Informing practice

Peripheral neuromodulation: part 2: somatosensory, head and facial pain

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A doctor demonstrating electrotherapy on a young woman (from the Wellcome Collection L0012521).

This is part 2 of a 3-part article on the history, current practice and future directions of peripheral neuromodulation.

In part 1, we previously covered the theory of peripheral nerve stimulation.

In part 2, we present the role of peripheral modulation for specific clinical indications.

Stimulation of nerve plexuses

Brachial plexus stimulation

Neuropathic pain in the upper limb is often difficult to treat effectively.[1] The upper limb is a very good target for neuromodulation. The peripheral stimulation of the brachial plexus is not only simpler but also seems to be more effective compared to SCS, dorsal root ganglion (DRG) stimulation and deep brain stimulation (DBS).

The first patient who underwent peripheral stimulation of the brachial plexus had extremely severe neuropathic pain (10/10) caused by brachial plexus injury; the pain co-occurred with arm paralysis on the affected side. A preliminary, direct stimulation of the brachial plexus with low-frequency electric current (2 Hz) for 5 minutes relieved the pain by 95% for 7 hours.[2] Subsequently, the stimulation electrode was inserted percutaneously into the brachial plexus from posterior access. Using the electrode in that site, stimulation with electric current at a frequency from 2 to 10 Hz reduced the pain by 95%, which was similar to the effect of the preliminary stimulation. Notably, after the treatment with the percutaneous electrode, allodynia resolved within several hours after the procedure, and a normal sense of touch returned within several weeks. The arm function continued to improve slowly over the next 3 months.[2] Currently, insertion of stimulation electrodes via the medial supraclavicular access under the guidance of stimulation, ultrasonography or fluoroscopy is the method of choice.[3] This method is effective and much easier than insertion from the posterior approach. An interesting variant of the medial approach, which involves ultrasound guidance, was proposed by Bouche from Nantes, who successfully gives this treatment to patients who have not responded to SCS.[4] To date, this brachial plexus stimulation (BPS) has been described in about 50 patients. Preliminary or trial stimulation, for up to 2–3 weeks, can be performed in most settings. This stimulation can be achieved with simple, inexpensive catheters that are typically used for continuous peripheral anaesthesia. Using brachial plexus neuromodulation, together with a continuous block to treat patients with upper limb ischaemia, may be a viable therapeutic option.[5] BPS may be considered as an attractive alternative method of nerve stimulation in patients with pain of the upper limb. However, trials to compare the effects of BPS with those of standard treatment are required.

The following images are of BPS and majority of implants are for severe neuropathic pain and/or CRPS (Figures 1–3).

Stimulation of the lumbar plexus/paravertebral stimulation

Stimulation of the lumbar plexus can be beneficial in patients with intractable pain in the hip and knee joints.

It is relatively simple to insert an electrode percutaneously into the lumbar plexus from paravertebral access at the L4 level

Figure 1. Brachial plexus neurostimulation trial, mono-lead. Majority of patients have implants for severe neuropathic pain and/or CRPS. (TG copyright, with permission).

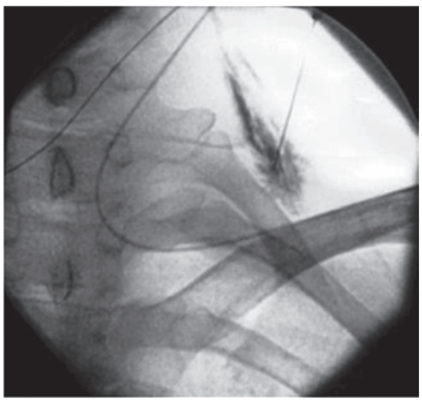
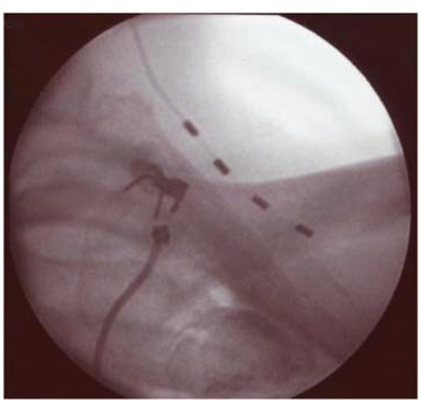


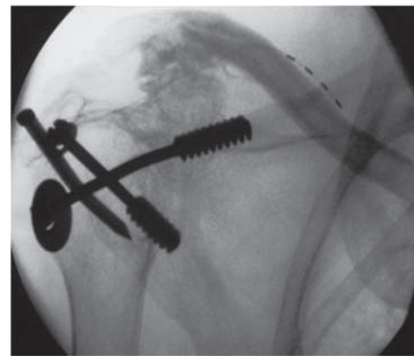
Figure 2. Brachial plexus stimulation (TG copyright, with permission).



with continuous diagnostic stimulation (2 Hz) and direct fluoroscopy or ultrasound guidance. In a small study among patients with knee pain, stimulation of the lumbar plexus relieved pain in three quarters of patients, and, in two patients, pain relief was achieved despite unsuccessful spinal cord stimulation.[6]

Paravertebral stimulation at the level of the chest can be a promising alternative to SCS or DRG stimulation for patients with unilateral chest pain. Paravertebral stimulation offers good electrode stability and substantial pain relief. The paravertebral

Figure 3. Brachial plexus stimulation (TG copyright, with permission).



stimulation is based on the same principle as the standard techniques of paravertebral anaesthesia.[7]

Nerve stimulation for headache and facial pain

Of the 15 occipital neuralgia patients of Weiner and Reed,[8] eight in fact actually suffered from chronic migraine for which it also proved successful. It is suggested that occipital nerve stimulation (ONS) is effective in chronic migraine because the signals from the trigeminal nerve, dura mater and cervical spinal nerves converge in the brainstem.[9]

The activation of the afferent fibres from the caudal portion of the trigeminal nucleus, at the C2 level, can cause pain in the trigeminal and cervical distributions. Thus, it is hypothesised that electrical stimulation modulating the function of occipital nerves can affect the mechanisms of pain in the areas innervated by the cervical nerves and the trigeminal nerve.[9]

The great occipital nerve is a branch of the C2 spinal nerve, and it is an easy target for stimulation-based treatments. In patients with chronic migraine who underwent ONS, position emission tomography (PET) showed increased blood flow in the areas assumed to mediate pain relief, that is, the posterior pons, anterior cingulate cortex and cuneus.[10]

Further series of case reports on the promising effects of ONS in patients with chronic headaches and migraine prompted large controlled trials assessing the effectiveness of this treatment.[10–13]

A total of 66 patients with drug-resistant migraine were enrolled in the ONSTIM study assessing the effects of bilateral ONS. The patients were randomly allocated to receive one of the three following treatments: variable ONS, fixed ONS and medical treatment.[11] Among the patients who received ONS, 39% responded to the variable ONS, and 6% of patients, to fixed ONS. Patients who received medications did not improve.

There may be a large placebo response as indicated in the PRISM study, when 132 patients were randomly allocated to undergo either nerve stimulation or sham stimulation.[12] The stimulation was given to patients for 12 weeks. The mean reduction in the number of days with migraine was 27% in the patients who received active stimulation, compared to 20% in those who underwent the sham stimulation, which was not significant.

In another study, 157 patients with refractory migraine were randomly allocated to receive either active stimulation or sham stimulation.[13] The results showed there was a significant difference between the groups that received either active or sham stimulation in achieving at least a 30% (but not 50%) reduction of headaches. This difference translated into a reduction in the number of days with headache by 3 days during a month and a decrease in the Migraine Disability Assessment Scale (MIDAS) scores by 44 points.

Cluster headache – ONS

Because the hypothalamus is known to be active during cluster headaches, it was the target of the first neuromodulation attempts to treat patients with cluster headaches who did not respond to medications.[14] However, the hypothalamus stimulation led to complications, and new targets for nerve stimulation in patients with cluster headaches were tested.[15,16] In patients with cluster headaches, PET showed an increased metabolism in the hypothalamus, pons and midbrain. This increased metabolism could be reversed by the stimulation of the occipital nerve.[17–21] A randomised, controlled trial comparing low-frequency and high-frequency paraesthesia is ongoing.[22]

Cluster headache – stimulation of the sphenopalatine ganglion

Stimulation of the sphenopalatine ganglion (SPG) is another neuromodulation target for cluster headache. The SPG lies in the pterygopalatine fossa, and the post-ganglionic parasympathetic and sensory fibres originating from the ganglion run along the blood vessels supplying the face, dura mater and brain. Initially, blockade and radiofrequency ablation of the SPG was used to treat patients with cluster headache who did not improve with standard treatment.[23,24] The SPG was chosen as the target for neuromodulation because, in animal studies, the electrical stimulation of this ganglion reversed hypoxia and increased blood flow in the relevant area.[25] A study among 28 patients with chronic cluster headache resistant to standard treatment tested the effects of a neurostimulator that was implanted through the mouth, with the tip of the electrode placed in the pterygopalatine fossa.[26] This device was controlled externally via a radiofrequency transmitter. The treatment with the SPG stimulator alleviated cluster headaches in 67.1% of patients, and it reduced the frequency of cluster headaches in 36% of all patients.[26] This improvement in cluster headache symptoms suggests that stimulation of the SPG is effective during acute episodes of cluster headache and can be also used in the prophylaxis of these headaches. Temporary sensory disturbances in the face were the most common adverse effects of the SPG stimulation.

Facial pain

Nerve stimulation, in the treatment of patients with facial pain, involves the stimulation of nerves located in the pain centres and pathways transmitting pain signals such as the trigeminal ganglion and its branches.[27–29] Clinical indications include trigeminal neuralgia, post-stroke pain, peripheral nerve injury, and post-herpetic neuralgia. Interestingly, in a case series, Taub et al.[30] observed that stimulation of the trigeminal ganglion successfully relieved pain in five of seven patients after stroke, but it did not improve post-herpetic neuralgia in any patient. Transcutaneous supraorbital nerve stimulation (tSNS) is promising, and it may prove to be an effective treatment for patients with migraine.[12,31,32]

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