Neuropathic pain and spinal-cord stimulation

Neuropathic pain can arise from injury to the nervous system and can involve spontaneous dysthaesias, allodynia, or hyperaesthesia. An estimated 8% of the population are thought to live with neuropathic pain. Several types of drugs can be used to treat neuropathic pain, but many patients have no relief. Stimulating the spinal cord with implanted electrodes can be an effective treatment, especially for failed back surgery syndrome. NICE issued guidance in October 2008 recommending spinal-cord stimulation and complex regional pain syndrome.

Dr Simon Thomson Consultant in Pain Medicine, Basildon and Thurrock University Hospitals, UK, and President Elect International Neuromodulation Society.
email simon.thomson@btuh.nhs.uk

Neuropathic pain arises from abnormal functioning of the sensory nervous system. This can come from injury to the central or peripheral nervous system by trauma, ischaemia, infection, or metabolic insult. Rather surprisingly the descriptions of reported pain are similar whatever the initiating cause and wherever that injury occurred. Neuropathic pain is usually described as "burning", "electrical", "shooting", and "tight bands".

The most common symptoms are spontaneous dysaesthesias (often described as burning or shooting pain) and evoked pain to non-painful stimuli (allodynia) and sensitivity to painful stimuli at low thresholds (hyperaesthesia). Commonly, skin in the affected area will have altered normal sensation with higher thresholds for some stimuli and lower thresholds for others.

Neuropathic pain can exist either as an isolated condition or with other pain mechanisms such as nociceptive pain (inflammatory pain). The differences between neuropathic pain and nociceptive pain become increasingly blurred when one considers the central sensitisation that occurs in the normal nervous system when chronic nociceptive pain is poorly relieved. This results in long-term sensitisation of pain perception pathways such that pain is maintained long after the initiating event has healed or diminished.

Nerve injury results in changes in expression of neurotransmitters and genes, and production of receptors throughout the pain perception pathway. Some patients might develop chronic neuropathic pain because of genetic differences or comorbid psychological distress.

Activation of pain receptors in turn activates a sensory discriminative pathway of neurones that project via the thalamus to the sensory cortex, and also the spinoreticulothalamic pathways that project to motivational and affective sites within the paleocortex. Thus, pain is as defined by the International Association for the Study of Pain—an unpleasant sensory and emotional experience which is caused by or described in terms of tissue damage.[1]

Epidemiology

A European epidemiological study showed that up to 17% of Europeans suffer chronic pain.[2] Torrance and colleagues reported that up to 8% of the population are living with neuropathic pain.[3] As might be expected from a condition that rarely recovers spontaneously, it will become more common in older people. Neuropathic pain is associated with poor function, psychological distress and depression, and poor health-related quality of life. Examples of neuropathic pain are post-herpetic neuralgia, diabetic neuropathy, post-traumatic or post-surgical neuropathy, and spinal entrapment neuropathy such as after spinal surgery or in spinal stenosis.

In recent years we have increasingly needed to challenge some of our beliefs about pain and some progress is being made at last. This progress has been slow, particularly for older patients, for several reasons. We have had to overcome beliefs that unrelieved pain is a natural part of getting old—which were an excuse to not even attempt to evaluate pain. Additionally, the general symptom

of pain has been left to non-pain experts to manage the pain as well as the disease, perhaps because of our disease-based model of treating illness. Finally, there is a belief that, apart from a limited selection of drug treatments, not much can be done.[4]

The rise of pain clinics

Pain medicine and pain clinics have been evolving in pockets throughout the country. Usually they are staffed by anaesthetists with a special interest in pain, who work with a multidisciplinary team from other medical specialties, such as psychology, physiotherapy, occupational therapy, and nursing. From March 2008, the Faculty of Pain Medicine of the Royal College of Anaesthetists came into being and represents the educational interests of this developing specialty.

Pain medicine is reaching out into primary care, is working with other specialties, and appears to be well recognised by the Department of Health to be required in many new initiatives such as musculoskeletal services. Patients with poorly controlled pain should be referred to local specialist pain services, if available.

Treatment of refractory neuropathic pain

An evidence-supported consensus exists on how to treat neuropathic pain.[1] Pharmacological treatment includes topical agents such as 5% lidocaine and capsaicin, and oral agents—tricyclic antidepressants, and sodium and calcium-channel blockers, and antiepileptics such as gabapentin, carbamazepine, and pregabalin. Educating patients about their condition and restoration of a sense of control over exacerbating factors is also important. Interventional and invasive techniques include neural blockade of the sensory somatic nerve with local anaesthetic and corticosteroids or by sympathetic nervous system blocks .

One of the main breakthroughs in managing refractory pain is the application of nerve-stimulation-induced analgesia such as spinal-cord stimulation. Transcutaneous electrical stimulation uses surface electrodes and is useful in some patients if used correctly but, even if it is effective, it is often difficult to maintain in the long term.

Spinal-cord stimulation

Spinal-cord stimulaiton is provided by specialised centres with adequate resources for multidisciplinary management and follow-up. Some devices are administered via neurosurgical centres and some via pain services. It is not a treatment for provision by the occasional enthusiast, but is best used in an integrated service with referral and follow-up, as suggested by guidelines published jointly by the British Pain Society and the Society of British Neurological Surgeons.[5]

Spinal-cord stimulation can be done under local anaesthesia as a day case. It involves insertion of cylindrical electrodes (like an epidural catheter) into the epidural space. Whilst the patient is awake on the operating table, a trial of stimulation is initiated such that pleasant parasthesiae are evoked within the painful area. The trial can be continued percutaneously for about a week, and if successful then a full implant is inserted with either local or general anaesthesia.

The implantable pulse generator (a little bigger than a cardiac pacemaker) is placed under the skin, usually in the abdomen or in the upper buttock area. The patient will have a small handheld programmer that can make desired adjustments to the pattern and style of stimulation from the fully implanted device.

Power supply to the implant is either from its own lithium oxide battery (non-rechargeable) or from a rechargeable battery. The rechargeable batteries are a new generation and are likely to improve upon the rate of minor complications seen with systems that employed fewer electrode contacts and whose batteries depleted quickly. A third type of power supply uses radiofrequency coupling whereby the implanted receiver obtains induced electrical stimulation from an antenna stuck to the skin over the receiver.[6] This method has become progressively obsolete.

Spinal-cord stimulation has been studied in medically refractory neuropathic pain of peripheral origin and for ischaemic pain syndromes such as critical limb ischaemia and angina pectoris.[7–22] Most devices are implanted in the UK for neuropathic pain that persists after surgically successful nerve decompression spinal surgery, the so-called failed back surgery syndrome.

Evidence of efficacy

In a study, 100 patients with this disorder were randomly assigned to receive either conventional medical management or conventional treatment and spinal-cord stimulation.[14] 48% of patients who had spinal-cord stimulation achieved a 50% reduction in

pain compared with only 9% on standard care. This increased pain relief was associated with increased functional capacity, treatment satisfaction, and most importantly, a dramatic improvement in health-related quality of life in the group having spinal cord stimulation.

Crossover was allowed at 6 months, but because so many patients crossed from the stimulation group to standard care and so few from standard to spinal-cord stimulation the groups were not statistically comparable for the 2-year outcome point. However, results from the group continuing with spinal-cord stimulation show that benefits are maintained at 2 years.[23,24]

One of the striking features of the participants was that 87% had received four or more treatment modalities before randomisation and their quality of life was similar to that seen with terminal heart failure. Compared with many other diseases with a similar incidence and prevalence such as rheumatoid arthritis, patients with failed back surgery syndrome had higher pain scores, greater work disability, higher use of opioids and lower quality of life (in press).

The Prospective, Randomized, Controlled, Multicenter Study of Patients with Failed Back Surgery Syndrome (PROCESS) study was the first to compare outcomes of spinal-cord stimulation in neuropathic pain due to failed back surgery syndrome with conventional medical management. Another high quality study[25] has shown spinal-cord stimulation to be superior to revision spinal surgery in a similar group of patients.

At first glance spinal-cord stimulation seems expensive, with devices costing between £9000 and £17,000. Data from the PROCESS study and others[26,27] show that annualised costs reduce from implantation with cost savings occuring about 2·5 years after initiation of treatment compared with the less effective conventional treatments. Available evidence on cost effectiveness for spinal-cord stimulation in failed back surgery syndrome and complex regional pain syndrome indicates that the incremental cost-effectiveness ratio is considerably less than the £30,000 figure used by NICE.[23]

Key points

- Neuropathic pain is more common in older patients
- Neuropathic pain causes pain, disability, and poor health-related quality of life, and thus deserves active management
- Several treatment strategies exist to help manage neuropathic pain
- Neuropathic pain is poorly recognised by health-care professionals
- Doctors need to be more aware of neuropathic pain and to build pain services to detect, treat, and refer treatment-refractory cases
- Pain services should have access to spinal-cord stimulation if required
- Spinal-cord stimulation has an impressive evidence base that demonstrates clinical and cost effectiveness in a variety of conditions
- It continues to develop technologically as well as refining its clinical indications
- NICE recommend spinal-cord stimulation for chronic refractory neuropathic pain such as due to failed back surgery syndrome or complex regional pain syndrome

NICE guidance

In October 2008, NICE issued final guidance[6] on use of spinal-cord stimulation for neuropathic pain. The PROCESS trial provided much of the data evaluated for using spinal-cord stimulation in failed back surgery syndrome, and evidence for use in complex regional pain syndrome was also considered. NICE recommends spinal-cord stimulation for neuropathic pain in patients who have pain of at least 50 mm on a visual rating scale of 0–100 mm for at least 6 months despite standard care and have had a successful trial of spinal-cord stimulation.

The assessment group did an economic analysis based on a device cost of £9000 with a lifespan of 4 years. For failed back surgery syndrome, the incremental cost-effectiveness ratio was £10,480 per quality-adjusted life year compared with conventional management alone, and £9219 per quality-adjusted life year compared with repeat surgery. For complex regional pain syndrome the incremental cost-effectiveness ratio was £16,596 per quality-adjusted life year.[6]

The evidence considered for spinal-cord stimulation in ischaemic pain was inconclusive. In a subset of patients with critical limb ischaemia, some beneficial effects of spinal-cord stimulation can be seen, but there was insufficient evidence to prove its clinical and cost effectiveness. Spinal-cord stimulation also appeared to be as good as coronary artery bypass grafting, coronary angioplaty, or percutaneous myocardial revascularisation, but evidence for its cost effectiveness in

refractory angina was insufficient. NICE have recommended that any existing patients having spinal-cord stimulation for ischaemia pain should continue to be funded by the NHS, but new patients should be funded only as part of robust clinical trials looking at clinical and cost effectiveness in these indications.[6]

I have no conflict of interest.

References

1. Attal N, Cruccu G, Haanpaa M, et al EFNS gudelines on pharmacological treatment of neuropathic pain. *Pain* 2006; **122** :156–162
2. Breivik H, Collett B, Ventafidda V, et al. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur J Pain* 2006; **10**: 287–333
3. Torrance N, Smith BH. Bennett MI, Lee AJ. The epidemiology of chronic pain of predominantly neuropathic origin. Results from a general population survey. *Eur J Pain* 2006; **7**: 281–89
4. Hall GC, Carroll D, Parry D, McQuay HJ. Epidemiology and treatment of neuropathic pain: the UK primary care perspective. *Pain* 2006; **122**: 156–62
5. Simpson K, Stannard C. Spinal cord stimulation for the management of pain: recommendations for best clinical practice. British Pain Society, 2005. www.britishpainsociety.org/SCS_2005.pdf (accessed 5 February, 2009)
6. NICE. Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin. Technology appraisal 159, October 2008. http://www.nice.org.uk/Guidance/TA159 (accessed 6 February 2009)
7. Taylor RS, Van Buyten JP, Buchser E. Spinal cord stimulation for chronic back and leg pain and failed back surgery syndrome: a systematic review and analysis of prognostic factors. *Spine* 2005; **30**: 152–60
8. Kemler MA, Barendse GA, van Kleef M, et al. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. *N Engl J Med* 2000; **343**: 618–24
9. Kemler MA, De Vet HC, Barendse GA, et al. Spinal cord stimulation for chronic reflex sympathetic dystrophy-five-year follow-up. *N Engl J Med* 2006; **354**: 2394–96
10. Turner JA, Loeser JD, Deyo RA, Sanders SB. Spinal cord stimulation for patients with failed back surgery syndrome or complex regional pain syndrome: a systematic review of effectiveness and complications. *Pain* 2004; **108**: 137–47
11. Taylor RS, Van Buyten JP, Buchser E. Spinal cord stimulation for complex regional pain syndrome: a systematic review of the clinical and cost-effectiveness literature and assessment of prognostic factors. *Eur J Pain* 2006; **10**: 91–101
12. Tesfaye S, Watt J, Benbow S, et al. Electrical spinal cord stimulation for painful diabetic peripheral neuropathy. *Lancet* 1996; **348**: 1698–701
13. Daousi C, Benbow SJ, MacFarlane IA. Electrical spinal cord stimulation in the long-term treatment of chronic painful diabetic neuropathy. *Diabet Med* 2005; **22**: 393–98
14. Kumar K, Toth C, Nath RK. Spinal cord stimulation for chronic pain in peripheral neuropathy. *Surg Neurol* 1996; **46**: 363–69
15. Mannheimer C, Eliasson T, Augustinsson LE, et al. Electrical stimulation versus coronary artery bypass surgery in severe angina pectoris: the ESBY study. *Circulation* 1998; **97**: 1157–63
16. Di Pede F, Lanza GA, Zuin G, et al. Immediate and long-term clinical outcome after spinal cord stimulation for refractory stable angina pectoris. *Am J Cardiology* 2003; **91**: 951–55
17. TenVaarwerk IA, Jessurun GA, DeJongste MJ et al. Clinical outcome of patients treated with spinal cord stimulation for therapeutically refractory angina pectoris. The Working Group on Neurocardiology. *Heart* 1999; **82**: 82–88
18. Hautvast RW, DeJongste MJ, Staal MJ, et al. Spinal cord stimulation in chronic intractable angina pectoris: a randomized, controlled efficacy study. *Am Heart J* 1998; **136**: 1114–20
19. Ekre O, Eliasson T, Norrsell H, et al. Electrical stimulation versus coronary artery bypass surgery in severe angina pectoris. Long-term effects of spinal cord stimulation and coronary artery bypass grafting on quality of life and survival in the ESBY study. *Eur Heart J* 2002; **23**: 1938–45
20. Di Pede F, Lanza GA, Zuin G, et al. Immediate and long-term clinical outcome after spinal cord stimulation for refractory stable angina pectoris. *Am Journal Cardiol* 2003; **91**: 951–55
21. Yu W, Maru F, Edner M, et al. Spinal cord stimulation for refractory angina pectoris: a retrospective analysis of efficacy and cost-benefit. *Coronary Artery Dis* 2004; **15**: 31–37
22. Amann W, Berg P, Gersbach P, et al. Spinal cord stimulation in the treatment of non-reconstructable stable critical leg ischaemia: results of the European Peripheral Vascular Disease Outcome Study (SCS-EPOS). *Eur J Vasc Endovasc Surg* 2003; **26**: 280–6
23. Kumar K, Taylor RS, Jacques L, et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with the failed back surgery syndrome *Pain* 2007; **31**: 179–88
24. Kumar K, Taylor RS, Jaques L, et al. The effects of spinal cord stimulation in neuropathic pain are sustained: a 24 month follow up of the prospective randomized controlled multicenter trial of the effectiveness of spinal cord stimulation. *Neurosurgery* 2008; **63**: 762–70
25. North RB, Kidd DH, Farrokhi F, Piantadosi SA. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. *Neurosurgery*. 2005; **56**: 98-106
26. Taylor RS, Van Buyten JP, Buchser E. Spinal cord stimulation for complex regional pain syndrome: a systematic review of the clinical and cost-effectiveness literature and assessment of prognostic factors. *Eur J Pain* 2006; **10**: 91–101
27. May MS, Banks C, Thomson SJ. A Retrospective, Long-term, Third-Party Follow-up of Patients Considered for Spinal Cord Stimulation. *Neuromodulation* 2002; **5**: 137–44