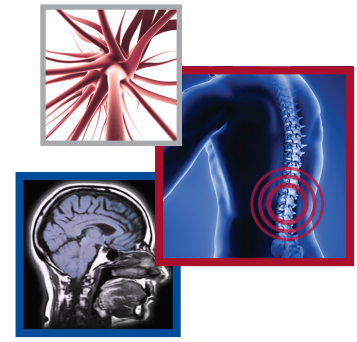
SYSTEMATIC REVIEW

Pain Management



A systematic review on the treatment of phantom limb pain with spinal cord stimulation

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Practice points

- The history of phantom limb pain (PLP) and how over the years spinal cord stimulation (SCS) has played a role in management for clinicians.
- The incidence and prevalence rates of PLP and importance of recognizing the pain and properly treating it.
- The paper goes into extensive detail with neurophysiological background the mechanisms and pathways of PLP, and how SCS neurologically plays a role in mitigating this pain neurologically.
- The aim of this systematic review is to provide evidence and well-established researched data on the efficacy of SCS for PLP.

Methods

- The authors utilized keyword searches in PubMed to ensure that a thorough, extensive search of the literature was carried out.
- Inclusion and exclusion criteria were used for this systematic review to help provide a more defined, focused systematic review.
- After using PRISMA method, and adequate analysis of the selected studies, a total of 12 research articles was decided on to be included in this systematic review.

Results

- The results of this review indicate that out of 12 studies, seven showed clinically significant results for pain relief, five did not show any pain relief.

Discussion

- There is discussion of the results, analyzing certain studies and highlighting the important findings amongst the 12 studies reviewed.
- There is discussion of potential complications of SCS management, as it is important for clinicians as well as patients to be aware of these.
- With the focus of this paper being on SCS, it is important to briefly discuss other treatment modalities for PLP (pharmacological and non-pharmacological).
- The limitations of our systematic review are presented in a concise, concluding manner.

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Phantom limb pain (PLP) is a challenging chronic pain syndrome to treat with pharmacologic agents being first line of management. However, when these agents fail to provide pain relief, other interventions must be considered in a clinical setting. Spinal cord stimulation (SCS) has been shown to provide analgesia in PLP, and should be considered by clinicians. **Methods:** This PRISMA systematic review analyzes the efficacy of SCS for treatment of PLP. **Results:** After review of 12 studies, there are mixed results to base a conclusion on. **Discussion:** While there is some evidence of efficacy, due to the relatively small number of patients in each study, further research is needed to demonstrate the benefits of SCS for PLP.

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KEYWORDS
• neuromodulation
• phantom pain • spinal cord stimulation

The first description of phantom limb pain (PLP) occurred in 1552, by French barber surgeon, Ambroise Pare, who witnessed injured soldiers on a battlefield, and were treated with amputation. However, the actual term was given in 1866 by neurologist Silas Weir Mitchell [1]. The International Association for the Study of Pain defines PLP as, 'pain referred to a surgically removed limb or portion thereof' [2]. Patients can perceive movement and position of that phantom limb. Sensations, additionally, in phantom limbs include temperature changes, pruritus, electrical sensations and tingling [3].

Sherman and Sherman discuss how PLP can be divided into four categories: intensity of pain sensations, frequency of episodes, duration of each episode and description of the pain [4]. Onset of PLP subsequent to amputation can vary from days to years according to Weeks *et al.* Weeks *et al.* report that the onset is usually immediately, in the majority of patients, with 50% experiencing the pain within 24 h after amputation, and within a week for another 25% of the patients [5].

The prevalence of PLP ranges from 50 to 85%, however, this is dependent on the site of amputation, anesthetic technique, patient population and time since amputation [6]. However, another study, by Subedi and Grossberg, reported that the prevalence of upper limb PLP was slightly lower, 43% in their conducted study [7].

Recent research indicates that the prevalence of PLP is more common in females than males. Even though as previously mentioned that PLP can occur from days to years, it should be noted that PLP has been described as having two peak periods of onset: within a month, and then after a year, postamputation. Prevalence of PLP is reported to decrease over time after amputation [8]. PLP is becoming more important due to the increase in prevalence of amputees in the population. A study report in 2005 US statistics describes that there were 1.6 million amputees, with a projected number of 3.6 million by the year 2050 [9]. Annually, there are roughly 185,000 limb amputations in USA, costing the healthcare US$12 billion [10]. On a global level, incidence of amputation is 4–68 per 100,000 people. Certain conditions, such as diabetes, can also contribute to an increased incidence rate [10]. For instance, Wrobel *et al.* reported an incidence of amputation in USA being 38 per 100,000 compared with over 380 per 100,000 in the diabetic population [10].

PLP is a challenging chronic pain syndrome to treat, with pharmacologic agents being first line of management [11]. Treating PLP can be divided into four interventions: pharmacological, surgical, anesthetic and psychological [1]. In 1967, spinal cord stimulation (SCS) was introduced, and considered as an intervention for a variety of pain syndromes [12]. SCS has been a modality for treatment of PLP since 1969, and the first published case series was in 1975 for PLP [13].

The widely accepted explanation behind SCS mechanism is 'gate-control theory,' which states electrical stimulation of the Aβ fibers within the dorsal columns inhibits the transmission of pain information to the brain via the Aβ and C fibers [14]. The theory behind pain transmission included 'gating mechanism,' involving the activation of large-diameter fibers modulating pain perception. More recent research describes SCS as an alteration of 'wide-dynamic-range' neuron excitability, facilitation of physiological inhibitory mechanisms and changes in activity of several neurotransmitters, including glutamate, adenosine, acetylcholine, substance P, calcitonin gene-related peptide, brain-derived neurotrophic factor and bradykinin [15]. Animal models show that SCS produce an increased spinal release of serotonin, and a decreased release of GABA in the periaqueductal gray region. More importantly, SCS is thought to have an

effect on neuropathic pain through application on dorsal column. Song *et al.* investigated the involvement of descending pain control from the rostral ventromedial medulla (RVM) with SCS. Their study demonstrated that activation of certain RVM neurons in animal models that responded to SCS. In addition, literature gives evidence of the correlation between activation and SCS responsiveness with the release of GABA, serotonin and acetylcholine in the spinal dorsal horn. Song *et al.* were able to demonstrate that the activation of descending inhibitory signals originating or relaying through the RVM plays a role in analgesia. Furthermore, this animal study showed that SCS responsive subjects produced an excitation of antinociceptive RVM off-like cells and serotonin like cells, while there was no effect on pro-nociceptive RVM on-like cells. In addition, there was no evidence of central opioid mechanisms being involved [16].

The basic unit of electrical stimulation in SCS is the 'pulse.' This pulse refers to a specific amount of current amplitude (measured in mill amperes) for a specific amount of time (pulse width, measured in μs). Frequency (number of pulses per second), pulse width and intensity can be adjusted to optimize patient therapy. SCS rates are normally in the range of 40–125 Hz, but frequencies of 50 Hz are most commonly used [17]. Frequencies of 50 Hz activate dorsal horn GABAergic neurons as well as interneurons that use transmitters such as acetylcholine and adenosine, serotoninergic cells in the ventromedial medulla and nuclei in the locus ceruleus region that contains norepinephrine [18].

We systematically reviewed literature to investigate the efficacy of SCS for the treatment of PLP. Since pharmacological treatment for PLP is somewhat limited, SCS is a noteworthy alternative. The aim for this review is to provide evidence and well-established, available research data on the efficacy of SCS for the treatment of PLP, and how beneficial it may be for clinicians to utilize this intervention. SCS is a relatively specialized treatment, when considered as a treatment modality for PLP. Our aim is to disclose the advantages and disadvantages of using this intervention, and whether or not clinicians should strongly consider this therapeutic option in the management of PLP.

Methods

A systematic review of all the published and ongoing literature was conducted via PubMed. The PRISMA method was used for each search. Keywords for searches include 'SCS and phantom', 'SCS and phantom limb', 'SCS and phantom', 'SCS and phantom limb', 'dorsal column stimulation and phantom' and 'dorsal column stimulation and phantom limb'. All articles from 1970 to July 2016 were searched on PubMed.

The exclusion criteria include omitting articles that were case reports, reviews, studies involving children (less than 18 years of age), nonhuman (animal model) studies, non-English studies and combination therapies. Therefore, the inclusion criteria were all clinical trials involving SCS and treatment of PLP, patients of all races and ethnicities and older than 18 years of age.

R Aiyer and R Barkin reviewed all trials for screening selection and extraction. The PRISMA method allowed for 123 articles to be screened. The first screening involved the reviews to exclude duplicate and irrelevant records. After this step, the remaining articles were screened, initially with the title of the research paper, then analysis of the abstract followed by analysis of the full texts. Fifteen full-text articles were obtained and analyzed. After applying the inclusion and exclusion criteria, the final number is 12 studies that were used in the literature review and included in the final manuscript. This process can be viewed on the PRISMA flow chart **(Figure 1)**.

The purpose of this review is to present a detailed and comprehensive review of all the literature involved with SCS and treatment of PLP. The level of evidence model was utilized, to break down the studies into different levels of review [19]. **Table 1** illustrates this model. The 12 articles represented level II evidence of SCS for PLP.

Results

The results of the data are summarized in **Table 2** [20–30]. A total of 12 studies were reviewed **(Table 2)**, which are organized chronologically. Of the 12 studies reviewed, seven illustrated clinically significant results for pain relief in patients with PLP. The other five studies showed no change in pain or any pain relief. All of the studies reviewed involved patients with an amputation that experienced PLP.

A couple of objective scales for measurement of pain were used throughout the literature review, including McGill pain questionnaire and visual analog scale (VAS). McAuley *et al.* used VAS, which showed that VAS scores were unchanged. Many of the researchers also used

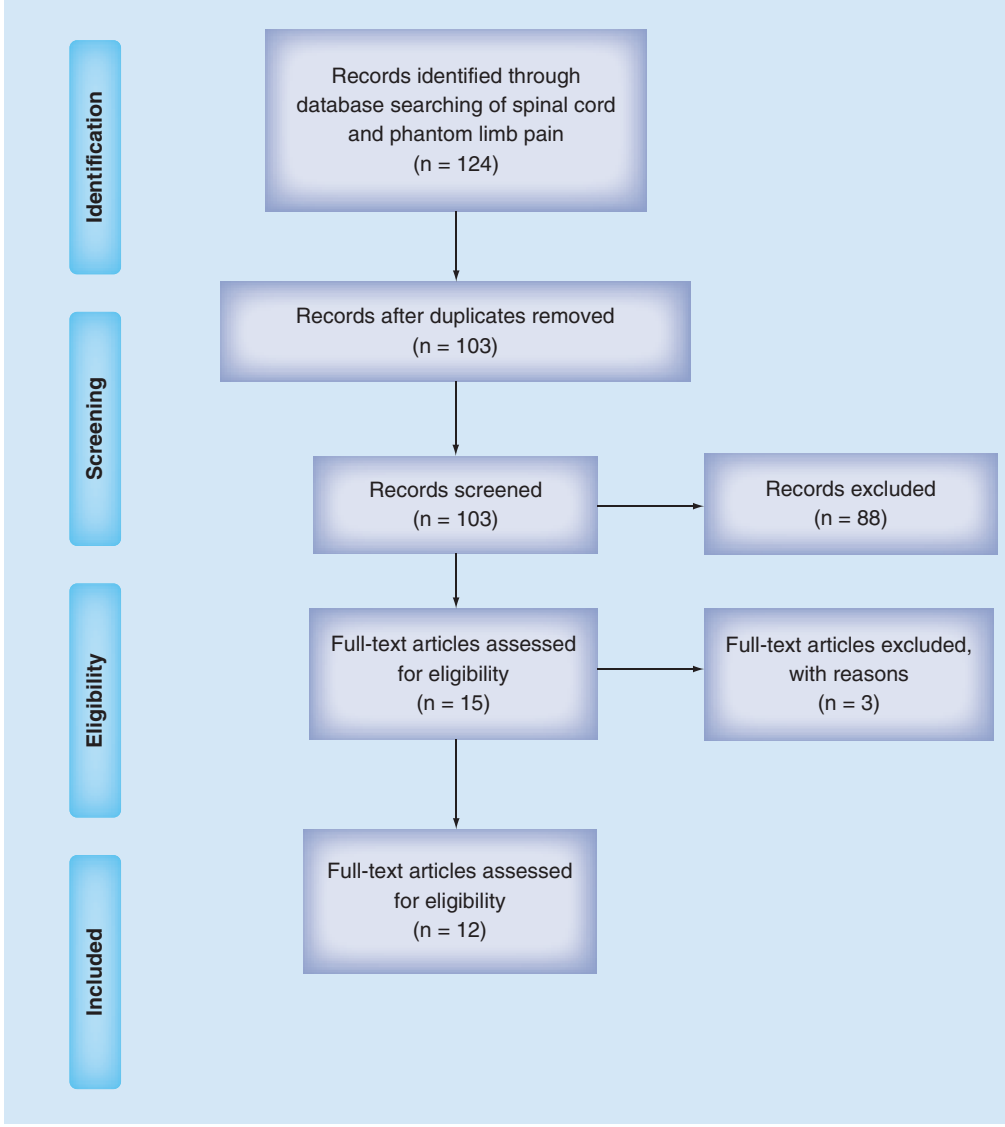

Figure 1. PRISMA flow chart of spinal cord stimulation and phantom limb pain.

subjective rating scales based on the patient's response. For instance, Wester used a simple system of 'good = 3', 'moderate = 2', 'weak = 1' and 'none = 0'. Based on this scale, average pain score before electrode implant: 2.50, and after SCS placement: 2.13, and therefore demonstrating a tendency toward pain amelioration [27]. Krainick *et al.* utilized a somewhat more structured subjective rating scale, with 'excellent' having more than 75% pain relief, 'good' having 51–75% and 'fair' having relief of 26–50% [28]. With this rating scale, 20.3% of patients had excellent relief, 25% had good relief and 11% had excellent results among a group of 64 patients [28].

Other factors such as pain intensity, frequency of pain occurrence, paresthesia and stump pain were also taken into consideration. Coverage of painful area with paresthesia (tingling sensation) is expected in traditional SCS, unless subthreshold parameters are used for paresthesia. However, sometimes the patients report paresthesia as unpleasant, and discontinuation of the SCS therapy may be required. In certain cases, SCS may be useful for stump pain if the pain is neuropathic in nature and originating from nerve injury or neuroma at the stump site. SCS, in general, does not provide pain relief for non-neuropathic pain conditions, at the stump site in case of mechanical causes (such as local irritation due to poorly fitting prosthesis) or inflammatory causes such as infection at the stump site.

Discussion

PLP has been proven to be a challenging condition to treat. It is evident from the data that SCS is a viable option for clinicians, when needed to treat PLP. Overall the studies evaluating the effectiveness of SCS for PLP demonstrate there are analgesic properties of this intervention, and thus an SCS implantation, provided that the trial period is successful, should be strongly considered in the management. The mixed results from this review illustrate the possible implications that SCS has to offer physicians in PLP. A major reason for the mixed results is that the pathophysiology of pain in PLP is still incompletely understood. Therefore, an SCS trial period with appropriate stimulation parameters (traditional dorsal column stimulation versus newer stimulation techniques such as high frequency stimulation, dorsal root ganglion (DRG) stimulation or burst stimulation) is important in the success of SCS therapy in PLP [30].

There is also evidence that not only does SCS provide pain relief upon initiation of this therapy, but also in the long term. Krainick *et al.* were able to show this objectively with having nearly half (45%) of their patients achieving good-to-excellent results initially, as well as 42.6% of patients reporting pain relief of more than 25% for pure phantom pain over a chronic time period [28]. McAuley *et al.* also showed good results initially and long term, with 65% of their patients reporting initial pain relief. After 5–20 years, five of the nine patients reported pain relief and benefit from stimulation [21]. Sanchez-Ledesma *et al.* also showed that of the 12 patients studied, ten had worthwhile benefit within the first year. Chronic follow-up, with a median of 11 years, showed that five of the six remaining patients had a continued benefit [25].

Nevertheless, Garcia-March *et al.* showed with their two patients that while initial pain relief is fair, after several months of long-term use, the relief is poor (14 and 19 months for both) [26]. Kumar *et al.* in both of their studies, illustrated that there was no pain relief in SCS for PLP [22,23].

It should also be noted that there were complications present in these 11 studies analyzed. For instance, Krainick *et al.* described radicular paresthesias that occurred at the level of stimulation, and presented in four patients in their trial [28]. However, it may be possible to improve paresthesia sensation by altering the certain parameters in programming [27]. Nielson *et al.* reported 12% of their patients experienced severe radicular chest pain. This is most likely due to stimulation of the radicular nerve fibers as opposed to stimulation of dorsal column fibers. three patients in that same study also experienced complication of cerebrospinal fluid leakage who underwent subdural implantations [30].

Eldabe *et al.* investigated eight patients with PLP and the use of a novel approach, DRG neuromodulation. At baseline, pain rating was 85.5 mm, and after following up (mean of 14.4 months) the pain by patients was reported at 43.5 mm, showing marked improvement. Quality of life and functional capacity, subjective reports, also showed improvement [2]. In addition, some patients also reduced or eliminated pain medications. Specifically, one patient's PLP was eliminated by the neuromodulation, while three of the patients experienced a diminution of pain relief, even though they initially had good outcome [2].

Analysis of SCS settings is important when considering SCS as an intervention for PLP management. Tonic, low frequency (50–100 Hz) SCS has been shown to activate the discharge pattern of neurons of the dorsal-column-medial-lemniscus system [31]. As a result, this activation can result in decreased hyperactivity of dorsal horn neurons. One study by Rasche *et al.* demonstrated decreased activity in the lateral sensory thalamic nuclei, prefrontal cortex, cingulate gyrus and postcentral gyrus in failed back surgical syndrome patients treated with tonic SCS [32]. High frequency (HF; 3–50 khz) SCS has been also extensively studied has been found to suppress or block spinal nociceptive transmission and possibly induced frequency-dependent conduction block of voltage-driven ion channels. Burst SCS, which is defined as application of more charges per second compared with tonic SCS with an amplitude below threshold required for activation of Aβ fibers. This may be the reason for the paresthesia-free characteristics of burst SCS. Research studies show that pulse SCS compared with tonic SCS has more neural suppression in gracile nucleus

Table 1. Levels of evidence for systematic review analysis.

Leve	Levels of evidence
Level I	Meta-analysis or systematic reviews
Level II	One or more well-powered randomized, controlled trials
Level III	Retrospective studies, open-label trials, pilot studies
Level IV	Anecdotes, case reports, clinical experience, among others

Table 2. Studies analyzed in PRISMA systematic review.

Study	Year	n	Lead location	Duration	Scale	Outcome and results	Ref.
De Caridi *et al.*	2016	3	T10–T11 intervertebral space	3 months	VAS	One patient's pain was maintained within 30/100 mm (on VAS) on both left and right side, and the use of opioid analgesics was decreased by more than 50% The second patient's pain was also maintained at 30/100 mm on VAS both left and right side, and the use of opioid analgesics was completely stopped The other patient was also maintained at 30/100 mm on VAS both left and right side, and the use of opioid analgesics was stopped	[20]
Eldabe *et al.*	2015	8	L3–S1 DRG for lower extremity pain and C6–C7 DRG for upper extremity pain	Mean of 14.4 months	VAS	Average baseline pain rating was 85.5. At follow-up, pain was rated 43.5 mm. Subjective ratings of quality of life and functional capacity improved One patient, stimulation eliminated PLP as well as nonpainful phantom sensations. Three patients experienced a diminution of pain relief, despite good initial outcomes All patients reported that the paresthesias generated with DRG neuromodulation were appropriately localized to the stump sites, and five patients reported that the paresthesia either could be perceived in their phantom limb or interacted with their perception of their phantom	[2]
McAuley *et al.*	2012	5	Epidural over cervical or thoracic spinal cord	5 years	VAS	Self-reported initial and final magnitudes of pain relief were unchanged, with a mean SD of 66% (18.2%). Benefits calculated from local and general visual analog pain scores were similarly unchanged (initial local 48.8% [18.7%]; final local 50.0% [17.6%]; initial general 60.8% [10.9%]; final general 57.9% [12.3%])	[21]
Kumar *et al.*	1998	3	N/A	N/A	VAS	Cases of stump pain or phantom limb pain responded poorly with no pain relief	[22]
Kumar *et al.*	1991	2	Between C6–T1 vertebral bodies for upper extremity pain and between T9–T11 for lower extremity pain	N/A	VAS and McGill questionnaire	Both patients failed to receive pain relief	[23]
Devulder *et al.*	1990	5	Percutaneous epidural	N/A	A: good pain relief, no need for medication B: good pain relief with non-narcotic agents C: little pain relief, need for narcotic analgesics D: no longer used the stimulation system	Three patients: A; one patient: C; one patient: D	[24]

DCS: Dorsal column stimulation; DRG: Dorsal root ganglion; N/A: Not applicable; SCS: Spinal cord stimulation; SD: Standard deviation; VAS: Visual analog scale.

Table 2. Studies analyzed in PRISMA systematic review (cont.).

Study	Year	n	Lead location	Duration	Scale	Outcome and results	Ref.
Sanchez-Ledesma *et al.*	1989	3	Epidural SCS	Mean follow-up of 5.5 years	Excellent: 75% pain relief Good: 50–75% pain relief Fair: 25–50% pain relief Not working	Two patients had no pain relief, one had good pain relief	[25]
Garcia-March *et al.*	1987	2	Epidural space	19 and 14 months	Excellent: 100% pain relief Good: 75–100% pain relief Fair: 25–75% pain relief Poor: less than 25% pain relief	Fair (early) and poor (late) for 19 months, fair (early) and poor (late) for 14 months	[26]
Wester	1987	5	DCS	4–60 months postoperatively (median 15 months)	Pain reducing effect: – Good: 3 – Moderate: 2 – Weak: 1 – None: 0	Average pain score before electrode implant: 2.50. With DCS, 2.13. Pain reducing effect of DCS (0.5) stimulation, whereas patients with phantom limb pain respond poorly, as they do to most other forms of pain treatment	[27]
Krainick *et al.*	1980	64	Electrodes were implanted subdurally in the first five patients and the rest were implanted endodurally	N/A	Subjective report of pain relief: – Excellent relief: with pain relief of more than 75% – Good pain relief: with pain reduction of 51–75% – Fair relief: with relief of 26–50%	Initial: excellent pain relief: obtained in 13 patients (20.3%); good pain relief: in 16 (25.0%); fair pain relief, in seven (10.9%) of the amputees. It is notable that all four arm amputees with poor results had brachial plexus root avulsions Chronic: 61 patients in the long-term group. A total of 42.6% reported pain relief of more than 25% for pure phantom pain as well as for stump pain. A significant decline in pain relief was observed in the patients with excellent results (pain relief or more than 75%). Only one of the 13 amputees evaluated initially remained in this group after a stimulation period of more than 2 years. Attacks of phantom and stump pain were generally less frequent and less severe after intermittent stimulation for several years	[28]
Miles *et al.*	1978	9	DCS	N/A	Excellent: excellent relief with no requirement of analgesics is graded as Some pain relief: some relief with the need for occasional simple analgesics No pain relief	Excellent pain relief: six patients Some pain relief: one patients No pain relief: two patients	[29]
Nielson *et al.*	1975	5	DCS at C3–C4 for arm pain, T2–T3 or T6–T7 for leg pain	2–7 years	Subjective report of pain relief: – 'Excellent' pain relief: freedom from significant pain, withdrawal from all medications except for occasional tranquilizers – 'Good' pain relief: still have some pain and require greater number of analgesics – 'Failure': could not tolerate pain at site of implant	Three out of five patients were considered to have had 'excellent' pain relief One patient had only a good result, since she still has some pain and requires a somewhat greater number of analgesics than the patients rated excellent The other patient is categorized as a failure, could not tolerate pain at the chest wall implant site	[30]

DCS: Dorsal column stimulation; DRG: Dorsal root ganglion; N/A: Not applicable; SCS: Spinal cord stimulation; SD: Standard deviation; VAS: Visual analog scale.

neurons which potentially translates to better analgesia [31].

While previously we investigated the complications that occurred in our 12 studies, it is critical to discuss morbidity and mortality observed with SCS in the literature. Mortality directly related to the SCS, independent of other causality, lacks in the literature. There are alerts in the manufacturers' product information by US FDA. With regards to morbidity, this is focused at morbidity during device placement (e.g., dural puncture, epidural and intrathecal hemorrhage, spinal cord or nerve trauma, paralysis) or after implantation such as lead migration, seroma formation and infection [32]

Broggi *et al.* discussed in their retrospective study that the most frequently occurring complication was the displacement of the leads (4.4%), and thus needed repositioning with revision [33]. In addition, 1.1% of the cases had infections of the subcutaneous pocket containing the pulse generator. Finally, two patients (0.6%) developed surgical wound infection at the lead entry incision site [33]. These complications are in reference to all SCS cases, not just PLP patients. Literature reviews by Turner *et al.* illustrated the following complications among the 34.3% of patients that were had complications secondary to stimulation: additional revision (23.1%), hardware malfunction (10.2%), infection (4.6%), biological complications (2.5%), pain at the pulse generator site (5.8%) and stimulator removal (11.0%) [34]. Mekhail *et al.* also reviewed over 700 cases that was managed with SCS, and the complication outcomes include: hardware-related (38%), lead migration (22.6%), lead connection failure (9.5%) and lead breakage (6%). Biologically related complications include pain at generator site (12%) and clinical infection (4.5%) [35]. According to the literature, the complication of most cause for concern for clinicians is neurological damage due to nerve root or cord injury [36]. Inadvertent dura puncture is not uncommon complication during the implantation of SCS, with the patient usually presenting with positional headache. This is treated with epidural blood patch [37].

While SCS is an intervention of choice for treatment of PLP, studies show that the first line is pharmacological therapies including tricyclic antidepressants (TCA) and sodium channel blockers [38]. Randomized, controlled clinical trials have shown to be beneficial for neuropathic pain, however, it should be noted that there are no controlled trials specifically for PLP. However, there are reported studies of efficacy of the TCA, doxepin and amitriptyline [39]. Carbamazepine, which is a sodium channel blocker anticonvulsant, has been proven to be effective PLP, along with lamotrigine (glutamate inhibitor and sodium channel blocker) and lidocaine [40]. The sodium channel blocker mexiletine was shown in an open-label study to produce pain relief in 18 of 31 patients [41].

Opioids have also been evaluated in randomized controlled trials for their efficacy of PLP. There have also been comparative trials carried out against TCAs and gabapentin, with opioids showing benefit, however, also associated with more side effects. The total amount of opioid required to achieve analgesia is less when used together with other pharmacologic treatments, such as anticonvulsant agents like gabapentin. Tramadol is an opioid with mechanism of action of weak μ-agonist and mixed serotonin–norepinephrine reuptake inhibition often used by clinicians for PLP treatment [42]. Recent literature demonstrates the efficacy of tapendatol for treatment of PLP. One particular case series reviewed five patients suffering from upper and lower extremity phantom pain, treated with tapendatol. The results illustrated four patients with strongly reduced pain intensity (between 4 and 6.5 on VAS). The fifth patient reported an increase in nocturnal sleep duration and a decrease in number of phantom pain attacks by 30% [43].

Nonpharmacological interventions, which include sympathectomy, dorsal-root entry-zone lesions, cordotomy and rhizotomy methods have a reported maximum benefit of 30% of PLP cases [44]. Specifically, two electrical stimulation treatments have been studied for PLP treatment. One is deep brain stimulation, which according to the literature is uncertain of its benefits for treatment of PLP. However, there are patients that do experience pain relief (>25%) and improved quality of life. The other stimulation is motor cortex stimulation (MCS), which is electrical stimulation of the precentral gyrus using epidural surgical leads and subthreshold stimulation. Studies from different centers show that PLP is an appropriate indication for MCS, with the upper limb represented in the convex part of the precentral gyrus, whereas the interhemispheric lead implants impact lower limb pain [45]. One particular review suggests pain relief in 53% of PLP patients that were treated with MCS [46].

The studies reviewed have several limitations. First, the variation in duration of time studied by the research groups provides a wide range of conclusions, including certain studies that had short duration. Second, the sample sizes of many of the studies are extremely small, with certain groups only having two patients. It should be noted that several of the studies used were unblended case series with small patient numbers. Third, there was variability in the selection of patients, as some studies investigated upper limb PLP, while others only investigated patients with lower limb pain. This is important, as the SCS lead positioning is different for the lower limb than upper extremity. Fourth, there is also not much information on particular studies with regards to the parameters used in stimulation, such as constant voltage versus constant current systems, pulse width and frequency, which may play a role in the clinical response. Fifth, psychological screening prior to placement of SCS were not well documented. Besides, individual personality traits, such as anxiety and pain coping mechanisms, could also mitigate against the success of neurostimulation. Sixth, pain scales used in these studies are sometimes very subjective and variable, and one study's 'fair' results may be interpreted as 'good' by another study. Seventh, there was not enough information as to the patient selection criteria and psychological screening prior to implementation of SCS. Appropriate patient selection is important for the success of SCS. Neuropathic pain in PLP responds more favorably to SCS therapy, as compared with non-neuropathic pain such as mechanical pain from the stump site or inflammation at the stump site. Appropriate clinical evaluation with diagnostic studies when necessary to rule out other causes of pain at the stump site prior to implementation of SCS therapy is necessary. For instance, mechanical pain, inflammation, infection or neuroma formation at the stump site contributing to pain perception must be ruled or treated appropriately prior to SCS therapy. Local injections or neuroablation techniques under image guidance may be considered for the neuroma at the stump site for diagnostic/therapeutic purposes prior to consideration of SCS therapy. While peripheral nerve surgery at times eliminates pain, it does not remove the PLP or phantom sensation.

Conclusion

While there is some evidence that SCS is relatively safe and can provide analgesia, further research is needed to determine if it is a suitable intervention compared with alternative management strategies. However, there is promising data that SCS can be an option when the more conservative noninvasive therapies fail to provide patient satisfaction. Further high quality studies are required for use of SCS techniques in the treatment of PLP, specifically with the use of more appropriate patient selection criteria such as inclusion of patients with predominantly neuropathic pain, after a careful psychological screening, and with the use of validated scales for pain, functional capacity and quality of life. Although SCS is an invasive therapy, there is a trial period that is completely reversible. If adequate pain relief and functional benefits are achieved by the trial period, SCS implantation may be highly considered for long-term therapy. Implanted SCS is also completely reversible therapy as it can be fully explanted in the case of failure of therapy. SCS therapy has a potential to reduce the PLP, improve function and quality of life, while reducing, simplifying or eliminating the medication use with potentially serious side effects and drug interactions. Furthermore, recent various novel applications of SCS such as high frequency SCS, burst SCS or DRG stimulation technology coupled with advances in MRI compatible devices minimizing the limitations of their clinical application, may be promising in the future treatment of patients with PLP.

Future perspective

Furthermore, recent novel applications of SCS techniques may also be promising in the treatment of patients with PLPs. Over the next few years, we can expect further refinement of current neuromodulation techniques, not only limited to SCS, but also other interventions such as deep brain stimulation and MCS. At present, while SCS may not be the definitive treatment for PLP, further knowledge on the mechanism of the physiology of the pain can help this intervention achieve better efficacy and perhaps become more widely used intervention for clinical management.

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