Current neurosurgical management of intractable central neuropathic pain

Introduction

Neuropathic pain arises from damaged neural tissue. It is deemed central when the neural injury is in the brain or spinal cord. Post stroke pain is one of the commonest forms of central neuropathic pain that affects about 2-8% of patients after a stroke1. This pain is usually resistant to analgesic medical therapy and is extremely unpleasant. Like other forms of neuropathic pain, it is generally described as a constant burning or lacerating sensation commonly associated with painful hyperesthesia in the same distribution2. Patients also complain of a crushing sensation, deep aching, allodynia and various other forms of unbearably altered sensory perception. Due to the generally intractable and incapacitating nature of this pain, various surgical management strategies have been tried over the years with varying rates of success. These include chronic deep brain stimulation (DBS), spinal cord stimulation (SCS), anterior cingulotomy, dorsal root entry zone (DREZ) lesions and in recent years, motor cortex stimulation (MCS)3-5,7. MCS has now become the preferred option (over DBS) in the neurosurgical management of medically intractable neuropathic pain of central origin (CNP)4-5. However, MCS provides satisfactory pain relief in only about 50%-75% of cases4-5. Our experience of managing CNP now comprises 16 patients who have been implanted with peri-ventricular gray (PVG) and / or sensory thalamic (ventroposterolateral) nucleus – VPL DBS electrodes and 6 patients with MCS. Based on this, we feel there still is a definite role for DBS in control of CNP.

Our experience with DBS for intractable central neuropathic pain

Patients and surgery

Twenty-two patients with CNP were treated between November 1995 and November 2002 at our functional neurosurgical clinic in the Radcliffe Infirmary, Oxford. Seventeen of these had post-stroke pain. All patients were referred by pain clinics as failures of drug treatment. They underwent neurological and neuropsychological assessment at our centre. Informed consent was obtained from each patient. All procedures were approved by the Local Ethics Committee, Radcliffe Hospitals NHS Trust, Oxford. Fourteen patients were stereotactically implanted with contralateral (to the side of pain) VPL DBS electrodes (Medtronic DBS 3387, Minneapolis, MN) in an area where stimulation induced paraesthesia in the area of pain and contralateral PVG DBS electrodes (Medtronic DBS 3387, Minneapolis, MN) where stimulation induced relief of pain or a sensation of warmth in the area of pain (Figure 1). One patient had only PVG and another only VPL DBS electrode implantation.

Six patients had a MCS (Resume’, Medtronic, Minneapolis, MN) implanted in the parietal cortex contralateral to the painful side. They were connected to a subcutaneous pulse generator (IPG, Synergy®, Medtronic, Minneapolis, MN).

Trial stimulation, field potential recording and pain assessment

In 12 of the 14 patients with both VPL and PVG implants the DBS electrodes were externalised for a week’s trial stimulation and recording of field potentials (FPs) to assess the degree of pain relief. Pain was assessed before and after surgery and during stimulation by a self-rated visual analogue scale (VAS, McGill-Melzack). FPs were recorded through the thalamic DBS leads during PVG stimulation in the ward after the patient had recovered from the operation and pain had returned to the pre-operative level.

Pulse generator

Patients who reported satisfactory relief from pain following trial PVG stimulation were then implanted with a subcutaneous pulse generator (IPG, Synergy®, Medtronic, Minneapolis, MN), placed in a pectoral pouch under general anaesthesia. The thalamic electrode was also connected but kept inactive in the initial period except in one patient who tolerated the VPL DBS better and hence that was the one used from the beginning.

Follow-up

All patients were regularly followed up to assess the degree of pain relief, adjust stimulator settings if required and to record any improvement in functional status. All the MCS cases were seen till withdrawal of treatment (range – 2 weeks to 4 years), while 14 of the DBS cases have now been seen for an average of 14 months (range - 3 to 34 months, Figure 2).

Figure 1. This figure is a MRI scan performed after implantation. It shows the two DBS electrodes placed in the left PVG and the left VPL, respectively in a patient with chronic post-stroke pain.

Figure 2. This figure illustrates the degree of reduction in pain scores during peri-ventricular gray (PVG) and / or sensory thalamic (VPL) stimulation. The red bars represent the reduction during the trial period while the green bars show the situation at the time of last follow-up (two patients with less than 3 months follow-up not shown). The number over each of the green bars is the length of follow-up in months.

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Professor Tipu A. Aziz studied physiology at University College London graduating in 1970. During this time he developed his keen interest in the role of the basal ganglia in movement disorders. He studied medicine at King’s College London (1970-1983) and obtained his surgical fellowship in 1987 following which he pursued a career in neurosurgery. He is currently a consultant neurosurgeon at the Radcliffe Infirmary, Oxford and Charing Cross Hospital, London. He is an expert in functional neurosurgery and has a special interest in the surgical treatment of movement disorders.
Results
Nine of the 12 patients who had trial PVG and VPL stimulation had satisfactory pain relief and opted to have the IPG implanted in a second procedure. Pain suppression was related to the frequency of stimulation of the PVG in all the cases of central pain. Maximum pain relief was obtained with 5 Hz – 35 Hz stimulation, while higher frequencies made the pain worse. All these patients responded better to PVG ± VPL stimulation than to VPL stimulation alone.

The FPs consisted of a very low frequency potential, of 0.2 - 0.4 Hz, in the sensory thalamus; the amplitude seemed to correlate with the intensity of pain perception. Figure 3 plots the VPL recordings from one of the patients and illustrates this point. These FPs were much stronger off stimulation and with higher frequency stimulation (≥50 Hz) when there was no pain suppression, than while stimulating the PVG at low frequencies (5 to 35 Hz) with accompanying pain relief.

Of the 6 patients who underwent MCS one was relieved of pain for four years, two had pain relief for only 2-3 weeks and three did not experience any appreciable relief.

Discussion
Eleven of the 16 patients with CNP recruited consecutively in this series had satisfactory pain suppression with PVG and / or VPL DBS. This was considerably better than our results with MCS. This also compares favourably with results reported with MCS by other groups2,6. As seen in Figure 2, the pain suppression obtained during trial stimulation is fairly robust and was maintained over the average follow-up period of 14 months in all but 2 patients.

Interestingly, we have found that there was correlation between the alleviation of pain sensation and the amplitude of the thalamic slow frequency FPs4,5. This may help the understanding of the complex nociceptive pathways.

Conclusions
Deep brain stimulation remains an important method of treatment of CNP. The most important challenge lies in selecting appropriate patients for either DBS or MCS. Both cost and potential complications are important considerations. There is a reported risk of 20% minor complications of which 4% are permanent and less than 1% risk of permanent disability or death. However, this needs to be viewed against the substantial cost of continued medical treatment, inability to work, the social and psychological toll on the patients and their families.

The future of this technique will depend on better knowledge of the neurobiology of the etiology of pain and pain pathways. It is also important to develop more objective indices to measure success in pain management and perhaps greater infrastructure to support patients with DBS implants outside the tertiary care hospital system.

Further reading