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## Masterclass

## The role of motor learning and neuroplasticity in designing rehabilitation approaches for musculoskeletal pain disorders

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## ABSTRACT

The extent of cortical neuroplastic changes has been shown to be a key neurophysiological feature that correlates with the level of functional recovery. Therefore, rehabilitation efforts that attempt to maximize cortical reorganization provide the greatest potential for rehabilitation success. This paper reviews the evidence of cortical neuroplastic changes that have been shown to occur in association with experimental or chronic pain disorders. Further, the promising role of novel motor-skill training is discussed in order to best direct the clinician to optimize rehabilitation strategies for patients with musculoskeletal pain disorders.

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## 1. Introduction

The extent of cortical neuroplastic changes has been shown to be a key neurophysiological feature that correlates with the level of functional recovery following a peripheral, spinal or cortical injury (Traversa et al., 1997; Hamdy et al., 1998; Byrnes et al., 2001; Gulino et al., 2007). For example, patients who recover their ability to swallow after having a unilateral hemispheric stroke also have a marked increase in the representation of the pharyngeal muscles in the unaffected hemisphere of the primary motor cortex (M1) (Hamdy et al., 1998). Further improvements in stroke rehabilitation success have also become evident upon the introduction of constraint induced therapy (CIT) (Kunkel et al., 1999; Miltner et al., 1999), which constrains the unaffected limb and forces the patient to maximize the usage of the affected limb. This strategy has been associated with marked cortical neuroplastic changes in the affected hemisphere (Taub et al., 1999; Oujamaa et al., 2009), which may be an underlying factor that contributes to the success of CIT in stroke patients. Thus, rehabilitation efforts that attempt to maximize the extent of cortical neuroplastic changes stand to provide the greatest potential for rehabilitation success. Although these notions are established in neurological rehabilitation, they have yet to be fully incorporated into motor rehabilitation strategies of musculoskeletal pain disorders. This brief review discusses the cortical neuroplastic changes that have been shown to occur in association with experimental or chronic pain disorders and the

role of novel motor-skill training in the rehabilitation of patients with musculoskeletal pain. The aim is to highlight key components of motor-skill training that stand to provide the greatest potential for rehabilitation success.

## 2. Cortical neuroplasticity and recovery of function

Cortical neuroplasticity is an intrinsic neurophysiological feature that occurs dynamically throughout life and can be defined as a morphological or functional change in neuronal properties, such as strength of internal connections, altered representational patterns or a reorganization of neuronal territories (Sanes and Donoghue, 2000; Calford, 2002). Cortical neuroplastic changes have been associated with altered motor function or behavior, such as that which occurs following the acquisition of novel motor-skills (Karni et al., 1995; Classen et al., 1998; Kleim et al., 2002; Korman et al., 2003; Svensson et al., 2003b; Hlustik et al., 2004; Perez et al., 2004; Koenke et al., 2006; Svensson et al., 2006; Boudreau et al., 2007; Boudreau et al., 2010a) or in the presence of experimental or chronic pain (Flor et al., 1997; Kofler et al., 1998; Le Pera et al., 2001; Cheong et al., 2003; Krause et al., 2006; Murray et al., 2006; Boudreau et al., 2007; Tsao et al., 2008). In novel motor-skill acquisition, cortical neuroplastic changes are often accompanied by behavior deemed to be advantageous, such as an increase in motor performance. Conversely, in experimental or chronic pain, neuroplastic changes are often accompanied by behavior deemed to be unfavorable, such as a decrease in performance. Since altered motor performance may be a factor for the maintenance of pain, motor rehabilitation approaches aimed at re-establishing normal motor strategies are a fundamental aspect of treatment of musculoskeletal

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pain disorders. The possibility of driving such changes in specific directions is based on the characteristics of motor-skill training

Evidence that neuroplastic changes underlie functional recovery have been best exemplified in stroke rehabilitation (Hamdy et al., 1998; Kunkel et al., 1999; Miltner et al., 1999). These demonstrations of functional recovery are also underscored by investigations of focal brain injury in the rat (Kleim et al., 2003; Ramanathan et al., 2006). Ramanathan et al. (2006) showed that the level of functional recovery, mediated by rehabilitation, is related to the ability of the M1 to re-express complex movement sequences that were initially abolished by the injury. These results suggest that the ability to promote cortical neuroplastic changes may not only be essential but may also serve as an indicator for the level of functional recovery.

Patients with musculoskeletal pain, in comparison to healthy individuals, have functional changes (reorganization) of the neuronal properties in the sensorimotor system representing the muscles most affected by pain. For example, patients with low back pain (LBP) have reduced cortical spinal drive in the lumbar spinal muscles (Strutton et al., 2005) and a shift in the representation of the lower back muscles in the somatosensory cortex (Flor et al., 1997). Additionally, a topography study of transversus abdominis responses to transcranial magnetic stimulation (TMS) in patients with recurrent episodes of LBP, showed a posterior and lateral shift in the center of gravity (CoG) and a greater representation of the transversus abdominis in the primary motor cortex, indicative of cortical reorganization, in comparison to healthy individuals (Tsao et al., 2008). The most intriguing finding, however, was that patients showed a delay in the activation of transversus abdominis EMG during a rapid arm movement task and this delay was correlated to the extent of MI reorganization. Moreover, it was recently shown that LBP patients who participated in a motor-skill training regime showed a reversal of the location of the CoG towards that previously demonstrated for healthy individuals and a reduction in self-reported pain (Tsao et al., 2010). These findings suggest that the cortical neuroplastic changes associated with pain may be reversed by motor-skill training.

Although the evidence is based on only a few studies, the extent of cortical neuroplastic changes in the sensorimotor system is emerging as a prominent factor for the maintenance of ongoing pain. For example, mean sustained pain levels are correlated to the difference of the median and ulnar nerve dipole localizations on the somatosensory cortex contralateral to the limb affected by complex regional pain syndrome (Pleger et al., 2004). A subsequent fMRI

study showed a similar correlation and a parallel reduction in tactile discrimination (Pleger et al., 2006). Further, a smaller representation of the long extensor muscles in the MI of the limb affected by complex regional pain syndrome has also been observed in comparison to the representation of the unaffected limb (Krause et al., 2006). However, following sensory and motor task training, a decrease in pain, an improvement in tactile discrimination, and an increase in the representation of the limb affected by complex regional pain syndrome was observed in the somatosensory cortices (Pleger et al., 2005). These findings of reduced pain and re-establishment of sensorimotor representations are also consistent with the results of sensory discrimination training in phantom limb pain patients (Flor et al., 2001). Together, these studies indicate that the representation of muscles affected by pain are altered in the sensorimotor system, that the extent of cortical neuroplastic changes is correlated to the level of motor function (recovery and deficit) and, most importantly, that the level of ongoing pain and the associated cortical neuroplastic changes may be reversed by sensory and motor task training.

### 3. Motor-skill training

In healthy individuals, novel motor-skill training, in contrast to passive assistance or repetitions of general exercise, has been associated with improvements in task performance and increased representation of the trained muscle in the MI (Karni et al., 1995; Pascual-Leone et al., 1995; Svensson et al., 2003b; Hlustik et al., 2004). For example, one-week of novel tongue-task training was associated with an increased motor representation of the tongue muscle and increased cortical excitability of the tongue MI (Svensson et al., 2003b) (Fig. 1). Increased cortical excitability has also been demonstrated for the hand MI following 2–4 weeks of novel motor training (Koenke et al., 2006). Furthermore, there is evidence to suggest that neuroplastic changes in the MI occur over very short training intervals. Improvements in motor performance and rapid changes in cortical excitability of the tongue MI occur immediately following 15 min of novel tongue-task training (Boudreau et al., 2007). Similar findings have been reported for training of a novel hand task (Classen et al., 1998; Boudreau et al., 2010a). These time scales of neuroplastic changes are supported by psychophysical studies which have demonstrated that the acquisition of a motor-skill follows two stages: first, an early, fast learning stage in which considerable improvement in performance is observed within a single training session and second, a later, slower learning stage in which further gains in performance can be

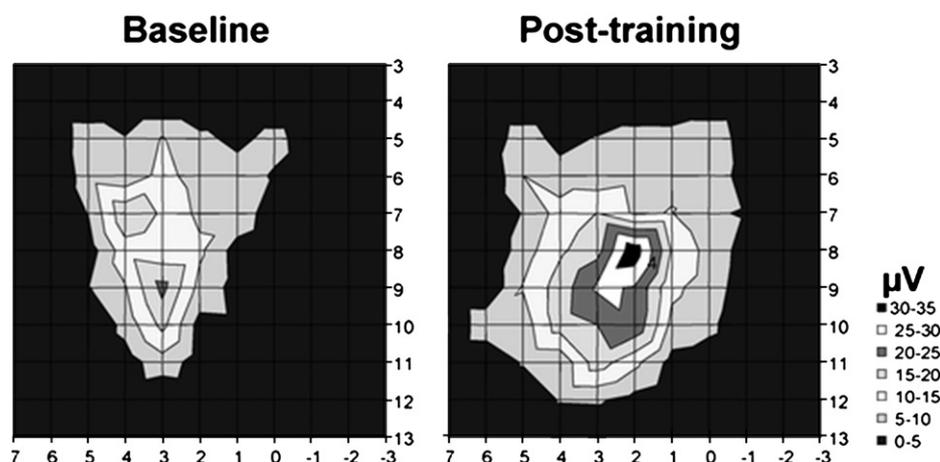


Fig. 1. Cortical motor maps of the face MI. The maps show a significant expansion of the tongue muscle representation following one-week of daily novel tongue-task training (Adapted from Svensson et al., 2003b).

observed across several sessions (and even weeks) of practice (Karni et al., 1998).

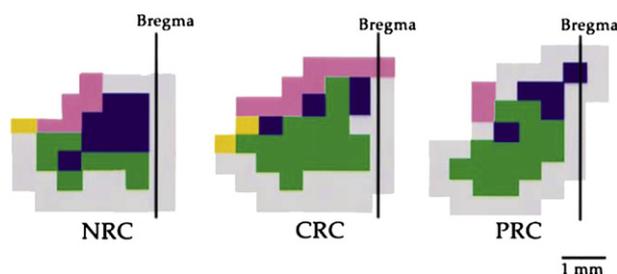
In summary, cortical neuroplastic changes in relation to motor-skill training occur rapidly and continually evolve with extended training.

Given the evidence that novel motor-skill training is associated with rapid changes in cortical excitability as well as cortical reorganization, this training type is considered relevant for treating patients with musculoskeletal pain. A common clinical approach that has been shown to be effective in the management of musculoskeletal pain disorders involves training the activation of a delayed or inhibited muscle with repeated isolated voluntary contractions (Richardson et al., 1998; Falla et al., 2007b; Jull et al., 2008; Jull et al., 2009; Tsao et al., 2010). For example, patients with neck pain may be treated by repeatedly activating their deep neck flexor muscles independently of the more superficial muscles, which constitutes a novel motor task (Jull et al., 2008). The rationale for using this approach is based on the principle of novel motor-skill training, which places emphasis on improved performance of a movement component rather than the simple execution of a sequence of movements (Fitts and Wasnor, 1967). There are, however, additional key components in motor-skill strategies that have recently surfaced and may provide a means to optimize rehabilitation success.

#### 4. Optimizing rehabilitation success

##### 4.1. Strength training does not achieve the same effect as skilled training

The ability to target a specific component of movement requires greater skill and increased levels of attention and precision than contraction of all muscles (e.g., strength training). Motor-skill training coupled with strength training does not promote greater cortical neuroplastic changes in the MI than motor-skill training alone (Remple et al., 2001) (Fig. 2). These findings support observations from patients with LBP who show a reorganization of the M1 following isolated training of the transversus abdominis muscle and not following a common exercise walking task (Tsao et al., 2010). Moreover in patients with neck pain, improvements in the amplitude and speed of activation of the deep cervical flexor muscles occur with isolated training of these muscles and not strengthening exercises (Jull et al., 2009). Such findings suggest that skilled or precision tasks should be used in order to facilitate the cortical neuroplastic changes that are known to occur in association with the learning stages of untrained functional tasks which will ultimately lead to improvements in motor behavior or performance.

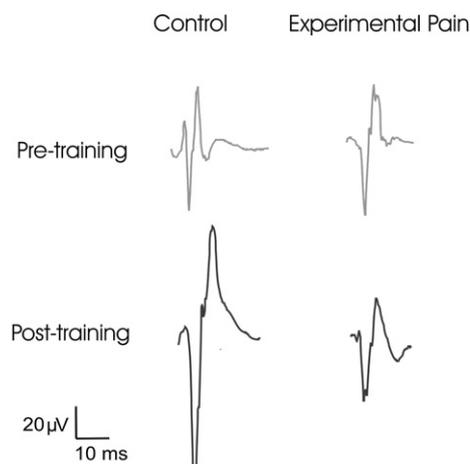


**Fig. 2.** Cortical motor maps of the rat M1. Skilled forelimb (CRC) and skilled power reaching paired with power or strength demand (PRC) result in significant increases in the representation of the forelimb (from blue to green) when compared to non-reaching (NRC). These motor maps also show that there are no additional cortical neuroplastic changes that occur for the strength protocol (Remple et al., 2001).

##### 4.2. Pain can hinder the cortical neuroplastic changes associated with novel motor-skill acquisition

To date, studies which have examined the effects of acute experimental pain have revealed that, as with novel motor-skill training, pain can rapidly alter the excitability of the MI (Farina et al., 2001; Le Pera et al., 2001; Cheong et al., 2003; Svensson et al., 2003a). Further research, however, is required to discern the features of the cortical neuroplastic changes associated with novel motor-skill training and that which occurs in association with experimental or chronic pain. In contrast to the rapid changes associated with novel motor-skill acquisition, the changes in cortical excitability that occur in association with acute pain are not necessarily consistent for the muscle groups represented in the MI. For example, noxious electrical stimulation of the finger induces an increased excitability of the hand MI but a simultaneous decreased excitability of the proximal (upper arm) muscles (Kofler et al., 1998). These pain-related changes in excitability of the MI may contribute to protective motor control strategies (e.g., reduced range of motion) that can occur in association with a painful limb or muscle and are consistent with alterations in muscle strategies observed following experimentally induced muscle pain (Graven-Nielsen et al., 1997; Falla and Farina 2008). For example, when pain is acutely induced in the neck muscles of healthy subjects, the coordination among neck muscles is substantially altered (Falla et al., 2007a). Similar findings are observed in patients with chronic musculoskeletal pain.

Notably, acute experimental pain has been shown to suppress the rapid increases in cortical excitability of the MI and to interfere with the incremental gains in task performance that would otherwise occur in association with a single-session of novel tongue-task training in humans (Boudreau et al., 2007) (Fig. 3). In line with these findings, animal studies have revealed that experimental pain interferes with the neuroplastic changes that underlie simple instrumental learning (condition and response) at the level of the spinal cord (Ferguson et al., 2006; Hook et al., 2008). The notion that pain may hinder novel motor-skill acquisition is in agreement with observations at various behavioral levels for chronic pain patients. Increased stress responses during a cognitive task (Thieme and Turk, 2006), reduced cognitive performance (Apkarian et al., 2004; Moseley, 2004a,b; Weiner et al., 2006; Dick and Rashiq, 2007), reduced quality of sleep (Roehrs and Roth, 2005), and



**Fig. 3.** Motor evoked potential (MEP) elicited in the tongue. The MEP amplitude increases following novel motor-skill training but it does not change when novel motor-skill training is performed in the presence of experimental pain (Boudreau et al., 2007).

attention deficits (Eccleston et al., 1997; Grisart and Plaghki, 1999), can affect learning. Furthermore, recent experimental pain studies have demonstrated that remote pain can also hinder motor learning, as pain itself can be a distraction (Tucker et al., 2010). Taken together, these findings suggest that motor-skill training should be performed in a pain-free manner in order to optimize success. The type, load and frequency of exercise should be tailored towards the patient to ensure that this criterion can be met.

#### 4.3. Motor-skill training can protect against the cortical neuroplastic changes associated with pain

While the experimental pain studies undoubtedly provide a link between pain and altered motor control (Falla and Farina, 2008; Graven-Nielsen and Arendt-Nielsen, 2008), there is less evidence to support the initiation of pain as a consequence of altered motor control. It can be speculated that deficits in motor control of the spine lead to poor control of joint movement, repeated micro-trauma and eventually to pain (Panjabi, 1992a,b). For example, augmented activity of the upper trapezius and the levator scapulae muscles, due to a poor working posture of the neck or of the arms, may over time increase compressive loads on the cervical segments and initiate a painful neck condition. Likewise, inhibition of the deep abdominal muscles may affect the stability and posture of the lumbar spine increasing the likelihood of LBP (Hodges and Moseley, 2003). Although there is no consensus on the cause-effect relationship between altered motor control and pain, there is a string of evidence that pain is associated with altered motor control.

A series of studies performed in animals has revealed that motor training prior to acute experimental pain can preclude the pain-associated neuroplastic changes in the spinal cord that would otherwise occur (Hook et al., 2008). Although these findings have yet to be reproduced in human studies, the notion that motor training can reduce the extent of cortical neuroplastic changes associated with pain is congruent with results of animals studies that have explored the possibility of exercise and motor enriched environments as a pre-emptive strategy to reduce the repercussions of brain injury (Kleim et al., 2003).

In summary, novel motor-skill training should be advocated upon the first presentation of pain symptoms so as to reduce the risk of further and unfavorable neuroplastic changes that are known to occur in association with pain.

#### 4.4. Encourage cognitive effort

Goal-oriented or 'cognitive' effort significantly contributes to the extent of cortical neuroplastic changes associated with novel motor-skill acquisition. For example, the performance of a goal-oriented sequential finger-tapping task over 5 days is associated with an increased representation of the trained muscle in the MI compared to a protocol that required mental rehearsal of the finger-tapping task and even more so than random non goal-oriented finger-tapping protocol (Pascual-Leone et al., 1995). Moreover, the performance of a complex finger-tapping task results in additional areas of cortical activation, as measured by fMRI, when compared to a simple finger-tapping task (Sadato et al., 1996). Further, the amount of overlapping cortical territories in the MI that is altered with training is greater when training of simple finger and wrist movements are paired with fine (finger sequence learning) rather than gross (squeezing a sponge) motor-skill training (Hlustik et al., 2004). In agreement with these human studies, animal studies show that increasing the complexity of a skilled reaching task results in a relatively larger expansion of the digit and wrist representations, as defined by intracortical microstimulation of the MI (Kleim et al., 2002).

In summary, slowly increasing the complexity of the novel motor-skill task over the duration of rehabilitation training may encourage cognitive effort and enhance the cortical neuroplastic changes that are known to occur in association with novel motor-skill acquisition.

#### 4.5. Quality versus quantity

A detailed analysis of the motor behavior associated with novel motor-skill training has revealed that significantly different within-session gains in an initial motor-skill training session do not differentially influence the time course of the initial or overall motor performance in subsequent training sessions (Boudreau et al., in press). The time course of these gains in overall motor performance were similar for protocols which consisted of 72 or 144 task-repetitions over a period of 15 and 30 min, respectively (Boudreau et al., 2010b), as also supported by earlier work (Svensson et al., 2003b). These studies provide evidence that extended within-session task-repetitions of a novel motor-skill may not facilitate additional gains in overall motor performance. Such findings suggest that excessive repetitions of a motor task within a training session may not result in additional benefits. This notion may be extended upon consideration that rapid changes in cortical excitability are already apparent following short (Approximately 60 within-session task-repetitions over a period of 10–15 min) training intervals (Boudreau et al., 2007, 2010b). Accordingly, task-repetitions should be limited in order to ensure that factors such as fatigue or pain are minimized. Further, the quality of training appears more important for improving the performance of a motor task. For example, changes in the timing of activation of the transversus abdominis muscle have been correlated to the quality of training and are associated with improvements in self-reported pain and function (Tsao et al., 2010).

## 5. Conclusion

Rehabilitation efforts that attempt to maximize the extent of cortical neuroplastic changes stand to provide the greatest potential for rehabilitation success. Clinical and experimental findings suggest that quality motor-skill training that encourages cognitive effort should be performed with a limited number of task-repetitions such that fatigue and pain are minimized in order to optimize the outcome of rehabilitation of patients with musculoskeletal pain.

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