Twitch Interpolation in Human Muscles: Mechanisms and Implications for Measurement of Voluntary Activation

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Herbert, R. D. and S. C. Gandevia. Twitch interpolation in human muscles: mechanisms and implications for measurement of voluntary activation. J. Neurophysiol. 82: 2271–2283, 1999. An electrical stimulus delivered to a muscle nerve during a maximal voluntary contraction usually produces a twitchlike increment in force. The amplitude of this ‘interpolated twitch’ is widely used to measure voluntary “activation” of muscles. In the present study, a computer model of the human adductor pollicis motoneuron pool was used to investigate factors that affect the interpolated twitch. Antidromic occlusion of naturally occurring orthodromic potentials was modeled, but reflex effects of the stimulus were not. In simulations, antidromic collisions occurred with probabilities of between ~16% (in early recruited motoneurons) and nearly 100% (in late recruited motoneurons). The model closely predicted experimental data on the amplitude and time course of the rising phase of interpolated twitches over the full range of voluntary forces, except that the amplitude of interpolated twitches was slightly overestimated at intermediate contraction intensities. Small interpolated twitches (4.7% of the resting twitch) were evident in simulated maximal voluntary contractions, but were nearly completely occluded when mean peak firing rate was increased to ~60 Hz. Simulated interpolated twitches did not show the marked force drop that follows the peak of the twitch, and when antidromic collisions were excluded from the model interpolated twitch amplitude was slightly increased and time-to-peak force was prolonged. These findings suggest that both antidromic and reflex effects reduce the amplitude of the interpolated twitch and contribute to the force drop that follows the twitch. The amplitude of the interpolated twitch was related to “excitation” of the motoneuron pool in a nonlinear way, so that at near-maximal contraction intensities (>90% maximal voluntary force) increases in excitation produced only small changes in interpolated twitch amplitude. Thus twitch interpolation may not provide a sensitive measure of motoneuronal excitation at near-maximal forces. Increases in the amplitude of interpolated twitches such as have been observed in fatigue and various pathologies may reflect large reductions in excitation of the motoneuron pool.

INTRODUCTION

A central question in human muscle physiology concerns how well the brain can “drive” muscles during maximal voluntary contractions. To answer this question it is necessary to determine whether the motoneuron pool has been excited sufficiently by volition to evoke all the force the relevant muscles can produce. This can be done by comparing the increment in muscle force produced when an electrical stimulus is delivered to a muscle during a voluntary contraction with the force increment produced when the same stimulus is delivered to the resting muscle (e.g., Allen et al. 1998; Bellemare and Bigland-Ritchie 1984; Merton 1954). When the stimulus consists of only a single pulse, the method is called twitch interpolation, and the force increment is referred to as the interpolated twitch. The amplitude of the interpolated twitch declines with increasing contraction intensity, so it has been used to measure the level of excitation of motoneurons (also referred to as “voluntary activation” or “neural drive”) (see Gandevia et al. 1995 for review). The method has also been used to estimate, by extrapolation, the muscle force that could be produced if voluntary activation were complete (e.g., Bellemare and Bigland-Ritchie 1984; De Serres and Enoka 1998; Merton 1954; Phillips et al. 1992; Rutherford et al. 1986). Twitch interpolation has been used to investigate limitations to muscle force production (usually under isometric conditions) (e.g., Allen et al. 1995; Belanger and McComas 1981; Merton 1954; cf. Gandevia et al. 1998), mechanisms of fatigue (e.g., Bigland-Ritchie et al. 1983a,b; McKenzie et al. 1992), the nature of weakness associated with various pathologies (e.g., Allen et al. 1993, 1997; McComas et al. 1983; Rice et al. 1992; Rutherford et al. 1986; Thomas et al. 1998), and neural adaptations associated with training voluntary isometric muscle strength (Herbert et al. 1998; Jones and Rutherford 1987).

When, in a maximal voluntary contraction, a subject manages to completely occlude the interpolated twitch, interpretation is usually straightforward: the level of excitation of motoneurons must have been sufficient to extract all of the force that the muscle could have produced (“maximal muscle force”) (cf. Allen et al. 1998 for a discussion of factors that may sometimes obscure interpolated twitches even when activation is truly maximal). Usually, however, subjects cannot completely occlude the twitch. In this case, the amplitude of the interpolated twitch is often used to infer the level of motoneuronal excitation. If quantitative inferences are to be made about excitation of motoneurons, it is necessary to know how interpolated twitch amplitude and excitation are related. It is not currently possible to measure excitation of the motoneuron pool any more directly than with the twitch interpolation method, so the relationship between interpolated twitch amplitude and excitation cannot be determined experimentally. Thus it is not certain what level of motoneuron excitation can be inferred from any particular interpolated twitch amplitude, nor how much of a change in excitation can be inferred from a change in interpolated twitch amplitude.
Sometimes the interpolated twitch method is used to make inferences about maximal muscle force. Interpolated twitches are measured as subjects intentionally contract to a range of submaximal intensities, and the relationship between interpolated twitch amplitude and voluntary force is extrapolated to the force at which the interpolated twitch would have been completely occluded (Bellemare and Bigland-Ritchie 1984; De Serres and Enoka 1998; Merton 1954; Phillips et al. 1992; Rutherford et al. 1986). This force is thought to correspond to maximal muscle force. Again, it is difficult to test the validity of these estimates of maximal muscle force because there is no completely satisfactory method for determining maximal muscle force. One comparison is between the force produced by tetanic stimulation and maximal voluntary force (Bigland and Lippold 1954; Merton 1954). However, this may be unsatisfactory because it is usually not possible to be certain that all of the agonists and none of the antagonist muscles are being stimulated supramaximally, and synergistic muscles will not usually be stimulated optimally.

The mechanisms that determine the amplitude of the interpolated twitch are complex and incompletely understood (Merton 1951). An interpolated stimulus evokes action potentials that propagate orthodromically and antidromically in nonrefractory motor and sensory axons. Orthodromic potentials in motor axons produce a near-synchronous twitch from muscle units. Antidromic potentials in motor axons may also influence the amplitude of the twitch, even at short latencies, because some collide with voluntarily produced potentials and reduce the rate of motoneuron discharge immediately after the stimulus. Other antidromic potentials reach the motoneuron soma and produce hyperpolarization (Brock et al. 1952) and may propagate along recurrent branches terminating on Renshaw cells, evoking inhibitory postsynaptic potentials in motoneurons. Motoneuron discharge after the interpolated stimulus may also be influenced by short-latency reflex effects of stimulated sensory axons and longer-latency reflex effects, including those due to the mechanical effects of the twitch (such as the decrease in spindle afferent discharge that accompanies unloading of muscle spindles). Presumably all the mechanisms described above can influence the period of prolonged “inhibition” (i.e., the electromyographic “silent period”), which follows the interpolated twitch.

The aim of the present study was to investigate properties of the interpolated twitch. We sought to determine the relationship between interpolated twitch amplitude and both motoneuronal excitation and muscle force, because knowledge of these relationships might enable quantitative inferences to be made about motoneuronal excitation or maximal muscle force when the interpolated twitch is not occluded. We also sought to examine factors that influence the amplitude of the interpolated twitch. Of particular interest was whether antidromic potentials reduce the amplitude of the interpolated twitch compared with the hypothetical situation in which antidromic conduction does not occur. In addition we examined the effect of motor-unit discharge rates and contractile properties on interpolated twitch amplitude. These questions are not easily investigated experimentally, so a computer modeling approach was used. Some of the results have been presented in preliminary form (Herbert and Gandevia 1998).

**Methods**

**Terminology**

Throughout the text we refer to maximal voluntary contraction, by which is meant the greatest muscle force that can be produced voluntarily, maximal voluntary excitation, by which is meant the level of excitation of the motoneuron pool required to excite all motoneurons to their peak voluntary firing frequencies, and maximal muscle force, by which is meant the greatest force the muscle can produce (i.e., with tetanic stimulation at 100 Hz). Excitation is used to mean “effective synaptic current” (Heckman and Binder 1988), which was assumed to be distributed uniformly to the motoneuron pool.

**Experimental data**

Experimental data were obtained from three subjects (healthy males, 29–44 yr of age) to assist in construction of the model and assignment of parameter values. Subjects were seated with the forearm resting on a bench, and brackets held the forearm halfway between full pronation and supination (Fig. 1A). Force produced by the adductor pollicis muscle was measured with a transducer (XTran, 250 N) firmly coupled to the proximal phalanx of the thumb, as described previously (Herbert and Gandevia 1996). The force signal was sampled at 5 kHz.

Twitch and force-frequency data were obtained by delivering stimulus trains at supramaximal intensities (constant current, 160–280 mA) to the ulnar nerve through a pair of surface electrodes (diameter 2 cm; interelectrode spacing ~4 cm) placed longitudinally over the ulnar nerve anteriorly and just proximal to the wrist. Care was taken to avoid inadvertent stimulation of the median nerve. Before each stimulus train, subjects performed a single, brief, maximal voluntary contraction to potentiate the adductor pollicis. Five seconds later, a stimulus train of 1-s duration was delivered. One minute of rest was allowed between each train. Stimulus frequencies were delivered in the following order: 1, 5, 10, 20, 50, 100, 100, 50, 20, 10, 5, and 1 Hz. The force produced by 100-Hz trains averaged 60.3% of maximal voluntary force. In additional trials, an extra stimulus was interpolated on constant frequency trains of 10 or 20 Hz. The results of these experiments were used to build the model, and so are given in the following methods.

![Diagram of motoneurons](http://jn.physiology.org/)

**FIG. 1.** Methods. A: positioning of subject for experiments. F, force transducer. B: schematic diagram of 3 motoneurons supplying adductor pollicis. Vertical arrows indicate the site of stimulation. Normally, the stimulus produces action potentials in motor axons that propagate orthodromically and antidromically. Antidromically conducting potentials may collide with one voluntarily produced action potential propagating orthodromically from the soma (shown as spikes in motoneurons 1 and 2) or, if they fail to meet orthodromic potentials, will propagate back to the soma (motoneuron 3). The effect of antidromic potentials is to remove motor axon potentials for a period of \( t_{\text{ref}} = \frac{2d}{v} \), after the stimulus (see text for details). The number of potentials removed will depend on the firing rates of the axons. The model was implemented with (top panel) and without (bottom panel) allowance for antidromic collisions.
In addition, interpolated twitches were obtained during contractions at a range of intensities. These data were used to test model predictions. Before each test contraction, subjects performed a single, brief maximal voluntary contraction. Five seconds later the subject contracted to a target proportion of maximal voluntary force using feedback of force on an oscilloscope. Target forces were 10% increments from 0 to 100% maximal voluntary force (MVC), presented in random order. A single supramaximal stimulus was delivered to the ulnar nerve during the force plateau of the contraction. At least 1 min of rest was given between contractions.

Model structure and modeling strategy

We modified the model of a motoneuron pool described in detail by Fuglevand et al. (1993) (see also Fuglevand 1989; Fuglevand and Bigland-Ritchie 1993) so that it could simulate interpolated twitches of the adductor pollicis muscle. The model consists of a pool of 120 motoneurons with varying excitation thresholds. When the motoneuron pool is excited, motoneurons excited above threshold begin to fire at a specified initial firing frequency. As excitation is increased above threshold, the firing rate of each motoneuron increases linearly with excitation according to an excitation-firing rate relationship analogous to the steady-state current-frequency relationship observed when single motoneurons are injected with current, up to a predetermined maximal firing frequency. A normally distributed random component is added to interspike intervals to simulate physiological variability in the instantaneous firing frequency. Then, once the firing pattern of each motoneuron has been determined, its force output is determined as follows. The twitch responses of motor units to a single stimulus are distributed so that the speeds and forces of twitches of early-recruited motor units are less than those of later recruited units. The force response to a train of stimuli is determined by summing twitch responses after scaling them according to the duration of the preceding interspike interval. The force of all motor units is then summed to give muscle force.

It is desirable, particularly in complex models with many parameters, that the structure of a model and the values of its parameters are determined without reference to the final outputs of the model. Thus values were assigned to parameters in a way that maximized goodness-of-fit to simple muscle behaviors observed experimentally (such as the response of the resting muscle to a single stimulus). The values of these parameters were then fixed. Values were assigned to more parameters as progressively more complex muscle behaviors were examined (see Fig. 2 and below for details). Data on the most complex behaviors (motor-unit firing patterns in voluntary contractions) were obtained from the literature. Once a good fit had been obtained to a complex set of muscle behaviors, values for all parameters were fixed, and the model was used to predict the effect of interpolated stimuli delivered during voluntary contractions of different strengths.

Model construction I: the resting twitch

The shape of the single twitch obtained from the resting adductor pollicis muscle could not be accurately modeled as the sum of motor

Based on our experimental data:

(i) model resting twitch

![Graph showing force over time for a model resting twitch](image)

(ii) model force-frequency relation

![Graph showing mean force over normalized frequency](image)

(iii) model force fluctuations with constant frequency stimuli, with & without interpolated stimulus

![Graph showing force over time for model force fluctuations](image)

Then, based on published data:

(iv) model mean firing frequency - voluntary force relationship

![Graph showing frequency over voluntary force](image)

FIG. 2. Flow chart to show how values were assigned to parameters in the model. Values were 1st assigned to those parameters that determined the simplest muscle behavior (the resting twitch), then to parameters that determined more complex behaviors. RP is the range of motor-unit twitch tensions (in multiples of the smallest twitch); $T_1$ is the contraction time of the slowest motor unit; $RT$ determines range of motor-unit contraction times (as the shortest contraction time = $T_1/(RT)$; $r$ determines the twitch:tetanus ratio; $c$ determines the curvature of the force-frequency relationship; $cutoff_{min}$ and $cutoff_{max}$ are filter coefficients that determine the amplitude of force fluctuations produced by trains of stimuli; $RR$ is the range of recruitment thresholds (in multiples of the threshold of the 1-st-recruited unit); $g_e$ is the slope of the relationship between current and firing frequency (in Hz excitation unit$^{-1}$, where 1 excitation unit is the excitation required to activate the 1-st-recruited unit); $MFR$ is the minimum firing frequency; $V$ is the coefficient of variation of interspike intervals, mean PFR and SD PFR are the mean and SD (respectively) of the normal distribution of peak firing rates of all motor units; and PFR distribution refers to how peak firing rates are distributed during a maximal voluntary contraction. Parameter values used in simulations are given in parentheses.
unit twitches if motor-unit twitches were modeled as the impulse response of a critically damped second-order system (as used by Fuglevand et al. 1993). If the duration of the rising phase was matched to experimental data, the falling phase was much too slow (Fig. 3A). Consequently only the rising phase of the motor-unit twitch was modeled as described by Fuglevand et al. (1993), that is

\[ F(t) = (P_i \times T_i) \times e^{-t/T_i}, \quad t \leq T_i \]

where \( F \) is motor-unit force, \( P_i \) is twitch force, \( t \) is time from the onset of the twitch, \( T_i \) is the motor unit’s twitch contraction time, and the subscript \( i \) refers to the \( i \)th motor unit. In the falling phase, twitch force decayed by an additional factor of \( e^{-t/T_f} \), so that

\[ F(t) = P_i \times (t/T_i) \times e^{-t/T_f}, \quad t > T_i \]

The whole muscle twitch is the sum of all motor-unit twitches, so it depends on the distributions of motor-unit twitch forces and twitch contraction times. Therefore we adjusted values of the relevant parameters (\( T_i \), the twitch contraction time of the slowest motor unit, \( RT \), the range of twitch contraction times, and \( Rp \), the range of twitch tensions) (Fuglevand 1989; Fuglevand et al. 1993) by trial and error within physiologically realistic ranges to match closely the resting muscle twitch observed experimentally. Excellent fits were obtained with \( T_i = 110 \) ms, \( RT = 1.83 \), and \( Rp = 50 \) (RMS error <4%; Fig. 3A). With these parameter values, twitch tensions for motor units 1, 10, 60, 110, and 120 were 0.07, 0.1, 0.5, 2.4, and 3.4% of the resting twitch, respectively. Corresponding twitch contraction times were 110, 105, 81, 63, and 60 ms, and corresponding excitation thresholds were 1.6, 2.1, 6.0, 24.9, and 32% of maximal voluntary excitation.

**Model construction II: trains of stimuli**

There have been few attempts to model the isometric forces produced by time-varying rates of stimulation in motor units or whole muscles [see Bobet and Stein (1999) and Ding et al. (1998) for references and descriptions of 2 successful models]. The approach used here is a modification of that used by Fuglevand et al. (1993).

When trains of stimuli are delivered to a motoneuron, motor-unit twitches do not sum linearly (e.g., Burke et al. 1976; Hartree and Hill 1921). The additional force produced by a single pulse in a stimulus train is a function of stimulation rate and history and may be more or less than the force produced in a resting twitch. The steady-state gain of a constant-frequency train of stimuli can be obtained from the force-frequency relationship, because the gain at any frequency is simply the ratio of force and frequency. For the present study, steady-state gains obtained from the force-frequency relationship were used to scale the amplitude of each motor-unit twitch according to the duration of the preceding interspike interval. The model assumed that the relationship between normalized force (per cent of maximum) and normalized frequency (frequency \( \times \) contraction time) was the same for all motor units (Fuglevand et al. 1993; Kernell et al. 1983; cf. Heckman and Binder 1991), and that forces from different motor unit summed linearly, so motor-unit gains were obtained from the experimentally obtained relationship between whole muscle force and normalized frequency. The experimentally obtained relationship was closely fitted by

\[ F_{\text{muscle}} = 100 \times [1 - r \times e^{3 \times 1/f}] \]

where \( F_{\text{muscle}} \) is muscle force as a percentage of force evoked with a 100-Hz stimulus, \( r \) is a constant that determines the ratio of twitch and tetanus forces, and \( c \) is a constant that determines the rate of increase in force with increasing normalized frequency, \( f \). At normalized frequencies of \( <0.4 \) (frequencies of \( 3–7 \) Hz), the gain was assigned a value of 1.0 (Fuglevand et al. 1993). Gains at normalized frequencies of \( \geq0.4 \) were subsequently normalized by dividing by the gain at a normalized frequency of 0.4, as described by Fuglevand et al. (1993). Values of \( r = 0.09 \) and \( c = 0.85 \) provided a good fit to data from a typical subject (RMS error = 4.1%; Fig. 3B). These values have been used in all simulations reported here.

Simulations of force responses to constant-frequency trains of stimuli at a range of frequencies (1, 5, 10, 20, 50, and 100 Hz) closely reproduced experimental measures of mean steady-state muscle force. Consequently the amplitude of simulated force fluctuations tended to be too large when the muscle was stimulated at all but the lowest frequencies. Consequently motor-unit twitches were filtered with a causal, critically damped, second-order low-pass filter. It was necessary to apply lower filter cutoffs at higher frequencies. (On the basis of experiments with brief interpulse intervals at low forces, we established that filter cutoffs should vary with stimulation frequency, not force.) To fit the force fluctuations well, filter cutoffs needed to decline progressively more slowly with increasing frequency, and thus they were modeled as

\[ \text{cutoff}(f) = \text{cutoff}_{\text{min}} + (\text{cutoff}_{\text{max}} - \text{cutoff}_{\text{min}}) \times e^{3 \times 1/f}, \quad |f| \geq 0.4 \]

\[ \text{cutoff}(f) = \text{cutoff}_{\text{max}} \quad |f| < 0.4 \]

Values for \( \text{cutoff}_{\text{min}} \) and \( \text{cutoff}_{\text{max}} \) were found by trial and error. Values of 10 and 30, respectively, produced good fits to experimental data from whole adductor pollicis for stimuli at constant frequency.

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**Fig. 3.** Comparison of simulated and experimental data. In all panels, heavy lines are simulations, and fine lines are experimental data from a typical subject (data from the same subject in all subsequent figures). A: resting muscle twitch. Traces have been scaled so that simulated and experimental data have same peak force. The simulated twitch response closely replicates experimental data (RMS error 3.7%). Also shown is a twitch simulated with Fuglevand et al.’s original model (---; model parameters were chosen to optimize the fit to rising phase of twitch; RMS error 30.4%) B: response to constant frequency trains of 1, 5, 10, 20, 50, and 100 Hz. Frequencies are shown at right margin. Traces have been scaled so that simulated and experimental data from 100-Hz stimulus trains have same force 500 ms after 1st stimulus. C: response to constant-frequency trains of 10 and 20 Hz with an additional stimulus interpolated at 542 ms (---). Traces have been scaled so that simulated and experimental data have comparable forces at the time of the interpolated stimulus.
Model construction III: simulated voluntary contractions

To simulate voluntary muscle force we used the approach described by Fuglevand (1989) and Fuglevand et al. (1993). Thus it was assumed that all motoneurons received a common level of excitation during a voluntary contraction. The threshold level of excitation required to cause the motoneuron to discharge was distributed so that many small units had low thresholds and relatively few units had high thresholds. The range of recruitment thresholds (in multiples of the threshold of the first-recruited unit) was \( RR \), and the minimum rate of discharge, attained when units were excited to their threshold, was \( MFR \). Above threshold, all motoneurons increased their firing frequencies linearly with increasing excitation, and the ratio of change in firing rate to excitation \( (g_e) \) was the same for all motoneurons. A normally distributed random component (with coefficient of variation \( V \)) was added to interspike intervals. Motoneurons increased their rate of firing to a predetermined maximum. In the model by Fuglevand et al. (1993), maximal firing frequencies were set as linear functions of excitation thresholds. As excitation thresholds are highly skewed, this produced a positively skewed distribution of peak firing rates (PFRs), but the best available experimental data suggest that PFRs of the adductor pollicis muscle are close to normally distributed (Bellemare et al. 1983); Fig. 4A. The mean and standard deviation of the distribution of PFRs to 35 and 7, respectively. This was done to simulate the narrower range of maximal firing frequencies observed in some individual subjects (Bellemare et al. 1983).

The best combination of values for these parameters was determined by exciting the motoneuron pool to different levels and examining their effects on the rate of increase in motoneuron firing frequency with force, and on the force threshold of the last recruited motoneuron. Experimental data suggest that some or all motoneurons increase their firing frequencies progressively more slowly with increasing muscle force, and that an acceleration of firing rates with increasing force is rarely or never seen in early recruited motoneurons (e.g., Kanosue et al. 1979; Monster and Chan 1977). In the adductor pollicis muscle, most units are recruited by 50% maximal voluntary force (Kukulka and Clamann 1981). When \( RR \) was set at 10, the rate of increase in motoneuron firing frequencies progressively increased, rather than declined, with force. On the other hand, if \( RR \) was set at 25 or 30, the force threshold of the last-recruited unit was too high (always \( >75\% \) maximal voluntary force), particularly with the regressive and random distributions. Thus \( RR \) was set to 20. With an \( RR \) of 20, the force threshold of the last recruited unit was 67, 71, 75, and 90\% maximal voluntary force for the progressive, progressive/random, random, and regressive/random distributions, respectively. Even if the minimum PFR was increased to 18 Hz, the regressive recruitment strategy used was and the minimum PFR was increased to 18 Hz by setting the mean and standard deviation of the distribution of PFRs to 35 and 7, respectively. This was done to simulate the narrower range of maximal firing frequencies observed in some individual subjects (Bellemare et al. 1983).

FIG. 4. Motor-unit firing patterns in simulated voluntary contractions. A: relationship between force and firing frequency of motor units 1 (smallest unit), 20, 40, 60, 80, 100, and 120 (largest unit). B: peak firing rate distributions. 1, simulated peak firing rates (mean rate of discharge in 1st 500 ms for each motor unit). 2, peak firing rates reported by Bellemare et al. (1983) for the adductor pollicis during maximal voluntary contractions (mean rate of discharge of brief trains of discharges, pooled data from 4 subjects).
as shown by Bigland-Ritchie et al. (1992) for the tibialis anterior muscle.

Model predictions: interpolated twitches

To simulate interpolated twitches obtained from contractions of varying intensities, the motoneuron pool was sequentially excited in increments of 10% from 0 to 100% of the maximal excitation level. Each level of excitation was sustained for 750 ms, and muscle force was determined every millisecond. To simulate a supramaximal stimulus, the muscle was excited with an interpolated stimulus at 500 ms, when muscle force had reached a plateau. The stimulus caused all nonrefractory motoneurons to fire synchronously. Motoneurons were considered to be refractory and therefore were not excited by the stimulus if they had discharged in the preceding 5 ms (Borg 1983). For simplicity, stimulation-contraction delays were ignored. After the stimulus, motoneurons fired as they would have if the stimulus had not been delivered, except that in some units action potentials were extinguished by collision with antidromically conducting potentials generated by the stimulus (Fig. 1B). This was modeled by preventing those units that were not refractory at the time of the stimulus from firing for a period equal to $t_{refr}^c + 2d/cv_i$, after the stimulus, where $t_{refr}^c$ is the refractory period of motor axons, $d$ is the distance from the stimulation site to the spinal cord, and $cv_i$ is the conduction velocity of the motor axon supplying unit $i$. Axonal conduction velocities were linearly related to the rank order of their twitch tensions (cf. Jamir and Petit 1985). The range of motor axon conduction velocities was 35–65 ms$^{-1}$, and, except where indicated, $d$ was set to 80 cm (the approximate distance of the site of stimulation of adductor pollicis from the spinal cord). Thus the period $t_{refr}^c + 2d/cv_i$ varied from 30 to 51 ms.

The amplitude of the interpolated twitch ($A_{int}$) was found by subtraction of the background force immediately preceding the stimulus from the force maxima occurring in a time window following the stimulus. This window was 20 ms longer than the contraction time of the slowest motor unit. Voluntary activation was calculated as 100 × $(1 - A_m/A_{int})$, where $A_m$ is the amplitude of a control twitch evoked from a resting muscle (e.g., Bigland-Ritchie et al. 1983b; McKenzie et al. 1992). The same procedures were used to calculate voluntary activation scores from experimental data.

In some simulations we examined the effects of interpolating two stimuli with a 20-ms interstimulus interval. Voluntary activation was measured in the same way as above except that a longer time window was used to detect the peak of the interpolated twitch, and the interpolated twitch was normalized to the amplitude of the resting muscle’s force response to paired stimuli. Antidromic collisions could occur following either stimulus.

Probability of refractoriness and of antidromic collision

To aid analysis, analytic expressions were developed to determine both the probability that an axon would be refractory at the time of stimulus and the probability that an antidromic collision would occur.

The probability of an axon being refractory at the time of the stimulus, $P_{refr}$, is the probability of an action potential having traversed the site of stimulation in a period $t_{refr}$ preceding the stimulus (Fig. 7A). In motor units excited above threshold, the probability density of an action potential in the period following the stimulus is zero between the time of stimulus and $t = t_{refr}$, then constant until $t = 1/f$, and then tapers to zero (Fig. 7B). Thus $P_{refr} = 2d/cv_i ≤ 1/f$

Note that here, $t_{refr}$ really refers to a motoneuron property rather than an axonal one; the difference does not materially affect model outputs.

If the motor unit is firing very rapidly, or if the distance to the spinal cord is great, or if the axon conducts slowly, $P_{refr}$ is (predictably) proportional to both $t_{refr}$ and $f$.

A similar approach can be used to determine the probability of antidromic collision. The probability of antidromic collision in an axon that has been excited above its threshold and is not refractory at the time of stimulus ($P_{ac}$) is the probability that an action potential would have traversed the site of stimulation (had the axon not been stimulated) within a period of $t_{refr} + 2d/cv_i$ following the stimulus. In these nonrefractory axons, the probability density of an action potential in the period following the stimulus is zero between the time of stimulus and $t = t_{refr}$, then constant until $t = 1/f$, and then tapers to zero (Fig. 7B). Thus $P_{ac} = (2d/cv_i) × f/(V × \sqrt{2\pi}) + 0.5 \left| t_{refr}^c ≤ 1/f \right.$

Note that here, $t_{refr}$ refers primarily to a motoneuron property rather than an axonal one; the difference does not materially affect model outputs.

If the motor unit is firing very rapidly, or if the distance to the spinal cord is great, or if the axon conducts slowly, $t_{refr} + 2d/cv_i$ can become $>1/f$. Then

\[ P_{ac} = \frac{\int_{1/f}^{t_{refr}^c} f/(V × \sqrt{2\pi}) + 0.5 \left| t_{refr}^c + 2d/cv_i > 1/f \right.}{(1/f - t_{refr}^c) × f/(V × \sqrt{2\pi}) + 0.5 \left| t_{refr}^c + 2d/cv_i > 1/f \right.} \]

The integral in the numerator is associated with the probability of an action potential between $1/f$ and $t_{refr} + 2d/cv_i$. The integral cannot be easily evaluated (Roscoe 1975) but can be obtained from tables of the area under the normalized normal curve, or evaluated numerically by many computer packages. In that case a more convenient notation is

\[ P_{ac} = \frac{(1/f - t_{refr}^c) × f/(V × \sqrt{2\pi}) + 0.5 \left| t_{refr}^c + 2d/cv_i > 1/f \right.}{(1/f - t_{refr}^c) × f/(V × \sqrt{2\pi}) + 0.5 \left| t_{refr}^c + 2d/cv_i > 1/f \right.} \]

Here $z$ is the standardized value.

Testing the effects of antidromic collisions, motor-unit contractile properties, and PFRs

In most simulations, both orthodromic and antidromic effects of the interpolated stimulus were studied. However, to determine the effects of antidromic collisions on interpolated twitch amplitude, the model was sometimes run without antidromic collisions (Fig. 1B). When the simulation was implemented this way, the sole effect of the stimulus was to interpolate an extra potential in motor axons of nonrefractory units.

To examine the effects of peripheral changes in contractile properties and variations in central drive on interpolated twitch amplitude,
we changed the distribution of motor-unit contraction times, PFRs of motoneurons, or both. Motor-unit contraction times were reduced (the contractile properties of the muscle were made “faster”) by reducing the contraction time of the slowest motor unit (T1) from 110 to 90 ms. The contraction times of all other motor units were referenced to this motor unit (Fuglevand et al. 1993), so the effect was to scale down the contraction times of all motor units. This reduced the contraction time of the whole muscle resting twitch from 69 to 55 ms (or by ~2 SDs) (Bellemare et al. 1983). To examine the effects of an increase in firing rate, the mean PFR was increased from 29.9 Hz in increments of 8.2 Hz. This number was chosen because the first increment (to 38.1 Hz) maintains the normalized firing frequency of the whole muscle (mean PRF × whole muscle twitch contraction time) when contraction time is reduced to 55 ms.

One set of simulations investigated the effect of occasional brief interpulse intervals (or “doublets”) that are sometimes observed experimentally (Bawa and Calancie 1983), by causing a random selection of 10% of all discharges to occur with an interpulse interval of 5 ms. The actual frequency of doublets is not known with any certainty, and there is no data on the frequency of doublets in human adductor pollicis during maximal voluntary contractions. A frequency of 10% probably represents the highest plausible frequency.

RESULTS

In METHODS we showed that the model provided a good fit to a range of experimental observations (Figs. 2–4). Here we present the predictions of the model. The results of a simulation in which interpolated stimuli were delivered to the muscle as it was sequentially excited to increasing proportions of maximal voluntary excitation are shown in Figs. 5 and 6A. The amplitude of the interpolated twitch declined with increasing excitation (and contraction intensity) as observed experimentally. The stimulus evoked twitches in all motor units at rest, but interpolated twitches were only discernible in the largest motor units at high contraction intensities (Fig. 5B). Randomness in interspike intervals did not produce a discernible degree of trial-to-trial variability in the force of simulated voluntary contractions or interpolated twitches, so the results from only one simulation are shown in this and subsequent figures.

When interpolated twitches were measured in experimental subjects during contractions to submaximal target intensities, both interpolated twitch amplitudes and times-to-peak were nearly linearly related to voluntary force (R² = 0.93 and 0.97, respectively; Fig. 6, B and C). Simulated amplitudes and times-to-peak were also linearly related to voluntary force (R² > 0.99) and closely approximated experimental data, although the amplitude of simulated interpolated twitches tended to overestimate experimental measures (mean overestimation of 12% of resting twitch, range 2–34%; Fig. 6, B and C). The relationship between simulated voluntary force and interpolated twitch amplitude was essentially unchanged by adding doublets to 10% of all discharges, or by using paired stimuli instead of a single interpolated stimulus (Fig. 6C). Force fell less, after the interpolated twitch, in simulated records compared with experimental records (Fig. 6A).

With simulated maximal voluntary excitation of the adductor pollicis motoneuron pool (the level of excitation required to make all motoneurons fire at their assigned peak rates, see METHODS), the amplitude of interpolated twitches was 4.7% of the resting twitch (Fig. 6A), giving a simulated voluntary activation of 95.3%. Very similar values were obtained when doublets were added to 10% of all discharges (activation, 95.2%) and when paired stimuli were used (activation, 94.2%). These values are all close to the median voluntary activation of 90.3% for the adductor pollicis, and well within the range of voluntary activation of individual subjects (81.2–100%) (Herbert and Gandevia 1996). The time-to-peak of the simulated interpolated twitch in a maximal voluntary contraction was 26 ms, slightly longer than the 19 ms (measured from time of force onset) observed in an experimental subject whose resting twitch had a similar contraction time to that used in the simulation (Fig. 6, A and B).

The force produced by simulated stimulus trains at 100 Hz (“maximal muscle force”) was 9.6% greater than the force produced in simulated maximal voluntary contractions (Fig. 6D). To investigate how well maximal muscle force could be estimated from the relationship between experimental interpolated twitch amplitude and voluntary force, the linear regression of these variables was extrapolated to the abcissa (Fig. 6D). This predicted a maximal muscle force of 97.9% of maximal voluntary force, an underestimation of maximal muscle force of 10.7%. The confidence intervals associated with this estimate (95% CI 88.2 to 111.4%) included simulated maximal voluntary force, but the limits of the confidence interval were wide. Nonlinear regression [using 3rd-order polynomial regression or a power transformation of interpolated twitch amplitude, as described by De Serres and Enoka (1998)] provided less accurate estimates of maximal muscle force (131.6 and 181.3% respectively), with even wider confidence intervals.

The probability of the interpolated stimulus arriving when an axon was refractory increased with firing frequency. For any single motoneuron that had been voluntarily excited above threshold, this probability increased from 3.2% at 8 Hz to 20.8% at 52 Hz (Fig. 7C), assuming a refractory period of 5 ms. If, instead, the refractory period was assumed to be 2.5 ms, the probability of refractoriness ranged from 1.6 to 10.4% over...
the same range of frequencies. The latter figure (2.5 ms) is likely to be closer to the true value (see Fig. 2 in Borg 1983). However, the degree of supramaximality probably varies with motor-unit size, so it is difficult to be certain which motor units will discharge in their relatively refractory periods. In practice, varying the refractory period from 2.5 to 5 ms had little effect on interpolated twitch amplitude.

In motoneurons excited above threshold but not refractory at the time of the stimulus, the probability of antidromic collision ranged from 16.3% in the first recruited motoneuron at its lowest firing frequency up to 99.8% in the last recruited motoneuron at its maximum firing frequency (Fig. 7C). The probability of antidromic collision was relatively insensitive to the “refractory” period (see also METHODS).

To assess the effect of antidromically conducting action potentials, interpolated twitches were compared when the model was run with and without extinction of potentials in nonrefractory motor axons after the stimulus (Fig. 1B). Without antidromic potentials, the amplitude and duration of interpolated twitches was slightly increased at all voluntary forces (Fig. 8) and, with high-intensity contractions, there was a conspicuous lack of the fall in force after the twitch (Fig. 8A).

FIG. 6. Simulated and experimental interpolated twitches. A: twitches obtained at rest and during contractions to ~34, ~82, and 100% maximal voluntary force (submaximal contraction intensities are given as approximations because they differed slightly between simulated and experimental data; actual values were 34.4 and 85.0% maximal voluntary force for simulations and 33.6 and 79.4% maximal voluntary force for experimental data). Twitches have been aligned with the time of onset of force, shown by the arrow, and the baseline force preceding the stimulus has been subtracted from all traces. B: time-to-peak of experimental and simulated interpolated twitches at contraction intensities of 0–100% maximal voluntary force. Time-to-peak has been measured from the onset of the increase in force. C: amplitude of interpolated twitches (expressed as a percentage of resting twitch amplitude) at contraction intensities of 0–100% maximal voluntary force. Experimental data are shown, as well as simulations with and without doublets, and also with paired stimuli. D: amplitude of experimental and simulated interpolated twitches (same data as in C, but high forces only are shown and axis scales have changed; simulation is with single stimulus and without doublets). Regressions through experimental data (thin line) and simulation data (thick line) are shown, along with their intercepts with the abcissa [predicted (exp) and predicted (sim)]. Also shown is maximal voluntary force [MVC (exp & sim), both 100% by definition] and force produced in simulated 100-Hz contractions [100 Hz (sim)].

FIG. 7. Probability of stimulating refractory axons and of antidromic collisions occurring in nonrefractory axons. A and B: probability density function of an action potential passing the site of stimulation at a given time before the interpolated stimulus (in A) or following the stimulus (in B). The dotted line is at the mean interspike interval before the stimulus (in A) and the mean interspike interval after the stimulus (in B). C: probability that a motor axon will be refractory at the time of the interpolated stimulus (P_{refr}, this probability is the same for all axons), and probability of antidromic collision in nonrefractory axons (P_{ac}; shown for motor units 1, 60, and 120) as a function of firing frequency. The following values were used: V = 0.2, \( d_p = 0.8 \text{ m} \), \( c_v = 35 \text{ to } 65 \text{ ms}^{-1} \). Solid lines, \( t_{refr} = 5 \text{ ms} \), dotted lines, \( t_{refr} = 2.5 \text{ ms} \).
During simulated maximal voluntary contractions, the amplitude of the interpolated twitch was increased to 8.7% of resting twitch (i.e., 91.3% activation) when there were no antidromic collisions, compared with 4.7% of the resting twitch (95.3% activation) when antidromic collisions occurred. This indicates that antidromic potentials slightly reduce the amplitude and duration of interpolated twitches and are responsible for at least some of the drop in force that occurs after the peak of the twitch. Because the effect of antidromic collisions on interpolated twitch amplitude was rather small, movement of the site of stimulation proximally from 0.8 m (i.e., wrist) to 0.4 m (i.e., elbow) from the spinal cord (a procedure that would reduce the number of antidromic collisions) only increased the amplitude of the interpolated twitch by 0.9% (to 5.6% of the resting twitch).

When simulations were performed in which motoneurons fired at the peak rates described in the literature for maximal voluntary efforts (Bellemare et al. 1983), small interpolated twitches were still observed. This suggests that subjects might attain higher PFRs than the “pooled” rates measured experimentally when, in experiments, the twitch is completely occluded. In the model, an increase of 8.2 Hz in mean PFR (to 38.1 Hz) increased muscle force to 4.4% above that observed during a simulated maximal voluntary contraction and reduced interpolated twitch amplitude to 2.9% (i.e., increased voluntary activation to 97.1%). Further increases in mean PFR by increments of 8.2 Hz increased voluntary force to 107.0% (at 46.3 Hz), 108.0% (at 54.5 Hz), and 108.7% (at 52.7 Hz) of maximal voluntary force, and increased voluntary activation to 98.4, 98.6, and 99.0%, respectively. Conversely, a reduction in whole muscle contraction time of ~2 SDs (or from 69 to 55 ms) reduced muscle force to 92.3% maximal voluntary force and increased interpolated twitch amplitude from 4.7 to 8.5% of the resting twitch (i.e., voluntary activation decreased from 95.3 to 91.5%). In one simulation, the contraction time of the muscle was reduced by ~2 SDs, but PFRs were increased to a mean of 38.1 Hz, so that the normalized frequency of the whole muscle remained constant. This resulted in an interpolated twitch amplitude of 4.8%, very similar to the 4.7% obtained with the default parameter values.
The relationship between the level of “excitation” of the motoneuron pool and muscle force was sigmoidal (Fig. 9C). Force initially increased rapidly with excitation, but above ~50% of the level of excitation required to elicit motoneurons to frequencies observed during maximal efforts, very large increases in excitation were required to produce small increases in force. This finding was robust, because it occurred with all plausible combinations of model parameters. Implications of the finding are considered in the DISCUSSION. The relationship between excitation and interpolated twitch amplitude was complementary (Fig. 9C). Interpolated twitch amplitude declined rapidly at low levels of excitation, but above ~50% of maximal voluntary excitation, decreases in interpolated twitch amplitude were very small. This was because all of the motoneuron pool was recruited, and most motor units had attained near-tetanic firing frequencies, at relatively low levels of excitation and force (Fig. 9, A and B). Thus at higher levels of excitation, the stimulus was only able to evoke additional force from the small number of motor units contracting at subtetanic frequencies.

DISCUSSION

In the present study a computer model based on experimental data from human adductor pollicis was used to simulate transients in muscle force produced by an interpolated stimulus. The model involved simplifying assumptions, and its implementation required that values were assigned to some parameters for which exact values were not available. Nevertheless, it incorporated realistic analogues of mechanisms known to influence muscle force, such as the orderly recruitment of motoneurons. Because there was unlikely to be a unique set of parameters that optimally fitted experimental data, we optimized the process of assigning values to parameters by first assigning values to those parameters that influenced the simplest muscle responses (e.g., resting twitch, response to stimulus trains of constant frequency), and then sequentially assigning values to parameters that determined more complex behaviors (e.g., irregular trains of stimuli, voluntary contractions). This approach minimized redundancy. The resulting model fitted complex muscle behaviors well and provided good predictions of the force responses to interpolated twitches over the full range of contraction intensities.

A primary aim of the present study was to investigate factors that influence the amplitude of the interpolated twitch. The time course and amplitude of the rising phase of simulated interpolated twitches obtained during maximal contractions closely resembled experimental data. However, the size of simulated interpolated twitches in submaximal contractions was slightly greater than observed experimentally. This may be because the model did not incorporate all consequences of the stimulus at spinal cord level, such as hyperpolarization of motoneuron somata, possible recurrent inhibition, and the inhibitory and disfacilitatory effects of stimulation of muscle afferents. Assuming the site of the stimulus was 0.8 m from the spinal cord and a maximal conduction velocity of 65 ms⁻¹, and ignoring synaptic delays, these effects could not influence adductor pollicis muscle forces until ~30 ms after the twitch (cf. Leis et al. 1991), and so would have no effect on the rising phase of interpolated twitches obtained during maximal contractions (which had times to peak force of ~19 ms). When the effects of antidromic collisions in motoneurons were eliminated (Fig. 1B), the amplitude of the interpolated twitch was slightly greater at all contraction intensities, especially between 40 and 80% maximal voluntary force. These data suggest that both antidromic collisions and the spinal (including reflex) effects of the stimulus can reduce the amplitude of the interpolated twitch at submaximal intensities, and that antidromic collisions slightly reduce the amplitude of interpolated twitches in maximal contractions.

A conspicuous feature of the force response to an interpolated twitch during a voluntary contraction is the large drop in force after the twitch. The precise mechanisms producing the drop in force are not known, but a number of studies have investigated the mechanisms that produce the accompanying electromyographic silence. Merton (1951) observed that the depth and duration of the silent period was closely associated with the size and duration of the interpolated twitch, and he argued that the later part of the electrical silence must therefore be due to afferent consequences of the twitch. More recent studies have shown that a silent period can be induced by the stimulation of afferent axons (Leis et al. 1991; McClelland 1973). In our simulations, which ignored the spinal effects of the stimulus, there was little or no decline in force after the twitch. This suggests that the primary mechanism producing the drop in force is of spinal origin. Moreover, when the model was run without antidromic collisions, the interpolated twitch became less peaked because force declined only slowly after the force maxima (Fig. 8). This suggests that antidromic collisions, as well as spinal mechanisms, contribute to the force drop after the stimulus. These findings are not surprising, because the interpolated stimulus advances the arrival of one potential in nonrefractory axons but may delay the arrival of the subsequent one (if an antidromic collision occurs; see Figs. 1B and 7). In real contractions, further delays may be produced when antidromic potentials that do not undergo collision “reset” membrane potential at the motoneuron soma.

Currently it is not possible to measure neural drive to the motoneuron pool more directly than with the interpolated twitch, as conventional measures of voluntarily generated electromyogram (EMG) cannot indicate if activation is truly “maximal.” Simulations by Heckman and Binder (1991) showed that the relationship between excitation of a cat motoneuron pool and muscle force is sigmoidal and, as muscle force is known to be near-linearly related to interpolated twitch amplitude, this implies that interpolated twitch amplitude is nonlinearly related to excitation. In the present study we showed that the relationship between excitation of a human motoneuron pool and interpolated twitch amplitude is also sigmoidal (Fig. 9C). This occurs because most motor units are recruited at low forces and attain near-tetanic frequencies at low levels of excitation, and because the firing rates of early recruited motor units plateau, rather than continue to increase markedly with force (Fig. 4A; e.g., Kanosue et al. 1979; Monster and Chan 1977; cf. Erim et al. 1996). The mechanisms that cause motor-unit firing frequencies to plateau are not known but may reflect nonhomogenous excitation of the motoneuron pool at high forces (Binder et al. 1996, 1998; Heckman and Binder 1993), the action of neuromodulators (Binder et al. 1996; Hounsgaard et al. 1988; see also Brownstone et al. 1992), or shunting of the synaptic current by active synaptic conductances located on proximal parts of dendrites (Binder et al. 1996; see also Jones...
The sigmoidal shape of the relationship between motoneuronal excitation and interpolated twitch amplitude means that large increases in motoneuronal excitation produce only small reductions in interpolated twitch amplitude during high-intensity contractions. Twitch interpolation is therefore not a sensitive measure of excitation at high forces. [A similar conclusion was drawn by Dowling et al. (1994), although their conclusion was based on observations of the relationship between interpolated twitch and voluntary force; cf. Allen et al. (1998).] These data imply that it may not be possible, in experiments, to distinguish between contractions of 60 and 100% of maximal voluntary excitation. Surface EMG is linearly or near-linearly related to muscle force (Woods and Bigland-Ritchie 1983), so it too probably provides insensitive measures of excitation at high forces. The lack of sensitivity of EMG is compounded by the high-frequency component in the EMG signal, which makes it more difficult to quantify than force (Allen et al. 1998).

The relationship between effective synaptic current and muscle force simulated by Heckman and Binder (1991) has been redrawn in Fig. 9D for comparison with our simulated relationship between excitation and force in Fig. 9C. The difficulty in comparing these data are that Heckman and Binder considered the effect of increasing effective synaptic current up to levels where muscle force was maximal, whereas we considered the effect of increasing “excitation” up to levels required to attain the firing frequencies observed in maximal voluntary contractions. In our simulations, force was essentially maximal at ~60% of maximal voluntary excitation. It is probable therefore that the maximal level of effective current investigated by Heckman and Binder is equal to ~60% of the maximal voluntary excitation in our simulations. When the Heckman and Binder data are drawn with the crest of the sigmoid at the same level of excitation (95 nA = 60% maximal voluntary excitation) the two curves essentially superimpose.

The plateau of the relationship between excitation and force (or interpolated twitch amplitude) at levels above ~60% maximal voluntary excitation may seem paradoxical. This may be because it is tempting to draw an analogy between excitation and “motor commands.” However, the concept of excitation used here is a notional one that may not, and is unlikely to, be directly related to a parameter that can be measured in volunteer subjects. Hence it would be speculative to attempt to relate excitation to the concepts of “effort” and corollary “motor commands” that are used in the literature on proprioception. There is no a priori reason to expect psychophysical “commands” to be linearly related to excitation of motoneurons. Increasing excitation from 60 to 100% of maximal voluntary excitation affects only a very small number of motoneurons: those recruited at high thresholds. This and other processes (such as nonhomogeneous distribution of commands) may cause the total excitatory drive summed across all motor units to be nonlinearly related to commands to generate force.

A more linear relationship between excitation and force would arise if less excitation was required to excite late-recruited units to maximal firing frequencies. This could occur if excitation thresholds were less skewed than in our model, or if the rate of increase in firing rate with excitation was greater for late-recruited units. The consequence would be that the sigmoid would have less curvature, but with any reasonable assumptions the relationship remains sigmoidal (see Figs. 3, 4, and 6 in Heckman and Binder 1991). Thus modification of the relationship between excitation and motor-unit firing frequencies may alter quantitative estimates of the sensitivity of the interpolated twitch to excitation of the motoneuron pool, but would not qualitatively change our conclusion about the insensitivity of the interpolated twitch to excitation at high forces. Nor would it change other conclusions that depend on the relationship between interpolated twitch amplitude and force rather than on the relationship between interpolated twitch amplitude and excitation.

For the adductor pollicis, comparison of experimental maximal voluntary force and 100-Hz force does not provide a valid experimental measure of activation. This is evident from the comparison of our experimental measures of voluntary force and 100-Hz force. Force produced by 100-Hz trains averaged 60.3% of maximal voluntary force. Maximal voluntary force was bigger than stimulated force, even though the stimulus was supramaximal and excited most or all of the intrinsic agonist muscles, because in stimulated contractions the rest of the hand was relaxed. In maximal voluntary contractions, other muscles (those not innervated by the ulnar nerve) may act synergistically to optimize force production by the thumb adductors (for example, synergistic muscles hold the thumb more internally rotated during maximal voluntary contractions) (see Merton 1954). In general, comparison of maximal voluntary force and 100-Hz force will not provide a valid measure of voluntary activation if nonstimulated muscles act synergistically to enhance measured muscle force.

Several studies have shown reduced levels of voluntary activation in fatigue and in some populations with pathology (e.g., Allen et al. 1993, 1997; Bigland-Ritchie et al. 1983; McComas et al. 1983; McKenzie et al. 1992; Rice et al. 1992; Rutherford et al. 1986). If, as the predictions of our model suggest, measures of voluntary activation obtained with the twitch interpolation method are insensitive to excitation, observations of even small reductions in voluntary drive must indicate significant failures of excitation to the motoneuron pool. Theoretically, such reductions may arise when there is a mismatch between the level of excitation to the motoneuron pool and the contractile properties of motor units. In the present simulations, voluntary activation was maintained when the normalized firing frequency (mean PFR × whole muscle twitch contraction time) was kept constant, for example, when a reduction in contraction time from 69 to 55 ms was matched by an increase in mean PFR from 30 to 38 Hz. An alternative mechanism is that fatigue could reduce the gain of the relationship between excitation and motoneuron firing frequency (for example, by reducing the level of synaptic “noise”).

In experiments, it is usual to see small interpolated twitches during maximal voluntary efforts. A small proportion of these twitches may actually be random fluctuations in voluntary force that coincide with the stimulus, but most are “real” interpolated twitches produced by the stimulus (an analysis of the experimental data shows that, for adductor pollicis, random force fluctuations in the plateau of maximal voluntary contractions is such that artifactual “twitches” with amplitudes of >5% of the resting twitch would be expected follow the stimulus in <10% of contractions, yet interpolated twitches >9.7% of the resting twitch are observed in 50% of maximal voluntary contractions). Interestingly, most subjects can fully activate the muscle (i.e., completely occlude the twitch) in
some maximal efforts (Allen et al. 1995; Herbert and Gandevia 1996). If the predictions of our model are correct, this cannot occur unless the distribution of PFRs is shifted toward higher values than those observed by Bellemare et al. (1983). The production of 200-Hz doublets in 10% of discharges of motoneurons (probably an extreme scenario) had little effect on the amplitude of interpolated twitches. However, interpolated twitch amplitude could be reduced to 1.0% (i.e., voluntary activation could be increased from 95.3 to 99.0%) by an increase in the mean firing frequency of all motoneurons from 29.9 to 62.7 Hz. Firing frequencies of this magnitude are unlikely to be sustained in maximal voluntary efforts (Bellemare et al. 1983), but perhaps could be attained transiently.

It is concluded that the amplitude of the interpolated twitch is influenced by reflex and antidromic effects. At forces greater than ~90% of maximal voluntary force, interpolated twitch amplitude is insensitive to motoneuron pool excitation, so real changes in interpolated twitch amplitude must indicate large changes in motoneuronal excitation.

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