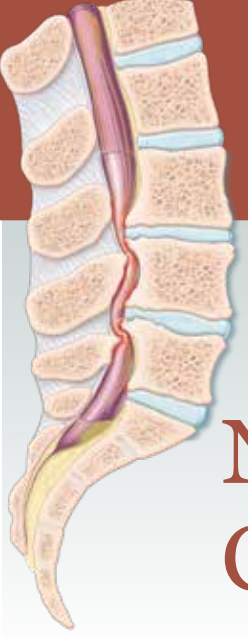

Neuromodulation for the Management of Chronic Pain After Spinal Surgery

ABSTRACT

Chronic neuropathic pain is associated with substantial disability and societal economic impact. Formerly called Failed Back Surgery Syndrome, and now labelled as Chronic Pain after Spinal Surgery by the ICD-11, this entity represents persistent neuropathic leg pain following structurally corrective spinal surgery, often refractory to pharmacological and interventional management,. In appropriately selected patients where medical management has been unsuccessful, the minimally invasive surgical technique of spinal cord stimulation can reduce disability and pain. Technological advances continue to improve this approach with greater success, lessened morbidity, and expanding indications.

KEYWORDS: chronic pain after spinal surgery, failed back surgery syndrome, neuropathic pain, spinal cord stimulation, neuromodulation

CME Pre-test Quiz

Introduction

The International Association for the Study of Pain (IASP) has defined pain as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage".[1] Chronic pain is defined as pain persisting beyond normal healing time.[2] With worldwide prevalence estimates of 13-53%, chronic pain can have profound socioeconomical impacts. It interferes with

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activities of daily living, increases rates of health-related unemployment, impairs psychological function, and increases utilization of health care resources.[3-6]

Neuropathic pain is a specific chronic pain subtype, defined as pain caused by a lesion or disease of the somatosensory nervous system.[1] Neuropathic pain presents clinically with spontaneous features including burning sensations, tightness, and unpredictable lancinating pain. It has stimulus-evoked features such as hyperalgesia, a heightened response to a painful stimulus, and allodynia, a painful response to normally non-painful stimuli.[1] The prevalence of neuropathic pain ranges up to 17.9% and includes diagnoses of painful diabetic neuropathy, lumbosacral radiculopathy, post-herpetic neuralgia, post-infectious or post-chemotherapy neuropathy, complex regional pain syndrome, and chronic pain after spinal surgery (CPSS), formerly designated failed back surgery syndrome (FBSS).[6-8]

CPSS with neuropathic pain is generally identified after ruling out structural spinal and compressive neural pathologies. Treatment is usually an escalating pharmacological and interventional regimen which can lead to neuromodulation. The use of electrical stimulation for analgesia was identified by the Roman physician Scribonius in 15AD, with the fortuitous observation that inadvertent contact with the electrified torpedo fish provided relief of gout pain.[9] Since the application of electrical stimulation to the dorsal columns of the spinal cord by Shealy *et al.* in 1967, spinal cord stimulation (SCS) has demonstrated clinical efficacy in the management of CPSS.[10] Originally, supported by prospective randomized controlled trials, SCS was reserved for leg-dominant CPSS. However, recent studies using newer stimulation paradigms have shown benefits of SCS in back-dominant CPSS and in non-surgical neuropathic pathologies.[11,12]

Overview of Neuropathic Pain

Despite the high prevalence of neuropathic pain, there remains substantial ambiguity about its pathophysiology. In the context of CPSS, the residual neuropathic pain is assumed to arise from ischemic or fibrotic changes to neural structures.[13,14] Since these changes may be invisible intraoperatively, a diagnosis may only be possible after adequate surgical decompression of the neural elements and successful restoration of spinal stability fail to resolve the patient's pain. Adding to the ambiguity is the fact that the diagnosis is made on a set of symptoms and subjective descriptions that are challenging to measure objectively. Most structural and functional investigations are only employed to rule out alternate diagnoses.

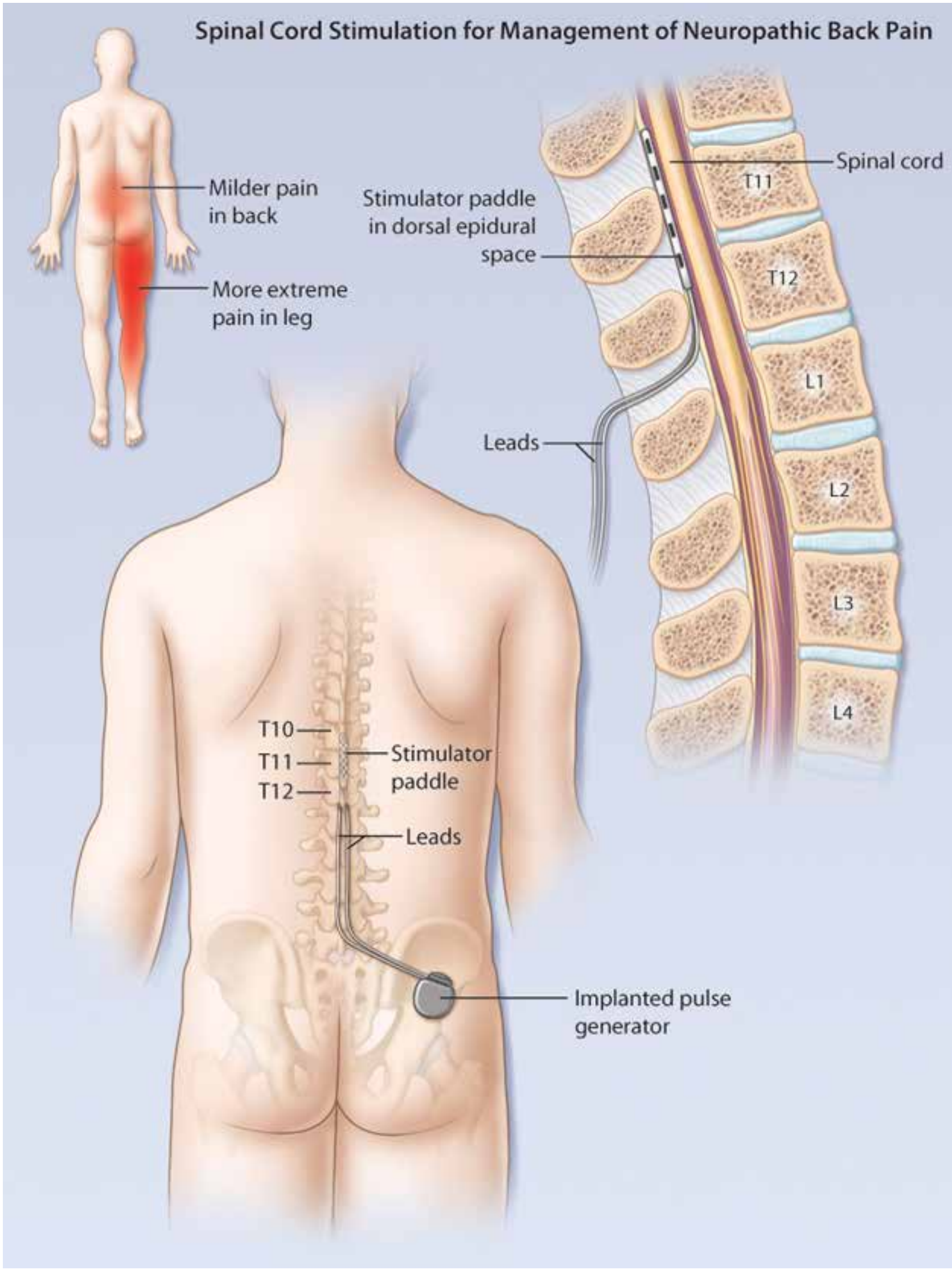
The IASP definition of neuropathic pain describes two main mechanisms, either a peripheral or central origin but the means by which practicing clinicians can distinguish neuropathic pain from other types of pain has remained elusive. The uncertainty has created a constellation of different features detected by various examination techniques and screening tools.[15,16] The specific qualities include allodynia, hyperalgesia, hyperesthesia, and hyperpathia. Hyperesthesia describes augmented sensitivity to all stimuli while hyperpathia is an abnormally painful response to a repetitively applied stimulus.

The clinician is faced with interpreting subjective responses into patterns of pain behaviour. The most consistent features include burning and a lancinating pain, the presence of paresthesia, and clinical findings of allodynia. More recent diagnostic methods include Quantitative Sensory Testing (QST) and electrodiagnostic studies.[17] QST is performed by administering various standard noxious stimuli (thermal, mechanical, electrical) under controlled settings to identify a dysfunctional sensory response. Electromyography (EMG) and nerve conduction studies (NCS) may offer additional confirmation of neural injury, supporting the pathophysiological basis of neuropathic pain.

What is Spinal Cord Stimulation?

In 1965 Melzack and Wall's Gate Control Theory, suggested that pain transmission in the spinal cord is modulated by nerve impulses from afferent fibers through a spinal gating mechanism in the dorsal column. This led to speculation about the use of electrical stimulation for pain management.[18] Melzack and Wall postulated that when small diameter C-fibers were activated, a "gate" opened allowing pain transmission. The gate closed with the activation of large afferent fibers blocking small fiber transmission. It was hypothesized that electrical stimulation of large afferent fibers would precipitate selective "gate closure" preventing painful input into the central nervous system. Two years later, Shealy and his group were the first to apply electrical stimulation to human dorsal columns, thereby demonstrating its clinical efficacy and corroborating the gate theory.[10]

Recent investigations and discoveries have shown that the mechanisms by which SCS achieves analgesia are more complicated than the original gate hypothesis. Evidence of complexity includes the lack of influence of SCS on nociceptive and induced acute pain, the ability to generate pain by activation of large afferent fibers, obliteration of cutaneous hyperalgesia by selective large fiber blocks and the fact that analgesic effects of


Spinal Cord Stimulation for Management of Neuropathic Back Pain
Milder pain in back
More extreme pain in leg
Stimulator paddle in dorsal epidural space
Spinal cord
T11
T12
L1
L2
L3
L4
Leads
T10
T11
T12
Stimulator paddle
Leads
Implanted pulse generator

SCS may outlast the duration of the stimulation.[19] Multiple sites within the central and peripheral nervous system are involved and there is modulation of the glial cell structure. Molecular analyses reveal that SCS can influence levels of cerebrospinal fluid neurotransmitters including increasing GABA, serotonin, Substance-P, norepinephrine, acetylcholine, and adenosine, while decreasing glutamate and aspartate.[20-22]

In the past, stimulation was considered successful when the pain in the target area was replaced by paresthesia. Now adjustments in stimulation amplitudes or frequency can modulate pain signals to produce paresthesia-free pain relief.[23] These new types of spinal cord stimulation have shown improved clinical outcomes and lower risk of therapeutic failure.[24]

Patient Selection for SCS

Correct patient selection is essential for SCS to successfully manage CPSS but selecting the proper subject is challenging even for experienced surgeons and pain physicians; a fact reflected in the variable rates of conversion from trial stimulation to permanent implantation.

Because of the difficulty in patient selection, a multidisciplinary team generally assesses patient suitability for SCS. The disciplines involved include surgery to identify structurally-correctable spinal pathologies, psychology to diagnose and manage comorbid mood and anxiety disorders, and comprehensive pain medicine for pharmacological and interventional treatment of neuropathic pain.

Contraindications to device implantation include untreated psychiatric comorbidity, presence of correctable structural pathology, coagulopathies, active infection and an inability to provide informed surgical consent or properly use the technology.[25,26]

Structural Spine Pain

Persistent post-surgical low back and/or leg pain may be due to a variety of different etiologies. It is important to examine the initial diagnosis, the effectiveness of the surgical intervention, the possibility of a new iatrogenic pain source and the sequelae of additional surgical intervention. The index surgery may not have achieved the intended goals and revision surgery may be warranted to complete the initial decompression, correct pre-existing or new deformity and stabilize any previous or newly created instability.

The diagnostic armamentarium includes structural and functional evaluations of the musculoskeletal and nervous systems. Magnetic resonance imaging with contrast can identify ongoing nerval compression or the development of epidural fibrosis. Computed tomography examines the bony anatomy and

can demonstrate lateral recess and foraminal stenosis while dynamic (flexion-extension) radiographs can show post-surgical instability.

Psychological Assessments

Individual pain experience and the response to various management modalities including SCS are influenced by comorbid psychopathology.[27] Mood and anxiety disorders, found in 50%-80% of patients with chronic pain, are the most common abnormalities. Self-reported levels of depression, anxiety, poor coping, somatization and hypochondriasis all correlate with poorer treatment benefits.[28] Other predictors of an unsuccessful outcome include pain chronicity, negative emotional impact, pain-related catastrophizing, substance abuse, cognitive dysfunction, poor social support and history of abuse or trauma.[28-30] Formal psychological assessment and optimization of mood and anxiety disorders should occur prior to permanent device implantation. The goal of SCS is to provide symptomatic pain control, and not to correct underlying pathology; complete pain relief is unrealistic. The early identification and treatment of significant vulnerabilities should improve patient satisfaction, heighten the response to SCS therapy and decrease the rate of unsuccessful trials.

Comprehensive Pain Management

Treating neuropathic pain secondary to CPSS requires a comprehensive pain medicine approach including pharmacologic, interventional and multidisciplinary initiatives.[31,32] Management begins with active physiotherapy and psychotherapy often followed by a stepwise multi-tier pharmacological approach. This should be supplemented with attempts to improve sleep and physical function. The goals of therapy must be clearly established; it rarely obliterates the pain completely but makes symptoms bearable and improves the quality of life.

SCS Process

When a patient is deemed an appropriate candidate, the first step is an externalized trialing process, which, if positive, is followed by the insertion of an implantable pulse generator (IPG). The procedural details vary. They may include general anesthesia or conscious sedation; trialing may be by percutaneous or surgically inserted leads. During the external trialing process, the patient has an opportunity to test various stimulation programs and try multiple modes of paresthesia-based and paresthesia-free stimulation. A trial is deemed successful when a patient demonstrates both 50% reduction in pain intensity and improved outcomes for physical function, mood and sleep.

When these criteria are met and the patient wishes to proceed, the IPG is internalized. For CPSS,

SUMMARY OF KEY POINTS

1. Managing chronic pain after spinal surgery is a challenging and requires combined pharmacological and interventional options.
2. Spinal cord stimulation is a modality with strong evidence to supports its efficacy in the management of patients with chronic pain after spinal surgery.
3. The workup of patients with chronic pain after spinal surgery must include multi-tier pharmacological approaches, psychological optimization, and structural spinal assessment from a multidisciplinary group of clinicians.

the location for implantation of the IPG in the dorsal epidural space ranges between T8-9 and T12-L1. The lead must be positioned so that it is symmetrical with the longitudinal axis of the spinal canal and its rostrocaudal location permits generation of limb paresthesia with minimal abdominal side effects. The IPG is generally anchored with an epifascial strain relief loop.

In addition to all the usual risks of spine surgery, unique risks associated with the SCS device include battery depletion, lead migration, hardware failure, cutaneous erosion, and infection; infected hardware can lead to epidural abscess.

SCS Outcomes

The value of SCS in the management of leg-dominant CPSS has been well established. The first randomized study, by Kumar *et al.*, demonstrated significant reduction in pain for SCS patients (58%) compared with conventional medical management (17%) along with improved self-reported quality of life, albeit with short term higher resource costs.[33,34] The second randomized study, by North *et al.*, showed 47% improvement in pain among SCS patients compared with 11% for patients undergoing repeated spinal surgery.[35] Traditionally SCS has been considered the "last resort treatment" for patient with chronic pain syndromes who have proven refractory to prolonged conventional medical management. But recent studies suggest that the long-term efficacy of SCS is inversely related to the duration of pain prior to implantation so some proponents recommend offering a trial of SCS if there is a suboptimal response to conventional multidisciplinary management after 12 to 16 weeks.[26] Kumar *et al.* reported success rates of over 85% if implantation occurs within 2 years following the onset of pain which decreases to as low as 9% with delays of 15 years or longer.[36,37]

Newer modes of SCS have shown promise for FBSS/CPSS.

Kapural *et al.* compared delivery of SCS at 10 kHz frequency, a paresthesia-free mode of stimulation, to conventional paresthesia-based stimulation for the management of chronic intractable back and leg pain in the SENZA randomized, parallel-arm, non-inferiority study.[12] The study randomized 198 subjects with both back and leg pain in a 1:1 ratio, with the primary outcome defined as having 50% or greater back pain reduction with no stimulation-related neurological deficit. Most of the enrolled patients, 77.1%, were diagnosed as FBSS/CPSS. At 3 months, 84.5% of implanted 10kHz therapy subjects with back-dominant pain and 83.1% with leg-dominant pain had a positive response. For the traditional SCS subjects, the results were 43.8% and 55.5% for back and leg dominant pain respectively. The superiority of 10kHz therapy over traditional SCS was sustained over 12 months.

Fishman *et al.* performed a prospective, open-label, multicentre cohort study assessing the feasibility of a novel form of SCS called differential target multiplexed stimulation for the management of low back pain.[11] Twenty-five patients, 72% diagnosed with FBSS, with a mean baseline numeric pain rating scale (NPRS) score for low back pain of 7.4, and mean pain duration of 18.0 years, received both the standard paresthesia-based and the differential target multiplexed (paresthesia-free) programs. The primary outcome was change in low back pain relative to baseline; a lower score indicates less pain. After standard programming subjects reported a reduction in their mean NPRS score from baseline to 4.2. That fell to 2.4 after the differential target multiplexed programming. The responder rate for low back pain relief was 50% for standard programming and 80% for differential target multiplexed programming.

CLINICAL PEARLS

Neuropathic pain is defined as pain caused by a lesion or disease of the somatosensory nervous system[1]. Spontaneous features include burning pain and tightness with unpredictable lancinating features.

The mechanism of spinal cord stimulation involves multiple sites within the central and peripheral nervous system. SCS can influence levels of cerebrospinal fluid neurotransmitters including increases in GABA, serotonin, Substance-P, norepinephrine, acetylcholine, and adenosine, and decreases in glutamate and aspartate.

The differential target multiplexed (paresthesia-free) spinal cord stimulation programs appear superior to the older standard paresthesia-based approach.

CME

Post-test Quiz

Members of the College of Family Physicians of Canada may claim MAINPRO-M2 Credits for this unaccredited educational program.

Conclusion

The management of persistent low back and leg pain following spinal surgery can be challenging with treatments ranging from psychotherapy to pharmacology to neuromodulation. As technology advances, the utility of SCS will continue to grow. The technique has been rigorously evaluated for treating CPSS and compares favourably to both medical management and conventional spinal surgery for pain control and cost effectiveness.

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