

Progress in Spinal Cord Electrical Stimulation for Spinal Cord Injury

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Abstract

Spinal cord injury (SCI) is a severe neurological disorder, with its incidence rising steadily each year. Following SCI, patients commonly experience sensory, motor, and autonomic nervous system dysfunction. The prolonged treatment duration and high medical costs impose a significant burden on both patients and their families. With the study of the mechanism of spinal cord injury, spinal cord electrical stimulation (SCS), as a new neuromodulation technique, has shown great potential in the field of spinal cord injury treatment. Evidence indicates that various stimulation paradigms—such as low-frequency, high-frequency, and variable-intensity stimulation—can effectively improve motor function, respiratory capacity, spasticity, and neuropathic pain by modulating neuronal excitability, enhancing neural plasticity, and regulating neural network dynamics. Although SCS therapy still faces technical challenges, with the continuous development of electrode design, stimulation strategies, and individualized treatment, SCS is expected to provide more effective rehabilitation for patients with spinal cord injury. In this paper, the present status and progress of spinal cord electrical stimulation on pain and motor sensory dysfunction in patients with spinal cord injury were reviewed, and the prospect of extensive application of spinal cord electrical stimulation in the field of spinal cord injury was discussed. The shortcomings of current spinal cord electrical stimulation research were analyzed, and it is expected to have a guiding role in future clinical work and clinical research.

Keywords

Spinal Cord Electrical Stimulation, Spinal Cord Injury, Pain, Motor Function, Sensory Function

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1. Introduction

Spinal cord injury (SCI) is a common type of central nervous system disease. According to the different segments of the injured spinal cord, sensory, motor, or autonomic nervous dysfunction occurs. Based on the cause of injury, it can be divided into traumatic SCI and non-traumatic SCI. Traumatic spinal cord injury is one of the most common serious injuries in spinal cord injury, mainly caused by external force trauma or fall [1]-[3]. SCI can also be divided into primary and secondary stages according to the stage of onset. Primary injury is central nervous system injury caused by traction or compression resulting from disc herniation, spinal dislocation, or displaced bone fragments after a fracture. Secondary injury is a series of complex processes involving multiple molecules and cells triggered on the basis of primary injury, including ischemia, tissue destruction, neuroinflammation, decreased neurotrophic factor content, ion imbalance, demyelination, and fine. It seriously intensifies the degree of spinal cord injury and is an important factor that hinders the protection and regeneration of injured nerves. Therefore, with the aging of the population and the continuous improvement of social modernization, the incidence of SCI shows a trend of increasing year by year [4]-[6]. Although traditional treatment methods (such as drug therapy, surgical therapy, etc.) can alleviate symptoms to some extent, these treatments are often difficult to completely recover the damaged nerve function, so they cannot effectively treat this destructive disease of the central nervous system. Some studies have found that neuromodulation techniques using electrical signals to stimulate the spinal cord have made effective progress in the treatment of spinal cord injury.

2. Principle of SCS

As shown in **Figure 1**, SCS technology is a neuromodulation approach that utilizes electrodes placed in the epidural space to generate artificial electric fields at corresponding spinal cord segments or targets under the control of pulse generator programs *in vitro* or *in vivo* to produce therapeutic effects [7] [8]. In addition, electrical stimulation blocks the transmission of pain signals through the spinal cord to the brain, preventing the signals from reaching the cerebral cortex, and at the same time promotes the release of endogenous analgesic substances to relieve patient pain. It has been widely used in the field of nervous system rehabilitation (such as SCI, NP, epilepsy, and stroke). Because traumatic SCI involves obvious physical compression, SCS is more effective at this time, as it can reduce the compression and alleviate the symptoms. However, for ischemic and hypoxic SCI caused by vascular occlusion, SCS technology may not be effective in improving local blood circulation and may lead to poor results, or even aggravate the ischemic state and further damage spinal cord function. Therefore, when formulating an SCI treatment plan involving SCS, clinicians should adopt an individualized, phenotype-driven strategy that integrates the injury level and completeness (e.g., AIS grade), the predominant functional deficits (motor, sensory, or auto-

nomic), and patient-specific factors (pain phenotype, spasticity, comorbidities, tolerance to paresthesia, and rehabilitation goals). Stimulation parameters (e.g., frequency, pulse width, amplitude, contact configuration, and waveform such as conventional, burst, or 10 kHz) should be iteratively optimized using intraoperative mapping and postoperative reprogramming, guided by objective outcomes (pain reduction, gait metrics, functional scales) and patient-reported responses. Such a precision approach acknowledges interindividual variability and disease heterogeneity and is more likely to maximize therapeutic benefit while minimizing adverse effects.

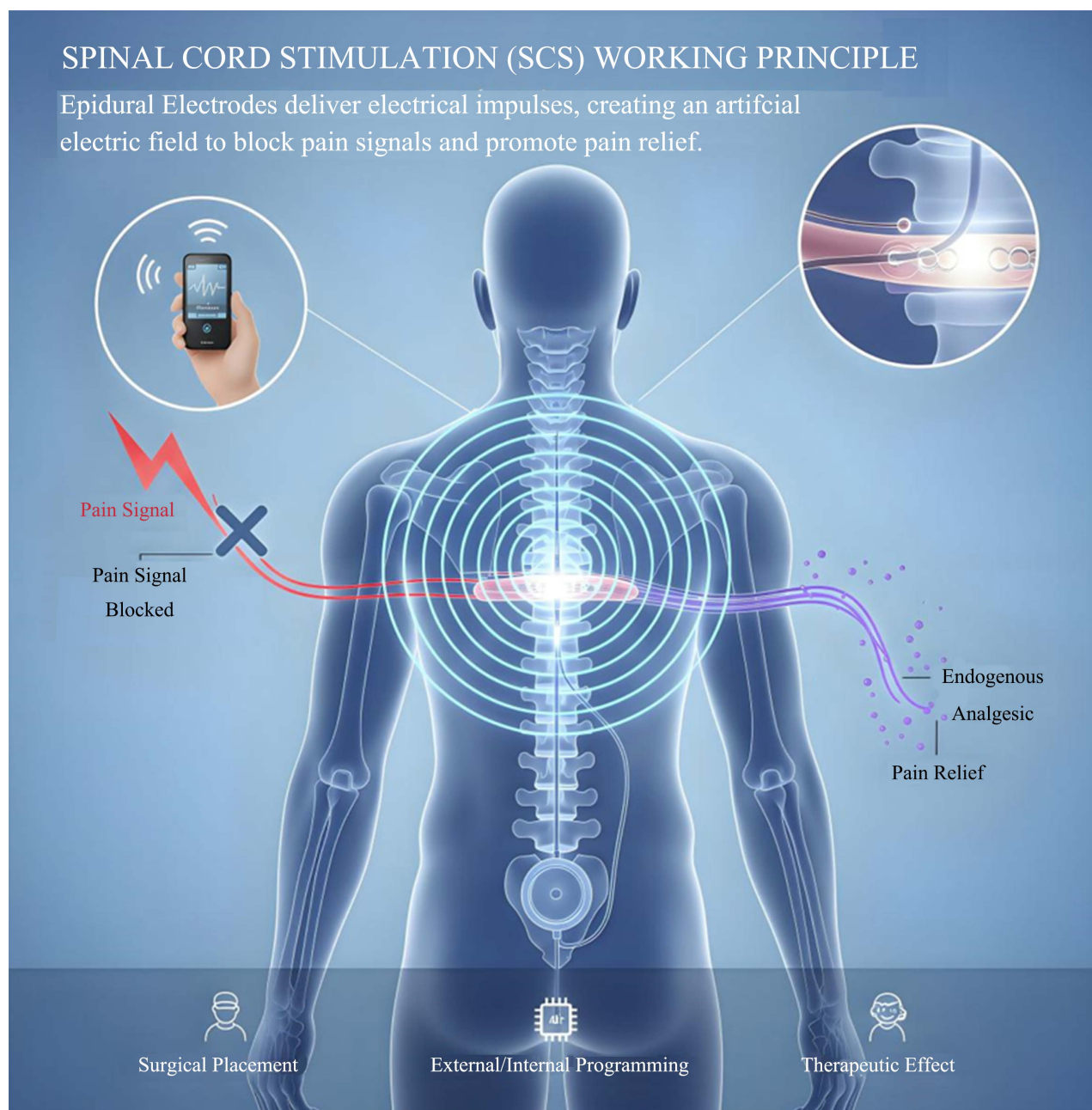


Figure 1. Spinal cord stimulation work principle.

3. Analgesic Effects of SCS

SCI patients often have different types of pain, among which refractory neuropathic pain has the greatest impact on patients' quality of life. Although analgesic drugs are the first-line treatment scheme for pain after SCI at present, for some patients who change medicine frequently or take drugs irregularly, long-term use of analgesic drugs will have side effects such as drug resistance, addiction, and damage to surrounding organs, and then appear drug failure, pain aggravation, and other phenomena. The authors note that pain types after SCI include multiple pain forms, such as needle-like, squeeze-like, caught-like, or laceration-like, and the pathological and physiological basis of pain onset is different, and the above pain types are difficult to effectively cover by currently marketed drugs [9]. Therefore, in the field of neuroanalgesic therapy, finding a safer, more effective, adjustable, and controllable analgesic therapy has become a hot and difficult point, rather than chemical drugs. In 1965, Melzack and Wall put forward the "Gating Theory", which provided a solid foundation for the improvement of SCS analgesic treatment mechanism; in 1975, Dooley *et al.* used puncture technology to insert electrode wires into the epidural space for low current stimulation to treat pain, which triggered the upsurge of using SCS to treat pain in Europe and America. In the 1980s, the advent of lithium batteries made possible the noninvasive SCS technique of percutaneous lead placement without incising the lamina, resulting in less trauma and rapid use for permanent implantation [10].

In recent years, more studies have focused on SCS therapy parameters, but so far, there is no uniform standard for SCS therapy parameter settings. In a prospective randomized double-blind crossover trial by Billot *et al.* [11], high-frequency electrical stimulation was defined as greater than 500 Hz, while traditional spinal cord electrical stimulation (TCS) is often treated with low-frequency electrical stimulation, which, depending on the distribution of abnormal sensation, can produce good pain relief, improve quality of life, and significantly reduce drug use; many early studies have demonstrated that SCS can successfully control long-term pathological pain in SCI patients [12]. However, paradoxically, multiple studies over the same period demonstrated that TCS treatment regimens did not achieve the desired effect on SCI pain, and the duration of pain suppression was relatively short and the effect gradually decreased over time [13]. With the progress of science and technology and materials and a large amount of basic research, the development of new technologies such as high-frequency spinal cord stimulation (HF-SCS) and differential target multiplexed spinal cord stimulation (DTM-SCS) makes the analgesic effect of SCS more significant [14]. Velásquez [15] retrospectively analyzed 12 patients with trigeminal neuralgia treated with SCS and found that 3 patients failed to relieve their long-term pain during an average follow-up period of 4.4 years, and the average pain relief rate of the remaining 9 patients was 57.10%. Edelbach and Lopez Gonzalez [16] treated a female patient with refractory trigeminal neuralgia with high cervical spinal cord electrical stimulation. The results showed that during the stimulation period (frequency

300 Hz, pulse width 170 μ s, intensity 0.50 - 0.80 mA), the pain relief rate was 60%; after 4 weeks of short-term follow-up, the patient reported significant improvement in quality of life after the first stimulation, diet and daily activities, and the VAS score was 6 points. Trigeminal postherpetic neuralgia (TG PHN) is one of the most common and complex forms of postherpetic neuralgia (PHN). It has unique clinical and pathophysiological characteristics, caused by varicella zoster virus (VZV) infection of the trigeminal ganglion, which can damage the ascending and descending neuroregulatory pathways of the head as the disease progresses [17]. An 83-year-old female patient with V2 and V3 trigeminal neuralgia was successfully treated with short-term high-cervical spinal cord stimulation (HSCS) combined with peripheral nerve stimulation (PNS). The stimulation parameters of HSCS were pulse width 400 μ s, frequency 60 Hz, intensity 5 mA, contact polarity 2+ and 6-; The stimulation parameters of peripheral nerve electrical stimulation were pulse width of 20 ms, frequency of 2 Hz, duration of 900 s and voltage of 40 - 80 V, and the pain was obviously relieved [18]. High cervical spinal cord stimulation (HSCS) stimulates the dorsal spinal cord by releasing electric current through the stimulation electrode in the epidural space, activates inhibitory interneurons and attenuates ascending pain transmission. It is suggested that short-term high cervical spinal cord stimulation at the C1 - 2 segment is an effective method for the treatment of elderly patients with post-herpetic neuralgia. In addition, neuromodulation techniques such as spinal cord electrical stimulation combined with trigeminal semilunar ganglion stimulation (TSGS) can also be used to treat trigeminal postherpetic neuralgia [19]. The combination of different neuromodulation techniques provides a more diversified approach to the treatment of this disease. Compared with TCS, HF-SCS (high frequency, low pulse, low amplitude) does not cause paresthesia and can cover a wider range of pain. In recent studies [20] [21], HF-SCS (especially 10 kHz stimulation) has been found to significantly reduce pain compared to low-frequency stimulation, and in combination with smartphone programs and remote programming modes, it has also been found to improve quality of life and function in chronic pain patients in the long term [22]. Moreover, 10 kHz stimulation can be used for rescue therapy when other forms of SCS therapy fail [23]. Lee [24] showed synergy between HF-SCS (10 kHz stimulation) and TCS (40 Hz), with 10 kHz SCS operating through selective activation of inhibitory interneurons in the superficial dorsal horn, while 40 Hz SCS is believed to operate primarily through dorsal column fiber activation, and a combination of 10 kHz SCS and 40 Hz SCS therapy can achieve more effective analgesic effects than electrical stimulation alone. Accordingly, while optimal SCS parameterization requires further high-quality study, current best practice supports a precision, iteration-based workflow. Target localization should be guided intraoperatively by fluoroscopy and neurophysiological monitoring (e.g., ECAP/EMG mapping when available), followed by systematic postoperative reprogramming to refine waveform, frequency, pulse width, amplitude, and contact configuration. Parameter adjustments ought to integrate objective endpoints (e.g.,

pain intensity, gait and spasticity metrics, functional scales) with patient-reported outcomes and tolerance to paresthesia, and be tailored to injury characteristics (level and completeness), dominant symptom domains (motor, sensory, autonomic), and comorbidities. In this individualized framework, timely modification of electrode configuration and stimulation settings is likely to maximize therapeutic benefit and minimize adverse effects in routine clinical practice.

4. SCS Treatment for Motor Function

Donald Hebb proposed Hebb's law in 1949. Hebb's law describes the basic principle of synaptic plasticity; that is, the continuous repeated stimulation transmitted by presynaptic neurons to postsynaptic neurons will lead to an increase in synaptic transmission efficiency. Later, this facilitation phenomenon was extended to homosynaptic facilitation and heterosynaptic facilitation. The proposal of Hebb's law provides theoretical guidance for the treatment of spinal cord injury. Bailey CH [25] showed that heterosynaptic and synsynaptic activation can promote synaptic connections between glutamate sensory neurons and motor neurons, so epidural stimulation can strengthen synaptic connections between sensory afferent fibers and motor neurons, thus promoting motor recovery. In addition, SCS helps to improve muscle strength, enhance muscle endurance, and thus improve motor function. Patients with spinal cord injury may have muscle atrophy, decreased oxygen content, increased fat mass, strength attenuation, and other conditions due to long-term bed rest [26] [27]. Studies have shown that SCS can trigger rhythmic muscle activity, promote the increase of autonomous movement amplitude of paralyzed limbs, and reduce muscle spasm in patients with incomplete spinal cord injury [28]. Rowald [29] showed that SCS targeting the lumbosacral dorsal root could be programmed to enable fully paralyzed patients to stand, walk, swim, etc. In addition, for patients with complete spinal cord injury, at least 5% body weight support is necessary to achieve lower limb movement [30]. Clinically, the most common way to promote paraplegic recovery is sports rehabilitation training with weight support. Ward PJ [31] conducted walking training for contusion rats for 1 h every day. After 3 months of training, the alternating activation mode of flexor and extensor muscles of the lower limbs of rats was significantly improved. Motor training is critical for regulating spinal circuits and improving motor recovery after spinal cord injury. Repeated practice of motor tasks affects training-induced neuroplasticity, resulting in dependence on specific movements, which affects the ability of the spinal cord to learn new motor tasks. Shah PK [32] studied rats with thoracic spinal cord transection and randomly divided them into three groups to perform bipedal walking training in the anterior, lateral, and posterior directions on a treadmill. Although all three impaired rats showed improvement in forward walking after training, the EMG peaks were higher and the consistency and coordination of the steps were more significant in the lateral and backward training groups. This study suggests that adding specific exercises to exercise tasks can improve exercise performance.

Variant exercise training also has a better therapeutic effect in the clinic. Gill ML [33] performed SCS and specific task training on L2 and S1 segments for patients with complete motor spinal cord injury, so that patients could finally move their legs on the ground with the assistance of a front wheel walker, such as standing and running on a treadmill. It is generally believed that spinal cord injury mainly cuts off the signal pathway from the brain to the body. In the later stage of spinal cord injury, besides stimulating muscle vitality and enhancing muscle strength, it is also possible to restore muscle control through neural prostheses. As shown in **Figure 2**, the principle of which is to replace the brain with electrical stimulation

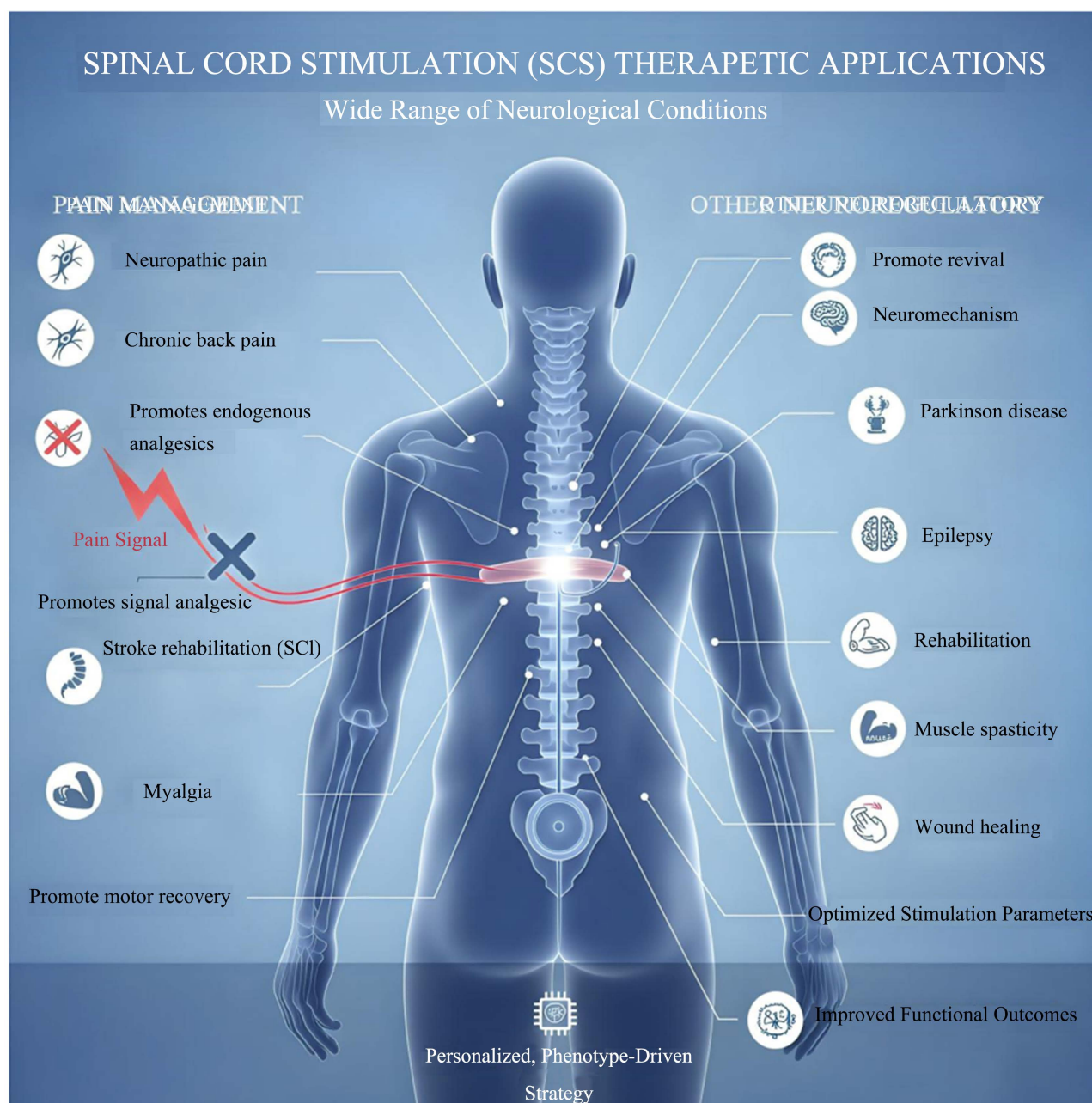


Figure 2. Spinal cord stimulation therapeutic applications.

to rebuild the nerve “electronic bypass” to regulate the peripheral nervous system to control muscle to restore motor function. Neuroprosthesis research has helped to reconstruct motor function in paralyzed people [34]. Compared with the improvement of lower limb function, spinal cord stimulation (SCS) is more challenging when it comes to improving upper limb function. For patients with high cervical spinal cord injury (SCI), upper limb paralysis severely limits their independence and quality of life. Multiple studies [35]-[37] have shown that transcutaneous spinal cord electrical stimulation (TSCS) can restore movement and function of the hands and arms in patients with complete paralysis and long-term SCI. TSCS delivers pulsed electrical currents to the dorsal skin surface of the spinal cord via surface electrodes, and it is mostly used to relieve pain and improve motor function. Sayenko DG *et al.* [38] applied TSCS to patients with chronic paralysis after spinal cord injury, and these patients were able to achieve independent standing and knee extension without assistance. Although TSCS has the advantages of being non-invasive and allowing easy adjustment of stimulation positions, it also has drawbacks such as the need for high electrode stimulation intensity, low stimulation specificity, and a tendency to cause co-activation of multiple muscles [8].

5. SCS Treatment of Sensory Function

Sensory nerves, as an important part of the human nervous system, play a key role in the process of transmitting external stimuli and internal information. Abnormal sensory function is also a common complication in patients with spinal cord injury. Studies have found that spinal cord electrical stimulation can induce inductive axon growth in the spinal dorsal column, promote myelin regeneration, and promote recovery of damaged inductive neural networks [39], thus improving sensory functions of patients with spinal cord injury such as touch, pain, and temperature sensation. It improves motor function by strengthening sensory-motor connections in the spinal cord and reducing hyperreflexia. This is also a prerequisite for SCI patients to improve their functions. For patients with severe complete spinal cord injury, the motor commands of the cerebral cortex have been completely cut off. Spinal cord electrical stimulation can be used as an upper spinal driving force to increase the excitability of spinal cord circuits. Combined with rehabilitation training, sensory feedback from dorsal root ganglia can be strengthened, allowing sensory input from the body and skin input as control sources to generate appropriate exercise patterns. Mahrous AA *et al.* [40] showed that motor input caused by dorsal root stimulation and spinal cord tissue stimulation can be activated simultaneously, which can induce large and stable motor output, and the application of neuromodulators can further enhance motor output. Collectively, these findings suggest that SCS may facilitate sensory restoration and sensorimotor integration through dorsal column/dorsal root-mediated plasticity (axon sprouting, remyelination, and circuit reweighting), and that coupling stimulation with task-specific rehabilitation and, where appropriate, pharmacologic

neuromodulators can amplify and stabilize motor outputs—supporting a multi-modal, rehabilitation-anchored strategy for sensory and functional recovery after SCI.

6. Summary and Outlook

Spinal cord stimulation (SCS) is emerging as a versatile neuromodulation modality with multi-domain benefits for spinal cord injury (SCI), spanning pain relief, sensorimotor recovery, autonomic modulation, and respiratory support. Converging preclinical and clinical evidence indicates that SCS can recalibrate spinal network excitability, engage inhibitory interneuronal circuits in the dorsal horn, and promote adaptive plasticity across dorsal column, dorsal root, and propriospinal pathways. Clinically, advances in waveform engineering—ranging from conventional low-frequency paradigms to kilohertz-frequency (10 kHz), burst, and differential target multiplexed (DTM) stimulation—have broadened the therapeutic toolbox, enabling paresthesia-free analgesia, wider pain coverage, and potentially more durable responses. In parallel, task-specific rehabilitation combined with epidural or transcutaneous SCS has demonstrated meaningful gains in standing, stepping, and upper-limb function among selected patients, emphasizing the necessity of pairing stimulation with intensive, goal-directed training.

Technological progress is rapidly refining SCS precision and usability. Multi-contact and multi-segment leads, high-resolution current steering, and closed-loop architectures leveraging ECAP/EMG or sensor feedback allow iterative, physiology-guided optimization of frequency, pulse width, amplitude, and contact configuration. Remote programming and smartphone-enabled monitoring improve adherence and long-term management, while wireless power transfer and battery-free designs promise reduced maintenance and enhanced compatibility with daily life. Imaging- and electrophysiology-guided targeting (DTI-informed placement, intraoperative mapping) further supports individualized programming that accounts for injury level and completeness (AIS grade), dominant symptom domains (motor, sensory, autonomic), pain phenotype, and tolerance to paresthesia.

Despite this momentum, key challenges remain. First, evidence heterogeneity hampers generalizability: many studies feature small sample sizes, mixed phenotypes, short follow-up, and inconsistent endpoints. Second, optimal parameter spaces are incompletely defined for distinct clinical goals (analgesia vs locomotion vs autonomic regulation), and head-to-head comparisons among waveforms (10 kHz, burst, DTM, closed-loop) in SCI-specific cohorts are scarce. Third, hardware-related complications (infection, lead migration, device malfunction), MRI conditionality, and reoperation rates require ongoing risk mitigation, while cost-effectiveness and equitable access merit rigorous evaluation. Mechanistically, the causal links between stimulation patterns, cell-type-specific recruitment (inhibitory interneurons, propriospinal neurons, glial modulation), and functional outcomes need further elucidation, along with biomarkers that can predict and monitor response.

Future research priorities should therefore include:

- Trial design and evidence standards: multicenter randomized or well-controlled prospective studies with SCI-specific stratification (injury level/completeness; acute, subacute, chronic phases), adequately powered samples, standardized primary endpoints (e.g., $\geq 50\%$ pain reduction, gait speed/6MWT, SCIM/WISCI II, autonomic outcomes), and follow-up of at least 12 - 24 months.
- Mechanism-to-parameter translation: integrative studies linking computational models, intraoperative neurophysiology, and longitudinal biomarkers (ECAP features, EMG patterns, QST, neuroimaging) to derive mechanistically informed, goal-specific parameter regimes.
- Personalization and closed-loop control: adaptive algorithms (including AI/ML) that adjust stimulation in real time based on neural and kinematic feedback; development of responder prediction tools incorporating lesion metrics, phenotyping, and psychosocial factors.
- Modality integration: combined approaches (SCS + task-specific rehabilitation, functional electrical stimulation, robotics/BCI, pharmacologic neuromodulators, and—where appropriate—regenerative strategies such as cell therapy or biomaterials) to leverage synergistic plasticity.
- Safety, usability, and access: refinement of MRI-conditional systems, infection prevention strategies, durable leads and anchors, patient-centered programming workflows, remote care pathways, and health-economic analyses to guide policy and reimbursement.

In conclusion, SCS has transitioned from a primarily analgesic intervention to a platform technology for circuit-level rehabilitation after SCI. As hardware, waveforms, and closed-loop control mature, and as trials adopt rigorous, phenotype-aware designs, SCS is poised to deliver more predictable, durable improvements in pain, sensorimotor function, and autonomy. Realizing this potential will depend on mechanistically grounded personalization, integration with intensive rehabilitation, and sustained attention to safety, cost-effectiveness, and equitable implementation. With continued scientific and clinical advances, SCS is likely to play an increasingly central role in comprehensive SCI care.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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