



Motor Cortex Stimulation in Patients Suffering from Chronic Neuropathic Pain: Summary of Expert Meeting and Premeeting Questionnaire, Combined with Literature Review

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Key words

- Expert meeting
- Neurosurgery
- Motor cortex stimulation
- Neuropathic pain
- Questionnaire

Abbreviations and Acronyms

BNS: Benelux Neuromodulation Society
fMRI: Functional magnetic resonance imaging
Hz: Hertz
IPG: Implantable pulse generator
MCS: Motor cortex stimulation
NRS: Numeric Rating Scale
QoL: Quality of life
rTMS: Repetitive transcranial magnetic stimulation
TMS: Transcranial magnetic stimulation
V: Volt
VAS: Visual Analog Scale
μs: Microseconds

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■ **BACKGROUND:** Motor cortex stimulation (MCS) was introduced in the early 1990s by Tsubokawa and his group for patients diagnosed with drug-resistant, central neuropathic pain. Inconsistencies concerning the details of this therapy and its outcomes and poor methodology of most clinical essays divide the neuromodulation society worldwide into “believers” and “nonbelievers.” A European expert meeting was organized in Brussels, Belgium by the Benelux Neuromodulation Society in order to develop uniform MCS protocols in the preoperative, intraoperative, and postoperative courses.

■ **METHODS:** An expert meeting was organized, and a questionnaire was sent out to all the invited participants before this expert meeting. An extensive literature research was conducted in order to enrich the results.

■ **RESULTS:** Topics that were addressed during the expert meeting were 1) inclusion and exclusion criteria, 2) targeting and methods of stimulation, 3) effects of MCS, and 4) results from the questionnaire.

■ **CONCLUSIONS:** Substantial commonalities but also important methodologic divergencies emerged from the discussion of MCS experts from 7 European Centers. From this meeting and questionnaire, all participants concluded that there is a need for more homogenous standardized protocols for MCS regarding patient selection, implantation procedure, stimulation parameters, and follow-up-course.

INTRODUCTION

Neuropathic pain due to a lesion or disease of the brain and/or spinal cord remains difficult to treat and can lead to a major disabling state.¹ After some unfruitful attempts to stimulate motor axons in the internal capsule to alleviate chronic pain, motor cortex stimulation (MCS) was introduced in the early 1990s by Tsubokawa and his group for patients diagnosed with this drug-resistant,

central neuropathic pain.² Because these syndromes were thought to be associated with thalamic hyperactivity, a cat model was used to approach the possible MCS mechanisms of action. Following a mesencephalic lesion that resulted in thalamic hyperactivity, stimulation of the primary motor cortex reduced the hyperactivity of the thalamus.³⁻⁵ Since then, clinical studies and systematical reviews have been published in order to confirm or discuss the efficacy of MCS in patients suffering from neuropathic pain.⁶⁻¹³ Although the exact mechanisms of MCS remain partially elusive, the technique has become a last-resort neurosurgical therapy for intractable central and sometimes peripheral neuropathic

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pain.^{3,5,14-22} Next to the fact that the exact mechanisms of action in MCS are incompletely understood, inconsistencies concerning the details of this therapy and its outcomes and poor methodology of most clinical essays divide the neuromodulation society worldwide into “believers” and “nonbelievers.” In order to determine the current clinical significance and the likely future developments of MCS, a European Expert Meeting was organized in Brussels, Belgium by the Benelux Neuromodulation Society (BNS). In addition, a questionnaire was sent out to all the invited participants before this expert meeting. The main topics, discussion points, and general conclusions are presented in this paper. Although this summary was written after the meeting, we checked the literature for more recent papers relevant to the topic, and included them in the discussion.

METHODS

European Expert Meeting

A European Expert Meeting was organized in Brussels by the BNS board in order to discuss the current state of the art concerning MCS treatment in patients with central neuropathic pain. Professionals with experience in MCS therapy from Brussels, Düsseldorf, Groningen, Lübeck, and Nijmegen attended this expert meeting. Colleagues from Lyon (L. Garcia-Larrea and J. Maarrawi) and Beirut (J. Maarrawi, worked before in Lyon till 2008) were not able to attend the expert meeting but provided their contribution to the questionnaire and participated to the written report. Participants of the expert meeting included neurosurgeons who perform MCS and anesthesiologists who specialize in the management of chronic pain and (clinical) neurophysiology experts. At the expert meeting, keynote speakers presented their expertise and led the group discussion. The entire expert meeting (327 minutes) was audiorecorded and later transcribed verbatim by one of the researchers (D. H.). The transcribed meeting was conscientiously analyzed with directed content analysis and independently coded line by line by 2 researchers (D. H. and E. K.). The coding process was performed using Atlas.ti 6 software (www.atlasti.com, Scientific Software Development GmbH, Berlin,

Germany). The 2 researchers discussed their findings and discrepancies in order to develop a codebook of themes organized by categories and codes to be discussed consecutively. Next, the initial draft was circulated among all the panel, rediscussed, edited, and completed in the light of recent literature and finally developed into the present form.

Questionnaire

Before the meeting, a questionnaire was sent electronically to all the invited participants. This questionnaire was created by the professionals of Nijmegen in order to determine the discrepancies in the methods of the whole MCS procedure in the different centers involved. The survey covered 3 main topics: 1) preoperative—indications and patient selection 2) intraoperative phase—surgical procedure, neurophysiological monitoring, and 3) postoperative phase—stimulation patterns, outcome, follow-up, and complications. The questionnaires were collected, categorized, and presented by 1 of the researchers (E. K.) at the meeting. The input and background information that was collected from the participants during the discussions and presentations at the expert meeting was used for the final results of the questionnaire by 2 researchers (E. K. and D. H.). Subsequently, the final results of the questionnaire were evaluated by 3 researchers (D. H., E. K., R. v. D.) independently, leading to material submitted for publication.

Ethical Statement

This article does not contain any material or study with patients that was performed by any of the participants in order to attend this expert meeting.

RESULTS

Topics that were addressed during the expert meeting were 1) inclusion and exclusion criteria, 2) targeting and methods of stimulation, 3) effects of MCS, and 4) results from the questionnaire. These topics are discussed separately in this manuscript, although these themes were intertwined in the expert meeting.

Inclusion and Exclusion Criteria

As Tsubokawa's cat model of a spinothalamic tractotomy and the newer

indications suggest, a lesion within the central nervous system must be identified.

“First of all, we must be able to identify a lesion in the spinothalamic, trigeminothalamic or thalamocortical tracts or their cortical targets. Secondly, we must be able to link the described pain to the objectified injury.”

This quote was a general remark in this session, and all agreed that we must try to ascertain that the patient suffers from definite neuropathic pain. The definition of neuropathic pain was revised in 2008 by the Neuropathic Pain Special Interest Group of the International Association for the Study of Pain and implies pain in a neuroanatomically plausible territory (i), with (ii) neurologic examination and history consistent with lesion or disease of somatosensory (mainly pain-related) pathways, and (iii) objective evidence of the existence of such a somatosensory lesion or disease by at least 1 confirmatory test.²³ Furthermore, the integrity of the corticospinal tract was considered obligatory for adequate analgesia. Patients who suffer from motor weakness are known to show less pain reduction (pain intensity score reduction of 15%), whereas patients with absent or mild motor deficits show significantly better pain reduction (pain intensity score reduction of 73%).²⁴

However, the etiology and diagnoses of patients suffering from pain that are included for MCS differed among the several centers. All participants agree on a number of causes. In the review by Lima and Fregni, they included not only central pain from brain or spinal cord injury but also peripheral causes such as trigeminal neuropathic facial pain, pain from peripheral nerve lesions, and brachial plexus avulsion and phantom limb pain.⁹ The etiology of the central lesions can be vascular (infarction, bleeding), neoplastic, degenerative, or inflammatory (multiple sclerosis) or due to damaged neural structures after radiation or brain surgery (or more specifically, a lesion or dysfunction of the spinothalamic tract). In a number of studies and experiences of the participants, atypical facial pain is not a clear diagnostic entity. Therefore the participants consider that patients who suffer from

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