Effect of Experimental Muscle Pain on Motor Unit Firing Rate and Conduction Velocity

Dario Farina,1,2 Lars Arendt-Nielsen,2 Roberto Merletti,1 and Thomas Graven-Nielsen2

1Centro di Bioingegneria, Dipartimento di Elettronica, Politecnico di Torino, 10129 Torino, Italy; and 2Center for Sensory-Motor Interaction, Aalborg University, Aalborg, DK-9220 Denmark

Submitted 30 June 2003; accepted in final form 29 October 2003


First published November 12, 2003; 10.1152/jn.00620.2003. The aim of this human study was to investigate the relationship between experimentally induced muscle pain intensity (i.e., amount of nociceptive activity) and motor unit (MU) firing decrease and MU conduction velocity (CV). In 12 healthy subjects, nociceptive afferents were stimulated in the right tibialis anterior muscle by three intramuscular injections of hypertonic saline (0.2, 0.5, and 0.9 ml) separated by 140 s. The subjects performed six isometric contractions (20 s long) at 10% of the maximal voluntary contraction during the experimental muscle pain. The same set of six contractions was performed without any infusion before the painful condition on the right leg. The procedure was repeated for the left leg with infusion of isotonic (nonpainful) saline. Intramuscular and surface electromyographic (EMG) signals were collected to assess MU firing rate and CV. The firing rate of the active MUs [range: 7.4–14.8 pulses/s (pps)] did not change significantly in the three control conditions (without infusion for the right and left leg and with infusion of isotonic saline in the left leg). There was, on the contrary, a significant decrease (on average, mean ± SE, 1.03 ± 0.21 pps) of the firing rates during the painful condition. Moreover, MU firing rates were inversely significantly correlated with the subjective scores of pain intensity. Single MU CV was 3.88 ± 0.03 m/s (mean ± SE, over all the MUs) with no statistical difference among any condition, i.e., the injection of hypertonic saline did not alter the muscle fiber membrane properties of the observed MUs. Progressively increased muscle pain intensity causes a gradual decrease of MU firing rates. This decrease is not associated with a change in MU membrane properties, indirectly assessed by CV. This study demonstrates a central inhibitory motor control mechanism with an efficacy correlated to the nociceptive activity.

INTRODUCTION

Decrease of motor unit (MU) firing rates has been documented during maximal and submaximal fatiguing contractions (e.g., Bigland-Ritchie et al. 1983; Carpentier et al. 2001; Garland et al. 1994; Griffin et al. 2001) where it has been argued that group III and IV afferent activity progressively increases during fatigue due to release of metabolic products, which centrally inhibits the motoneuron pool via reflex circuitry (Bigland-Ritchie et al. 1986; Garland et al. 1988; Woods et al. 1987). Evidence for involvement of thin afferent fibers came from studies in ischemic conditions during electrically induced contractions in humans (Garland 1991; Garland and McComas 1990). However, ischemia can affect other important parameters such as conduction velocity (CV) of efferents and muscle fibers and eventually evoke unintentional afferent activity (Gandevia 2001). Nonetheless, if group III and IV afferent activity is relevant in modulation of MU activity in fatigue, a correlation between the decrease of MU firing rate and nociceptive activity mediated by group III and IV afferents should exist in nonfatigued conditions. Thus the main aim of this study is to assess the MU firing rate in submaximal, nonfatiguing contractions during progressively increasing muscle pain intensities and simultaneously record the muscle fiber CV to control for changes in muscle fiber membrane properties.

A major proportion of small diameter group III and IV muscle afferents are sensitive to noxious mechanical and chemical stimuli (Mense and Meyer 1985; Mense and Stahnke 1983). According to the pain adaptation model (Lund et al. 1991), the activity of thin nociceptive muscle afferents facilitates inhibitory pathways when the muscle acts as an agonist and facilitates excitatory pathways during antagonist activity. Thus smaller and slower movements are generated, which probably represents a functional adaptation to muscle pain (Arendt-Nielsen et al. 1996; Graven-Nielsen et al. 1997). In isometric contractions, infusion of hypertonic saline was associated with lower surface electromyographic (EMG) activity compared with a nonpainful condition at the same force level (e.g., Graven-Nielsen et al. 1997; Wang et al. 2000a). This led to the assumption that experimental muscle pain altered MU recruitment, inhibiting muscle activity (Wang et al. 2000a). However, direct measurement of MU activity in the masseter muscle indicated no effect of experimental muscle pain on the recruitment curve while decline of MU firing rates was observed with pain (Sohn et al. 2000). Although the effect of pain observed by Sohn et al. (2000) was similar for different MUs at different contraction levels, it may not be evident when different MU samples are studied in painful and nonpainful contractions (Birch et al. 2000).

It is essential to validate that the experimental muscle pain per se does not compromise the peripheral apparatus. Experimental muscle pain does not modulate the M-wave during electrical stimulation of the motor nerve (Svensson et al. 1998); thus the electrophysiological properties of the muscle fibers are probably unchanged. In addition, attenuation of maximal voluntary contraction (MVC) force during experimental muscle pain was not associated with changes of contractile
properties but to a pure central effect (Graven-Nielsen et al. 2002). However, there are no studies directly assessing single MU membrane properties during experimental muscle pain.

CV indirectly reflects the contractile properties of the MUs in fresh muscle (Andreassen and Arendt-Nielsen 1987; Sadoyama et al. 1988), as CV and twitch force are related by the size principle. Moreover, changes of muscle fiber CV reflect changes of the contractile properties, for example, due to fatigue, temperature, or ischemic conditions (Bigland-Ritchie et al. 1981; Van der Hoeven and Lange 1994; Zhou et al. 1998). Single MU CV may thus be indicative of eventual modifications in the peripheral properties of the neuromuscular system.

The hypotheses of the present study are that 1) MU firing rate decrease is correlated to the muscle pain intensity, and 2) MU firing rate decrease during experimental muscle pain is not related to changes in muscle fiber CV. If both hypotheses are accepted, the most likely modulation of muscle pain on motor control is inhibition via a centrally mediated reflex mechanism and as such represents a potential mechanism involved in the MU inhibition seen in fatigue when accumulation of metabolites is a potential activator of muscle nociceptive afferents.

METHODS

Subjects

Twelve healthy subjects (5 males, 7 females) with ages ranging from 20 to 28 yr (mean age: 23.2 yr) participated in the study. None of the subjects reported symptoms of neuromuscular disorders, problems with the ligaments, 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 prior to inclusion.

Experimental muscle pain

Experimental muscle pain was induced by infusion of sterile hypertonic saline (5.8%) into the deep midportion of the tibialis anterior muscle. Infusion of hypertonic saline was accomplished with a computer-controlled syringe pump (IVAC, model 770) and a 10-ml plastic syringe. A tube (IVAC G30303, extension set with polyethylene inner line) was connected from the syringe to a disposable plastic catheter (Venflon, 22 G, 25 mm). The infusion paradigm was designed so that a stepwise progressive increment of the muscle pain intensity was obtained. Hypertonic saline was infused in three bolus of different volumes (0.2, 0.5, and 0.9 ml) at the same site and with an interval between each infusion of 140 s. The first bolus (0.2 ml) was infused at a rate of 18 ml/h, thus 40 s was needed for the injection. At intervals of 140 s between each other, the other two infusions were performed at a rate of 18 ml/h, thus 40 s was needed for the injection. At intervals of 140 s between each other, the other two infusions were performed at a rate of 18 ml/h, thus 40 s was needed for the injection. At intervals of 140 s between each other, the other two infusions were performed at a rate of 18 ml/h, thus 40 s was needed for the injection. At intervals of 140 s between each other, the other two infusions were performed at a rate of 18 ml/h, thus 40 s was needed for the injection. At intervals of 140 s between each other, the other two infusions were performed at a rate of 18 ml/h, thus 40 s was needed for the injection. At intervals of 140 s between each other, the other two infusions were performed at a rate of 18 ml/h, thus 40 s was needed for the injection.

EMG signal detection

Surface and intramuscular EMG signals were recorded simultaneously. Figure 1 shows an example of the location on the muscle of surface and intramuscular electrodes during an experimental session. The procedure of electrode positioning has been described in detail in a previous work (Farina et al. 2002a) and will be summarized briefly below.

Surface EMG

For the recording of surface EMG signals, a linear array of 16 equispaced electrodes was used (interelectrode distance 5 mm, bar electrodes 5 mm long, 1 mm diam) (Masuda et al. 1985; Merletti et al. 1999). The linear array allowed the detection of surface EMG signals from a number of equally spaced locations along the muscle fibers.

For electrode positioning, the array was moved over the tibialis anterior muscle during test contractions to observe clear propagation of the detected MU action potentials (MUAPs) from the innervation zone to the tendon region (the signal quality was assessed by visual inspection) (Merletti et al. 1999). The multichannel approach allows optimal location of the detection system with respect to the muscle fibers, thus decreasing the bias of CV estimation (Broman et al. 1985).

After determination of the main anatomical landmarks of the MUs (innervation zones and tendon regions), the array was moved distally to detect the propagation of the action potentials between the most distal innervation zone and the distal tendon region, without covering the part of muscle between the innervation zone and the proximal tendon region. An example of surface EMG signals detected in this way from the tibialis anterior muscle during a contraction at 10% MVC is seen in Fig. 2. Note the potentials propagating from the proximal muscle region to the distal part, indicating electrode placement between the innervation zone and the distal tendon. The skin was slightly abraded in the selected location for the array placement and the array was fixed by adhesive tapes. Surface EMG signals were detected in single differential configuration and amplified (EMG amplifier, LISIN-SEMA Elettronica, Turin, Italy, gain in the range 10,000–20,000, cutoff frequencies 10–500 Hz), sampled at 2048 Hz, and stored by a 12-bit A/D conversion. The torque exerted by the subject was sampled in parallel with EMG signals at 2048 Hz.

Intramuscular EMG

Four wire electrodes made of Teflon-coated stainless steel (A-M Systems, Carlsborg, WA) were inserted with a 23 G needle, 10–20 mm proximal with respect to the surface array top (Fig. 1). The angle of insertion of the needle was about 45° and the depth was a few millimeters below the muscle fascia. The detection point of the wires was between the innervation zone and the proximal tendon region and corresponded to MUs with territory under the surface electrodes (i.e., the insertion point was in line with the electrodes of the surface array). Approximately 1 mm of the wires was uninsulated at the tip to detect intramuscular EMG signals. The wires in the insertion needle were bent at the tip at different lengths to record from as many MUs as possible. The needle was removed with the wire electrodes left inside the muscle. After needle removal, the subject was asked to perform a maximal voluntary dorsiflexion to fix the wires. The position of the wires was slightly adjusted until the signal-to-noise ratio was sufficiently high for the majority of the four channels (signal quality was assessed by visual inspection). Intramuscular EMG signals were amplified (EMG amplifier, Aalborg University, Denmark), band-pass filtered (500 Hz to 5 kHz), sampled at 20,480 Hz, and stored after 12-bit A/D conversion.

General procedures

The subject sat comfortably on a chair with his/her foot fixed in an isometric force brace incorporating one torque transducer (Aalborg University, Denmark). The angle of the ankle was fixed at 90° while the angle of the knee varied between 110 and 130° depending on the height of the subject (the thigh was always in the horizontal position). The MVC torque in dorsiflexion was recorded three times. The three MVC measures were separated by 2 min rest and the maximal of the
three recorded MVC was considered as the reference for the definition of submaximal torque contraction levels. Invasive and surface electrodes for EMG signal detection were mounted as described above.

After 5 min rest, the subject performed six 20-s-long isometric contractions at 10% MVC each, separated by 50 s of rest. The subject was given a verbal command to begin the contraction and was continuously provided with visual feedback of torque on an oscilloscope. After 10 min of recovery, the hypertonic saline infusion paradigm described above was applied while the subject repeated the same set of six contractions with the same resting periods, as performed without infusion of saline. The first, third, and fifth contractions in the painful conditions started at the end of infusion of the three saline bolii, respectively.

After the right leg assessment, in the same experimental session, a similar procedure was performed for the left leg but with infusion of isotonic saline as a control condition to the experimental muscle pain induced by hypertonic saline.

**Signal analysis**

The intramuscular recordings were automatically decomposed to detect MU activities. The surface EMG signals were then averaged with the intramuscularly detected single MUAPs as triggers (spike triggered averaging). In each 20-s-long contraction, all the detected firings belonging to the same MU were used for the averaging process. The MUs accepted for further processing were those that led to...
averaged surface potentials with peak-to-peak value higher than three times the noise level after the averaging. Based on template matching (Farina et al. 2002a), it was assured that the same MUs were followed during the 12 contractions of each leg.

CV of single MUs was estimated from the averaged multichannel double differential surface MUAPs by a maximum likelihood technique (Farina et al. 2002a). The CV estimation technique provides estimates of delay from a number of surface EMG signals traveling in one direction; the larger the number of signals, the lower the CV estimation variance. The channels of the surface array selected for CV estimation were automatically chosen with the criterion of minimal shape changes (Farina et al. 2002a). The selected signals of the array were aligned by the estimated delay and the cross-correlation coefficient between all the possible pairs of aligned signals was computed; only estimates of delay leading to a correlation coefficient higher than 0.85 were included in the further statistical analysis of CV.

Conduction velocity could be assessed with high resolution (approximately 0.15 m/s) from the noninvasive recordings. It was possible in this way to assess both control and conduction properties of single MUs during the voluntary contractions. Validation of the method used has been reported (Farina et al. 2002a).

In addition to single MU CV, the average rectified value and mean power spectral frequency were computed as global variables from surface EMG signal epochs of 1 s during all the contractions to assess global modifications in EMG activity. The mean values over the 20 estimates were used for the statistical analysis. The surface channel selected for the estimation of the global amplitude and spectral variables was that in the middle of the channels used for single MU multichannel CV estimation. Global variables were estimated from single differential signals, with algorithms described in previous works (for a recent review, see Farina and Merletti 2000).

Statistical analysis

Data are presented as mean ± SE. One- and two-way repeated measures ANOVA were applied to assess the dependency of the results on the contraction type. The posthoc Student–Newman–Keuls (SNK) test for multiple comparisons was applied when necessary. Linear regression analysis was used to assess correlation between experimental variables. Significance was accepted for P values < 0.05.

RESULTS

Experimental muscle pain

The average VAS score after the three infusions of hypertonic and isotonic saline is illustrated in Fig. 3. A two-way (hypertonic/isotonic saline, 6 contractions) ANOVA of VAS score was significant for both factors (F > 36.29, P < 0.001). The posthoc SNK test revealed pair-wise differences after contractions with isotonic and hypertonic saline infusion (P < 0.001) and among all the six contractions (P < 0.05), except between the second and the third and the fourth and the fifth.

Electrode placement

The most proximal electrode of the array was located 19.3 ± 0.7 cm distant from the distal apex patellae for the right leg and 19.1 ± 0.6 cm for the left leg. The insertion point of the wires was 16.8 ± 0.6 mm distant from the most proximal electrode of the array for the right leg and 16.3 ± 0.9 mm for the left leg.

Torque and global surface EMG variables

For both legs, two-way ANOVA (condition with and without infusion, 6 contractions) of the mean torque level sustained by the subject was not significant (average torque level over all subjects and contractions, 10.6 ± 0.03% MVC). Moreover, there was no statistical dependence of the coefficient of variation (SD divided by the mean value) of the torque exerted by the subjects in the different conditions (for both legs, 2-way ANOVA with factors the condition with and without infusion and the 6 contractions; average coefficient of variation, 0.59 ± 0.01%).

A two-way (condition with and without infusion and contraction) ANOVA of the average rectified value and mean frequency for both the right and left leg was not significant (Fig. 4). Together with the torque, this illustrates an intact ability to generate the required submaximal contraction.
MU firing rates

A typical example of detection and classification of the intramuscular and surface action potentials from the same MU after 12 contractions with the infusion of hypertonic saline is shown in Fig. 5. The intramuscular MUAP waveforms are stable in the 12 recordings and no effects on the averaged multichannel surface EMG signals are visible.

The total number of MUs detected from recordings in right tibialis anterior was 55 while in left tibialis anterior it was 49. Figure 6 shows an example of instantaneous firing rate analysis of 4 MUs detected from one subject. A decrease in MU firing rate following the infusions of hypertonic saline is seen in contrast to no changes of the firing rate after isotonic saline infusion.

The mean firing rates are constant in all conditions except when hypertonic saline is infused (Fig. 7). A two-way (condition with and without infusion and contraction) ANOVA of the firing rate for the right leg was significant for the infusion ($F = 13.17, P < 0.001$), with the infusion condition leading to lower firing rates. There was no significant effect of the condition with or without infusion and of the contraction for the left leg (2-way ANOVA).

A one-way (contraction) ANOVA of the firing rate for the contractions during infusion of hypertonic saline was significant ($F = 2.98, P < 0.05$). The posthoc SNK test revealed a pair-wise decrease in firing rate between the first contraction and the fourth, fifth, and sixth, and between the second and the sixth contraction. VAS scores and firing rates after infusion of hypertonic saline were significantly correlated (Fig. 8, linear regression analysis, $R = -0.45, P < 0.001$; pooling together results from the infusion of hypertonic and isotonic saline, $R = -0.34, P < 0.001$).

Besides the case of infusion of hypertonic saline, there was no significant difference in the MU firing rates of the contractions in all the other conditions.

Motor unit conduction velocity

The number of double differential channels selected for CV estimation was 5.8 ± 0.3 for the right leg and 4.9 ± 0.2 for the left leg. The number of detected MUs from which CV could be reliably estimated (according to the criterion on cross-correlation, see METHODS) was 32 for the right leg and 28 for the left leg. A two-way (condition with and without infusion and contraction) ANOVA of CV for both the right and left leg was not significant (Fig. 9).

DISCUSSION

Low threshold MU activity in the tibialis anterior muscle during painful conditions was investigated. Experimental muscle pain caused a decreased MU firing rate correlated to the pain intensity without compromising CV of MUs. This model may be useful to investigate some of the central changes associated with muscle fatigue as the model provides MU firing rate changes without the associated slowing of muscle fiber CV, as seen during contraction-induced muscle fatigue.

Prepain MU firing rates and conduction velocity

Compared with our previous study (Farina et al. 2002a), the average CV estimated from the active MU pool was smaller (in average 3.88 with respect to 4.11 m/s). The average initial firing rates were smaller in this study with respect to the previous (10.5 vs. 12.7 pps). These differences are explained by the torque contraction levels in the two studies. In the present study, the force level was less than half of that of the previous one, thus slower MUs were recruited (Andreassen and Arendt-Nielsen 1987) and lower firing rates were achieved (DeLuca et al. 1982a,b; Milner-Brown et al. 1973). The results obtained, in agreement with the Henneman principle (Henneman 1980), indicate the reliability of the applied technique.
FIG. 5. Intramuscular and multichannel surface motor unit action potentials (MUAPs) belonging to the same MU and detected in the 12 contractions performed by 1 subject (right leg). In each case, 1 intramuscular detected potential of every 10 is superimposed (only 1 channel among the 4 detected is reported). All the detected firings were used for the averaging process, which led to the average multichannel surface potentials shown for the 12 contractions. The surface EMG signals are reported as double differential recordings (14 channels in total). The pain intensity for the recordings during hypertonic saline infusion is indicated (by mean VAS over the contraction duration). Note the stability of the intramuscular potential shapes during the entire period of recording (about 20 min separated the first and last of the 12 contractions). Note also that muscle pain is not significantly altering the MUAP shape.

FIG. 6. Firing rate of 4 MUs whose action potentials were detected during the 12 contractions of the right and left leg of one subject. The first 6 contractions of each set were separated by 50 s, the 2 blocks of 6 contractions in the set of 12 were separated by 10 min. These resting periods are not reported in the plots. Thus the instantaneous firing rates in the 12 contractions (of 20 s each) is reported consecutively on the same time axis (resulting in 240 s of activity). The arrows indicate the time points corresponding to the end of the injection of the 3 boli of hypertonic (right leg) and isotonic (left leg) saline. In the 4 cases, the firing rate does not change significantly during the first 6 contractions. Moreover, there is no change in firing rate after the injections of isotonic saline. The firing rates progressively decreased during experimental muscle pain induced by hypertonic saline.
Decrease of MU firing rate following nociceptive afferent stimulation

The observed decreased MU firing rate during muscle pain could not be due to fatigue since no decrease was observed when nonpainful contractions were investigated. Moreover, the injection of nonpainful (isotonic) saline did not induce any change in firing rate, indicating that the increase of intramuscular pressure due to the saline was not the cause of the observed changes following hypertonic saline injection.

The result is in agreement with the pain adaptation model that predicts a decrease of muscle activity in response to pain (Lund et al. 1991). However, the central mechanisms involved in the MU inhibition are not fully clear.

The decrease in firing rate in the present study was rather small (about 1 pps on average), although the pain level reached was relatively high, as shown by the VAS scores (Fig. 3). However, compared with decreased MU firing rate due to fatigue, the decrease of firing rate caused by noxious stimulation is in the same range. For example, after 60 s of 25% MVC sustained, nonpainful contractions of the tibialis anterior muscle, the MU firing rates decreased on average about 1.5 pps (Farina et al. 2002a). A similar decreased firing rate in painful, nonfatiguing conditions and in fatiguing contractions may suggest a reflex-mediated inhibition caused by muscle pain, as also observed during muscle fatigue (Bigland-Ritchie et al. 1986), most likely involving group III and IV afferent activity (Garland 1991). However, during fatigue, the peripheral neuromuscular system properties also change, as assessed by CV (Farina et al. 2002a), and this is opposed to the painful condition. Thus the decreased firing rate in fatiguing conditions may follow changes in the contractile and membrane properties of the active MUs. In addition, the decrease of firing rate during fatigue may also be mediated by other afferent mechanisms, such as a progressive withdrawal of spindle support (Macefield et al. 1991). The result that noxious stimulation produces similar decreases in firing rate as seen in sustained contractions does not prove but indicates that the same mechanism may mediate the two phenomena.

The central mechanisms potentially involved in the decrease

FIG. 7. Mean ± SE of the firing rate estimated from the detected MUs in the 12 subjects for the right and left leg (n = 55 and n = 49 MUs, respectively). For each leg, the values obtained in the 12 contractions are shown.

FIG. 8. The relationship between average firing rate and VAS scores (±SE) for the 6 contractions after the infusion of hypertonic (empty squares, n = 55 motor units) and isotonic (filled squares, n = 49 motor units) saline.
of firing rate during pain may be indeed numerous. Inhibition through peripheral reflex circuitries is an interpretation in agreement with the many studies showing an effect of pain on spinal reflexes. The motor potentials evoked by transcranial magnetic stimulation are reduced during muscle pain (Le Pera et al. 2001). The motor cortex inhibition is followed by decreased amplitude of the H-reflex in resting conditions, indicating inhibition of spinal motoneurons (Le Pera et al. 2001; Rossi et al. 1997). However, the H-reflex inhibition is not a common finding in other studies using different experimental paradigms with respect to pain duration and background muscle activity (Matre et al. 1998; Svensson et al. 1998). The stretch reflex on the contrary is robustly facilitated during experimental muscle pain (Matre et al. 1998; Svensson et al. 1998; Wang et al. 2000b). Moreover, the long-latency inhibitory reflex (silent period) is disinhibited (i.e., net facilitation) during experimental muscle pain (Wang et al. 1999). There is no logical relation between the latter findings describing muscle pain–induced facilitation and progressively decreased firing rate of MUs during muscle pain. Most experimental studies assessing the effect of muscle pain on excitatory and inhibitory reflexes have, however, not assessed the potential effect of postsynaptic modulation by nociceptive activity, since the MU firing rate or global muscle activity were kept constant before assessing the reflex. A recent study has demonstrated facilitated homonymous recurrent inhibition of the soleus muscle during experimental muscle pain with a close relation between the temporal aspects of the pain and efficacy of recurrent inhibition (Rossi et al. 2003). The functional effects of facilitated recurrent inhibition on MU firing rate are complex (Katz and Pierrot-Deseilligny 1999), but the present findings might reflect facilitated recurrent inhibition by muscle pain.

As an alternative interpretation, the possible role of conscious changes in the neural drive cannot be ruled out. It is indeed possible that the subjects reacted to the muscle pain by a voluntary change of control strategy, aimed at the decrease of the activity of the synergic and/or antagonist muscles. However, recent results indicate that all major synergic muscles are inhibited during isometric dorsiflexion (Ciubotariu et al. 2004). Thus to obtain unchanged force during muscle pain, the MU control strategy within the painful muscle is probably changed.

Changes in muscle fiber CV

The MU control mechanisms can be influenced by the peripheral conditions of the neuromuscular system and vice versa. As an indicator of peripheral properties of the neuromuscular system, single MU CV is particularly attractive since it can be assessed at any physiological firing rate–firing rate, on the contrary, limits the twitch-force averaging technique (Callec and Bawa 1986; Stein et al. 1972)—and can be estimated with good temporal resolution, allowing detection of sudden CV changes.

In the present study it could not be ruled out a priori that the injection of hypertonic saline affected the extracellular environment, thus changing conduction and contractile membrane muscle fiber properties. This could have altered the MU control properties regardless of the activity of thin nociceptive afferents. However, we found no significant change of single MU CV in all the conditions examined. This is in contrast with what we observed in fatiguing conditions (Farina et al. 2002a), in which a statistically significant change of single MU CV was documented together with firing rate decrease. During fatigue, the changes in MU CV might suggest changes in MU contractile properties. Since membrane MU properties, indirectly assessed by CV, did not change, it may be assumed also that the contractile properties of the detected MUs did not change with the injection of the hypertonic saline.

Motor unit firing and contractile properties

Marsden et al. (1983) suggested that MU firing rates during constant force contractions are regulated to match the slowing muscle contractile properties during fatigue. Thus decreased MU firing rates should be associated with the increase of MU twitch force contraction time, so that the central drive is just enough to produce the force and minimize fatigue. The results on experimental muscle pain suggest that decrease of MU firing rate may be induced by excitation of small diameter muscle afferents without changing the muscle fiber membrane properties, thus the mechanisms for the maintenance of the required force are not likely based on the adaptation to the muscle fiber contractile properties at the single MU level.

Absence of correlation between firing rate modulation and changes of contractile properties has been indirectly observed.
in normal muscle operating conditions, such as changing muscle length or muscle temperature (Bigland-Ritchie et al. 1992a,b). It has also been observed that, during submaximal contractions, firing rates may decrease without increasing the global muscle force twitch contraction time (Garland et al. 1997). These observations suggest that single MU contractile properties and firing rates do not change accordingly during submaximal contractions. Thus the muscle wisdom theory does not seem to apply, at least for submaximal contractions and at the single MU level.

Aside from changes in contractile properties of the observed MUs, possible interpretations of the decrease in MU firing rate with maintenance of constant force are 1) changes in contractile properties of MUs not detected by the intramuscular wires, 2) recruitment of additional MUs in the painful condition, or 3) modifications of the activity of the synergistic and/or antagonist muscles.

Recruitment of additional MUs was not observed in the subjects investigated, in line with a previous study (Sohn et al. 2000). This does not imply that the phenomenon did not occur, since the detection volume of intramuscular signals is rather small (Basmajian and DeLuca 1985). However, the global surface EMG amplitude, as well as the characteristic spectral frequencies, did not show any change in all the conditions tested. Surface EMG amplitude is directly related to recruitment (Fuglevand et al. 1993; Woods and Bigland-Ritchie 1983) and was expected to increase if new MUs were activated. However, EMG amplitude also depends on firing rates, thus the two opposite effects (firing rate decrease and possible MU recruitment) could be balanced. Finally, it cannot be excluded that newly recruited MUs were in deep muscle layers and out of the surface detection volume. Similar considerations arise for mean power spectral frequency. Thus absence of changes in surface EMG amplitude and frequency content do not rule out the possible recruitment of new MUs as a compensatory mechanism.

A change in motor control at the level of a muscle group, rather than of a single muscle, is also a possible interpretation. Synergistic muscles may indeed increase their activity to compensate for the decrease in the force produced by the painful muscle. Effect of pain on muscles other than the painful one (i.e., antagonist and synergist) has been documented in dynamic contractions (Graven-Nielsen et al. 1997; Zedka et al. 1999) but direct extrapolation of results from dynamic tasks to isometric conditions is not possible. Indeed, the activity of synergic muscles is also decreased by experimental muscle pain during isometric contractions (Ciubotariu et al. 2004). Since also the activity of synergic muscles decreases with pain, the amount of surface EMG crosstalk (Farina et al. 2002b) from other muscles in the tibialis anterior muscle does not increase in the pain condition. Thus an increased crosstalk from synergic muscles is not likely to account for the absence of changes in surface EMG amplitude in the different conditions. Absence of changes of surface EMG amplitude with decreased MU firing rate may be due to lack of sensitivity of EMG amplitude to detect small changes in neural drive.

CONCLUSIONS

Decrease of MU firing rate was correlated to the intensity of muscle pain. This confirms the pain adaptation model (Lund et al. 1991) while it contrasts the vicious circle model (Johansson and Sojka 1991), at least in conditions of acute experimental pain and for low threshold MUs. The use of combined surface and intramuscular EMG techniques allowed exclusion of alternative explanations for the decrease of firing rate, such as the changes of muscle fiber membrane properties, as assessed indirectly by muscle fiber CV. The central mechanisms involved in the MU firing rate decrease are not clear. In particular, a reflex inhibition through the activity of small diameter muscle afferents as well as a voluntary change in the neural drive to the different muscles contributing to the contraction need further assessment.

GRANTS

This work was supported by the Danish Technical Research Council. The surface electrode arrays were developed within the European Shared Cost Project NEW (QLRT-2000–00339).

REFERENCES


EXPERIMENTAL MUSCLE PAIN AND MOTOR CONTROL


