Neuromodulation: what is its place in pain management?

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Neuromodulation has an expanding role in chronic pain management. Appropriate patient selection, education, standardised care and attention to detail are crucial for successful outcomes in neuromodulation and to reduce the risks of complications.

Key points

- **Neuromodulation is the modulation of nerve activity by delivering electrical or pharmaceutical agents directly to a target area.**
- **Long-term opioid therapy in chronic noncancer pain has limited efficacy and is associated with significant complications in people with chronic noncancer pain. Alternative management techniques should therefore be considered in these patients.**
- **Patients should be considered for referral for spinal cord stimulation if they have ongoing moderate to high levels of persistent neuropathic pain and if more conservative strategies have been comprehensively trialled and failed.**
- **Specific indications for consideration for spinal cord stimulation include failed back surgery syndrome, complex regional pain syndrome, peripheral neuropathic pain, chronic peripheral ischaemic pain and refractory angina pectoris.**

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Neuromodulation refers to the therapeutic alteration of the central or peripheral nervous system. According to the International Neuromodulation Society, the definition of neuromodulation is: '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 includes: spinal cord stimulation and peripheral nerve stimulation for neuropathic pain; sacral nerve stimulation for pelvic pain or urinary/defaecatory disorders; intrathecal therapy for pain or spasticity; and deep brain stimulation for Parkinson's disease and other movement disorders. This concise review focuses mainly on spinal cord stimulation, peripheral nerve stimulation, sacral nerve stimulation and intrathecal therapy.

Spinal cord stimulation

Spinal cord stimulation was first performed in 1967 by the pioneer neurosurgeon, Norman Shealy,[1] only months after the seminal publication of the 'gate control theory of pain' by Ronald Wall and Patrick Melzack.[2] Technical issues hampered the rapid uptake of spinal cord stimulation by neurosurgeons for difficult pain conditions. These technical issues included lead migration, device failure and clinical failures in patients subsequently determined to be unsuitable for the procedure. Now, after more than 40 years of clinical experience with this therapy, its value has been clarified, its cost effectiveness has been proven,[3] the indications for implant have been determined[4] and society statements and guidelines have been published.[5] Spinal cord stimulation is now effectively being used to reduce pain and improve quality of life in carefully selected patients.

Indications

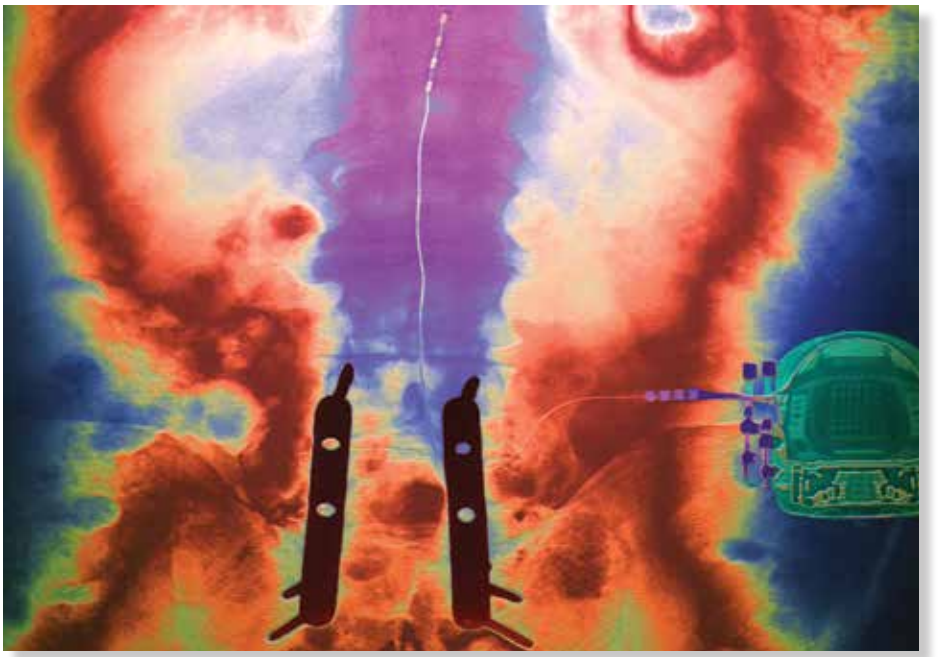
Spinal cord stimulation is indicated for patients with neuropathic conditions of the upper or lower limbs in whom more conservative strategies have been comprehensively trialled and failed, and the patient has ongoing moderate to high levels of persistent pain. Typical conditions known to be responsive to this therapy include:

- back and leg pain after spine surgery (referred to as failed back surgery syndrome)[6]
- complex regional pain syndrome (formally known as reflex sympathetic dystrophy)[7]
- peripheral neuropathic pain (e.g. diabetic neuropathy)[8]

- chronic ischaemic pain of the lower limbs due to peripheral vascular disease that is nonreconstructable[9]
- refractory angina pectoris.[10]

Some conditions that rarely respond to spinal cord stimulation include:

- pain following spinal cord damage (i.e. where there is loss of the spinal cord posterior column integrity or function)
- central pain of nonspinal cord origin (e.g. poststroke pain)
- brachial plexus injury (30% may respond to spinal cord stimulation and these cases usually have some form of intact nerve roots).



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Patient selection

Spinal cord stimulation is contraindicated in patients with significant, uncontrolled psychiatric or psychological conditions. This includes active suicidal ideation, homicidal ideation, severe uncontrolled depression, and severe levels of catastrophising, fear-avoidance behaviour or severely impaired pain self-efficacy ratings.

Patients with clear issues of enmeshment within the compensation system, with issues of drug addiction or drug dependency (morphine equivalents of more than 100 mg/day) or in the process of active litigation should also be excluded. This is because the clinical outcome in this group is one of poor response to the therapy and neither the results nor the cost can be justified. This group of patients may better respond to intensive cognitive behavioural therapy or acceptance and commitment therapy for their pain management.

Patient management

Typically, a patient with severe persistent pain will be referred to a specialist pain medicine physician, who holds the degree of Fellowship of the Faculty of Pain Medicine Australian and New Zealand College of Anaesthetists (FFPMANZCA) and is working in a multidisciplinary pain clinic. The patient will be assessed across multiple domains of functioning and a treatment plan will be devised, using components of pharmacotherapy, psychological therapy, physical rehabilitation and interventional pain therapy, which are deemed appropriate for the patient's condition. If patients do not respond to these therapies then spinal cord stimulation will be indicated, and patients will undergo a thorough psychological assessment as part of their work up to determine the appropriateness of spinal cord stimulation. This intervention may span more than one session and will also include psychological preparation and education on spinal cord stimulation.

If the patient is deemed suitable for neuromodulation therapy, he or she will typically have a percutaneous trial of the therapy for four to 14 days. This is carried out by placing the stimulator leads (each lead contains up to 16 active electrodes) percutaneously into the thoracic epidural space. The leads are brought out through the skin and connected to a battery-powered device. Each device is programmed to deliver stimulation to cover the patient's individual and specific pain(s). The patient has control over the device and stimulation parameters (via a remote control) and can choose different settings and programs. Typically, 60% of patients demonstrate a positive response to the trial experiencing a 30 to 50% reduction in pain scores. The cut-off figure of over 50% pain reduction has been demonstrated to be highly correlated with long-term clinical success of a permanent spinal cord stimulation implant, with an implanted pulse generator (IPG) to power the unit. If the trial is successful, the whole system is implanted permanently. Patients who have an unsuccessful trial should not receive a permanent implant.

After permanent implant, the patient can usually be weaned off oral analgesic medications and undergo, if necessary, a physical rehabilitation program. It is generally thought that 10 or more cases per year constitute an adequate caseload to deliver excellent technical outcomes. Therefore, some pain physicians will refer patients onto colleagues who regularly perform such surgery and have the resources in place to offer excellence in clinical care. There are estimated to be 50 or more such implanters in Australia, with total implant numbers suggested to be about 1000 per year.

Peripheral nerve stimulation

Peripheral nerve stimulation refers to placement of the stimulating electrode either in the subcutaneous tissue of the pain area, or more specifically on a peripheral nerve (guided by ultrasound), to provide stimulation (a pleasant tingle or paresthesia) over the area of the pain thereby reducing or modulating the pain. Peripheral nerve stimulation can be used for both peripheral focal neuropathic pain or for axial low back pain. It has also been used for refractory occipital neuralgia (namely occipital based headache syndromes) in the form of occipital nerve stimulation.[11] Data collection and literature support

is at an earlier stage for peripheral nerve stimulation compared with spinal cord stimulation.

Sacral nerve stimulation

Sacral nerve stimulation has been documented to be effective not only for perineal pain[12] but also for voiding disorders (retention or incontinence) and defaecatory disorders (retention or incontinence).[13] Sacral nerve stimulation is now practised by urologists, urogynaecologists and colorectal surgeons as well as pain specialists. The stimulator lead is typically placed over the S3 nerve through the S3 foramen or the sacral hiatus. Use of the device allows modulation of the pelvic organ dysfunction in cases of over or under activity.

Intrathecal therapy

Intrathecal therapy refers to placement of a permanent catheter into the cerebrospinal fluid (subarachnoid space), which is connected to an automated pump (placed subcutaneously). The pump contains a fluid reservoir used for the long-term delivery of medication directly into the intrathecal space.

Baclofen is used for refractory spasticity in people with multiple sclerosis, stroke and cerebral palsy, whereas analgesic agents, such as opioids, clonidine and local anaesthetics, are generally used for people with refractory cancer pain in whom survival is judged to be more than three months.

Intrathecal analgesic administration can also be used for people with chronic noncancer pain, but in these circumstances it is associated with multiple long-term side effects (e.g. intrathecal opioids can cause testosterone and oestrogen suppression and hyperalgesia [increased pain] at high doses). Intrathecal therapy systems for opioid delivery for people with noncancer pain are currently being withdrawn and have been superseded by other techniques such as spinal cord stimulation. However, intrathecal therapy may still have a role to play in a small group of selected cases.

GPs and neuromodulation

GPs are increasingly likely to encounter patients receiving neuromodulation for persistent pain conditions. GPs may wish to play a role in patient selection and should consider referring such patients to pain physicians who offer this technology. Appropriate patient selection, education, standardised care and attention to detail are crucial for successful outcomes in neuromodulation and to reduce the risks of complications. Complications of neuromodulation include:

- technical issues: lead migration, lead fracture, connection failure, system malfunction
- minor issues: pain at battery site, superficial infection
- major issues (uncommon): deep infections, haematomas, cerebrospinal fluid leak requiring the system to be explanted.

Early recognition of any of these complications by either the patient or GP, and prompt discussion together with the implanting team, should minimise significant adverse outcomes.

Conclusion

There are currently five competing neuromodulation/stimulation companies with a range of products. It is expected that the cost of these devices will fall significantly in the next decade due to innovation and competition. The use of neuromodulation/stimulation technology is likely to become more widespread in future due to its increasing evidence base, falling costs and the recognition of the limited role opioids play in treating patients with chronic noncancer pain.[14] **PMT**

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