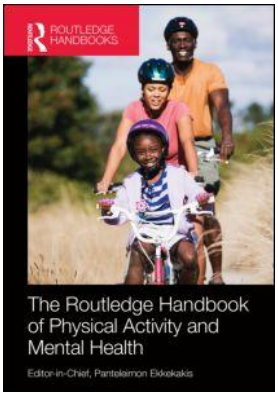

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PART 7

Pain

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24

THE INTERACTION OF MUSCULOSKELETAL PAIN AND PHYSICAL ACTIVITY

Human studies

Thomas Graven-Nielsen, Henrik B. Madsen, and Lars Arendt-Nielsen

This chapter is intended to provide an overview of the research regarding exercise and muscle pain in humans, focusing on both the potential for exercise to reduce pain sensitivity and for pain to interfere with muscle function. In order to accomplish this, the chapter is divided into two sections. The first will describe the acute effects of exercise on pain in both healthy individuals and those with chronic pain conditions. The second will discuss the effects of pain on motor control systems with an emphasis on understanding how acute pain may translate into chronic pain conditions.

Effects of exercise on pain: exercise-induced hypoalgesia

Anecdotes about athletes who did not report pain following severe injuries during sports competition have contributed to the notion that exercise may alter pain perception. Over the past 30 years a number of studies have examined whether analgesia occurs during or following exercise. This area of research has produced evidence that one potential benefit for healthy individuals performing acute exercise is a reduction in pain sensitivity.

Exercise-induced hypoalgesia in healthy subjects

Several studies on healthy subjects have reported that pain intensity and unpleasantness are decreased (Koltyn, Garvin, Gardiner, & Nelson, 1996; Koltyn, 2000; Umeda, Newcomb, Ellingson, & Koltyn, 2010; Droste, 1991; Hoffman et al., 2004) and that pain thresholds as well as pain tolerance increased during and after aerobic, isometric and resistance exercise. Early research in this area was limited by significant methodological flaws (e.g., no control group), leading some to conclude that reduced pain sensitivity following exercise was simply a phenomenon of pre-exposure to painful stimuli (Padawer & Levine, 1992). However, subsequent research has clearly demonstrated that reduced pain sensitivity occurs following acute exercise when compared to no-exercise control conditions (Gurevich, Kohn, & Davis, 1994; Koltyn et al., 1996). This phenomenon has been referred to as exercise-induced analgesia or more recently, exercise-induced hypoalgesia (EIH). Most research on EIH has been conducted using aerobic exercise (bicycling or running), although studies using isometric exercise are common. Only a

few studies have investigated the effect of resistance exercise on pain perception. Several types of experimental pain modalities, including mechanical, thermal and electrical stimuli, have been used to assess pain sensitivity following exercise. Although evidence exists that exercise reduces sensitivity to all the pain modalities tested, EIH is most consistently observed for mechanical and electrical stimuli (Koltyn, 2000; Hoeger Bement, 2009). Changes in pain intensity and unpleasantness occur not only in the exercised body part or within a few segmental levels, but also at distant sites, indicating that the central nervous system could play an important role in modulating pain during and following exercise (Kosek & Lundberg, 2003).

Exercise intensity and duration: Aerobic exercise most consistently produces a hypoalgesic effect when performed at intensities equal to or higher than 200 Watts or at 60–75% of maximal oxygen uptake ($\dot{V}O_2$ max) (Koltyn, 2002; Droste, 1991; Hoffman et al., 2004). Duration of exercise is also important and there appears to be an interaction between intensity and duration. Hoffman et al. (2004) assessed the pain sensitivity in healthy subjects before and after treadmill running and found that pain sensitivity decreased after exercise at high intensity (75% of $\dot{V}O_2$max) and longer duration (30 minutes). Pain sensitivity was not affected by exercise at the same intensity for a shorter time (10 minutes) or at reduced exercise intensity (50% of $\dot{V}O_2$max) that was of longer duration (30 minutes). Similar results have been reported in an animal study, where animals that run more have higher pain thresholds than animals that run less (Shyu, Andersson, & Thoren, 1982). Interestingly, in healthy subjects passive cycling induced pressure hypoalgesia compared with a control condition (Figure 24.1) (Nielsen, Mortensen, Sorensen, Simonsen, & Graven-Nielsen, 2009), indicating the role of joint movement or proprioception in EIH.

In contrast to aerobic exercise, EIH is produced with isometric exercise at both low and high intensity. Hoeger Bement and colleagues reported that isometric contractions at longer duration

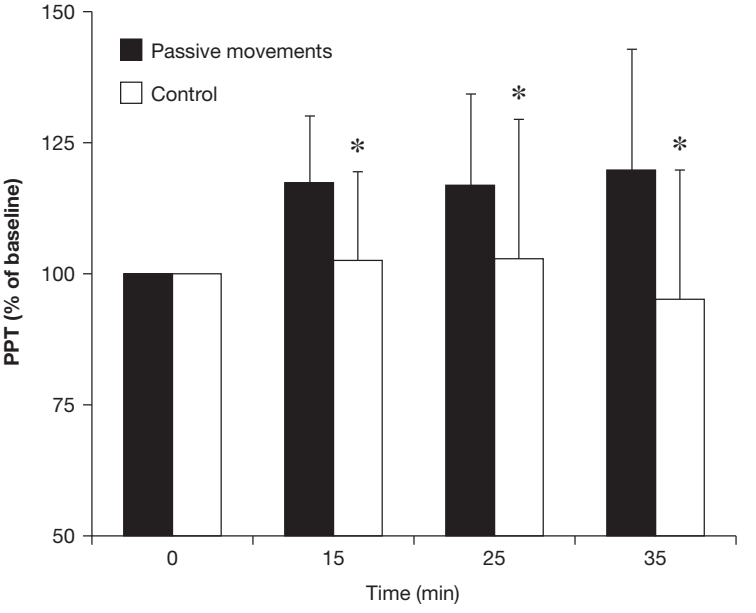

Figure 24.1 Average PPT (+ SD, N = 14, percentage of baseline) before and during passive physiological movements. Passive joint mobilization of the knee joint was implemented by an electrical bicycle (30 rpm) in blocks of 10–15 minutes in between assessment of the pressure pain thresholds. The pressure pain thresholds were increased at the lower leg compared with baseline and during control sessions (⋆: $P < 0.05$) (based on data from Nielsen, Mortensen, Sorensen, Simonsen, & Graven-Nielsen et al., 2009).

and lower intensity caused a greater decrease in pain sensitivity compared with contractions at low and high intensities of shorter duration (Hoeger Bement, Dicapo, Rasiarmos, & Hunter, 2008). However, Umeda and colleagues (Umeda, Newcomb, Ellingson, & Koltyn, 2010) failed to find a dose-response relationship for isometric handgrip performed at 25% of maximal voluntary contraction for 1, 3 and 5 minutes. Although blood pressure was found to increase in a dose-response manner, pain sensitivity did not differ among the three durations. Thus, it appears that isometric exercise can be performed at lower intensities to produce EIH and that the duration of exercise may be less important for isometric than aerobic exercise.

Compared to aerobic exercise, EIH to resistance exercise has been less studied. Koltyn and Arbogast (1998) assessed pain threshold and pain ratings in healthy subjects before and after 45 minutes of resistance exercise performed as four different exercises with three sets of ten repetitions at 75% of maximal voluntary contraction and found increased pain threshold and decreased pain ratings compared to quiet rest 5 minutes after exercise, but not 15 minutes after. Anshel and Russell (1994) studied the effect of 12 weeks of strength training compared to aerobic training and no training on pain tolerance and mood in unfit males and found that strength training had no positive influence on pain or mood, but, oddly, increased depressed mood.

Duration of exercise-induced analgesia: The hypoalgesic effect of exercise is larger during exercise compared with post-exercise measurements (Kosek, Ekholm, & Hansson, 1996), but the results on the duration of EIH are inconsistent. Hoffman et al. (2004) found a significant decrease in pain sensitivity 5 minutes after high-intensity aerobic exercise, which was not maintained after 10 minutes. However, Janal and colleagues (Janal, Colt, Clark, & Glusman, 1984) reported hypoalgesic effects 30 minutes after high-intensity aerobic exercise and Droste (1991) reported decreased pain sensitivity for up to 60 minutes post-exercise. In general, aerobic exercise appears to produce longer-lasting hypoalgesia than resistance exercise modalities (Koltyn & Arbogast, 1998).

Gender and exercise-induced analgesia: Most studies on EIH in healthy subjects have been conducted in males, but studies including both genders have shown comparable effects on pain sensitivity after exercise (Umeda et al., 2010; Hoffman et al., 2004; Kosek & Lundberg, 2003). Nonetheless, Sternberg, Bokat, Kass, Alboyadjian, and Gracely (2001) reported EIH in women but not men after treadmill running for 10 minutes at 85% of $\dot{V}O_2$max. Similarly, decreased pain sensitivity was found in women after submaximal isometric contractions, whereas male subjects did not present with decreased pain sensitivity. Phases of the menstrual cycle do not appear to influence the magnitude of EIH in women (Hoeger Bement et al., 2009). However, the complexity of the gender, pain and exercise relationship deserves more systematic study.

Exercise-induced hypoalgesia in chronic pain patients

Exercise is frequently used in pain management settings. Systematic reviews have concluded that exercise is beneficial for a variety of pain conditions, including neck pain, low back pain, pelvic girdle pain, osteoarthritis, knee osteoarthritis, fibromyalgia and rheumatoid arthritis (for a more detailed review refer to Chapter 27 in this volume). Decreased pain sensitivity to mechanical pressure at the index finger (Hoffman, Shepanski, Mackenzie, & Clifford, 2005), arm, leg and back (Meeus, Roussel, Truijen, & Nijs, 2010) has been reported after submaximal bicycling in chronic low back pain patients, and this decrease was similar to healthy controls (Meeus et al., 2010). In contrast to the EIH in chronic low back pain patients, exercise has been shown to induce pressure hyperalgesia post-exercise in patients with chronic fatigue syndrome (Meeus et al., 2010; Whiteside, Hansen, & Chaudhuri, 2004). To date, the influence of acute exercise on pain sensitivity and symptoms in patients with fibromyalgia has been equivocal. Several studies

(Kosek et al., 1996; Staud, Robinson, & Price, 2005; Vierck et al., 2001; Hoeger Bement et al., 2011; Lannersten & Kosek, 2010) have reported increased pain ratings and hyperalgesia during and after exercise while several others have reported decreases or no change (Newcomb, Koltyn, Morgan, & Cook, 2011; Kadetoff & Kosek, 2007; Staud, Robinson, Weyl, & Price, 2010). Newcomb and colleagues (Newcomb et al., 2011) recently reported that a low-intensity bout of cycle ergometry resulted in reduced sensitivity to pressure pain stimuli and improved symptoms up to 4 days following the acute exercise bout. In patients with chronic trapezius myalgia, multi-segmental increases in pressure pain thresholds were found post-exercise when performed by a body part distant from the painful muscles (Lannersten & Kosek, 2010), but not when exercise was performed in the area of the painful muscles (Lannersten & Kosek, 2010). Together, these data suggest that intensity, duration and exercise modality can influence EIH and symptom responses to acute exercise in chronic pain patients.

Effects of pain on motor control systems

There are dense synaptic connections from nociceptive fibres to both motoneurons and sensory neurons involved in motor control (tendon organs and muscle spindles) located in the ventral horn of the spinal cord (Schomburg, Steffens, & Kniffki, 1999). Moreover, fibres with nociceptive properties have a prominent influence on reflex control (Schomburg & Steffens, 2002). Because exercise involves increases in several physiological systems, including skeletal muscle activity, there are several mechanisms through which exercise may be communicating with the pain system. Based on this, there are several models that have been discussed with respect to the bilateral effects of pain on motor control systems.

An early explanatory model described the cause of muscle pain as based on muscle hyperactivity, which was maintained by a vicious cycle due to muscle ischemia (Travell, Rinzler, & Herman, 1942). In line with this, hyperactivity was also suggested to be important in the stress-causality and reflex-spasm models (deVries, 1966; Cohen, 1978). The model suggesting that muscle pain induces ongoing muscle hyperactivity was not systematically assessed in humans until the late 1990s. However, animal data indicate that muscle nociception results in muscle hyperactivity due to facilitation of γ-motoneurons (Schmidt, Kniffki, & Schomburg, 1981; Johansson & Sojka, 1991). The implication of such facilitation was discussed as a reflex-mediated spread of muscle stiffness and potentially the launch of a vicious cycle of hyperactivity. However, recent animal studies did not corroborate facilitation of the muscle spindle activity during muscle nociception (Ro & Capra, 2001; Masri, Ro, & Capra, 2005), but instead demonstrated that a modified spindle sensitivity was responsible for the change in proprioceptive function.

The pain-adaptation model links activity in nociceptive afferents, a central pattern generator, motor function and muscle coordination (Lund, Stohler, & Widmer, 1993). This model predicts that during muscle pain, muscle activity in antagonistic phases is facilitated and muscle activity in agonistic phases is inhibited, which may produce a decrease in movement amplitude and velocity. The pain-adaptation model is organized as inhibition and facilitation of motoneurons depending on the functional phases (agonist or antagonist) of the painful muscle. Recently this model was revised based on human experimental and clinical data, incorporating a more functional adaptation described by redistribution of activity between and within muscles to protect the painful structure (i.e., joint or muscle) instead of the specific agonist inhibition and increased antagonist activity originally proposed (Hodges, 2011).

The influence of muscle pain on the resting muscle

Increased resting muscle activity after experimental facial muscle pain compared with baseline recordings has been reported (Ashton-Miller, McGlashen, Herzenberg, & Stohler, 1990), but not compared with a sham pain condition where subjects recalled a painful condition without having the actual pain stimulation (Stohler, Zhang, & Lund, 1996). This indicates that the increased muscle activity is not related to the pain per se but rather is due to activities related to facial expressions. In a later study, a transient increase in the resting EMG activity was recorded during i.m. injection of hypertonic saline, which was not found after injection of the non-painful isotonic saline (Svensson, Graven-Nielsen, Matre, & Arendt-Nielsen, 1998). The transient increased muscle activity was not maintained during the ongoing muscle pain. Likewise, the resting EMG activity between repeated maximal voluntary contractions was not increased during experimental muscle pain (Graven-Nielsen, Svensson, & Arendt-Nielsen, 1997).

Musculoskeletal pain patients present both with increased and unchanged resting EMG activities. In fibromyalgia patients an increased resting EMG activity between contractions has been reported (Elert, Dahlqvist, Henriksson-Larsén, & Gerdle, 1989) in contrast to other studies where no changes in the resting muscle EMG activity was found in fibromyalgia (Zidar, Bäckman, Bengtsson, & Henriksson, 1990), low back pain (Collins, Cohen, Nailboff, & Schandler, 1982; Ahern, Follick, Council, Laser-Wolston, & Litchman, 1988), temporomandibular pain (Bodéré, Tea, Giroux-Metges, & Woda, 2005) and chronic neck pain due to trapezius myalgia (Larsson, Öberg, & Larsson, 1999). Spontaneous muscle activity (deVries, 1966) and unchanged (Howell, Chila, Ford, David, & Gates, 1985; Bobbert, Hollander, & Huijing, 1986) resting muscle activity were detected at the time for maximal soreness induced by eccentric exercise (delayed onset muscle soreness).

The influence of muscle pain on contractions without movement

In experimental muscle pain models, the maximal voluntary contraction (MVC) is attenuated as illustrated in Figure 24.2 (Graven-Nielsen, Lund, Arendt-Nielsen, Danneskiold-Samsøe, & Bliddal, 2002; Graven-Nielsen et al., 1997; Wang, Arima, Arendt-Nielsen, & Svensson, 2000).

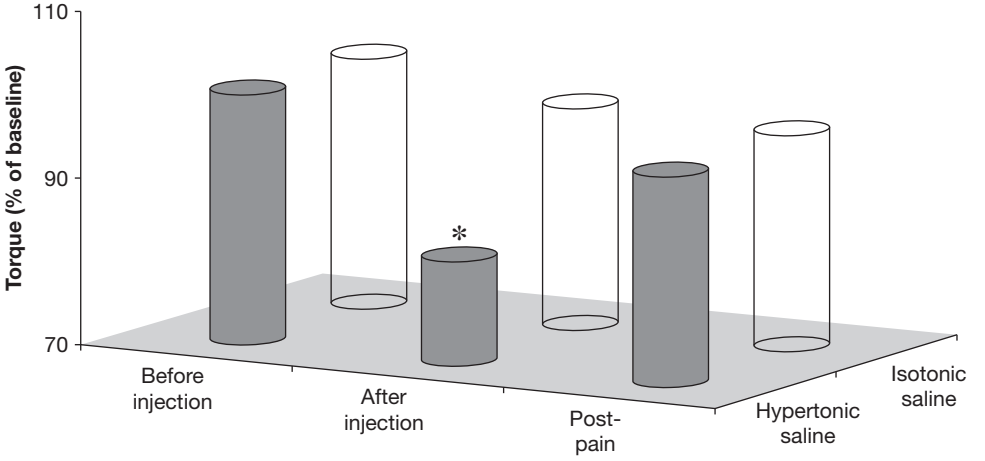

Figure 24.2 Mean maximal voluntary knee extension torque recorded before and after infusion (during, 10 minutes and 30 minutes post-infusion) of isotonic and hypertonic saline into m. rectus femoris. Significantly decreased torque compared with both pre-pain and post-pain recordings and compared with the recording immediately after infusion of isotonic saline is indicated (*) (based on data from Graven-Nielsen, Lund, Arendt-Nielsen, Danneskiold-Samsøe, & Biddell, 2002).

This decrease in MVC is not associated with modified contractile properties of muscle fibres and is likely better explained by a central inhibitory effect (Graven-Nielsen et al., 2002; Farina, Arendt-Nielsen, & Graven-Nielsen, 2005a). In fibromyalgia patients supramaximal stimulation of the ulnar nerve shows no difference in the strength of the adductor pollicis muscle between patients and control subjects, suggesting a deficient central activation of motor units in these patients explaining the reduced strength (Bäckman, Bengtsson, Bengtsson, Lennmarken, & Henriksson, 1988). Also, in localized pain conditions, attenuated MVC has been reported, e.g., in lateral epicondylalgia patients reduced strength is recorded in their sore arm compared to asymptomatic arms in controls (Slater, Arendt-Nielsen, Wright, & Graven-Nielsen, 2005). Interestingly, in trapezius myalgia patients, increased muscle activity during static contractions has been reported (Larsson et al., 1999).

Submaximal static contractions (e.g., 80% of the MVC before pain) are possible to maintain during experimental muscle pain, although with a significant reduction in endurance time (Ciubotariu, Arendt-Nielsen, & Graven-Nielsen, 2004). The different findings between the maximal contraction force, which is reduced by muscle pain, and submaximal contraction force, where the required force can be obtained during pain, is probably due to changes in descending neural drive to motoneurons. During MVC the descending neural drive cannot be voluntarily increased, and a pain-related inhibitory mechanism controlling the motoneurons may therefore explain the decreased MVC. In contrast, during submaximal contractions the voluntary neural drive can be increased and thus compensate for pain-related inhibitory mechanisms. Experimental muscle pain can also delay the recovery phase after fatiguing contractions (Ciubotariu, Arendt-Nielsen, & Graven-Nielsen, 2007), illustrating that the combination of pain and fatigue has a detrimental effect relevant in occupational conditions.

A decreased endurance time is reported in muscle pain patients performing a submaximal contraction compared with sex- and age-matched controls (Clark, Beemsterboer, & Jacobson, 1984; Elert, Dahlqvist, Almay, & Eisemann, 1993; Bengtsson, Bäckman, Lindblom, & Skogh, 1994; Gay, Maton, Rendell, & Majourau, 1994). When submaximal painful contractions are completed, at the cost of increased voluntary neural drive, then a more pronounced central fatigue may explain the decreased endurance time (James, Sacco, & Jones, 1995). Various physiological factors (e.g., microcirculation in the muscle) can influence endurance time in patients, which is not likely to occur in healthy volunteers exposed to experimental muscle pain. These results suggest that chronic pain can interfere with muscle activity/physical activity and that unique mechanisms may be involved.

Reduced muscle activity during pain has been recorded by surface EMG for contraction levels above 25% MVC (Falla, Farina, Dahl, & Graven-Nielsen, 2007) and impaired firing of single motor units during low contraction levels has been reported (Sohn, Graven-Nielsen, Arendt-Nielsen, & Svensson, 2000; Farina, Arendt-Nielsen, Merletti, & Graven-Nielsen, 2004; Tucker, Butler, Graven-Nielsen, Riek, & Hodges, 2009). The reduction in firing rate of motor units has been shown to be correlated with experimental muscle pain intensity (Farina et al., 2004). In fatiguing but non-painful contractions, reduced motor unit firing over time has also been found. During experimental muscle pain, the initial firing rate is reduced to the same level as at the end of fatiguing non-painful contractions (Farina, Arendt-Nielsen, & Graven-Nielsen, 2005b). This suggests that the nociceptive system in muscles is potentially linked with the mechanism causing reduced motor unit firing during fatigue.

The effect of muscle pain during static contractions not only decreases muscle activity of the painful muscle, but importantly also attenuates the synergistic muscles (Ciubotariu et al., 2004; Falla et al., 2007). Within muscles the spatial distribution of activity can be recorded by surface matrix EMG electrodes. With this method trapezius muscle activity was found to be fully

reorganized and decreased by experimental muscle pain (Madeleine, Leclerc, Arendt-Nielsen, Ravier, & Farina, 2006). Generating the required contraction force and compensating for the muscle inhibition requires a new muscle coordination that eventually results in overload of otherwise non-painful muscles. This may also explain the larger movement variability seen in acute pain, whereas chronic or prolonged pain seems to reduce the movement variability (Madeleine, 2010). The contraction force is, among other factors, determined by the motor unit firing rate, and it is unclear how constant force can be maintained during muscle pain despite the decrease in motor unit firing rate. Motor unit twitch properties can change, which has been suggested as a compensatory mechanism for the decreased motor unit firing during pain. Accordingly, during experimental muscle pain, increased twitch force of low-threshold motor units has been reported (Sohn, Graven-Nielsen, Arendt-Nielsen, & Svensson, 2004; Farina, Arendt-Nielsen, Roatta, & Graven-Nielsen, 2008). On the contrary, muscle membrane properties seem to be unaffected by experimental muscle pain as both the M-wave (Farina et al., 2005a) and motor unit conduction velocity (Farina et al., 2005b) are unchanged. In post-pain conditions, when the motor unit firing rate returns to normal, the peak twitch force remains elevated (Farina et al., 2008), which strongly suggests that the facilitated twitch force is not the main mechanism compensating for the decline in motor unit firing rate. The maintenance of force may also be achieved if the nervous system increases the activity of muscles with a synergistic role to compensate for the decreased force produced by the painful muscle. Nevertheless, motor units in synergistic muscles neighbouring a painful muscle also demonstrate reduced firings (Figure 24.3) (Hodges, Ervilha, & Graven-Nielsen, 2008), and do not account for maintenance of force

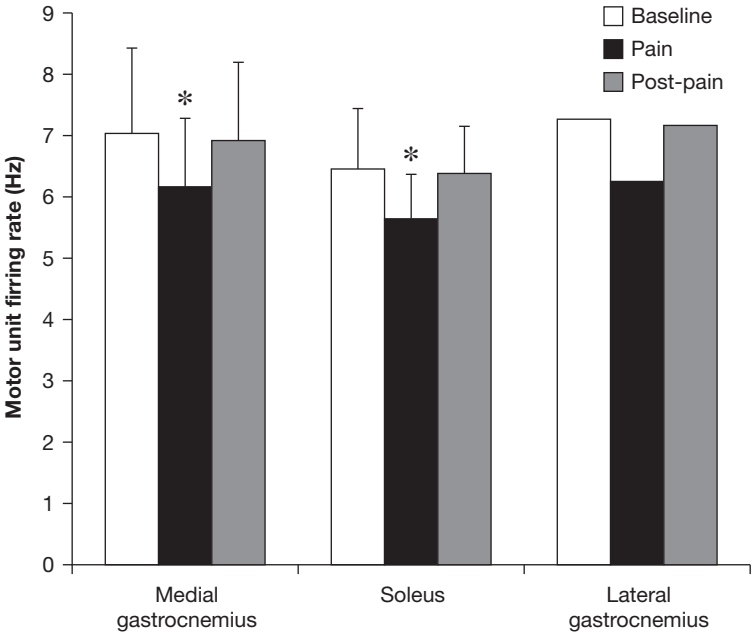

Figure 24.3 Mean discharge rate of single motor units during plantar-flexion at low-level contractions. Experimental pain was induced by injection of hypertonic saline in the lateral gastrocnemius muscle. The single motor units were identified and recorded before (open bars), during (solid bars) and post-pain (grey bars) in synergistic muscles (soleus, medial gastrocnemious). During pain the instantaneous firing rate is significantly reduced in synergistic motor units (*: $P < 0.05$). In one session a single motor unit was recorded in the lateral gastrocnemious (based on data from Hodges, Ervilha, & Graven-Nielsen, 2008).

during painful contractions without movements. Recruitment of additional motor units (e.g., high threshold units) during pain is an attractive mechanism to explain the maintained force with reduced motor unit firing. Recent data demonstrate such recruitment in combination with decreased motor unit firing in painful muscles (Tucker et al., 2009).

The experimental pain model, based on injections of hypertonic saline, does not affect the contractile apparatus (Graven-Nielsen et al., 2002). On the contrary, delayed onset muscle soreness (DOMS) is probably related to ultra-structural damage, which may affect the contractile properties resulting in loss of force. Reported loss of force within the first 24 hours of DOMS may be explained by inhibition of motor cortex and/or spinal motoneurons (Prasartwuth, Taylor, & Gandevia, 2005). Another study showed that eccentric contractions caused reduced EMG amplitude during sustained contractions, which was not found before DOMS, suggesting a modification of contractile properties (Hedayatpour, Falla, Arendt-Nielsen, & Farina, 2008). Increased (Kroon & Naeije, 1991), decreased (Nie, Arendt-Nielsen, Kawczynski, & Madeleine, 2007) and no differences in (Bajaj, Madeleine, Sjogaard, & Arendt-Nielsen, 2002) EMG activity during DOMS with constant contractions have also been reported. Therefore, when conditions include changes of the contractile properties in addition to modulation of motor control parameters by nociception, the results should be interpreted with caution.

The influence of muscle pain on contractions with movement

In conditions with experimental and clinical low back pain it was found that the low back muscle activity was increased in phases where the EMG activity normally is silent, and not affected or decreased in phases with strong EMG activity in control subjects (Arendt-Nielsen, Graven-Nielsen, Svarrer, & Svensson, 1996). Similarly, gait muscle pain often causes decreased EMG in the agonistic phase and increased EMG in the antagonistic phase of leg muscle activity (Graven-Nielsen et al., 1997). A similar finding is reported during trunk flexion-extension movements, where the antagonist phase showed increased activity in low back pain patients, which is normally silent in pain-free controls (Sihvonen, Partanen, Hänninen, & Soimakallio, 1991). The functional outcome of this reorganized motor control is reduced movement amplitudes in experimental and clinical musculoskeletal pain conditions (Graven-Nielsen & Arendt-Nielsen, 2008), which may protect the painful muscle by reducing the load on the painful structure. Individual combinations of increased, decreased and co-contraction activity of trunk flexors and extensors may be another strategy adopted to maintain spine stability in conditions of experimental low back pain (Hodges, Cholewicki, Coppieters, & MacDonald, 2006).

During muscle pain another strategy is characterized by decreased activity in both the agonistic and antagonistic muscles without significantly impairing the movement amplitude or acceleration (Ervilha, Arendt-Nielsen, Duarte, & Graven-Nielsen, 2004). Interestingly, the initial (100 ms) agonistic EMG burst activity was decreased during muscle pain suggesting a reorganized motor strategy. Reduced feed-forward responses of the abdominal muscles were found in conditions of experimental low back muscle pain and this change in motor planning may compromise spine stability (Hodges, Moseley, Gabrielsson, & Gandevia, 2003). Another example is gait initiation, which also depends on specific motor control strategies and is perturbed by experimental muscle pain (Madeleine, Voigt, & Arendt-Nielsen, 1999). In occupational settings abnormal motor planning results in compensatory action from other muscles to achieve the required movement, and this may possibly contribute to the development of musculoskeletal pain problems. During pointing movements increased trapezius activity was found with experimental pain induced in the biceps brachii muscle and this could constitute a compensatory response (Ervilha et al., 2004). Reorganized trapezius muscle activity during repetitive shoulder flexion has been characterized

as reduced activity of the upper trapezius (with experimental pain) accompanied by increased muscle activity of the lower trapezius as compensation (Falla, Farina, & Graven-Nielsen, 2007).

The reorganized muscle coordination caused by muscle pain has strong biomechanical impact on the other skeletal structures. During experimental pain induced in the vastus medialis muscle, the functional significance of knee joint control during gait was assessed by three-dimensional gait analyses (Henriksen et al., 2007). The quadriceps muscle activity was reduced by muscle pain causing an impaired knee joint control and joint instability during walking. Similar changes have been observed in patients with osteoarthritic knee pain and experimental knee pain (Henriksen, Graven-Nielsen, Aaboe, Andriacchi, & Bliddal, 2010). The impaired joint control may place the knee joint prone to injury and as such participate in the chronicity of musculoskeletal problems. In recent studies, Hirata et al. (Hirata, Arendt-Nielsen, & Graven-Nielsen, 2010; Hirata, Ervilha, Arendt-Nielsen, & Graven-Nielsen, 2011) reported that pain induced in knee muscles challenged postural control, which may increase the risk of falls. Such biomechanical effects have important clinical implications for training and rehabilitation of patients with knee pain.

Summary and future directions

Aerobic, isometric and resistance exercises produce hypoalgesic effects in healthy subjects. Exercise-induced hypoalgesia following aerobic exercise is more likely to occur with higher intensity and longer duration, whereas EIH occurs after isometric contractions at both low and high intensity and may be independent of duration. Future studies are needed to examine chronic pain patients developing post-exercise pain in contrast to EIH, since hyperalgesia may block the mental health benefits of exercise.

A fundamental aspect of musculoskeletal pain conditions is motor control reorganization, which is most likely one crucial mechanism in understanding how acute pain may translate into a chronic pain condition. The interaction between musculoskeletal pain and motor control depends on the specific motor task. During dynamic exercise muscle pain causes a change in the coordination and changes in the co-contraction pattern. The functional adaptation to muscle pain may also involve increased muscle activity reflecting reorganized muscle coordination and strategy. In general, these findings do not support the 'vicious cycle' theory but rather an adaptive model predicting how muscle activity is reorganized in order to protect painful structures. Future pain models should address the variability and redundancy/reorganization in the motor control system, how this is affected by deep-tissue pain, and how this will interfere with motor performance and physical activity behaviours. Unfortunately the impaired functional effects caused by pain will counteract a potential positive effect of training on mental health.

References

Ahern, D. K., Follick, M. J., Council, J. R., Laser-Wolston, N., & Litchman, H. (1988). Comparison of lumbar paravertebral EMG patterns in chronic low back pain patients and non-patient controls. *Pain*, *34*, 153–160.

Anshel, M. H., & Russell, K. G. (1994). Effect of aerobic and strength training on pain tolerance, pain appraisal and mood of unfit males as a function of pain location. *Journal of Sports Science*, *12*, 535–547.

Arendt-Nielsen, L., Graven-Nielsen, T., Svarrer, H., & Svensson, P. (1996). The influence of low back pain on muscle activity and coordination during gait: A clinical and experimental study. *Pain*, *64*, 231–240.

Ashton-Miller, J. A., McGlashen, K. M., Herzenberg, J. E., & Stohler, C. S. (1990). Cervical muscle myoelectric response to acute experimental sternocleidomastoid pain. *Spine*, *15*, 1006–1012.

Bäckman, E., Bengtsson, A., Bengtsson, M., Lennmarken, C., & Henriksson, K. G. (1988). Skeletal muscle function in primary fibromyalgia. Effect of regional sympathetic blockade with guanethidine. *Acta Neurologica Scandinavica*, 77, 187–191.

Bajaj, P., Madeleine, P., Sjogaard, G., & Arendt-Nielsen, L. (2002). Assessment of postexercise muscle soreness by electromyography and mechanomyography. *Journal of Pain*, *3*, 126–136.

Bengtsson, A., Bäckman, E., Lindblom, B., & Skogh, T. (1994). Long term follow-up of fibromyalgia patients: Clinical symptoms, muscular function, laboratory test – an eight year comparison study. *Journal of Musculoskeletal Pain*, *2*, 67–80.

Bobbert, M. F., Hollander, A. P., & Huijing, P. A. (1986). Factors in delayed onset muscular soreness of man. *Medicine and Science in Sports and Exercise*, *18*, 75–81.

Bodéré, C., Tea, S. H., Giroux-Metges, M. A., & Woda, A. (2005). Activity of masticatory muscles in subjects with different orofacial pain conditions. *Pain*, *116*, 33–41.

Ciubotariu, A., Arendt-Nielsen, L., & Graven-Nielsen, T. (2004). The influence of muscle pain and fatigue on the activity of synergistic muscles of the leg. *European Journal of Applied Physiology*, *91*, 604–614.

Ciubotariu, A., Arendt-Nielsen, L., & Graven-Nielsen, T. (2007). Localized muscle pain causes prolonged recovery after fatiguing isometric contractions. *Experimental Brain Research*, *181*, 147–158.

Clark, G. T., Beemsterboer, P. L., & Jacobson, R. (1984). The effect of sustained submaximal clenching on maximum bite force in myofascial pain dysfunction patients. *Journal of Oral Rehabilitation*, *11*, 387–391.

Cohen, M. J. (1978). Psychophysiological studies of headache: Is there similarity between migraine and muscle contraction headaches? *Headache*, *18*, 189–196.

Collins, G. A., Cohen, M. J., Nailboff, B. D., & Schandler, S. L. (1982). Comparative analysis of paraspinal and frontalis EMG, heart rate and skin conductance in chronic low back pain patients and normals to various postures and stress. *Scandinavian Journal of Rehabilitation Medicine*, *14*, 39–46.

deVries, H. A. (1966). Quantitative electromyographic investigation of the spasm theory of muscle pain. *American Journal of Physical Medicine*, *45*, 119–134.

Droste, C. (1991). Physical exercise, endogenous opiates and pain regulation. *Schmerz*, *5*, 138–147.

Elert, J. E., Dahlqvist, S. R., Almay, B., & Eisemann, M. (1993). Muscle endurance, muscle tension and personality traits in patients with muscle or joint pain – A pilot study. *Journal of Rheumatology*, *20*, 1550–1556.

Elert, J. E., Dahlqvist, S. B. R., Henriksson-Larsén, K., & Gerdle, B. (1989). Increased EMG activity during short pauses in patients with primary fibromyalgia. *Scandinavian Journal of Rheumatology*, *18*, 321–323.

Ervilha, U. F., Arendt-Nielsen, L., Duarte, M., & Graven-Nielsen, T. (2004). Effect of load level and muscle pain intensity on the motor control of elbow-flexion movements. *European Journal of Applied Physiology*, *92*, 168–175.

Falla, D., Farina, D., Dahl, M. K., & Graven-Nielsen, T. (2007). Muscle pain induces task-dependent changes in cervical agonist/antagonist activity. *Journal of Applied Physiology*, *102*, 601–609.

Falla, D., Farina, D., & Graven-Nielsen, T. (2007). Experimental muscle pain results in reorganization of coordination among trapezius muscle subdivisions during repetitive shoulder flexion. *Experimental Brain Research*, *178*, 385–393.

Farina, D., Arendt-Nielsen, L., & Graven-Nielsen, T. (2005a). Experimental muscle pain decreases voluntary EMG activity but does not affect the muscle potential evoked by transcutaneous electrical stimulation. *Clinical Neurophysiology*, *116*, 1558–1565.

Farina, D., Arendt-Nielsen, L., & Graven-Nielsen, T. (2005b). Experimental muscle pain reduces initial motor unit discharge rates during sustained submaximal contractions. *Journal of Applied Physiology*, *98*, 999–1005.

Farina, D., Arendt-Nielsen, L., Merletti, R., & Graven-Nielsen, T. (2004). Effect of experimental muscle pain on motor unit firing rate and conduction velocity. *Journal of Neurophysiology*, *91*, 1250–1259.

Farina, D., Arendt-Nielsen, L., Roatta, S., & Graven-Nielsen, T. (2008). The pain-induced decrease in low-threshold motor unit discharge rate is not associated with the amount of increase in spike-triggered average torque. *Clinical Neurophysiology*, *119*, 43–51.

Gay, T., Maton, B., Rendell, J., & Majourau, A. (1994). Characteristics of muscle fatigue in patients with myofascial pain-dysfunction syndrome. *Archives of Oral Biology*, *39*, 847–852.

Graven-Nielsen, T., & Arendt-Nielsen, L. (2008). Impact of clinical and experimental pain on muscle strength and activity. *Current Rheumatology Reports*, *10*, 475–481.

Graven-Nielsen, T., Lund, H., Arendt-Nielsen, L., Danneskiold-Samsøe, B., & Bliddal, H. (2002). Inhibition of maximal voluntary contraction force by experimental muscle pain: A centrally mediated mechanism. *Muscle & Nerve*, *26*, 708–712.

Graven-Nielsen, T., Svensson, P., & Arendt-Nielsen, L. (1997). Effects of experimental muscle pain on muscle activity and co-ordination during static and dynamic motor function. *Electroencephalography and Clinical Neurophysiology*, *105*, 156–164.

Gurevich, M., Kohn, P. M., & Davis, C. (1994). Exercise-induced analgesia and the role of reactivity in pain sensitivity. *Journal of Sports Science*, *12*, 549–559.

Hedayatpour, N., Falla, D., Arendt-Nielsen, L., & Farina, D. (2008). Sensory and electromyographic mapping during delayed-onset muscle soreness. *Medicine and Science in Sports and Exercise*, *40*, 326–334.

Henriksen, M., Alkjaer, T., Lund, H., Simonsen, E. B., Graven-Nielsen, T., Danneskiold-Samsoe, B. et al. (2007). Experimental quadriceps muscle pain impairs knee joint control during walking. *Journal of Applied Physiology*, *103*, 132–139.

Henriksen, M., Graven-Nielsen, T., Aaboe, J., Andriacchi, T. P., & Bliddal, H. (2010). Gait changes in patients with knee osteoarthritis are replicated by experimental knee pain. *Arthritis Care Research (Hoboken)*, *62*, 501–509.

Hirata, R. P., Arendt-Nielsen, L., & Graven-Nielsen, T. (2010). Experimental calf muscle pain attenuates the postural stability during quiet stance and perturbation. *Clinical Biomechanics (Bristol, Avon)*, *25*, 931–937.

Hirata, R. P., Ervilha, U. F., Arendt-Nielsen, L., & Graven-Nielsen, T. (2011). Experimental muscle pain challenges the postural stability during quiet stance and unexpected posture perturbation. *Journal of Pain*, *12*, 911–919.

Hodges, P., Cholewicki, J., Coppieters, M., & MacDonald, D. (2006). *Trunk muscle activity is increased during experimental back pain, but the pattern varies between individuals*. In Proceedings of International Society for Electrophysiologyand Kinesiology, Turin.

Hodges, P. W. (2011). Pain and motor control: From the laboratory to rehabilitation. *Journal of Electromyography and Kinesiology*, *21*, 220–228.

Hodges, P. W., Ervilha, U. F., & Graven-Nielsen, T. (2008). Changes in motor unit firing rate in synergist muscles cannot explain the maintenance of force during constant force painful contractions. *Journal of Pain*, *9*, 1169–1174.

Hodges, P. W., Moseley, G. L., Gabrielsson, A., & Gandevia, S. C. (2003). Experimental muscle pain changes feedforward postural responses of the trunk muscles. *Experimental Brain Research*, *151*, 262–271.

Hoeger Bement, M. K. (2009). Exercise-induced hypoalgesia: An evidence-based review. In K. A. Sluka (Ed.), *Mechanisms and management of pain for the physical therapist* (pp. 143–166). Seattle: IASP.

Hoeger Bement, M. K., Dicapo, J., Rasiarmos, R., & Hunter, S. K. (2008). Dose response of isometric contractions on pain perception in healthy adults. *Medicine and Science in Sports and Exercise*, *40*, 1880–1889.

Hoeger Bement, M. K., Rasiarmos, R. L., DiCapo, J. M., Lewis, A., Keller, M. L., Harkins, A. L. et al. (2009). The role of the menstrual cycle phase in pain perception before and after an isometric fatiguing contraction. *European Journal of Applied Physiology*, *106*, 105–112.

Hoeger Bement, M. K., Weyer, A., Hartley, S., Drewek, B., Harkins, A. L., & Hunter, S. K. (2011). Pain perception after isometric exercise in women with fibromyalgia. *Archives of Physical Medicine and Rehabilitation*, *92*, 89–95.

Hoffman, M. D., Shepanski, M. A., Mackenzie, S. P., & Clifford, P. S. (2005). Experimentally induced pain perception is acutely reduced by aerobic exercise in people with chronic low back pain. *Journal of Rehabilitation Research and Development*, *42*, 183–190.

Hoffman, M. D., Shepanski, M. A., Ruble, S. B., Valic, Z., Buckwalter, J. B., & Clifford, P. S. (2004). Intensity and duration threshold for aerobic exercise-induced analgesia to pressure pain. *Archives of Physical Medicine and Rehabilitation*, *85*, 1183–1187.

Howell, J. N., Chila, A. G., Ford, G., David, D., & Gates, T. (1985). An electromyographic study of elbow motion during postexercise muscle soreness. *Journal of Applied Physiology*, *58*, 1713–1718.

James, C., Sacco, P., & Jones, D. A. (1995). Loss of power during fatigue of human leg muscles. *Journal of Physiology (Lond.)*, *484*, 237–246.

Janal, M. N., Colt, E. W., Clark, W. C., & Glusman, M. (1984). Pain sensitivity, mood and plasma endocrine levels in man following long-distance running: Effects of naloxone. *Pain*, *19*, 13–25.

Johansson, H., & Sojka, P. (1991). Pathophysiological mechanisms involved in genesis and spread of muscular tension in occupational muscle pain and in chronic musculoskeletal pain syndromes: A hypothesis. *Medical Hypotheses*, *35*, 196–203.

Kadetoff, D., & Kosek, E. (2007). The effects of static muscular contraction on blood pressure, heart rate, pain ratings and pressure pain thresholds in healthy individuals and patients with fibromyalgia. *European Journal of Pain*, *11*, 39–47.

Koltyn, K. F. (2000). Analgesia following exercise: A review. *Sports Medicine*, *29*, 85–98.

Koltyn, K. F. (2002). Exercise-induced hypoalgesia and intensity of exercise. *Sports Medicine*, *32*, 477–487.

Koltyn, K. F., & Arbogast, R. W. (1998). Perception of pain after resistance exercise. *British Journal of Sports Medicine*, *32*, 20–24.

Koltyn, K. F., Garvin, A. W., Gardiner, R. L., & Nelson, T. F. (1996). Perception of pain following aerobic exercise. *Medicine and Science in Sports and Exercise*, *28*, 1418–1421.

Kosek, E., Ekholm, J., & Hansson, P. (1996). Modulation of pressure pain thresholds during and following isometric contraction in patients with fibromyalgia and in healthy controls. *Pain*, *64*, 415–423.

Kosek, E., & Lundberg, L. (2003). Segmental and plurisegmental modulation of pressure pain thresholds during static muscle contractions in healthy individuals. *European Journal of Pain*, *7*, 251–258.

Kroon, G. W., & Naeije, M. (1991). Recovery of the human biceps electromyogram after heavy eccentric, concentric or isometric exercise. *European Journal of Applied Physiology and Occupational Physiology*, *63*, 444–448.

Lannersten, L., & Kosek, E. (2010). Dysfunction of endogenous pain inhibition during exercise with painful muscles in patients with shoulder myalgia and fibromyalgia. *Pain*, *151*, 77–86.

Larsson, R., Öberg, P. Å., & Larsson, S.-E. (1999). Changes of trapezius muscle blood flow and electromyography in chronic neck pain due to trapezius myalgia. *Pain*, *79*, 45–50.

Lund, J. P., Stohler, C. S., & Widmer, C. G. (1993). The relationship between pain and muscle activity in fibromyalgia and similar conditions. In H. Værøy & H. Merskey (Eds.), *Progress in fibromyalgia and myofascial pain* (pp. 311–327). Amsterdam: Elsevier.

Madeleine, P. (2010). On functional motor adaptations: From the quantification of motor strategies to the prevention of musculoskeletal disorders in the neck-shoulder region. *Acta Physiologica (Oxf). 199 Suppl 679*, 1–46.

Madeleine, P., Leclerc, F., Arendt-Nielsen, L., Ravier, P., & Farina, D. (2006). Experimental muscle pain changes the spatial distribution of upper trapezius muscle activity during sustained contraction. *Clinical Neurophysiology*, *117*, 2436–2445.

Madeleine, P., Voigt, M., & Arendt-Nielsen, L. (1999). Reorganisation of human step initiation during acute experimental muscle pain. *Gait and Posture*, *10*, 240–247.

Masri, R., Ro, J. Y., & Capra, N. (2005). The effect of experimental muscle pain on the amplitude and velocity sensitivity of jaw closing muscle spindle afferents. *Brain Research*, *1050*, 138–147.

Meeus, M., Roussel, N. A., Truijen, S., & Nijs, J. (2010). Reduced pressure pain thresholds in response to exercise in chronic fatigue syndrome but not in chronic low back pain: An experimental study. *Journal of Rehabilitation Medicine*, *42*, 884–890.

Newcomb, L. W., Koltyn, K. F., Morgan, W. P., & Cook, D. B. (2011). Influence of preferred versus prescribed exercise on pain in fibromyalgia. *Medicine and Science in Sports and Exercise*, *43*, 1106–1113.

Nie, H., Arendt-Nielsen, L., Kawczynski, A., & Madeleine, P. (2007). Gender effects on trapezius surface EMG during delayed onset muscle soreness due to eccentric shoulder exercise. *Journal of Electromyography and Kinesiology*, *17*, 401–409.

Nielsen, M. M., Mortensen, A., Sorensen, J. K., Simonsen, O., & Graven-Nielsen, T. (2009). Reduction of experimental muscle pain by passive physiological movements. *Manual Therapy*, *14*, 101–109.

Padawer, W. J., & Levine, F. M. (1992). Exercise-induced analgesia: Fact or artifact? *Pain*, *48*, 131–135.

Prasartwuth, O., Taylor, J. L., & Gandevia, S. C. (2005). Maximal force, voluntary activation and muscle soreness after eccentric damage to human elbow flexor muscles. *Journal of Physiology*, *567*, 337–348.

Ro, J. Y., & Capra, N. F. (2001). Modulation of jaw muscle spindle afferent activity following intramuscular injections with hypertonic saline. *Pain*, *92*, 117–127.

Schmidt, R. F., Kniffki, K.-D., & Schomburg, E. D. (1981). Der Einfluss kleinkalibriger Muskelafferenzen auf den Muskeltonus. In H. Bauer, W. P. Koella, & H. Struppler (Eds.), *Therapie der spastic* (pp. 71–86). München: Verlag for angewandte Wissenschaft.

Schomburg, E. D., & Steffens, H. (2002). Only minor spinal motor reflex effects from feline group IV muscle nociceptors. *Neuroscience Research*, *44*, 213–223.

Schomburg, E. D., Steffens, H., & Kniffki, K. D. (1999). Contribution of group III and IV muscle afferents to multisensorial spinal motor control in cats. *Neuroscience Research*, *33*, 195–206.

Shyu, B. C., Andersson, S. A., & Thoren, P. (1982). Endorphin mediated increase in pain threshold induced by long-lasting exercise in rats. *Life Sciences*, *30*, 833–840.

Sihvonen, T., Partanen, J., Hänninen, O., & Soimakallio, S. (1991). Electric behavior of low back muscles during lumbar pelvic rhythm in low back pain patients and healthy controls. *Archives of Physical Medicine and Rehabilitation*, *72*, 1080–1087.

Slater, H., Arendt-Nielsen, L., Wright, A., & Graven-Nielsen, T. (2005). Sensory and motor effects of experimental muscle pain in patients with lateral epicondylalgia and controls with delayed onset muscle soreness. *Pain*, *114*, 118–130.

Sohn, M. K., Graven-Nielsen, T., Arendt-Nielsen, L., & Svensson, P. (2000). Inhibition of motor unit firing during experimental muscle pain in humans. *Muscle & Nerve*, *23*, 1219–1226.

Sohn, M. K., Graven-Nielsen, T., Arendt-Nielsen, L., & Svensson, P. (2004). Effects of experimental muscle pain on mechanical properties of single motor units in human masseter. *Clinical Neurophysiology*, *115*, 76–84.

Staud, R., Robinson, M. E., & Price, D. D. (2005). Isometric exercise has opposite effects on central pain mechanisms in fibromyalgia patients compared to normal controls. *Pain*, *118*, 176–184.

Staud, R., Robinson, M. E., Weyl, E. E., & Price, D. D. (2010). Pain variability in fibromyalgia is related to activity and rest: Role of peripheral tissue impulse input. *Journal of Pain*, *11*, 1376–1383.

Sternberg, W. F., Bokat, C., Kass, L., Alboyadjian, A., & Gracely, R. H. (2001). Sex-dependent components of the analgesia produced by athletic competition. *Journal of Pain*, *2*, 65–74.

Stohler, C. S., Zhang, X., & Lund, J. P. (1996). The effect of experimental jaw muscle pain on postural muscle activity. *Pain*, *66*, 215–221.

Svensson, P., Graven-Nielsen, T., Matre, D., & Arendt-Nielsen, L. (1998). Experimental muscle pain does not cause long-lasting increases in resting electromyographic activity. *Muscle & Nerve*, *21*, 1382–1389.

Travell, J. G., Rinzler, S., & Herman, M. (1942). Pain and disability of the shoulder and arm. *Journal of the American Medical Association*, *120*, 417–422.

Tucker, K., Butler, J., Graven-Nielsen, T., Riek, S., & Hodges, P. (2009). Motor unit recruitment strategies are altered during deep-tissue pain. *Journal of Neuroscience*, *29*, 10820–10826.

Umeda, M., Newcomb, L. W., Ellingson, L. D., & Koltyn, K. F. (2010). Examination of the dose-response relationship between pain perception and blood pressure elevations induced by isometric exercise in men and women. *Biological Psychology*, *85*, 90–96.

Vierck, C. J., Jr., Staud, R., Price, D. D., Cannon, R. L., Mauderli, A. P., & Martin, A. D. (2001). The effect of maximal exercise on temporal summation of second pain (windup) in patients with fibromyalgia syndrome. *Journal of Pain*, *2*, 334–344.

Wang, K., Arima, T., Arendt-Nielsen, L., & Svensson, P. (2000). EMG-force relationships are influenced by experimental jaw-muscle pain. *Journal of Oral Rehabilitation*, *27*, 394–402.

Whiteside, A., Hansen, S., & Chaudhuri, A. (2004). Exercise lowers pain threshold in chronic fatigue syndrome. *Pain*, *109*, 497–499.

Zidar, J., Bäckman, E., Bengtsson, A., & Henriksson, K. G. (1990). Quantitative EMG and muscle tension in painful muscles in fibromyalgia. *Pain*, *40*, 249–254.