Interactions between pain and the motor cortex:
Insights from research on phantom limb pain and complex regional pain syndrome

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ABSTRACT

Purpose: Pain is a significantly disabling problem that often interacts with other deficits during the rehabilitation process. The aim of this paper is to review evidence on interactions between pain and the motor cortex in order to attempt to answer the following questions: (1) Does acute pain interfere with motor cortex activity? (2) Does chronic pain interfere with motor cortex activity and, conversely, does motor cortex plasticity contribute to chronic pain? (3) Can the induction of motor plasticity by means of motor cortex stimulation decrease pain? (4) Can motor training result in both motor cortex reorganization and pain relief? Summary of Key Points: Acute experimental pain was clearly shown to exert an inhibitory influence over the motor cortex, which can interfere with motor learning capacities. Current evidence also suggests a relationship between chronic pain and motor cortex reorganization, but it is still unclear whether one causes the other. However, there is growing evidence to the effect that interventions that aim to normalize motor cortex organization can lead to pain relief. Conclusions: Interactions between pain and the motor cortex are complex, and more studies are needed to understand these interactions in our patients, as well as to develop optimal rehabilitative strategies.

Keywords: pain, motor control, motor cortex, plasticity, rehabilitation
Pain is one of the most common and disabling symptoms in numerous diseases. For many years, pain was considered and treated as a symptom of pathology or injury and as a sensory phenomenon only. Steering away from this view of pain as a purely sensory process, contemporary integrative models of pain include a sensory-discriminative component of pain (processing information about the location and the type of pain) and a motivational-affective component (processing the subjective feeling of unpleasantness associated with pain). Brain imaging techniques have revealed a complex network of cerebral structures associated with the different dimensions of pain including the primary (S1) and secondary (S2) somatosensory, insular (IC), anterior cingulate (ACC), and prefrontal (PFC) cortices and thalamus (Th). In addition to this brain network which is classically associated with pain processing, some functional neuroimaging studies have also reported hemodynamic changes in brain regions related to motor function during pain, including primary motor cortex (M1), although this aspect of pain-related brain activity is rarely discussed. These neuroimaging results do not necessarily indicate that motor areas are involved in pain processing and perception, but they certainly raise the possibility of interactions between pain and motor function. Although the possible link between pain and motor functions was recognized several years ago, research into the nature and the extent of these interactions is very recent.

Physiotherapists are generally aware that pain can interact with other functions during the rehabilitation process, and in particular with motor functions, but these motor dysfunctions are often simply regarded as a consequence of movement-related pain or anticipated movement-
related pain (e.g. kinesiophobia). The interactions between pain and motor control are much more complex however, and more in-depth knowledge about these interactions is necessary to understand the physiology of the motor and nociceptive systems in patients suffering from both pain and motor deficits, as well as to develop rehabilitative strategies that take these interactions into account. One important aspect to consider from a rehabilitation perspective is that these interactions might be bidirectional, i.e. that pain might have an effect on motor cortex activity, but that motor cortex activity might also have an impact on pain. The aim of this paper is to review evidence on interactions between pain and motor cortex activity in order to try to answer the four following questions: (1) Does acute pain interfere with motor cortex activity? (2) Does chronic pain interfere with motor cortex activity, and conversely, does motor cortex plasticity contribute to chronic pain? (3) Can the induction of motor plasticity by means of motor cortex stimulation decrease pain? (4) Can motor training result in both motor cortex reorganization and pain relief? As these four questions target the motor cortex rather than the motor system in general, the effect of pain on the muscle itself and on spinal reflexes will not be addressed in details in this paper. The effects of focal muscle pain on muscle activity during rest, contraction and fatigue have already been reviewed elsewhere.8,9 This review will focus mainly on two models of chronic neuropathic pain, phantom limb pain and complex regional pain syndrome. As the idea of a role of maladaptive plasticity within the sensorimotor cortex as a potential cause of chronic pain (or of pain maintenance) has emerged from research in the field of neuropathic pain,10,11 most of the research on the interaction between motor cortex plasticity and pain was therefore conducted in these populations.
Does acute pain interfere with motor cortex activity?

Plasticity has been clearly observed in the sensory systems in response to both acute and chronic pain, including changes in the dorsal horn, the thalamus and the somatosensory cortex, but the idea that pain may also affect the motor system is still relatively new. Most studies that have focused on the interactions between pain and motor function have dealt with the effects of experimental acute pain on spinal cord reflexes (see for instance Sandrini et al. and Clark & Harris for reviews). During the withdrawal reflex response, nociceptive information from skin, muscles and/or joints makes synapses with motoneurons located in various spinal cord segments, inducing a complex flexion synergy of the stimulated limb. This flexion synergy would play a protective role against potential limb damage, and attest that the interactions between pain and motor function occur as early as in the spinal cord. Interestingly, applications of previous noxious stimuli to specific regions of the limb, as well as the presence of certain injuries, have been shown to increase the magnitude of the withdrawal reflex response (see Clark & Harris for a review). These increased withdrawal responses are thought to be caused by changes occurring at the sensory level (e.g. central sensitization) and would enhance the protective function of the withdrawal reflex after tissue injury.

It has been demonstrated that pain leads to a reduction of maximal voluntary contraction, a decrease in endurance during submaximal contraction and changes in coordination during dynamic tasks (see Graven-Nielsen & Arendt-Nielsen and Arendt-Nielsen & Graven-Nielsen for reviews). Moreover, recent studies using intra-muscular EMG recordings have shown that pain (induced either in muscular or non-muscular tissue) results in changes in the motor unit
recruitment strategy, revealing that the effect of pain is not limited to a uniform inhibition of the motoneuron pool, but rather includes more subtle changes in the distribution of output to the motoneuron pool.\textsuperscript{20,21} However, it is still unclear whether these alterations in motor function observed at the muscular level reflect changes at the peripheral, spinal or cortical level. Two different models have been proposed regarding the interactions between pain and movement: the vicious circle model,\textsuperscript{22} and the pain-adaptation model.\textsuperscript{23} The vicious circle model suggests that musculoskeletal pain is sustained by the fact that pain-related muscle spasms lead to muscle ischemia that in turn increases pain and contributes to its maintenance.\textsuperscript{22} However, this model has not received much support from experimental data.\textsuperscript{8,23} Alternately, the pain-adaptation model predicts a reduction of the agonist motoneuron output and an increase in antagonist motoneuron firing during movement in the presence of pain.\textsuperscript{23} According to this model, changes in motor output in response to pain result from interneurons receiving convergent afferent information and having a reciprocal effect on agonist and antagonist muscles in the spinal cord and the brainstem. Two common features of these models on interaction between pain and movement are (1) that they have arisen from clinical observations and experiments focusing on localized muscle pain and (2) that they focus on changes in the spinal cord and periphery, without considering any potential role of cortical mechanisms.

More recently, several studies using transcranial magnetic stimulation (TMS) have shown that pain also influences the excitability of the primary motor cortex.\textsuperscript{6} TMS is a method of stimulating the brain non-invasively. The rapid time-varying magnetic field generated by the TMS coil penetrates the scalp and skull, and induces electrical currents in the area of the brain beneath the coil that activate the axons of neurons in the cortex. Stimulation of the motor cortex
evokes muscles responses termed motor evoked-potentials (MEPs), which are measured using EMG. A variety of parameters of MEPs can be studied in order to assess changes in corticospinal or intra-cortical excitability. The motor threshold is generally defined as the minimal intensity of stimulation required to produce a MEP of small amplitude in 50% of trials. Therefore a decrease in motor threshold reflects an increased excitability of the corticospinal tract and vice versa. The size of the MEP (amplitude, duration or area) also reflects the excitability of the corticospinal pathway, which can be affected by a number of mechanisms at both the cortical and spinal level. Paired pulse stimulation, where a suprathreshold test stimulus is preceded by a subthreshold conditioning stimulus, can be used to gain insight into the contribution of local inhibitory and excitatory interneurons in order to assess changes in intra-cortical facilitation or intra-cortical inhibition mechanisms. TMS can also be used to create a cortical map of a target muscle’s representation by measuring MEP amplitudes evoked by TMS applied to different positions over the motor cortex. This allows to study the extent and the location (often defined by the center of gravity of the map) of the cortical representation of a given muscle target.

Although the effect of pain on the motor system can vary depending on variables such as duration of the painful stimulus (phasic vs. tonic pain), submodality (deep vs. superficial pain), and location (proximal vs. distal pain), a common finding of TMS studies is that acute experimental pain exerts an inhibitory influence on corticospinal excitability.24-29 This inhibitory effect of experimental pain was however not observed by Romaniello and colleagues.30 Changes in responses evoked by TMS do not necessarily reflect changes at the motor cortex level, but could alternatively be the result of changes occurring in various neural structures between the primary motor cortex and the motoneurons in the spinal cord. However, there is evidence that the
origin of these effects can at least be partially attributed to the cortex. For example, laser-evoked pain was found to attenuate motor responses to TMS, but not to transcranial electrical anodal stimulation (which directly activates the pyramidal tract rather than cortical interneurons).\textsuperscript{24,27} Another study showed that during the initial phase of tonic pain induced by injection of hypertonic (5\%) saline, there was a reduction of motor responses evoked by TMS stimulation in the absence of any effect on the H-reflex (H-reflex amplitude was decreased in a later phase, about 1 minute after the peak in pain, which suggests that the change initially occurred at the motor cortex level).\textsuperscript{25} Pain induced by application of capsaicin on the skin was also found to reduce the amplitude of motor responses evoked by TMS without alteration of spinal excitability.\textsuperscript{26} It is noteworthy that these different experimental pain models recruit different types of nociceptive afferents. For example, injection of hypertonic saline, often used to mimic musculoskeletal pain, excites nociceptive muscle afferents (groups III and IV),\textsuperscript{31,32} while capsaicin or laser-evoked pain selectively activate A\(\delta\) and C fibres in the superficial skin layers.\textsuperscript{33,34} Even though nociceptive inputs from muscle and skin have been shown to induce distinct changes in trigeminal motoneuronal excitability,\textsuperscript{35} changes at the motor cortex level appear to be consistently inhibitory across the different pain models (i.e. muscle vs. cutaneous pain, phasic vs. tonic pain).\textsuperscript{24-29}

In patients with motor deficits who experience acute pain, the inhibitory influence of pain on the motor cortex might hamper optimal motor cortex activation during voluntary movement and preclude motor improvement during rehabilitation. There is striking evidence supporting this view from a recent study in healthy individuals showing that acute pain can prevent motor cortex plasticity associated with novel motor training and impair the ability to learn a new motor task.\textsuperscript{36}
In this study, healthy volunteers participated in two cross-over training sessions in which they were trained in a tongue-protrusion task. Prior to each training session, a cream was applied to the tongue that either contained capsaicin (inducing moderate intra-oral tonic pain) or an inert substance (control condition). Even though participants improved their performance in the motor task following training in both the painful and nonpainful conditions, the improvement was significantly lower when the training was performed in the presence of pain (capsaicin condition). Moreover, measurements of corticospinal excitability with TMS showed that the presence of pain suppressed training-induced motor plasticity effects (e.g. increased excitability) observed in the control condition, despite a similar amount of practice. Although these results were obtained in healthy individuals, they strongly suggest that pain can interfere with the effect of motor rehabilitation, both at the cortical and the behavioural levels.

**Does chronic pain interfere with motor cortex activity, and conversely, does motor cortex plasticity contribute to chronic pain?**

While increased inhibition has been systematically observed in acute experimental pain models, changes in motor cortex excitability in patients with chronic pain are less consistent. Some TMS studies report increased motor cortex excitability (reflected by decreased motor threshold, increased map volume or reduced intracortical inhibition) in patients with chronic pain from diverse origins, but the opposite has also been found. Studying the relationship between pain and changes within the motor cortex in patients with chronic pain is very complex, as these patients also have other sensorimotor deficits that likely impact motor cortex excitability. The presence of these sensorimotor deficits may explain why there is more variability in the results of
studies on clinical pain compared with acute experimental pain. In order to illustrate the complex nature of the relationship between changes within motor cortex, motor deficits, and pain in patients with chronic pain disorders, two examples of neuropathic chronic pain will be discussed here: phantom limb pain and complex regional pain syndrome (CRPS).

*Phantom limb pain, phantom limb movement, and motor reorganizations.* One particularly interesting model used to study interactions between the motor system and pain is the phantom limb phenomenon, which is the vivid sensation that a missing body part is still there after an amputation. Fifty to eighty percent of amputees also report pain in the missing limb, a phenomenon called phantom limb pain. Phantom limb pain often persists chronically and is recognized as very difficult to treat.\(^45\) Interestingly, most amputees (including those with and without phantom limb pain) feel that they are able to perform voluntary movements with their phantom limb.\(^{46-52}\) Most amputees are able to move their phantom limb easily soon after the amputation, but in many cases this ability diminishes over time, with the phantom limb becoming more and more difficult to move, and in some cases becoming completely paralyzed.\(^{49-51}\) Clinical observations and experimental data provide some evidence of interactions between pain and motor control in the phantom limb phenomenon. As the physical limb is no longer there, it is likely that these interactions reflect central mechanisms, and the phantom limb phenomenon is therefore an interesting model for studying interactions between changes in motor cortex and pain.

Amputees often report the feeling that if they could move the limb into a new position it would ease their pain. However, moving the phantom limb is often difficult, and attempts to move it
tend to increase the pain.\textsuperscript{49} We recently developed an approach to assess phantom limb motor control and showed that distinct movements of the phantom limb were associated with distinct patterns of EMG activity in the remaining stump muscles.\textsuperscript{46,51} Using this method, we demonstrated that phantom limb motor control is decreased in patients with pain compared with amputees who are pain-free.\textsuperscript{46} Indeed, phantom movement speed was systematically decreased in subjects with phantom limb pain compared to amputees that were pain free, suggesting decreased phantom limb motor control in patients with phantom limb pain.\textsuperscript{46} Also, the presence of a clear phase-dependent modulation of stump muscle EMG activity during phantom hand movements was associated with more severe phantom limb pain. Since movement–related EMG patterns in above-elbow stump muscles during phantom hand movements can be considered a marker of motor system reorganization (as above-elbow muscles are not normally activated during hand movements), this result indirectly supports the hypothesis that amputation-induced plasticity within the motor system is associated with phantom limb pain severity.\textsuperscript{46}

At the cortical level, this amputation-induced plasticity is observable as a marked increase in the excitability of the representation of stump muscles compared to the same muscles on the intact side,\textsuperscript{37,53-56} although it is important to note that this excitability asymmetry was not related to pain severity in most studies. Indeed, only one study found such an association, with an increase in excitability of the representation of stump muscles (i.e. muscle responses evoked by TMS were larger) compared to the intact side in patients with phantom limb pain but not in patients who were pain-free.\textsuperscript{37} Such association between pain and cortical excitability has been challenged by the findings of another study showing that the reduction of cortical excitability in patients with chronic phantom limb pain following treatment with memantine was not paralleled
by a reduction of phantom pain intensity.\textsuperscript{57} Therefore the relationship between motor excitability and phantom limb pain remains unclear, and it is possible that deafferentation/ defferentation plays a larger role in post-amputation excitability changes than post-amputation pain. Evidence to the contrary comes from neuroimaging studies, which generally support the existence of a relationship between phantom limb pain and the spatial extent of amputation–induced reorganization in motor cortex, this reorganization being characterized as a medial shift of the face muscle representation in upper limb amputees (i.e. displacement toward the former hand area).\textsuperscript{37,58-60} As these studies have shown that more reorganization is associated with more pain, this reorganization induced by amputation is generally considered as an example of maladaptive plasticity. Altogether, results of studies using EMG, TMS, and other neuroimaging techniques suggest the existence of some relationship between motor reorganization and pain after amputation, but the exact nature of this relationship remains unclear.

\textit{Complex regional pain syndrome and motor reorganization.} Complex regional pain syndrome type I (CRPS-I) is a painful disorder that develops after trauma (or even in the absence of trauma), and is characterized by pain and related sensory abnormalities that are disproportionate to the initial problem. These abnormalities include edema, autonomic dysfunction, motor symptoms, and trophic changes.\textsuperscript{61} There is some evidence for motor cortex reorganization in patients with CRPS-I. Although TMS studies found no significant inter-hemispheric difference in the motor thresholds,\textsuperscript{38,40,42} the size of the cortical representation of muscles on the affected side was found to be reduced compared to the unaffected side.\textsuperscript{42} In addition, intra-cortical inhibition has been found to be decreased in the motor cortex contralateral to the affected limb, or bilaterally.\textsuperscript{38,40} Interestingly, this reduction in intra-cortical inhibition of the motor cortex
contralateral to the affected limb was linked with pain severity. Consistent with this decreased inhibition, an fMRI study showed greater activation within the motor cortex (among other regions) during a finger tapping task performed with the affected hand as compared to activations for the unaffected hand or activations seen in healthy controls. Moreover, the degree of activation within the motor cortex was correlated with the amount of motor impairment evaluated during reach-to-grasp movements. However, no significant correlation was found between pain intensity and motor performance deficits.

Overall, it can be concluded from studies in these two clinical populations that reorganization occurs within the motor cortex of patients with different chronic pain syndromes but that this reorganization is not always consistent with what is seen in acute experimental pain models (increased excitability and/or decreased inhibition in these chronic pain populations vs. decreased excitability and/or increased inhibition with acute experimental pain). There are several possible explanations for these differences. First, it is possible that the effect of pain on the motor cortex changes depends on the duration of the exposure to pain. Second, several factors other than pain might contribute to the changes observed in motor excitability in the clinical populations, such as the lack of somatosensory input, disuse of the limb, loss of muscle targets, etc. For example, in the absence of pain, immobilization has been shown to induce motor cortex reorganization. Finally, it is possible that the cortical changes vary depending on the pain population. Such hypothesis is supported from studies observing the changes that occur at the somatosensory cortices level. These studies showed that the representation of the painful area decreased in patients with phantom limb pain and in patients suffering from CRPS, but increased in patients with low back pain and patients suffering from fibromyalgia. Because
of the high concordance of changes in the somatosensory and motor systems, it is conceivable that these opposite changes could also be present in the motor cortex. In that sense, the experimental pain models (using stimulations that recruit peripheral nociceptors) are quite different from the phantom limb pain patients suffering from neuropathic pain. Additional studies focusing on the changes of excitability of the motor cortex in patients suffering from somatic pain are needed to better understand the relationship between chronic pain and motor cortex activity.

Consequently, at the moment it is not possible to give clear answers to the questions “Does chronic pain interfere with motor cortex activity?” and “Does motor cortex plasticity contribute to chronic pain?”. In the two clinical populations discussed, there is evidence of some associations between changes within the motor cortex, changes in motor control and pain intensity. However, such associations do not allow us to reach any conclusions regarding causal relationships, and it is still unclear whether these associations indicate that pain drives plasticity within the motor cortex, or conversely that motor cortex plasticity contributes to the development of chronic pain. The presence of relationships between changes at the motor cortex level and pain suggest that existing models (i.e. vicious circle model and pain-adaptation model) are incomplete and cannot account for observations made in patients with neuropathic pain. It is important to keep in mind that these models were developed based on models of musculoskeletal pain. That said, reorganization of trunk muscle representation was recently shown in the motor cortex of individuals with recurrent low back pain, and this reorganization was shown to be associated with deficits in postural control. Although motor cortex reorganizations have been much less studied in populations with musculoskeletal pain than in populations with neuropathic
pain, this finding suggests that alterations within the motor cortex should be taken into consideration in a model of pain-movement interactions, even in the context of musculoskeletal pain.

One way to gain more insight into the causal relationships between pain and changes in motor cortex activity is to examine whether interventions inducing changes in motor performance and/or in motor cortex organization also modify pain. The next two sections will address the impact of motor cortex stimulation (presumably inducing motor cortex plasticity) and motor training on chronic pain.

Can the induction of motor plasticity by means of motor cortex stimulation decrease pain?

Chronic motor cortex stimulation (MCS) with surgically implanted electrodes has been performed in people with neuropathic pain over the last 20 years, and the results of several studies indicate that MCS is useful in neuropathic pain of central or peripheral origins. Given that electrical stimulation of the motor cortex can induce analgesic effects, researchers wondered whether similar effects could be induced using TMS. Repetitive TMS (rTMS) is a noninvasive method that can induce immediate and lasting changes in cortical excitability. Over the last decade, several studies have shown that rTMS applied over the motor cortex can also, at least temporarily, alleviate neuropathic pain. Until now, about 20 studies have assessed the efficacy of rTMS in more than 300 persons with drug-resistant chronic neuropathic pain from diverse origins (post-stroke pain, CRPS, trigeminal neuralgia, amputation, spinal cord injury,
brachial plexus avulsion, etc.), and recent meta-analyses show that high-frequency rTMS is associated with significant pain relief.

Does the reduction in pain following stimulation of the motor cortex indicate that motor cortex plasticity is a cause of chronic neuropathic pain? Not necessarily. The neurophysiological changes at the origin of the analgesic effects induced by motor cortex stimulation may be far from the stimulation site. In fact, electrophysiological and PET-scan studies in people receiving MCS have failed so far to demonstrate significant changes within the primary motor cortex. Current hypotheses suggest that MCS may act through other mechanisms such as: (1) activation of perigenual cingulate and orbitofrontal areas modulating the emotional appraisal of pain; (2) top-down activation of brainstem periaqueductal grey matter driving descending inhibition toward the spinal cord; and (3) triggering of mechanisms resulting in the secretion of endogenous opioids. However, changes within the motor cortex itself might also contribute to the effect of motor cortex stimulation. It has been shown that 10 Hz rTMS applied over the motor cortex can restore defective intra-cortical inhibition in people with neuropathic hand pain. Interestingly, the increase in intra-cortical inhibition was found to be correlated with the concomitant pain relief. This result suggests that restoring defective inhibitory mechanisms within the motor cortex might contribute to pain relief, but more TMS studies on the relationship between local changes induced by rTMS and pain relief are needed in order to draw definitive conclusions about whether motor plasticity induced by rTMS (or MCS) can decrease pain.
Can motor training result in both motor cortex reorganization and pain relief?

Another way to look at the relationship between motor cortex reorganization, motor control, and pain is to examine whether motor cortex plasticity driven by motor training is associated with pain relief. The changes driven by motor training are of particular interest for physiotherapists who commonly use such strategies (motor relearning, therapeutic exercises) in various pain populations. Besides the changes occurring at the level of the musculoskeletal system, activation of the motor system by the means of therapeutic exercises could indeed help to explain how active rehabilitation (focusing on movement and exercises) can help to decrease pain. This question has received particular attention in the field of phantom limb pain.

The first line of evidence that motor training can affect both motor cortex organization and pain comes from the observation that intensive use of a prosthetic hand controlled via stump muscle contractions (which can be considered as a type of motor training involving the residual limb) is associated with less sensorimotor reorganization (presumably a reversal of the maladaptive plasticity) and also with reduced phantom limb pain. However, not all studies have found an association between prosthesis use and pain and/or cortical reorganization. Moreover, the two studies that did find an association used transversal or retrospective designs, which make it difficult to ascertain that this association reflects a causal relationship. A larger cohort of patients with a longitudinal follow-up is needed in order to be able to relate motor cortex reorganization to the amount of motor training and to pain relief. At this stage it is also difficult to determine whether it is the motor act of controlling the prosthesis that is important in the reversal or
prevention of the maladaptive plasticity, or whether other factors are involved, for example the visual feedback provided by the artificial limb or the cutaneous stimulation of the stump.

A second line of evidence that motor training affects motor cortex organization and pain comes from longitudinal intervention studies showing that rehabilitation interventions can induce pain relief that is associated with changes in motor control of the phantom limb and/or motor cortex activity in people with amputations. These rehabilitative approaches targeting phantom limb motor control emerged from the observation that viewing a virtual limb moving (achieved by looking at the reflection of the intact arm in a mirror box, an approach called mirror therapy) could induce sensations of movement in the phantom limb and alleviate pain. These observations led to the idea that performing a motor training task with the phantom limb while providing visual feedback that is congruent with the movements attempted with the phantom limb might lead to a parallel improvement of motor control of the phantom limb and a reduction in phantom pain. Two randomized controlled studies have shown that such approaches lead to significantly greater improvement in pain and in the ability to move the phantom limb as compared to repeated attempts to move it without visual feedback and to mental visualization of movements of the limb. Pain reduction was also found in patients with amputation or brachial plexus avulsion using visuomotor training in which a virtual image of a missing-paralyzed limb performing different movements was presented while the patient was asked to follow the movements with his phantom limb. Interestingly, in one of these studies, an fMRI examination performed before and after the intervention showed that the amount of activity in the primary motor cortex during attempts to move the phantom hand increased after
the treatment in the two patients who experienced pain relief, while no change occurred in the patient that did not experience a decrease in pain. 83

Another fMRI study focused on cortical reorganization within primary motor and somatosensory cortices prior to and after mental imagery training that included movements of the phantom limb. 60 After training, the reduction in constant pain scores covaried significantly with the decreased activation of the contralateral hand/ arm area within the motor cortex during a lip purse movement (i.e. an indication of reversal of the presumably maladaptive motor reorganization). Patients also reported improvement in freedom of movement of the phantom limb as training progressed. Studies in patients with CRPS-I have also shown that mirror therapy, or a graded imagery program - including tasks of recognition of limb laterality (implicit motor imagery), imagined movements (explicit motor imagery), and mirror therapy - can provide a sustained decrease in pain and disability. 84-86 However, none of the studies in patients with CRPS-I documented whether these treatments resulted in motor cortex reorganization, making it impossible to ascertain whether the analgesic effect is related to motor changes.

Conclusion

In summary, acute experimental pain has clearly shown to exert an inhibitory influence over the motor cortex. This inhibition can hamper proper motor cortex activation and not only limit the immediate ability to perform a motor task, but also interfere with the ability to learn a new one. Current evidence also suggests that there is a relationship between chronic pain and motor cortex reorganization, but the causal relationship is still unclear. That said, there is growing evidence
that rTMS approaches and rehabilitation treatments whose goal are to normalize motor cortex organization can reduce pain in patients with chronic pain. One important aspect to consider from a rehabilitation perspective is that these interactions might be bidirectional and sometimes paradoxical. For example, on the one hand, pain can restrain learning during motor training, while on the other hand interventions based upon motor training can alleviate pain. Altogether the evidence reviewed here indicates that interactions between pain and motor cortex are complex. They demonstrate the need for new models of interaction between pain and movement that will take cortical mechanisms into account and will contribute to our understanding of neuropathic pain. They also underline the importance of conducting further research to better understand these interactions in patients suffering from both pain and motor deficits, as well as to develop optimal rehabilitative strategies that take these interactions into account.

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Key Messages

“What is already known on this subject”
Physiotherapists are generally aware that pain can interact with other functions during the rehabilitation process, and in particular with motor functions. These motor dysfunctions are often regarded simply as a consequence of movement-related pain or anticipated movement-related pain (e.g. kinesiophobia).

“What this paper adds”
This review paper shows that the interactions between pain and motor control are however much more complex. Acute pain exerts an inhibitory influence over the motor cortex that can interfere with motor learning capacities. Current evidence also suggests a relationship between chronic pain and motor cortex reorganization, but it is still unclear whether one causes the other. Interestingly, there is growing evidence that interventions that aim to normalize motor cortex organization can also lead to pain relief.
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