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EFFECT OF ECCENTRIC EXERCISE AND DELAYED ONSET MUSCLE SORENESS ON THE HOMOLOGOUS MUSCLE OF THE CONTRALATERAL LIMB

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ABSTRACT

High intensity eccentric exercise induces muscle fiber damage and associated delayed-onset muscle soreness (DOMS) resulting in an impaired ability of the muscle to generate voluntary force. This study investigates the extent to which DOMS, induced by high intensity eccentric exercise, can affect activation and performance of the non-exercised homologous muscle of the contralateral limb. Healthy volunteers performed maximal voluntary contractions of knee extension and sustained isometric knee extension at 50% of maximal force until task failure on both the ipsilateral exercised limb and the contralateral limb. Surface electromyography (EMG) was recorded from the ipsilateral and contralateral knee extensor muscles (vastus medialis, rectus femoris, and vastus lateralis). Maximal isometric knee extension force (13.7% reduction) and time to task failure (38.1% reduction) of the contralateral non-exercised leg decreased immediately after eccentric exercise, and persisted 24 h and 48 h after ($p<0.05$). Moreover, the amplitude of muscle activity recorded from the contralateral knee extensor muscles was significantly lower during the post exercise maximal and submaximal contractions following high intensity eccentric exercise of the opposite limb ($p<0.05$). Unilateral high intensity eccentric exercise of the quadriceps can contribute to reduced neuromuscular activity and physical work capacity of the non-exercised homologous muscle in the contralateral limb.

Key Words: EMG, contralateral, pain, eccentric exercise

INTRODUCTION

Musculoskeletal pain can induce cortical reorganization in both somatosensory and motor area (Flor, 2013), which in turn can reduce motor abilities of both the affected and unaffected limb. For example, deficits in motor output of the ipsilateral and contralateral limb have been identified during acute pain (Falla et al., 2007, Hedayatpour et al., 2008, Schabrun et al., 2016) and /or in chronic pain conditions (Akseki et al., 2008, Smeulders et al., 2002, Arguis et al., 2008).

Pain is also common after high intensity eccentric exercise, most likely due to the pathophysiological changes within the injured muscle. It has been reported that pathophysiological changes associated with tissue injuries ((Ebbeling & Clarkson, 1989), such as progressive necrosis of the contractile elements (Fridén et al. 1998), and the release of algesic substances (e.g., prostaglandins) (Amaya et al., 2013; Tegeder et al., 2002) enhances the responsiveness of nociceptive endings (Mense, 2003; Tegeder et al., 2002), large mechanoreceptor afferents, muscle spindles and tendons (Barlas et al., 2000; Taguchi et al., 2005), which in turn results in delayed onset muscle soreness (DOMS) 24 to 72 hours after the exercise. Although considerable research has been devoted to the effect of DOMS on muscle activity and the force-generating capacity of the exercised muscles (Hedayatpour et al., 2009, Hedayatpour & Falla, 2014b), less attention has been devoted to the effect of DOMS on the functional parameters of non-exercised

homologous muscle in the contralateral limb. There are several potential mechanisms by which pain induced by eccentric exercise may contribute to reduced motor output of the contralateral non-exercised side.

For example, nociceptor sensitization associated with tissue injury can influence the primary afferents of muscle spindles at superficial layers of the dorsal horn of the spinal cord which cross to the contralateral side of brainstem and thalamus (Le Pera et al., 2001; Todd et al., 2003). Moreover, the presence of pain within the damaged muscle could mediate inhibitory effects on both ipsilateral and contralateral human motor cortex (Dimou et al., 2013). Accordingly, a ‘cross-over’ effect of muscle adaptations (e.g., fatigue) has been reported for the upper and lower limbs after different types of exercise (Amann et al., 2008; Ruohonen et al., 2002; Todd et al., 2003; Willis, 1985). This evidence suggests that exercise induced change in motor ability of the exercised limb could also change motor output of the contralateral non-exercised side, most probably due to modulation of neural circuits at the level of spinal cord and motor cortex.

Based on these findings, we hypothesized that pain induced by high intensity eccentric exercise could contribute to the reduced motor ability not only in the exercised muscle, but also in the non-exercised homologous muscle in the contralateral limb. Therefore, the aim of this study was to evaluate whether high intensity eccentric exercise and subsequent DOMS in the exercised muscle affects neuromuscular activity of the non-exercised homologous muscle in the contralateral limb. Surface electromyography (EMG) was recorded from the ipsilateral and contralateral knee extensor muscles during maximal voluntary contractions and submaximal sustained knee extension before, 24 h, and 48 h after eccentric exercise.

METHODS

Experimental design and approach. This experiment investigates whether high intensity eccentric exercise induced DOMS can affect activation and performance of the non-exercised homologous muscle of the contralateral limb. Time to task failure and MVC of the non-exercised quadriceps muscle measured, before, immediately after, and 24 and 48 h after eccentric exercise. Moreover EMG activities of the non-exercised quadriceps muscle were recorded during MVC and over sustained contraction at 50% MVC before and after eccentric exercise.

Participants

Fifteen healthy men (age, mean ± standard deviation; SD, 20.5 ± 2.2 years, body mass 70.5 ± 8.4 kg, height 1.75 ± 0.06 m) volunteered to participate in the study which followed a repeated measures design. All subjects were right-leg dominant (self-reported) and were not involved in regular exercise of their knee extensor muscles for at least 6 months before the experiment. The study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee. Subjects provided informed written consent before participation in the study.

Warm up

Subjects initially warmed up on a bicycle ergometer (LC4, Monark Exercise AB, Sweden) for 10 min. After the warm-up, they performed bilateral maximum and submaximal knee extension contractions and an eccentric exercise protocol on their right leg as detailed below.

Eccentric exercise

Subjects performed eccentric exercise of their right quadriceps using a weight-training machine (Universal Gym, USA) whilst positioned in supine. The workload was determined for each subject based on their initial one repetition maximum (1-RM) and load was defined as 150% of the initial value of 1-RM. One repetition maximum was defined as the heaviest load that can be moved over a specific range of motion (90 º - 180º), one time, and with correct performance. The subject performed 4 sets of 25 repetitions with 150% of the 1-RM with three minutes of rest between sets. Timing of the lowering and lockout phases of the exercise was established using a metronome. The metronome emitted an audible stimulus at a frequency of 1 Hz. Subjects were asked to lower the load to the end position in a controlled manoeuvre, in time with the metronome. The leg press was brought to the starting position (170 º - 180 º knee extension, 180 º = full knee extension) using two assistants, and the subject lowered the load to the end position (60 º knee extension) in a controlled manoeuvre. This allowed the subjects to perform multiple repetitions against relatively high loads and delayed the onset of fatigue by eliminating the concentric contraction.

Maximum and sustained knee extension contractions

The subject sat comfortably on a chair fixed with a belt at the hip flexed at 90º and with the right knee in 90º of flexion. A strap, connected by a chain to a load cell, was attached to the ankle to measure knee extension isometric force. Force was provided to the subject as visual feedback on an oscilloscope. The subject performed a total of six 5-second maximum voluntary contractions (MVC) of knee extension on the ipsilateral and contralateral limb (three MVCs for each limb) each separated by 2-min rest. During each MVC, verbal encouragement was provided to exceed the previous force level. MVCs were performed in random order for the ipsilateral and contralateral leg. The highest MVC value was considered as a reference value to define the submaximal load.

Participants also performed an isometric knee extension contraction at 50% MVC sustained until task failure on both the ipsilateral and contralateral leg, with the participant in the same position as in the MVCs. In order to prevent any cross over effect of muscle fatigue, sustained contractions were performed in a random order for the ipsilateral and contralateral leg across participants with 25 minute rests in between. Additionally, EMG signals were recorded from same muscle locations and from same channels of the EMG amplifier by a single experimenter, factors that can reduce data variability across a testing session.

Submaximal force was defined relative to the highest MVC measured on the same day of the test. This allowed us to assess the muscles ability to maintain force output over a sustained contraction with respect to the maximal muscle force produced on the same day of the test. Task failure was defined as a drop in force >5% MVC for more than 5 s after strong verbal encouragement to the subject to maintain the target force value (Hedayatpour et al., 2014b).

Pain assessment

A 10-cm visual analogue scale (VAS), labelled with end points on no pain and worst pain imaginable, was used to assess the perceived pain intensity measured 24 and 48 h after eccentric exercise. The subjects were asked to rate the average pain intensity in their quadriceps during their regular activities of daily living (e.g., climbing stairs) since their last visit to the laboratory (during the past 24 h).

Limb girth

Thigh girth was measured using a tape-measure around the distal portion of the thigh of the ipsilateral limb (at 10% of the distance between the superior border of the patella and the anterior superior iliac spine) to monitor changes in limb girth which may change because of muscle swelling (Soderberg et al., 1996)

Electromyography

Surface electrodes (Ag–AgCl surface electrodes, Ambu Neuroline, conductive area, 28 mm^2) were placed bilaterally in bipolar configuration (inter-electrode distance, 2 cm) between the medial border (vastus medialis, VM), superior border (rectus femoris, RF) and lateral border (vastus lateralis, VL) of the patella and anterior superior iliac spine, according to the SENIAM recommendations (Hermens et al. 2000)

A reference electrode was placed around the right ankle. The positions of the electrodes were marked on the skin during the first session (day 1) so that the locations could be replicated 24 h and 48 h after exercise. Surface EMG signals were amplified (EMG amplifier, EMG-16, OT Bioelettronica, Torino, Italy, bandwidth 10–500 Hz), sampled at 2048 Hz and stored after 12-bit A/D conversion.

Signal analysis

To assess the amplitude of muscle activation during the MVC, the average rectified value (ARV) for each individual muscle were calculated over 200-ms windows within each 5-s MVC. The peak ARV obtained from the highest MVC was retained for further analysis. For the sustained contractions, the ARV was estimated from the EMG signals for epochs of 1 s. The values obtained from 1-s-long epochs in intervals of 10% of the time to task failure were averaged to obtain one representative value for each 10% interval. This was performed to allow comparison between subjects with different times to task failure.

Statistical Analysis

Two-way repeated-measures analysis of variance (ANOVA) was used to analyse MVC force and time to task failure in the ipsilateral and contralateral leg before and after eccentric exercise (pre-exercise, immediately after, 24 h and 48 h). A two-way repeated-measures ANOVA was also used to assess the EMG ARV of the knee extensors (averaged for VM, RF and VL muscle) with time (pre-exercise, immediately after, 24 h and 48 h), and leg (ipsilateral and contralateral) as dependent factors. Moreover, three-way repeated measures ANOVA were used to assess ARV (averaged for VM, RF and VL muscle) across the sustained contraction at 50% MVC (change from the first to the last epoch), with time (pre exercise, immediately after, 24 h and 48 h) and leg (injured/ipsilateral and uninjured/contralateral) as dependent factors.

One-way repeated-measures ANOVA was applied to asses muscle inflammation in the injured leg after eccentric exercise with time as the dependent factor. Pearson correlation coefficients were obtained to assess the relationship between change in EMG and change in maximal knee extension force across testing sessions. The significance

level was set at $p<0.05$ for all statistical procedures. Results are reported as mean and SD in the text and standard error (SE) in the figures.

RESULTS

A significant difference was observed for both maximum force ($F=9.0$, $p< 0.001$ and time to task failure ($F=14.0$, $p<0.0001$) between sides with the dominant leg producing higher force and greater endurance compared with the non-dominant leg ($p< 0.05$).

A significant reduction in maximum isometric knee extension force was observed for both the ipsilateral and contralateral leg ($F=27.7$, $p<0.001$) after eccentric exercise. A significant interaction was observed revealing that the extent of reduction in the maximum knee extension force was significantly greater for the ipsilateral injured leg compared to the contralateral un-injured leg ($p<0.05$; Figure 1). A significant reduction in time to task failure was also observed for both the ipsilateral and contralateral leg ($F=20.5$, $p<0.001$) after eccentric exercise. A significant interaction was also observed indicating a greater percentage of decrease in time to task failure observed for the injured leg compared with the un-injured leg ($p<0.05$) (Figure 2). MVC and time to task failure were not significantly different between the three post exercise sessions (immediately after, and at 24 and 48 h, $p>0.05$).

Figure 1 about here

Figure 2 about here

Additionally, the quadriceps EMG amplitude measured from both the ipsilateral and contralateral leg was significantly decreased during the post exercise MVCs ($F=21.0$,

p<0.001; Figure 3) and during the sustained isometric contractions (in the final epoch with respect to the initial epoch) (F=46.0, p<0.0001), compared with the pre-exercise condition (Table 1).

Figure 3 about here

Table 1 about here

In the non-exercised leg, the change in maximal force and change in ARV over the maximal contraction were significantly correlated (p<0.05; r = 0.39). The positive correlation indicates that variation in maximal force of the un-injured leg was partially a result of localised changes in muscle activation.

Figure 4 about here

Pain intensity increased over the quadriceps muscle as self-reported by the participants at 24 h (5.3±1.1/10) and 48 h post exercise (5.5±0.9/10). No difference in pain intensity was observed between 24 h and 48 h post exercise measurements. Thigh girth measured on the injured leg during the post exercise sessions was also significantly larger compared with the pre-exercise session measure (F=4.5, p<0.05).

DISCUSSION

Unilateral eccentric exercise was associated with an immediate decrease in strength (13.7%) and time to task failure (38.1%) of the contralateral side, which persisted for 48 hours. This may indicate that unilateral high intensity eccentric exercise of the quadriceps can modify neuromuscular activity and physical work capacity of the non-exercised homologous muscle in the contralateral limb.

Muscle performance before eccentric exercise

Before the eccentric exercise, the dominant leg produced higher muscle force and longer time to task failure as compared with the non- dominant leg. Previous studies have also demonstrated a greater force production for the dominant leg with respect to the non-dominant leg (Noguchi et al. 2014, Lanshammar& Ribom, 2011). This difference between two leg may be related to higher capacity of the dominant leg to produce force most likely due to the lower ratio between hamstrings and quadriceps strength in the dominant leg (H:Q), (Noguchi et al. 2014).

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Muscle performance after eccentric exercise

In the current study, participants reported that their quadriceps muscle of the injured leg was sore 24 and 48 h after eccentric exercise, which might be related to muscle fiber injuries, which in turn sensitizes the intramyofibril group IV afferents (Smith, 1991). The average pain intensity reported by participants for the injured leg was 5.3±1.1 and 5.5±0.9 at 24 and 48 h, respectively which is in agreement with the level of pain reported post eccentric exercise of the quadriceps in previous studies (Hedayatpour

et al., 2014a; Vila-Chã et al., 2012). This level of pain intensity has been reported to be a potential mechanism for the reduced muscle force and time to task failure after eccentric exercise. The observation of reduced muscle performance after eccentric exercise indirectly confirms that the muscle was injured by the exercise.

Cross-over effect of fatigue

In this study, the observed reduction in force output immediately after eccentric exercise, is most likely explained by a combination of muscle fiber damage and metabolite accumulation within the exercised muscle. An acute muscle adaptation to eccentric exercise such as early sarcomere damage (Proske & Morgan, 2001) and/or metabolites accumulation (e.g., hydrogen ions, lactate and inorganic phosphate) (Wan et al., 2017), alters contractile process within the exercised muscle, which, in turn reduce muscle force. Additionally, we also observed a significant reduction in force output for the non-exercised leg immediately after eccentric exercise. Although direct damage to the muscle fibers and contractile elements was not present within the non-exercised leg and therefore these changes in muscle function cannot be explained by changes in the contractile process. However, neural processes beyond excitation- contraction coupling such as corticospinal pathways may be involved (Hortobágyi et al., 2003; Sotgiu et al., 2004).

In agreement with our finding, other studies have also reported a ‘cross-over’ effect of central fatigue for both upper and lower limbs after fatiguing exercise (Ruohonen et al., 2002; Todd et al., 2003; Zijdewind et al., 1998). Doix et al. (2016) reported that unilateral fatiguing exercise resulted in a significant torque decline of 10.6% in the contralateral

non-exercised limb. Similarly, Martin and Rattey, (2007) found a significant force decline (<13%) in the non-exercised lower limb after unilateral fatiguing exercise. Others studies also showed that fatigue induced by exercise, produced a 'cross-over' effect of central inhibition, which in turn resulted in a reduction in force and /or motor output of the contralateral non -exercised limb (Halperin et al., 2014, Todd et al., 2003).

Cross-over effect of DOMS

Maximal voluntary force and time to task failure in the contralateral non-exercised leg were also significantly decreased 24 h after eccentric exercise of the opposite limb which persisted up to 48 h. A significant reduction in maximal isometric force and time to task failure observed for the contralateral non-exercised leg, indicates that eccentric exercise contributes to reduced muscle force and physical work capacity not only in the exercised muscle, but also in the non-exercised homologous muscle in the contralateral limb.

Reduction in muscle force observed at 24 and 48 h post eccentric could be related to fiber injuries of exercised muscle, since muscle can recover from fatigue within 24 h after exercise.

Additionally, a significant reduction in the amplitude of quadriceps muscle activity was observed during the post exercise MVCs and sustained contractions for the contralateral non-exercised leg with respect to the pre-exercise session, indicating that the reduced muscle force of the contralateral non-exercised leg was partially associated with decreased muscle activation.

Potential mechanisms for cross-over effect of DOMS

There are several potential mechanisms by which DOMS, induced by eccentric exercise, may contribute to the reduced motor output of the non-exercised leg. Typically, nociceptor sensitization associated with tissue injury can influence primary afferents of muscle spindles at superficial layers of the dorsal horn of the spinal cord 24h after eccentric exercise (Le Pera et al., 2001; Sotgiu et al., 2004). The axons of nociceptive dorsal horn neurons cross to the contralateral anterolateral quadrant to form an ascending tract (Carpenter, 1985), which terminates in the brainstem and several distinct areas of the thalamus (Todd, 2010). These ascending pathways, which mediate nociceptive information (Willis, 1985), may inhibit motor cortex regions associated with the contralateral limb which, in turn, reduces neural output (Cotofana et al., 2015; Gossard & Rossignol, 1990; Barr& Kiernan, 1993) and, consequently, reduces maximal force (Farina et al., 2005; Hedayatpour et al., 2009).

Reduced muscle force in the contralateral non-exercised leg could be further explained by a pain-induced change in motor planning and/or by change in potential signalling pathways on the contralateral side. The perception of pain within the injured quadriceps muscle can alter cerebral motor plans (Svensson et al., 1997) and as a consequence may contribute to reduced muscle performance of the contralateral non-exercised leg (Byl & Melnick, 1997; Halperin et al., 2014). Finally, damage to muscle fibers results in the release of a number of immunomodulatory agents that can be transported to the contralateral part of the body with possible effects on signalling pathways and consequently changed motor behaviour (Dennis, 1998; Ruohonen et al., 2002).

A number of studies have investigated 'cross-over' effect of exercise training and indicated that both positive and negative effects of exercise can be transferred to the contralateral non-effected limb, most likely due to the modulation of neural circuits at the level of spinal cord and motor cortex. For example, previous studies reported that pain can impair motor performance of the contralateral, unaffected arm of patients with chronic unilateral tennis elbow (Pienima et al., 1997). Patients with chronic wrist pain also demonstrated disturbances of fine motor output of the contralateral, unaffected wrist (Smeulders et al., 2002). Accordingly, deficits in motor function of the contralateral unaffected side have been identified in some musculoskeletal pain conditions including osteoarthritis (Cotofana et al., 2015) and patellofemoral pain (Akseki et al., 2008) as well as following some experimental paradigms (Moseley et al., 2005). The contralateral effects of pain have also been demonstrated by earlier electrophysiological studies in response to laser-evoked somatic and trigeminal pain (Tarkka & Treede, 1993). Additionally, positive effects of exercise has been reported to be transferred to the contralateral non-exercised limb. Previous studies reported an increase in muscle force for the contralateral untrained limb after 4 to 12 weeks of unilateral training (Carroll et al. 2006), and eccentric training resulted in a greater increase in isometric force of the contralateral untrained limb (39%) as compared to concentric training (22%) (Hortobágyi et al. 1997).

In line with these findings, we also observed for the first time, a decrement in force output of the contralateral non-exercised leg after a unilateral knee eccentric exercise, most likely due to cross-over effect of DOMS at the level of spinal cord and /or motor cortex. This cross-over effect of DOMS may be necessary to reduce force

generating capacity of the non-exercised leg through lower voluntary activation to cope with the weaker force of the exercised leg, and therefore to regulate bilateral coordination between two limbs during high intensity exercise.

CONCLUSION

Maximal knee extension force and time task failure during sustained knee extension contractions of the contralateral non-exercised leg were significantly reduced immediately after unilateral eccentric exercise, and this persisted 24 and 48 h post exercise. This original finding indicates that DOMS induced by eccentric exercise at 24 and 48 h post eccentric may partly contribute to reduced muscle force and physical work capacity in the unaffected homologous muscle of the contralateral limb. This change should be taken into consideration when developing training and rehabilitation programmes since these changes may leave the limb at risk of greater injury if the training volume is not adjusted according to the reduced motor capacity. Further studies are needed to determine the underlying mechanisms of reduced motor output in the contralateral non-exercised limb and to identify the time required for motor function to return to normal.

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TABLE

Table 1- Mean ± SD (n=15) for the percent change in the EMG average rectified value (ARV) recorded from the quadriceps during sustained knee extension contractions at 50% MVC (change from the first to the last epoch), and measurement of thigh circumference.

ARV (% decrease) Ipsilateral leg	-1.5 ± 0.09	-15.5 ± 3.4 *	-14.8 ± 2.7 *	-12.9 ± 3.8 *
ARV (% decrease) Contralateral leg	- 0.85 ± 0.02	-10.7 ± 2. 5*	-9.5 ± 2. 3*	-7.7 ± 1.8 *
Thigh girth (cm)	40.7 ±2. 4	41.6 ± 3.1 *	41.5 ± 2.8 *	41.5 ± 3. 1*

*Indicates significant difference to baseline ($p<0.05$).

FIGURES

FIGURE 1- Maximal isometric knee extension force (mean ± SE, N.m, n = 15) recorded before the eccentric exercise (pre exercise), immediately after, 24 H and 48 h after the eccentric exercise. Ipsilateral leg (black circle) and contralateral leg (white circle). $*p \leq 0.05$.

FIGURE 2- Time to task failure (mean ± SE, s, n = 15) during sustained isometric knee extension 50% of the maximal voluntary contraction (MVC) measured before the eccentric exercise (pre exercise), immediately after, 24 h and 48 h after the eccentric exercise. Ipsilateral leg (black circle) and contralateral leg (white circle). $*p \leq 0.05$.

FIGURE 3- Average rectified value of EMG (ARV; mean ± SE, µV , n = 15) recorded from the knee extensors muscles (average for the VM, RF and VL muscles) during maximal voluntary contraction of the knee extension before the eccentric exercise (pre exercise), immediately after, 24 h and 48 h after the eccentric exercise. Ipsilateral leg (black circle) and contralateral leg (white circle). $*p \leq 0.05$.

FIGURE 4. Scatter plot of change in average rectified value of EMG (average for vastus medilais, vastus lateralis and rectus femoris) versus change in maximal isometric muscle force, performed at pre-exercise compared with the post- exercise sessions (average for

all post- exercise sessions). In the non-exercised leg, the change in maximal force and change in ARV over the maximal contraction were significantly correlated ($p<0.05$; $r = 0.39$). The positive correlation indicates that variation in maximal force of the non-exercised leg was partially a result of changes in muscle activation.