Impact of Clinical and Experimental Pain on Muscle Strength and Activity

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Current Rheumatology Reports 2008, **10:**475–481
Current Medicine Group LLC ISSN 1523-3774

A reorganized motor control system is a key factor in musculoskeletal pain conditions, and its relevance in the transition from acute pain to chronic pain is most likely underestimated. The interaction between muscle pain and motor control depends on the specific motor task. Muscle pain causes no increase in electromyographic activity at rest and reduces maximal voluntary contraction and endurance time during submaximal contractions. Furthermore, muscle pain causes an adaptive change in the coordination during dynamic exercises. Increased muscle activity reflecting reorganized muscle coordination and strategy is also a component of the functional adaption to muscle pain. In general, the "vicious cycle" hypothesis is not supported by these findings. Instead, they support an adaptive model predicting reduced agonistic muscle activity eventually advanced by changed antagonistic muscle activity. The motor control assessment procedures provide complementary clinical information and give further support for optimizing treatment regimens and prevention procedures for musculoskeletal pain.

Introduction

Deep-tissue pain constitutes a special diagnostic and therapeutic challenge, and new knowledge on peripheral and central neurobiological mechanisms is necessary to improve diagnosis and management strategies. Human experimental pain models applied to healthy volunteers are a potential strategy to investigate functional aspects of deep-tissue pain. Experimental muscle pain research involves two separate topics: 1) standardized excitation of the nociceptive system, and 2) quantitative assessment of the related sensory and motor responses. In this situation, healthy volunteers transiently become patients with a well-defined muscle pain where the sensory–motor interaction can be assessed in line with the sensory manifestations. Several techniques have been used to induce human muscle pain [1], and this article describes the basic effects of induced muscle pain on muscle coordination. The mutual link between experimental muscle pain and changes in motor control cannot be directly transferred to the clinical conditions with chronic muscle pain. Nonetheless, many groups of patients suffering from chronic muscle pain, such as low back pain, fibromyalgia, and myofascial temporomandibular pain, demonstrate similar changes in the muscle coordination as found in groups with experimental muscle pain. One important advantage with experimental muscle pain studies is that the cause and effect relationship is known (ie, the effects of pain on movement coordination can be described by electromyographic [EMG], kinematic, and force recordings). Thus, the use of experimental muscle pain can elucidate basic biological motor-control mechanisms, which are affected by muscle pain. These mechanisms are likely involved in chronic muscle pain conditions, in parallel with the mechanisms responsible for the transition from acute to chronic pain.

Functional implications of muscle pain are evident from daily life, where pain from joints and muscles affects motor performance or causes facial expressions (ie, the painful limb or area is protected by voluntary or reflex-based movements with reduced amplitude or strength). Associated with the impact of pain on the motor performance is the contrary condition, which is that muscle work can induce musculoskeletal pain. Within occupational health, it is still not clear why some individuals develop musculoskeletal pain and others do not, even though they are exposed to the same working conditions. Potentially, the interactions of pain to motor function and motor function to pain are related in a mechanistic manner.

Experimental Muscle Pain

Acute deep-tissue pain is caused by activation of group III (Aδ-fiber) and group IV (C-fiber) polymodal muscle

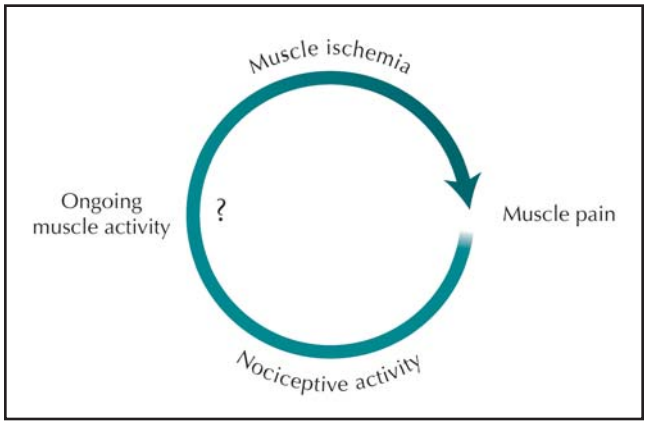

Figure 1. The vicious cycle hypothesis posits ongoing muscle activity triggered by muscle pain. Ischemia is a natural course of increased muscle activity, and over time ischemia might also lead to deep-tissue pain. The other part of this model assumes that ongoing muscle activity is evoked by muscle nociception, but this notion is disputed.

nociceptors [2]. Strong mechanical stimuli and algesic substances can excite the nociceptors contrary to muscle contraction, normal movements, or muscle stretch.

Algesic substances

Various algesic substances have been used to induce experimental muscle pain in humans [1]. In particular, the hypertonic saline model has been used to characterize the sensory and motor effects involved in muscle pain because the quality of the induced pain is comparable with acute clinical muscle pain and shows localized and referred pain characteristics. Jonas Kellgren and Sir Thomas Lewis introduced the method of experimental muscle pain induced by injection of hypertonic saline. Manual bolus injections of hypertonic saline were often used, and the model was later improved by computer-controlled infusions of hypertonic saline, which gave a more standardized model and allowed the induction of tonic muscle pain by continuous infusion. The saline-induced muscle pain intensity is dependent on concentration, volume, and infusion rate. The quality of saline-induced muscle pain is typically described as "aching," "cramping," "boring," "drilling," "taut," "tight," "spreading," and "radiating." The saline-induced pain model has been used to a great extent in studies on the influence of muscle pain on motor control, and adverse effects associated with saline-induced muscle pain have been reported [1]. Animal studies did not show muscle toxicity by this method, which underpins its use for human experimentation.

Robust excitation of group III and IV afferent fibers by hypertonic saline has been shown in animal studies [3], in contrast to excitation of thick, fast afferent fibers [3]. Iggo [4] reported, however, that other afferent fibers (eg, related to muscle spindles) than group III and IV were excited by hypertonic saline, although no specific details were given. The predominant excitation of thin caliber afferents by hypertonic saline is also substantiated by an inverse relationship between the nerve conduction velocity and saline-evoked cumulative afferent discharges [3]. Other algesic substances (eg, capsaicin, glutamate, acidic buffers) have also been used for induction of experimental muscle pain [1].

Exercise-induced muscle pain

Muscle pain induced by concentric muscle work (eg, cycle ergometry) is normally brief and a result of impaired blood flow during work. Thus, it may resemble the condition of ischemic muscle pain. Eccentric muscle work causes delayed onset of muscle soreness, with peak soreness after 24 to 48 hours. Delayed onset muscle soreness (DOMS) has been widely used to explore pathophysiologic components of the musculoskeletal system. The mechanism underlying delayed-onset muscle soreness is not clear but is probably related to ultrastructural damage resulting in the release of algesic substances. The release of algesic substances may cause an inflammatory reaction, as NSAIDs appear to have an effect on this type of muscle soreness in some conditions.

Models of Pain–Motor Interaction

Like the classical sensory afferent fibers involved in motor control (eg, tendon organs and muscle spindles), there is dense connectivity (via interneurons) from group III and IV afferents to the motoneurons in the ventral horn. Group III afferents with nociceptive properties were recently reported to have the strongest influence on the reflex control [5].

The vicious cycle model

From daily life activities, it is evident that muscle pain interacts with the movement capabilities. Muscle hyperactivity sustained by a vicious cycle due to muscle ischemia was one of the first theories explaining the cause of muscle pain (Fig. 1) [6]. The part of the model suggesting that muscle pain will induce ongoing muscle activity was not systematically investigated until recently. Based on animal data, a physiologic model proposes muscle hyperactivity due to facilitation of the fusimotor system by muscle pain [7]. A facilitated fusimotor system was suggested to cause a reflex-mediated spread of muscle stiffness and possible initiation of a vicious cycle. The muscle spindle activity is, however, not facilitated by muscle nociception, but rather by a change in spindle sensitivity affecting the proprioceptive function [8].

The pain-adaptation model

This model was proposed by Lund et al. [9] to explain the link between activity in nociceptive afferents, a central pattern generator, the motor function, and coordination of muscles. This pain-adaptation model predicts increased muscle activity in antagonistic phases and decreased muscle activity in agonistic phases during muscle pain; such a

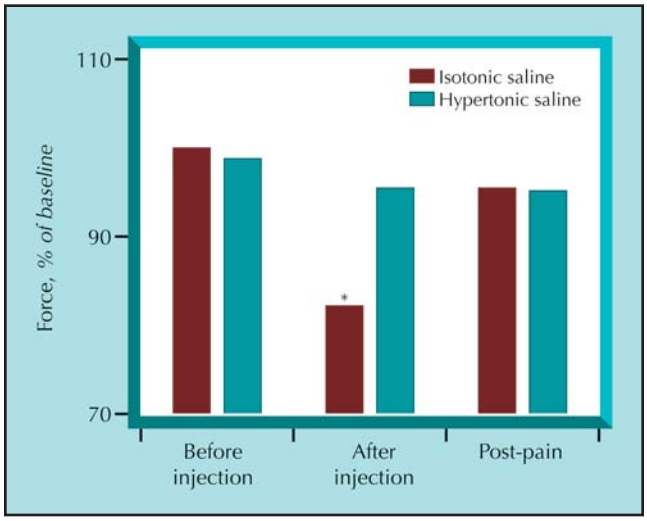

Figure 2. Mean maximal voluntary knee extension force assessed before and after injection of isotonic and hypertonic saline into the rectus femoris muscle. There is significantly decreased torque compared with both before and after recordings and compared with the recording immediately after injection of isotonic saline (*asterisk*). (*Data from* Graven-Nielsen et al. [23].)

coordination may produce a decrease in movement velocity and amplitude. The pain-adaptation model includes an inhibitory and excitatory facilitation of motoneurons according to the functional phases (agonist or antagonist) of the painful muscle. This supports the need for assessing functional effects of muscle pain in the various functional phases of dynamic contractions as well as in contractions without movements (static) and in resting conditions.

Spontaneous Muscle Activity at Rest

A small increase (less than 1% of EMG from maximal voluntary contraction [MVC]) in the resting activity of the sternocleidomastoid muscle was reported after injecting 5 mL of hypertonic saline (5%) into this muscle [10]. Pain in this muscle may be associated with changes in facial expression, and the observed increase in the EMG activity was likely due to cross-talk from the platysma muscle. Compared with baseline recordings, but not compared with a sham pain condition where patients recalled a painful condition (without the actual pain stimulation), increased resting muscle activity after saline-induced muscle pain was found [11]. This indicates that increased muscle activity is not caused by the muscle pain per se. In a later study, a transient increase in the resting EMG activity during intramuscular infusion of hypertonic saline was recorded in contrast to recordings after the infusion of isotonic saline [12]. It is important to note that ongoing muscle pain did not produce sustained increased EMG activity. Moreover, saline-induced muscle pain does not cause any changes in the resting EMG activity between repeated MVCs [13]. Other models of experimental muscle pain (eg, glutamate induced) have shown increased resting activity in neck and facial muscles, suggesting a difference between pain modalities or muscles [14]. The increased resting muscle activity during glutamate-induced muscle pain is found predominately when assessed in fatigued muscle [15], and this seems to be more evident in men compared with women [16].

Spontaneous muscle activity in clinical studies

Increased and unchanged resting EMG activities have been reported in musculoskeletal pain patients, in contrast to patients in experimental pain studies. An increase in the resting EMG activity between contractions was recorded in fibromyalgia patients [17]. Other clinical studies report no increase in the resting muscle EMG activity in fibromyalgia [18], temporomandibular disorder [19], chronic neck pain caused by trapezius myalgia [20], and low back pain patients [21]. Moreover, spontaneous muscle activity and unchanged resting muscle activity have been reported at the time for maximal soreness caused by eccentric contractions (delayed-onset muscle soreness).

The findings of increased human EMG activity during muscle pain are limited, which is in strong contrast to the increases in EMG activity in animal studies [22]. The most expressed responses in animal studies are seen in jaw-opening muscles and a weaker effect in the jaw-closing muscle; this may be interpreted as a reflex reaction in order to avoid movements.

Contractions Without Movement (Static)

During saline-induced muscle pain, the MVC force is significantly lower than in a control condition (Fig. 2) [13,23]. The decrease of MVC force during experimental muscle pain was not related to changes in the contractile properties of muscle fibers but rather to a central effect on the motor control system [23,24]. Decreased muscle strength during voluntary isometric contractions of a painful muscle has also been found in musculoskeletal pain patients. The reduction in strength in fibromyalgia patients is suggested to be caused by a deficient central activation of motor units, because supramaximal stimulation of the ulnar nerve shows no difference in the strength of the adductor pollicis muscle between patients and a control group [25]. Attenuated MVC is also found in more localized pain conditions; in lateral epicondylalgia patients, reduced strength is recorded in their sore arm compared with asymptomatic arms in control patients [26]. In contrast, increased muscle activity during static contractions in trapezius myalgia patients has also been reported [20].

Effects of muscle pain on submaximum contractions

Decreased surface EMG activity is detected for contraction levels above 25% MVC [27••], and at low contraction levels decreased muscle activity is evident by reduced firing rate of single motor units [28]. The pain intensity and the amount of reduced motor unit firing

are correlated [28]. Decreased motor unit firing rate is also detected in nonpainful but fatiguing contractions, and the initial firing rate is reduced to the same level as during fatiguing contractions, indicating that the nociceptive activity in group III and IV afferents is related to the reduced motor unit firing during fatigue [24].

Effects of muscle pain on synergistic muscle activity

A significant observation is that the muscle pain during static contractions does not only decrease the muscle activity of the painful muscle, but also attenuates the synergistic muscles [27••]. The distribution of muscle activity across a muscle can be assessed by surface matrix EMG electrodes, allowing recordings from multiple EMG electrodes within one muscle; the trapezius muscle activity pattern was found to be reduced and reorganized by experimental muscle pain [29••]. The generalized pain-related inhibition calls for a changed muscle coordination and eventual overload of otherwise nonpainful muscles if the required force must be archived. The motor unit firing rate is an important determinant of the force generated by a muscle, and therefore it is unclear how a constant force requirement can be archived and maintained in case of a pain-related decrease in motor unit firing rate. Motor unit twitch properties may change as a compensatory mechanism for the decreased motor unit firing during pain, and increased twitch force of low-threshold motor units has been recorded during experimental muscle pain [24]. However, the muscle membrane properties seem not to be affected by experimental muscle pain, as both motor unit conduction velocity and M-wave recordings are unchanged [24]. The peak twitch force also remains increased in post-pain conditions, as the motor unit firing rate returned to normal [24]. This interesting finding suggests that the facilitated twitch force is not the mechanism compensating for the decline in motor unit firing rate during pain. An alternative mechanism for the maintenance of force is that the nervous system may increase the activity of synergistic muscles to compensate for decreased force production by a painful muscle. Nonetheless, a recent study found that motor units in synergistic muscles neighboring a painful muscle show reduced firings [30], and therefore increased firing of low threshold motor units in synergist muscles does not account for maintenance of force during painful constant force contractions. Recruitment of higher threshold motor units during pain is a potential mechanism to explain the maintained force with reduced motor unit firing.

Facilitated fatigue by muscle pain

In submaximal contractions (80% of the MVC before pain), experimental muscle pain causes a significant reduction in endurance time [13]. The different findings between the submaximal contraction (where the required force can be obtained during pain) and the maximal contraction force (which is reduced by muscle pain) may be explained by changes in the descending drive to motoneurons. During MVC, the descending neural drive cannot be voluntarily increased; therefore, an inhibitory mechanism controlling the motoneurons might explain the decreases in MVC. In contrast, when submaximal contractions are performed, the voluntary neural drive may be increased and thus compensate for potential inhibitory mechanisms. The shorter endurance time with experimental muscle pain is accompanied by a prolonged recovery period after fatiguing contractions [31•], obviously making the combination of pain and fatigue a detrimental condition.

Decreased endurance time is reported in muscle pain patients performing a submaximal contraction compared with age- and sex-matched controls [32], which is in line with experimental findings [13]. Submaximal contractions during muscle pain may be achieved by increased voluntary neural drive, and the decreased endurance time may therefore be due to a more pronounced central fatigue. Various physiologic factors within the muscle (eg, microcirculation) could influence the endurance time in patients, but this is not likely to occur in healthy volunteers exposed to experimental muscle pain.

Delayed-onset muscle soreness and motor function

The saline-induced muscle pain model has been widely used and has been shown not to affect the contractile apparatus [23]. DOMS is probably based on ultrastructural damage affecting the contractile properties, resulting in loss of force. Inhibition of motor cortex and/or spinal motoneurons may contribute to the loss of force, especially in the first 24 hours [33]. Recently, it was reported that eccentric contractions caused reduced EMG amplitude over time during sustained contractions, which was not seen prior to DOMS, indicating a change in the contractile properties [34]. No change [35], increased [36], and decreased [37] EMG activity of static contractions in DOMS have also been reported. Therefore, in conditions including changes of the contractile properties in addition to modulation of motor control parameters by nociception, caution is needed when delimiting involved mechanisms.

Contractions During Movement (Dynamic)

In one of the first studies assessing effects of pain on dynamic contractions, low back muscle activity during gait on a treadmill was recorded in experimental and clinical low back pain. During pain, the low back muscle activity was increased in phases where the EMG activity is normally silent, and it was not affected or decreased in the phases with strong EMG activity in controls [38]. Muscle pain during gait generally causes decreased activity in the agonistic phase and increased activity in the antagonistic phase of the leg muscle [13]. A similar example is found in trunk flexion-extension movements, where the antagonist phase, normally silent in pain-free controls, showed increased activity in patients with low back pain [39].

This suggests that the pain modulation of muscle activity is dependent on the specific muscle function (agonist/antagonist phases), a finding that also has been reported in several clinical studies [9]. Reduced movement amplitudes are the functional consequence of pain and have been found in experimental and clinical musculoskeletal pain conditions such as low back pain [38].

Reorganized motor control

The reorganized motor control may protect the painful muscle by a reduction of the muscle activity and contraction force. Other strategies might also be adopted, as individual combinations of decreased, increased, and cocontraction activity of trunk flexors and extensors were reported during experimental low back pain [40]. Reduced activity in both the agonistic and antagonistic muscles during muscle pain has been reported without significantly impairing the movement amplitude or acceleration [41]. Specifically, the initial (100 ms) EMG burst recorded from the agonist muscle was decreased, illustrating the reorganized motor strategy caused by muscle pain. A similar example of changes in motor planning is illustrated by reduced feed-forward responses of the abdominal muscles in conditions of pain induced in the lower back muscles, which might compromise the spinal stability [40]. Gait initiation is also dependent on specific motor control strategies, and these were affected by experimental muscle pain [42]. Anomalous motor planning is highly important in working conditions where such a change may need compensatory activity from other muscles to fulfil the required movement, and such a scenario may contribute to the development of musculoskeletal pain problems in occupational settings. A potential compensatory action may be the increased trapezius activity recorded during biceps muscle pain [41]. Similarly, reorganization of trapezius muscle activity during repetitive shoulder flexion has been found as decreased activity of the upper trapezius (where pain was induced), whereas the lower trapezius showed compensatory actions by increased muscle activity [43].

Functional impact on joint stability

Deep-tissue pain can have significant biomechanical impact on the other skeletal structures. The functional significance of muscle pain on knee joint control during gait was recently assessed by three-dimensional gait analyses during experimental pain (medial muscle of vastus medialis); impaired knee joint control and joint instability during walking was the functional consequence of the induced muscle pain [44••]. Similar changes are observed in patients with osteoarthritic knee pain. The deficit of joint control may leave the knee joint prone to injury and potentially participate in the translation from acute to chronic musculoskeletal problems. Such biomechanical effects of pain will have clinically important implications for the rehabilitation and training of patients with knee pain of musculoskeletal origin.

Excitability of Motoneurons

The neuronal mechanisms potentially involved in the pain-related reduction of muscle activity may be numerous. The H-reflex is not changed in contrast to the stretch reflex, which is facilitated during experimental muscle pain [45]. Microneurography recordings from spindle afferents showed no increased discharge activity during experimental pain, indicating that muscle pain does not cause a reflex increase in the fusimotor drive, in contrast to the hyperactivity theory [46••]. Facilitated stretch responses might be related to a more pronounced stiffness in the painful motor system and cause impaired motor performance. The long-latency inhibitory reflex (silent period) is disinhibited (ie, net facilitation) during experimental muscle pain [47]. There is no consistent relation between the findings of reflex facilitation and decreased muscle activity during muscle pain. However, most studies assessing the effect of experimental muscle pain on reflexes have not assessed the potential effect of postsynaptic modulation by nociceptive activity because the muscle activity was kept constant before assessing the reflex. Recently, facilitated homonymous recurrent inhibition of the soleus muscle during experimental muscle pain was reported with a close relation between the temporal aspects of the pain and strength of recurrent inhibition [48]; reduced muscle activity during muscle pain might be a result of facilitated recurrent inhibition.

Differential effects of muscle nociception on spinal and cortical motoneurons illustrate the complex changes in the motor neuronal system due to pain. Muscle nociception facilitated spinal motoneurons innervating elbow flexor and extensor muscles, and at the same time depressed motor cortical neurons projecting to these muscles [49••]. Another study showed reduced motor evoked potentials (by transcranial magnetic stimulation) from the abductor digiti minimi muscle during muscle pain, and with a time delay the spinal motoneurons also showed reduced excitability assessed by the H-reflex [50]. The complex interaction between pain and reflexes is probably due to the highly flexible and plastic motor control system.

Conclusions

A reorganized motor control system is a key factor in musculoskeletal pain conditions (Table 1), and its relevance in the transition from acute pain to chronic pain is probably underestimated. In general, the vicious cycle hypothesis is not supported by the reviewed data, but the data do support an adaptive model predicting reduced agonistic muscle activity eventually advanced by decreased antagonistic muscle activity. Recent animal data also suggest a similar reorganized motor control system. The current experimental pain approach is essential when translating basic findings with clinical manifestations. The motor control assessment procedures can provide complementary clinical information and give further support for optimizing treatment regimens and developing prevention procedures for musculoskeletal pain.

Table 1. Typical effects of experimental muscle pain on the motor control system

Resting conditions	No ongoing spontaneous activity
Static contractions	Reorganized and reduced muscle activity
	Attenuated synergistic muscle activity
	Reduced firing of single motor units (pain-intensity dependent)
	Aggravated fatigue effects
Dynamic contractions	Decreased agonist muscle activity
	Adaptive change of antagonistic activity (increased or decreased)
Functional effects	An adaptive function potentially protecting the painful structure
	Decreased amplitude and velocity of movements

Disclosures

No potential conflicts of interest relevant to this article were reported.

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