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REVIEW

Peripheral Nerve Stimulation: A Review of Techniques and Clinical Efficacy

Alan D. Kaye · Sasha Ridgell · E. Saunders Alpaugh · Aya Mouhaffel ·

Aaron J. Kaye · Elyse M. Cornett · Azam A. Chami · Rutvij Shah ·

Bruce M. Dixon · Omar Viswanath · Ivan Urits · Amber N. Edinoff ·

Richard D. Urman

ABSTRACT

Chronic pain is a common source of morbidity in many patient populations worldwide. There are growing concerns about the potential side effects of currently prescribed medications and a continued need for effective treatment. Related to these concerns, peripheral nerve stimulation has been regaining popularity as a potential treatment modality. Peripheral nerve stimulation components include helically coiled electrical leads, which direct an applied current to afferent neurons providing sensory innervation to the painful area. In theory, the applied current to the peripheral nerve will alter the large-diameter myelinated afferent nerve fibers, which interfere with the central processing of pain signals through small-diameter afferent fibers at the level of the spinal cord. Multiple studies have shown success in the use of peripheral nerve stimulation for acute post-surgical pain for orthopedic surgery, including post total knee arthroplasty and anterior cruci-

A. D. Kaye · S. Ridgell · A. Mouhaffel ·
E. M. Cornett · A. A. Chami · R. Shah ·
B. M. Dixon · O. Viswanath · I. Urits
Department of Anesthesiology, LSU Health
Shreveport, Shreveport, LA, USA

A. D. Kaye · E. S. Alpaugh
Department of Anesthesiology, LSU HSC New
Orleans, New Orleans, LA, USA

A. J. Kaye
Department of Anesthesiology, Medical University
of South Carolina, Charleston, SC, USA

O. Viswanath
University of Arizona College of Medicine-Phoenix,
Phoenix, AZ, USA

O. Viswanath
Department of Anesthesiology, Creighton
University School of Medicine, Omaha, NE, USA

O. Viswanath
Valley Anesthesiology and Pain Consultants,
Envision Physician Services, Phoenix, AZ, USA

I. Urits
Southcoast Physicians Group Pain Medicine,
Southcoast Health, Wareham, MA, USA

A. N. Edinoff
Department of Psychiatry and Behavioral Medicine,
Louisiana State University Health Science Center
Shreveport, Shreveport, LA, USA

R. D. Urman
Department of Anesthesiology, Perioperative and
Pain Medicine, Brigham and Women's Hospital,
Harvard Medical School, Boston, MA, USA

A. D. Kaye (✉)
Department of Academic Affairs, LSU Health
Shreveport, 1501 Kings Hwy, Shreveport, LA 71103,
USA
e-mail: alan.kaye@lsuhs.edu

ate ligament surgery, and chronic knee pain. Many studies have investigated the utility of peripheral nerve stimulation for the management of chronic shoulder pain. Peripheral nerve stimulation also serves as one of the potential non-pharmacologic therapies to treat back pain along with physical therapy, application of transcutaneous electrical neurostimulation unit, radiofrequency ablation, epidural steroid injections, permanently implanted neurostimulators, and surgery. Studies regarding back pain treatment have shown that peripheral nerve stimulation led to significant improvement in all pain and quality-of-life measures and a reduction in the use of opioids. Further studies are needed as the long-term risks and benefits of peripheral nerve stimulation have not been well studied as most information available on the effectiveness of peripheral nerve stimulation is based on shorter-term improvements in chronic pain.

Key Summary Points

Chronic pain is a significant cause of morbidity in a wide variety of patient populations throughout the world. Concerns about the potential side effects of currently prescribed medications continue to grow, as does the need for effective treatment.

Peripheral nerve stimulation has been regaining popularity as a potential treatment modality in response to these concerns. Components of peripheral nerve stimulation include helically coiled electrical leads that direct an applied current to afferent neurons that innervate the painful area sensory.

Numerous studies have demonstrated success with peripheral nerve stimulation in the treatment of acute post-surgical pain following orthopedic surgery, including total knee arthroplasty and anterior cruciate ligament reconstruction, and chronic knee pain.

Peripheral nerve stimulation has been shown to significantly improve all pain and quality-of-life measures and to decrease the use of opioids in studies examining back pain treatment. Additional research is needed to determine the long-term risks and benefits of peripheral nerve stimulation, as the majority of available information on its effectiveness is based on short-term improvements in chronic pain.

INTRODUCTION

Chronic pain is a common source of morbidity in many patient populations worldwide. Studies link chronic pain with limitations to mobility, interference with daily activities, dependence on opioid analgesics, and psychiatric illness [1]. With growing concerns about potential side effects of currently prescribed medications and a continued need for effective treatment, the medical community is open to alternatives that provide safe and effective measures to control patient pain. Related to these concerns, peripheral nerve stimulation (PNS) has been regaining popularity as a potential treatment modality.

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

History of Peripheral Nerve Stimulation

The concept of PNS for the management of pain originated in the first century AD with the discovery that torpedo fish produce electrical discharges that were noted to provide relief of pain

[2, 3]. Following this discovery, several attempts were made to produce man-made electrical nerve stimulators that replicate the effects observed from torpedo fish. The earliest concept of peripheral nerve stimulation as we know it today was introduced in 1967 [4]. In this study, the authors demonstrated temporary pain relief following a sustained, 2-min electrical stimulation. The first clinical studies of implantable nerve stimulators were performed in 1976 at Johns Hopkins, with the investigators citing reduced opioid requirement, increased ability to work, better sleep, improvements in depressive symptoms, and reduced pain as potential benefits [5].

Mechanism of Peripheral Nerve Stimulation

Several mechanisms have been proposed to explain the effectiveness of PNS. The potential benefits of counterirritation were reported decades prior to Wall and Sweet's landmark publication. Temporary pain relief was observed on withdrawal of many irritating stimuli; irritants used for this study included heat, ice, and vibration [6]. The gate control theory of pain was published later [7]. This theory proposed that pain nerve fibers of different sizes act as "gates" for different types of sensory information and suggested that one can decrease the perception of pain by providing competing, non-painful stimulation through large fiber neurons to close the small-fiber pain "gates." Current thinking suggests that, although the gate control theory is likely involved, it is unlikely to be the sole mechanism by which PNS works. Several additional theories have been proposed, many relating the effects of PNS to changes in various neuromodulators [8–10]. Despite these lingering questions, PNS continues to be a heavily studied treatment modality for the management of pain. It has shown possible effectiveness in the management of trigeminal neuropathic pain [11–13], chronic migraine headaches [14–16], complex regional pain syndrome [17–19] and many other conditions. It is with this background in mind that we look into the clinical efficacy of PNS and the

techniques used for the placement and management of various musculoskeletal painful conditions.

PERIPHERAL NERVE STIMULATION FOR ACUTE PAIN AFTER SURGERY

Providing optimal postoperative pain control while improving mobility and time to ambulation, beginning physical therapy, and reducing overall opioid consumption still poses many challenges to the anesthesia provider. To achieve these goals, providers often utilize multiple approaches consisting of a variety of multimodal pharmacologic and interventional approaches. PNS serves as an additional method to treat post-operative pain while reducing overall opioid consumption and avoiding difficulties associated with other more-invasive modalities, including continuous epidural infusions, perineural stimulators, continuous peripheral nerve blocks, or even a single shot nerve block [20]. By utilizing PNS in the treatment of acute postoperative pain, there is an opportunity to improve recovery time and reduce overall opioid consumption [21].

Peripheral nerve stimulators are composed of helically coiled electrical leads, which direct an applied current to the afferent neurons providing sensory innervation to the painful area. In theory, the applied current to the peripheral nerve will alter the large-diameter myelinated afferent nerve fibers, which interfere with the central processing of pain signals through small-diameter afferent fibers at the level of the spinal cord. Placement of the leads requires ultrasound guidance and depends on the specific nerve of the target. Leads are placed at a distance of 0.5–0.3 cm of the nerve. This is in contrast to perineural stimulators that are frequently implanted immediately adjacent to and within the same fascial plane as the target nerve, which holds a higher risk of neurologic injury due to needle–nerve contact [21].

Multiple studies have shown success in the use of peripheral nerve stimulation for acute post-surgical pain for orthopedic surgery, including post total knee arthroplasty (TKA) and anterior cruciate ligament (ACL) surgery.

One study reported a case series following eight patients post TKA showing significant improvements in Western Ontario and McMaster Universities arthritis index (WOMAC). WOMAC is a clinical scale that reports pain, stiffness, and difficulty with activities of daily living. On average, subjects in this study had improvement in WOMAC by 76% and 86% at 6 and 12 weeks, respectively, in comparison to prior to surgery [22]. Another case series followed five patients measuring pain tolerance post-TKA within 2 h after lead implantation and determination of stimulation parameters. Following application of stimulation to the femoral or sciatic nerve subjects showed an average of 63% and 14% reduction of their pain at rest and active range of motion, respectively [21]. This study used a small-diameter (0.2-mm), open-coiled, helical electrical lead with an anchoring wire preloaded within a 20-gauge insertion needle. The timing of the insertion was postsurgical for all patients, however, the time after surgery was not within the 72 h for any of the subjects, which is usually defined as the acute postoperative period. Time since surgery varied among subjects from 8 to 97 days. A third study followed five patients within 60 days post-TKA with knee pain inadequately controlled with oral pain medication. In this study, leads were inserted 8–58 days postoperatively, with four out of five subjects having complete resolution of their pain and an average pain reduction of 27% and 30% during passive and active knee range of motion, respectively [20]. A similar study reported improvement in pain control and reduced total opioid requirements post ACL surgery following femoral nerve stimulation [23]. Although these studies are promising, the sample sizes are small and larger studies are warranted.

There was a study that looked at acute postoperative pain control following upper extremity surgery, however, it was a proof-of-concept study to look at lead implantation sites and to see if this could be feasible in the postoperative period. Leads were placed using ultrasound guidance intended to target the suprascapular nerve or brachial plexus, preoperatively. Patients received stimulation in 5-min periods or a sham followed by a 5-min crossover period and then continuous stimulant until the leads were removed between postoperative days 14–28. This study found that it was feasible, however, the analgesia immediately following the surgery did not appear to be as potent as local anesthetic-based peripheral nerve blocks [24]. This study showed that PNS could be useful in the possible reduction of opioid use in the postoperative period.

In addition to improvement in pain control and disability, the relative size of PNS devices allows the user to wear a small pulse generator comfortably in an ambulatory setting. This is much more feasible than requiring the user to have an attached infusion pump and to carry a local anesthetic reservoir [20]. Additionally, typical post-operative pain in extremities will outlast the length of pain relief provided by a continuous peripheral nerve block, which may only be utilized for 3–4 days postoperatively [21, 25]. Continuous local anesthetic infusion also induces sensory and motor blockade, while PNS does not produce these effects. These procedures are also more invasive, costly, hold a higher risk of infection, and may prolong the time to ambulation and increase the risk of falls in comparison to peripheral nerve stimulators [20]. These continuous infusions would also increase the number of days in the hospital, which goes against the current trend of trying to reduce the days spent in the hospital after surgery.

Among the range of potential therapies in the acute setting and PNS provides adequate therapy while avoiding challenges and possible complications of more-invasive techniques. Related to the relative size of PNS devices and small associated risks, PNS devices can be applied feasibly to treat acute postoperative pain immediately following surgery and extending to the ambulatory setting. By introducing PNS to the spectrum of analgesic treatments, patients can experience better overall outcomes by improving mobility, time to ambulation, and reducing overall opioid consumption, while adequately treating pain [20].

SHOULDER

Chronic shoulder pain is a common condition with an estimated prevalence of 20–33%, with 40% of all cases proceeding longer than 1 year [26, 27]. Many studies have investigated the utility of PNS for the management of chronic shoulder pain. Hemiplegic shoulder pain (HSP), a condition causing decreased mobility and increased pain in stroke patients, is the most frequently studied chronic shoulder pain diagnosis in terms of response to PNS. Other diagnoses commonly implicated in shoulder pain include rotator cuff disorders, adhesive capsulitis, shoulder instability, and shoulder arthritis [26, 28]. Current interventional shoulder pain relief options, such as medications, steroid injections, physical therapy, and acupuncture, are available but are limited as many of these only provide short-term relief for long-term symptoms. It is this conundrum that drives the search for alternative shoulder pain treatment options.

Anatomy and Placement Technique

Innervation of the shoulder joint primarily comes from two nerves: the axillary and suprascapular nerves [29]. The suprascapular nerve provides sensory innervation to the posterior glenohumeral joint and motor to the supraspinatus and infraspinatus muscles. The deltoid and teres minor are innervated by the axillary nerve. These two nerves are the primary focus of most studies investigating the use of PNS for the management of shoulder pain.

Nerves can be targeted for PNS using a variety of techniques. Open surgical placement can be performed by dissecting down to the nerve in question and placing a lead alongside the nerve for stimulation. Nerve-stimulation trials sometimes precede permanent stimulator placement, although this practice is of questionable benefit in patients with shoulder pain as patients with failed trials have been observed to benefit from the placement of a permanent peripheral nerve stimulator [30]. Open surgical placement is also associated with higher rates of post-operative pain, a concerning finding in patients being treated for chronic pain. The major benefit of percutaneous placement is that it is faster and less traumatic. Usage is limited by the need for superficial nerve targets, higher rates of post-placement lead migration, and susceptibility to equipment malfunctions [30, 31]. Ultrasound-guided lead placement has been studied for the shoulder, which provides an alternative to open placement for deeper nerve structures. The suprascapular and axillary nerves can be targeted from any location throughout their courses, although the suprascapular notch and the posterior humerus, respectively, are the most common locations picked [30, 32, 33]. For either nerve, a needle can be advanced under ultrasound guidance until it is just past the nerve. Once the target is reached, a guide can be placed to facilitate lead placement, and the needle is removed; a dilator is used to open the target space. The lead can be placed through the dilator. This technique reliably places leads within 0.5 cm of the target nerve in most patients [33]. There is a problem of placing the lead too close to the nerve as it may lead to motor stimulation of the nerve.

PERIPHERAL NERVE STIMULATION FOR BACK PAIN

The treatment of chronic lower back pain (CLBP) consists of a continuum of pharmacologic and procedural therapies. The use of multimodal analgesic medications, rehabilitation, and percutaneous interventions have been clinically shown to reduce total opioid consumption and better overall pain control. PNS serves as one of the potential non-pharmacologic therapies to treat CLBP along with physical therapy, application of transcutaneous electrical neurostimulation (TENs) units, radiofrequency ablation, epidural steroid injections, permanently implanted neurostimulators, and surgery [34]. Due to PNS having fewer associated risks and relative feasibility, it can serve as an effective option prior to the application of permanently implanted systems or even surgical intervention [35].

Another way to treat CLBP is spinal cord stimulators (SCS), which work by activating

large, rapidly conducting fibers [36]. Spinal cord stimulation involves the generation of electric fields, which are conducted between metal contacts residing in the epidural space. These applied fields change the electric potential across membranes leading to one or more action potentials depending on the axon's diameter, myelination status, and electric threshold [36]. In North et al., patients who were treated with spinal cord stimulators had a 50% or greater pain relief and satisfaction [36]; while in Kumar et al., spinal cord stimulators had greater success compared to conservative medical management [36]. The study by Kemler et al. compared physical therapy to a conventional spinal cord stimulator and found that stimulators were superior to physical therapy in patients suffering from complex regional pain syndrome [36].

The proposed mechanism of action is through the modulation of central sensitization. More specifically, the applied current interferes with processing afferent pain signaling fibers to the spinal cord and central nervous system through the commonly accepted gate mechanism [34]. Anatomic targets of PNS include the medial branches of the dorsal rami. Leads are placed under ultrasound guidance adjacent to the medial branches using known anatomical landmarks as the dorsal rami exits the intervertebral foramen. Confirmation of the correct position of lead placement requires stimulating the probe into the tissue with selective activation of the lumbar multifidus and comfortable contractions overlapping the region of pain [34]. One study reported an optimal lead depth of 10–12 mm from the surface of the skin to maximize the target sensation for CLBP [37]. Stimulators can also have programmable settings that allow each individual to receive an optimal strength of stimulation while still providing comfortable sensations [34].

PNS can serve as a preferred option for the treatment of back pain prior to implanting permanent spinal cord stimulation and surgery. Due to the placement of leads near the spinal cord, spinal cord stimulation (SCS) has more complications that are consequential and have a higher associated expense. For these reasons,

SCS is typically reserved as a treatment of last resort. Additionally, more invasive surgical procedures, including spinal fusion and disc replacement, do not always adequately improve pain or reduce disability. For these cases, there remains a therapeutic gap before opting for treatments with higher associated risks [34].

Utilizing PNS early in treatment has been suggested to improve patient outcomes by potentially reducing the number of hospitalizations, clinic visits, and reducing overall opioid consumption [34]. Providing this option gives the patient an opportunity to avoid the need for a permanently implanted system or surgery prematurely or altogether in chronic back pain. PNS shows promise to function as an early and effective option in the treatment continuum while reducing pain, opioid use, and disability [35, 38].

PERIPHERAL NERVE STIMULATION FOR KNEE PAIN

Chronic knee pain and knee pain following surgery are commonly treated with a range of pharmacologic, interventional, rehabilitative methods. PNS provides an additional line of therapy in the treatment of both post-operative and chronic knee pain [20, 39]. The addition of PNS to the spectrum of therapeutic options gives patients the ability to utilize non-pharmacological pain control sooner before opting for more invasive interventions. Its application can additionally reduce overall opioid consumption and provide better overall pain relief. While PNS does not completely eradicate pain in all refractory cases, it can serve as a bridge in the gap in therapy between pharmacologic modalities and more-invasive interventions [21].

Similar to the application of PNS stimulator to other regions of pain, the implanted leads target the large diameter myelinated afferent nerve fibers, which interfere with central processing of pain signals through small-diameter afferent fibers in the spinal cord and central nervous system [20]. Depending on the origin of knee pain, common nerve targets include the femoral and the sciatic nerve. Leads are placed

under ultrasound guidance and usually aim to place the lead between 0.5 and 3.0 cm from the nerve. Since the generated current can be applied at a distance, placement of the leads avoids the associated risk of peripheral nerve damage.

One potential risk of PNS placement is lead migration. Reducing the risk of lead migration prevents failure of providing analgesia, activation of cutaneous pain fibers. Avoiding lead placement across large joints such as the knee or hip can help prevent this risk [40]. Additionally, the helical design of the leads limits the risk of lead migration by providing a more flexible composition that allows the wire to stretch when the subject moves. This feature also promotes tissue ingrowth between the coils, providing additional support. Additionally, the design can even decrease the risk of infection to 0.03 per 1000 indwelling days [21]. In short, the design can help decrease the risk of both infection and lead migration.

In the setting of acute, post-operative knee pain, PNS can provide specific advantages in comparison to continuous peripheral nerve blockade and epidural local anesthetic infusions. Epidural local anesthetic infusions can provide pain relief for 3–4 days due to the risk of infection and local anesthetic reservoir exhaustion. Epidural infusions are further associated with urinary retention, motor weakness, hypotension, and risk of epidural hematoma [20]. In comparison to continuous peripheral nerve blocks, PNS devices are lightweight and can be worn comfortably with a stimulator attached either to the ipsilateral limb or the abdomen. Continuous blocks are also associated with dislodgement, fluid leakage, and require the patient to have attached infusion pumps and anesthetic reservoirs [23].

Peripheral nerve stimulators have also shown efficacy in the treatment of chronic and post-operative knee pain. While providing adequate pain relief, peripheral nerve stimulators are less invasive, costly, and have less associated risk of infection than other traditional approaches. Neurostimulation avoids potential risks of common pharmacologic and invasive treatments and can serve a key role in the management of knee pain.

CLINICAL STUDIES: SAFETY AND EFFICACY

Peripheral nerve stimulators have been studied for use in patients of several different types of pain. In a study where 28 lower-extremity amputees with post-amputation pain were enrolled, subjects underwent ultrasound-guided implantation of the percutaneous leads, and patients either received peripheral nerve stimulators or placebo [41]. This was a crossover study in which the placebo group received a peripheral nerve stimulator for four additional weeks [41]. In this study, a significantly greater number of patients who received peripheral nerve stimulators demonstrated 50% or more reduction in postamputation pain during the 1–4 weeks as compared to placebo [41].

Back Pain

Multiple studies have reported improvements in overall pain control, disability, and opioid consumption following PNS implantation for the treatment of CLBP. One case series followed nine patients and measured their reported pain scores following PNS lead placement. This report showed a significant, sustained level of therapeutic relief of CLBP and disability with clinical reductions of ≥ 50% in two-thirds of patients for at least 12 months following lead removal [34]. Additionally, a prospective multicenter study following 118 patients during therapy with PNS showed significant improvement in all pain and quality-of-life measures and an overall reduction in the use of opioids, non-steroidal anti-inflammatory drugs, and anticonvulsants [42]. A third study followed 100 patients with a variety of chronic pain syndromes and measured pain, complications, disability, and depression outcomes following PNS treatment. One cohort in this study showed significant improvement to pain and disability following receiving lumbosacral PNS as measured by the Oswestry Disability Index without any long-term reported complications [43].

In another study with patients who have CLBP, the subjects received percutaneous peripheral nerve stimulator leads that targeted

the medial branch of the dorsal ramus in the region of lower back pain [44]. The leads remained in place for 30 days of therapy. Even after the removal of the peripheral nerve stimulator leads, there were sustained long-term benefits of the peripheral nerve stimulator leads in treating chronic lower back pain. Patients showed improvement in pain through a reduction in pain and disability and sustained reduction in the use of analgesic medication; this continued long term at the 4-month follow-up visit [44]. Subjects also reported clinically significant reductions in disability (based on the Oswestry Disability Index), pain interference, and the patient's global impression of change.

Knee Pain

Percutaneous peripheral nerve stimulation has been studied with the intention to control the often severe, long-lasting postoperative pain following total knee arthroplasty [45]. In a study of patients undergoing primary, unilateral total knee arthroplasty, the patients received both a femoral and sciatic open coil percutaneous leads that were placed 1 week prior to surgery. Although the study was small ($n = 7$), the majority of subjects using percutaneous peripheral nerve stimulation had well-controlled postoperative pain during the first week following total knee arthroplasty. In six out of seven patients, pain was well controlled even 4 weeks after total knee arthroplasty. Additionally, four out of the seven subjects studied had such well-controlled pain that opioid use was discontinued in the first week. One of the four subjects did not even require opioids during the duration of therapy. The study suggests that perioperative percutaneous peripheral nerve stimulators may enable patients to experience reduced post-operative pain, earlier cessation of opioid use, and accelerated functional recovery following the total knee arthroplasty. However, it is important to note that the study was limited by small size ($n = 7$), and future studies should be designed to further investigate the risks and benefits of the above intervention [45].

While PNS for knee pain has mostly been studied in acute postoperative knee pain, there is also evidence that PNS can be used among other therapies for chronic knee pain. One study showed effective pain relief using PNS for treatment of chronic intractable knee pain following TKA. The patients participating in the study had chronic knee pain for greater than 1-year post-surgery, which was intractable to NSAIDs, physical therapy, TENS unit, oral antidepressants, opioids, and surgical revisions. This study showed a significant improvement in functional capacity and reduction in pain visual analog scale scores [40]. Another study reported the effectiveness of PNS in improving chronic knee pain following an 8-week course receiving PNS therapy three times a week. This study showed improvement in pain, stiffness, and physical function utilizing the Western Ontario and McMaster Universities arthritis index (WOMAC) and the short-form 36-item health survey (SF-36), suggesting its effectiveness to treat chronic knee pain [39].

Shoulder Pain

Hemiplegic shoulder pain is a common condition that affects stroke survivors within the first 12 months of their stroke [46]. This hemiplegic shoulder pain is associated with poor rehab outcomes and interferes with activities of daily living, which leads to very poor quality of life [46] and poor functional outcomes [47]. There is a study that examined the effects of peripheral nerve stimulation, which focused on hemiplegic shoulder pain in stroke survivor patients. The study explored the safety and feasibility of a single lead peripheral nerve stimulator, which was fully implanted and placed so that it stimulated the axillary nerve of the affected shoulder, leading to contractions of the middle and posterior deltoid muscles for 6 h a day for 3 weeks [46]. Around 57% of patients enrolled in the trial had a two-point reduction in pain during active stimulation [46]. Patients experienced improvement in pain-free external range of motion and reduction in pain and pain interference with no serious adverse events related to the device or the procedure [46].

Another randomized controlled trial was performed to compare physical therapy to peripheral nerve stimulation on shoulder biomechanics in patients with chronic hemiplegic shoulder pain [47]. The study focused more on the effects peripheral nerve stimulators had on the patient's shoulder strength, range of motion, and motor function. The purpose of the study was to determine if there is a correlation between pain reduction and biomechanical outcomes [47]. Participants were randomized to either receive a 3-week treatment with a single-lead peripheral nerve stimulator or physical therapy (PT). Outcomes were measured at baseline and weeks 1, 4, 12, and 16 [47]. Participants were approximately split in half, with 13 patients assigned to a peripheral nerve stimulator and 12 assigned to PT sessions [47]. Patients in the PT treatment group received 8 h of outpatient PT over a 4-week period from a licensed therapist, and they also were advised to perform a home exercise program as well. Interestingly, the results of the study suggested that both peripheral nerve simulators and physical therapy were associated with improvements in biomechanics but that biomechanics alone did not account for the greater pain relief in patients with PNS compared to physical therapy [47]. There are numerous reasons for this finding, with the first being that shoulder biomechanics may not be as important in the maintenance of chronic vs. acute hemiplegic shoulder pain [47]. The study above may also have been too small of a population size to detect a difference in shoulder biomechanics [47].

CONCLUSIONS

PNS has shown great promise in the management of a wide variety of common musculoskeletal pains. Several trials have predicted its effectiveness without the side effects and could reduce the need for potentially addictive medications given for management of pain. Further studies are needed as the long-term risks and benefits of PNS have not been well studied as most information available on the effectiveness of PNS is based on shorter-term improvements in chronic pain. Early investigations suggest that nerve stimulators are safe to use for up to 18 years, with wide differences in biostability noted for stimulators placed in different locations [48–51].

The utility of newer technology also requires further investigation. New techniques for placement of peripheral nerve stimulation will likely open the possibility of targeting deeper neural structures for PNS. Smaller devices create opportunities to use PNS for smaller nerves that the modern stimulators are able to effectively stimulate. This widens the array of possible chronic pain syndromes for which PNS can provide relief of symptoms not well managed by traditional medical and physical therapies.

PNS can play a large role in the future of chronic pain management. Although there is still much to learn in regard to specific mechanisms, patient selection, and long-term safety, early results have shown promise. Currently, many devices placed for treatment of chronic pain are placed as an off-label use of the device. Obtaining this important safety data is an important next step. More information allows for expansion of the number of relevant diagnoses for which this therapy can be applied. It also allows for standardized safety protocols to be developed to optimize short-term and long-term safety. Through further investigation, a useful adjunct for management of chronic pain can be developed with PNS.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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