

**Alexander Adam and Carlo J. De Luca**

*J Appl Physiol* 99:268-280, 2005. doi:10.1152/jappphysiol.01344.2004

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C. J. De Luca, A. Adam, R. Wotiz, L. D. Gilmore and S. H. Nawab

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K. Sogaard, S. C. Gandevia, G. Todd, N. T. Petersen and J. L. Taylor

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## Firing rates of motor units in human vastus lateralis muscle during fatiguing isometric contractions

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**Adam, Alexander, and Carlo J. De Luca.** Firing rates of motor units in human vastus lateralis muscle during fatiguing isometric contractions. *J Appl Physiol* 99: 268–280, 2005. doi:10.1152/jappphysiol.01344.2004.—We investigated the firing rate of motor units in the vastus lateralis muscle in five healthy young men (mean = 21.4 yr, SD = 0.9) during a sequence of isometric constant-torque contractions repeated to exhaustion. The contractions were sustained at 20% of the maximal voluntary level, measured at the beginning of the test sequence. Electromyographic (EMG) signals were recorded via quadrifilar fine-wire electrodes and subsequently decomposed into their constituent motor unit action potentials to obtain the motor unit firing times. In addition, we measured the whole muscle mechanical properties during the fatigue task using electrical stimulation. The firing rate of motor units first decreased within the first 10–20% of the endurance time of the contractions and then increased. The firing rate increase was accompanied by recruitment of additional motor units as the force output remained constant. The elicited twitch and tetanic torque responses first increased and then decreased. The two processes modulated in a complementary fashion at the same time. Our data suggest that, when the vastus lateralis muscle is activated to maintain a constant torque output, its motoneuron pool receives a net excitatory drive that first decreases to compensate for the short-lived potentiation of the muscle force twitch and then increases to compensate for the diminution of the force twitch. The underlying inverse relationship between the firing rate and the recruitment threshold that has been reported for nonfatigued contractions is maintained. We, therefore, conclude that the central nervous system control of vastus lateralis motor units remains invariant during fatigue in submaximal isometric isotonic contractions.

muscle fatigue; motoneuron; twitch potentiation; motor control; common drive

THE BEHAVIOR OF MOTOR UNIT firing rates during muscle contractions, even the most commonly studied isometric constant-force contractions, is not well understood. Although the decreasing trend of motor unit firing rates during isometric contractions of moderate length (<30 s) and moderate to maximal voluntary effort has been well established (3, 4, 10, 11, 43), the firing behavior of motor units during prolonged contractions remains an issue of controversy.

During submaximal fatiguing contractions, several studies have reported a decrease in firing rates for the majority of motor units in the following muscles: thenar muscles, 45–90% maximal voluntary contraction (MVC) (19); biceps brachii, 11–60% MVC (17); triceps brachii, 20% MVC (18). In some of these studies, a fraction of the observed motor units was found to increase or not change their firing rate during the isometric fatigue task, leaving some investigators (17) to sug-

gest the coexistence of three distinct patterns of behavior: decrease, increase, and no change in firing rate. In a study of the biceps brachii at contraction levels of 20–30% MVC, firing rates reportedly did not decrease but remained either stable or increased (30). Yet, another study in the biceps brachii (15) reported a “triphasic” adaptation of motor units during a series of sustained isometric contractions at 20% MVC. These researchers noted a short-term decrease in firing rates over 2–3 min, followed by a progressive increase in firing rates and the recruitment of new motor units. In that particular study, the observations were based on pooled contractions from 10 subjects at 10 different recording sites each. The firings of individual motor units could not be followed throughout the length of the prescribed 45-min exercise period. In another set of studies (2, 6, 7, 16), in which fatigue was induced through repeated short-duration contractions with brief rest periods, the reported results were also varied. An increase in the population average firing rate, for example, was seen in intermittent fatiguing contractions at 30 and 50% MVC in the quadriceps and adductor pollicis muscle (2). In contrast, intermittent contraction in the biceps brachii at 30–50% MVC showed a decrease in firing rates (7). In the first dorsal interosseous muscle, threshold firing rates were reduced after repeated 50% MVC contractions until force failure (16). Using a similar protocol, Carpentier et al. (6) reported a progressive decrease in the firing rates during a fatigue task, with the exception of newly recruited motor units, which increased their firing rates. To add to the confusion, a study of fatiguing extension movements in the triceps brachii at a mean contraction level of 17% MVC reported increasing, decreasing, or constant firing rates to the extent that, in two of three subjects, concurrently active units were reported to present diverging behavior (31). These previous studies were performed with various recording techniques and protocols, factors that may account for the differing results. Yet another cause may be the widespread reliance on pooled firing rate data. Averaging or comparison of firing data across subjects, motor unit populations, and measurement times most certainly would obscure the underlying time course of individual motor unit firing rate patterns. In this study, we systematically investigated the behavior of the firing properties of individual motor units during sustained contractions to exhaustion in an attempt to resolve some of the apparent inconsistencies of earlier reports. Parts of this study, dealing with the behavior of the recruitment of motor units, have been reported previously (1). In this report we describe the behavior of the firing rates of the motor units and the interaction between firing rate and recruitment.

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## METHODS

**Subjects.** Five healthy men, age 20–22 yr [21.4 yr (SD 0.9)], having no known neuromuscular disorders participated in this study. All subjects provided informed consent, and the study was approved by the Institutional Review Board at Boston University.

**Experimental procedures.** The experimental protocol has been described in detail elsewhere (1). Briefly, subjects were seated in a special chair to restrain hip movement and fix the dominant leg at a knee angle of 60° flexion. Isometric knee-extension torque was measured via a lever arm and a pad positioned against the tibia 3 cm above the medial malleolus. Subjects controlled the knee extension torque via a feedback display on a computer screen. The subjects performed three brief (3 s) maximal knee extension contractions, the highest of which was used to establish the initial MVC torque and the maximal surface EMG signal levels of knee extensor muscles. In a similar fashion, three maximal knee flexion contractions were performed to establish the maximal flexor EMG activity. Subjects then traced target trajectories by exerting the appropriate amount of extension torque. To ensure smooth and consistent torque output, subjects performed 7–10 practice contractions with 3 min of rest time. The fatigue protocol consisted of repeated contractions of a constant target level, which was set to 20% of the initial MVC value. Each cycle started with a 5-s ramp up to 50% MVC and a brief hold phase after which the torque was decreased to the target value of 20% MVC and held constant for 50 s. Apart from its importance for the estimation of recruitment thresholds, the ramp and hold phase of the torque profile at the beginning of each cycle served two additional purposes. 1) It allowed for the measurement of firing rates under dynamic conditions as the contraction series progressed, and 2) it revealed that the recruitment order of the motor units was not active at the beginning of the 20% MVC level. Thus we were able to verify that the motor units recruited during the plateau phase of the contraction followed the same recruitment order executed during an increasing force contraction. A brief (6 s) period of rest at the end of each cycle was used to measure the electrically evoked muscle response and to allow the subject to prepare for the next contraction. The sequence of contractions was performed until the subject could no longer maintain the target level. When the torque trace repeatedly dipped below the constant target value of 20% MVC, the subject received strong verbal encouragement. The trial was terminated by the experimenter at the end of a cycle if the torque trace dipped below the target value by 1% MVC more than twice per 10 s of constant target torque.

**Surface and intramuscular EMG recordings.** A parallel bar bipolar surface electrode (DE2.1, Delsys) was placed on the vastus lateralis (VL) muscle of the dominant leg to record global muscle activity. Synergist and antagonist muscle activity was monitored via additional surface electrodes placed on vastus medialis, rectus femoris, and biceps femoris. Torque and surface EMG signals were band-pass filtered from 0–100 Hz and 10 Hz–1 kHz, respectively, and digitized at 2 kHz.

Intramuscular EMG signals from the VL muscle of the dominant leg were recorded by using a quadrifilar fine-wire electrode. The electrode was placed in close proximity to the surface electrode, in the distal one-third of the VL muscle. Each electrode consisted of four 50- $\mu$ m-diameter nylon-coated Ni-Cr wires (Stablohm 800A, California Fine Wire) glued together and cut to expose only the cross section of the wires (8). The fine-wire electrode was inserted into the muscle via a 25-gauge disposable hypodermic needle, which was withdrawn leaving the electrode in place. This arrangement permits the experimenter to reliably record motor units with minimal discomfort to the subject and provides stable recordings of up to 1 h (42). Three combinations of wire pairs were selected and differentially amplified to yield three separate EMG channels. The signals were band-pass filtered (1–10 kHz) to accentuate the differences in the wave shapes, sampled at 50 kHz, and stored on a personal computer for offline data analysis.

**Electrical stimulation.** On three subjects, the voluntary fatigue protocol was repeated on a separate occasion without intramuscular EMG recordings but with the addition of transcutaneous electrical stimulation delivered during each 6-s rest period between successive voluntary contractions. The VL muscle was stimulated by use of two self-adhesive surface electrodes (4.5 cm  $\times$  4.5 cm) placed proximally and distally over the lateral aspect of the thigh. Optimal electrode placement was determined by observing the elicited muscle twitch at a fixed current intensity as the proximal electrode position was varied slightly. The electrode was secured to the skin at the location that produced the largest twitch amplitude. During the testing, electrical square-wave pulses (0.2 ms in duration) from a constant-current stimulator (S88 and SIU6, Grass Instruments) were administered at supramaximal (110%) intensity. Maximum intensity was achieved by gradually increasing the stimulation current until no further increase in twitch amplitude could be observed. Supramaximal stimulation ensured that the largest possible muscle mass was activated for a given electrode location. During the recording of the elicited M-waves, the output stage of the EMG amplifier was blanked at the time of the stimulation pulse to reduce stimulus artifact. Constant area of the M-wave obtained from the VL surface electrode was taken as evidence that the same or a similar population of muscle fibers were stimulated during the fatigue protocol. The knee extension torque during maximal voluntary effort was examined 3 min before and 1 min after the voluntary fatigue protocol. A test stimulation train consisting of a brief train of 11 stimuli at 50 Hz was administered before, during, and immediately after the voluntary fatigue protocol. In two subjects, the 50-Hz train was followed, with a 1-s delay, by a single stimulus to measure the twitch response.

**Analysis.** The amplitude of the surface EMG signals was measured by calculating the root mean square (RMS) value for nonoverlapping segments of 0.5-s duration. Plots of RMS values for each contraction were examined for antagonist coactivation and alternating activation patterns among synergist muscles. The RMS values of VL, vastus medialis, and rectus femoris were normalized by the respective peak values obtained during the maximal knee extension contraction, those of biceps femoris by the peak value observed during maximal knee flexion.

The intramuscular EMG signals were separated into the constituent action potential trains via the Precision Decomposition technique. This technique has been used by our group for over three decades and has been described in numerous publications (5, 8, 26). Briefly, this technique uses rule-based artificial intelligence algorithms to identify action potentials and allocate them to motor units via template matching, template updating, calculation of firing probabilities, and resolution of superpositions. With assistance from the operator, the decomposition of the EMG signal can achieve an accuracy of 100% in some cases (26, 28), including the ones reported in this paper. The accuracy of this technique has been established by Mambrito and De Luca (28), who decomposed signals obtained from two separate electrodes. The two signals contained some motor unit action potentials common to both recording sites with the remainder being unique to each signal. Accuracy was established by comparing the firing times of the in-common motor units. The procedure for decomposing the EMG signal required considerable time, up to 200 h for some contractions of this study.

We only considered sets of contractions in which we had assurance that the same motor units were tracked repeatedly in all the contractions. We confirmed the presence of the same motor unit set with two tests. First, the shape of the action potentials in the three channels did not change across successive contractions. Second, the shape and amplitude of the spike-triggered averaged surface action potential of the motor unit remained similar throughout the set of contractions. (The spike-triggered averaging was performed in contractions for which more than 50 consecutive firings were available.)

The recruitment threshold of a motor unit was calculated as the torque level at the first consistent firing (next firing within 250 ms) of

the unit. The time-varying mean firing rate of the motor units was computed by passing the impulse train corresponding to the firing times of each motor unit through a unit-area Hanning window filter of 1.6-s duration (12). The length of the window was chosen to capture slowly varying trends in the mean firing rate (10). The time-varying behavior of the mean firing rates during the plateau phase (20% MVC target torque) of the contraction was parameterized by the slope of a linear fit as well as the average value for each motor unit. If a motor unit was not active from the start of the plateau phase, firing statistics were calculated over the longest time interval in which the unit discharged with an average rate of at least 4 pulses per second (pps). (This is typically the lowest sustained firing rate for this muscle.) In addition, the firing rate during the initial torque peak (50% MVC target torque) of each contraction, hereafter referred to as peak firing rate, was estimated by computing the inverse of the average interpulse interval in a 1-s window. The position of the window was chosen to include the peaks in the mean firing rate curves of all motor units. These peaks in the mean firing rate typically occurred before the torque achieved a maximum value because of the mechanical delay in the muscle-tendon apparatus (see also Ref. 13).

The recruitment and firing rate properties were analyzed, for all contractions in the set and in greater detail in the first, middle, and last contraction of the fatigue protocol. Data are presented as means and standard deviation [mean (SD)]. A critical significance level of 0.05 was set for all statistical tests.

## RESULTS

The number of successive contractions performed up to exhaustion ranged from 6 to 10 [8.2 (SD 2.0)] in our cohort of five subjects. The total number of contractions performed by each subject was not significantly dependent on the pre-fatigue knee extension torque MVC values ( $r = -0.65$ ,  $P > 0.05$ ), which ranged from 139.6 to 220.9 N·m [198.4 N·m (SD 33.6)]. The pre-fatigue torque values were measured at the start of each experimental session.

During each contraction, the surface EMG signal of the monitored muscle, the VL and the synergist muscles, the vastus medialis, and the rectus femoris along with the antagonist, the biceps femoris, were monitored to ensure that the torque of the knee joint measured in this experiment reflected the behavior of the force produced by the VL muscles where the motor unit activity was studied. The plots in Fig. 1 show examples of the time course of the normalized RMS amplitude of EMG signals from these muscles during the first, middle, and last contraction in two subjects. Note that the relative amplitudes of the EMG signals from the agonist and antagonist muscles remained constant throughout each contraction, i.e., without alternating activity among knee extensors or between flexor and extensors. This indicates that the relative force contribution of each muscle remained constant with respect to the measured torque around the knee joint. Also the RMS amplitude curves of the knee extensors for the first and last contraction have a similar, parallel pattern, indicating that the relative contribution of the forces from the individual muscles to the measured torque remains similar from the first to last contraction. This pattern of synergist and antagonist muscle activity was confirmed in all subjects, although the extent of the increase in RMS amplitude of the surface EMG signals at exhaustion differed among subjects as illustrated here by plots in Fig. 1. Our results are consistent with those of a recent study of the activity of knee extensor muscles during sustained low-level contractions that reported emergence of alternate activation of the superficial

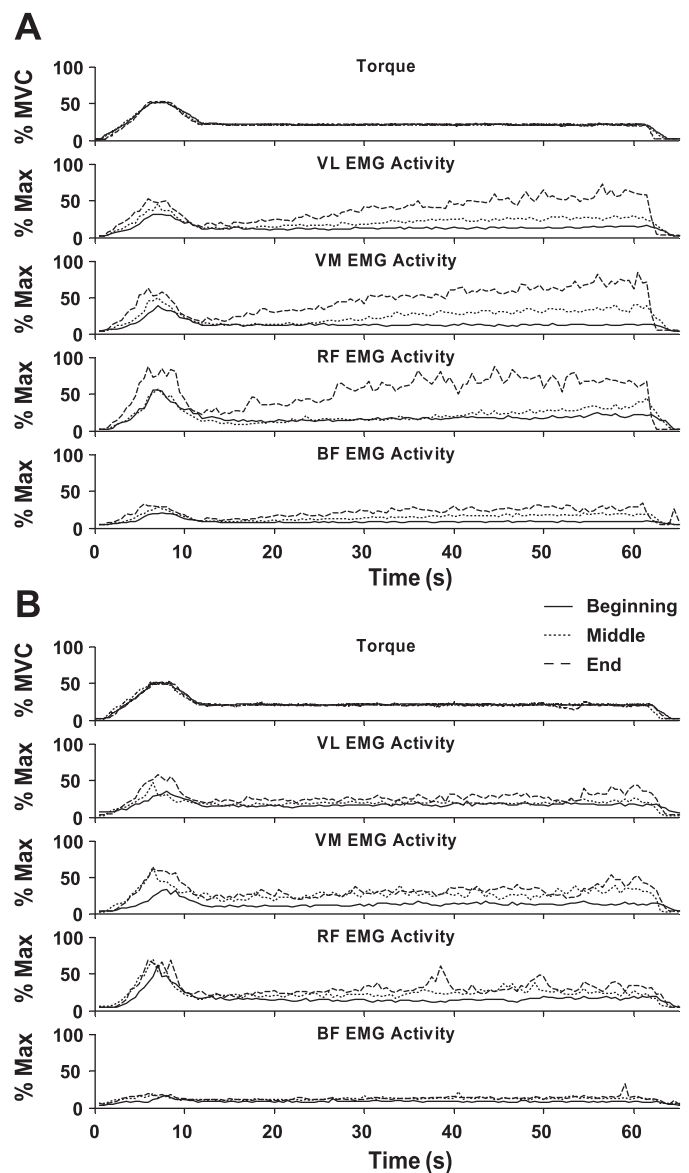


Fig. 1. A: surface EMG activity pattern in 1 subject (*subject C*) during the beginning (solid line), middle (dotted line), and end (dashed line) of the fatigue series. Shown are (from top to bottom) the knee extension torque and the root mean square (RMS) amplitude of the surface EMG signals of the monitored synergist muscles, the vastus lateralis (VL), the vastus medialis (VM), the rectus femoris (RF), and 1 antagonist muscle, the biceps femoris (BF). Torque and EMG amplitude are expressed as a percentage of the maximal voluntary contraction (MVC) values established at the beginning of the experiment. B: same plot as in A with data from another subject (*subject B*).

quadriceps musculature at contraction levels of 5% MVC or less, but none at higher contraction levels (25).

*Motor unit firing patterns during a fatigue task.* An example of the knee torque and the underlying motor unit firing data from one subject is given in Fig. 2. Figure 2 shows the first, middle, and last contraction in a series of 10 repeated contractions. Motor unit firings, represented by vertical bars, are linked to the torque record by a common time axis. The mean firing rates, derived from the firing trains of each motor unit through low-pass filtering (see METHODS), are shown in the three graphs of the center column. To the right of each graph, insets depict snapshots of the motor unit action potential shapes



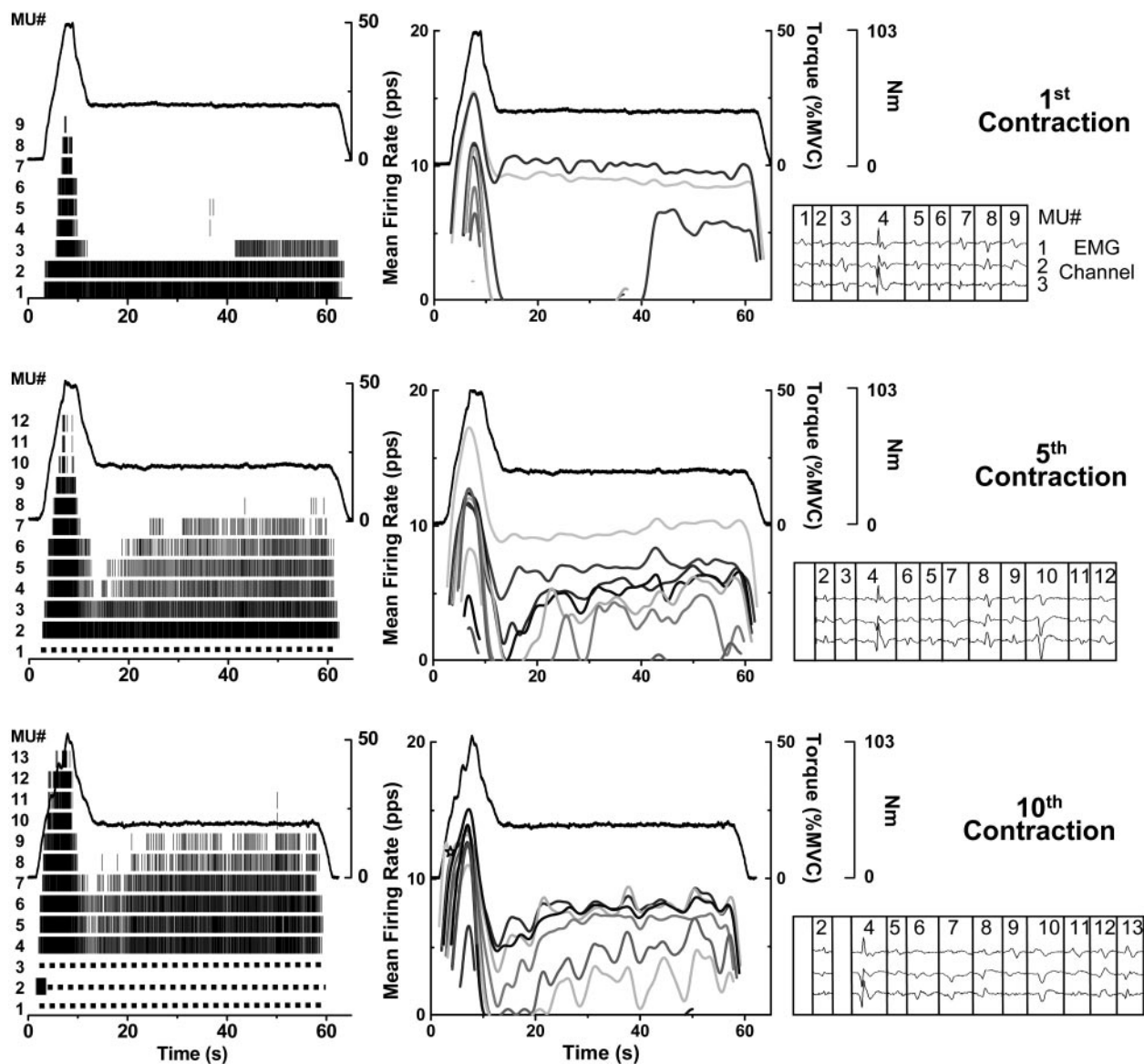


Fig. 2. Motor unit (MU) firing pattern during the first, middle (5th), and last contraction in a series of 10 successive VL contractions performed by 1 subject. *Left*: isometric knee extension torque (solid black line, right vertical axis), both in absolute (N·m) and relative measures (%MVC), and the firing times of concurrently active MUs (vertical bars). Dotted lines indicate that a MU shape could no longer be reliably detected. *Middle*: isometric knee extension torque (uppermost solid line, right vertical axis) and the mean firing rates of concurrently active MUs (shaded lines, left vertical axis). Mean firing rates, expressed in pulses per second (pps), were calculated by passing the impulse trains corresponding to firing times of MUs through a 4-s Hanning window to accentuate slowly varying trends in the discharge rate. In the *bottom* plot (10th contraction), ☆ indicates that the MU shape could no longer be reliably detected (cf. Fig. 3). *Right*: insets to the right of each graph depict MU action potential shapes (in 3 channels) used to identify individual firing trains. The shapes were sufficiently different from one another (and only changed gradually over time) to allow the tracking of continuously active MU and to identify newly recruited MUs during the fatigue protocol. Numbers above the 3-channel EMG signatures correspond to the MU tracked across successive contractions. (Adapted from Ref. 1, used with permission.)

that were used to identify individual firing trains. Each shape consists of the motor unit action potential waveform in three channels.

In the first contraction, nine motor units were activated during the initial ramp, some of which only contributed a few discharges as the torque trace reached its peak (Fig. 2, *top left*). The ordered recruitment was complemented by the layering of mean firing rates, clearly visible during the first 10 s of the plot (Fig. 2, *top center*). All motor units modulated their firing rates in a pattern resembling the increase and subsequent decrease of the torque output. As the contraction entered the next phase,

the 50-s low-level torque plateau, the majority of motor units in the detection volume of the recording electrode were derecruited, and only two motor units remained active during the next segment of the contraction. Note the gradual decrease in the mean firing rate from 15 s onward, as the joint torque was kept stable at the target level (Fig. 2, *top center*). At 41 s into the contraction, the third motor unit to be recruited during the initial torque ramp became active again, discharging with a lower mean firing than the other two units, but also decreasing its rate until the end of the contraction. This slow decay in firing rates was only seen during the first contraction in this

contraction series. As shown in the middle and bottom row of plots in Fig. 2, which depict the middle and last contraction in the series, mean firing rates increased slowly over time as the torque level continued to remain constant. This change in the firing rate behavior occurred in conjunction with three other phenomena: 1) additional motor units were recruited during the torque plateau phase, 2) fewer motor units were derecruited after the initial torque peak, and 3) those that stopped firing tended to be reactivated sooner.

In addition to derecruitment and recruitment events, de novo recruitment of motor units was observed during the torque ramp as the contraction series progressed. In the fifth contraction (Fig. 2, middle row), three new motor units were recruited during the initial torque peak (*motor units 10, 11, and 12*), and a larger fraction of the units was active during the constant torque plateau. An additional motor unit was recruited by the end of the contraction series (Fig. 2, bottom row), amounting to 13 distinct motor units identified in the EMG signal for this subject. All throughout, the layering of mean firing rates with the earliest recruited motor unit having the greatest firing rate and the last recruited motor unit having the lowest was maintained during both the torque peak as well as the plateau phases.

It was not always possible to follow all the detected motor units that contributed to the EMG signal throughout the full set of contractions. However, we were always able to distinguish cases of true derecruitment from cases in which the decomposition algorithm lost track of a motor unit because of a change in its signal-to-noise ratio. For example, *motor unit 1* in the middle panel, and *motor units 1, 2, and 3* in the bottom panel of Fig. 2 were not derecruited; they could not be tracked. Their EMG signatures exhibited amplitude and/or shape changes, which rendered them unreliable for firing rate analysis in these contractions. Frequently, when decomposing a complex, motor

unit-rich, superimposed EMG signal, it becomes difficult, if not impossible, to track the firings of the lowest threshold motor units because they have the action potentials with the lowest energy. At times, these action potentials disappear in the background noise of the signal from which they are being extracted. For example, the amplitude and shape changes for *motor units 2 and 5* shown in Fig. 3 occurred gradually while the motor units were not changing their firing characteristics. This behavior indicates that the cause was due to movement of the recording electrode with respect to the muscle fibers, as the action potentials of all motor units were affected at the same time.

Among our five subjects, 37 of all detected motor units were active during the first contraction, of which 15 participated in the plateau phase of the contraction. At the endurance limit, 56 motor units were active during the peak and 34 during the plateau, representing a 51% and a 117% increase, respectively, in motor unit activation. The time course of motor unit activation for each of the subjects is shown in Fig. 4. Note that for both peak (50% MVC) and plateau (20% MVC) torque, the total number of motor units increased with endurance time, and this increase was more pronounced during the first one-half of the contraction series.

**Peak firing rates.** All motor units exhibited a similar increase in their peak firing rate as the contraction series progressed such that the hierarchical arrangement of the firing rates remained strikingly unchanged from that of the initial contraction (see Fig. 2). Newly recruited motor units always discharged at a lower peak firing rate than all previously active motor units. Nineteen motor units had sufficiently stable action potential waveforms during the peak in the torque trace to yield reliable peak firing estimates. A paired *t*-test revealed the mean value of the peak firing rates during the last contraction [14.7 pps (SD 1.9)] to be significantly higher than that during the first

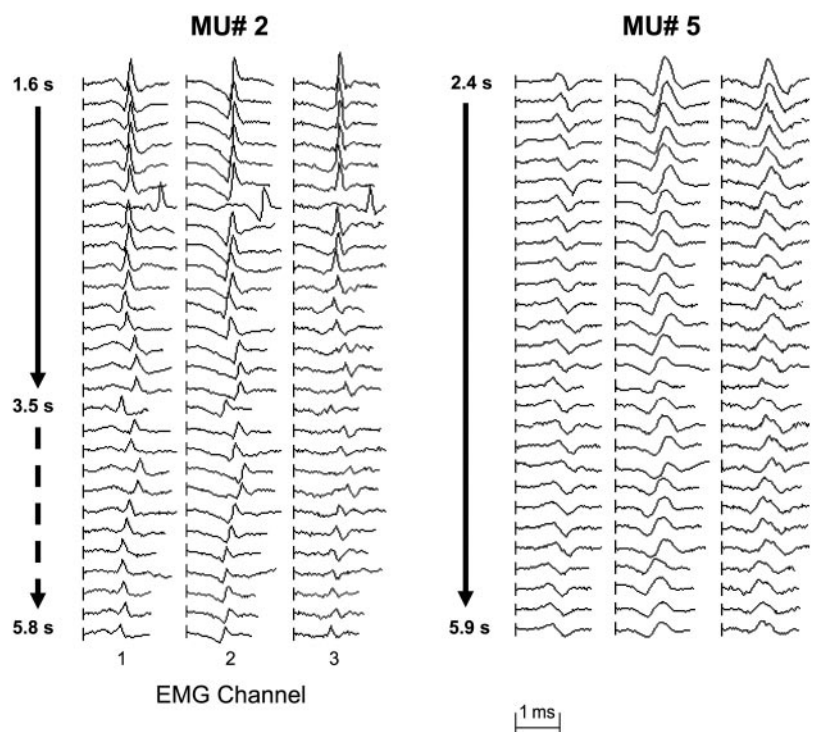


Fig. 3. Raster plot of 3-channel EMG wave shapes for 2 simultaneously recorded MUs. The amplitude of the EMG signature of *motor unit 2* (on all 3 channels) and *motor unit 5* (on channels 2 and 3) continually decreased, indicating that the electrode was moving away from the fibers of both MUs (solid arrows). In the case of *motor unit 2* the amplitude became indistinguishable from the noise in the signal; hence it could no longer be tracked reliably from 3.5 s onward, although firings continued to be detected (dashed arrow). The amplitude of *motor unit 5* also decreased but remained sufficiently large to enable continued identification of this MU. The effect of the electrode displacement on the observed EMG signature of each MU varied, depending on the orientation of the fibers and the distance from the recording surfaces. Shape changes due to electrode movement are reflected in the EMG signatures of all MUs and are a pure artifact of the recording technique.

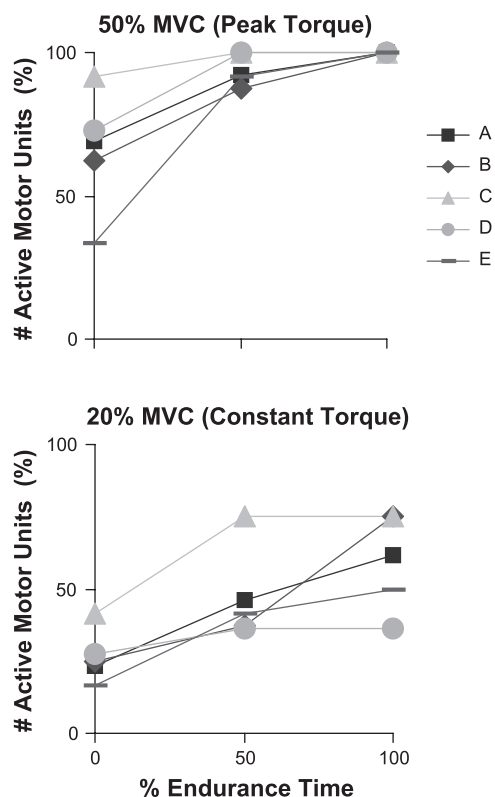


Fig. 4. Number of MUs active during the 50% MVC torque peak (*top*) and the 20% MVC torque plateau (*bottom*) plotted as a function of normalized endurance time. Values for the first, middle, and last contraction are shown, corresponding to endurance times of 0, 50, and 100%. The number of active MUs at any time is expressed relative to the number of MUs recruited during the final torque peak (13, 8, 12, 11, and 12 MUs for subjects A–E, respectively). Different symbols and shadings denote different subjects. In this and the following Figs. 5 and 6, the letters A–E refer to the same 5 subjects.

[11.9 pps (SD 3.2),  $P < 0.001$ ,  $n = 19$ ]. An additional 15 units were recruited between the first and the middle contraction of all subjects. The mean values of peak firing rates for these newly recruited units were not statistically different between the middle and last contraction [11.2 pps (SD 2.4) vs. 11.8 pps (SD 3.0),  $P > 0.05$ ,  $n = 15$ , paired  $t$ -test].

**Behavior of mean firing rates during the torque plateau.** The time course of the mean firing rate of motor units in all but one subject decreased during the first 10–20% of the endurance time and subsequently increased continuously until exhaustion (Fig. 5, A–E). The top left graph (Fig. 5A) indicates that in this subject three motor units were active during the torque plateau of the first contraction (see also Fig. 2, *top row*). The average value of the firing rate in these units decreased in the second contraction, but another motor unit was also recruited during this contraction, discharging at the lowest rate of the group. With the recruitment of the additional motor unit and the recruitment of more units in subsequent contractions, the downward trend in the average firing rate adaptation was reversed. Subsequently, all motor units increased their average firing rates, surpassing their initial rate, despite the transient drop in contractions two and three. Thus, for motor units that were active during the torque plateau and could be tracked throughout the contraction series, the population means at 0 and 100% endurance time were significantly different [8.3 pps

(SD 1.8) vs. 10.4 pps (SD 1.0),  $P < 0.05$ ,  $n = 8$ ]. Similarly, motor units gradually recruited during the plateau exhibited an increase in the average firing rate, as quantified in the population means at 50 and 100% endurance time [5.8 pps (SD 1.5) and 8.7 pps (SD 2.6),  $P < 0.001$ ,  $n = 12$ ]. The percentage increase in firing rates was 24% for the continuously active motor units and 51% for the motor units recruited in the course of the torque plateau.

By itself, the average value of the firing rate does not fully capture the behavior of the mean firing rates during the constant-torque phase of the contraction. As already pointed out in the description of Fig. 2, mean firing rates were not constant; they had a time-varying trend during each contraction. This trend was parameterized by fitting a linear least square line through the mean firing rate curves. The resulting slopes are plotted as a function of normalized endurance time in Fig. 5, *a–e*. Only motor units that fired consistently at an average rate  $> 4$  pps for  $\geq 10$  s were considered. In four of five subjects, negative slopes were dominant in the first contraction, indicating that firing rates slowly decreased as the torque was held constant. This behavior shifted toward increasing mean firing rates, or predominantly positive slopes at the end of endurance time for all subjects. To quantify the percentage of motor units exhibiting a certain firing rate trend, motor units firing rate slopes were classified into three categories: decreasing, slope  $< -0.03$  pps<sup>2</sup>; increasing, slope  $> +0.03$  pps<sup>2</sup>; and quasi-constant, for slope values in between. This classification scheme followed that of De Luca et al. (10), with the exception that the boundaries were set tighter. The previous transition slope had been set to 0.1 pps<sup>2</sup>, which amounted to a mean firing rate change of 0.8–1.5 pps for the length of the constant-force contractions studied in that investigation. Because the constant-torque phase of the contractions in the present study lasted 50 s, a factor of 3 longer than the longest interval considered in the previous study, the slope boundaries were adjusted by one-third. The results of the classification are summarized in Table 1. Note that, during the first contraction, 80% of the motor units displayed either a decreasing or quasi-constant firing rate slope, whereas during the final contraction, none showed a decreasing slope and only 28% a quasi-constant slope. Furthermore, all instances of increasing firing rate slope during the first contraction were observed in the same subject (Fig. 5c). If the analysis is limited to motor units that could be tracked continuously, the results are qualitatively the same. On the average, these motor units increased their firing rate slope from the beginning to the end of endurance time. There was a significant increase in the mean value of the slope when comparing the first and the last contraction [0.02 pps<sup>2</sup> (SD 0.06) and 0.11 pps<sup>2</sup> (SD 0.12),  $P < 0.01$ ,  $n = 8$ ]. Similarly, for motor units that were progressively recruited during the plateau phase, an increase in the mean firing rate slope from middle to last contraction was observed [0.04 pps<sup>2</sup> (SD 0.04) and 0.12 pps<sup>2</sup> (SD 0.13),  $P < 0.05$ ,  $n = 12$ ].

**Interaction between recruitment threshold and firing rate.** For each subject scatterplots of motor unit firing rate vs. recruitment threshold were constructed. Figure 6 shows the resulting plots for the peak firing rates (A–E) and for the average firing rates (*a–e*) during the contractions. Each plot presents data from one subject at three endurance times (diamonds, first contraction; squares, middle contraction; triangles, last contraction). Note that recruitment thresholds are ex-

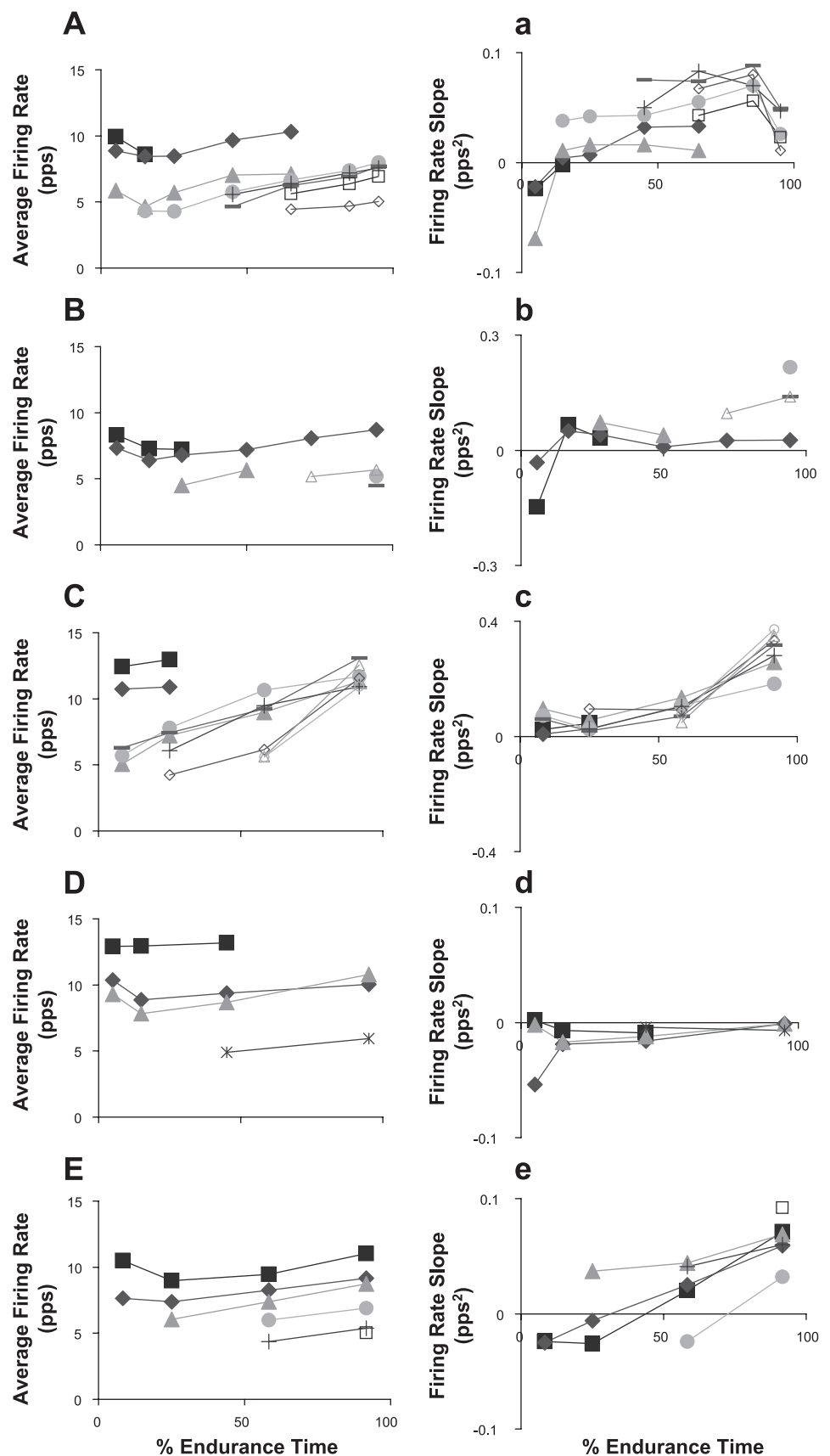


Fig. 5. Average firing rate (*left column, A–E*) and the slope of the mean firing rate (*right column, a–e*) of MUs from each of the 5 subjects plotted as a function of normalized endurance time. Each data point represents the firing rate parameter of 1 MU during the constant torque region of 1 contraction. Data points are shown at endurance times corresponding to the first 2 contractions, the middle, and the last contraction for each subject. In 2 subjects (*A, B*), additional data points were available at intermediate endurance times and have been included in the plots. Because average firing rate and firing rate slope were determined over the entire length of the torque plateau, normalized endurance times were calculated by using the midpoint of each of the contractions.



Table 1. Summary of motor unit firing patterns during the plateau phase of the first, middle, and last contraction in the fatigue series

Contraction	Slope			Total
	Decreasing	Quasi-Constant	Increasing	
First	4 (26.7%)	8 (53.3%)	3 (20.0%)	15 (100%)
Middle	1 (4.2%)	9 (37.5%)	14 (58.3%)	24 (100%)
Last	0 (0.0%)	7 (28.0%)	18 (72.0%)	25 (100%)

Each table entry shows the number (and percentage) of active motor units exhibiting a particular firing pattern. A motor unit was considered to be active during the plateau phase of the contraction if it fired continuously for a minimum of 10 s and had a mean firing rate > 4 pulses/s (pps). Categorization of mean firing rate slopes: Decreasing, slope < -0.03 pps<sup>2</sup>; Quasi-Constant, -0.03 ≤ slope ≤ 0.03 pps<sup>2</sup>; Increasing, slope > 0.03 pps<sup>2</sup>.

pressed as a percentage of the pre-fatigue MVC value. Straight-line fits through the data points indicate the trend in the relationship between recruitment and firing rate variables. If more than two motor units were available for analysis, the slope and the coefficient of the linear regression were computed. In all subjects, a negative correlation between the peak firing rates and the recruitment thresholds of motor units was observed, irrespective of the contraction number. The range of negative correlation coefficients was narrower during the first (-0.67 to -0.97) and the middle contraction (-0.55 to -0.87) than during the last contraction (-0.15 to -1.00). Averaging across all subjects, the inverse relationship between peak firing rate and recruitment threshold during the first contraction was well described by a straight line ( $y = -0.30x + 23.00$ ,  $r = -0.84$ ,  $P < 0.001$ ,  $n = 34$ ). Similar regression results were obtained for the middle ( $y = -0.15x + 17.75$ ,  $r = -0.62$ ,  $P < 0.001$ ,  $n = 41$ ) and the last contraction ( $y = -0.20x + 18.35$ ,  $r = -0.72$ ,  $P < 0.001$ ,  $n = 38$ ).

The plots of the mean firing rates as a function of recruitment threshold revealed an inverse relationship (Fig. 6, *a-e*). However, because fewer motor units were active during the plateau phase, in particular during the first contraction, the sample size was much smaller than that for the peak firing rate analysis. In two of five subjects, fewer than three data points were available to establish the relationship between average firing rate and recruitment threshold for the first contraction. In one subject, no recruitment threshold could be obtained for motor units active during the torque plateau. Hence, only four plots appear in the right column of Fig. 6. Collapsing the data across the four subjects, significant negative correlations between average firing rate and recruitment threshold were obtained for the first ( $y = -0.13x + 11.42$ ,  $r = -0.65$ ,  $P < 0.05$ ,  $n = 12$ ), middle ( $y = -0.14x + 9.68$ ,  $r = -0.62$ ,  $P < 0.01$ ,  $n = 19$ ), and last ( $y = -0.16x + 10.81$ ,  $r = -0.47$ ,  $P < 0.05$ ,  $n = 19$ ) contractions in the fatigue series. (This averaging across subjects is valid in this instance because all the subjects have the same trend.)

**Whole muscle mechanical changes with fatigue.** The fatigue protocol was repeated in three of the subjects in the volunteer group to quantify the effect on the mechanical properties of the VL muscle. Electrical stimulation was delivered to the muscle before, in between, and after each voluntary contraction. Figure 7 shows the series of elicited torque responses to 50 Hz and single-twitch stimulation for the subject whose motor unit firing data is presented in Fig. 2. The tetanic and twitch torque

amplitude declined to 53 and 48% of the initial value. Note, however, the initial increase in the peak torque from the first measurement, immediately before the start of the fatigue protocol (0% endurance time), to the second measurement, immediately after the first voluntary contraction (10% endurance time). A qualitatively similar result was obtained for the second subject, where peak torque at 50 Hz was slightly elevated after the first contraction and then declined to 51% of the initial value. In a third subject, peak torque of twitch and tetanus were decreased immediately after the first contraction and subsequently fell to 12 and 33% of the initial value (see also Fig. 6 in Ref. 1).

Figure 8 presents plots of the peak torque of the elicited tetanic and twitch response (circles and X's) as a function of endurance time overlaid on the mean firing rates (shaded lines) obtained from the same subjects. For clarity, mean firing rates are only shown for the constant torque region of the contraction. Note that the firing rates were initially decreasing in the same two subjects (A and B) for which the peak tetanic torque was potentiated (106 and 101% of initial values) after the first contraction. Potentiation was absent in one subject, as was the decrease in the firing rates during the first contraction (Fig. 8C, same subject as in Fig. 5C).

## DISCUSSION

The firings of several concurrently active motor units were followed successfully through a series of contractions to exhaustion. This data set allowed us to study the interaction between the recruitment threshold and firing rate for a group of motor units as fatigue progressed to exhaustion. At the beginning of the series of contractions, the firing rate decreased and then increased during the subsequent contractions. The increase in the firing rates was concomitant with the observed recruitment of new motor units. This trend in the firing rates complemented the opposite behavior of the force twitch and tetanic torque measured in the whole muscle.

An example of the initially decreasing firing rates can be seen in the top panel of Fig. 2, which represents the first of the series of contractions. Overall, 80% of the motor units showed decreasing or quasi-static firing rates during the first contraction (Table 1). The results are in line with those of De Luca et al. (10), who reported that firing rates of the tibialis anterior and first dorsal interosseous muscles decreased during the first 8–15 s in 80% of all the contractions that met their stringent criteria of constant force. In addition, that report established that the decrease in firing rate was, in general, proportional to the force level of the contraction, such that lower contraction levels yielded lesser firing rate decreases. As the contraction series progressed, a change in the time-varying firing rate behavior was observed. During the middle contraction, only 1 motor unit was found to meet the decreasing firing rate criterion, whereas 58% of the motor units exhibited increasing mean firing rates (Table 1 and Fig. 5). At 100% endurance time, the proportions had shifted to 72% increasing and none decreasing. In other words, for motor units that started out with a negative firing rate slope, a reversal in sign had taken place. In two subjects (Fig. 5, *a* and *b*), where firing rates during intermediate contractions had been analyzed, this reversal could be pinpointed to the second contraction in a series of 10 and 9 contraction, respectively. Note that concomitant changes

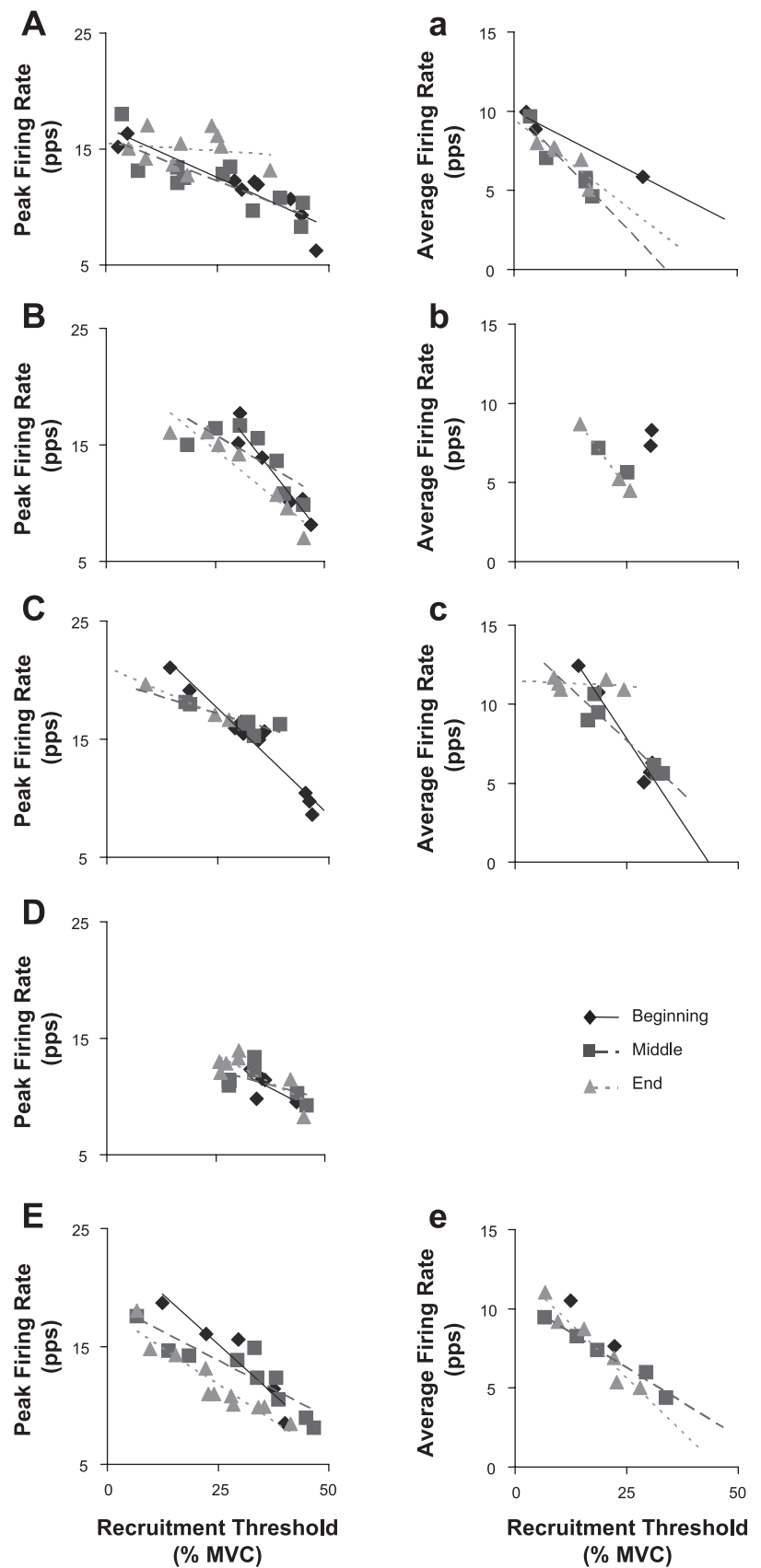


Fig. 6. Peak firing rate (A–E) and average firing rate (a–c, e) plotted as a function of recruitment threshold for MUs from each of the 5 subjects. In each plot, concurrently active MUs are denoted by identical symbols corresponding to first (diamonds, solid line), middle (squares, dashed line), and last (triangles, dotted line) contraction. Note that in 1 subject no reliable recruitment data could be obtained for MUs that were active during the torque plateau. (Recruitment thresholds and peak firing rates were estimated for higher threshold MUs as shown in D). No systematic change in the slope of the regression line as a function of endurance time was observed, although the slope was always steeper in the first contraction. The important observation is that the negative correlation between firing rate and recruitment threshold was maintained throughout the fatiguing contraction set.

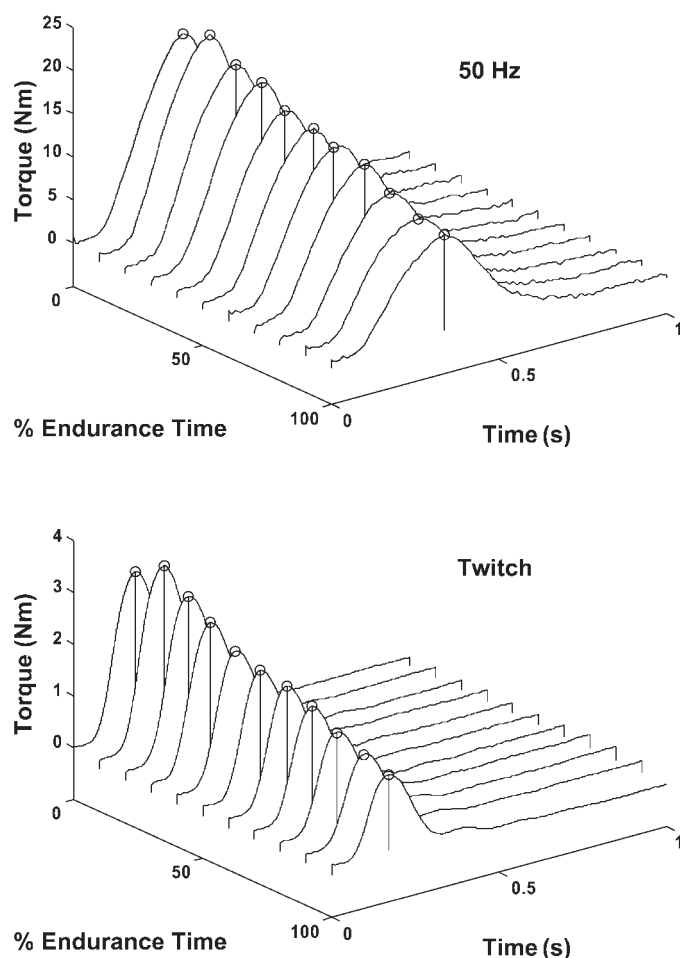


Fig. 7. Waterfall plots of the electrically evoked contractions in the VL muscle of *subject A* recorded during the fatigue task. The electrical stimulation consisted of 11 supramaximal current pulses at 50 Hz (*top*), followed by a single pulse (*bottom*) separated by 1 s. Each plot shows the amplitude (*z*-axis) and contraction time (*y*-axis) for individual torque responses as a function of normalized endurance time on the *x*-axis. The torque response at 0% endurance time was elicited immediately before the first voluntary contraction; the one at 100% endurance time, immediately after the last contraction. Superimposed vertical lines and circles mark the peak torque level and the time to peak torque. Note the increases in peak torque after the first contraction and the steady decline thereafter for both tetanic (50 Hz) and single-twitch stimulation. The initial increase in peak torque was not observed in 1 of the subjects (see also Ref. 1). The time courses of peak torque values for all 3 subjects are shown in Fig. 8.

in the average firing rate curves (Fig. 5, *A* and *B*) and the start of the progressive recruitment of additional motor units mark the transition point. The firing rate reversal occurred at different times for different subjects. This was likely a function of the fatigue state of the muscle.

A short-term decline in mean firing rates followed by an increase and the recruitment of additional motor units was previously only described by Dorfman et al. (15) and De Luca et al. (10) for submaximal contractions in the biceps brachii and first dorsal interosseous muscle, respectively. In other studies of ensemble averages of motor unit firing rates, an initial decrease was not detected (30) or, if apparent, not discussed (2). In at least one report on single motor unit firing rates, an initial decline of firing rates was quantified, but the subsequent increase was not measured (18). That study re-

ported a significant decline in the firing rate of the majority of motor units that were active from the start of a sustained 20% MVC contraction in the biceps brachii. Yet careful examination of the time course of motor unit firing rates (Ref. 18, their Fig. 1) revealed that only 7 of 20 such units could be followed until the endurance limit, the majority of which increased their firing rates toward the end (3 surpassing their initial firing rate). In addition, 11 of 13 newly recruited motor units showed an increase in the average firing rate over time, which is in agreement with our findings.

Our finding that the firing rate can present three phases (decreasing, near-constant, and increasing) at different sections of the fatiguing contraction sets can explain the differing reports in the literature that describe one or the other of these

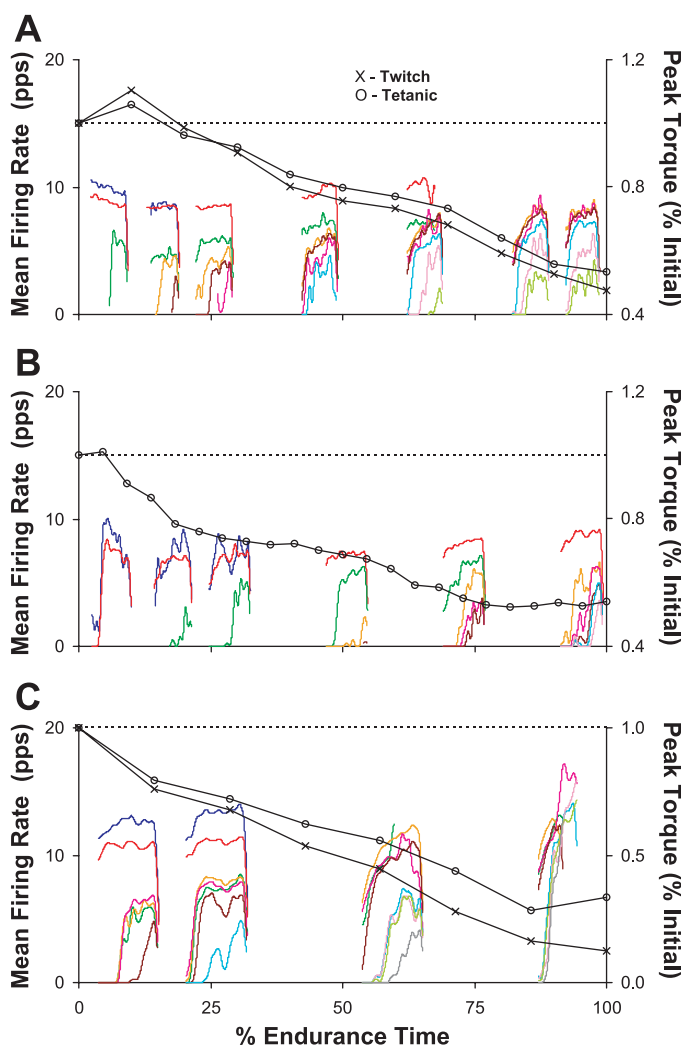


Fig. 8. *A*: overlay of time course of firing rate adaptations and elicited torque responses during the fatigue protocol for *subject A*. Shown are mean firing rates of MUs during the plateau phase (colored lines, left vertical axis) and the peak torque of a single twitch and of the tetanic stimulation at 50 Hz ( $\times$  and  $\circ$ , right vertical axis). Note that the firing rates were obtained during the voluntary contractions, whereas the electrical stimulation was administered during the brief rest periods in between successive voluntary contractions. Mean firing rates in this figure were computed by using an 8-s Hanning window. *B*: mean firing rate and peak tetanic torque data for *subject B*. No single-twitch measurements during the fatigue protocol were available for this subject. *C*: note the absence of torque potentiation and of decreasing firing rates in the first contraction.

phases. It may well be that the differing reports analyzed data collected from different locations along the fatigue continuum and consequently obtained different and, at times, opposing results.

*Twitch potentiation and diminution.* Changes in the mechanical properties of the muscle can explain the observed firing rate adaptations.

The twitch and tetanic torque response declined in amplitude by 52–85 and 46–67%, respectively. A closer look at the time course of both revealed that the decline in amplitude was not monotonic in two of three subjects, but briefly increased after the first contraction (Fig. 7). This increase was only short lasting, as the peak torque declined below the initial value at subsequent 1-min intervals. This observation is consistent with the short-term manifestation of twitch potentiation (20–60 s) that has been established by other investigators (24, 27, 35, 40, 41). The amount of twitch potentiation is dependent on the extent of voluntary activity (40, 41), with the highest potentiation values reported for brief (~10 s) maximal force contractions. These previous reports indicate that in our study the actual peak twitch potentiation in the subject shown in Fig. 8A may have been greater than the measured 111% and likely occurred during the first voluntary contraction. That this might be the case is supported by two observations: 1) the firing rate decrease in two motor units leveled off at 41 s into the contraction, and 2) an additional motor unit was recruited during the first contraction. Although the conditions of motor unit recording and electrical stimulation trials were not exactly identical in the present study, our data are consistent with those of Klein et al. (24), who provided evidence for the link between motor unit firing rates and muscle twitch properties. These researchers reported a positive correlation between the percent decrease in single motor unit firing rates, at three different target force levels, and the potentiation of muscle twitch force after a brief conditioning contraction at 75% MVC. In our study the steady decline in peak torque values after the first 10% of endurance time was mirrored by an increase in the mean firing rate and the recruitment of motor units. The occurrence of twitch potentiation at the 20% MVC level contractions of thigh muscles is plausible and has been reported by other investigators. Vøllestad et al. (41) argued that twitch potentiation in the quadriceps muscle was in part due to mechanical changes in the low-threshold motor units.

The initial increase and subsequent diminution of the whole muscle torque response to electrical stimulation offer a straightforward explanation for the complementing behavior of the observed firing rate adaptations. As can be seen in Fig. 8, the firing rates decrease when the elicited torque response increases, and it increases when the elicited torque decreases. This is so because the task was to maintain the force output of the muscle constant. This complementary, but opposite, behavior is evident even in Fig. 8C, where the elicited torque response only decreases. This subject did not perform more practice contractions than the others before initiating the fatigue contraction series. Thus it seems unlikely that the early-onset twitch potentiation would have occurred during the practice contractions. Furthermore, the subject did not perform any practice contractions in the second experimental session, when the electrical stimulation was applied to the muscle. This is a strong indication that the changes in motor unit firing rate and the changes in mechanical response of the muscle were not

affected by the practice trajectories. It may simply be that different subjects present different profiles in the manifestation of twitch potentiation. The important point is that the behavior of the force twitch and the firing rate is complementary.

The mechanism of twitch potentiation had been previously implicated by De Luca et al. (10) to account for the maintenance of force over the first 15 s of a voluntary isometric contraction when firing rates were found to decline. In the absence of additional recruitment, the authors concluded that twitch potentiation enhanced force production such that lower firing rates sufficed to produce the target forces. We cannot exclude that the initial decline in firing rates is an adaptation due to motor unit intrinsic properties, such as those described in cat motoneurons in response to sustained intracellular (23) or extracellular (37) activation. If indeed the firing rate changes are due to motoneuron adaptation, the coincidence of the firing rate changes with the increase and subsequent decrease in twitch properties would be truly remarkable. The more likely explanation is that the changes in twitch properties necessitate adjustment of the central drive to the muscle, which then results in the observed firing rate changes.

*The motor control scheme remains invariant throughout fatigue.* As early as the 1970s, researchers have reported that the mean firing rates of motor units are inversely proportional to their recruitment thresholds, such that earlier recruited, low-threshold motor units maintain higher firing rates than later recruited, higher threshold units (11, 32, 39). Subsequent work from our group (9, 10, 12, 13), focusing on contractions of less than 30-s duration from various limb muscles, confirmed this relationship. Other independent investigators have confirmed this phenomenon in limb muscles in human as well as animal studies (22, 29, 34, 38), and recently our group has shown that this relationship is present during nonisometric, dynamic contractions in laryngeal muscles (33). The layered appearance of the plots of the firing rates of successively recruited motor units led us to refer to this phenomenon as “onion skin” (9).

The few dissensions found in the literature are due to the aggregation of data from separate contractions from different subjects. This practice introduces intersubject variability that obscures the real underlying organization of the motor unit firing rate hierarchy that exists within each muscle.

In conjunction with the size principle of motor unit recruitment (20, 21), the inverse relation of recruitment threshold and firing rate form a set of rules that govern the firing behavior of a pool of motor units in response to an excitatory “common drive.” From the companion study to this work we have previously reported (1) that the ordered recruitment of motor units is maintained during submaximal fatiguing contractions. This was established by direct measurement of the recruitment order during a ramp up to 50% MVC at the beginning of each contraction in the series as well as the observation that additional recruitment of motor units during the course of the hold phase at 20% MVC occurred according to the initial order. We now add that the inverse relationship between the recruitment threshold and firing rates is also maintained during fatiguing contractions. The plots in Fig. 6 demonstrate that the peak and average firing rate are inversely proportional to the recruitment threshold at the beginning, middle, and end of a fatiguing contraction series lasting up to 10 min.



The finding that the activation pattern among muscles and motor units follows the same scheme during repeated contraction is indeed remarkable given the redundancy in the system of muscles around the knee joint. In contrast, previous studies of other muscle groups have indicated that activation of agonist and antagonist muscle groups may not be predictable and are not consistent from contraction to contraction (36, 44). Scutter and Türker (36) reported varying levels of cocontraction during repeated slow-ramp contractions of jaw muscles within the same subject. Zijdwind et al. (44) demonstrated several different activation patterns in the first dorsal interosseous muscle but not in the adductor pollicis during isometric force contractions. The variability in the first dorsal interosseous muscle was attributed to alternating synergistic activity (i.e., index finger flexion vs. abduction) as well as different distributions of activity within a muscle (revealed by multiple electrode recordings). These contrasting observations might reflect variability in the control of muscles by the central nervous system (CNS) in less constraint motor tasks of multiple degrees of freedom, compared with the simple isometric knee extension task of the present study. Our results show consistent changes in surface EMG as well as motor unit recruitment and firing rate patterns from contraction to contraction, although the amount of change varied among subjects. The seemingly different behavior of one subject could be explained by considering the measured mechanical response of the muscle. A recent report by de Ruyter et al. (14) on quadriceps muscle activation patterns during a sustained, isometric knee extension task described a large variation in the VL motor unit firing rates among subjects, especially toward the end of the endurance time. The authors interpreted these results as reflecting differences in voluntary drive among subjects. However, as in our study, within each contraction, the changes in motor unit firing rates were similar. A possible explanation for the discrepancy in intersubject variability is that our subject group was more homogenous, both in terms of age and gender. In addition, antagonist muscle activity was not monitored in the previous study, leaving increased cocontraction as a possible contributor to differences in task performance among subjects.

**Recruitment vs. rate coding.** It has been argued that the control strategy to regulate motor unit firings might adapt, depending on whether a muscle is producing a brief force-varying, or a fatiguing, static contraction. Bigland-Ritchie et al. (2) stated that, in contrast to brief voluntary contractions, the CNS used motor unit recruitment over rate coding in the quadriceps as the predominant method to compensate for the effects of muscle fatigue. Their conclusion was based on the observation that the surface-rectified EMG signal increased fourfold during 40–50 min of intermittent contractions at 30% MVC, whereas the population average firing rate only increased by 80%. Furthermore, they speculated that the increase in average firing rates toward the end of the experiments was probably due to the recruitment of faster type II muscle fibers, which (according to them) would require higher firing rates to achieve twitch fusion. Our present results in the VL muscle are consistent with our results in the first dorsal interosseous (10), and all clearly indicate that, in a contraction of increasing force, the newly recruited (higher threshold) motor units have in fact lower average firing rates than the already active units. Additionally, all motor units increased their firing rate as fatigue progressed and recruitment threshold and firing rate

always remained highly correlated (Fig. 6), disfavoring independent adjustment of either of those variables. In fact, our results indicate that the control strategy during a fatiguing contraction series remains essentially the same, but the excitatory drive to the motor unit pool increases once the initial twitch potentiation has subsided. The apparent prevalence of motor unit recruitment in the fatiguing VL muscle appears to be a consequence of a broad recruitment range and moderate firing rate dynamics in the VL motor unit pool, both of which are indeed observed in the nonfatigued state of the muscle at the beginning of the fatigue series.

In summary, we have shown that, during a series of fatiguing contractions, the firing rate of motor units in the VL muscle first decreased and then subsequently increased, along with the recruitment of additional motor units. The firing rate modulation complemented an opposite modulation in the amplitude of the elicited mechanical response of the muscle. These data suggest that, during maintenance of a constant force output, the motoneuron pool receives a net excitatory drive that, in the presence of short-lived potentiation of the muscle twitch, first decreases and then increases to compensate for the diminution of the twitch. However, the inverse relationship between recruitment threshold and firing rate is maintained. We therefore conclude that in VL muscle the control strategy used by the CNS to regulate muscle output is invariant during isometric contractions sustained until exhaustion.

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