Changes in Motor Unit Firing Rate in Synergist Muscles Cannot Explain the Maintenance of Force During Constant Force Painful Contractions

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Abstract: The firing rate of low threshold motor units is decreased in constant force contractions during experimental pain. However, as firing rate is a determinant of force, it is unclear how force is maintained. Increased synergist muscle activity may compensate. This was investigated by evaluation of motor unit firing rate in synergist ankle plantar flexor muscles (triceps surae). Single motor unit action potentials were recorded in medial gastrocnemius and soleus muscles with fine wire electrodes in 10 subjects. Gross muscle activity was estimated from surface electromyographic (EMG) recordings. Bolus injections of 5% hypertonic saline were injected into lateral gastrocnemius to induce pain (low intensity, 0.5 mL; high intensity, 1.5 mL). Subjects gently plantar-flexed the ankle to recruit 1 to 4 motor units and performed 3 20-second contractions to this target before, during, and after pain. Firing rate decreased $\approx 12\%$ in synergist heads of triceps surae during pain and recovered after pain. Despite reduced firing rate, root-mean-square surface EMG amplitude did not change. The effect of nociceptor stimulation is not restricted to painful muscles but reduces motor unit firing in synergist muscles. Changes in synergist muscles cannot explain the maintenance of muscle force. Maintenance of surface EMG amplitude suggests recruitment of additional motor units.

Perspective: This study showed that activity of synergist muscles can be affected by muscle pain. However, the changes in activity of synergist muscles may not compensate for changes in the painful muscle. This finding provides evidence of more widespread effects of pain on muscle control.

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Key words: Motor unit, firing rate, muscle pain, motor control.

Muscle pain is associated with reduced amplitude of electromyographic (EMG) activity in a painful muscle during strong isometric contractions.$^{3,5,10,19,25}$ In addition, more recent studies have shown that the firing rate of low threshold motor units is reduced during pain in the homonymous muscle.$^{7,8,23}$ This has been argued to be linked to inhibitory processes due to input from nociceptive afferents on the motor neuron pool. This observation appears consistent with the predictions of the pain adaptation of Lund et al,$^{18}$ which predicts that activity is inhibited in a painful muscle in order to reduce force and movement amplitude. However, as motor unit firing rate is a determinant of the force generated in a muscle it is unclear how constant force can be maintained despite the decrease in firing rate.

Changes in motor unit twitch properties have been suggested as a compensatory mechanism for the decreased motor unit firing during pain. Indeed, increased twitch force of low-threshold motor units have been reported during experimental muscle pain.$^{9,24}$ In contrast, the muscle membrane properties seems not to be affected by experimental muscle pain as both motor unit conduction velocity$^{7,8}$ and M-wave$^6$ are unchanged. Interestingly, the peak twitch force remained increased...
also in post-pain conditions where the motor unit firing rate returned to normal. This strongly suggests that the facilitated twitch force is not the mechanism compensating for the decline in motor unit firing rate.

Another likely mechanism for the maintenance of force is that the nervous system may increase the activity of muscles with a synergist action to compensate for decreased force production by a painful muscle. However, variable data are available in the literature. Schulte et al reported no change in firing rate in a small number of units of some synergist muscles estimated using a surface array electrode during 40% maximal voluntary contraction (MVC) static elbow flexion contraction with pain in biceps. In contrast, Ciubotariu et al reported a decrease in surface EMG amplitude of synergist muscles during 80% and 50% MVC contractions. However, changes in motor unit firing rate cannot be extrapolated from changes in surface EMG recordings due to partial cancellation of motor unit action potential representation in the surface EMG signal. To clarify whether adaptation in motor unit firing rate in synergist muscles accounts for the maintenance of force in a constant force contraction it is necessary to record motor unit action potentials in a larger population of motor units in all synergist muscles that contribute to force generation.

This study aimed to investigate whether the maintenance of force during pain in a constant force contraction can be explained by changes in low-threshold motor unit firing properties in synergist muscles. The ideal anatomical system to study this question is to evaluate the firing properties of motor units in 3 heads of the triceps surae muscle (medial and lateral gastrocnemius and soleus) which act synergistically to plantar-flex the ankle.

Materials and Methods

Subjects

Ten healthy subjects (all male) with ages ranging from 20 to 33 years participated in the study. Subjects were excluded if they had any symptoms of neuromuscular disorders or musculoskeletal pain. The study was conducted in accordance with the Declaration of Helsinki, approved by the local ethics committee, and written informed consent was obtained from all participants before inclusion.

Electromyography

Recordings of single motor unit action potentials were made from the right medial gastrocnemius (MG) and soleus (SO) in 10 subjects and lateral gastrocnemius (LG) in 1 subject. Fine-wire electrodes (13R71; Dantec, Skovlunde, Denmark) were inserted into the middle of the muscle belly of LG for infusion of sterile hypertonic saline (5%). The cannula was attached to a 10-mL syringe via an extension set and infusion was controlled with a computer-controlled syringe pump (ALARIS Medical Systems, Asena, UK). Hypertonic saline was infused at 2 different volumes (0.5 mL and 1.5 mL) to induce pain of a lower and higher intensity. Bolus injections were infused at a rate of 90 mL/h. No attempt was made to titrate the volume to match the pain reported between individuals. Subjects reported pain continually throughout the study on a 10-cm electronic visual analog scale (VAS). The extremes of the scale were marked “no pain” and “maximum pain.” Subjects rated their pain from onset to resolution and the data was automatically sampled every 2 seconds. Peak pain scores were extracted offline.

Procedure

In sitting, the right foot was firmly strapped to a plate attached to a torque transducer with the axis aligned approximately to the ankle joint. The knee was maintained at approximately 45° from full extension (Fig 1). Both the knee and the thigh were fixed with a custom-made device attached to the chair. In this setup, the subjects could only perform isometric contractions at the ankle. With visual feedback of force on an oscilloscope, subjects plantar-flexed gently against the plate until 1 to

![Figure 1. Experimental setup. A, The right ankle was fixed to the plate of the torque transducer. Subjects plantar-flexed to a target force that was sufficient to recruit 1 to 4 motor units in each muscle. This target force was kept constant throughout the experiment. B, Fine-wire and surface electromyography (EMG) recordings were made from medial gastrocnemius (MG) and soleus (SO) before, during, and after pain was induced in the lateral gastrocnemius (LG) muscle.](image-url)
4 motor units could be identified in each muscle. This torque was marked on the oscilloscope to act as the target for all subsequent trials. Subjects performed 3 20-second contractions to the target force before pain (pre-pain), 1 to 2 minutes after the onset of pain when the pain intensity had reached a plateau (high/low-pain), and then after complete resolution of pain (post high/low pain). Subjects rested for 40 seconds between each contraction. The procedure was then repeated with the second injection of hypertonic saline after ~10 minutes of rest. The order of low and high intensity pain trials was randomized.

**Data Analysis**

Single motor unit action potentials were sorted on the basis of motor unit morphology using Spike2 software (Cambridge Electronic Design, Cambridge, UK). The mean firing rate was calculated over each 20-second trial and averaged over the three repetitions. Root mean square EMG amplitude was calculated for the surface EMG electrodes over the same 20-second period.

Data are presented as means and standard deviations, except for pain data, which are presented as mean and standard error of the mean. Mean firing rate and RMS EMG amplitude were compared between trials (repeated measure) and between muscles (independent factor) with a mixed-model analyses of variance (ANOVA). Post hoc testing was undertaken with Duncan’s multiple range test. Pain ratings were compared by a paired t test. Spearman correlations coefficient was used to test for association between pain intensity and the motor unit firing rate (absolute firing rate and change in firing rate between pre-pain and pain). The significance was set at \( P < .05 \).

**Results**

Pain intensities reported by the subjects following the 1.5-mL and 0.5-mL injections are presented in Fig 2. Peak pain intensities were 4.9 (3.8) and 3.3 (3.0) cm on the 10 cm VAS for the high and low volume, respectively, and were significantly different (paired t test, \( P < .01 \)). Pain was reported locally at the injection site in LG with no referral distally and no referral to the MG or SO muscles.

Single motor unit recordings were made from 10 units in MG (in 8 subjects), 10 motor units in SO (in 8 subjects), and 1 motor unit in LG in all conditions (pre-pain, high pain, post high pain, low pain, and post low pain). Fig 3 shows data for a representative subject. Insets show overlaid motor unit action potentials which confirm that identical motor units were identified before and during pain. Inspection of the motor unit firing rate during the maintenance of constant force indicates that motor unit firing rate of the target motor unit in MG and SO was decreased during pain. Fig 4 shows group data for MG and SO and the firing rate for the single motor unit recorded in LG. Individual data are shown in Fig 5. Group and individual data show a consistent reduction in motor unit firing rate in all muscles (main effect: condition, \( P < .0001 \), despite the localization of pain in LG, and no pain in the MG or SO. Motor unit firing rate of the target units in MG and SO were reduced by an average of 12.3% and 12.3%, respectively, during high pain and 10.1% and 7.5% during low pain. There was no difference in motor unit firing rate between MG and SO (main effect: muscle, \( P = .33 \); interaction: muscle \times \) condition, \( P = .95 \), and no difference between the motor unit firing rate during the pre-pain, post high pain, and post low pain conditions. Although there was no significant difference between the motor unit firing rates during the high and low pain conditions there was a tendency towards a greater reduction in the high pain condition (post hoc: \( P = .16 \) (Fig 4A). There was no relationship between the absolute reported pain intensity and motor unit firing rate (or change in firing rate) for either muscle (absolute firing rate: MG: \( R^2 = .06 \); SO: \( R^2 = .01 \), change in firing rate: MG: \( R^2 = .004 \); SO: \( R^2 = .01 \)).
Despite the reduction in motor unit firing rate in the target motor units, there was no change in RMS EMG amplitude between any of the conditions (main effect: condition, $P = .30$; interaction: muscle $\times$ condition, $P = .66$; Fig 4B).

**Discussion**

These data point to 2 new observations. First, motor unit firing rate is reduced, not only in the painful muscle but also the muscles that synergistically contribute to the torque produced by the painful muscle. Second, motor unit firing rate of the synergist muscle is not increased to compensate for the reduction in force from the painful muscle. These observations provide novel insight into the problems associated with generation of force during pain.

**Motor Unit Firing Rate Is Reduced in Heteronymous Muscles**

In the present study, decreased firing rate was shown in the homonymous muscle in the one subject in whom LG motor unit activity was recorded. Although decreased motor unit firing rate such as this has been consistently reported in muscles with homonymous nociceptive afferent activity, this was not found in 2 studies. However, of those studies, one assessed few motor units (ie, underpowered) and the other estimated motor unit firing properties in a population of units without tracking the same units between conditions. The contrasting findings could also be due to differences in motor control strategy between different muscles. Reduced firing rate has been observed for masseter and tibialis anterior but not biceps brachii or extensor carpi ulnaris. The current study is the first to report a clear reduction in motor unit firing rate of motor units in synergist muscles during muscle pain.

In previous studies, a robust excitation of group III and IV afferent fibers by hypertonic saline has been shown, in contrast to the thick, fast nerve fibers. Thus, it is unlikely that muscle efferent nerve fibers or muscle fibers are excited by hypertonic saline. In line, no increased EMG activity has been detected with tonic muscle pain after administration of hypertonic saline compared with isotonic saline. Furthermore, the conduction velocity of single muscle fibers is unaffected by injections of hypertonic saline, indicating that muscle fiber membrane properties are unlikely to be disturbed by hypertonic saline. There is experimental evidence from animal studies that excitation of III and IV afferents inhibit both homonymous and synergistic $\alpha$-motoneurons and extensive branching of nociceptive muscle afferents and their interneuronal relay at spinal level. Thus nociceptive afferent discharge could...
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The Maintenance of Force Is Not Due to Increased Motor Unit Firing Rate in Synergist Muscles

The key finding of the present study is that changes in firing rate of low threshold motor units in muscles with a synergistic function to the painful muscle do not account for the maintenance of force during a painful constant force contraction. Instead, motor unit firing rate was also reduced in synergist muscles. This suggests the effect of nociceptor stimulation is not localized and has a broad effect on synergist muscles. Similar findings have been reported for whole muscle recordings during strong contractions (>20% MVC) assessed by surface EMG. For instance, MG EMG amplitude is reduced during submaximal contractions during pain in the LG muscle, extensor hallucis longus EMG is reduced in dorsiflexion efforts during tibialis anterior pain, temporalis EMG is reduced during contralateral masseter muscle pain and sternocleidomastoid EMG decreases when their is pain in the contralateral muscle during cervical flexion.

The current funding rejects the hypothesis that the rate of discharge of motor units in synergistic muscles could be increased to compensate for decreased firing rates of motor unit in the painful muscle. Instead motor unit firing rate was decreased in the synergist muscles. This appears consistent with the purpose of the adaptation of muscle activity during pain; to reduce force of a painful movement. However, this highlights the problem—in the present study, the adaptation in muscle activity did not result in reduced force as subjects were provided with feedback to maintain constant force between painful and nonpainful contractions, and this was achieved despite reduced firing rate of the painful muscle and its synergists. This begs the question “how was force maintained?”

It has been proposed that force could be maintained at lower motor unit firing rates if twitch force is modified. However, this is unlikely to be the explanation as changes in twitch force persist in the period immediately after pain when motor unit firing rate has recovered. Recent data suggest that changes in twitch force during pain may be an artefact of the triggered averaging technique due to reduced half relaxation time caused by changes in adrenaline concentration due to sympathetic activity.

Another alternative possibility is that additional higher threshold motor units may be recruited during the painful contraction to maintain force. This could explain why surface EMG amplitude remained constant despite reduced firing rate of the low threshold units. It is possible inhibition may not be uniform and could selectively affect the lower threshold units. In a study on the human first dorsal interosseous muscle, Masakado et al. showed that electrical percutaneous stimulation over the first digit decreased the recruitment threshold of higher threshold motor units recruited over 30% MVC, increases the firing rate of those units, and at the same time decreases the recruitment threshold for the low threshold motor units. In the case of muscle pain, Sohn et al. were unable to find any reversal of the normal recruitment order of masseter motor units or change in recruitment threshold, but that study only investigated low threshold motor units that were active under 20% MVC. However, they did not exclude the recruitment of additional higher threshold units.

Increased synchronization of discharge of separate motor units, which increases twitch force, could provide another possible mechanism to maintained force despite decreased motor unit firing rate. Increased motor unit synchronization has been demonstrated during various conditions such as fatigue and during common inhibitory effects that would affect a large population of motoneurons.

Conclusion

Increased firing of low threshold motor units in synergist muscles does not account for maintenance of force during painful constant force contractions. Data hint at the possible recruitment of additional higher threshold motor units during pain. Further work is required to investigate activity of higher threshold units, and if such changes are apparent, to determine the mechanism and possible advantage of recruitment of different motor units.
References


