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Motor Cortex Stimulation for Chronic Central and Peripheral Neuropathic Pain: State of Art

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Abstract

Motor cortex stimulation (MCS) was proposed by Tsubokawa in 1991 for the treatment of post-stroke thalamic pain. Since that time, the indications enlarged including trigeminal neuropathic pain and other types of central and peripheral deafferentation pain. Clinical knowledge of MCS derives mainly from published individual cases and case series. Mechanisms underlying the effects of MCS are not yet clearly known. Empirical approach is generally used to select the optimal parameters by adjusting the combination of contacts, polarity, frequency, pulse width and amplitude, according to the patient's pain relief. Complications are relatively rare but long-term loss of efficacy is reported.

Keywords: Motor cortex stimulation; Chronic pain; Central pain; Post-stroke pain; Neuropathic pain; Deafferentation pain; Trigeminal neuropathy

Introduction

Motor cortex stimulation (MCS) is an effective and less invasive treatment for central and peripheral refractory neuropathic pain. It is confirmed in the last years because of the risks and unfavorable outcomes associated with traditional deep brain stimulation (DBS) in chronic pain. Patients experiencing long-lasting pain have a reduced quality of life and multidimensional impairments [1,2]. In 1954 Penfield and Jasper were the first to notice the involvement of the motor cortex in sensory phenomena when they reported a sensory response after stimulation of the precentral gyrus during an epilepsy surgery [3]. Chronic stimulation of the precentral cortex for the treatment of pain was first reported by Tsubokawa in 1991 He observed that chronic stimulation of the precentral gyrus below the threshold produced a motor response and was able to alleviate certain types of deafferentation pain [4,5]. Afterwards Meyerson observed that the technique was particularly effective for trigeminal neuropathic pain [6,7]. Since that time, many reports confirmed efficacy of MCS for intractable pain syndromes including post-stroke pain, phantom limb pain, spinal cord injury pain, postherpetic neuralgia and trigeminal neuropathic pain.

Mechanisms of action

The mechanisms of action underlying the effects of MCS is actually still unknown. A corticospinal system relatively intact is necessary, but not sufficient, to achieve pain control with MCS, while success in treating MCS does not require an intact somatosensory system. Under normal conditions noxious and non-noxious inputs from the thalamus converge at cortical level and the non-noxious stimulus is able to inhibit the noxious afferences. Under pathological conditions of thalamus, MCS may antidromically and orthodromically activate large fibers reciprocal connections between the motor and sensory cortex [8-10]. It has been proposed that the mechanism of action for MCS may be attributed to modulation of pathologic hyperactivity in thalamic relai nuclei by reinforcing the control of non-nociceptive sensory inputs on nociceptive systems not only at the level of the thalamus but also dorsal column nuclei and spinal cord [8,7]. Drouot discovered that MCS influences the structures of the sensory system and modifies the transmission of pain stimuli [11]. Coulter et al. reported that the direct influence of the pyramidal tract on the posterior horn of the spinal cord plays a role in the analgesic effects of MCS [12]. Saitoh et al. observed an increased perfusion of the thalamus at the collateral side when MCS was applied controlaterally. This could lead to the explanation of partial benefits for patients who do not show a reorganization of the thalamus [13]. Other proposed mechanisms involve supraspinal structures (cingulate gyrus, orbitofrontal cortex and brainstem) and MCS may reduce the emotional component of chronic pain by activating the anterior cingulate cortex and the anterior insula [8,9,14]. MCS-induced pain relief is associated with an improved sensory discrimination within the painful zone suggesting that MCS acts on somatosensory pathways and sensory processing [15].

Biochemical processes such as action on the endorphin sites in the brainstem or control on the GABAergic interneurons at cortical level, may also be implicated in the mechanisms of MCS.

Clinical indications and results

By the time MCS indications have been extended to various types of peripheral and central deafferentation pain refractory to common treatments included, when indicated, spinal cord stimulation. MCS is used for intractable pain syndromes including post-stroke pain, brachial plexus and roots avulsions pain, phantom limb pain, spinal cord injury pain, postherpetic neuralgia and trigeminal neuropathic pain: the most common pain type treated is post-stroke with a percentage of 60% followed by trigeminal neuropathic pain with 30%.

The potential benefits of MCS used to treat peripheral and central neuropathic pain were firstly described by Tsubokawa [4]. There is a lack of consistency across published studies regarding the methods used to evaluate the outcome and the pain reduction to define MCS as successful treatment. The most reliable assessment measures are visual analogue scale (VAS) or numeric rating scale (NRS) and the global impression of change (GIC), which can be implemented utilizing multidimensional scales such as the SF-36 or the Oswestry questionnaire. Many articles

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report only the percentage of pain relief, other papers report the VAS/NRS score and few utilize multidimensional scales. A pain relief of 50% is the usual cut-off for success [16-18] but also pain relief of 40% or even 30% during medical treatment has been considered sufficient to define MCS treatment as effective. Meyerson et al. published the first use of MCS for the treatment of trigeminal neuropathic pain (TNP) or trigeminal deafferentation pain (TDP), reporting that 5 of 12 patients had complete pain relief and 8 of 12 patients had some degree of pain relief 1 year after surgery [6]. Ebel et al. studied 7 patients with TNP with MCS electrode implantation: initially 5 patients experienced >80% pain relief, of which 2 lost their benefits over the months [19]. Nguyen et al. reported a larger series of patients who underwent MCS for central pain, all of whom experienced 40-100% pain relief. This review of the literature reports that patients with neuropathic facial pain achieved ≥ 50% pain relief with MCS. Post-stroke pain responds nearly as well, with almost two-thirds of patients obtaining good to excellent relief [20,21]. A study by Brown and Barbaro demonstrated a long-lasting benefit of MCS in patients with central pain after stroke [22]. Lefaucheur et al. reported a mean of 48% of pain relief (as measured by VAS) [23]. In patients with facial pain Rasche, Meyerson and Nguyen reported a pain reduction ranging from 75 to 100% [6,24,25]. Tani, Saitoh and Katayama recommended MCS for pain after spinal cord injury, reporting a pain amelioration between 50 and 70% [14,25-28]. Raslan et al. treated 8 of 11 patients with trigeminal neuropathic or deafferentation pain with permanent implantation of a MCS system. All 8 patients reported initial satisfactory pain control but only 5 (62,5%) continued to experience long-term pain control [29,30]. Kolodziej et al. implanted 20 of 22 patients with central pain, deafferentation pain and neuropathic trigeminal pain. Of these 20 patients, 55% reported complete pain relief, 40% reported satisfactory pain relief and 5% reported no satisfactory pain relief [31,32]. Im et al. studied 21 patients with central post-stroke pain, central pain after spinal cord injury and peripheral neuropathic pain who underwent MCS. Of the 21 patients, 76,2% had a successful trial and underwent chronic MCS [33]. Slotty et al. retrospectively analyzed 23 patients treated with MCS. About half of the patients (47,8%) experienced a satisfactory reduction in pain during the first month of treatment [33,34].

Stimulation parameters

An empirical approach is generally used to select the optimal parameters by adjusting the combination of contacts, polarity, frequency, pulse width and amplitude, according to the patient's pain relief. Reported amplitudes range from 0.5 V to 10 V, rates from 5 Hz to 130 Hz and pulse widths from 60 μs to 450 μs, increasing the intensity by 20% if necessary [35]. In all cases, similar to Rasche et al, bipolar stimulation of the motor cortex (negative over the motor cortex and positive over the nearby region) is chosen [24]. Other authors reported higher stimulation intensities, taking into account the shorter battery life of the stimulator. Stimulation is always sub-threshold to avoid muscle contraction or any sensation [36]. Patients who have undergone permanent implantation of a MCS pulse generator require multiple programming sessions, the number of which is directly proportional to treatment durability [29]. Some patients that experience return of their symptoms can be "recaptured" through programming changes [37]. The amount of cerebrospinal fluid (CSF) between the dura and the cortex underneath the stimulating electrode is the most important factor affecting the distribution of the electrical field over the cortex and the stimulation amplitude [35].

Complications

Complications are relatively rare (11,4% of all published cases) [17,25,26,37]. The most common ones described in literature are infection and epidural hematoma but also cerebrospinal fluid fistula and headache related to stimulation are reported. Seizures induction occurred during the intraoperative motor mapping, following MCS programming and during chronic MCS, not necessary leading to the development of epilepsy. In several studies publications long-term loss of efficacy is described due to cortical plasticity, scarring of the epidural electrode, depressive disorders.

Conclusion

MCS has emerged as an effective technique of neurostimulation in relation to severe medically intractable pain and it is more frequently used than DBS because it is easier to perform, has a wider range of indications and lack of risk of intracranial hemorrhage. Atypical facial pain or trigeminal deafferentation pain and central post-stroke pain had more favorable response to MCS. Complications are relatively rare. Many aspects of MCS still remain unclear, especially the neural circuits involved and their response to long-term stimulation.

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