Motor cortex stimulation for neuropathic pain


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Motor cortex stimulation is increasingly reported in the literature as a surgical option for the alleviation of neuropathic pain. The authors review the published literature and present their results including those demonstrated in a randomized controlled trial that confirmed the efficacy of the procedure. Patient selection and prediction of outcomes, however, remain difficult issues.

KEY WORDS • motor cortex stimulation • neuropathic pain
### TABLE 1

*Summary of published data on the effects of MCS*

<table>
<thead>
<tr>
<th>Authors &amp; Yr</th>
<th>No. of Cases</th>
<th>Diagnosis</th>
<th>Response</th>
<th>Optimum Settings</th>
<th>Adverse Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsubokawa, et al., 1990</td>
<td>25</td>
<td>deafferentation pain (thalamic &amp; MCS) persistent vegetative state (possible DBS as opposed to MCS)</td>
<td>NA</td>
<td>75% response rate at 7 mos DBS increased p250 in 4 patients up to 4 mos</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Katayama, et al., 1991</td>
<td>8</td>
<td>central deafferentation pain (burning dysesthesia contralateral side of body), 5 w/ poststroke, 1 w/ postresection of lt parietal AVM</td>
<td>6 w/ complete relief</td>
<td>2–3 mo FU: 4 w/ excellent relief, 1 w/ 30%, 1 w/ 0%; 9–30 mos: 3 w/ excellent relief</td>
<td>Irel II: 3–5 V, PW 180–160 msec, frequency 20–30 Hz, cycling mode, 1 hr on, 6 hrs off</td>
<td>NS</td>
</tr>
<tr>
<td>Hosobuchi, et al., 1993</td>
<td>6</td>
<td>central deafferentation pain (burning dysesthesia contralateral side of body), 5 w/ poststroke, 1 w/ postresection of lt parietal AVM</td>
<td>6 w/ &gt;50% relief during TS (for up to 4 wks); no relief in poststroke pain</td>
<td>subthreshold for muscle spasm stimulation (pulse duration 0.3 msec, 50 Hz); stimulation during test period 20–30 mins 3–5 times/day</td>
<td>most had 1–2 short-lasting seizures during TS; no long term motor effects; 2 w/ pain over electrode site; 1 of 2 had epidural clot requiring surgery, resulting in expressive aphasia &amp; long-term dysphasia; no equipment failures; 2 of 6 had electrodes re-situated due to local irritation</td>
<td>no response in poststroke pain; placing of electrodes crucial for response</td>
</tr>
<tr>
<td>Meyerson, et al., 1993</td>
<td>10</td>
<td>central &amp; neuropathic pain</td>
<td>6 w/ &gt;50% relief during TS (for up to 4 wks); no relief in poststroke pain</td>
<td>subthreshold for muscle spasm stimulation (pulse duration 0.3 msec, 50 Hz); stimulation during test period 20–30 mins 3–5 times/day</td>
<td>most had 1–2 short-lasting seizures during TS; no long term motor effects; 2 w/ pain over electrode site; 1 of 2 had epidural clot requiring surgery, resulting in expressive aphasia &amp; long-term dysphasia; no equipment failures; 2 of 6 had electrodes re-situated due to local irritation</td>
<td>no response in poststroke pain; placing of electrodes crucial for response</td>
</tr>
<tr>
<td>Tsubokawa, et al., 1993</td>
<td>11</td>
<td>thalamic pain</td>
<td>NA</td>
<td>5 of 8 had prolonged relief at 2 yrs; in 3 of 8 pain relief diminished</td>
<td>NA</td>
<td>none</td>
</tr>
<tr>
<td>Katayama, et al., 1994</td>
<td>7</td>
<td>4 w/ bulbar pain (caused by lat medullary infarct): 3 MCS, 1 MCS + TS</td>
<td>2 of 3 w/ satisfactory relief</td>
<td>subthreshold for muscle spasm stimulation (pulse duration 0.1–0.5 msec; intensity 2–8 V)</td>
<td>NS</td>
<td>MCS better than TS for poststroke pain</td>
</tr>
<tr>
<td>Canavero &amp; Bonicalzi, 1995</td>
<td>2</td>
<td>1) male: cervical syringomyelia (pain lt arm &amp; hemitorno), propofol responsive; 2) female: poststroke pain, propofol unresponsive</td>
<td>1) 30–50%; 2) no relief</td>
<td>Irel II 5–7 V, 50 Hz, 300 μsec, 0-3 setting, dosing 30 min on, 60 min off, cycling mode (off at night)</td>
<td>NS</td>
<td>1) parietal cortex stimulation; no motor effects intraop but parasthesia reported; 2) no response</td>
</tr>
<tr>
<td>Herregodts, et al., 1995</td>
<td>7</td>
<td>2 w/ central poststroke pain, 5 w/ TGN</td>
<td>7 w/ &gt;50% reduction in pain during TS</td>
<td>FU 9–22 mos w/ at least 50% relief in 5 of 7; 1 of 7 (poststroke) w/ no relief at 4 mos; 1 of 7 (anesthesia dolorosa) w/ only 20% relief at 6 wks &amp; no relief at 13 mos</td>
<td>motor response elicited during TS</td>
<td>NS</td>
</tr>
</tbody>
</table>

* amp = amplitude; AVM = arteriovenous malformation; DBS = deep brain stimulation; fMR = functional magnetic resonance; GABA = γ-aminobutyric acid; FU = follow-up; NA = not available; NS = not stated; PAG = periaqueductal gray area; PW = pulse width; RCT = randomized controlled trial; TGN = trigeminal neuralgia; TS = test stimulation.

† Results reported in conference proceedings.
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</thead>
<tbody>
<tr>
<td>Peyron, et al., 1995</td>
<td>2</td>
<td>poststroke pain</td>
<td>both w/ good response based on VAS score</td>
<td>1 w/ pain relief maintained at 22 mos; 1 w/ pain relief only for 3 wks</td>
<td>NA</td>
<td>1 withdrew as stimulation produced unacceptable burning pain in lower Lt limb; long term response in 3 of 6 who responded; decreased response over time in some</td>
</tr>
<tr>
<td>Ebel, et al., 1996</td>
<td>7</td>
<td>TGN</td>
<td>6 of 7 w/ &gt;50% reduction in VAS pain intensity following TS</td>
<td>3 of 6 w/ good to excellent pain control; long-term FU 5–24 mos; 3 of 6 positive effects decreased over several mos</td>
<td>settings subthreshold for motor effects (Irel II), amp 3.5–10.5 V, frequency 60–130 Hz, PW 180–350 µsec, cycling mode except for 1 patient w/ continuous stimulation; 20 mins–2 hrs on, 3–10 hrs off, no difference for pain relief between 10 Hz &amp; 100 Hz</td>
<td>1 of 7 w/ prolonged focal seizure (post-ictal speech arrest) during TS &amp; did not undergo implantation of internal system</td>
</tr>
<tr>
<td>Fujii, et al., 1997</td>
<td>7</td>
<td>thalamic pain</td>
<td>6 of 7 fair to excellent relief during TS</td>
<td>6 of 6 fair to excellent relief at 1 mos; 5 of 6 fair relief at 3 mos FU time NS</td>
<td>fatigue in upper limbs at 100 Hz</td>
<td>decreased response over time in all</td>
</tr>
<tr>
<td>Garcia-Larrea, et al., 1997</td>
<td>9</td>
<td>w/ poststroke pain; 3 w/ brachial plexus pain</td>
<td>3 w/ &gt;80% relief; 2 w/ 40–50% relief; 4 w/ &lt;40%</td>
<td>14–39-mo (mean 25.1 mos) FU: 14 reported 40–100% reduction in pain (7 of 7 w/ TGN, 1 of 1 w/ peripheral nerve injury, 80% relief); 5 of 10 w/ central pain; 1 of 2 w/ spinal cord lesion excellent relief</td>
<td>mean frequency 40 Hz (25–55 Hz), duration 90 msec (60–180 msec) amp 2.4 V (1.3–4 V) 3 hrs on, 3 hrs off</td>
<td>extradural hematoma in 1, resolved spontaneously; 3 w/ dysesthesia at &gt;3 mA; 1 w/ speech disorder 6.6 mA; no technical problems or seizures</td>
</tr>
<tr>
<td>Nguyen, et al., 1997</td>
<td>20</td>
<td>deafferentation pain (7 w/ TGN, 10 w/ central pain, 1 w/ peripheral neuralgia, 2 w/ spinal cord lesions)</td>
<td>12 w/ at least satisfactory improvement during TS; 3 failed to respond</td>
<td>12-mo plus FU: 13 (76%) of 28 had positive response to MCS; 10 (71%) of 14 morphine-resistant &amp; thiamylal-resistant or ketamine-sensitive patients had positive response to MCS</td>
<td>continuous stimulation for 15–30 mins several times a day; intensity 2.5 V at 25–50 Hz</td>
<td>N/A</td>
</tr>
<tr>
<td>Rainov, et al., 1997</td>
<td>2</td>
<td>chronic facial pain</td>
<td>satisfactory relief in both</td>
<td>stable reduction in pain in both at 18 mos</td>
<td>NA</td>
<td>N/A</td>
</tr>
<tr>
<td>Yamamoto, et al., 1997</td>
<td>28</td>
<td>poststroke, hemibody pain</td>
<td>NA</td>
<td>12-mo plus FU: 13 (76%) of 28 had positive response to MCS; 10 (71%) of 14 morphine-resistant &amp; thiamylal-resistant or ketamine-sensitive patients had positive response to MCS</td>
<td>continuous stimulation for 15–30 mins several times a day; intensity 2.5 V at 25–50 Hz</td>
<td>N/A</td>
</tr>
<tr>
<td>Canavero, et al., 1998†</td>
<td>9</td>
<td>5 w/ central pain, 3 w/ neuropathic pain, 11 w/ atypical facial pain</td>
<td>central pain, 3 of 5 responded, neuropathic TGN, 1 of 3 responded; facial pain, no response</td>
<td>central pain, 1 of 3 continued to respond at 2 mos; 0 of 1 w/ TGN responded</td>
<td>NA</td>
<td>N/A</td>
</tr>
</tbody>
</table>

* amp = amplitude; DBS = deep brain stimulation; fMR = functional magnetic resonance; GABA = γ-aminobutyric acid; FU = follow-up; NA = not available; NS = not stated; PAG = periaqueductal gray area; PW = pulse width; RCT = randomized controlled trial; TGN = trigeminal neuralgia; TS = test stimulation.
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### TABLE 1, continued

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<tbody>
<tr>
<td>Katayama, et al., 1998</td>
<td>31</td>
<td>poststroke pain</td>
<td>initial testing for 1 wk; 23 (74%) w/ good relief</td>
<td>Frequency 20–25 Hz, NS intensity 2–8 V</td>
<td>NS</td>
<td>preop evaluation of motor strength in painful area appears useful for predicting response to MCS for poststroke pain</td>
</tr>
<tr>
<td>Nguyen, et al., 1998†</td>
<td>37</td>
<td>central &amp; peripheral neuropathic pain</td>
<td>12 of 15 w/ neuropathic pain &amp; 12 of 14 w/ central pain; at least 80% improvement complete relief of pain (face) &amp; tremor (arm)</td>
<td>1.8 V, cycling mode: 3 hrs on, 3 hrs off, PW 60 nsec, frequency 50 Hz; bipolar stimulation (no. 1 electrode positive, no. 2 negative)</td>
<td>NS</td>
<td>good long-term relief; positive response in 5 of 5 in RCT</td>
</tr>
<tr>
<td>Canavero, et al., 1999</td>
<td>1</td>
<td>poststroke pain</td>
<td>initial testing showed lt arm–ripping &amp; squeezing-induced pain totally gone; burning pain reduced by 50%</td>
<td>at 5 wks burning pain returned; at 6 weeks pain fully returned; MCS switched off</td>
<td>NS</td>
<td>reduced response over 5 wks, pain returned in 6 wks; presence of lt supernumerary arm</td>
</tr>
<tr>
<td>Franzini, et al., 2000</td>
<td>1</td>
<td>thalamic hand syndrome</td>
<td>complete recovery</td>
<td>up to 2 years</td>
<td>NS</td>
<td>full recovery in 2 yr FU</td>
</tr>
<tr>
<td>Nguyen, et al., 2000</td>
<td>32</td>
<td>13 w/ central pain;12 w/ neuropathic facial pain; 3 w/ postparaplegic pain; 1 w/ plexus avulsion; 1 w/ intercostal herpes zoster</td>
<td>10 (77%) of 13 substantial relief; 9 (75%) of 12 substantial relief; 1 of 3 clearly improved; 2 with satisfactory improvement same relief w/ a mean FU of 27.3 mos</td>
<td>NS</td>
<td>none developed epileptic seizures</td>
<td></td>
</tr>
<tr>
<td>Saitoh, et al., 2000</td>
<td>8</td>
<td>4 w/ thalamic pain; 4 w/ peripheral deafferentation pain</td>
<td>6 w/ pain relief (2 excellent, 2 good, 2 fair)</td>
<td>FU time NS</td>
<td>NS</td>
<td>no correlation between pharmacological results &amp; MCS</td>
</tr>
<tr>
<td>Roux, et al., 2001</td>
<td>1</td>
<td>phantom-limb pain</td>
<td>70% reduction based on VAS scores</td>
<td>FU time NS</td>
<td>NS</td>
<td>used fMR imaging as an indicator for electrode placement</td>
</tr>
</tbody>
</table>

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...some patients. Effects attributed to surgery include epidural clots.13 Other effects directly attributed to MCS include epileptic and focal seizures, aphasia and dysphasia, upper-extremity fatigue, burning sensations in the area of stimulation, and the presence of left-sided supernumerary arm in the affected area.3,13,15,18,19 No seizures or other complications have been reported as a result of long-term stimulation delivered at optimum settings.

**CLINICAL MATERIAL AND METHODS**

**Indications for MCS**

Given the reported outcomes of this procedure, patients in whom chronic neuropathic pain was refractory to conventional analgesic intervention were considered eligible for surgical implantation of an MCS device (Itrel II or III; Medtronic, Inc., Minneapolis, MN).

**Preoperative Investigations**

Predicting which patients will likely benefit from stimulation is a major clinical problem. Response does not appear to be condition specific. Barbiturate sensitivity and opioid insensitivity have been suggested as possible predictors of response.1,12,24 Transcranial magnetic stimulation may be another useful predictor of response.1,14 Another possible predictor in patients with poststroke pain could be the level of muscle strength demonstrated in the painful area.10 Results of such preoperative testing, however, are no guarantee of a successful outcome, as not all patients who respond to propofol respond to MCS and, equally, morphine-insensitive patients have been shown to respond to stimulation.1

We have not, therefore, routinely performed any specific investigations other than head computerized tomography and magnetic resonance imaging, preoperative chest radiography, electrocardiography and blood count, clotting screen, and serum chemistry.

**Surgical Technique**

At the Radcliffe Infirmary, the procedure is performed in two stages. After induction of general anesthesia the patient is positioned such that the side contralateral to pain lies uppermost, with a sandbag under the same shoulder to prevent venous congestion. The position of the central sulcus is marked using standard anatomical landmarks, but no other image guidance is used. The patient’s hair is not shaved but is cleansed with chlorhexidine shampoo followed by alcoholic chlorhexidine. After draping the operative field, a horseshoe-shaped incision is marked 3 cm on either side of the central sulcus and extended to the midline for the leg and for faciobrachial pain the exposure extends 2 cm lateral to the midline. A free bone flap is raised, lateral to the central sulcus while applying stimuli to elicit motor contractions in the area of pain, until the patient reports sensations, usually of muscle contractions in the nonexistent limb. The stimulus parameters for exploration are 5 to 10 Hz, and 3 to 5 V for demarcation of the motor strip. If the patient feels any discomfort from dura-related pressure, a lidocaine-soaked swab is placed over the dura to induce local anesthesia.

Once the best placement has been identified, the electrode is secured to the dura with silk sutures, the bone flap wired back in place, and most of the wound closed in two layers, except posterolaterally where the free end of the lead is placed under the skin and interrupted suture placed. This allows the drapes to be removed, induction of anesthesia, and redraping to incorporate the scalp neck and upper chest. The posterior part of the scalp wound is reopened, and the free electrode is connected to the extension lead, which is the tunneled to a subcutaneous subclavicular pocket to be connected to a pacemaker (Itrel III, Medtronic, Inc.). All wounds are then closed in two layers, and the patient is reawakened. Antibiotic agents are given for up to 3 days. No attempt to program the stimulator is made on this admission. All patients receive long-term anticonvulsant medication.

**Postoperative Care**

Within 6 weeks postoperatively the patients are routinely admitted to the Pain Relief Unit where they stay for a week to optimize the stimulation parameters to achieve the best possible reduction in pain. The specialist nurse performs all assessments of pain independently of the surgeon. The specialist nurse then conducts follow-up review of the patients on a regular basis, either by telephone or outpatient examination.

**RESULTS**

Details of the 12 patients are shown in Table 2. A motor response was elicited in all 12 patients during intraoperative stimulation, and implantation of the MCS device was performed in all 12. The effects of the procedure on pain relief were then independently assessed in the Pain Relief Unit. The protocol used included the following items: 1) pain intensity: a four-point verbal rating scale (severe pain, 3; moderate, 2; mild, 1; and no pain, 0) and a 10-point numerical scale (0–10); 2) the McGill Pain Questionnaire; 3) pain relief: a five-point scale (no pain relief, 0; slight, 1; moderate, 2; good, 3; and complete pain relief, 4) and percentage of pain relief; 4) volunteered and observed adverse effects of treatment; 5) details of stimulator parameters (amplitude, pulse width, pulse rate, and electrode settings); and 6) use of other analgesic interventions.

Six of the 12 patients reported experiencing relief of pain during the first postoperative titration of the stimulator setting (Cases 1, 2, 4, 5, 8, and 12). In six patients stim-
ulation failed to achieve any pain relief despite extensive attempts during titration (Cases 3, 6, 7, and 9–11).

Patients With Pain Relief

Of the six patients who reported pain relief during MCS, three suffered from central poststroke pain (Cases 1, 4, and 12), one posttraumatic neuralgia (Case 2), and two from phantom-limb pain (Case 5 [lower limb] and Case 8 [upper limb]), of 2 to 13 years’ duration. There was a clear reproducible motor response (muscle spasm, tightness, or tingling sensation) evoked in the area of pain during both intra- and postoperative titration in all six patients.

### TABLE 2
Summary of data in 12 patients in whom an MCS device was implanted for refractory pain*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Diagnosis/Year of Onset</th>
<th>Site of Pain/Characteristics</th>
<th>Age (yrs), Sex</th>
<th>1st Stage of MCS (2nd Stage)</th>
<th>Adverse Effects/Complications</th>
<th>Optimum Settings</th>
<th>Pain Relief/Duration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>poststroke pain (thalamic infarct), 1991</td>
<td>hemibody; constant, severe</td>
<td>62, M</td>
<td>11/95 (11/95)</td>
<td>subdural hematoma, secondary wound infection; explantation 4/96</td>
<td>not documented</td>
<td>&gt;50%, 2–3 wks</td>
<td>initial pain relief (&gt;50%) lasted 2–3 wks, died of unrelated cause 6/96</td>
</tr>
<tr>
<td>2</td>
<td>posttraumatic neuralgia (brainstem gunshot injury), 1993</td>
<td>face, neck, arm, &amp; shoulder; constant, severe</td>
<td>54, F</td>
<td>7/96 (7/96)</td>
<td>tender over implant; secondary wound infection; high amp stimulation gave sense of tightness in area of pain, impaired speech</td>
<td>amp 2.1 V, PW 450 µsec, PR 20 Hz</td>
<td>50–60%, 36 mos</td>
<td>&gt;50% relief overall; titration limited by tightness &amp; other symptoms</td>
</tr>
<tr>
<td>3</td>
<td>poststroke pain (thalamic infarct), 1985</td>
<td>facial; constant, severe</td>
<td>80, M</td>
<td>3/96 (3/98)</td>
<td>none found</td>
<td>none</td>
<td>no relief; no clear postmortem response</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>poststroke (occipital infarct), 1990</td>
<td>hemibody; constant, severe</td>
<td>70, M</td>
<td>7/96 (12/96)</td>
<td>Irel II affected by exposure to external magnetic field</td>
<td>amp 5.0 V, PW 450 µsec, PR 15 Hz</td>
<td>100%, 31 mos</td>
<td>no since 10/98; stimulator switched off 2/99 w/ no recurrence of pain; died of unrelated cause 7/99</td>
</tr>
<tr>
<td>5</td>
<td>phantom &amp; stump pain, 1992</td>
<td>leg; constant, severe</td>
<td>48, M</td>
<td>1/97 (1/97)</td>
<td>higher amp yielded tightness in area of pain</td>
<td>amp 7.0 V, PW 450 µsec, PR 25 Hz</td>
<td>70% phantom 0% stump, 30 mos</td>
<td>good relief phantom pain; no relief of stump pain</td>
</tr>
<tr>
<td>6</td>
<td>neurofibromatosis, 1990</td>
<td>arm; constant, severe</td>
<td>55, F</td>
<td>1/97 (1/97)</td>
<td>no postop motor response</td>
<td>none</td>
<td>none</td>
<td>no pain relief; no postmortem response; MCS discontinued</td>
</tr>
<tr>
<td>7</td>
<td>poststroke pain (thalamic infarct), 1990</td>
<td>hemibody; constant, severe</td>
<td>63, F</td>
<td>3/97 (3/97)</td>
<td>none found</td>
<td>none</td>
<td>no pain relief; no postmortem response; MCS discontinued</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>phantom limb pain, 1975</td>
<td>arm &amp; hand; constant, severe</td>
<td>56, F</td>
<td>4/97 (4/97)</td>
<td>secondary wound infection; pain over implant site</td>
<td>amp 2.5 V, PW 450 µsec, PR 75 Hz</td>
<td>arm 75%, hand 5%, 27 mos</td>
<td>good long-term relief of phantom pain</td>
</tr>
<tr>
<td>9</td>
<td>phantom limb pain, 1979</td>
<td>arm; constant severe</td>
<td>39, M</td>
<td>10/97 (10/97)</td>
<td>no postop motor response; possible contact w/ external magnetic field</td>
<td>none found</td>
<td>none</td>
<td>technical failure; MCS discontinued</td>
</tr>
<tr>
<td>10</td>
<td>poststroke pain (brainstem &amp; TGN, 1992)</td>
<td>facial burning; constant, severe, episodic</td>
<td>80, F</td>
<td>2/98 (3/98)</td>
<td>fit induced during postop titration (9.6 V); no pain relief despite motor response during postop titration</td>
<td>none found</td>
<td>none</td>
<td>clear reproducible postmortem response (8 V); no pain relief; MCS discontinued</td>
</tr>
<tr>
<td>11</td>
<td>brachial plexus avulsion, 1976</td>
<td>hand &amp; arm; constant, variable intensity</td>
<td>36, F</td>
<td>11/99 (1/99)</td>
<td>strong motor response during intraop TS; during intraop TS &amp; postop titration</td>
<td>none found</td>
<td>none</td>
<td>evidence of motor response postop, no pain relief; MCS discontinued</td>
</tr>
<tr>
<td>12</td>
<td>poststroke pain, 1997</td>
<td>hemibody; constant, moderate-to-severe</td>
<td>68, M</td>
<td>3/99 (3/99)</td>
<td>strong motor response during intraop TS</td>
<td>awaiting retitration</td>
<td>2 wks relief from initial postop titration; awaiting further titration</td>
<td>complete relief of pain from propofol; initial postop titration produced 70% relief of pain in arm &amp; hand for 2–3 wks</td>
</tr>
</tbody>
</table>

*PR = pulse rate.
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who reported pain relief. Pain relief varied from 50 to 90% (compared with baseline pain). No patient reported complete relief of pain for any significant period of time during titration. Long-term pain relief (most recent assessment ranged between 21 months and 50 months postimplantation) was maintained in all except two patients (Cases 1 and 12). The patient in Case 1 was in poor general health before MCS surgery and reported a reduction in pain after 2 to 3 weeks of stimulation. This was associated with a low impedance, and surgical exploration confirmed that the insulation of the electrode cable was damaged and this was replaced. Postreplacement, it was not possible to replicate the same level of pain relief previously attained (> 50% relief). Unfortunately this patient developed a secondary wound infection and the device had to be removed. Postoperatively a subdural hematoma formed, which required further surgery. The patient later died of a pulmonary embolism.

Hardware-related problems were demonstrated in five patients who responded to MCS. Such problems always presented as a sudden and unanticipated increase in pain. The patient in Case 4 suffered three episodes in which the pain returned to its original intensity. On each occasion the device had unexplainably switched off. We believe that the patient had been exposed to a magnetic field (ultrasoundography on one occasion) which interfered with the device. In two patients (Cases 5 and 8) damaged leads needed to be replaced. In Case 5 this was because the patient sustained trauma while rapidly elevating his arms above his head. In Case 8 there was no clear explanation for the damage. Unfortunately in this same patient a previously faulty pulse generator (Itrel II), had been replaced with a different model (Itrel III). Interestingly, as with the patient in Case 1, in Case 8 titration after the second and third operations was far from straightforward. Although excellent pain relief was eventually achieved, this required several inpatient sessions. In the patient in Case 2, the titration process was not straightforward because of preexisting neurological symptoms related to the original severe brainstem injury that were exacerbated whenever the stimulation was increased. She could not tolerate stimulation above 2.5 V because of dysarthria and increased tightness over the site of her pain, even though increased pain relief was achieved at higher levels. Similar stimulation-related problems were encountered in the patient in Case 5, in whom a 7-V stimulation induced a 90% reduction of phantom-arm pain. Increasing the intensity of during titration produced 100% relief of pain, but the patient could not tolerate the feeling of tightness and tiredness, which appeared to replace the phantom pain. Titration was hindered by the presence of multiple pain sites in four (Cases 2, 4, 5, and 8) of the six patients in whom a positive response to MCS was found. Although the patient in Case 5 experienced good relief of most of the pain in the phantom limb, it was not possible to relieve the burning pain in his toes, nor the local stump pain, which was aggravated by an ill-fitting prosthesis; overall he reported a 70% improvement in his pain. Similarly, although the patient in Case 8 experienced good relief of pain in the phantom arm, which was the site of her worst pain before MCS implantation, it was not possible to produce any significant pain relief in her hand without diminishing the pain relief in her arm.

No patient who reported MCS-induced pain relief experienced epileptic or focal seizures at any time. The patients in Cases 2 and 8 complained of local tenderness and hypersensitivity over the electrode site, which neither resolved nor diminished over time. The patient in the latter case developed a secondary wound infection after the operation to repair the electrodes, which was successfully treated with antibiotic therapy. The patient in the former case developed a scalp infection that required surgical debridement.

Patients Without Pain Relief

Six patients failed to respond to MCS despite extensive attempts to determine optimum stimulation parameters during postoperative titration. Details are given in Table 2. No clear postoperative motor response was ever elicited in four of these patients (Cases 3, 6, 7, and 9). In these four patients no clinically observable signs of active stimulation were demonstrated after implantation of the system. We failed to elicit any motor response postoperatively in Case 7. Case 9 was considered to be a clear technical failure as the patient succeeded in wiping the identification number from his internally implanted programming device when repairing large high-fidelity speakers. He inflicted deliberate damage to the stimulator leads by repeatedly rotating the pulse generator under his skin. In the patients in Cases 10 and 11, a clear and reproducible motor response was elicited. The former patient exhibited muscle spasm in the right side of her face directly in the area of pain, together with expressive dysphasia. There was a clear dose response for these motor signs. Even very small increases in the stimulation (0.5 V) were sufficient to change the initial expressive dysphasia into a focal arrest, together with a marked increase in muscle spasm. This patient did not experience any change in her pain status, even with prolonged periods of continuous stimulation at amplitudes up to 5 V. Stimulation at higher levels resulted in a full epileptic seizure, and the device was eventually switched off. Such extreme effects were not seen in any other patients, even at high levels of stimulation (for example, 10 V in Case 9). The patient in Case 11 exhibited muscle tightness and spasm in her arm; she, too, also experienced seizures, both intra- and postoperatively.

Randomised, Double-blinded, Within-Patient Cross-Over Trial

Patients reporting at least 50% long-term (> 6 months) intermittent MCS–induced pain relief were invited to take part in this randomized, double-blind, within-patient repeated cross-over study, which was approved by the local hospital ethics committee.

Study Procedure

For practical reasons, patients were admitted to hospital for the duration of the study.

Eligible patients were allocated to receive up to 10 sequential treatment periods of both: 1) active stimulation (five treatments); and 2) no stimulation (five treatments).

Study treatments were given in a random order (tossing of coin), and the randomization schedule was concealed (sealed envelopes for each treatment, identified by patient
name and treatment number [1–10]). The treatments were double blinded. The person operating the IPG (on/off stimulation switch) was not involved with study assessments and had no other contact with patients. The nurse observer was unaware of the randomization schedule, and active stimulation was at subthreshold levels for any motor response.

Each treatment was given for a minimum of 1 hour and until the patients were able to make a prospective judgment as to whether the stimulator was currently on or off during each treatment (because of subjective changes in pain).

Pain intensity and pain relief were assessed immediately before each study treatment and then immediately before patients requested that they be switched over to the next treatment, according to the randomization schedule.

Pain was assessed using the following measures: 1) four-point verbal rating scale for pain intensity (severe pain, 3; moderate, 2; mild, 1; and no pain, 0); 2) five-point verbal rating scale for pain relief (no pain, 0; slight, 1; moderate, 2; good, 3; and complete pain relief, 4); 3) a 10-cm VAS for pain intensity (from least possible pain [0] to worst possible pain [10]); and 4) a 10-cm VAS for pain relief (from no relief of pain [0] to complete relief of pain [10]).

Patients were also asked to make an overall rating of each treatment (poor, 0; fair, 1; good, 2; very good, 3; and excellent, 4) before receiving the next study treatment.

Results of the Trial

Three of the six patients with long-term MCS-induced pain relief were willing and able to take part in the study (Table 2). Two of these patients died of unrelated causes before the study was set up.

Of the three patients who took part, two were able to judge correctly when they received the active- and no-stimulation treatments on eight of 10 occasions because of clinically relevant changes (decrease/increase) in their pain. Each cross-over treatment lasted for 1 hour, and treatments were given across 2 consecutive days.

One patient only guessed correctly which treatment she had received on four of 10 occasions. She reported that the study treatment periods (1 to 2 hours) were not long enough for her to have made a reliable judgment.

Conclusions of the Trial

In our experience, 50% of patients treated so far have responded positively to MCS (> 50% pain relief). A positive response was achieved in phantom pain (two cases), poststroke pain (three cases), and posttraumatic neuralgia (one case). We found that it is impossible to predict which patients are likely to respond to MCS prior to treatment, as response does not appear to be condition specific. Once pain relief is achieved patients may need further retitration and fine tuning of the stimulator setting. The findings of the randomized double-blind trial suggest that patients are able to distinguish between active- and no-stimulation treatments because of a clinically relevant change in pain.

DISCUSSION

Multiple surgical procedures have been attempted over the years to manage the intractable nature of neuropathic pain. Surgery in which lesions are created is fraught with hazardous side effects that can be as bad or worse than the original complaint and should be avoided. Hence, neuro-modulatory techniques have been explored. Over the last decade the authors of several series have reported on in the efficacy of MCS. As Table 1 shows there is still no obvious clear-cut indication for the procedure except that it would appear most effective in cases of facial and phantom pain syndromes. Poststroke pain in the presence of severe motor deficits, however, should be considered a contraindication.

Hardware-related failure (lead fractures, migration, and insulation fractures) is another important issue. Because the leads are placed extradurally, as the skull heals over any problems that occur, revision procedures are much more difficult. In very few papers have the authors addressed this issue, but in our experience hardware-related problems were encountered in five of those patients in whom MCS-induced responses occurred: two lead fractures; two pacemakers (Itrel IIs) stopped working and were replaced; and one pacemaker switched on and off the times unpredictably in one patient. Consequently there were four additional operative procedures. These complications are in agreement with the those reported by authors implanting neurostimulators for movement disorders in which hardware-related problems occurred in 8 to 65% of patients (with associated morbidity and additional costs of treatment).

Our experience and a review of the literature suggest that MCS is an effective therapy for neuropathic pain in approximately 50% of cases in the long term. Very little is published regarding potential technical problems associated with this technique, but hopefully as larger series accrue with longer follow-up periods these questions may be addressed.

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