Somatotopic organization of the analgesic effects of motor cortex rTMS in neuropathic pain

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Abstract—*Background:* Motor cortex repetitive transcranial magnetic stimulation (rTMS) was found to relieve chronic neuropathic pain, but the optimal parameters of stimulation remain to be determined, including the site of stimulation. *Objective:* To determine the relationship between cortical stimulation site and pain site regarding the analgesic efficacy of rTMS of motor cortex in chronic neuropathic pain. *Methods:* Thirty-six patients with unilateral chronic neuropathic pain located at the face or the hand were enrolled. Motor cortex rTMS was applied at 10 Hz over the area corresponding to the face, hand, or arm of the painful side, whatever pain location. Analgesic effects were daily assessed on visual analogue scale for the week that followed each rTMS session. *Results:* All types of rTMS session, whatever the target, significantly relieved pain, compared with baseline. However, analgesic effects were significantly better after hand than face area stimulation in patients with facial pain and after face than hand or arm area stimulation in patients with hand pain. *Conclusion:* Repetitive transcranial magnetic stimulation was more effective for pain relief when the stimulation was applied to an area adjacent to the cortical representation of the painful zone rather than to the motor cortical area corresponding to the painful zone itself. This result contradicts the somatotopic efficacy observed for chronic epidural motor cortex stimulation with surgically implanted electrodes.

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Chronic motor cortex stimulation (MCS) with surgically implanted epidural electrodes was developed in the early 1990s and was found effective for inducing analgesia in patients with chronic, drug-resistant, neuropathic pain.[1-3] In such patients, repetitive transcranial magnetic stimulation (rTMS) applied at high frequency (10 to 20 Hz) over the motor cortex was also shown to produce analgesic effects.[4-6] The rate and duration of pain relief provided by rTMS are variable and seem to depend on stimulation frequency,[4] as well as on the origin of pain and on the location of the stimulated cortical target regarding the site of pain.[7] In a previous study, we showed that facial pain improved better than hand pain when the hand motor area was stimulated.[7] This result suggested that rTMS target for pain control might be not the cortical area corresponding to the painful zone, as for the implanted MCS procedure,[3] but an adjacent one. However, in our previous study, it was difficult to determine whether rTMS applied over hand area was more effective on facial vs hand pain or on trigeminal neuralgia vs other etiologies. The current study was designed to address specifically the question of the relationship between the site of stimulation and the site of pain. In a series of patients with chronic neuropathic pain of various origins, we assessed the ability of rTMS applied over face, hand, or arm motor cortical area to relieve pain according to its location at the face or the hand.

Methods. *Patients.* Thirty-six patients with chronic, unilateral neuropathic pain and no past history of seizures were enrolled. These patients were referred to evaluate the indication of chronic MCS. This study was included within the framework of a research program on MCS for pain treatment with authorization from local ethics committee. The pain located at the face for one-half of patients (15 women and 3 men, mean age: 56.8 years, range: 36 to 79 years) and at the hand for the other half (7 women and 11 men, mean age: 49.1 years, range: 30 to 66 years). In the group of patients with facial pain, etiologies were trigeminal neuralgia with past history of surgical treatment (microvascular decompression, percutaneous balloon compression, or radiofrequency thermocoagulation) (n = 7), orofacial pain secondary to dental (n = 4) or facial (n = 3) surgery, and brainstem stroke (pontine hemorrhage or infarction) (n = 4). In the group of patients with hand pain, causes were cervical spondylotic or traumatic myelopathy (n = 2), cervical syringomyelia (n = 3), thalamic stroke (hemorrhage or infarction) (n = 4) or tumor (n = 1), and traumatic lesion of the brachial plexus (n = 4) or of a single nerve trunk in the upper limb (n = 4). The thalamic tumor was a thalamopeduncular anaplastic astrocytoma (World Health Organization grade III), treated after diagnostic biopsy by radiotherapy plus temozolomide more than 6 years before the current study. No clinical or radiologic sign of tumor progression or recurrence was observed since then in this patient. She was presenting drug-resistant chronic neuropathic pain at the right upper limb, predominating at the hand and attributed to the thalamic lesion, from the time of the

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treatment of the tumor. Additional clinical information for each patient is presented in table 1.

rTMS procedure. The patients were seated in a comfortable reclining chair with a tightly fitting Lycra swimming cap placed over the head. In patients with facial pain, two different sessions of rTMS were performed, targeting the face or hand motor cortical area corresponding to the painful side. In patients with hand pain, three different sessions of rTMS were performed, targeting the face, arm, or hand area corresponding to the painful side. The sessions were performed in a random order, separated by at least 4 weeks, the patients being unaware of the exact condition of each rTMS session.

All sessions were identical in their course. First, we located the motor cortical representation of the face, arm, or hand corresponding to the painful side using the single-pulse program of a Super-Rapid magnetic stimulator and a 70-mm 8-shaped coil (Magstim Co., Whitland, UK). Targeting was performed by recording motor responses in the masseter muscle at the face, the biceps brachii muscle at the arm, and the first dorsal interosseus muscle at the hand, using surface electrodes and standard electromyography machine (Phasis II, EsaOte, Florence, Italy). The optimal sites for evoking motor responses (motor hot spots) were marked on the cap. Then, we determined the rest motor threshold, defined as the lowest stimulation intensity that evoked motor responses greater than 50 μV in 5 of 10 trials with the patient at rest.[8] Finally, rTMS was performed with the 8-shaped coil centered over one of the motor hot spots. Twenty trains of 10-second duration (50-second intertrain interval) were applied at 10 Hz and 90% of rest motor threshold intensity. The 8-shaped coil was maintained steady the whole session long, tangentially to the scalp, oriented in a posteroanterior direction. Immediately after each rTMS session, we checked on the absence of coil shift from the motor hot spot marked on the cap and made sure of still eliciting motor evoked potentials in the targeted muscle at suprathreshold stimulus intensities.

In view of this study, we sought to optimize coil positioning for targeting the lower face according to previously published data.[9-12] The largest motor responses of cortical origin, not contaminated by short latency responses due to facial nerve stimulation, were obtained when the coil was centered 10 cm lateral to the vertex and 2 cm anterior to the interaural line. This was corresponding to an approximate mean distance of 4 cm to the motor cortical representation of the hand.[10,11]

Pain assessment. First, patients were instructed to rate their ongoing pain on a 0 to 100 visual analogue scale (VAS) drawn on a sheet of paper, at home, for 1 week, each day at the same hour, prior to the first rTMS session. Then, they were asked for the same task, the week following each rTMS session, as maximal rTMS efficacy on pain score was previously found to occur between 2 and4 days after the session.[13] From each week of assessment, the averaged and the lowest (minimal) daily pain scores were determined.

The Clinical Global Impression Scale (CGI) was used to assess the global impression of the patients regarding rTMS efficacy on pain.[14] This scale includes seven categorical responses to measure improvement or aggravation of a symptom. The global change in chronic pain that the patients felt during the week after rTMS was rated by a clinician according to the following propositions: 1 = very much relieved, 2 = moderately relieved, 3 = slightly relieved, 4 = unchanged, 5 = slightly aggravated, 6 = moderately aggravated, 7 = very much aggravated. In all cases, the investigator who recorded pain scores was blinded for the type of stimulation.

Statistical analyses. Various clinical characteristics (age, pain intensity at baseline, pain duration) were compared between the two groups of patients (facial pain vs hand pain) using unpaired t test. The intensity of stimulation was compared between the two groups of patients and between the different rTMS sessions in each group using unpaired or paired t tests, or repeated measure one-way analysis of variance (ANOVA). The averaged and minimal daily pain scores assessed on VAS initially and after each rTMS session and the resulting CGI scores were compared in each group of patients using paired t tests and repeated measure one-way ANOVA followed by post-hoc tests with Bonferroni correction. We performed parametric tests after confirming that data were sampled from Gaussian distributions with the method of Kolmogorov and Smirnov. Significance was considered as less than 0.05 for the two-tailed p values of t tests or ANOVA (StatView; Abacus Concepts, Berkeley, CA). Regarding individual results, χ^2 tests were performed to assess the relationship between the type of rTMS session and its clinical outcome, assessed on mean VAS (more vs less than 30% pain relief[7]) or CGI score (improved, CGI 1 to 3, vs unchanged or aggravated patients, CGI 4 to 7).

Results. Patients with facial pain were older than patients with hand pain (mean [SEM]: 56.8 [2.5] vs 49.1 [2.5] years, unpaired t test, $p = 0.03$). However, the both groups were similar regarding VAS pain scores at baseline (79.3 [2.9] vs 81.6 [2.4], $p = 0.55$), pain duration (9.1 [1.6] vs 7.8 [1.9] years, $p = 0.62$) and stimulus intensity when all rTMS sessions were pooled (64.4 [2.5] vs 64.7% [1.6], $p = 0.92$). The intensity of stimulation did not vary with the location of the targeted cortical area in patients with facial pain (paired t test, $p = 0.63$) or with hand pain (repeated measure one-way ANOVA, $p = 0.13$).

No adverse effects were observed in the weeks that followed the different rTMS sessions. In particular, no seizures were induced. The evolution of the pain scores for each week of assessment in each group of patients is presented in figure 1. The averaged and minimal daily pain scores from each week of assessment are presented in figures 2 and 3. These scores varied with the time of assessment in each group of patients (repeated measure one-way ANOVA, $p < 0.0001$). Post-hoc tests showed a reduction of these scores after any type of rTMS session compared with pre-rTMS baseline (p values ranging between 0.01 and 0.001). By comparing all pairs of post-rTMS values, we found that pain relief was higher after hand vs face area stimulation in patients with facial pain ($p < 0.001$) and after face vs hand or arm area stimulation in patients with hand pain (face vs hand: $p < 0.001$ for averaged pain scores and $p < 0.01$ for minimal pain scores; face vs arm: $p < 0.05$ for both scores). The effects of hand or arm area stimulation were similar in patients with hand pain ($p > 0.05$).

In patients with facial pain, the averaged pain scores improved by 27% after hand area rTMS and 11% after face area rTMS. In patients with hand pain, the averaged pain scores improved by 37% after face area rTMS, 18% after hand area rTMS, and 22% after arm area rTMS. Regarding individual results assessed on VAS score, 8 of the 18 patients with facial pain presented significant pain relief after hand area stimulation (VAS score reduced by more than 30%) but only 3 patients after face area stimulation. In contrast, face area stimulation produced significant pain relief in 11 of the 18 patients with hand pain, whereas arm and hand area stimulation relieved only 2 and 4 patients in this group. The χ^2 test showed that a pain relief was associated with the type of rTMS session for patients with hand pain ($p = 0.003$) and for patients with facial pain ($p = 0.07$).

Similar results were obtained regarding the CGI scores. The patients reported a greater improvement after hand vs face area rTMS in case of facial pain (paired t test, $p = 0.003$) and after face vs hand or arm area rTMS in case of hand pain (ANOVA post-hoc test, face vs hand, $p < 0.001$; face vs arm, $p < 0.01$), whereas the effects were similar between hand and arm area stimulation ($p > 0.05$).

Regarding individual results assessed on CGI scores, 11 patients with facial pain experienced a global impression of pain relief after hand area rTMS but only 4 patients

Table 1 *Clinical characteristics of patients with face (F1 to F18) or hand (H1 to H18) pain*

Patient	Sex	Age, y	Pain origin	Pain location	Pain duration, y	Pain intensity (VAS)	Analgesic medication
F1	F	79	Resistant trigeminal neuralgia	R face	10	70	Bromazepam
F2	F	42	Resistant trigeminal neuralgia	R face	13	71	Carbamazepine, clomipramine, clonazepam, lamotrigine
F3	F	57	Resistant trigeminal neuralgia	L face	25	96	Baclofen, carbamazepine, gabapentin
F4	F	69	Resistant trigeminal neuralgia	R face	10	67	Baclofen, carbamazepine
F5	F	58	Resistant trigeminal neuralgia	L face	22	95	Bromazepam, clonazepam, gabapentin
F6	F	64	Resistant trigeminal neuralgia	L face	20	100	Bromazepam, clomipramine, clonazepam, gabapentin
F7	F	70	Resistant trigeminal neuralgia	R face	10	100	Amitriptyline, bromazepam, clonazepam, lamotrigine
F8	F	55	Orofacial pain (dental surgery)	R face	6	95	Clonazepam, morphine sulfate, oxcarbazepine
F9	F	57	Orofacial pain (dental surgery)	R face	7	72	Clonazepam, venlafaxine
F10	F	51	Orofacial pain (dental surgery)	L face	4	77	Clonazepam, gabapentin
F11	F	36	Orofacial pain (dental surgery)	L face	2	74	Bromazepam, buprenorphine, clonazepam, venlafaxine
F12	M	45	Orofacial pain (facial surgery)	R face	2	73	Paracetamol, tramadol
F13	F	55	Orofacial pain (facial surgery)	R face	5	65	Fentanyl, fluoxetine, morphine sulfate
F14	F	69	Orofacial pain (facial surgery)	L face	6	80	Clomipramine
F15	M	52	Pontine hemorrhage	R face	2	66	Clomipramine, clonazepam, oxcarbazepine, tramadol
F16	F	51	Pontine hemorrhage	L face	3	80	Clonazepam
F17	F	53	Pontine hemorrhage	L face	6	69	Clonazepam, codeine, gabapentin, paracetamol
F18	M	59	Pontine infarction	L face	10	77	Amitriptyline
H1	M	55	Cervical spondylotic myelopathy	R hand	3	91	Carbamazepine, clomipramine, clonazepam, morphine sulfate
H2	M	48	Cervical traumatic myelopathy	L hand	6	86	Amitriptyline, gabapentin, morphine sulfate, tramadol
H3	M	66	Cervical syringomyelia	R hand	12	79	Codeine, gabapentin, paracetamol, sertraline, tramadol
H4	M	58	Cervical syringomyelia	R hand	29	90	Amitriptyline, fentanyl, oxcarbazepine, sertraline
H5	F	38	Cervical syringomyelia	R hand	9	90	Amitriptyline
H6	F	57	Thalamic hemorrhage	L hand	6	73	Dantrolene, lamotrigine, topiramate
H7	F	41	Thalamic infarction	R hand	3	89	Clonazepam, gabapentin, oxcarbazepine
H8	M	46	Thalamic infarction	R hand	3	90	Clonazepam, codeine, paracetamol
H9	M	56	Thalamic infarction	R hand	2	90	Clonazepam, gabapentin
H10	F	30	Thalamic astrocytoma	R hand	3	73	Amitriptyline, clonazepam
H11	F	42	Brachial plexus lesion	R hand	3	71	Dextropropoxyphene, fluoxetine, paracetamol
H12	M	47	Brachial plexus lesion	L hand	27	64	Amitriptyline, gabapentin
H13	M	51	Brachial plexus lesion	L hand	10	65	Clonazepam
H14	M	41	Brachial plexus lesion	L hand	4	86	Codeine, paracetamol
H15	M	57	Ulnar nerve lesion (elbow)	L hand	3	71	Gabapentin
H16	F	55	Median nerve lesion (forearm)	L hand	4	89	Amitriptyline, clonazepam
H17	M	64	Median and ulnar nerve lesion (wrist)	L hand	7	73	Amitriptyline, carbamazepine, tramadol
H18	F	31	Median nerve lesion (wrist)	L hand	7	98	Bromazepam, gabapentin, morphine sulfate, topiramate

VAS = visual analogue scale.

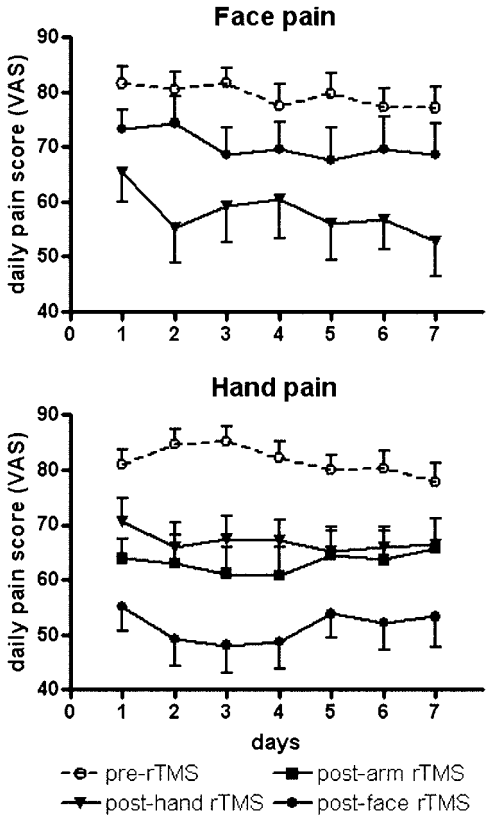

Figure 1. Evolution of the pain scores (mean ± SEM) observed daily for a week before and after the different sessions of repetitive transcranial magnetic stimulation applied over the face, hand, or arm motor cortical area, in patients with face or hand pain.

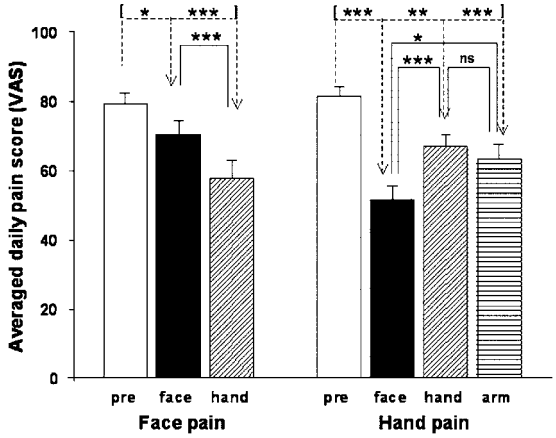

*Figure 2. Mean (±SEM) values of the pain level scored on 0 to 100 visual analogue scale and averaged from a week of assessment before and after repetitive transcranial magnetic stimulation (rTMS) of the face, hand, or arm motor cortical area in patients with face or hand pain. The p significance values of post-hoc tests are indicated for comparisons with baseline pre-rTMS values (above dotted lines) and between all pairs of post-rTMS results (above solid lines) (NS $p > 0.033$; *$p < 0.033$; **$p < 0.010$; ***$p < 0.001$).*

after face area rTMS (table 2). In contrast, 16 patients with hand pain experienced pain relief after face area rTMS, but only 7 and 8 patients after hand and arm area rTMS (table 2). No patients reported pain exacerbation after rTMS, whatever the session. χ^2 test showed that the outcome (improved vs unchanged) was associated with the type of rTMS session for patients with facial pain ($p = 0.018$) as for patients with hand pain ($p = 0.004$).

Discussion. This study confirmed that subthreshold 10-Hz rTMS trains delivered over the primary motor cortex were able to relieve chronic drug-resistant neuropathic pain of central or peripheral origin. Analgesic effects were significant for the week that followed the rTMS session, whatever the cortical target site. However, the best conditions were hand area stimulation for patients with facial pain and face area stimulation for patients with hand pain.

First, the possible influence of retest and placebo effects should be discussed. As the sessions, and then the post-rTMS assessments, were randomly performed, order effect should not be responsible for the differential results according to the type of stimulation. In contrast, we could not rule out carry-over effects because baseline was not assessed before every sessions. Regarding placebo effect, a mean rate of 4 to 11% improvement in VAS scores could be expected from the previous sham-controlled rTMS studies reported in chronic pain.[4,6,7] In the current study, mean pain relief ranged between 11 and 37%, thereby precluding a placebo response. The facial twitch induced by rTMS could also have interfered with the clinical outcome in patients with facial pain, particularly in case of face area stimulation. This condition was marked by a poor improvement and thereby nocebo effects resulting from the rTMS-

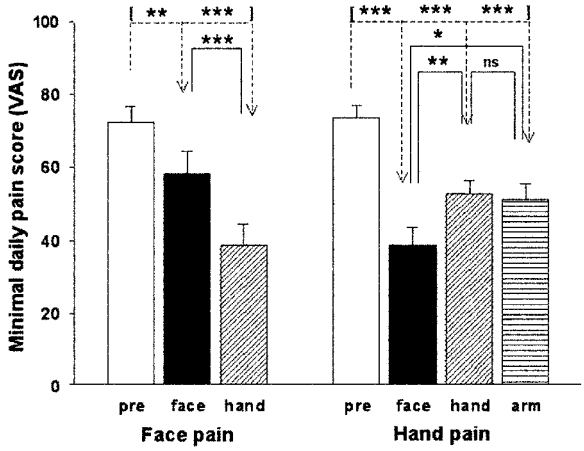

*Figure 3. Mean (±SEM) values of the minimal pain scores measured on 0 to 100 visual analogue scale from a week of assessment before and after repetitive transcranial magnetic stimulation (rTMS) of the face, hand, or arm motor cortical area in patients with face or hand pain. The p significance values of post-hoc tests are indicated for comparisons with baseline pre-rTMS values (above dotted connecting lines) and between all pairs of post-rTMS results (above solid connecting lines) (NS $p > 0.033$; *$p < 0.033$; **$p < 0.010$; ***$p < 0.001$).*

Table 2 *Clinical Global Impression (CGI) in patients with face (F1 to 18) or hand (H1 to 18) pain after single session of repetitive transcranial magnetic stimulation (rTMS) applied over the face, hand, or arm motor cortical area*

Patient	Pain origin	CGI post face rTMS	CGI post hand rTMS	CGI post arm rTMS
F1	Resistant trigeminal neuralgia	—	—	
F2	Resistant trigeminal neuralgia	3	1	
F3	Resistant trigeminal neuralgia	—	—	
F4	Resistant trigeminal neuralgia	—	2	
F5	Resistant trigeminal neuralgia	—	2	
F6	Resistant trigeminal neuralgia	—	—	
F7	Resistant trigeminal neuralgia	—	—	
F8	Orofacial pain (dental surgery)	2	2	
F9	Orofacial pain (dental surgery)	—	—	
F10	Orofacial pain (dental surgery)	—	—	
F11	Orofacial pain (dental surgery)	—	3	
F12	Orofacial pain (facial surgery)	1	1	
F13	Orofacial pain (facial surgery)	—	2	
F14	Orofacial pain (facial surgery)	—	1	
F15	Pontine hemorrhage	—	—	
F16	Pontine hemorrhage	—	2	
F17	Pontine hemorrhage	1	1	
F18	Pontine infarction	—	2	
H1	Cervical spondylotic myelopathy	2	3	3
H2	Cervical traumatic myelopathy	1	—	3
H3	Cervical syringomyelia	1	2	2
H4	Cervical syringomyelia	1	—	—
H5	Cervical syringomyelia	2	3	—
H6	Thalamic hemorrhage	—	—	2
H7	Thalamic infarction	3	—	—
H8	Thalamic infarction	3	—	—
H9	Thalamic infarction	3	—	3
H10	Thalamic astrocytoma	1	—	—
H11	Brachial plexus lesion	3	—	1
H12	Brachial plexus lesion	2	2	—
H13	Brachial plexus lesion	2	—	—
H14	Brachial plexus lesion	1	3	—
H15	Ulnar nerve lesion (elbow)	2	3	—
H16	Median nerve lesion (forearm)	—	—	2
H17	Median and ulnar nerve lesion (wrist)	1	—	3
H18	Median nerve lesion (wrist)	2	2	—

CGI: 1 = very much relieved; 2 = moderately relieved; 3 = slightly relieved; (—) = unchanged.

induced facial twitches might have lowered the efficacy of rTMS on chronic pain. Such nocebo effects were unlikely to occur, because "peripheral" repetitive magnetic stimulation was found effective for the treatment of myofascial tender points,[15] even at a higher level than transcutaneous electrical nerve stimulation, which can be successfully applied for the management of facial pain.[16] Therefore, we assumed that the current results account for a true efficacy of motor cortex rTMS on pain and that rTMS was more effective when the stimulation was applied to an area adjacent to the cortical representation of the painful zone than to the motor cortical area corresponding to the painful zone.

A somatotopic efficacy has been observed for chronic MCS with implanted epidural electrodes.[3] Even if this remains controversial,[17] most investigators reported that an appropriate targeting of the

motor cortical area corresponding to the painful zone was representing a crucial step in obtaining pain relief. This was leading to the development of sophisticated radiologic guidance.[18] The current study suggests that cortical targeting might, however, differ in rTMS from the implanted MCS procedure.

First, this could result from differences in the nature of the current flow induced in the brain by these two techniques. In a model of epidural MCS for chronic pain, it was suggested that bipolar MCS was rather a bifocal stimulation with both active anode and cathode, due to the large distance between stimulating electrodes.[19] Horizontal fibers, parallel to cortical surface, were excited under the cathode, whereas efferent fibers perpendicular to cortical surface were excited under the anode.[19] In contrast, rTMS, at least performed with a figure-of-8 coil oriented in posteroanterior direction, as in the current study, was found to activate only corticocortical interneuronal fibers, tangentially oriented to the surface of the cortex.[20,21] Therefore, motor cortex rTMS likely evokes various indirect I waves, whereas epidural MCS could evoke different I waves, but also D waves, due to the direct activation of the corticospinal fibers, perpendicularly oriented to the surface of the cortex.[22] These observations could explain targeting differences between noninvasive rTMS and implanted MCS procedures. Nevertheless, the both techniques probably share common mechanisms of action to produce analgesic effects, whatever their differences regarding the pattern of cortical activation and its location. In particular, their effects on chronic pain are likely to depend on the recruitment of fibers located within the motor cortex but projecting to remote structures, functionally connected with the motor cortex, and involved in pain and sensory processing.

The rTMS-induced current was able to modulate outputs from the nearby cortical representation better than from the stimulated area. The optimal rTMS target was medial to the affected area in patients with facial pain, whereas rTMS was more efficient in patients with hand pain when applied laterally to hand representation. Lesion-induced plasticity might explain such a difference in the across-representation shift of the effective cortical rTMS target.

Patients with chronic pain secondary to neurologic lesions could present a functional reorganization in cortical areas with maladaptive plasticity. Imaging or electrophysiologic studies disclosed strong representation plasticity in the motor cortex in various types of neuropathic pain, possibly correlated with the amount of pain.[23] It was shown in amputees that adaptive cortical plasticity was influenced by the presentation, the duration, and the intensity of pain, according to features of phantom limb pain.[24] In case of upper limb amputation, the former hand area of the cortex was shown to be invaded either by a lateralization of the arm area, corresponding to overactivated muscles in the stump,[25-27] or by a medialization of the face area,[25,27,28] particularly in case of phantom limb pain.[24] In patients with facial palsy, a TMS study showed an enlargement of the hand field in a lateral direction, into the site of the face area.[29] A transient ischemic deafferentation of the hand could also result in a lateralized increase of motor cortical output from arm representation.[30]

In this study, the duration and intensity of pain, which were similar in both group of patients, were unlikely to influence the direction of across-representation shifts. In contrast, the origin of pain, mostly due to peripheral nervous system lesion in patients with facial pain and to CNS lesion in patients with hand pain, could have contributed to the difference observed between the two groups of patients.

Deafferentation results in the "invasion" of the cortical representation of the affected part of the body by adjacent cortical representations of intact parts. This can result from the unmasking of normally inhibited connections or the sprouting of new connections. This might also relate to altered cortical projections from brainstem structures or thalamic nuclei[31] that in turn could affect distant regions involved in pain processing, like the insula or the anterior cingulate cortex. Sensory deafferentation leads to various changes in motor cortex excitability, including enhanced motor output (motor disinhibition) in areas adjacent to the affected area.[32] Low-rate rTMS was shown to induce within-representation increase but across-representation decrease of cortical disinhibition around the affected area in subjects with ischemic deafferentation.[32] The involvement of such a mechanism of bidirectional plasticity in the process of pain relief induced by rTMS was not supported by our negative experience of low-frequency motor cortex rTMS in chronic pain,[4] but remains to be explored for cortical stimulation applied at higher rates.

This study has investigated the influence of target location on the somatotopy of the analgesic effects induced by motor cortex rTMS in patients with chronic neuropathic pain. These effects were better when the stimulation was applied to a cortical area adjacent to that of the painful zone and thereby differed from the somatotopy observed in chronic MCS procedure. Although significant, the mean rate of pain relief was moderate: 27% in patients with facial pain for the optimal condition (hand area stimulation) and 37% in patients with hand pain for the optimal condition (face area stimulation). Cortical plasticity and stimulation settings condition rTMS outcome in chronic pain. How cortical reorganization due to the underlying neurologic lesion impacts the analgesic efficacy of rTMS should be further explored for motor targets and also for other cortical targets that can be tested in pain control, such as prefrontal and medial frontal targets.

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