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Insight into motor adaptation to pain from between-leg compensation

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Running title: between-leg compensations during pain

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Abstract (250 words)

Purpose: Although it appears obvious that we change movement behaviours to unload the painful region, non-systematic motor adaptations observed in simple experimental tasks with pain question this theory. We investigated the effect of unilateral pain on performance of a bilateral plantarflexion task. This experimental task clearly allowed for stress on painful tissue to be reduced by modification of load sharing between legs. **Methods:** Fourteen participants performed bilateral plantarflexion at 10%, 30%, 50% and 70% of their MVC during 5 conditions (Baseline, Saline-1, Washout-1, Saline-2, Washout-2). For Saline-1 and -2, either isotonic saline (Iso), or hypertonic saline (Pain) was injected in the soleus. **Results:** The force produced by the painful leg was less during Pain than Baseline (range: -52.6% at 10% of MVC to -20.1% at 70% of MVC; $P<0.003$). This was compensated by more force produced by the non-painful leg (range: 18.4% at 70% of MVC to 70.2% at 10% of MVC; $P<0.001$). The reduction in plantarflexion force was not accompanied by a significant decrease in soleus electromyographic activity at 10% and 30% of MVC. Further, no significant linear relationship was found between changes in soleus electromyographic activity and change in plantarflexion force for the painful leg (with the exception of a weak relationship at 10% of MVC, i.e. $R^2=0.31$). **Conclusion:** These results show that when the nervous system is presented with an obvious solution to decrease stress on irritated tissue, this option is selected. However, this was not strongly related to a decrease in soleus (painful muscle) activity level.

Key words: electromyography; stress; hypertonic saline; load; plantarflexion; force plate

Abbreviations:
EMG: Electromyography
GM: Gastrocnemius medialis
GL: Gastrocnemius lateralis
Iso: Isotonic
MVC: Maximal Voluntary Contraction
SOL: Soleus
TA: Tibialis anterior
WO: Washout

Introduction

The effects of pain on movement have been widely studied in clinical populations, (e.g. Crossley et al. 2012; Mundermann et al. 2005). This underpins the conclusion that we move differently when we are in pain. The principle theory is that adaptation aims to reduce load on painful tissue to protect from further pain and/or injury (Hodges and Tucker 2011). Although logical and generally assumed to be correct, there is surprisingly little experimental evidence for a purposeful strategy to decrease load in the painful tissue.

It is difficult to isolate the effect of nociceptive stimulation in clinical populations. This is because chronic musculoskeletal pain is often associated with other impairments (e.g. structural tissue changes, weakness and disuse) and the link between nociceptive input and pain is complicated by sensitization (central and peripheral). To circumvent this problem, experimental pain is used to replicate the nociceptive component of these complex conditions. Experimental pain induction most frequently involves intramuscular injection of hypertonic saline (Graven-Nielsen et al. 2003; Staahl and Drewes 2004), which produces acute nociceptive stimulation with local and referred pain. Similar to the prediction based on data from clinical pain studies, motor adaptations to this acute nociceptive stimulation are thought to reduce load on the painful tissue (Bank et al. 2013; Hodges and Tucker 2011). Yet, results are conflicting. Consistent with a decrease in load, some studies report a decrease in gross myoelectrical activity of the painful muscle (Ciubotariu et al. 2004; Graven-Nielsen et al. 1997) but this is not always observed, especially at low contraction intensities (Farina et al. 2004a; Hodges et al. 2008; Madeleine and Arendt-Nielsen 2005). Increased muscle activity associated to an increase in corticospinal excitability has also been reported (Fadiga et al. 2004). Variability in the mechanical outcome of

pain adaptations also exists. For example, although the direction of knee extension force is modified when pain is induced in the infrapatellar fat pad (presumably to modify loading of the pad), the direction of angle change (i.e. medially or laterally) is not uniform between individuals (Tucker and Hodges 2010).

Three issues could explain the inconsistency between studies/individuals. First, the theory may be wrong and the adaptation to pain may not serve to unload irritated tissue. Second, hypertonic saline may not provide a suitable model to study the adaptation to pain, as pain level might not be related to tissue loading in a manner that is identical to that in clinical conditions. Third, the isometric single joint tasks classically used to study motor adaptation have limited options available to vary the manner in which a task is performed while output is maintained. As a consequence, the failure to observe a consistent adaptation may be explained by to the inability to unload painful tissues consistently.

To test whether experimental nociceptive stimulation induces a motor adaptation that systematically modifies tissue load, nociceptive stimulation can be induced in a task that involves an obvious option to modify force distribution (tissue stress), while maintaining the task objective. Here we investigated the effect of *unilateral* nociceptive stimulation on performance of a *bilateral* plantarflexion task that clearly allows for stress on the painful tissue to be reduced by modification of load sharing between legs. Although between-leg compensation would appear an obvious strategy to unload painful tissue, previous results are inconsistent. In quiet stance, weight is redistributed to the non-painful leg when pain is induced in some leg muscles but not others (Hirata et al. 2010; Hirata et al. 2011). We hypothesized that, during bilateral plantarflexion; 1) force produced by the painful leg would consistently decrease, with compensation by the non-painful side, regardless of the

contraction intensity, and that 2) these adaptations would involve consistent changes in activity of plantarflexor muscles, i.e., decreased activity in painful leg compensated by increased activity in the non-painful leg.

Materials and methods

Participants

Fourteen healthy volunteers participated in this experiment (age: 22 ± 2 years; 7 males and 7 females). Participants were excluded if they had a history of leg pain that had limited function or for which they had sought treatment. Participants were recruited through advertisements on the University's website and no participants had previously participated in a pain experiment. The Institutional Medical Research Ethics Committee (The University of Queensland) approved the study and all the procedures conformed to the Declaration of Helsinki.

Experimental set up

Participants sat on a chair with the feet on separate force plates. The hip, knee and ankle were positioned at ~90° from full extension (Fig. 1A) to limit contribution of gastrocnemii muscles to plantarflexion (Cresswell et al. 1995). Consequently, the soleus muscle (SOL) was primarily responsible for the plantarflexion torque produced during the experimental task. This experimental set-up ensured participants were provided with an obvious potential solution to decrease load within the painful leg (and thus, the irritated tissues), i.e., compensation by the contralateral leg. A horizontal bar pressed against the distal thighs resisted movement of the legs during the isometric plantarflexion (Fig. 1A). To minimize movement of the body or changes in posture between contractions, the hips were fixed with a strap attached to the chair.

Force data

Separate force plates (Model 9260AA6, Kistler, Switzerland) measured the plantarflexion force produced by each leg. Data were sampled at 1 kHz (Power1401 Data Acquisition System, Cambridge Electronic Design, UK) and low-pass filtered (20 Hz, 4th order Butterworth filter) off-line. Total plantarflexion force (Fz_{Tot}) was provided as a feedback to the participants and calculated as the sum of the left and the right plantarflexion force (Fz_L and Fz_R, respectively).

Electromyography

Myoelectric activity was recorded bilaterally with surface EMG electrodes from four leg muscles: SOL, gastrocnemius medialis (GM) and lateralis (GL), and tibialis anterior (TA). For each muscle, a pair of self-adhesive Ag/AgCl electrodes (Blue sensor N, Ambu, Denmark) was attached to the skin with an inter-electrode distance of 20 mm (center-to-center) (Fig. 1B). The skin was cleaned with abrasive gel (Nuprep, D.O. Weaver & Co, USA) and alcohol. The ground electrode (half a Universal Electrosurgical Pad, 3M Health Care, USA) was placed over the right tibia. EMG data were pre-amplified 1,000 times, band-pass filtered (20 Hz to 500 Hz) on-line (Neurolog, Digitimer, UK), and sampled at 1 kHz using a Power1401 Data Acquisition System with Spike2 software (Cambridge Electronic Design, UK).

Experimental tasks

Three bilateral maximal isometric voluntary plantarflexion efforts were performed for 3 s and separated by 90 s. Maximum Fz_{Tot} was considered the best performance (maximum voluntary contraction [MVC]). The experimental task involved matching a target Fz_{Tot} set at 10, 30, 50, or 70% of MVC during short (≈10 s) constant force isometric contractions performed in random order with 30 s rest between each repetition. An experimenter verified that the force was well matched throughout the data collection, and verbal encouragement was provided to the

participants if required to assist in the appropriate maintenance of force. Participants were aware that feedback (Fz_{Tot}) was provided by summation of force produced by both legs but were not instructed regarding any load sharing strategy to produce force. This was repeated in 5 experimental conditions: Baseline, Saline 1, Washout 1, Saline 2, Washout 2. The Baseline condition without injection preceded a Saline condition with either isotonic saline (Iso), or hypertonic saline (Pain) injected into the left SOL (see below). Each Saline condition was followed by a Washout condition (Fig. 2). In order to test the variation of force data that could be expected between repetitions of the task (without nociceptive stimulation), two contractions were performed for the Baseline condition at each force level. The order of isotonic and hypertonic saline injection was counterbalanced (an equal number of participants received isotonic and hypertonic saline injection as their first Saline condition). The Washout condition following the Pain condition was initiated >2 min after pain had completely resolved.

Experimental Pain

The procedure was identical for both Pain and Iso conditions, except that hypertonic saline (0.5 mL bolus 6.7% NaCl) was injected to stimulate nociceptors, and isotonic saline (0.7 mL bolus 0.9% NaCl) was injected as a control for the injection of a fluid bolus into the test muscle. Isotonic saline was injected with larger volume to account for possible greater diffusion of water from surrounding tissue following hypertonic saline injection (Tsao et al. 2010). Saline was injected using a 25G × 19 mm hypodermic needle into the lateral soleus of the left leg ~1/3 the distance from the ankle to the posterior knee crease. This location was confirmed to be the soleus by manual palpation. Participants rated pain intensity on an 11-point numerical rating scale (NRS), anchored with “no pain” at 0 and “worst imaginable pain” at 10. Immediately following each contraction, participants rated pain intensity

experienced during the task, and during the rest period. Participants recorded the area of pain on a standardized diagram of the lower leg after completion of the pain condition (Fig. 1B).

Data analysis

All data were processed using Matlab (The Mathworks, Nathick, USA). A typical example of the raw data is depicted in Fig. 3. From each force-matched contraction, a 5-s period of data at the middle of the force plateau was used for analysis. The baseline force (i.e. weight of the legs) measured prior to the first Baseline contraction was subtracted from all force data. The average amplitude of Fz_L, Fz_R and Fz_{Tot} during each contraction was calculated.

EMG amplitude of SOL, GM and GL was quantified as Root Mean Square (RMS) calculated over the same 5-s period as that used for the mechanical data. These values were normalized to the peak RMS calculated from a 500-ms windows centered on maximum EMG recorded during the MVCs. As no maximal dorsiflexion was performed, TA EMG activity was not normalized and activity of that muscle was compared between conditions using un-normalised data.

Statistical analysis

Statistical analyses were performed in Statistica (Statsoft, USA). Distributions consistently passed the Shapiro-Wilk normality test and thus all data are reported as mean±SD. P-values below 0.05 were considered significant.

Variation of Fz_L and Fz_R between the 2 contractions performed during the Baseline condition was assessed using the Intraclass Correlation Coefficient (ICC) and the Standard Error in Measurement (SEM). For all analyses the mean of the two Baseline contractions was used.

To verify that the two legs contributed similarly to MVC, a paired t-test was used to compare Fz_R and Fz_L (as % Fz_{Tot}). Pain intensity was compared between Conditions (Pain vs. Iso), Intensities (10, 30, 50 vs. 70% of MVC) and Contraction state (during contraction vs. rest) using a repeated measures ANOVA. Plantarflexion force and EMG amplitude for each muscle (separately) was compared between Conditions (Baseline, Pain, Iso, Washout 1, Washout 2), Intensities (10%, 30%, 50% vs. 70% of MVC) and Legs (painful vs. non-painful) using a repeated measures ANOVA. Because TA EMG activity was not normalized, separate ANOVAs were performed for each leg to determine whether antagonist muscle activity differed between Conditions (Baseline, Pain, Iso, Washout 1, Washout 2) and Intensities (10%, 30%, 50% vs. 70% of MVC). To determine whether the amount of change in plantarflexion force produced by the painful leg depend on the target force, we compared the changes in Fz_L observed during Pain (expressed in % of Baseline) between the 4 intensities using a repeated measures ANOVA. Finally, to determine whether the changes in plantarflexion force were linearly related to changes in EMG of the agonist muscles, we calculated the linear regression between these variables (expressed in % of MVC) for each leg and each intensity separately.

When required, post hoc analyses were performed using the Fisher test. To limit the bias induced by multiple comparisons, only changes from the Baseline conditions and differences between Pain and Iso were analyzed (limiting to 5 comparisons between Conditions for each leg). In addition, a correction was applied resulting in a significance set at P-value below 0.01 (i.e., 0.05/5 comparisons) for the post hoc analyses. Finally, Cohen's *d* values are reported as measures of effect size, with 0.2, 0.5 and 0.8 as small, moderate and large effect, respectively (Cohen 1988).

Results

Pain

Pain was reported at the site of hypertonic saline injection (Fig. 1B) except for one participant who reported pain over the proximal calf. Average pain intensity was higher during Pain than Iso (5.6±1.8 vs. 0.3±0.8, P<0.0001, *d*=4.0). Pain did not differ with contraction Intensity (P=0.71) or Contraction state (i.e., contracted vs. relaxed; P=0.33).

Force

MVC force was 1124±306 N. The contribution to MVC did not differ between legs (52.8±4.8 vs. 47.2±4.9% of Fz_{Tot} for the left and right leg, respectively; P=0.11), which suggest a similar maximal capacity for each leg. Variation of the contribution of each leg to Fz_{Tot} between repetitions of the task in the Baseline condition was low (ICC= 0.72, 0.69, 0.91, and 0.72; SEM=4.7, 4.6, 1.9, and 3.4 % of Fz_{Tot} for 10%, 30%, 50%, and 70% of MVC, respectively). This indicates that the sharing of load between legs to produce Fz_{Tot} during Baseline contractions was robust over time.

The typical error of Fz_{Tot} (target force) calculated as a coefficient of variation over the 5 conditions was low (3.4%, 1.4%, 0.9%, and 1.6% for 10%, 30%, 50% and 70% of MVC, respectively) indicating that the target force was well matched at each contraction level. There was a significant interaction between Condition × Intensity × Leg (P=0.023) for plantarflexion force. As shown in Fig. 4, the force produced by the painful leg was less during Pain than Baseline at 10% of MVC (-52.6±54.3%, P=0.003, *d*=1.2), 30% of MVC (-32.9±32.3%, P<0.0001, *d*=1.0), 50% of MVC (-27.3±27.5%, P<0.0001; *d*=0.8), and 70% of MVC (-20.1±18.3%, P<0.0001, *d*=0.5). Further, the force produced by the non-painful leg was greater during Pain than Baseline at 10% of MVC (+70.2±57.5%, P=0.001, d=1.8), 30% of MVC

(+40.1±34.9%, P<0.0001, *d*=1.0), 50% of MVC (+31.3±32.9%, P<0.0001, *d*=1.0), and 70% of MVC (+18.4±18.3%, P<0.0001, *d*=0.6). Note that only 1 participant did not exhibit this compensation strategy but rather exhibited an opposite compensation, i.e. slight increase in force produced by the painful leg for all target force levels. Isotonic and Washout conditions were not different from Baseline (all P values > 0.42).

Differences in load sharing were also observed between Pain and Iso conditions for each intensity and both legs (Fig. 4). Force produced by the painful leg was lower during Pain than Iso at 10% of MVC (P=0.008, *d*=1.1), 30% of MVC (P=0.002, *d*=0.7), 50% of MVC (P<0.001, *d*=0.5) and 70% of MVC (P<0.001, *d*=0.5). Force produced by the non-painful leg was higher during Pain than Iso at 10% of MVC (P=0.005, *d*=1.3), 30% of MVC (P=0.001, *d*=0.8), 50% of MVC (P<0.001; *d*=0.6) and 70% of MVC (P<0.001, *d*=0.6).

When the changes in force produced by the painful leg during Pain (expressed in percentage of Baseline) were compared between the four intensities, a significant effect was found (P=0.017). The decrease in force was greater at 10% of MVC (-52.6±54.3%) compared to both 50% of MVC (-27.3±27.5%; P=0.016; *d*=0.6) and 70% of MVC (-20.1±18.3%; P=0.002; *d*=0.8). No other differences were found (all P values >0.06).

Surface EMG

There was a significant Condition × Intensity × Leg interaction (P=0.030) for SOL RMS EMG. SOL RMS EMG of the painful leg was less during Pain than Baseline at both 50% of MVC (-21.1±19.3%, P=0.0007, *d*=0.7) and 70% of MVC (-14.6±23.9%, P=0.0002, *d*=0.6) (Fig. 5). SOL EMG activity of the non-painful leg was greater during Pain than Baseline at 30% of MVC (+47.6±93.3%; P=0.0002, *d*=0.7),

50% (+40.0±93.3%, P<0.0001, *d*=0.6) and 70% of MVC (+20.2±31.9%, P<0.0001, *d*=0.6) (Fig. 5). Greater SOL RMS EMG of the non-painful leg was also observed during Iso conditions at 50% of MVC (+17.5±40.8%, P=0.008; *d*=0.4) and during Washout (following the Pain condition) at 70% of MVC (+17.0±28.3%, P<0.0001, *d*=0.5), despite the complete resolution of pain. SOL RMS EMG of the painful leg was only different between Pain and Iso at 70% of MVC (P=0.0008, *d*=0.6), however, differences were observed for the non-painful leg at 30% of MVC (P=0.004; *d*=0.5), 50% (P=0.004, *d*=0.3), and 70% of MVC (P=0.0037; *d*=0.3) (Fig. 5).

For GL, a significant Condition × Intensity × Leg interaction (P=0.016) was found. GL RMS EMG of the painful leg was less during Pain than Baseline at both 50% of MVC (-10.6±38.5%, P=0.005, *d*=0.5) and 70% of MVC (-10.3±38.5%, P=0.004, *d*=0.4). GL EMG of the non-painful leg was greater during Pain than Baseline at 30% of MVC (+40.5±60.1%, P=0.001, *d*=0.4), 50% of MVC (+30.3±33.5%, P<0.0001, *d*=0.7) and 70% of MVC (+19.3±33.4%, P<0.0001, *d*=0.6). For GM, only a main effect of Intensity (P<0.0001) and a significant Condition × Leg interaction (P=0.004) was found. GM RMS EMG of the non-painful leg was higher during Pain (+28.9±46.4%, P<0.0001, *d*=0.7) than Baseline.

Antagonist TA RMS EMG was affected by contraction intensity (main effect Intensity for both legs: P<0.0001), but did not differ between Conditions for either leg (main effect Condition: P>0.13; Intensity × Condition interaction: P>0.12).

Relationship between EMG and force

The relationship between the change of SOL RMS EMG between the Baseline and Pain conditions and the change in Fz was tested for each leg and each intensity separately. For the painful leg, no significant linear regression was found (P values ranged from 0.10 to 0.41) except at 10% of MVC (P=0.037, R^2=0.31; i.e. SOL EMG

decreased in a linear manner with the decreased force for the painful leg). For the non-painful leg, SOL EMG increased in a linear manner with the increased force at 30% of MVC ($P<0.001$, $R^2=0.68$), 50% of MVC ($P<0.001$, $R^2=0.82$), and 70% of MVC ($P=0.03$, $R^2=0.31$). The P-value was also close to significant ($P=0.06$) at 10% of MVC.

Discussion

The present study provides evidence that when the nervous system is presented with an obvious solution to decrease stress on irritated tissue (decrease force produced by the painful leg and increase force in the non-painful leg in a bilateral task), this option is selected. A surprising observation was that although the obvious solution to reduce force would involve reduced SOL EMG of the painful leg (the most mechanically efficient muscle for this task) no significant reduction in SOL EMG amplitude was observed in the painful leg at 10% and 30% of MVC. In addition, no significant linear relationship (except for a weak relationship at 10% of MVC, i.e. $R^2=0.31$) was found between changes in SOL EMG amplitude and change in plantarflexion force for the painful leg. This suggests that participants did not systematically select what could be reasonably argued to be the most straightforward solution (reduced SOL activation).

The consistent “between-leg” compensation to maintain the task objective (maintain target total plantarflexion force), combined with the complex relationship between force and EMG during acute experimental pain provide important insight into motor adaptations with acute nociceptor stimulation and pain. As muscle force is directly related to muscle stress during isometric contractions, the consistent decrease in force observed in the painful leg suggests a decreased stress (or load) within the painful SOL muscle (which is the primary contributor to the plantarflexion task when

the knee is flexed (Cresswell et al. 1995)). We argue that when the nervous system is presented with a clear solution to reduce load in a painful tissue while maintaining task performance, this new strategy is consistently adopted (only 1 participant out of 14 did not exhibit between-leg compensation for any contraction intensity). Although such between-leg compensation would appear obvious and predictable, similar adaptations have not been consistently observed during bilateral balance tasks with unilateral pain (Hirata et al. 2010; Hirata et al. 2011). For example, a shift in body weight to the non-painful side during quiet stance was reported when pain was simultaneously induced in multiple leg muscles (Hirata et al., 2010). However, this was less commonly observed when pain was isolated to a single leg muscle (Hirata et al., 2011). One interpretation is that other options (including a redistribution of activity between muscles of the painful leg, or a change in the position of multiple body segments) were available to the nervous system in response to application of nociceptive stimuli to a single muscle during the bilateral standing task. The shift of load to the non-painful leg was therefore not the only solution, and may not have been the most energy efficient solution.

No significant change in SOL EMG was observed in the painful leg at 10% and 30% of MVC. In addition, no significant linear regression was found between change in SOL EMG and change in plantarflexion force in the painful leg at 30%, 50% and 70% of MVC. Taken together, these results imply that reduced plantarflexion force was not achieved exclusively by reduced SOL activation. Because the task was designed to limit the contribution of the gastrocnemii muscles and because no significant decrease in GM and GL activity was observed in the painful leg at 10% and 30% of MVC, it is unlikely that these muscles explain the reduced plantarflexion force. It is important to consider that we did not record EMG

from deep muscles that can contribute to plantarflexion (flexor digitorum longus, tibialis posterior, and flexor hallucis longus). Although triceps surae is thought to contribute > 85% (van Zandwijk et al. 1998) during plantarflexion, the activity of other plantarflexors may have contributed to our results. Further, although the experimental task was designed to reduce the contribution of other joints (knee, hip), it is possible that altered activation of other muscles contributed to this change in plantarflexion force. Finally, it is possible that increased antagonist muscle activation could account for reduced total plantarflexion force, but this was also not observed. Rather, we argue that within the painful limb, there remains a complex adaptation of activity within and between muscles that precludes identification of systematic changes in EMG recorded with surface electrodes. This is because the surface recorded EMG signal represent the net activation of a large area of muscles and do not enable identification of subtle redistribution of activity that may vary between individuals (Hodges et al. 2008; Tucker et al. 2009; Hug et al. 2013). This is particularly important because activity may have changed heterogeneously within the muscle, i.e., decreased in a region or in some fibres, but no others, as has be shown previously during a similar plantarflexion task (Hug et al. 2013). Alternatively, it is possible that surface EMG signals cannot provide an accurate indication of loading within the muscle tissue (i.e., muscle stress). This is because the EMG signal is influenced by numerous physiological (e.g. fibre membrane properties, depth of motor units) and non-physiological factors (e.g. muscle geometry, crosstalk, detection system, summation of action potentials from multiple motor units) (Farina et al. 2004b; Hug 2011). In addition, EMG cannot account for passive force and putative between-muscle force transmission, which has been argued to be significant between SOL and GM (Tian et al. 2012).

The complex relationship between EMG and muscle stress can explain some discrepancies among previous results, i.e., decrease in EMG activity within the painful muscle (Ciubotariu et al. 2004; Graven-Nielsen et al. 1997), no change (Farina et al. 2004a; Hodges et al. 2008; Madeleine and Arendt-Nielsen 2005), or even an increase (Fadiga et al. 2004) in muscle activity with pain. Despite these conflicting results it is possible that the intention of the adaptation to reduce stress (at least locally) in the painful tissue may have been achieved in all of these studies, but not reflected by interpretation of the gross surface EMG recording. This is particularly relevant to consider in a muscle with complex muscle architecture such as SOL. Martin et al. (2001) reported considerable variation in muscle fibre orientation in SOL between individuals, which can underpin wide variation in SOL aponeurosis strain (Finni et al. 2003) for the same activation level. A weak association between EMG amplitude and muscle stress has been shown during single joint isometric contractions (Bouillard et al. 2012; Bouillard et al. 2011), and during gait where changes in knee contact forces were poorly estimated from EMG measures (Meyer et al. 2013). Together these results demonstrate that there is a limited ability to interpret changes in tissue stress based on surface EMG alone, and highlights the need for more direct techniques to measure stress such as elastography.

In addition to the primary outcomes of this study, we have also shown no difference in pain intensity between contraction levels during isometric force-matched contractions (similar to previous work (Ciubotariu et al. 2004)). However, this analysis might be compromised by the counter-balanced order of force level because the reported pain induced by this hypertonic saline injection gradually decreases over time (e.g. peak at ≈2 min after injection, decreasing <2 (out of 10) after ≈7 min; Hirata et al., 2010). In contrast to previous works showing that pain intensity is

decreased during muscle stretching and muscle contraction (Tsao et al. 2010), pain intensity was not worsened or relieved by contraction in our experiment. This observation could be interpreted in 2 ways. First, it may indicate that the adaptation to motor strategy decreased tissue load sufficiently to avoid additional tissue irritation during the contraction, or second, that pain intensity using this experimental model may be unrelated to tissue load.

In conclusion, we have shown that when provided with a clear solution to unload the painful tissue this solution is adopted. However, considering that SOL is the main plantarflexor at this knee angle (Cresswell et al. 1995), the absence of significant decrease in SOL activity at 10 and 30% of MVC suggests that the CNS did not select the most straightforward option to unload the painful tissue. We argue this latter observation is explained by subtle variation between individuals and/or inherent limitations to interpretation of tissue loading from surface EMG recordings. Experimental techniques to quantify tissue stress are needed to determine if the observed changes in plantarflexion force are associated with reduced tissue load in the painful region.

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Figures

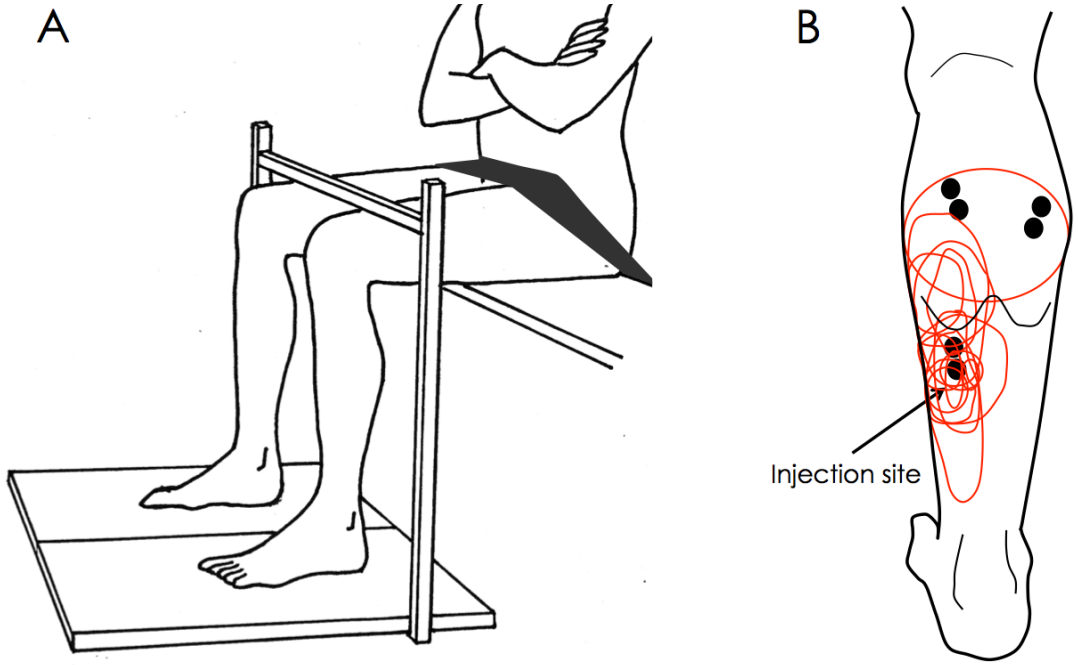

Figure 1. Experimental setup (A) and area of pain (B).

A) Lateral view of the position of the legs, support bar and force plates. Participants sat comfortably on a chair with each foot positioned on a separated force plate. B) The injection site (arrow) and the area of reported pain for each participant (red) are shown. The position of the surface EMG electrodes is also shown (black circles).

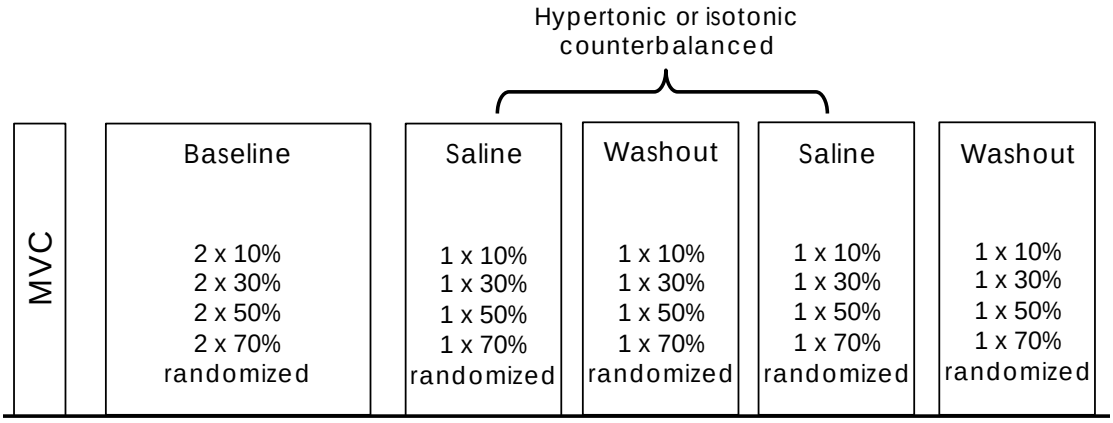

Figure 2. Experimental design.

The experimental task involved matching a target Fz_{Tot} set at 10, 30, 50, or 70% of maximal voluntary contraction (MVC) during short (10 s) constant force isometric contractions performed in randomised order with 30 s rest between each. This was

repeated in 5 experimental conditions: Baseline, 2 × Saline (1 × hypertonic; 1 × isotonic), 2 × Washout.

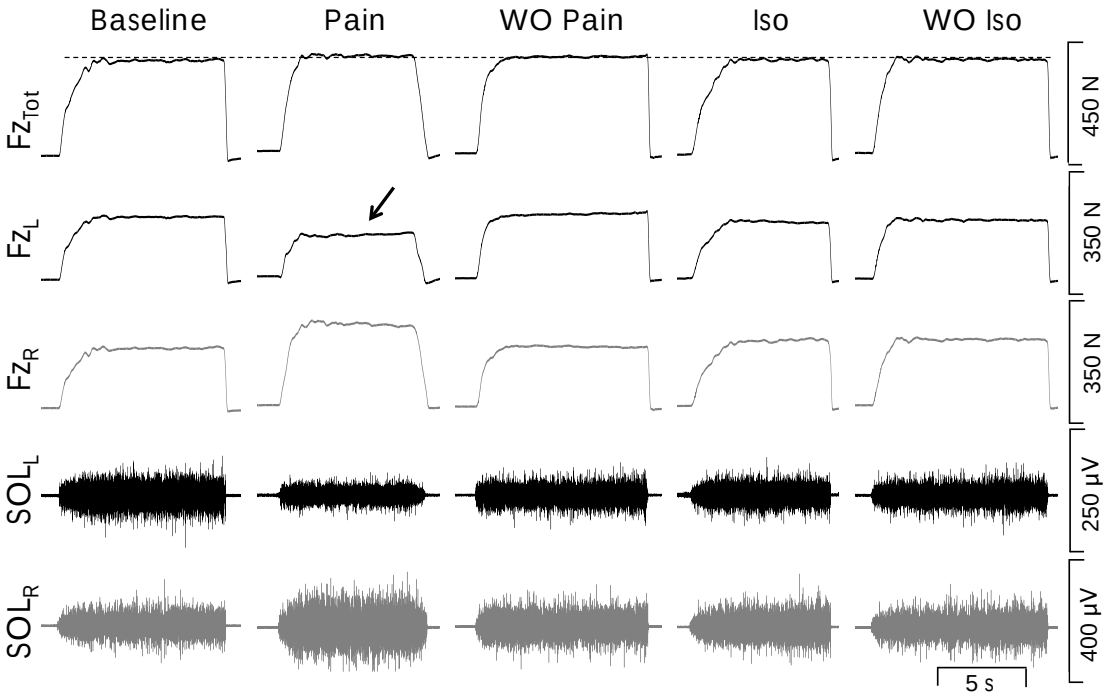

Figure 3. Typical example of force and EMG data.

Total plantar flexion force (sum of the force produced by both legs, Fz_{Tot}) was maintained between the 5 contractions performed at 50% of maximal voluntary contraction. Saline injection was performed in the left leg. Pain induced a decrease in the force produced by the painful leg ($Fz_{L;}$ indicated by an arrow) compensated by an increase in force produced by the non-painful leg (Fz_R). Despite similar changes were observed after the injection of isotonic saline, their magnitude was lower.

SOL, soleus; Fz, Plantarflexion force

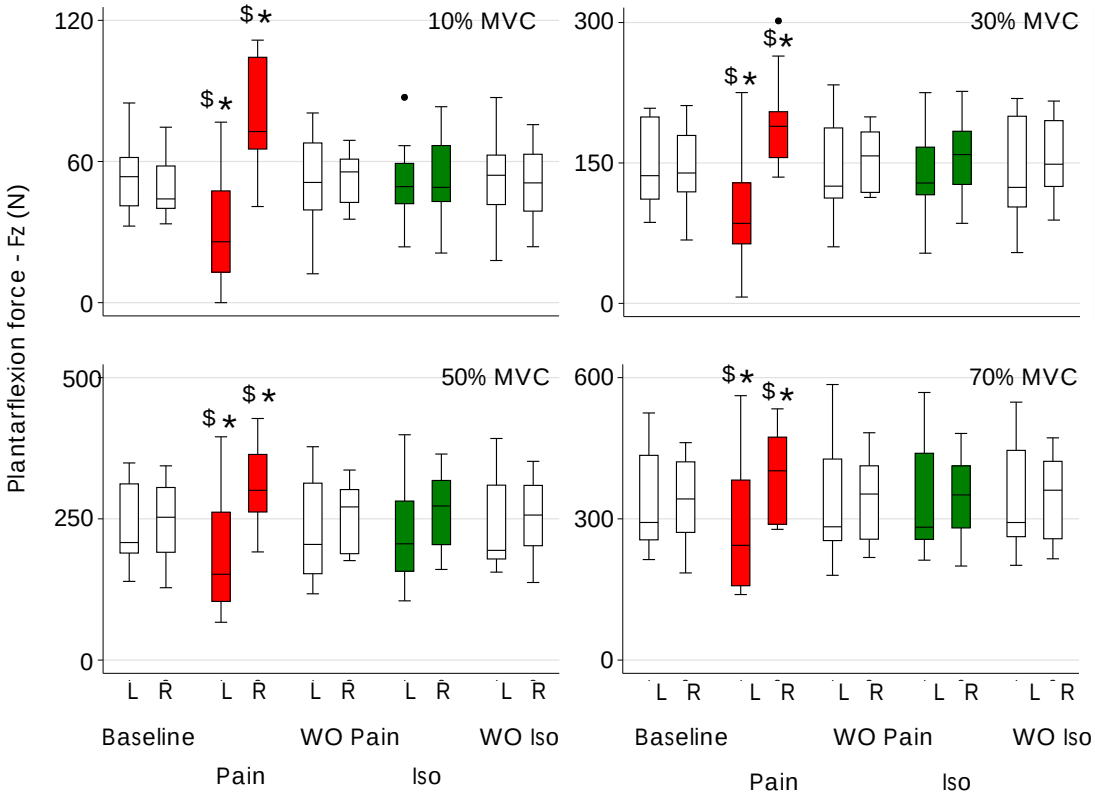

Figure 4. Plantarflexion force produced by the left (painful: Fz_L) and right (non-painful: Fz_R) leg.

During contraction at each intensity, the force produced by the painful leg was less during pain than Baseline, and the force produced by the non-painful leg was greater. Error bars denote the 95% confidence interval; box denotes the 25-75 percentile with the median and dots indicate outliers. * - significant difference from Baseline using the Fisher test for post hoc comparison, $, significant difference from Iso using the Fisher test for post hoc comparison.

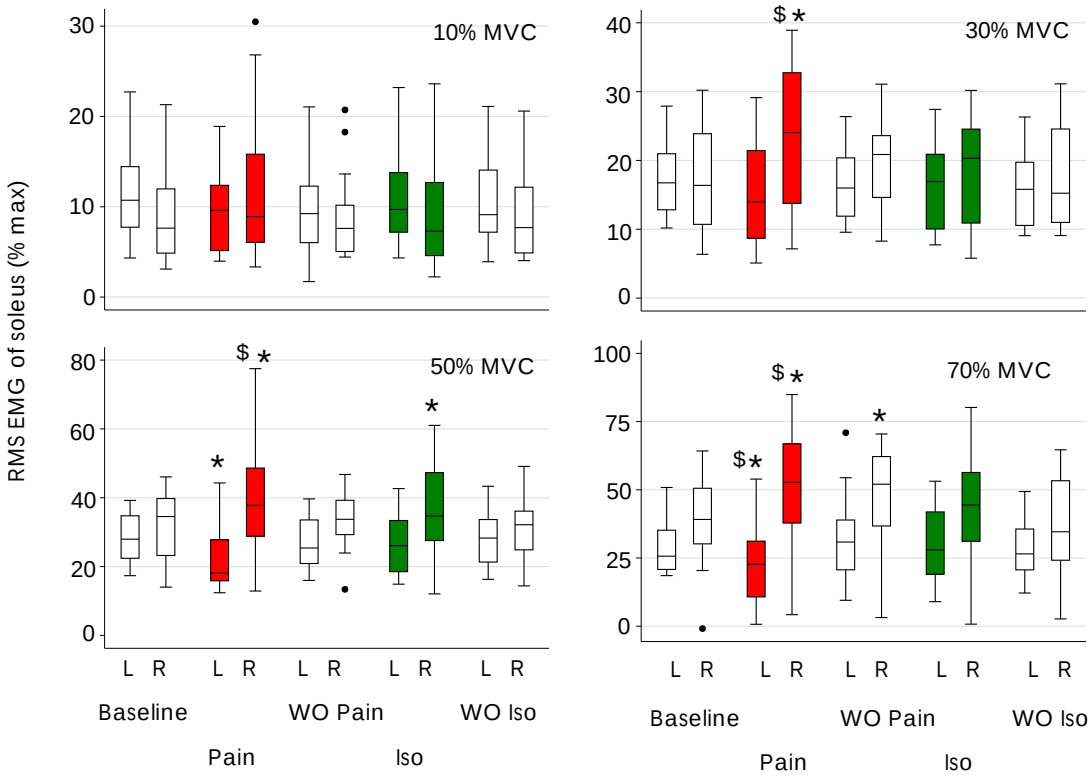

Figure 5. Soleus EMG amplitude during all conditions.

SOL RMS EMG (normalised to maximal values measured during MVC) is shown for all Conditions, Legs and Contraction intensities. Note the different scales were used. SOL EMG activity of the painful leg was lower during Pain than Baseline at 50% and 70% of MVC while SOL EMG activity of the non-painful leg was greater during Pain at 30, 50 and 70% of MVC than Baseline. Error bars denote the 95% confidence interval; box denotes the 25-75 percentile with the median and dots indicate outliers. * - significant difference from Baseline. $, significant difference from Iso.