While TSCS alone can increase spinal excitability and facilitate voluntary motor activation, its combination with functional, task-specific therapies significantly amplifies neuromodulatory effects and accelerates motor recovery in individuals with SCI. A growing body of evidence supports the use of TSCS as an adjunct to locomotor training, upper limb rehabilitation, and activity-based physical therapy, underscoring its role in promoting neuroplasticity and functional restoration.

Inanici et al. [12] provided compelling evidence of functional gains when TSCS was integrated into a structured upper limb rehabilitation program for individuals with cervical SCI. The intervention included two months of therapy, with the first month involving motor training alone and the second combining training with cervical TSCS. Participants demonstrated significant improvements in strength, coordination, and functional use of the hands, with benefits sustained up to six months post-intervention. These findings support the idea that TSCS can prime the spinal cord to respond more effectively to therapeutic input and enhance motor learning through increased spinal excitability [12].

Samejima et al. [66] expanded this concept by combining multisite TSCS (cervical and

lumbosacral) with intensive locomotor training over eight weeks. Their results showed improvements not only in motor outcomes but also in somatosensory processing, as evidenced by reduced P40 latency in somatosensory evoked potentials (SSEPs) and increased motor evoked potentials (MEPs). These findings illustrate how TSCS, when integrated into a high-repetition gait training program, enhances both motor and sensory neuroplasticity. The rhythmic stepping movements provided afferent input that, when paired with sub-threshold spinal stimulation, helped to engage and reorganize CPGs and segmental reflex networks [66].

Estes et al. [46] conducted a randomized clinical trial evaluating TSCS combined with locomotor training in individuals with subacute SCI. Their findings showed that although both the TSCS and sham groups improved, the TSCS group demonstrated greater gains in walking speed and endurance. These results support the feasibility of integrating TSCS into standard gait training protocols to augment locomotor recovery. Importantly, this study highlights TSCS as a neuromodulatory facilitator rather than a stand-alone therapeutic agent.

In a case study by Sharma et al. [48], the participant with motor complete C2 SCI underwent 60 sessions of activity-based recovery training (ABRT) paired with multi-site TSCS. Although there was no overt volitional movement, neurophysiological data revealed new activation in previously silent muscle groups, and the participant reported enhanced sensation and functional use of the hand. This study reinforces the potential of integrating TSCS with intensive, goal-oriented rehabilitation to engage residual neural circuits, even in cases of severe injury [48]. Despite these promising findings, integrating TSCS into clinical practice poses several challenges. Individual variability in response, differences in injury level and severity, and the absence of standardized stimulation protocols make it difficult to develop universal guidelines. Moreover, the optimal timing, intensity, and sequencing of TSCS relative to therapeutic tasks

remain under investigation. Some studies have applied TSCS before rehabilitation sessions to “prime” the nervous system, while others deliver stimulation during active movement to promote task-specific neuroplasticity.

Future research should focus on multicentred trials using standardized outcome measures and stimulation protocols to advance clinical translation. The development of wearable and portable TSCS devices may facilitate home-based therapy integration, further enhancing accessibility and long-term adherence. As research continues to evolve, personalized rehabilitation strategies that incorporate TSCS into broader neurorehabilitation frameworks hold great promise for improving functional recovery in SCI populations.

Translating TSCS into Clinical Practice

The use of TSCS in clinical settings is growing, with many ongoing studies exploring its benefits in different areas of SCI recovery. However, it is still not widely used in everyday practice because of differences in stimulation methods and varied patient responses. To make TSCS more effective, personalized treatment plans are needed. These should take into account the severity of the injury, each person’s unique nerve function, and their specific rehab goals. Tailoring treatment in this way will help unlock the full benefits of TSCS for a wider range of patients.

Although TSCS is considered more accessible than ESCS, several practical barriers may limit its widespread clinical adoption. These include the cost of stimulation devices, the need for trained clinicians to ensure accurate electrode placement and parameter optimization, and the requirement for supervision during the initial phases of therapy [12]. In home-based settings, additional challenges such as patient adherence, safety monitoring, and device usability must be addressed. Furthermore, variability in patient response necessitates individualized parameter adjustment, which may not be easily achievable without clinical expertise. These real-world

constraints suggest that, despite its non-invasive nature, effective implementation of TSCS requires structured clinical protocols and adequate training to ensure safe and consistent delivery.

Current clinical trials on TSCS have provided important insights into its potential benefits, but have also revealed challenges in standardization and patient selection. For example, studies such as Tharu et al. [63] and Inanici et al. [12] demonstrated significant improvements in motor function when TSCS was combined with rehabilitation therapies, whereas Sharma et al. [48] found that while upper limb activation increased, functional improvements were limited. These findings suggest that TSCS alone may not be sufficient for functional restoration but can serve as an adjunct therapy in structured rehabilitation programs.

A key consideration in clinical translation is injury-specific customization of TSCS protocols. Evidence from Krenn et al. [13] and Lin et al. [64] suggests that individual differences in injury type (motor-complete vs. incomplete SCI) significantly influence response to TSCS, reinforcing the need for personalized stimulation parameters. While lower limb applications (locomotor rehabilitation) have shown more consistent improvements, upper limb interventions require further optimization due to greater variability in response.

Furthermore, Engel-Haber et al. [24] have recently highlighted regional differences in autonomic modulation, demonstrating that TSCS applied at the lumbosacral level can influence blood pressure regulation, whereas cervical TSCS does not elicit the same autonomic effects. These findings highlight the importance of placing electrodes correctly based on the desired outcome. As TSCS becomes more widely used, rehab programs should include personalized assessments to see how each patient responds and help choose the right settings. Using tools like EMG and autonomic monitoring can help clinicians adjust stimulation in real time, making

sure the treatment is given at the best intensity and frequency for each person.

Overall, this review proposes a response-stratified neuroplasticity model of TSCS in SCI. In this model, TSCS should not be viewed as a uniform neuromodulation intervention, but rather as a spinal priming tool whose effectiveness depends on the interaction of three key factors: residual neural connectivity, spinal excitability, and rehabilitation-driven afferent input. TSCS increases the excitability of spinal networks, creating a temporary physiological window that enables dormant or weakened neural circuits to be more responsive to voluntary and sensory inputs. However, the transition from short-term neuromodulation to long-term functional recovery is hypothesized to occur only when stimulation is consistently paired with task-specific rehabilitation that reinforces neural pathways through activity-dependent plasticity. This framework challenges the prevailing assumption that standardized stimulation parameters can produce similar outcomes across individuals with SCI. Instead, it suggests that individuals with preserved descending pathways and greater sensorimotor integration may achieve more sustained improvements, whereas others may demonstrate only transient or limited responses. By incorporating these factors, this model provides a conceptual basis for predicting treatment responsiveness and supports the development of more personalized and targeted TSCS protocols in clinical practice.

The short-term and long-term effects of TSCS

TSCS demonstrates a compelling capacity to enhance motor function and autonomic regulation in individuals with SCI. Both short- and long-term effects have been documented, with distinctions in onset, underlying mechanisms, and clinical impact. Short-term effects are typically observed within or immediately after a stimulation session and are often linked to heightened neural excitability. For example, Inanici et al. [12] found that TSCS significantly

improved upper extremity function after just one session, with enhanced voluntary movement observed in participants with both complete and incomplete cervical SCI. Notably, these improvements were comparable to or superior to those reported with invasive epidural stimulation. Likewise, Hofstoetter et al. [42] showed that a single session of 50 Hz TSCS could significantly reduce spasticity through reflex modulation mechanisms, reflecting a short-term neuromodulatory influence on hyperexcitable spinal circuits

Conversely, long-term effects emerge from repeated applications of TSCS and are largely attributed to neuroplastic adaptations. Inanici et al. [12] studied over 8 weeks with functional task practice during the first month and stimulation combined with training in the second. Participants maintained motor gains for up to six months post-intervention, indicating sustained reorganization of spinal pathways and cortical inputs. Similarly, Estes et al. [46] implemented a 4-week intervention with subacute SCI patients, showing greater improvements in walking speed and endurance in the TSCS group versus sham, although between-group differences were not statistically significant due to small sample size and variability.

The main difference between short- and long-term effects of TSCS is how long the benefits last. Short-term effects happen due to temporary changes in spinal activity and may include stronger muscle contractions, reduced reflexes, or better motor unit use. These benefits usually fade once the stimulation stops. In contrast, long-term effects involve lasting improvements in movement control, likely due to changes in the nervous system, like new connections between nerves. Signs of these lasting changes include increased motor evoked potentials (MEPs) and better timing in sensory signals seen in longer-term TSCS use.

Samejima et al. [66] extended this finding by demonstrating improvements in somatosensory pathways (P40 latency reduction) after two months of paired cervical and lumbosacral TSCS

with locomotor training. However, some findings also indicate the challenges of observing clear autonomic effects in the short term. For instance, Sandler et al. [25] found no group-level reductions in spasticity after a single TSCS session, although individuals with more pronounced baseline spasticity did show significant benefits.

Table 3 outlines the temporal effects of TSCS in individuals with SCI, distinguishing between short-term and long-term outcomes. This comparison highlights a crucial aspect of TSCS application, namely its dual role as both an immediate neuromodulatory tool and a potential driver of sustained neuroplastic changes.

In the short term, TSCS produces rapid effects that are often observable within a single session. These effects are primarily attributed to increased spinal excitability and modulation of segmental reflex pathways [14, 25]. Such neuromodulatory changes facilitate enhanced voluntary motor output, reduction in spasticity, and temporary improvements in functional performance. Clinically, these effects are reflected in measurable indicators such as increased muscle torque, reduced clonus, and transient facilitation of motor evoked potentials (MEPs) [12]. However, these benefits are typically reversible and diminish once stimulation ceases, indicating that short-term effects are largely dependent on ongoing neuromodulatory input rather than structural neural adaptation.

In contrast, long-term effects of TSCS emerge following repeated and structured stimulation over weeks to months. These effects are associated with activity-dependent neuroplasticity, including corticospinal reorganization and strengthening of synaptic connectivity [66; 46]. Sustained improvements in motor function, including enhanced walking ability, coordination, and voluntary control, suggest that TSCS may facilitate lasting changes within both spinal and supraspinal networks. Neurophysiological markers such as improved MEP and somatosensory evoked potential (SSEP) latency, as well as increased intracortical

facilitation, further support the presence of long-term neural adaptation.

Despite these promising findings, the distinction between short-term and long-term effects is not always clearly delineated in the literature. Many studies report overlapping outcomes, and the transition from transient neuromodulation to durable neuroplasticity remains poorly understood. Moreover, long-term benefits are highly dependent on the integration of TSCS with task-specific rehabilitation, suggesting that stimulation alone may be insufficient to induce meaningful and lasting functional recovery.

Another critical consideration is the variability in individual response. Factors such as injury severity, chronicity, and the integrity of residual neural pathways appear to influence both the magnitude and persistence of TSCS effects. Individuals with incomplete SCI and preserved descending pathways are more likely to demonstrate long-term improvements, whereas those with complete injuries may experience predominantly short-term, transient benefits.

Furthermore, the lack of standardized stimulation protocols complicates the interpretation of temporal effects. Differences in frequency, intensity, electrode placement, and duration across studies make it difficult to establish clear dose-response relationships and optimal intervention strategies. As a result, while the conceptual distinction between short-term neuromodulation and long-term neuroplasticity is well recognized, its clinical translation remains inconsistent.

Overall, Table 3 underscores the importance of viewing TSCS not merely as an acute intervention but as a modality with potential cumulative effects when applied systematically over time. Future research should focus on elucidating the mechanisms underlying the transition from immediate excitability changes to sustained neuroplastic adaptation, as well as identifying optimal stimulation protocols that maximize long-term functional recovery in individuals with SCI.

In summary, TSCS provides both short- and long-term benefits for people with SCI. Short-term use boosts immediate nerve and muscle activity, while long-term use supports ongoing recovery and functional gains. Together, these effects make TSCS a valuable part of structured rehab programs, although current studies differ in sample size and methods, overall findings support the use of TSCS at both early and late stages of SCI rehabilitation.

Future Research Recommendations

Although early studies show promise, larger clinical trials and improved technology are needed to confirm the long-term benefits of TSCS and make it more widely available. Future research should focus on testing its effectiveness in different SCI populations, finding the best stimulation settings for consistent results, and developing wearable TSCS devices for home use and long-term self-care.

A critical frontier in advancing TSCS toward personalized rehabilitation lies in the identification of reliable neurophysiological biomarkers. Measures such as motor evoked potentials (MEPs), somatosensory evoked potentials (SSEPs), and H-reflex modulation have been proposed as indicators of spinal excitability and neural pathway integrity, with potential to predict individual responsiveness to stimulation [14, 29]. The integration of these biomarkers with real-time monitoring tools, including electromyography (EMG) and autonomic assessments, may enable data-driven optimization of stimulation parameters. Such approaches could facilitate individualized dosing strategies, improve treatment consistency, and enhance the precision of TSCS interventions in clinical practice [13, 51].

Despite positive findings from small studies, large randomized controlled trials (RCTs) remain lacking. Studies such as Solinsky et al. [23] and Chandrasekaran et al. [11] reported short-term improvements in cardiovascular regulation and sensory recovery, but the long-term effects

remain unclear. Future research should determine whether TSCS-induced benefits persist over time, supporting sustained neuroplastic adaptation.

A major challenge in TSCS research is the lack of standardized stimulation parameters. Variations in frequency, intensity, and electrode placement lead to inconsistent results. For instance, Choi et al. [26] found no significant impact on neuropathic pain, whereas Sandler et al. [25] reported short-term relief from spasticity-related pain, suggesting pain modulation may depend on stimulation frequency. Multi-center trials should establish standardized protocols and identify patient subgroups that respond best based on injury type and residual neural function.

Limitations and Challenges

Despite encouraging preliminary findings, several limitations must be acknowledged. Current evidence on the use of TSCS for neurogenic bladder and bowel dysfunction is primarily derived from small-scale studies and pilot trials. Larger, randomized controlled trials are urgently needed to validate the efficacy, safety, and clinical applicability of this intervention. Furthermore, patient responses to TSCS vary considerably due to factors such as the level and completeness of SCI, individual anatomical differences, and heterogeneity in stimulation parameters. This variability presents a challenge for developing standardized treatment protocols and predicting therapeutic outcomes.

Conclusion

TSCS has emerged as a promising non-invasive neuromodulation technique for SCI rehabilitation, demonstrating potential in motor recovery, autonomic function regulation, and sensory restoration. While current research highlights its efficacy across multiple domains, challenges such as variability in patient responses, lack of standardized protocols, and the need for long-term studies must be addressed before TSCS becomes a mainstream clinical intervention. Key

findings from studies such as Tharu et al. [63], Chandrasekaran et al. [11], and Engel-Haber et al. [24] confirm that TSCS can enhance locomotion, hand function, and autonomic stability. However, contrasting results from Choi et al. [26] and Sharma et al. [48] indicate that its effects are not uniform across all patients, necessitating individualized rehabilitation strategies. Moving forward, large-scale clinical trials are essential to establish evidence-based TSCS protocols, while technological advancements in wearable neuromodulation devices could revolutionize home-based SCI rehabilitation. If these research priorities are met, TSCS has the potential to become a standardized, accessible, and effective intervention for enhancing neuroplasticity and functional recovery in SCI patients. By addressing these challenges, TSCS could transition from an experimental therapy to a clinically validated intervention, significantly improving the quality of life for individuals with SCI and expanding neuromodulation's role in rehabilitative medicine.

Clinical take-away

TSCS is a non-invasive, emerging intervention for SCI that holds potential across motor, autonomic, and sensory domains. When combined with physiotherapy, it may offer greater neuroplastic recovery. Clinicians should stay informed about optimal protocols, and future implementation should consider individual injury profiles and long-term monitoring.

Conflict of interest

The authors declare no conflicts of interest related to the content of this manuscript. No commercial or financial relationships were involved that could be construed as a potential conflict of interest.

Financial support and acknowledgements

We thank our 'Geran Galakan Penyelidik Muda' (GGPM 2023-071) and 'Early Career Research Award' (NN-2024-023), Universiti Kebangsaan Malaysia (UKM) as well as colleagues from the Physiotherapy Department and Centre for Rehabilitation and Special Needs Study, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, who provided insight, advice, and expertise that hugely assisted in this study.

Author contributions

HH led the conceptualization, supervision, methodology, validation, literature search, data curation, drafting, figure/table preparation, and final approval. SAI and NAH provided literature review, writing and editing, neurophysiology and rehabilitation input, spinal stimulation expertise, critical revisions, and resources. SAB and NACS handled data interpretation, writing and review, clinical applications input, literature screening, data organization, and supporting sections. ZZ contributed biomedical insights, review and editing, and future directions input.

Table 1. Comparison of key features between Transcutaneous Spinal Cord Stimulation (TSCS) and Epidural Spinal Cord Stimulation (ESCS) in the context of spinal cord injury rehabilitation.

Feature	TSCS (Transcutaneous Spinal Cord Stimulation)	ESCS (Epidural Spinal Cord Stimulation)
Electrode Placement	Surface electrodes on the skin over the vertebrae	Implanted electrodes in the epidural space
Invasiveness	Non-invasive (no surgery required)	Invasive (requires surgical implantation)
Mechanism	Sub-threshold stimulation (modulates excitability, engages dormant circuits)	Direct neural activation (stimulates specific spinal segments)
Neural Engagement	General spinal modulation influences CPGs, and propriospinal circuits	Targeted stimulation allows volitional movement
Effect on Motor Function	Enhances residual movement, modulates reflexes	Can restore standing and stepping in complete SCI
Effect on Autonomic Function	Improves blood pressure regulation and bladder control	Stronger autonomic effects due to direct neural targeting
Spasticity Reduction	Temporary attenuation of spasticity	Can provide longer-term spasticity control
Clinical Implementation	Easier to administer, lower cost, accessible	Expensive, requires specialized implantation & programming
Limitations	Less precise, individual response variability	Surgical risks, high cost, limited accessibility

Table 2. Summary of key studies investigating the effects of TSCS on motor recovery, cardiovascular function, and neuropathic pain in individuals with spinal cord injury.

Domain	Author(s)	Primary Mechanism	Physiological Target	Key Outcomes	Injury characteristics	Stimulation Parameters	Study Design
Motor Recovery	Hofstoetter et al. [42]; Sharma et al. [48]	Modulation of spinal reflexes (excitatory & inhibitory); activation of CPGs	Lumbosacral spinal cord; interneurons	Improved gait, stepping, and voluntary muscle activation	Chronic SCI; varying completeness (including motor complete cases)	Typically 30–50 Hz; surface electrodes over lumbosacral segments; multi-session protocols	Experimental studies and case study
	Chandrasekaran et al. [11]	Targeted cervical TSCS to enhance descending drive and upper limb motor control	Cervical cord (C5–T1); corticospinal tract	47% improvement in hand strength; increased tactile sensation	Cervical SCI (motor incomplete)	Cervical TSCS; task-specific upper limb training; repeated sessions (~6 weeks)	Case study
	Inanici et al. [12]; Samejima et al. [66]	Multisite TSCS with task-specific training; cortical reorganization	Cervical + lumbosacral pathways; motor cortex	Sustained motor recovery post-stimulation; enhanced MEP and SSEP responses	Chronic cervical SCI; both complete and incomplete injuries	Multisite TSCS; ~30 Hz; integrated with intensive rehabilitation (8 weeks)	Interventional study and longitudinal experimental study
	Tajali et al. [41]; MacKay-Lyons [35]	Sub-threshold modulation; Hebbian neuroplasticity via repetitive activation	Interneuronal circuits; residual supraspinal tracts	Improved coordination, balance, and long-term neuromuscular control	Motor-incomplete SCI; preserved descending pathways	Sub-threshold stimulation; variable frequency (5–30 Hz); repetitive training paradigms	Conceptual and experimental studies
Cardiovascular Function	Kumru et al. [55]	Enhanced respiratory motor drive; stimulation of phrenic and accessory muscles	C3–C4 spinal level; phrenic nerve pathways	Improved inspiratory/expiratory pressures; better respiratory performance	Cervical SCI (predominantly chronic, tetraplegia)	Cervical (C3–C4) + thoracic (T9–T10) stimulation; combined with inspiratory muscle training; repeated sessions	Randomized controlled trial (n = 22)
	Engel-Haber et al. [24]	Segmental autonomic stimulation; site-dependent BP modulation	Lumbosacral sympathetic circuits	Increased systolic BP with lumbosacral stimulation; cervical TSCS had no BP effect	High-thoracic SCI ($\geq T6$; severe autonomic impairment)	TSCS applied during autonomic testing; variable parameters targeting thoracic segments	Comparative experimental study
	Solinsky et al. [23]	Overactivation of sympathetic pathways; autonomic dysreflexia	High-thoracic cord; baroreceptor pathways	Increased BP instability; worsened dysreflexia in high-level SCI	High-thoracic SCI ($\geq T6$; severe autonomic impairment)	High-thoracic SCI ($\geq T6$; severe autonomic impairment)	High-thoracic SCI ($\geq T6$; severe autonomic impairment)
Neuropathic Pain	Inanici et al. [12]; Zhang et al. [39]	Activation of sensory afferents and cortical	Dorsal column pathways;	2-point tactile sensation improvement;	Chronic SCI (cervical & thoracic);	Cervical TSCS; ~30–50 Hz; sub-motor	Case series / experimental study

	plasticity via paired motor-sensory training	sensory cortex	lasting post-stimulation	predominantly incomplete)	threshold; combined with task-specific training	
Choi et al. [26]	Sub-threshold TSCS; unclear modulation of pain-processing centers	Dorsal horn; pain pathways	No significant pain relief vs. sham; limited effect on chronic NP	Chronic SCI (mixed levels; complete & incomplete)	Thoracic TSCS; low intensity; sub-threshold stimulation	Randomized controlled trial (sham-controlled)
Sandler et al. [25]	Stimulation of inhibitory interneurons; reduced spasticity-linked discomfort	Spinal afferents; gamma motor neurons	Temporary spasticity and pain reduction up to 45 mins post-session	Chronic SCI with spasticity-related pain (incomplete SCI)	Lumbosacral TSCS; ~20–30 Hz; short-duration sessions	Experimental (within-subject design)
Gerasimenko et al. [60]	Afferent activation to facilitate cortical reorganization	Somatosensory cortex; ascending pathways	Improved sensory responsiveness; potential secondary effect on pain perception	Chronic SCI (varied levels; predominantly incomplete)	Multisite TSCS; moderate frequency; combined with rehabilitation training	Pilot study

Table 3. Comparison of short-term and long-term effects of TSCS in individuals with SCI.

Category	Short-Term Effects	Long-Term Effects
Onset of Effects	Immediate or within a single session	After repeated sessions (weeks to months)
Primary Mechanism	Increased spinal excitability; reflex modulation	Neuroplasticity; corticospinal reorganization
Functional Improvements	Enhanced voluntary movement; reduced spasticity	Sustained motor gains; improved walking, coordination
Reversibility	Transient effects may fade after stimulation ends	Durable; effects persist beyond the stimulation period
Clinical Indicators	Increased torque, reduced clonus, MEP facilitation (temporarily)	Improved MEP/SSEP latency, intracortical facilitation
Examples from Literature	Inanici et al. [12]; Hofstoetter et al. [14]; Sandler et al. [25]	Estes et al. [46]; Samejima et al. [66]

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