Motor cortex stimulation and neuropathic facial pain

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Trigeminal neuropathic facial pain is a syndrome of severe, constant facial pain related to disease of or injury to the trigeminal nerve or ganglion. Causes of this type of pain can include injury from sinus or dental surgery, skull and/or facial trauma, or intentional destruction for therapeutic reasons (deafferentation) as well as intrinsic pathological conditions in any part of the trigeminal system. Motor cortex stimulation (MCS) is a relatively new technique that has shown some promise in the treatment of trigeminal neuropathic pain. This technique has the potential to revolutionize the treatment of chronic pain. The authors present a review of the literature, focusing on surgical technique, device programming, safety, and efficacy, and suggest some initial guidelines for standardization of these aspects. It is important to evaluate MCS critically in a prospective, controlled fashion.

Key Words • facial pain • neuropathic pain • motor cortex stimulation • trigeminal nerve • neurosurgery

Abbreviations used in this paper: MCS = motor cortex stimulation.
gramming, pain relief cannot always be achieved. There is a risk of seizures during stimulator programming.4,12,17,23,30 Although the development of epilepsy has not been reported, thus, there exists clinical equipoise regarding the true risk/benefit ratio of MCS for the treatment of trigeminal neuropathic pain.

In addition, programming parameters vary from investigator to investigator, with some groups achieving pain relief by using parameters that other groups find ineffective. A review of the literature, focusing on surgical technique, device programming, safety, and efficacy suggests some initial guidelines for standardization of these aspects.

**Surgical Technique**

Following the initial report of Tsubokawa et al.,44 several studies were published in which a similar technique of introducing the electrode through a bur hole after application of local anesthetic was used.1,4,16,18,20–23,26,27,30,31,36,39,43 In several cases, groups that started out using a bur hole technique later switched to placement of the electrode through a craniotomy,1,23,26,27, and the majority of surgeons now perform a craniotomy after induction of either local1,12,20–23,26,27,30,31,36,39,41 or general anesthesia.4,16,18,20–23,26,27,30,31,36,39,41 Nearly all investigators place the electrodes epidurally, although subdural placement has been described.34,40 Image-guided neuronavigation is used for precise identification of the motor cortex intraoperatively,1,4,24,28,29,36 and proper placement is confirmed with physiological testing.

**Stimulation Parameters**

There is tremendous variation in the reported parameters for MCS. Pain relief can occur at amplitudes from 0.5 to 10 V, rates from 5 to 130 Hz, and pulse widths from 60 to 450 µsec.2 In Table 1 we summarize several key publications and illustrate the wide variety of stimulus parameters that have been used. Although in most studies rates of approximately 40 Hz have been used, in others higher rates have been found to be necessary in some cases. There is also no agreement on whether wide or narrow pulse widths provide more effective stimulation. Amplitudes have been chosen empirically in many cases, whereas other investigators base stimulation amplitude on a percentage of motor threshold.

Pain relief is most commonly achieved at amplitudes of 6 V or less, with mean amplitudes of 5 V or less in most studies. Amplitudes above 6 V are more likely to be associated with seizures during programming, with seizures commonly induced at amplitudes approaching 9 V.17 Many investigators have noted that MCS frequently produces a period of poststimulus pain relief that can range from minutes to hours. Thus, the majority of publications report the use of a cycling mode of stimulation, with 10 minutes to 3 hours on stimulation followed by 15 minutes to 6 hours off stimulation. In one study, switching from a continuous to cycling mode (in addition to other programming changes) may have contributed to improvement in pain relief.17

**Safety of MCS**

Like any neurosurgical procedure, MCS can be associated with risks and complications, including bleeding, infection, and neurological deficits. Although in many studies no adverse events with MCS have been reported,16,18,19,38–40,42,44 there have been some serious complications reported in the literature. Two epidural hematomas have been reported, one small and asymptomatic,26 and the other requiring evacuation and associated with persistent dysphasia.23 One group reported on two patients with devastating cerebral hemorrhages, with one patient dying of this complication and the other remaining in a persistent vegetative state.33,34 It is possible that these complications resulted from this group’s use of subdural rather than epidural electrode placement. Infection of the hardware requiring removal and/or treatment with antibiotics has been reported in a number of studies.1,4,8,28,29,34,37 Some patients have also experienced wound dehiscence, which resolved after surgical revision.1 Breakage of the hardware can also occur.8 Two patients in one study experienced transient postoperative neurological deficits (one speech, one motor).28

Programming of MCS systems as well as long-term treatment with MCS can also be associated with certain risks and side effects. Foremost among these is the risk of seizures, which have been frequently reported in the literature. These have been variously described as brief focal seizures during programming, unspecified seizures during programming,17,33,35,36 prolonged focal seizure with postictal speech arrest,11 brief generalized seizures during programming29 (occurring in the majority of patients in one study23), and generalized seizures after activation of the stimulator.30,35 In one recent study of intensive MCS reprogramming, the mean threshold for inducing seizures was 8.9 V.17 There is at least one report of a patient in whom severe epilepsy developed after long-term motor cortex stimulation.1 To investigate further the epilepto-
genic potential of chronic MCS. Bezard et al. undertook a study in three macaque monkeys that were implanted with MCS electrodes. These investigators found that with stimulation at a rate of 40 Hz and a pulse width of 90 μsec no seizures occurred, even at stimulus intensities up to 3 mA above the motor threshold. Higher frequencies and pulse widths induced muscle twitching at lower amplitudes and consequently also induced seizures at lower amplitudes.

Other reported side effects from stimulation include painful stimulation of the dura mater,12,21,23 stimulation-induced dysesthesias,15,20,26 dysarthria,6 and fatigue.4 There are two case reports of unusual side effects: impairment in a motor imagery task,41 and development of a painful supernumerary phantom arm in a patient with poststroke pain.7 In addition, there is a suggestion that MCS may adversely affect cognitive function, especially in older patients.25

It is therefore important that this procedure be performed by experienced groups who have developed techniques to minimize surgical risks and deal with complications in an expeditious manner.

Efficacy of MCS

Published studies have been uniformly laudatory regarding the efficacy of MCS for the treatment of neuropathic facial pain, beginning with the 1993 publication by Meyerson et al.23 In their study of a group of 10 patients with different types of neuropathic pain, all five patients with the trigeminal type obtained between 60 and 90% pain relief at 8 to 28 months. A follow-up study by Herroodts et al.19 showed a 50 to 100% reduction in visual analog scale pain scores in four of five patients with trigeminal neuropathic pain.

In a 1996 study by Ebel et al.,12 seven patients with trigeminal neuropathic pain of various origins were treated with MCS. Six of the seven patients underwent permanent implantation of electrodes, with five of six achieving 80% or greater pain relief. Two patients subsequently lost pain relief over the course of several months, leaving three (50%) of six patients with a satisfactory result at their last follow-up visit.

Nguyen and colleagues12,26,27 have published several descriptions of their surgical technique and programming approach. In their series, all patients with neuropathic facial pain achieved 40 to 100% pain relief.

More recently, Brown and Pilitsis1 reported on 10 patients who underwent a trial of MCS for facial pain of various origins, including trigeminal neuropathic pain, postherpetic neuralgia, and central poststroke pain. All eight patients with a peripheral neuropathic mechanism for their pain underwent placement of a permanent system after a successful trial. In 88% of these patients immediate pain relief of 50% or more was obtained, and 75% experienced sustained reduction in pain at 3- to 24-month follow-up intervals. In a review of the literature they corroborated these results, showing that 29 (76%) of 38 patients with neuropathic facial pain achieved 50% or more pain relief. All patients in the cohort that underwent implantation of the devices experienced a decrease in their medication requirements of more than 50%.

The definition of success for MCS is not clear from the published literature. In several studies investigators have suggested that a 30% reduction in pain intensity, or a decrease of 2 points on a scale of 1 to 10, represents a minimum clinically meaningful reduction in pain.9,13,14 In most studies of therapeutic interventions for pain, a 50% reduction in baseline visual analog scale pain ratings is regarded as clearly significant.

Conclusions

Despite the reported success with MCS for the treatment of trigeminal neuropathic pain, there have been no large, controlled, prospective, randomized trials of this modality. We face a situation similar to that experienced with the advent of deep brain stimulation for pain in the 1970s and 1980s. The procedure was widely used despite little strong evidence for efficacy, until two prospective trials were eventually performed in the 1990s. These trials showed that deep brain stimulation for pain could be effective, but the researchers suggested that a very low percentage (13.5–17.8%) of patients could be proven to have clinically significant pain relief at long-term follow up.16 The lesson learned from this study was that future trials of analgesic devices should follow structured protocols for patient selection and use uniform implantation and treatment paradigms. It is imperative that MCS be subjected to this type of scrutiny prior to its widespread adoption as a potential standard therapy for chronic pain.

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