Peripheral Nerve Stimulation

3

Konstantin V. Slavin, Alexios G. Carayannopoulos, Mark Plazier, Sven Vanneste, and Dirk De Ridder

Introduction

Within the family of neuromodulation procedures, peripheral nerve stimulation (PNS) has a unique place. Despite several decades of clinical use, PNS struggles to become a widely used and, to some extent, legitimate counterpart to its more established siblings, which include deep brain (DBS) and spinal cord stimulation (SCS). PNS is defined as electric stimulation performed on the peripheral nervous system and applied to a specific nerve [1]. Electrical current can be delivered to nerves transcutaneously (transcutaneous electrical nerve stimulation: TENS), percutaneously with a temporary electrode (the so-called percutaneous electrical nerve stimulation: PENS), and with help of surgically or percutaneously implanted electrodes (PNS).

Historically, the first published report of PNS for treatment of neuropathic pain described procedure performed on October 9, 1965 when Drs. Wall and Sweet implanted electrodes around the median and ulnar nerves of a 26-year-old woman with a clinical presentation consistent with complex regional pain syndrome (CRPS). Electrical stimulation of the median nerve provoked pleasant paresthesias and modulated pain in the medial three fingers [2]. During that same year, Drs. Melzack and Wall published the seminal "gate-control" theory of pain in their article in *Science*, postulating that innocuous sensory information may suppress the transmission of pain [3]. This was the scientific foundation for the development of a new treatment modality, coined neuromodulation, which subsequently grew in its number of indications and types of procedural applications. Soon thereafter, the famous 1969 book "Pain and the neurosurgeon" by White and Sweet was published and detailed a description and an X-ray image of a PNS device implanted on the ulnar nerve of a patient with post-traumatic neuropathy [2]. Shortly after, dozens of clinical reports detailed various aspects of PNS in the 1970s thru 1990s, and PNS has remained relatively unchanged since: the target nerve was exposed, and a paddle-type electrode lead was placed in direct contact with the nerve trunk [4]. To facilitate this procedure, a specially designed paddle lead was created; it had an integrated mesh attached to the paddle, allowing the surgeon to wrap the electrode around the nerve, rather than to struggle with suturing it in situ.

Introduction of a percutaneous PNS insertion technique in the late 1990s [5] has since revolutionized the PNS field. Although the approach initially appeared to be most applicable to craniofacial stimulation, it gradually spread to use in the lower parts of the body, including the extremities, abdomen, chest wall, upper and lower back, groin area, and neck. The next development was introduction of the peripheral nerve field stimulation (PNFS) concept (sometimes called subcutaneous nerve stimulation, subcutaneous target stimulation, or peripheral field stimulation). Considered a variation of PNS, PNFS targets more distal neural structures, including unnamed nerve branches and subcutaneous nerve endings [1]. More recently, the PNS approach was augmented by addition of ultrasound

K.V. Slavin
Department of Neurosurgery, University of Illinois at Chicago, 912 South Wood Street, M/C 799, Chicago, IL 60612
e-mail: kslavin@uic.edu

A.G. Carayannopoulos
Spine Center, Department of Neurosurgery, Lahey Clinic, 41 Mall Road, 7 Central, Burlington, MA 01805
e-mail: Alexios.G.Carayannopoulos@Lahey.org

M. Plazier
Department of Neurosurgery, University Hospital Antwerp, Wilrijkstraat 10, Edegem, Antwerp 2650, Belgium
e-mail: Mark.plazier@uza.be

S. Vanneste
School for Behavioral and Brain Sciences, University of Texas at Dallas, 1966 Inwood Rd, Dallas, TX 75235, USA
e-mail: sven.vanneste@utdallas.edu

D. De Ridder (✉)
Department of Surgical Sciences, Section of Neurosurgery, Dunedin Public Hospital, 201 Great King Street, Dunedin, Otago 9016, New Zealand
e-mail: dirk.deridder@otago.ac.nz

H. Knotkova and D. Rasche (eds.), *Textbook of Neuromodulation*,
DOI 10.1007/978-1-4939-1408-1_3,

guidance, which helps in visualization of peripheral nerves during percutaneous lead insertion [6]. Finally, progress in PNS was facilitated by technical innovations of several new companies, each of which came up with surgical techniques specifically developed for PNS applications.

The Spectrum of Peripheral Nerve Stimulation

Transcutaneous Electrical Nerve Stimulation

TENS is an external neuromodulation modality that involves delivery of electrical current through intact skin, over the course of a nerve. Generally, it is used as a noninvasive neuromodulation approach, in conjunction with modalities used in physical therapy. It often serves as an alternative or prelude to more invasive interventions. Ostensibly, it is by far the most common application of peripheral neuromodulation in contemporary medical practice.

Recent reviews have analyzed the strength of evidence in the application of TENS to the treatment of neuropathic pain [7] and cancer pain [8]. Additionally, acupuncture-like application of TENS has also been reviewed in detail of late [9]. Outside of pain practice, posterior tibial nerve stimulation for the treatment of overactive bladder [10] and fecal incontinence [11] are the most commonly used TENS indications in patients. This modality has also been applied to stimulation of the phrenic and vagus nerves in the treatment of persistent hiccups [12] and seizures [13], and stimulation of the trigeminal nerve in treatment of epilepsy [14] and depression [15]. Trigeminal TENS has also been tried for treatment of trigeminal neuralgia [16]. In the mid-1970s, several groups used TENS for selection of candidates to undergo permanent PNS implants; however, no difference was found in the long-term success rate among those who did and those who did not respond to TENS prior to PNS procedure [17, 18].

Percutaneous Electrical Nerve Stimulation

PENS treatment is a technique performed with bipolar needle-like temporary electrodes, which are inserted into the tissues (as opposed to TENS where electrical stimulation is delivered through the skin) and then removed at the end of the session. This relatively noninvasive neuromodulation approach has been used in the treatment of a variety of painful conditions including low back pain, sciatica, diabetic neuropathy, acute herpetic pain, and headaches (for detailed review see PENS section in [4]).

PENS treatment is not an accepted means of PNS screening. It may have value for the treatment of cancer related pain, whereby permanent implantation is not possible [19] or in some cases of facial pain, whereby trigeminal neuropathy does not respond to medical treatment [20]. PENS equipment has recently become commercially available (NeuroStimulator PENS therapy, Algotec Ltd., West Sussex, UK) but to this date, has not been approved for clinical use in the USA. Interestingly, the original illustration of the "gate-control" theory of pain came from Drs. Wall and Sweet, who used PENS to suppress pain sensation by inserting stimulating electrodes into their own infraorbital foramina [21].

Peripheral Nerve Stimulation

PNS requires implantation of an electrode lead across or along a nerve trunk to provide stimulation-induced paresthesias. When originally approved by the US Food and Drug Administration (FDA), this old modality was defined as a way to electrically stimulate a peripheral nerve in patients to relieve severe intractable pain. The FDA used the following definition for PNS devices: "An implanted peripheral nerve stimulator for pain relief is a device that is used to electrically stimulate a peripheral nerve in a patient to relieve severe intractable pain" [22]. This definition later added the following statement: "The stimulator consists of an inplanted (sic) receiver with electrodes that are placed around a peripheral nerve and an external transmitter for transmitting the stimulating pulses across the patient's skin to the implanted receiver" [22], which referred to the radiofrequency (RF) coupled systems that were used in the past, including the original report of White and Sweet [2].

By limiting approved PNS devices to RF-coupled systems, current FDA approval effectively excludes all currently used implantable pulse generators [23] (these include prime-cell and rechargeable generators by Medtronic, Minneapolis, Minn.; St. Jude Medical, St. Paul, Minn.; and rechargeable generators by Boston Scientific, Natick, Mass.) In a surprising twist of technological development, a new, non-RF-coupled device, which satisfies FDA requirements, was recently introduced (StimRouter, Bioness, Valencia, Calif.) specifically for PNS applications [24].

The first decade of the twenty-first century has witnessed a dramatic increase in the use of PNS, not just for the treatment of chronic, intractable pain but also for the treatment of refractory epilepsy [25], treatment-resistant depression with vagal nerve stimulation [26] (VNS Pulse and Demipulse, Cyberonics, Houston, Tex.), diaphragmatic pacing by phrenic nerve stimulation for respiratory failure treatment [27] (Breathing Pacemaker System, Avery Biomedical Devices, Comack., N.Y.), reduction in apnea with implantable hypoglossal nerve stimulation systems [28] (Inspire II, Inspire Medical, Maple Grove, Minn.; HGNS, Apnex

Medical Inc., St Paul, Minn.; and Aura6000, ImThera Medical, San Diego, Calif.), somatic nerve stimulation of the extremities in patients after stroke [29] (NESS L300, Bioness; ActiGait, Neurodan, Aalborg, Denmark), and finally autonomic stimulation for urinary and gastrointestinal disorders [30] (InterStim, Medtronic).

A renewed interest in PNS treatment modality has been supported by ongoing technological advances in the field as well as adoption of minimally invasive neuromodulation techniques by non-neurosurgical colleagues, including interventional pain physicians.

PNS/PNFS Techniques

Two peripheral neuromodulation techniques are used by physicians for various types of neuropathic pain: (1) PNS, whereby leads are implanted in the subcutaneous tissue near a specific nerve, which has sensory distribution over the painful area; (2) PNFS, whereby leads are implanted within an area of pain perception [1, 31]. The aim of PNS is to produce paresthesias along the territory of the stimulated nerve, while the aim of PNFS is to distribute paresthesias in an electrical field around the lead's active electrodes, without achieving a clearly defined nerve distribution. Generally, this results in concentric stimulation-induced sensation in a specific area of precise painful zone, without radiation.

Implantation of a peripheral nerve stimulator is performed in two stages, which are similar to spinal cord stimulation. During the first stage, an electrode lead is inserted in the vicinity of the targeted nerve branch. This is followed by a trial of stimulation that lasts several days or weeks. If the trial is successful, the second stage of surgery involves insertion of a permanent electrode, which is anchored in place, usually to the underlying fascia, with subsequent tunneling of the electrode lead or an appropriate extension cable to an implantable pulse generator (IPG).

Indications and Patient Selection

Patient selection in PNS is generally consistent with guidelines used in the family of neuromodulation procedures. PNS is indicated for cases of chronic, severe, disabling neuropathic pain that has been refractory to medical treatments, which is associated with a clear diagnostic impression, and which occurs in the absence of correctable pathology. Additionally, patients are expected to be familiar with the modality and willing to use it, have a favorable neuropsychological profile, and respond positively to a trial of PNS before the permanent device is implanted. The usual contraindications, such as short life expectancy, active infection, uncorrectable coagulopathy or thrombocytopenia, and generally poor medical condition, which would preclude patients from undergoing elective surgery and/or anesthesia, should all be taken into consideration.

The most common indications for PNS in the extremities are chronic pain due to peripheral nerve injury, persistent pain from compressive neuropathy (following adequate decompression), complex regional pain syndromes (CRPS) type 1 (formerly known as reflex sympathetic dystrophy) and type 2 (formerly known as causalgia), and painful peripheral neuropathy. For PNS (of PNFS) of the chest wall, abdomen, neck, upper and lower back, groin area, and other parts of the trunk, the most common indications are postsurgical neuropathic pain, post-infectious (particularly post-herpetic) pain, and posttraumatic neuropathy.

In the last few years, most patients undergoing PNS below the head and face carried the diagnosis of failed back surgery syndrome (FBSS). At one point, this category of patients was dominated by pain from peripheral nerve injury and CRPS. This shift reflects the growing prevalence of back pain in the general population and is also likely secondary to recent growth in the number of spinal interventions, as well as the general ineffectiveness of other treatment modalities, including SCS, in management of axial back pain or paraspinal lumbar pain.

For extremity pain, patients with pain limited to the distribution of a single nerve are better candidates for PNS, whereas patients with pain in the trunk, chest, abdomen, generally respond better to PNS/PNFS. Pure sensory nerves tend to be better targets for PNS than mixed motor/sensory or pure motor nerves, whereby stimulation may also provoke undesired motor phenomena.

Neuropathic Limb Pain

Traditionally, complex regional pain syndromes from to an injury to a nerve (CRPS Type 2) or to a tissue (CRPS Type 1) have been the main indications for use of PNS in a limb [32]. Selection of PNS for patients with CRPS depends on chronicity as well as severity of pain, failure of less invasive treatment approaches, and mediation of pain by primary sensory nerves, since mixed and predominantly motor nerves may not tolerate stimulation [33]. Historically, PNS electrode lead implantation in the limbs was done by an open surgical approach due to the proximity of nerves to vessels and the deep course of nerves in the soft tissues. However, the risk of perineural scarring made the open approach less attractive. At the same time, introduction of ultrasound guidance has gained acceptance, as it allows one to use minimal access techniques for percutaneous electrode insertion [34, 35]. The variable course and depth of the nerves to be stimulated, as well as proximity to vessels, makes ultrasound guidance particularly helpful. Well documented class III evidence from two studies on limb neuropathic pain

suggests that PNS could provide good relief for CRPS, which is limited to the distribution of one major nerve in 60 % of patients [32, 36].

Neuropathic Facial Pain

Post herpetic neuropathy, incidental trauma, and iatrogenic injury to the face are major causes of trigeminal neuropathic pain (TNP). PNS in the face is indicated for the management of TNP with clear anatomic distribution within one or several of the trigeminal branches. PNS of supraorbital, infraorbital, and mandibular branches of the fifth cranial nerve, alone or in combination, has been published [37–39]. In one recent case series, TNP was successfully treated with PNS with up to a 2 years follow-up [40].

Neuropathic Trunk Pain

Case reports and small series have documented successful application of PNS and PFNS to chronic neuropathic pains of the neck [41], chest wall [42], abdominal wall [43, 44], and low back [45–48]. Post-herpetic neuralgia and postoperative pain due to thoracic and abdominal surgeries were the common etiologies of neuropathic pain in these patients. Among newly introduced developments are the "cross talk" concept [49, 50] for low back PNS as well as "hybrid" stimulation concept that combines spinal cord stimulation with PNFS [51–55].

The largest PNFS series was based on an Austrian nationwide retrospective study, which analyzed 111 patients with non-cancer pain with successful trial and subsequent implantation with a permanent neurostimulation system [56]. Of these, 97 had pain in the trunk (lower back, neck, chest wall) with an impressive reduction in the average pain intensity, measured by the numerical rating scale before and after the implantation. This difference was particularly significant in patients with low back pain and failed back surgery syndrome [56] ($P < 0.0001$). Out of 111 patients, 27 (24 %) developed complications, including 7 infections (6 %), 14 lead migrations (13 %), and 6 (5 %) lead fractures; all of these developed within 6 months after implantation [56].

Another recent study showed that peripheral neuromodulation is a safe and effective treatment option for intractable chronic pain conditions. Results of a prospective, observational Australian study of 100 consecutive patients receiving PNFS for the treatment of chronic craniofacial, thoracic, lumbosacral, abdominal, pelvic, and groin pain conditions included 16 adverse events without any report of long term complications [57]. The frequency of adverse events were as follows: lead infection—1, hardware erosion—7, hardware migration—2, leads too superficial—3, leads too tight—1, hardware failure—2, with a total rate of complications reaching 14 %, with some patients having more than one complication [57]. The greatest reduction in pain was observed in the abdominal PNFS group, in which there was an average drop of 7.0 ± 1.0 pain scale points ($P < 0.007$). A statistically significant reduction in pain was observed in the lumbosacral group, with a reduction of 3.3 ± 2.3 pain scale points ($P < 0.000$) [57].

With ongoing accumulation of clinical and research data in the field of PNS, more in-depth understanding on the mechanisms of action, technical details, and complications will become available for review [58]. Further research in PNS will allow new indications, new targets, and new devices. For example, development of a dedicated PNS system for post-amputation pain with special cuff-like electrodes is now undergoing clinical trials [59] (Electrical Nerve Block, Neuros Medical, Willoughby, Ohio). A single piece ultra-compact electrode/generator combination (BION, Boston Scientific) is currently under evaluation for the effectiveness for chronic cluster headache [60]. In a very different approach, intramuscular nerve stimulation with a dedicated device (IMN, SPR Therapeutics, Cleveland, Ohio) is being tested for stimulation of the deltoid muscle for refractory shoulder pain in hemiplegic patients [61]. There are multiple recent reports of pioneering PNS applications including the use of splanchnic nerve PNS for chronic pancreatitis pain [62, 63], paravertebral plexus PNS for thoracic neuropathic pain [64], inguinal and genitofemoral PNS for postoperative testicular pain [65], and vagus nerve stimulation for migraines [66].

With recent regulatory approval of PNS in Europe for the treatment of chronic lower back pain and intractable chronic migraines, clinical interest in this modality will continue to grow and is expected to stimulate accrual of objective evidence in terms of safety, efficacy, best indications, and optimal stimulation parameters. All of these will be necessary for regulatory approval worldwide and for greater benefit to the patients who are still suffering from chronic neuropathic pain.

Peripheral Nerve Field Stimulation of the C2 Nerve

Electrical stimulation of the occipital branch of the C2 nerve takes a special place in PNFS, because of its seemingly widespread effects, most of which are not fully explained, even though hypotheses have been proposed of its hypothetical working mechanism [67].

The greater occipital nerve is a branch of the second cervical spinal nerve which leaves the spinal cord at the level of the second cervical vertebral body. It provides sensory innervation of occipital area of the scalp up to the vertex of the head. The main branches of the nerve arise in the subcutaneous tissue in a small area just underneath the occipital protuberance [68]. It usually has medial and lateral branches which spread and divide into smaller branches in the subcutaneous area from this point on. The greater occipital nerve afferents enter the C2 segment of the spinal cord at the level of the nucleus caudalis of the trigeminal nerve

forming the trigeminocervical complex [69]. The nucleus caudalis projects to the thalamus, which relays sensory input to the cortex. Furthermore, animal studies have shown connections between neurons of the C2 spinal cord and the hypothalamus [70], the thalamus [71], the periaqueductal grey [71], the amygdala [70], anterior cingulate cortex [72], and posterior insula [72]. Thus, the C2 neurons in the spinal cord are directly connected to most areas of the pain matrix, and both to the medial and lateral spinothalamic pain pathways. C2 PNFS can thus theoretically modulate both the discriminatory (pain intensity, localization, etc.) and affective (attention to pain, unpleasantness, distress, etc.) components of the pain. This was also demonstrated in a recent fMRI study, showing that depending on the stimulation pattern (burst vs. tonic) and frequency, different brain areas are modulated [73]. For example burst stimulation exerts a BOLD activation of the dorsal anterior cingulate cortex, an activity which is related to unpleasantness, whereas tonic stimulation seems to exert a BOLD deactivation in a healthy volunteer [73]. But it also influences the thalamus, somatosensory cortex, and periaqueductal grey in a different way depending on the stimulation design [73]. PET scans performed during C2 stimulation in patients revealed significant changes in the regional cerebral blood flow in the dorsal rostral pons, anterior cingulate cortex, and the cuneus, correlated to pain scores. Changes in the anterior cingulate cortex and the left pulvinar correlated to paresthesia scores [74]. As these structures are well known to be involved in the brain pain matrix, these data might suggest that stimulation of the greater occipital nerve results in a modulation of brain activity in pain related cortical and subcortical structures.

Indications for C2 PNFS

Headache

Introduction of percutaneous insertion technique in the field of PNS allowed treatment of the craniofacial region [31]. PNS of occipital nerves has been successfully used for treatment of chronic headaches due to occipital neuralgia, cluster headache, and migraine [58]. In addition, occipital PNS was recently reportedly successful in the management of chronic headaches [75] as well as a complicated case of occipital neuralgia [76].

Headache: Occipital Neuralgia

Occipital neuralgia, or Arnold's neuralgia, has been one of the first clinical indications in which greater occipital nerve stimulation has been used. In this pathology, patients suffer from an aching, burning pain at the occipital nerve area which can be triggered by neck movements and touching trigger points at the occipital scalp. PNFS seemed to have a strong effect in pain reduction in this syndrome [17]. Further publications confirmed these results in a group of 17 patients with a follow-up of 1.5–6 years. Percutaneous cylindrical leads were placed on a horizontal line at the level of the occipital protuberance. Approximately two-third of the patients experienced a pain relief described as excellent and one-third described as good [5]. A more recent publication describes similar results in a group of 14 patients; however, 4 patients did not pass the trial phase of their study [77]. However, the results seem to be reproducible in various studies [78–82] (see Table 3.1 for overview).

Headaches: Chronic Migraine

The main developments in occipital PNS came from its use in migraine headaches. Despite disappointing results of the first two multicenter prospective randomized studies investigating occipital PNS in patients with intractable migraines [93, 95], the third multicenter double-blind, controlled study aimed to assess safety and efficacy of occipital PNFS for the management of chronic migraine. This sponsored study showed a significant difference between the active and control groups in essentially every monitored indicator [92], including a decrease in days of headache (22.5 vs. 3.4), improvement in MIDAS scores (64.6 vs. 20.4), improvement in Zung Pain and Distress Scales (13.3 vs. 5.5), improvement in visual analogue scale of pain severity (14.1 vs. 7.0) and improvement in quality-of-life measures. Furthermore, there was only a 1 % rate of serious device and procedure-related events in the entire cohort of 157 patients [92]. Based on these results, the authors concluded that occipital PNS is safe and effective in treatment of headache pain and disability associated with chronic migraine [92].

These studies were initiated after some evidence derived from smaller scale studies suggesting C2 PNFS could benefit migraine patients. In a publication of Oh et al. patients were included suffering from both occipital neuralgia and transformed migraine. The results were positive in nine out of ten patients at 6 months. Pain relief was rated as good to excellent [79]. Other studies achieved similar results [74, 84, 91]. A recent review by Young et al. provides an overview of these results [96] (see Table 3.1).

Simultaneous neuromodulation of occipital and supraorbital [97] or occipital and auriculotemporal nerve [98] has been used for challenging cases of severe migraine. PNFS of occipital nerves alleviates headache by acting on the trigeminocervical nucleus complex in the brainstem. In a multicenter retrospective study of 31 patients with various type of headache, 56 % had no headache after 1 year of peripheral neuromodulation, and 47 % stopped taking medication [99]. These results indicate that this treatment might have beneficial effects on the overall quality of life in

Table 3.1 Occipital nerve stimulation for headache syndromes

Study	Indication	Responders	Effect
Melvin et al. (2007) [83]	Occipital headache ($n = 11$)	11/11	67 %
Popeney et al. (2003) [84]	Migraine ($n = 25$)	20/25	88.7 % improvement MIDAS
Oh et al. (2004) [79]	Occipital neuralgia ($n = 20$)	18/20	90 %
Weiner et al. (1999) [5]	Occipital neuralgia ($n = 13$)	13/13	100 % good to perfect
Matharu et al.(2004) [74]	Migraine ($n = 8$)	8/8	100 % good to perfect
Kapural et al. (2005) [80]	Cervicogenic headache ($n = 6$)	6/6	70 %
Rodrigo-Royo et al. (2005) [82]	Occipital neuralgia ($n = 4$)	4/4	100 %
Slavin et al. (2006) [77]	Occipital neuralgia ($n = 10$)	10/10	>50 %
Magis et al. (2007) [85]	Cluster headache ($n = 8$)	7/8	50 %
Schwedt et al. (2007) [86]	Cluster headache ($n = 3$)	15/19	52 %
	Hemicrania ($n = 6$)		
	Migraine ($n = 8$)		
	Post-trauma ($n = 2$)		
Burns et al. (2007) [87]	Cluster headache ($n = 8$)	6/8	64 %
Picaza et al. (1977) [17]	Occipital neuralgia ($n = 6$)	3/6	100 % good to perfect
Schwedt et al. (2006) [88]	Hemicrania Continua ($n = 2$)	1/2	70 %
Ghaemi et al. (2008) [89]	Post cervical fusion pain ($n = 1$)	1/1	90 %
Amin et al. (2008) [90]	Supraorbital neuralgia ($n = 10$)	10/10	77 %
Brewer et al. (2012) [91]	Migraine ($n = 12$), Cluster headache ($n = 5$), Miscellaneous headaches ($n = 8$)	5/10, 4/5, 5/8	18 % decrease of headache, 27 % decrease in severity and 50 % decrease in MIDAS
Silberstein et al. (2012) [92]	Chronic Migraine ($n = 105$)	NA	22.5 % decrease in headache days, 64.6 % decrease in MIDAS scores, 14.1 % improvement in VAS of pain severity
Saper et al. (2011) [93]	Chronic migraine ($n = 110$)	43/110	>50 % decrease in headache days or/plus 3 or more points decrease in VAS
Burns et al. (2009) [94]	Cluster headache ($n = 14$)	10/14	52 %

chronic migraine patients and that the onset of beneficial effects can be expected after a period of 3 months of stimulation.

Headaches: Cluster Headache

Recently, a group from Belgium presented results of long-term follow-up (mean 36.82 months) of 15 chronic cluster headache patients, who were resistant to drug treatment, implanted with occipital stimulators [100]. This approach resulted in sustained disability reduction. Results indicated that 60 % became pain-free for prolonged periods [100]. PNS of occipital nerves in patients with cluster headache appears to stimulate metabolic normalization in the pain neuro-matrix, seen on PET scan [101]. Frequency, duration and severity of the cluster attacks were reduced in 90 % of the patients with refractory chronic cluster headache in a different series of ten patients [102]. Refractory cases of cluster headache may require trigeminal peripheral neuromodulation in addition to occipital PNS [97].

Burns et al. published their results on eight patients, with a 26 months follow-up period with an improvement in severity and frequency in six out of eight patients in the Lancet [87, 103]. Magis et al. describe similar results and a difference in the nociceptive blink reflex after stimulation [85, 104]. These studies teach us that the clinical beneficial effect starts after weeks, as well as the wash-out of the beneficial effects of stimulation after switching of the stimulator.

Fibromyalgia

Fibromyalgia is a disease which consists of chronic pain in all four limbs of the body, without any abnormalities on clinical, physical, and technical examinations. The syndrome is accompanied by other symptoms like fatigue, sleeping disorders, irritable bowel syndrome, and headaches [105, 106]. It has a prevalence of up to 4 % and the socioeconomic burden is high. Berger et al. report a mean total healthcare cost of $ 9,573 per patient per year in the USA [107, 108].

Thimineur and De Ridder published results on a group of 12 patients suffering from chronic migraine and fibromyalgia, treated with PNFS of the occipital branch of the C2 nerve. They implanted percutaneous cylindrical leads at a horizontal line underneath the occipital protuberance. Patients reported a reduction in the visual analogue scale

for bodily pain of approximately 60 %. Besides these findings the authors report a decrease in fatigue and depressive mood as well as an increase in life quality [109]. Plazier et al. describe their results in a group of 11 patients, implanted with a cylindrical lead at the occipital nerve area. A double-blinded placebo controlled crossover design was applied for 10 weeks. A significant decrease in pain could be reported between the active stimulation scores and the sham stimulation (approximately 40 %). At 6 months these results remained stable. Besides the decrease in visual analogue scale a significant decrease in pain catastrophizing behavior could be found [110].

Pain catastrophizing behavior defines the emotional aspects of the total pain experience. As these scores get higher, patients get more distressed, worried, and occupied by their pain. Negative correlations between pain catastrophizing and life quality have been described [111, 112]. This might suggest that the overall beneficial effects of this form of stimulation on fibromyalgia might partially be caused by decreasing pain catastrophizing behavior.

The various functional imaging as well as source localized EEG studies (Plazier et al., unpublished data) reveal activity changes in various brain regions involved in catastrophizing behavior [73, 74, 101, 113–116].

In an ongoing sponsored trial the effects of this form of stimulation on the symptoms of fibromyalgia are being evaluated. Ad interim analysis reveals similar findings to the previously mentioned studies (Plazier et al., unpublished data).

Peripheral Pain

A case report shows that C2 PNFS might be capable of suppressing neuropathic pain in the setting of failed back surgery syndrome (FBSS) [117]. In summary, a subcutaneous C2 electrode was inserted under local anesthesia, and attached to an external pulse generator in a patient with FBSS. Classical tonic stimulation, consisting of 40 Hz stimulation, a placebo and a burst stimulation, consisting of 40 Hz burst mode, with five spikes delivered at 500 Hz at 1,000 μsec pulse width and 1,000 μsec interspike interval were tested. All stimulations were performed subthreshold for paresthesias. Burst mode was superior to placebo and tonic mode, and she received a fully implanted C2 electrode connected to an IPG via an extension wire. The burst design was capable of both suppressing the least and worst pain effectively, and she has remained almost pain-free for over 3 years.

Its mechanism is unclear but has been suggested to be related to similar mechanisms involved in fibromyalgia related pain suppression by ONS.

C1–C3 cells represent 45 % of all spinothalamic neurons and relay information from all levels of the cord to periaqueductal grey and/or thalamus [118] via a calbindin positive pathway [119]. C1–C3 spinothalamic tract neurons process sensory information from widespread regions of the body [120]. Upper spinal cord stimulation at C1–C3 modifies firing rate of >90 % of lumbosacral spinothalamic cells [121], and may therefore modulate transmission of noxious stimuli from lumbosacral origin, analogous to what has been proposed for the modulation of widespread bodily pain in fibromyalgia [67, 109].

Tinnitus

C2 nerve stimulation has been performed for suppressing tinnitus, using both TENS [122] and implanted electrodes [123]. The concept is based on well described somatosensory–auditory interactions [124]. Several studies have demonstrated the interactions between the somatosensory and auditory system, either at the dorsal cochlear nucleus (DCN) or at the inferior colliculus [125]. The aim of somatosensory stimulations is to decrease dorsal cochlear nucleus activity, as increased DCN activity has been implicated in tinnitus [126, 127]. The DCN receives auditory input from the cochlear nerve and somatosensory input, directly from the ipsilateral dorsal column and spinal trigeminal nuclei [128–130] or indirectly via the dorsal raphe and locus coeruleus [131]. The pinna and the neck are innervated by the upper cervical nerves (C1–C3), which project to spinal trigeminal nuclei [132–134]. C2 electrical stimulation produces a pattern of inhibition and excitation, of the principal cells [135] in the ventral and dorsal division of the cochlear nucleus [136–138], and can hereby suppress or enhance responses to sound [136, 137]. Not only C2 electrical stimulation can modulate the DCN. Electrical stimulation in the cat spinal trigeminal nuclei also yields strong inhibition and weak excitation of DCN principal cells [138, 139]. Thus both C2 and trigeminal stimulation can be proposed as treatments for tinnitus. For C2 electrical stimulation, noninvasive electrical stimulations using TENS have shown that it is possible to change the tinnitus percept [140, 141]. In a large study of 240 patients, only 17.9 % ($N = 43$) of the patients with tinnitus responded to C2 TENS. They had an improvement of 42.92 %, and only 6 of 240 patients had a reduction of 100 %. The first uncontrolled data do also show that similar results can be obtained by implanting wire electrodes subcutaneously in the C2 dermatome, as can implants on the spinal cord at the C2 level [123]. It can be expected that only very few people will respond to implants of the C2 or trigeminal dermatome, analogous to the amount of responders to TENS. A recent fMRI study demonstrated that subthreshold and suprathreshold stimulations are possible and evoke similar BOLD activation patterns in the brain [73], suggesting that placebo-controlled studies are feasible.

Device Choice

Traditionally, equipment used in PNS was originally designed for SCS. There was a wrap-around design of initial custom made electrode leads used in PNS for phrenic and vagal nerve stimulation for the treatment of diaphragmatic palsy, epilepsy, and depression. Subsequent introduction of the "multi-button" electrode design for PNS never went into mass production. These were designed to specifically stimulate separate fascicles of a large mixed nerve, such as sciatic, but for variety of reasons, the standard paddle electrodes already available for SCS applications became the preferred PNS delivery device. To overcome formation of scar tissue between the nerve and the electrode, paddles were then modified by attaching an integrated Dacron mesh, which could be wrapped around the nerve [142]. However, the open surgical approach with nerve exploration required for implantation of these electrodes meant this technique was mostly abandoned with the advent of percutaneous PNS techniques.

Although percutaneous placement now dominates the field of PNS, some neuromodulators still use paddle leads for PNS because of several important benefits of paddle leads. First, modern paddles have several rows of electrode contacts (between 1 and 5 rows), separated by a preset distance. This facilitates multiple stimulation paradigms in the longitudinal, transverse and oblique directions, with electrode contact configuration that matches the course of sensory fibers inside the nerve trunk. Second, the paddle structure ensures unidirectional stimulation, whereby electrical energy gets directed toward the nerve, while the surrounding tissue gets shielded by the insulation of the paddle's backing. Thereby, paddle leads consume less energy to produce the desired effect and may be associated with longer implantable pulse generator (IPG) battery life. Third, the use of paddle electrodes in PNS, similarly to SCS experience, is associated with a lower migration rate.

The invasiveness of paddle insertion and need for highly refined surgical skills to expose peripheral nerves were among the reasons for the lack of widespread acceptance of paddle-based PNS. Additionally, there have been multiple reports of perineural fibrosis following long-term PNS with paddle leads, which has raised concern about their safety and appropriateness, even though this phenomenon occurred in a very small percentage of patients. Nevertheless, percutaneous lead insertion for PNS/PNFS application has become so widespread that, by some estimates, this application accounts for between 25 and 50 % of the devices implanted in the USA in 2011.

Currently, percutaneous electrode leads are generally chosen when the nerve of interest is located in a predictable area, when stimulation may be delivered without direct contact with the nerve, and whenever the painful area may require coverage with one or more leads, whereby stimulating paresthesias are concordant with the pain distribution. Additionally, insertion of percutaneous PNS leads may be facilitated by the use of ultrasound guidance, which helps in localizing the nerve pathway and depth while avoiding adjacent vascular structures.

The choice of power source for PNS is usually determined by stimulation energy requirement. In the past (and even now in the USA), the only approved devices for PNS applications were radiofrequency (RF)-coupled systems. In such systems, the power source is external and delivers energy by means of a RF link between a transmitting antenna and an implanted receiver, which is connected to the electrode-leads either directly or via extensions. Once popular, these RF-coupled systems are rarely, if ever used today.

Initial IPGs were powered by a prime cell battery, which meant that the entire device had to be replaced when the battery became depleted. Such depletion could occur within a year after implantation, if high power settings were used in stimulation, or if stimulation was used continuously. The need for frequent IPG replacement was eliminated by the introduction of rechargeable technology. Today, rechargeable IPG devices dominate the neuromodulation marketplace. However, in some parts of the world, this technology is not available due to a lack of regulatory approval or the high cost of rechargeable IPGs. In PNS applications, use of rechargeable technology makes great sense since the low profile and smaller size of rechargeable IPG leads to less discomfort and better cosmoses for this patient population.

Of interest, several old PNS designs, including wrap-around electrode leads and RF-coupled power sources have been reincarnated with modern PNS applications. Two new companies have put their main focus on PNS-oriented devices. One company uses specially designed coil-like electrode leads, which are designed to be wrapped around peripheral nerves while delivering high-frequency electrical stimulation to eliminate pain of amputation neuroma [59]. Another company developed an RF-coupled implantable system whereby the electrode lead itself serves as an antenna linked to an external miniature power source, which is taped to the skin above it [24].

Procedural Details

Techniques used for PNS implantation depend on both the stimulation target and the choice of hardware. For direct stimulation of a specific peripheral nerve, the electrode lead may be implanted through open exploration of the nerve segment or by percutaneous placement in the vicinity of the nerve. In both scenarios, anatomical knowledge of the nerve course is important.

For percutaneous placement, electrode insertion may be facilitated by fluoroscopy (to define known skeletal landmarks) or ultrasound (to directly visualize the nerve and adjacent vascular bundle). Identification of the surgically accessible segment of the nerve, where branching is minimal, is important. Additionally, it is critical to plan electrode lead position, entry, and tunneling path in advance, to avoid major joints, since repetitive movement of the lead or extension cable may result in material fatigue or fracture. Furthermore, constant manipulation of metal wires and external plastic insulation may damage the equipment. Surgical experience is essential for implanting paddle electrodes for PNS, as is a great familiarity with intraoperative ultrasound, for PNS targeting.

Conversely, detailed knowledge of peripheral nerve anatomy is not as essential for PNFS applications. Here, the electrode leads are implanted either in the middle of the painful area, or on its edges. Traditionally, it was thought that one cylindrical electrode could cover an area the size of a business card (or a credit card) if the electrode was placed medially. Any larger treatment area, within a 10–12 cm limit, should be treated with two leads placed on the periphery of the painful region. More recently, this initial placement paradigm has evolved subsequent to the introduction of the "cross talk" approach, which postulates that very large areas can be covered with separate electrode leads placed far from each other [50]. This approach has been validated with theoretical modeling and in small clinical series, but thus far has not received widespread acceptance.

For both PNS and PNFS applications, the ideal depth of the electrode is just above the deep subcutaneous fascia. Placing leads in the epifascial plane has limited the development of muscle spasms, which would occur when the electrode was placed too deep. Additionally, this has limited the risk of lead erosion, which would occur if the lead were placed too superficially.

Depth of electrode placement is important in selection of an appropriate anchoring device. Some commercially available anchors have a high profile, which may lead to discomfort or visible deformation of the skin, and in turn, may lead to erosion over time. Anchoring electrode lead(s) in place is an important step in device implantation given the high mobility of soft tissues in PNS/PNFS applications. Improper anchoring may result in even higher migration rate than seen in SCS, where leads are relatively immobile in the epidural space or in DBS, where leads are skull mounted.

Whichever anchor or anchoring technique is used, it is generally recommended to use non-absorbable sutures and to fix the lead to a hard tissue, such as thick deep fascia. Additionally, it is recommended to use "strain relief" loops, which are intended to minimize lead displacement during the patient's body movement. These loops should be placed, if possible, next to the anchor (between the anchor and the generator) and next to the IPG, minimizing the chance of electrode migration and/or fracture.

The location and depth of IPG implantation should also be preplanned. Position of the IPG in PNS cases is usually dependent on the location of pain and electrode leads. Placing the IPG over bony prominences (edge of the rib cage, iliac crest, scapula, etc.), or too close to the midline, should be avoided to prevent patient discomfort. Placing the IPG too deep in the soft tissues may interfere with the ability to recharge the device. Alternatively, placing the IPG too superficially, immediately under the dermis increases the risk of poor wound healing, device erosion, and implant site pain.

Occipital Nerve Stimulation Techniques

The implantation and trial and permanent implantation phase of occipital nerve stimulation does not, technically, differ from the above mentioned. The electrode(s) are normally located in an area just underneath the occipital protuberance. This is the region where the main branches of the greater occipital nerve can be found [68]. Both techniques with paddle leads and percutaneous leads have been published [143]. Weiner et al. published their technique with introduction of the lead with a Tuohy needle [5] The lead is positioned in the subcutaneous tissue in a horizontal line between the two pinnae of the ears. If the lead is placed to low or to deep, it might stimulate the cervical muscle tissue. This will cause undesirable effects [144].

The lead can be anchored to the muscle fascia, or periosteum tissue, or be tunneled in a steep angle to prevent lead migration. Trial can be performed by connecting the lead to an extension cable and externalize the contacts of this cable. After successful stimulation, the extension cable can be removed and a full system can be implanted with the IPG at the desired site of the body. In some indications where the onset of effects might take long periods, like chronic migraine, the IPG can be implanted directly.

PNS Complications

Complications of all neuromodulation techniques are generally divided into ten main groups [145]. Some occur primarily with intrathecal pumps and other means of chemical neuromodulation; some others are specific to the central nervous system and apply to the electrical stimulation of spinal and cerebral structures. Several categories, however, are applicable to PNS including infection, hemorrhage, injury to nervous tissue, placement of device in the wrong compartment, hardware migration, erosion, and device malfunction, which includes lead fracture and disconnection.

Through advancement in technology, many initial PNS complications are rarely seen today, while others remain essentially unchanged.

In the early stages of PNS practice, electrodes were custom-made. Some wrap-around electrodes had Silastic backing [146] with platinum wires facing the nerve being stimulated. In some circumstances, this backing accumulated a significant amount of fluid, which subsequently affected electrical impedance, leading to loss of electrical conductivity [146]. Later, as cuff electrodes were designed to be more biocompatible, the principal complication was nerve injury secondary to development of fibrosis and possible ischemia, which was caused by electrodes strangling the nerve within the soft tissues. Reporting of multiple incidents of this complication significantly contributed to abandonment of this device [18, 33, 147]. Furthermore, despite meticulous dissection and secure anchoring, some cuff electrodes became displaced, necessitating electrode revision.

The migration incidence increased with introduction of the percutaneous PNS technique, whereby tissue friction is minimal and the only thing that holds the electrode in place is the anchor and the so-called "strain relief loop," which is commonly placed next to the anchoring site. Most surgeons who have revised percutaneous PNS electrode would agree that these electrodes easily migrate, and the tissue reaction around them is minimal. Migration is unlikely to happen in lateral (relative to the electrode axis) electrode placement. Most commonly, migration occurs secondary to the electrode pulling out from its original lead position. Sometimes, if the anchor is completely incompetent, or if the patient presents with hypermobility over the electrode path, migration can be dramatic. In addition to this "pull-out" phenomenon, the electrode lead may also migrate "in", shifting more distally along the electrode path. If migration is suspected, simple plain films compared to original images at time of electrode placement can help to differentiate. Thereby, it is important to obtain and save radiographic images of initial electrode lead position at time of original implantation. Incidence of migrations is variable, and ranges from 0 to 100 % depending on series [143, 148, 149]. Revision of malpositioned or migrated electrodes, which are still functioning, is relatively easy. A simple technique allows for repositioning without reopening the generator pocket [150, 151]. However, it is important to have the generator pocket prepped and ready for exploration should the electrode lead turn out to be damaged or otherwise unsuitable for reinsertion.

Electrode leads may break at any time after implantation. Breakage (fracture) is usually secondary to kinking in the electrode's lead insulation. The lead insulation of internal wires may break due to repetitive movement that involves repetitive stretch or compression of the device, resulting in material fatigue and eventual failure. This issue should be considered when choosing the path of electrode lead placement and generator location. Crossing large joints and tunneling greater distances is associated with higher rate of fractures and migrations.

Both infection and hemorrhage have occurred with PNS devices, but incidence is rare. Since most devices are placed in superficial locations, hemostasis is generally obtainable and hematoma formation is rarely symptomatic. Infection, on the other hand, may occur soon or late post-implantation. Surgical infection may result from poor surgical technique or insufficient dissection of anchors and connectors, resulting in excessive tissue tension, which prevents wound healing. In our series of 40 patients with PNS implants that were followed for longer than 30 months, there were two infections [23]; in each case, the device had to be removed. Infection was managed with systemic antibiotics specific to antibiotic sensitivities, once established. PNS systems may be reimplanted several months after infection is eradicated, as long as the cause of infection is understood and addressed.

Placement of the PNS device in the wrong compartment is a theoretical concern, since most PNS electrodes are inserted in a subcutaneous epifascial plane. However, since the proximity of electrode lead to the nerve being stimulated is extremely important in obtaining adequate paresthesias and maintaining stimulation parameters within reasonable range, various techniques have been suggested to improve the placement accuracy. Most PNS implanters rely on use of fluoroscopy for localization [152], but now multiple reports suggest ease of use of intraoperative ultrasound for localization of the nerve trunk and the surrounding structures [6, 153, 154]. Insertion of electrodes too deep into soft tissues can cause unpleasant muscle spasms during stimulation [144]; insertion too superficially may result in lead tip erosion [155].

Overall, most PNS complications are minor and rarely, if ever, require hospitalization. Recently, we analyzed our institutional experience with PNS. Among nearly 100 PNS cases since April 2000, we identified 40 patients who underwent original PNS trial at our institution, who were then followed up for 30 months or longer [23]. The remaining patients had either shorter follow-up, or had their initial surgery at another institution. Out of 40 patients, 8 did not sufficiently improve during the trial and 32 proceeded with permanent implantation. In a long-term follow-up series, 27/32 patients underwent subsequent operations (including 12 battery replacements) but only 1/32 had an infection requiring hospital admission. Out of 15 reoperations, there were 6 revisions (1 for electrode erosion 4 weeks after implantation, 4 for electrode migration at 1, 3, 5, and 9 months after original implantation, 1 for device disconnection), and 9 device removals (2 from infections at 1 and 49 months, due to a loss of effectiveness

at 9, 10, and 25 months, and 4 due to improvement of symptoms at 13, 17, 21, and 56 months after original implantation) [23]. This experience illustrates the well-known observation about the high rate of complications but relatively minor morbidity associated with PNS [143, 149].

Outcomes

The long-term outcome of more recently introduced PNFS is still unknown. The large series from Australia and Europe, some of which were used for getting regulatory approval on these continents, discussed outcomes of 3 months in a heterogeneous cohort of 111 patients (the Austrian multicenter study [56]) and 7 months in 13 patients (the Australian experience [156]). All published studies documented consistently observed more than 50 % reduction in pain level in every group of PNS/PNFS patients.

In traditional PNS cases, much longer follow-up has been summarized in multiple publications. An average follow-up of more than 10 years in a combined German–Israeli experience of Dr. Waisbrod showed that among 46 implanted PNS patients, good results were observed in 22/30 (73 %) of lower extremity implants and in 10/12 (83 %) of upper extremity implants [157]. The patients with postsurgical nerve injury and entrapment neuropathy exhibited significant improvement in >80 % of cases, while those with pain after traumatic injections had 50 % success rate, and those with pain after nerve graft—0 %. Even longer follow-up (more than 20 years) was reported in the Belgian study of Drs. Van Calenbergh and Gybels where patients implanted in the 1980s continued to enjoy >50 % improvement in pain intensity when using their PNS devices [158].

Conclusions

The peripheral neuromodulation approach includes the following three modalities: (1) PNS, which requires implantation of stimulating electrode leads over the affected peripheral nerves; (2) percutaneous PNS, which involves insertion of stimulating electrode leads in the vicinity of the nerve with proper guidance; (3) PNFS that stimulates smaller nerves and nerve endings in the region of pain. Peripheral neuromodulation is an effective way to control chronic, disabling, neuropathic pain of various etiologies, which is refractory to medical treatment. Peripheral neuromodulation is expected to be more widely accepted (and properly covered by regulatory agencies and payers) once there is more prospective data showing long-term clinical efficacy and cost-effectiveness.

Although commonly used in clinical practice, peripheral nerve stimulation (PNS) for treatment of chronic neuropathic pain is mostly performed using devices developed and marketed for spinal cord stimulation applications. This may be one reason why PNS is marked by a relatively high complication rate, since the anatomy of peripheral nerves and surrounding soft tissues is quite different from the epidural spinal space, for which the current devices are designed. Based on literature data and analysis of the authors' experience with PNS, despite the high rate of complications, morbidity associated with the PNS approach is low, and most problems may be resolved with simple revision surgeries performed on an outpatient basis. Reduction in the complication rate is expected to occur when the hardware used in PNS procedures is appropriately adapted and designed for PNS applications. Introduction of dedicated PNS/PNFS devices will not only reduce complication rates, but will also likely improve reliability and sustainability of optimal outcomes. Based on the authors' observations and expectations, the next decade will bring both technical advances and clinical experience in the PNS/PNFS arena.

References

1. Abejon D, Perez-Cajaraville J. Peripheral nerve stimulation: definition. Prog Neurol Surg. 2011;24:203–9.
2. White JC, Sweet WH. Pain and the neurosurgeon. A forty-year experience. Springfield, IL: Thomas; 1969. p. 894–9.
3. Melzack RA, Wall PD. Pain mechanisms: a new theory. Science. 1965;150:971–9.
4. Slavin KV. History of peripheral nerve stimulation. Prog Neurol Surg. 2011;24:1–15.
5. Weiner RL, Reed KL. Peripheral neurostimulation for control of intractable occipital neuralgia. Neuromodulation. 1999;2:217–21.
6. Huntoon MA, Burgher AH. Ultrasound-guided permanent implantation of peripheral nerve stimulation (PNS) system for neuropathic pain of the extremities: original cases and outcomes. Pain Med. 2009;10:1369–77.
7. Johnson MI, Bjordal JM. Transcutaneous electrical nerve stimulation for the management of painful conditions: focus on neuropathic pain. Expert Rev Neurother. 2011;11:735–53.
8. Hurlow A, Bennett MI, Robb KA, Johnson MI, Simpson KH, Oxberry SG. Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. Cochrane Database Syst Rev. 2012;3:CD006276. doi:10.1002/14651858.CD006276.pub3.
9. Francis RP, Johnson MI. The characteristics of acupuncture-like transcutaneous electrical nerve stimulation (acupuncture-like TENS): a literature review. Acupunct Electrother Res. 2011;36:231–58.
10. Levin PJ, Wu JM, Kawasaki A, Weidner AC, Amundsen CL. The efficacy of posterior tibial nerve stimulation for the treatment of overactive bladder in women: a systematic review. Int Urogynecol J. 2012;23:1591–7.
11. Findlay JM, Maxwell-Armstrong C. Posterior tibial nerve stimulation and faecal incontinence: a review. Int J Colorectal Dis. 2011;26:265–73.
12. Schulz-Stubner S, Kehl F. Treatment of persistent hiccups with transcutaneous phrenic and vagal nerve stimulation. Intensive Care Med. 2011;37:1048–9.
13. Stefan H, et al. Transcutaneous vagus nerve stimulation (t-VNS) in pharmacoresistant epilepsies: a proof of concept trial. Epilepsia. 2012;53(7):e115–8.

14. Pop J, Murray D, Markovic D, DeGiorgio CM. Acute and long term safety of external trigeminal nerve stimulation for drug resistant epilepsy. Epilepsy Behav. 2011;22:574–6.
15. Schrader LM, Cool IA, Miller PR, Maremont ER, DeGiorgio CM. Trigeminal nerve stimulation in major depressive disorder: first proof of concept in an open pilot trial. Epilepsy Behav. 2011;22:475–8.
16. Singla S, Prabhakar V, Singla RK. Role of transcutaneous electrical nerve stimulation in the management of trigeminal neuralgia. J Neurosci Rural Pract. 2011;2:150–2.
17. Picaza JA, Hunter SE, Cannon BW. Pain suppression by peripheral nerve stimulation: chronic effects of implanted devices. Appl Neurophysiol. 1977–1978;40:223–34.
18. Kirsch WM, Lewis JA, Simon RH. Experiences with electrical stimulation devices for the control of chronic pain. Med Instrum. 1975;9:217–20.
19. Bhaskar A, White A, Patel K. Percutaneous electrical stimulation (PENS) therapy for management of focal neuropathic pain: a case series of 42 cancer patients. Neuromodulation. 2011;14:558. (abstract of the 10th INS conference)
20. Bhaskar A, Patel K, White A. Trigeminal field stimulation using percutaneous electrical nerve stimulation (PENS) therapy – preliminary case series of 8 patients. Neuromodulation. 2011;14:558. (abstract of the 10th INS conference)
21. Wall PD, Sweet WH. Temporary abolition of pain in man. Science. 1967;155:108–9.
22. U.S. Food and Drug Administration: Code of Federal Regulations. Title 21, Volume 8, 21CFR882.5870. http://www.gpo.gov/fdsys/pkg/CFR-2011-title21-vol8/pdf/CFR-2011-title21-vol8-sec882-5870.pdf
23. Slavin KV. Technical aspects of peripheral nerve stimulation: hardware and complications. Prog Neurol Surg. 2011;24:189–202.
24. Deer TR, Levy RM, Rosenfeld EL. Prospective clinical study of a new implantable peripheral nerve stimulation device to treat chronic pain. Clin J Pain. 2010;26:359–72.
25. Kotagal P. Neurostimulation: vagus nerve stimulation and beyond. Semin Pediatr Neurol. 2011;18:186–94.
26. Daban C, Martinez-Aran A, Cruz N, Vieta E. Safety and efficacy of vagus nerve stimulation in treatment-resistant depression. A systematic review. J Affect Disord. 2008;110:1–15.
27. DiMarco AF. Phrenic nerve stimulation in patients with spinal cord injury. Respir Physiol Neurobiol. 2009;169:200–9.
28. Oliven A. Treating obstructive sleep apnea with hypoglossal nerve stimulation. Current Opin Pulm Med. 2011;17:419–24.
29. Van Swigchem R, Weerdesteyn V, van Duijnhoven HJ, den Boer J, Beems T, Geurts AC. Near-normal gait pattern with peroneal electrical stimulation as a neuroprosthesis in the chronic phase of stroke: a case report. Arch Phys Med Rehabil. 2011;92:320–4.
30. Norderval S, Rydningen M, Lindsetmo RO, Lein D, Vonen B. Sacral nerve stimulation. Tidsskr Nor Laegefore. 2011;131:1190–3.
31. Levy RM. Differentiating the leaves from the branches in the tree of neuromodulation: the state of peripheral nerve field stimulation. Neuromodulation. 2011;14:201–5.
32. Hassenbusch SJ, Stanton-Hicks M, Schoppa D, Walsh JG, Covington EC. Long-term results of peripheral nerve stimulation for reflex sympathetic dystrophy. J Neurosurg. 1996;84:415–23.
33. Nashold Jr BS, Goldner JL, Mullen JB, Bright DS. Long-term pain control by direct peripheral-nerve stimulation. J Bone Joint Surg Am. 1982;64:1–10.
34. Kent M, Upp J, Spevak C, Shanon C, Buckenmaier C. Ultrasound-guided peripheral nerve stimulator placement in two soldiers with acute battlefield neuropathic pain. Anesth Analg. 2012;114:875–8.
35. Bouche B, Eisenberg E, Meigner M, Durand S, Papaniaou M, Suarez A, Verlysen M, Lemarie J. Facilitation of diagnostic and percutaneous trial lead placement with ultrasound guidance for peripheral subcutaneous field stimulation on infrapatellar branches of saphenous nerve. Neuromodulation. 2011;14:564.
36. Mobbs RJ, Nair S, Blum P. Peripheral nerve stimulation for the treatment of chronic pain. J Clin Neurosci. 2007;14:216–21.
37. Reverberi C, Dario A. The treatment of trigeminal neuralgia and atypical facial pain with peripheral nerve field stimulation (PNFS): a clinical case report. Neuromodulation. 2011;14:552.
38. Yakovlev A, Karasev SA, Resch BE, Yakovleva V, Strutsenko A. Treatment of atypical facial pain using peripheral nerve stimulation. Neuromodulation. 2011;14:553.
39. Deogaonkar M. Peripheral nerve/field stimulation for post-intervention trigeminal neuropathic pain. Neuromodulation. 2011;14:555.
40. Stidd DA, Wuollet A, Bowden K, Price T, Patwardhan A, Barker S, Weinand ME, Annabi J, Annabi E. Peripheral nerve stimulation for trigeminal neuropathic pain. Pain Physician. 2012;15:27–33.
41. De Carolis G, Paroli M, Psy Ciaramela A, Tollapi L, Paolo P. A case of successful treatment of post herpetic neuralgia using subcutaneous targeted neuromodulation. Neuromodulation. 2011;14:555.
42. Desai M, Sayal P, Leiphart J. Immediate outcomes of peripheral field nerve stimulation trials for thoracic neuropathic pain: a case series. Neuromodulation. 2011;14:559.
43. Bouche B, Eisenberg E, Meigner M, Durand S, Papaniaou M, Suarez A, Verlysen M, Dixneuf V, Lemarie J. Facilitation of diagnostic and percutaneous trial lead placement with ultrasound guidance for peripheral nerve stimulation on ilioinguinal neuralgia. Neuromodulation. 2011;14:563.
44. Bouche B, Eisenberg E, Meigner M, Durand S, Papaniaou M, Suarez A, Verlysen M, Lemarie J. Facilitation of diagnostic and percutaneous trial lead placement with ultrasound guidance for peripheral nerve stimulation on lateral cutaneous nerve. Neuromodulation. 2011;14:565.
45. Yakovlev AE, Resch BE, Yakovleva VE. Peripheral nerve field stimulation in the treatment of postlaminectomy syndrome after multilevel spinal surgeries. Neuromodulation. 2011;14:534–8.
46. Courtney P. Superior and middle cluneal nerves: an important target for stimulation in the treatment of failed back surgery syndrome (FBSS). Neuromodulation. 2011;14:552.
47. Djian MC, Page P, Viala A, Cherroun C, Roux FX. Successful back pain relief with peripheral nerve stimulation: case series of 3 patients. Neuromodulation. 2011;14:554.
48. Perruchoud C, Durrer A, Bovy M, Rutschmann B, Koeppel C, Kirchhofer E, Leberre J, Buchser E. Subcutaneous field stimulation for low-back pain: a 96-month follow-up. Neuromodulation. 2011;14:557.
49. Burgher A, Huntoon M, Turley TW, Doust MW, Stearns LJ. Subcutaneous peripheral nerve stimulation with inter-lead stimulation for axial neck and low back pain: case series and review of the literature. Neuromodulation. 2012;15:100–7.
50. Falco FJ, Berger J, Vrable A, Onyewu O, Zhu J. Cross talk: a new method for peripheral nerve stimulation. An observational report with cadaveric verification. Pain Physician. 2009;12:965–83.
51. Salmon J. Neuromodulation for refractory, truncal or diffuse neuropathic pain states. Clinical experience with subcutaneous (including C2 area) and combined subcutaneous and spinal cord stimulation treatment. Neuromodulation. 2011;14:550.
52. Reverberi C. The treatment of complex pain with combination of spinal cord stimulation (SCS) and peripheral nerve field stimulation (PNFS): our experience. Neuromodulation. 2011;14:551.
53. Hamm-Faber TE, Aukes HA, de Loos F, Gultuna I. Subcutaneous stimulation as an additional therapy to spinal cord stimulation for the treatment of lower limb pain and/or back pain. Neuromodulation. 2011;14:553.
54. Cioni B, Tufo T, Conforti G, De Simone C, Meglio M. Combined spinal cord and peripheral subcutaneous filed stimulation. Neuromodulation. 2011;14:560.

55. Barolat G, Wolkowitz RM, Meyer J, McRoberts P, Lipov EG, Joshi J, Davis B, Cairns KD. A randomized controlled feasibility trial to evaluate peripheral nerve field stimulation (PNFS) using subcutaneous placement of neurostimulation leads in the management of localized chronic intractable pain of the back. Neuromodulation. 2011;14:562.
56. Sator-Katzenschlager S, Fiala K, Kress HG, Kofler A, Neuhold J, Kloimstein H, Ilias W, Mozes-Balla EM, Pinter M, Loining N, Fuchs W, Heinze G, Likar R. Subcutaneous target stimulation (STS) in chronic noncancer pain: a nationwide retrospective study. Pain Pract. 2010;10:279–86.
57. Verrills P, Vivian D, Mitchell B, Barnard A. Peripheral nerve field stimulation for chronic pain: 100 cases and review of the literature. Pain Med. 2011;12:1395–405.
58. Slavin KV, editor. Peripheral nerve stimulation. Basel: Karger; 2011.
59. Soin A, Kilgore K, Bhadra N, Fang ZP. Feasibility study on high-frequency electrical nerve block for amputation pain. Neuromodulation. 2011;14:561.
60. Strand NH, Trentman TL, Vargas BB, Dodick DW. Occipital nerve stimulation with the Bion microstimulator for the treatment of medically refractory chronic cluster headache. Pain Physician. 2011;14:435–40.
61. Chae J, Wilson RD, Bennet ME, Lechman TE, Stager KW. Single-lead percutaneous peripheral nerve stimulation for the treatment of hemiplegic shoulder pain: a case series. Pain Pract. 2013;13:59–67.
62. Goroszeniuk T, Khan R. Permanent percutaneous splanchnic nerve neuromodulation for management of pain due to chronic pancreatitis: a case report. Neuromodulation. 2011;14:253–7.
63. Atallah J, Davidov M, Davila V. Feasibility of placement of peripheral nerve stimulator in the splanchnic nerves for treatment of chronic abdominal pain, cadaveric study. Neuromodulation. 2011;14:556.
64. Hegarty D, Goroszeniuk T. Peripheral nerve stimulation of the thoracic paravertebral plexus for chronic neuropathic pain. Pain Physician. 2011;14:295–300.
65. Rosendal F, Moir L, de Pennington N, Green AL, Aziz TZ. Successful treatment of testicular pain with peripheral nerve stimulation of the cutaneous branch of the ilioinguinal and genital branch of the genitofemoral nerves. Neuromodulation. 2012;16:121–4.
66. Jenkins B, Tepper SJ. Neurostimulation for primary headache disorders: part 2, review of central neurostimulators for primary headache, overall therapeutic efficacy, safety, cost, patient selection, and future research in headache neuromodulation. Headache. 2011;51:1408–18.
67. Plazier M, et al. Peripheral nerve stimulation for fibromyalgia. Prog Neurol Surg. 2011;24:133–46.
68. Bovim G, et al. Topographic variations in the peripheral course of the greater occipital nerve. Autopsy study with clinical correlations. Spine. 1991;16(4):475–8.
69. Pfaller K, Arvidsson J. Central distribution of trigeminal and upper cervical primary afferents in the rat studied by anterograde transport of horseradish peroxidase conjugated to wheat germ agglutinin. J Comp Neurol. 1988;268(1):91–108.
70. Newman HM, Stevens RT, Apkarian AV. Direct spinal projections to limbic and striatal areas: anterograde transport studies from the upper cervical spinal cord and the cervical enlargement in squirrel monkey and rat. J Comp Neurol. 1996;365(4):640–58.
71. Edvinsson L. Tracing neural connections to pain pathways with relevance to primary headaches. Cephalalgia. 2011;31(6):737–47.
72. Keizer K, Kuypers HG. Distribution of corticospinal neurons with collaterals to the lower brain stem reticular formation in monkey (Macaca fascicularis). Exp Brain Res. 1989;74(2):311–8.
73. Kovacs S, et al. Central effects of occipital nerve electrical stimulation studied by functional magnetic resonance imaging. Neuromodulation. 2011;14(1):46–55. discussion 56-7.
74. Matharu MS, et al. Central neuromodulation in chronic migraine patients with suboccipital stimulators: a PET study. Brain. 2004;127(Pt 1):220–30.
75. Shin JH, Kim YC, Jang IK, Kim JH, Park SY, Lee SC. Occipital nerve stimulation in a patient with an intractable chronic headache - a case repot. Korean J Anesthesiol. 2011;60:298–301.
76. Skaribas I, Calvillo O, Delikanaki-Skaribas E. Occipital peripheral nerve stimulation in the management of chronic intractable occipital neuralgia in a patient with neurofibromatosis type 1: a case report. J Med Case Reports. 2011;5:174.
77. Slavin KV, Nersesyan H, Wess C. Peripheral neurostimulation for treatment of intractable occipital neuralgia. Neurosurgery. 2006;58(1):112–9. discussion 112-9.
78. Hammer M, Doleys DM. Perineuromal stimulation in the treatment of occipital neuralgia: a case study. Neuromodulation. 2001;4(2):47–51.
79. Oh MY, et al. Peripheral nerve stimulation for the treatment of occipital neuralgia and transformed migraine using a C1-2-3 subcutaneous paddle style electrode: a technical report. Neuromodulation. 2004;7(2):103–12.
80. Kapural L, et al. Occipital nerve electrical stimulation via the midline approach and subcutaneous surgical leads for treatment of severe occipital neuralgia: a pilot study. Anesth Analg. 2005;101(1):171–4.
81. Johnstone CS, Sundaraj R. Occipital nerve stimulation for the treatment of occipital neuralgia-eight case studies. Neuromodulation. 2006;9(1):41–7.
82. Rodrigo-Royo MD, et al. Peripheral neurostimulation in the management of cervicogenic headache: four case reports. Neuromodulation. 2005;8(4):241–8.
83. Melvin Jr EA, Jordan FR, Weiner RL, Primm D. Using peripheral stimulation to reduce the pain of C2-mediated occipital headaches: a preliminary report. Pain Physician. 2007;10:453–60.
84. Popeney CA, Alo KM. Peripheral neurostimulation for the treatment of chronic, disabling, transformed migraine. Headache. 2003;43:369–75.
85. Magis D, et al. Occipital nerve stimulation for drug-resistant chronic cluster headache: a prospective pilot study. Lancet Neurol. 2007;6(4):314–21.
86. Schwedt TJ, Dodick DW, Hentz J, Trentman TL, Zimmerman RS. Occipital nerve stimulation for chronic headache: long-term safety and efficacy. Cephalalgia. 2007;27:153–7.
87. Burns B, Watkins L, Goadsby PJ. Treatment of medically intractable cluster headache by occipital nerve stimulation: long-term follow-up of eight patients. Lancet. 2007;369(9567):1099–106.
88. Schwedt TJ, Dodick DW, Trentman TL, Zimmerman RS. Occipital nerve stimulation for chronic cluster headache and hemicrania continua: pain relief and persistence of autonomic features. Cephalalgia. 2006;26:1025–7.
89. Ghaemi K, Capelle HH, Kinfe TM, Krauss JK. Occipital nerve stimulation for refractory occipital pain after occipitocervical fusion: expanding indications. Stereotact Funct Neurosurg. 2008;86:391–3.
90. Amin S, Buvanendran A, Park KS, Kroin JS, Moric M. Peripheral nerve stimulator for the treatment of supraorbital neuralgia: a retrospective case series. Cephalalgia. 2008;28:355–9.
91. Brewer AC, et al. Long-term outcome in occipital nerve stimulation patients with medically intractable primary headache disorders. Neuromodulation. 2012;16:557.
92. Silberstein SD, Dodick DW, Saper J, Huh B, Slavin KV, Sharan A, Reed K, Narouze S, Mogilner A, Goldstein J, Trentman T, Vaisma J, Ordia J, Weber P, Deer T, Levy R, Diaz RL, Washburn SN, Mekhail N. Safety and efficacy

of peripheral nerve stimulation of the occipital nerves for the management of chronic migraine: results from a randomized, multicenter, double-blinded, controlled study. Cephalalgia. 2012;32:1165–79.
93. Saper JR, Dodick DW, Silberstein SD, McCarville S, Sun M, Goadsby PJ. ONSTIM Investigators: occipital nerve stimulation for the treatment of intractable chronic migraine headache: ONSTIM feasibility study. Cephalalgia. 2011;31:271–85.
94. Burns B, Watkins L, Goadsby PJ. Treatment of intractable chronic cluster headache by occipital nerve stimulation in 14 patients. Neurology. 2009;72:341–5.
95. Lipton RB, Goadsby PJ, Cady RK, Aurora SK, Grosberg BM, Freitag FG, Silbersteon SD, Whiten DM, Jaax KN. PRISM study: occipital nerve stimulation for treatment-refractory migraine. Cephalalgia. 2009;29 Suppl 1:30.
96. Young WB, Silberstein SD. Occipital nerve stimulation for primary headaches. J Neurosurg Sci. 2012;56(4):307–12.
97. Royster EI, Crumbley K. Initial experience with implanted peripheral nerve stimulation for the treatment of refractory cephalgia. Ochsner J. 2011;11:147–50.
98. Deshpande KK, Wininger KL. Feasibility of combined epicranial temporal and occipital neurostimulation: treatment of a challenging case of headache. Pain Physician. 2011;14:37–44.
99. Abejon D, Calvo R, Arranz J, Perez-Cajaraville J, del Saz J, Aguierre-Jaime A. Peripheral nerve stimulation in the treatment of various types of headache. Rev Esp Anesthesiol Reanim. 2011;58:589–94.
100. Magis D, Gerardy PY, Remacle JM, Schoenen J. Sustained effectiveness of occipital nerve stimulation in drug-resistant chronic cluster headache. Headache. 2011;51:1191–201.
101. Magis D, Bruno MA, Fumal A, Gérardy PY, Hustinx R, Laureys S, Schoenen J. Central modulation in cluster headache patients treated with occipital nerve stimulation: an FDG-PET study. BMC Neurol. 2011;11:25.
102. Mammis A, Gudesblatt M, Mogilner AY. Peripheral neurostimulation for the treatment of refractory cluster headache, long-term follow-up: case report. Neuromodulation. 2011;14:432–5.
103. Burns B, Watkins L, Goadsby PJ. Treatment of hemicrania continua by occipital nerve stimulation with a bion device: long-term follow-up of a crossover study. Lancet Neurol. 2008;7 (11):1001–12.
104. Magis D, Schoenen J. Neurostimulation in chronic cluster headache. Curr Pain Headache Rep. 2008;12(2):145–53.
105. Salaffi F, Sarzi-Puttini P. Old and new criteria for the classification and diagnosis of fibromyalgia: comparison and evaluation. Clin Exp Rheumatol. 2012;30(6 Suppl 74):3–9.
106. Fitzcharles MA, et al. The 2010 American college of rheumatology fibromyalgia survey diagnostic criteria and symptom severity scale is a valid and reliable tool in a French speaking fibromyalgia cohort. BMC Musculoskelet Disord. 2012;13:179.
107. Bennett RM, et al. An internet survey of 2,596 people with fibromyalgia. BMC Musculoskelet Disord. 2007;8:27.
108. Berger A, et al. Characteristics and patterns of healthcare utilization of patients with fibromyalgia in general practitioner settings in Germany. Curr Med Res Opin. 2008;24(9):2489–99.
109. Thimineur M, De Ridder D. C2 area neurostimulation: a surgical treatment for fibromyalgia. Pain Med. 2007;8(8):639–46.
110. Plazier M, Dekelver I, Vanneste S, Stassijns G, Menovsky T, Thimineur M, De Ridder D. Occipital nerve stimulation in fibromyalgia: a double-blind placebo-controlled pilot study with a six-month follow-up. Neuromodulation. 2014;17:256.
111. Velly AM, et al. The effect of catastrophizing and depression on chronic pain–a prospective cohort study of temporomandibular muscle and joint pain disorders. Pain. 2011;152(10):2377–83.
112. Arnow BA, et al. Catastrophizing, depression and pain-related disability. Gen Hosp Psychiatry. 2011;33(2):150–6.
113. Vanneste S, et al. The neural correlates of tinnitus-related distress. Neuroimage. 2010;52(2):470–80.
114. Gracely RH, Ambrose KR. Neuroimaging of fibromyalgia. Best Pract Res Clin Rheumatol. 2011;25(2):271–84.
115. Nebel MB, Gracely RH. Neuroimaging of fibromyalgia. Rheum Dis Clin North Am. 2009;35(2):313–27.
116. Gracely RH, et al. Pain catastrophizing and neural responses to pain among persons with fibromyalgia. Brain. 2004;127(Pt 4):835–43.
117. De Ridder D, Plazier M, Menovsky T, Kamerling N, Vanneste S. C2 subcutaneous stimulation for failed back surgery syndrome: a case report. Neuromodulation. 2013;16:610.
118. Mouton LJ, Klop EM, Holstege G. C1-C3 spinal cord projections to periaqueductal gray and thalamus: a quantitative retrograde tracing study in cat. Brain Res. 2005;1043(1–2):87–94.
119. Craig AD, Zhang ET, Blomqvist A. Association of spinothalamic lamina I neurons and their ascending axons with calbindin-immunoreactivity in monkey and human. Pain. 2002;97 (1–2):105–15.
120. Chandler MJ, Zhang J, Foreman RD. Vagal, sympathetic and somatic sensory inputs to upper cervical (C1-C3) spinothalamic tract neurons in monkeys. J Neurophysiol. 1996;76(4):2555–67.
121. Djouhri L, Brown AG, Short AD. Effects of upper cervical spinal cord stimulation on neurons in the lumbosacral enlargement of the cat: spinothalamic tract neurons. Neuroscience. 1995;68 (4):1237–46.
122. Vanneste S, De Ridder D. Noninvasive and invasive neuromodulation for the treatment of tinnitus: an overview. Neuromodulation. 2012;15(4):350–60.
123. De Ridder D, et al. Surgical brain modulation for tinnitus: the past, present and future. J Neurosurg Sci. 2012;56(4):323–40.
124. Shore SE, Zhou J. Somatosensory influence on the cochlear nucleus and beyond. Hear Res. 2006;216–217:90–9.
125. Szczepaniak WS, Moller AR. Interaction between auditory and somatosensory systems: a study of evoked potentials in the inferior colliculus. Electroencephalogr Clin Neurophysiol. 1993;88 (6):508–15.
126. Kaltenbach JA. The dorsal cochlear nucleus as a contributor to tinnitus: mechanisms underlying the induction of hyperactivity. Prog Brain Res. 2007;166:89–106.
127. Kaltenbach JA. Summary of evidence pointing to a role of the dorsal cochlear nucleus in the etiology of tinnitus. Acta Otolaryngol Suppl. 2006;556:20–6.
128. Wright DD, Ryugo DK. Mossy fiber projections from the cuneate nucleus to the cochlear nucleus in the rat. J Comp Neurol. 1996;365(1):159–72.
129. Itoh K, et al. Direct projections from the dorsal column nuclei and the spinal trigeminal nuclei to the cochlear nuclei in the cat. Brain Res. 1987;400(1):145–50.
130. Weinberg RJ, Rustioni A. A cuneocochlear pathway in the rat. Neuroscience. 1987;20(1):209–19.
131. Zhang J, Guan Z. Pathways involved in somatosensory electrical modulation of dorsal cochlear nucleus activity. Brain Res. 2007;1184:121–31.
132. Abrahams VC, Lynn B, Richmond FJ. Organization and sensory properties of small myelinated fibres in the dorsal cervical rami of the cat. J Physiol. 1984;347:177–87.
133. Hekmatpanah J. Organization of tactile dermatomes, C1 through L4, in cat. J Neurophysiol. 1961;24:129–40.
134. Abrahams VC, Richmond FJ, Keane J. Projections from C2 and C3 nerves supplying muscles and skin of the cat neck: a study using transganglionic transport of horseradish peroxidase. J Comp Neurol. 1984;230(1):142–54.
135. Kanold PO, Young ED. Proprioceptive information from the pinna provides somatosensory input to cat dorsal cochlear nucleus. J Neurosci. 2001;21(19):7848–58.

136. Shore SE. Multisensory integration in the dorsal cochlear nucleus: unit responses to acoustic and trigeminal ganglion stimulation. Eur J Neurosci. 2005;21(12):3334–48.
137. Shore SE, El Kashlan H, Lu J. Effects of trigeminal ganglion stimulation on unit activity of ventral cochlear nucleus neurons. Neuroscience. 2003;119(4):1085–101.
138. Young ED, Nelken I, Conley RA. Somatosensory effects on neurons in dorsal cochlear nucleus. J Neurophysiol. 1995;73 (2):743–65.
139. Davis KA, Miller RL, Young ED. Effects of somatosensory and parallel-fiber stimulation on neurons in dorsal cochlear nucleus. J Neurophysiol. 1996;76(5):3012–24.
140. Vanneste S, et al. Transcutaneous electrical nerve stimulation (TENS) of upper cervical nerve (C2) for the treatment of somatic tinnitus. Exp Brain Res. 2010;204(2):283–7.
141. Herraiz C, Toledano A, Diges I. Trans-electrical nerve stimulation (TENS) for somatic tinnitus. Prog Brain Res. 2007;166:389–94.
142. Mobbs RJ, Blum P, Rossato R. Mesh electrode for peripheral nerve stimulation. J Clin Neurosci. 2003;10:476–7.
143. Jasper J, Hayek S. Implanted occipital nerve stimulators. Pain Physician. 2008;11:187–200.
144. Hayek SM, Jasper JF, Deep DR, Narouze SN. Occipital neurostimulation-induced muscle spasms: implications for lead placement. Pain Physician. 2009;12:867–76.
145. Slavin KV. Placing neuromodulation in the human body: limiting morbidity. In: Arle JA, Shils JL, editors. Essential neuromodulation. Philadelphia, PA: Elsevier; 2011. p. 301–20.
146. Shelden CH, Paul F, Jacques DB, Pudenz RH. Electrical stimulation of the nervous system. Surg Neurol. 1975;4:127–32.
147. Nielson KD, Watts C, Clark WK. Peripheral nerve injury from implantation of chronic stimulating electrodes for pain control. Surg Neurol. 1976;5:51–3.
148. Franzini A, Messina G, Leone M, Broggi G. Occipital nerve stimulation (ONS). Surgical technique and prevention of late electrode migration. Acta Neurochir (Wien). 2009;151: 861–5.
149. Falowski S, Wang D, Sabesan A, Sharan A. Occipital nerve stimulator systems: review of complications and surgical techniques. Neuromodulation. 2010;13:121–5.
150. Slavin KV, Vannemreddy PSSV. Repositioning of supraorbital nerve stimulation electrode using retrograde needle insertion: a technical note. Neuromodulation. 2011;14:160–3.
151. Mammis A, Mogilner AY. A technique of distal to proximal revision of peripheral neurostimulator leads: technical note. Stereotact Funct Neurosurg. 2011;89:65–9.
152. Trentman TL, Zimmerman RS. Occipital nerve stimulation: technical and surgical aspects of implantation. Headache. 2008;48:319–27.
153. Carayannopoulos A, Beasley R, Sites B. Facilitation of percutaneous trial lead placement with ultrasound guidance for peripheral nerve stimulation trial of ilioinguinal neuralgia: a technical note. Neuromodulation. 2009;12:296–301.
154. Skaribas I, Aló K. Ultrasound imaging and occipital nerve stimulation. Neuromodulation. 2010;13:126–30.
155. Trentman TL, Dodick DW, Zimmerman RS, Birch BD. Percutaneous occipital stimulator tip erosion: report of 2 cases. Pain Physician. 2008;11:253–6.
156. Verrills P, Mitchell B, Vivian D, Sinclair C. Peripheral nerve stimulation; a treatment for chronic low back pain and failed back surgery syndrome? Neuromodulation. 2009;12:68–75.
157. Eisenberg E, Waisbrod H, Gerbershagen HU. Long-term peripheral nerve stimulation for painful nerve injuries. Clin J Pain. 2004;20:143–6.
158. Van Calenbergh F, Gybels J, Van Laere K, Dupont P, Plaghki L, Depreitere B, Kupers R. Long term clinical outcome of peripheral nerve stimulation in patients with chronic peripheral neuropathic pain. Surg Neurol. 2009;72:330–5.