BRITISH JOURNAL OF HOSPITAL MEDICINE

REVIEW

Neuromodulation

Sarah Love-Jones[1]

Author details can be found at the end of this article

Correspondence to:
Sarah Love-Jones; Sarah.Love-Jones@nbt.nhs.uk

Abstract

Spinal cord stimulation is the main neuromodulation therapy for certain chronic neuropathic pain conditions. This article describes neuromodulation and the process of spinal cord stimulation therapy. It also clarifies the suitability of a patient for referral and consideration for spinal cord stimulation.

Key words: Neuromodulation, Neuropathic pain, Spinal cord stimulation

Submitted: 2 December 2020; Accepted: 3 February 2021

Chronic pain and the impact it has on a patient's quality of life

Chronic pain is defined as pain that persists or recurs for more than 3 months (Treede et al, 2019). It is persistent pain beyond normal expectation, continuing after the diagnosis and treatment of a condition. Ongoing pain becomes the disease process rather than a symptom.

Chronic pain affects between one-third and one-half of the population of the UK, corresponding to just under 28 million adults (Fayaz et al, 2016).

Chronic pain has significant consequences for patients, as well as for their families, and their social and professional environment, causing deterioration in the quality of life of patients and those close to them (Dueñas et al, 2016). It can affect the patient's ability to work, wellbeing, mood, sleep and activity.

What is neuromodulation and what is the role of neuromodulation in chronic pain?

Neuromodulation is a technology that acts directly upon nerves. It is the alteration (or modulation) of nerve activity by delivering electrical or pharmaceutical agents directly to a target area.

Neuromodulation devices and treatments are life improving. They can provide an alternative to long-term drug therapy for the symptomatic relief of persistent or chronic conditions. The most common indication for neuromodulation is chronic neuropathic pain (Caylor et al, 2019). Neuromodulation devices used to treat chronic neuropathic pain include spinal cord stimulation, intrathecal drug delivery devices, peripheral nerve stimulation and dorsal root ganglion stimulation (which can treat focal neuropathic pain). The most common type of neuromodulation used in patients with chronic pain is spinal cord stimulation.

Spinal cord stimulation involves applying low current electrical stimulation directly to the dorsal column of the spinal cord (Figure 1) with leads in the epidural space. It involves the generation of electric fields between metal contacts of the spinal cord stimulation lead within the epidural space. The applied electrical fields change the electrical potential across membranes.

A pain psychology review is required before implantation. The spinal cord stimulation leads (Figures 2 and 3) are placed in the dorsal epidural space, either percutaneously through a narrow-gauge needle (Tuohy needle) or surgically. Electrical stimulation is delivered to the spinal cord (Figure 4). Insertion of lead(s) for spinal cord stimulation trials is first carried out under fluoroscopy, with at least 50% relief demonstrated in a pre-intervention trial. When successful, patients using spinal cord stimulation may find improvement in pain level and function, as well as improved mood and sleep. Following a successful trial, the leads are tunnelled under the skin to the battery which is usually implanted in the buttock area (Figure 1). Any changes to stimulation can be made via telemetry by the patient,

How to cite this article:
Love-Jones S. Neuromodulation. Br J Hosp Med. 2021. https://doi.org/10.12968/hmed.2020.0709

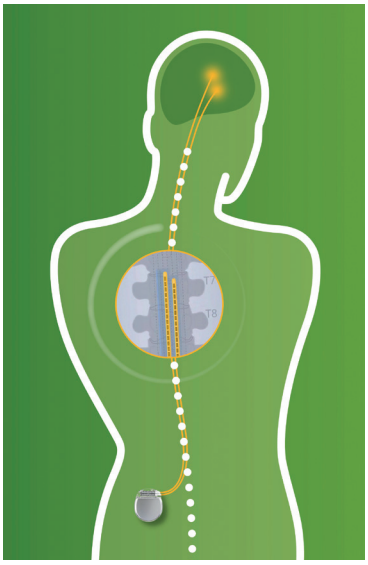

Figure 1. Leads in epidural space and battery in buttock area.

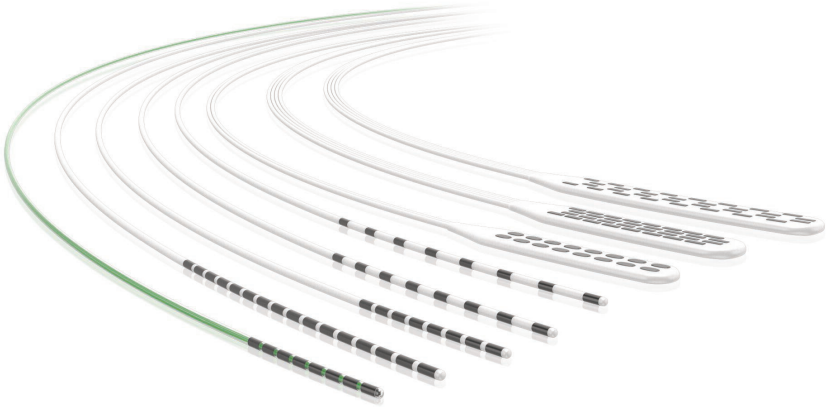

Figure 2. Percutaneous and surgical paddle leads.

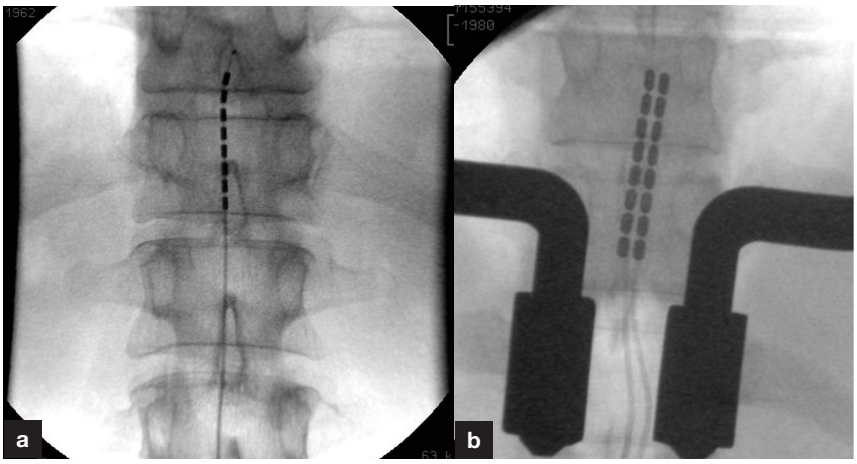

Figure 3. X-rays of (a) percutaneous and (b) surgical leads in the epidural space.

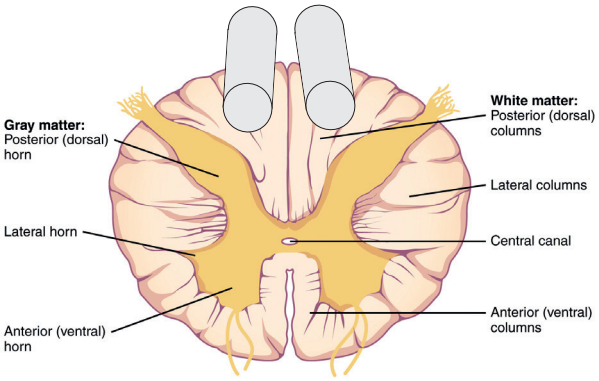

Figure 4. Electrical stimulation is delivered to the dorsal column of the spinal cord.

using a wireless handheld remote control (Figure 5). The implanted battery is charged using a cordless system.

The mechanism of action proposed for spinal cord stimulation was initially via the gate-control theory; however, this has been challenged with multiple potential mechanisms proposed (Caylor et al, 2019). The patient feels a sensation of a pleasant tingling instead of

Figure 5. Battery, leads and handheld programmer.

their pain. Some spinal cord stimulation devices can deliver multiple waveforms (including programmes with no tingling) so that the patient can receive maximum benefit and pain relief.

Advanced pain treatments: the referral pathway and which patients are suitable candidates for neuromodulation?

Spinal cord stimulation can help patients with chronic neuropathic pain (not nociceptive or mechanical pain). The National Institute for Health and Care Excellence (2008) Technology Appraisal Guideline 159 recommends spinal cord stimulation for patients with failed back surgery syndrome or complex regional pain syndrome. It can also help those with other peripheral or limb neuropathic pain. Patients with chronic neuropathic pain will normally have been seen in a pain clinic and tried other options such as medications, injection, transcutaneous electrical nerve stimulation, acupuncture, physiotherapy and pain management (includes cognitive–behavioural therapy, acceptance therapy and sleep hygiene, in order to manage the effects pain has on quality of life, rather than trying to cure the pain). Spinal cord stimulation is usually a last resort after other simpler treatments have been tried. It must be made clear that spinal cord stimulation is not a treatment for the condition but a way of reducing the intensity of the pain. Patients who are suitable for consideration for spinal cord stimulation are listed in Table 1 (National Institute for Health and Care Excellence, 2008). Patients who are not suitable for or excluded from spinal cord stimulation are listed in Table 2.

Review of the evidence: what does the research say?

There are now several randomised trials in spinal cord stimulation. The key trials are summarised as follows:

The landmark PROCESS trial by Kumar et al (2007) randomised 100 patients with failed back surgery syndrome with predominant leg pain of neuropathic radicular origin to receive spinal cord stimulation plus conventional medical management (spinal cord stimulation group) or conventional medical management alone for at least 6 months. Compared with the conventional medical management group, the group who had spinal cord stimulation experienced improved leg and back pain relief, quality of life, and functional capacity, as well as greater treatment satisfaction. Between 6 and 12 months after the start of the trial, five patients crossed from the spinal cord stimulation to the conventional medical management group, and 32 patients crossed from the conventional medical management group to the spinal cord stimulation group. This trial found that in selected patients with failed back surgery syndrome, spinal cord stimulation provided better pain relief and

Table 1. Patients who are suitable for treatment with spinal cord stimulation
Patients with complex regional pain syndrome
Patients with failed back surgery syndrome or post laminectomy syndrome
Patients with neuropathic pain in the limbs

Table 2. Patients who are not suitable for spinal cord stimulation
Patients waiting for elective surgery for anything (once patients have a spinal cord stimulator it may preclude them from magnetic resonance imaging and monopolar diathermy cannot be used)
Patients who have not been seen in a pain clinic (spinal cord stimulation is a last resort treatment, only used when all other pain clinic options have been exhausted)
Patients with nociceptive pain or mechanical back pain (spinal cord stimulation only works for neuropathic pain)
Patients taking high doses of opioids (>100 mg morphine equivalent in 24 hours)
Patients with active psychosis or suicidal ideation
Patients with major uncontrolled depression or other mood disorders
Patients with alcohol or drug dependency
Patients in the process of suing for compensation or litigation resolution regarding their pain condition (spinal cord stimulation should be provided only after any legal case is resolved)
Patients without appropriate social support
Patients with neuro-behavioural or cognitive deficits

improved health-related quality of life and functional capacity compared with conventional medical management alone.

North et al (2005) conducted a prospective, randomised, controlled trial to test the hypothesis that spinal cord stimulation is more likely than lumbar spine reoperation to result in a successful outcome. Patients were followed up 3 years postoperatively. If the results of the randomised treatment were unsatisfactory to them, patients could cross over to the alternative. Among 45 patients (90%) available for follow up, spinal cord stimulation was more successful than reoperation (9 of 19 patients vs 3 of 26 patients). Patients who were initially randomised to spinal cord stimulation were significantly less likely to cross over than were those randomised to reoperation (5 of 24 patients vs 14 of 26 patients). Patients randomised to reoperation required increased amounts of opiate analgesics significantly more often than those randomised to spinal cord stimulation. Spinal cord stimulation is more effective than reoperation as a treatment for persistent radicular pain after lumbosacral spine surgery and, in the great majority of patients, it obviates the need for reoperation.

Kemler et al (2008) looked at spinal cord stimulation in patients with complex regional pain syndrome with a 2-year comparison of spinal cord stimulation with physiotherapy, followed by a non-randomised follow up for a further 3 years during which some patients received spinal cord stimulation. They concluded that while at 24 months spinal cord stimulation is superior in pain relief to physiotherapy, this effect was lost from the third year onwards. This is the only randomised controlled trial of spinal cord stimulation in patients with complex regional pain syndrome and although the study showed the effect was lost from 3 years, many patients still derive good long-term effect from their spinal cord stimulation beyond this.

Conventional spinal cord stimulation was compared to medical management in patients with painful diabetic peripheral neuropathy in two prospective randomised controlled trials (de Vos et al, 2014; Slangen et al, 2014). These studies demonstrated the superiority of spinal cord stimulation over best medical management, as approximately 60% of patients in the spinal cord stimulation group, but only 5–7% of patients in the control arm, met

success criteria at 6 months. Results in the spinal cord stimulation group were sustained over time, with 80% of patients using their devices and 55% of patients achieving treatment success at 5 years (van Beek et al, 2018).

Guidelines and recommendations for clinical practice

Neuromodulation is best provided in a multidisciplinary setting with selection of patients after failure of other pain clinic interventions. The team usually consists of a pain physician (anaesthetist) and/or neurosurgeon, specialist nurses, physiotherapists, psychologists and occupational therapists. In the UK National Institute for Health and Care Excellence (2008) have specified recommendations for considering patients for spinal cord stimulation. This includes patients with intractable neuropathic pain, having a numeric rating score of pain above 5/10. Patients usually undergo a trial of spinal cord stimulation before permanent implant – this may include on-table trials; temporary trials of up to 2 weeks or permanent trials up to 1 month's duration. Patients are usually selected from pain clinics once they have tried other therapies.

Conclusions

Neuromodulation refers to the technology of altering nerve activity with either electricity or chemicals. Spinal cord stimulation which uses electricity is the most common type of neuromodulation used in patients with chronic neuropathic pain such as complex regional pain syndrome and failed back surgery syndrome (or post laminectomy syndrome). The technology involved in spinal cord stimulation has advanced rapidly over the last 10 years and there are now multiple therapies available with multiple waveforms. Patients now have the choice of paraesthesia therapy (where they feel a tingling sensation), sub-perception or high frequency therapy (where they feel no tingling) or a combination of both. Spinal cord stimulation can deliver combination therapy simultaneously (Metzger et al, 2020). It must be made clear that spinal cord stimulation is not a treatment for the cause of pain, but it is an excellent therapy for reducing the intensity of neuropathic pain in well-selected patients.

Author details

[1]Department of Anaesthesia, Southmead Hospital, North Bristol NHS Trust, UK

Conflicts of interest

Dr Love-Jones has undertaken paid consultancy work for Abbott Medical, Boston Scientific, Medtronic, Nevro Corporation and Pfizer. She has research support from Boston Scientific, Medtronic, Abbott Medical, Nevro Corporation, Nalu Medical and Mainstay Medical.

Acknowledgement

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Key points

- Spinal cord stimulation can be helpful in reducing the intensity of chronic neuropathic pain.
- Failed back surgery syndrome is the most common indication for spinal cord stimulation.
- Appropriate patient selection and education is key to successful spinal cord stimulation.
- Spinal cord stimulation involves applying low current electrical stimulation to the spinal cord.

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