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Comprehensive Review of the Four Stimulation Modes in Spinal Cord Stimulation (SCS) Therapy

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Abstract:

Chronic pain is a global health problem with a significant patient and socioeconomic burden. The technology of spinal cord stimulation (SCS), an efficient strategy for managing persistent pain, has undergone significant development in the previous couple of decades. The purpose of this paper is to review the development of SCS techniques, compare the efficacy of different SCS modalities, and explore future research directions. The article reviewed the development of SCS, including traditional tonic SCS, high-frequency SCS, burst SCS, and closed-loop SCS. Clinical trial and research data analysis were used to assess the safety and effectiveness of the different SCS modalities in the treatment of chronic pain. The study showed that high-frequency SCS and burst SCS were effective in relieving pain without producing paresthesia compared with conventional SCS. Closed-loop SCS provides a more personalized treatment plan by modulating stimulation through real-time feedback. However, the application of SCS still faces technical challenges, such as electrode displacement and equipment malfunction. SCS technology shows great potential in chronic pain management. With technological advances, SCS is expected to provide more effective and personalized treatment options for chronic pain patients. Subsequent investigations ought to concentrate on enhancing device stability, mitigating issues, and investigating astute and customized therapeutic alternatives.

Keywords: chronic pain, tonic SCS, high-frequency SCS, burst SCS, closed-loop SCS.

1. Introduction

Chronic pain is a major public healthcare problem worldwide, especially in industrialized countries. A European survey showed that almost 20% of adults endure chronic pain and almost two-thirds of patients

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consider their pain to be inadequately controlled [1]. In the UK, the economic burden of back pain exceeds £10 billion per year, higher than the indirect costs of any other condition [2]. Similarly, chronic pain costs the U.S. economy between $560 and $635 billion annually. These figures not only reflect the prevalence of chronic pain but also show its enormous impact on economic and social activities [3]. As a result of pain, many patients are severely limited in their ability to perform daily living and work, which in turn leads to an increase in days missed from work and a decrease in social activities. This situation is prevalent globally and puts enormous pressure on the healthcare and socio-economic systems of countries [4].

Facing this growing public health crisis, spinal cord stimulation (SCS) therapy is gaining attention and recognition as an effective intervention. SCS was first used as early as 1967, based on the gating theory proposed by Melzack and Wall in 1965 [5]. Early SCS systems relied on an external power source that delivered energy via radiofrequency. However, with technological advances, lithium batteries, especially after their introduction in the 1980s, have been used in a variety of applications, fully implantable systems have gradually replaced the early externally powered systems, dramatically improving patient quality of life and outcomes [6]. Under conventional SCS, the patient's pain, which is typically accompanied by paresthesia, is concealed by low-frequency electrical stimulation by the implantation of electrodes in the epidural space [7]. However, more options for treating chronic pain are now available because of recent technical advancements including burst SCS and high-frequency SCS, which both effectively relieve pain without paralyzing the patient.

This paper aims to present a side-by-side comparison of the most widely used SCS models now. Due to the increasing complexity and diversification of SCS applications, different SCS models have been gradually formed and developed individually in practice. However, these models differ significantly in terms of specific applications, management strategies, and technical support. Therefore, this paper will explore the characteristics of different SCS models in depth through systematic analysis to provide valuable references for academic research and practical operation.

2. Common Spinal cord stimulation

In this chapter, spinal cord stimulation (SCS) will be classified into the following broad categories in terms of the different stimulation modes: Tonic SCS, Burst SCS, High-Frequency Stimulation (HF SCS), and Closed-loop SCS. Next, the mechanisms, indications, and clinical outcomes of each SCS modality will be explored in detail to provide guidance for selecting an appropriate spinal cord stimulation protocol.

2.1 Tonic SCS

Tonic spinal cord stimulation is the most traditional form of SCS, as the original form of electrical waveforms whose electrical impulses are delivered to the spinal cord through implanted electrodes connected to a pulse generator, producing a tonic waveform consisting of continuous stimulation, usually at a low frequency, with a sufficiently high amplitude to deliver pulses, usually at a constant frequency and with a constant pulse width, inducing a non-painful tingling sensation, which in turn produces a paralyzing sensation in the area of pain, called paresthesia [7]. The mode of action of conventional spinal cord stimulation is based on the pain gate control theory, which is derived from depolarizing the large myelinated Aβ fibers in the dorsal columns of the spinal cord with electrical impulses [5]. According to the theory, pain information typically travels between the rapid A-delta fibers, which provide sharp pain, and the sluggish C-fibers, which cause dull pain. Pain signaling is dependent on the balance of activity of the bigger A-beta fibers, the smaller A-delta fibers, and the C-fibers [8]. Stimulation of A-Beta fibers, which are sensitive to touch, activates inhibitory neurons, which weaken pain signals before they reach the brain and reduce the sensation of pain [8]. Nevertheless, when using conventional low-frequency spinal cord stimulation, patients invariably experience abnormal sensations at the site of stimulation. Over time, tolerance to this sensation may develop in certain patients, leading to a diminished masking effect, which reduces the inhibitory effect on pain [9].

2.2 HF SCS (High frequency SCS)

For patients with refractory pain, including complicated regional pain syndrome and FBSS, conventional spinal cord stimulation is recommended in less than half of cases [10]. At the same time, there are certain drawbacks to traditional SCS, including a small number of clinical indications, insufficient or subpar pain suppression, and a gradual decline in therapeutic efficacy [9]. Although traditional SCS remains a primary neurostimulation therapy, new stimulation protocols are becoming more and more necessary to increase the common indications of SCS and enhance both its short-term and long-term therapeutic efficacy.

High Frequency SCS provides an alternative therapy that delivers high frequency stimulation without causing paralysis and has shown promising results in reducing low back and leg pain. While early results are positive, long-term follow-up is critical, as traditional SCS efficacy tends to wane over time. This was further investigated in a prospective multicenter study in which Adnan studied individuals with persistent back pain who did not improve with traditional therapy for at least 6 months [11]. Patients try the HF10 SCS system first and then receive a permanent implant after a successful trial. Unlike conventional systems with lower frequencies, the rechargeable system used in the study had a maximum stimulation frequency of 10 kHz. Three-fifths of the 83 individuals had shown an overall decrease in back pain of more than half at the 2-year follow-up. Of these, 72 patients had successfully finished the trial phase and obtained permanent implants, and 71 percent had similar reductions in leg pain. The results of the study compare favorably with traditional SCS tests. In addition, a large number of patients (38%) stopped using opioids altogether, and overall opioid use declined significantly. This extended trial showed that in patients with chronic low back pain, HF SCS provides long-lasting pain alleviation. Significantly, the absence of paralysis associated with HF SCS improves patient satisfaction and contributes to treatment adherence [11].

2.3 Burst SCS

Recently developed burst stimulation allows paralysis-free stimulation [12,13], similar to high-frequency stimulation [14], in which five pulses are emitted per burst at a frequency of 500 Hz, and 40 bursts are emitted per second, with a period of quiescence between them, called the burst interval [14]. Each burst consists of a sequence of pulses with a consistent pulse width, amplitude, and inter-pulse frequency. The transmission pattern of these pulses is akin to that of burst-firing neurons, which are found in certain pain pathways in addition to tonic-firing neurons [15]. In the SCS experiment, De Ridder and associates examined the tonic and burst waveforms in individuals with chronic pain [16]. The study showed that burst SCS provided better pain relief, there were no reports of adverse effects, and all subjects preferred the pulsed string mode to tonic stimulation. Schu et al. examined the pain results of one-week tonic stimulation, burst stimulation, and placebo stimulation in FBSS individuals who had used tonic stimulation for a minimum of three months in another prospective randomized trial [16]. When burst stimulation was used, the subjects' pain scores were the lowest. Based on this data, it appears that burst SCS relieves pain more effectively than tonic SCS.

2.4 Closed-loop SCS

The available evidence for SCS has been restricted to fixed-output, open-loop sensory stimulation in the roughly 50 years since SCS was originally investigated. The fixed output, open-loop SCS activates spinal cord fibers that help limit pain transmission only when the patient reports paresthesia or when the actual position of the SCS causes paresthesia-free stimulation. Prior to the implantation of a permanent SCS device, the patient's perceived pain response is often evaluated in a screening trial following lead placement [17].

Recently, A novel approach to closed-loop spinal cord stimulation has been created, and its appearance signifies yet another significant paradigm change in SCS strategy. Whereas former open-loop, fixed-output stimulation techniques functioned, Real-time feedback can be integrated with closed-loop stimulation. SCS system's linear electrode array architecture makes it possible to evaluate electrically evoked compound action potentials [18]. Systems that use closed-loop SCS (CL-SCS) make use of evoked compound action potentials (ECAP). ECAP is generated as a result of therapeutic stimulation from one of the electrodes, and it then spreads across retrograde and orthodontic orthopedics. With the remaining, discarded electrodes, ECAP can be obtained in either or both directions [19]. The electrode to target site distance is directly proportional to the difference in charge generated at the electrode and the charge transferred to the spinal cord. The distance for electrodes positioned epidurally is predominantly dictated by the dorsal layer of cerebrospinal fluid and the dura mater thickness [6]. To maximize neuronal activation and stimulation accuracy and to assist programming, ECAP offers an objective physiological biomarker for therapeutic spinal cord activation. Personalized CL-SCS ECAP amplitude targets are used to deliver controlled energy to maintain the accuracy of neural activation. The ECAP-controlled CL-SCS uses real-time ECAP measurements to automatically adjust the output of each electrical pulse in reaction to the changing conditions between the spinal cord and the electrode [17].

Avalon's analysis of the first closed-loop SCS system assessed the ECAP system's effectiveness in managing chronic pain [20]. Research demonstrates that the closed-loop device reduced back pain by an average of 77.3% 24 months following implantation [21]. Comparing open- and closed-loop SCS, it was found that three-fifths of patients in the open-loop group met the primary outcome criteria after three months, while approximately four-fifths of patients in the closed-loop group experienced pain reduction of at least one-half and no increase in baseline medications [22]. Evoke has indicated in his research that when ECAP is combined with closed-loop SCS patients can achieve sustainable pain control without manual adjustments during physical movement.

In comparing different spinal cord stimulation techniques,

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Tonic SCS provides pain relief through continuous low-frequency stimulation and is suitable for chronic pain management. Burst SCS, on the other hand, utilizes brief pulses of stimulation that mimic natural nerve activity, potentially improving patient comfort and efficacy. High-frequency SCS utilizes high-frequency pulsed stimulation, which is typically associated with lower pain perception and is appropriate for certain types of pain. Closed-loop SCS has real-time monitoring and modulation capabilities to optimize pain control by dynamically adjusting stimulation parameters based on the patient's physiological feedback. Each of these techniques has advantages and disadvantages and is adapted to different clinical needs and patient characteristics. There is a more detailed cross-sectional comparison of common spinal cord stimulation (SCS) treatment options in Table 1. Meanwhile, Fig. 1 shows the current versus time profile of four modes of SCS to visualize the effects of different stimulus forms in pain relief.

Table 1. Cross-sectional comparison of common spinal cord stimulation

	Tonic SCS	Burst SCS	HF SCS	Closed loop SCS
Principle	Constant activation of the spinal cord's dorsal columns	Intermittent pulse stimulation of nerve bundles	High-frequency pulses do not trigger sensory electrical stimulation	Adjusting stimuli to match neural responses based on real-time feedback
Frequency	40-60 Hz	500 Hz	10 kHz	40-60 Hz
Current Form	Continuous constant current	Short pulse current	Continuous high frequency current	Constant current with real-time closed-loop control
Pain Masking Effect	Masking of pain signals, at times accompanied by numbness	Reducing pain and numbness	Highly effective in masking pain without numbness	Dynamically optimizing pain relief and individualizing treatment effects
Effects on Nervous System	Direct inhibition of pain signaling	Improvement of neuroplasticity and modulation of pain thresholds	Blocking pain signal transmission without eliciting a sensory nerve response	Precise feedback regulation to reduce nervous system fatigue
Battery Life	Long (lasts for many years, varies according to setup and use)	Relatively short (fast power consumption at higher frequencies)	Short (due to higher frequencies requiring more power)	Similar to Tonic SCS, but energy efficiency may be better
Population	Suitable for most chronic pain patients	Especially appropriate for individuals not responding to tonic SCS	Patients with intractable pain not responding to conventional SCS	People whose response to pain changes rapidly and who need more precise and individualized treatment plans
Potential Side Effect	Numbness, occasional tingling	Less tingling and fewer side effects	Long-term effects unknown, may be sensitive to high-frequency currents	Requires more sophisticated equipment and may be more prone to equipment failure

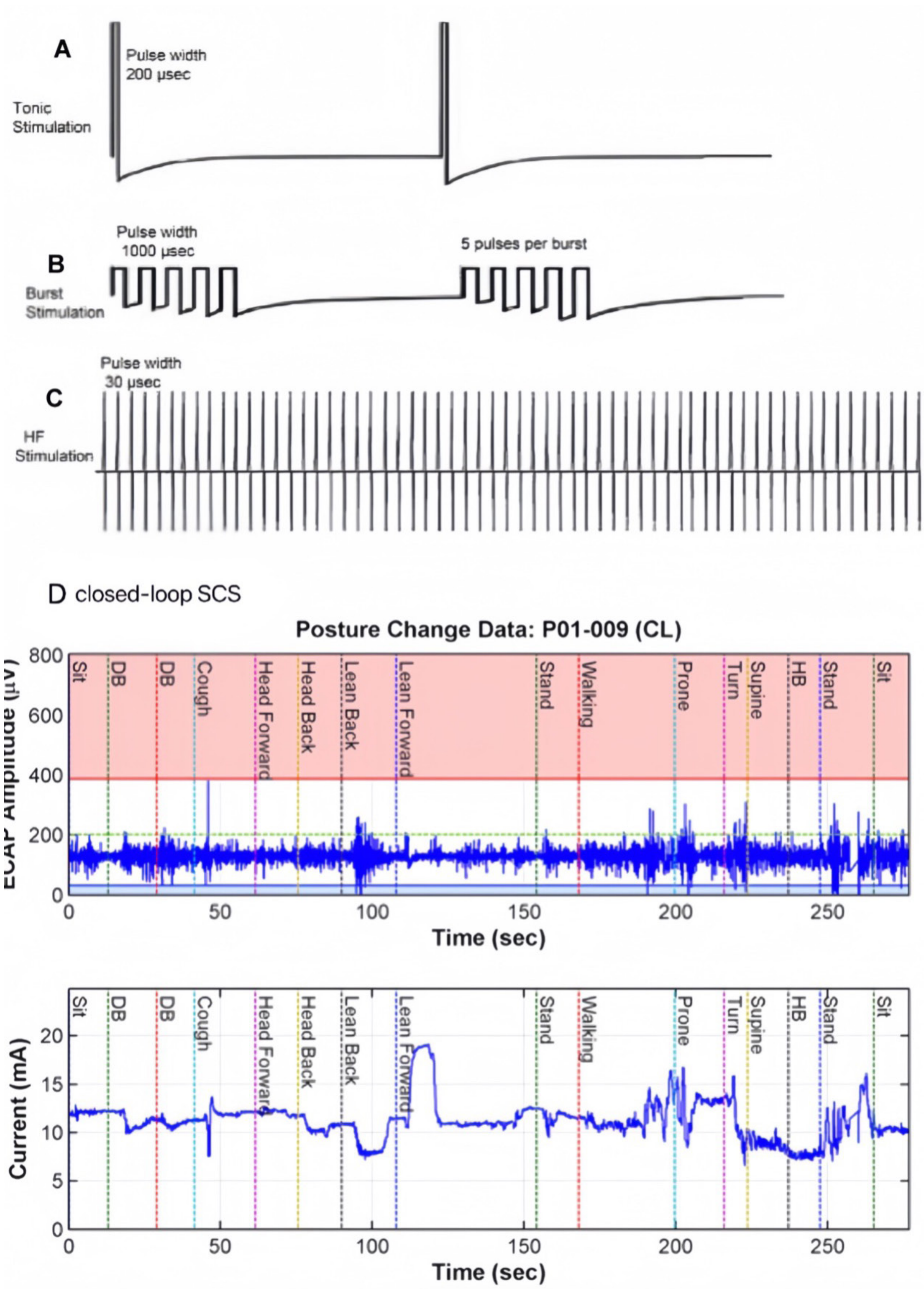

Fig. 1 Waveforms that allow tonic (A), burst (B), and high-frequency (C) SCS relative pulse lengths, frequencies, and amplitudes to be compared [20]. (D) shows how the closed-loop system responds to ECAPs by automatically adjusting its stimulation levels, thereby preventing periods of over- or under-stimulation [21].

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3. Complications of SCS

A typical side effect of spinal cord stimulation is electrode displacement, with studies showing an incidence between 1.5% and 13.2%. Cameron's study showed that electrode displacement occurred in approximately 13.2% of 2753 patients [23], An incidence of 11.3% was observed by Kumar et al [24], whereas Mekhail et al.'s study found that 119 out of 527 patients experienced lead displacement [25]. This situation often leads to failure of pain control and increases the risk of infection, as each surgical repair is accompanied by an elevated risk of infection.

Electrode displacement is usually confirmed by radiographic examination and typically manifests as a change in stimulation or an adjustment in voltage requirements. In some cases, patients may still feel symptoms even if the shift is not detected by radiography. In this case, comparing radiographic images postoperatively and at the time of suspicion of displacement is an effective way to confirm displacement [26]. In addition, cerebrospinal fluid displacement in the epidural space of the spinal cord may also affect the distance between the electrode and the spinal cord in different positions, leading to failure of pain control, but this is not related to the displacement of the lead [27].

Although electrode displacement can be corrected by reprogramming the device, surgical repositioning is often required in cases of severe displacement. However, even with the most advanced electrode technology, reprogramming may not help in cases of severe displacement, requiring surgical intervention [28].

In conclusion, although lead displacement is a common complication of SCS, the need for surgical repair has diminished through improved implantation techniques and multi-contact electrode systems. However, in cases of severe displacement, surgical repositioning remains an unavoidable option.

4. Future directions

4.1 Intelligent implantable devices

Currently, conventional SCS devices require the stimulation parameters to be manually adjusted in reaction to variations in pain or changes in patient posture. Future smart implantable devices may be able to automatically adjust through integrated sensors and algorithms. For example, position-sensing technology could be used to monitor a patient's body posture and automatically modify the electrical stimulation's intensity in response to variations in the spinal cord's and spine's distance from one another. This technology may be able to address the problem of over-stimulation or under-stimulation of patients in different positions, improving efficacy and reducing discomfort. In addition, the personalization capabilities of smart SCS devices can be enhanced. Through machine learning and big data analytics, the device can automatically optimize stimulation patterns and parameters based on historical patient data and real-time feedback. Future devices may use a closed-loop control system that monitors nerve activity in real time and automatically modifies stimulation levels to always match the patient's pain state. This advancement could improve the accuracy of treatment and reduce the need for frequent manual adjustments.

4.2 Advances in neurofeedback techniques

Neurofeedback technology could also be an important direction for SCS innovation. While traditional SCS devices only provide external electrical stimulation, future systems may incorporate neurofeedback to monitor and respond to the patient's neural signals in real time. This means that the device can rely not just on a fixed current pattern, but dynamically adjust the stimulation based on the immediate state of the nervous system. This technique is expected to significantly improve treatment outcomes, especially in the long-term management of chronic pain. For example, closed-loop neurofeedback systems are being investigated by directly monitoring neural signals (e.g., firing patterns of pain neurons) and automatically adjusting stimulation parameters based on the feedback. This technology will not only increase the efficiency of pain relief, but also reduce patients' dependence on opioids. By interacting with the nervous system in real time, these systems will be able to capture small changes in pain and provide more personalized and continuous pain management.

4.3 Multimodal electrical stimulation

Future SCS devices may also incorporate multimodal electrical stimulation, in which different types of stimulation modes (e.g., high-frequency, pulse train, and low-frequency stimulation) are used simultaneously to allow for greater flexibility in responding to different types of pain. For example, certain patients respond better to high-frequency stimulation, while others may require pulse train or mixed-mode stimulation. By integrating multiple stimulation modalities, future devices will be able to treat complex pain problems more precisely and maximize relief through personalized treatment plans [29,30].

5. Conclusion

In the treatment of vascular and chronic neuropathic pain, spinal cord stimulation technology has become increasingly important, especially for patients with refractory leg and back pain. The existing literature suggests that SCS has significant benefits in terms of improving patients' pain, and quality of life, and reducing the use of analgesic medications (especially opioids). With the development of different stimulation modalities, such as tonic SCS, high-frequency SCS, burst SCS, and closed-loop SCS, the efficacy of SCS has been further enhanced, showing strong potential, especially in terms of decreasing side effects, improving patient satisfaction, and increasing the durability of pain relief.

However, despite important clinical advances in SCS, a number of challenges and limitations remain. Electrode displacement, device malfunction, and inconsistent treatment results for specific pain types (e.g., low back pain) are currently the main technical challenges. In addition, most of the available studies have focused on short-term efficacy, with relatively limited data on long-term efficacy and device safety. Future research should focus on improving device stability, reducing complications, and continuing to explore intelligent and personalized treatment options, such as closed-loop control systems incorporating neurofeedback.

Overall, the role of SCS in chronic pain management cannot be ignored and its potential technological innovations will further expand its applicability. With new device development and technological advancements, it is projected that SCS will play a major role in the treatment of a greater variety of pain types and develop into a feasible long-term option for people with chronic pain. Long-term follow-up studies and higher caliber randomized controlled trials will be necessary in the future to confirm the long-term safety and effectiveness of SCS.

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