Neurological Characteristics of Post-stroke Pain Patients with Favorable Therapeutic Responses to Motor Cortex Stimulation

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Abstract

We previously reported that subthreshold stimulation of the motor cortex (MCX) provided satisfactory pain control in approximately a half of patients with thalamic post-stroke pain. In the present study, we attempted to identify the neurological characteristics of patients who respond favorably to MCX stimulation. We analyzed data obtained from 28 patients with thalamic post-stroke pain. Among them, satisfactory pain control was observed during a 1-week test stimulation period in 21 (76 %). The effect of MCX stimulation was unchanged in 13 patients (46 %) for follow-up period of more than 2 years. No significant difference in age, gender or location of lesion was observed between the patients who reported favorable effects for a long-term and others. It was found that pain control from MCX stimulation tended to be unsatisfactory in patients with severe motor weakness and absent muscle twitch to MCX stimulation. Nevertheless, the pain inhibition usually occurred at intensities below the threshold of muscle contraction, suggesting that activation of corticospinal tract neurons themselves is not crucial for accomplishing pain inhibition. It may be that intercortical neuronal circuits maintained by the presence of corticospinal tract neurons play an important role in pain control with MCX stimulation.

Key words : motor cortex, motor deficit, stroke, central pain, deafferentation

INTRODUCTION

Central post-stroke pain, such as thalamic pain¹⁾, has proved the most difficult pain syndrome to control even with stimulation therapy^{2,8,10,11)}. We previously reported that excellent pain control is sometimes provided in thalamic pain patients with subthreshold stimulation of the motor cortex (MCX). Analysis of our own experience has indicated that excellent pain control was accomplished more frequently with this form of stimulation therapy as compared to stimulation of the dorsal column, thalamic relay nucleus, internal capsule or somatosensory cortex^{5,12)}.

In our initial experience¹²⁾, the beneficial effect of MCX stimulation has been obtained for follow-up periods of more than 2 years in 5 (45 %) of 11 patients with thalamic post-stroke pain. Hosobuchi³⁾ has independently confirmed that MCX stimulation provides excellent pain control in 3 (50 %) of 6 patients with cortical, thalamic and midbrain post-stroke pain. In the present study, we attempted to identify the neurological characteristics of patients who respond favorably to MCX stimulation from a new series of patients who have been treated since 1993.

MATERIALS AND METHODS

We analyzed data obtained from 28 patients with thalamic pain who were subjected to MCX stimulation⁵⁾. Among these patient, 20 had either a small thalamic infarct or thalamic hemorrhage, and the remaining 8 had a small lesion in the posterior limb of the internal capsule caused by a putaminal hemorrhage. Patients with midbrain or medullary lesions were excluded from the present study. The patients had been treated with various kinds of medication (anticonvulsants and/or antidepressants). These patients did not report any beneficial effect of peripheral or dorsal

column stimulation. The patients complained of spontaneous pain of great intensity which they described as burning, tearing or deep boring, mostly in the upper extremities and trunk area.

The surgical procedures employed in the present series of patients are basically similar to those we have reported previously^{5,12)}. Under local anesthesia, a paramedian linear skin incision 1~4 cm lateral to the midline or a oblique linear skin incision parallel to the estimated MCX is made depending on the location of the painful area. A small craniotomy of 3~4 cm in diameter is then carried out. An electrode array with 4 plate electrodes (diameter, 5 mm, Medtronic Inc M3587), each separated by 10 mm, is inserted from the edge of the craniotomy into the epidural space. In general, the location of MCX was determined from muscle contraction in response to stimulation with the electrode. Bipolar stimulation employing 2 appropriate electrodes was performed (interpolar distance, 10~30 mm), usually playing the electrode array parallel to the mediolateral orientation of the MCX^{4,5)}. Exploration of the MCX were performed with electrical pulses of low frequency less than 1 Hz because of following two reasons. Firstly, motor response to high frequency stimulation of the MCX is relatively susceptible to habituation. Secondly, high-frequency stimulation of the MCX at intensity above motor response threshold may cause seizures.

Once the best location and orientation of the electrode array for producing muscle contraction of the painful area with the lowest threshold is established, the electrode array is tightly sutured on the surface of the dura. During test stimulation period for approximately 1 week, stimuli are delivered by monophasic pulses mostly with duration of 0.2 ms (0.1~0.5 ms). Stimulation is usually applied continuously for 10~20 min on each occasion, and no stimulations are given at night. The stimulation system is internalized

Table 1 Level of lesion and pain control with MCX stimulation

Level of lesions	Group I (long-term success)	Group II (failure)
Suprathalamic lesion	3 (33 %)	5
Thalamic lesion	10 (50 %)	10
Total	13 (46 %)*	15

*initial success (internalization) rate in pain control, 76 %.

when satisfactory pain control is obtained during test stimulation period. Chronic stimulation is performed using wireless stimulation system (Medtronic Inc M3425 or more recent version). While the parameters for chronic stimulations are chosen so that the best pain inhibition was achieved, frequency and intensity are restricted to a level slightly lower than the threshold for muscle contraction.

The effects of stimulation are evaluated at predetermined intervals after initiation of the therapy. Each patient is asked to express the pain level on a visual analog scale. The effects of stimulation are classified into 4 categories; excellent, reduction of the pain level by 80~100 %; good, reduction of the pain level by 60~79 %; fair, reduction of the pain level by 40~59 %; and poor, reduction of the pain level less than 40 %. The pain level was evaluated every day during the period of test stimulation and once a month subsequently.

RESULTS

Among the 28 patients, satisfactory pain control was observed during a 1-week test stimulation period in 21 (76 %). The stimulation system was internalized in these patients. The effect of MCX stimulation was unchanged in 13 patients (46 %) for follow-up period of more than 2 years. In the remaining 8 patients (29 %), the effect decreased gradually over several months and became unsatisfactory. These results (Table 1) were very similar to those obtained

Table 2 Sensorimotor functions and pain control with MCX stimulation

Sensorimotor function	Group I (long-term success)	Group II (failure)
N ₂₀ component of somatosensory evoked potential*		
present	3 (38 %)	5
absent	4 (44 %)	5
Motor weakness		
mild (MMT, 4, 5)	11 (73 %) **	4
moderate or severe (MMT, 1, 2, 3)	2 (15 %)	11
Muscle twitch to MCX stimulation		
present	12 (55 %) **	5
absent	1 (16 %)	10

MMT, muscle maneuver test; *only patients with pain in hand area; **p<0.01

in our initial series of patients. No significant difference in age, gender or location of lesion was observed between the patients (Group 1; n=13) in which satisfactory pain control continued for more than 2 years and the patients (Group 2; n=15) in whom no satisfactory pain control was observed during the test stimulation period, or in whom satisfactory pain control was initially achieved but the effect faded away over several months.

Deficits or an increased threshold of pin-prick and thermal sensation (hypoalgesia) was observed in all the patients. A decrease in tactile and/or vibration sensations of varying degrees (hypesthesia) in painful area was noted in 10 patients. There was no noticeable difference in the presence of severe deficits in tactile and/or vibration sensation between the Group 1 patients and the Group 2 patients. We evaluated this aspect of clinical characteristics with N20 component of median nerve-evoked somatosensory scalp potential in 16 patients with pain in hand area. Among them, 9 patients revealed no detectable N20 component. No significant difference in the presence or absence of N20 component was

demonstrated between the Group 1 patients and the Group 2 patients (**Table 2**).

Despite the increased threshold of pinprick and thermal sensation, 18 patients reported that an abnormally painful sensation was produced when repetitive or sufficiently strong painful stimuli were applied (hyperpathia). In 7 patients, one of the cardinal symptoms was abnormally painful sensation elicited by external stimuli which are not normally painful, such as tactile, pressure or cold stimuli, or movements (allodynia). No noticeable difference in the presence of hyperpathia or severe allodynia was detected between the Group 1 patients and the Group 2 patients. MCX stimulation appeared to suppress hyperpathia and/or allodynia when it is effective to control spontaneous pain. In contrast, MCX stimulation did not attenuate non-painful paresthesia.

While motor weakness in painful area was virtually absent or mild (4 or 5 on Muscle Maneuver Test) in 15, it was moderate or severe (1, 2 or 3 on Muscle Maneuver Test) in 13. Only two of the Group 1 patients demonstrated moderate or severe motor weakness. In contrast, more than two-third of the Group 2 patients were suffered of moderate or severe motor weakness (**Table 2**). This difference was statistically significant ($p < 0.01$). Muscle twitch was induced in painful area in 22 patients when the MCX was stimulated with higher intensity current at 2Hz. No such muscle response was inducible in the remaining 6 patients, even though extensive exploration was performed to determine appropriate stimulation site. In the Group 1 patients, only one patients failed to demonstrate muscle twitches. In contrast, muscle twitch was not inducible in many of the Group 2 patients (**Table 2**). This difference between these two groups was again statistically significant ($p < 0.01$).

DISCUSSION

Since our initial experience of MCX stimulation¹²⁾, results of this form of stimulation therapy in 3 series of patients with different pain syndromes have been published: thalamic pain¹²⁾, bulbar pain⁵⁾ and trigeminal neuropathic pain⁶⁾. In addition, Parrent and Tasker⁹⁾ have reported a patient with a large supratthalamic infarct causing pain. Due to the lack of sufficient MCX on the affected hemisphere to be stimulated, they stimulated MCX of the unaffected hemisphere. The stimulation consistently produced ipsilateral paresthesia and substantial pain relief at amplitudes below the threshold for motor response.

Since good pain inhibition was evidently achieved only when stimulation is applied in the area from which muscle contractions are induced^{5,12)}, the pain inhibition obtained by cortical stimulation appears to be attributable to activation of the MCX. Furthermore, Meyerson, et al.⁶⁾ have reported that each stimulation site demonstrates spatial specificity regarding peripheral areas. Two of their patients with trigeminal neuropathy spontaneously reported that certain pairs of stimulation sites selectively influenced the pain in different parts of the face and neck. The spatial specificity of stimulation was also evident in the patients in whom an electrode grid with multiple poles was temporarily implanted. It appears that pain control provided by MCX stimulation is probably caused by activation of some neural element within the MCX.

The present study demonstrated that pain control from MCX stimulation tends to be unsatisfactory in patients with severe motor weakness and absent muscle twitch to MCX stimulation. This finding suggests that pain control from MCX stimulation requires intact corticospinal tract neurons originating from the MCX. Nevertheless, the pain inhibition usually occurred at

intensities below the threshold for production of muscle contraction (intensity, 3~8V)^{5,12)}. Similar observation has been reported in patients with trigeminal neuropathic pain⁶⁾, suggesting that activation of corticospinal tract neurons themselves is not crucial for accomplishing pain inhibition. It may be that intercortical neuronal circuits maintained by the presence of corticospinal tract neurons play an important role in producing pain control from MCX stimulation. There is a highly organized set of reciprocal connections between the MCX and the somatosensory cortex. It may be hypothesized that MCX stimulation activates such reciprocal connections, either orthodromically, which in turn inhibits hyperactive nociceptive neurons within the somatosensory cortex and other areas⁷⁾.

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