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THE CONTRACTILE PROPERTIES OF HUMAN MOTOR UNITS DURING VOLUNTARY ISOMETRIC CONTRACTIONS

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SUMMARY

1. The electrical activity of single motor units has been recorded from the first dorsal interosseus muscle of normal human subjects during voluntary, isometric contractions, together with the force generated by the muscle.

2. By averaging the force correlated with the impulses from a single motor unit, the contraction time and twitch tension generated by that motor unit could be measured. When the rate of discharge was limited, either voluntarily or by automatic selection of intervals for analysis, the time for the tension to decline to half its maximum value (half-relaxation time) could also be measured for some motor units.

3. Under our experimental conditions the trains of impulses from different motor units in most subjects were generated quite independently as tested by (*a*) measuring the correlation between activity in single units and that in the whole muscle as recorded by the surface electromyogram (e.m.g.), (*b*) measuring the cross-correlations between pairs of single units and (*c*) comparing the tension generated by stimulating single motor units with the average tension correlated in time with voluntary activity of single units in the same location.

4. In one normal subject evidence of synchronization between separate motor units was obtained. Cross-correlation studies suggested that the cause of the synchronization was the presence of substantial common excitation received by the various motor units in the muscle.

5. The frequency response for the contractions of single motor units was well fitted by that for a linear, second-order system with nearly critical damping. However, when stimulation of a few motor units was superimposed on a voluntary contraction, underdamped (oscillatory) responses were seen which were probably of reflex origin.

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6. The significance of these results in relation to the normal postural tremor in hand muscles is discussed.

INTRODUCTION

The electrical activity of single motor units can be recorded so easily during normal voluntary contractions that these recordings are used routinely in the diagnosis of diseases affecting nerves and muscles (Lenman & Ritchie, 1970). However, only recently have attempts been made to record the contractile tension generated by single motor units in man (Buchthal & Schmalbruch, 1970; Sica & McComas, 1971). The methods used to measure tension involve the more difficult task of stimulating single motoneurones in whole nerves or branches of nerves after they divide close to the motor end-plates. With these methods fast and slow twitch motor units have been identified in human muscles, but whether different fibre types are used differently during normal voluntary contractions remains unclear.

In a preliminary report (Stein, French, Mannard & Yemm, 1972) we suggested that the early time course of the isometric contractions produced by single motor units during voluntary contractions could be easily measured using the following technique. Impulses recorded from a single motor unit are used to trigger a signal averager, which sums the forces recorded from the whole muscle as a function of time before and after these impulses. If the impulses from other motor units occur at random times relative to those of the single motor unit being studied, averaging will extract the tension changes produced by the single unit from the overall tension fluctuations in the muscle.

In this paper we will extend this technique and determine its power and limitations, compared to the stimulation methods, for studying the contractile properties of single human motor units. In addition to its simplicity, the averaging technique has the advantage that the contractile properties can be associated with the function of the motor units, either in normal subjects or in patients having various diseases affecting their nerves or muscles. For example, we have recently found (Milner-Brown, Stein & Yemm, 1972) that motor units are recruited during voluntary contractions of increasing force approximately in the order of the contractile force that they generate.

METHODS

One hundred and thirty-seven single motor units have been studied from the first dorsal interosseus muscles in the hands of seven normal subjects. This particular muscle was chosen for extensive study because it is the only one producing movement of the index finger away from the middle finger (there is no corresponding ventral interosseus muscle). Therefore, the problems of recording the tension generated by a single muscle are minimized (Stephens & Taylor, 1972). Also, since we intended to correlate the tension generated with the discharge of single motor units, a fairly small muscle having a limited number of motor units was desirable.

E.m.g. recording. One or two bipolar needle electrodes were inserted into the muscle and positioned so that the discharge of single motor units could be distinguished at a moderate level of voluntary contraction. The electrodes consisted of two fine (75 μm) wires for differential recording fixed with epoxy in the barrel of a needle (25 gauge) which served as an earth connexion. The electrical activity was (1) amplified using a preamplifier with 10 MΩ input impedance and 90 dB common mode rejection, (2) filtered with a low frequency cut-off between 20 and 200 Hz and a high frequency cut-off of 1000 or 10,000 Hz, (3) displayed on an oscilloscope, and (4) recorded on an FM tape recorder. Subjects were provided with both visual and auditory feed-back of the electrical signals, as suggested by Basmajian (1963), and were asked to maintain the discharge of a single motor unit at a slow, fairly steady rate (e.g. 5–10 impulses/sec). Single units were identified in the usual way, by triggering the oscilloscope from the amplified electrical signal, and observing the occurrence of a repetitive waveform with (1) invariant amplitude and time course, and (2) no intervals shorter than several msec. Although some units could be made to discharge steadily at somewhat lower rates, this often proved difficult to maintain for the periods of recording used (3–5 min). The voluntary force level was then varied to change the firing rate or to recruit other motor units and the process was repeated. After recording all the motor units that could be distinguished at one electrode location, the position of the electrode was changed. Attempts were made in each session to record motor units which were recruited over a range of forces from very weak ones up to a kg or more. Pulse height analysers (Stein, 1968) were available to analyse smaller units which were recorded simultaneously with units producing larger electrical signals. In addition to a needle inserted into the muscle, silver disk surface electrodes (with a diameter of 9 mm) were often placed $3 \pm 0{\cdot}5$ cm apart on the skin on opposite sides of the needle and electrode paste was used for good electrical contact. The three electrodes were then in a line parallel to the long axis of the muscle. Similar amplification, filtering and recording were used for the surface e.m.g.

Tension recording. Subjects held a force transducer between their thumb and first finger, while resting their arm comfortably on a support. The force transducer was rigidly clamped to the support. Brackets were mounted on the frame of the transducer for the thumb and on the lever attached to the strain gauges to accommodate the lateral portion of the first finger, approximately midway between the base of the finger and the proximal interphalangeal joint. The transducer was virtually isometric, allowing only 1 mm of movement, and was used with springs for recording forces up to about 2 kg. The natural frequency of the transducer when loaded by the bracket was about 400 Hz. Where the records after averaging were noisy, the higher frequencies were sometimes filtered, taking care not to distort the recorded waveform. Low frequency fluctuations were commonly seen in the tension records, and these were reduced before recording by a high-pass filter with a time constant of 1 or 2·5 sec. This does not appreciably distort the time course of any traces shown here which have, at most, a duration of 320 msec.

Correlation and averaging methods. The four-channel FM tape recorder was used to record (1) the unfiltered force at low gain, (2) the force at higher gain after filtering out low frequency fluctuations (see *Tension recording*), (3) motor unit activity from a needle electrode, and (4) the activity from either a second needle electrode or the surface e.m.g. The activity from motor units could be replayed through a predetection facility about 270 msec before the corresponding force records. The impulses from single motor units were used to:

(1) trigger an averager. The averager would then sum the force records and/or the surface e.m.g. from a number of sweeps (typically 512) to determine the magnitudes of the signals correlated in time with the impulses from a single motor unit;

(2) generate an *autocorrelation* histogram (Moore, Perkel & Segundo, 1966) using a computer programme (French, 1970) which measured the numbers of impulses occurring at various time intervals after the occurrence of an impulse in a single motor unit. The numbers of impulses were divided by the number of sweeps and bin width to give the rate of discharge following an impulse which is referred to in various applications as an autocorrelation histogram, as a renewal density function or an intensity function (Stein, 1972). The numbers of impulses were also summed and divided by the number of sweeps to give the cumulative mean number of impulses occurring in various intervals following an impulse;

(3) generate a *cross-correlation* histogram for distinct trains of impulses recorded with two needle electrodes (Moore *et al.* 1966). The numbers of impulses in one train which occur at various times before or after the occurrence of an impulse in the second train were measured and converted to a rate of discharge as for the autocorrelation histogram.

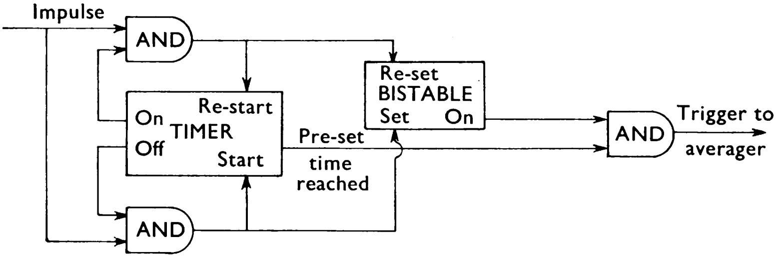

Fig. 1. Block diagram for the rate limiter. The circuit contains three gates which perform a logical AND function; e.g. a trigger pulse is sent to the averager only if a preset time T has been reached *and* the bistable is on. The timer switches off after reaching the time T and the bistable is only set if an impulse arrives when the timer is off; i.e. when no impulse has occurred for the time T beforehand. Thus an output is produced a time T after an impulse only if both the preceding and succeeding intervals are greater than T. This corresponds to choosing impulses occurring with a maintained rate less than $1/T$. Using the predetection facility of the tape recorder, the trigger pulses could actually start the sweeps $270 - T$ msec before the corresponding force or surface e.m.g. records.

Rate limitation. It was often desirable for reasons explained under Results to average only those impulses which occurred at least a time T msec removed from other impulses. A block diagram of a simple circuit to select such impulses automatically is shown in Fig. 1 (further specifications are available on request from the authors).

Rectification of surface e.m.g. To obtain records such as shown in Fig. 8, the surface e.m.g. was passed through a full-wave rectifier, and then averaged as a function of time before or after the occurrence of impulses from a motor unit recorded by a needle electrode. The effect of this process is shown schematically in Fig. 2. The time of occurrence of impulses recorded by the needle electrode are indicated by a vertical line in Fig. 2*A*. Associated with these impulses will be some wave form on an unrectified average (indicated schematically by a triangular wave form in Fig. 2*B*). Impulses from other units which are not tightly synchronized (approximately to within the time T) will be 'averaged out' because there will be an equal probability that they will give a positive or a negative contribution on successive sweeps. (Because of the a.c. recording, the time average of these e.m.g. wave forms must be zero.) It can be shown (Cox & Miller, 1965) that the probability density function $f(\nu)$ for the total voltage ν contributed by other uncorrelated units in individual traces will be Gaussian with a standard deviation σ, i.e.

$$f(\nu) = (2\pi\sigma^2)^{-\frac{1}{2}} \exp\left(-\frac{\nu^2}{2\sigma^2}\right). \tag{1}$$

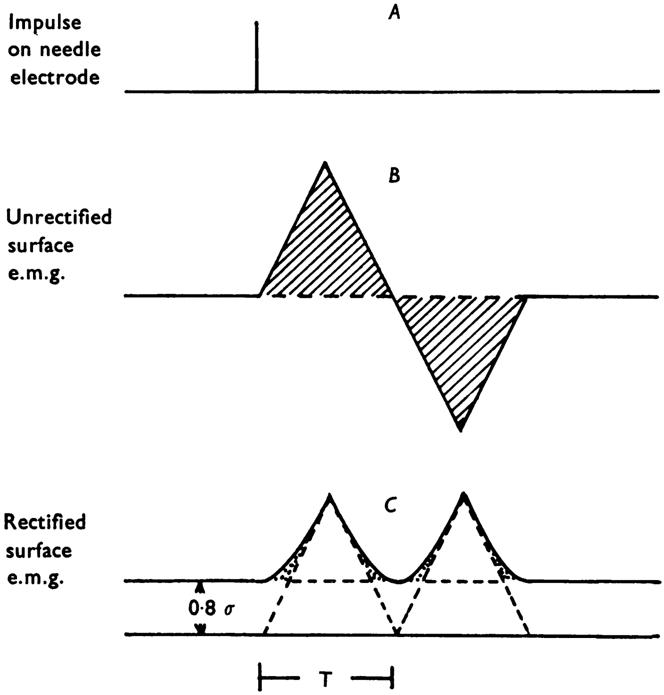

Fig. 2. Schematic representation of a test for synchronization of motor units using the surface e.m.g. If a signal averager is triggered by impulses from a single unit *A* recorded by a needle electrode, a wave form *B* is obtained by directly averaging the surface e.m.g. When impulses in different motor units are generated independently (no synchronization), this average will simply represent the voltage generated by the single unit which is recorded by the surface electrodes (the area is indicated by diagonal lines in *B*). If averaging is done after rectification *C*, there will be a net contribution to the average of (1) the wave form in *B* after rectification, (2) the ongoing activity of other units (0·8σ, see explanation of notation in text) and (3) a partial summation of these two (dotted area). However, if the discharge of several units tends to be grouped (synchronization) over a period greater than T, a broader and larger increase in the rectified surface e.m.g. will be observed than can be accounted for by (1) to (3) above.

After rectification there will be a net contribution where

$$\bar{\nu} = 2(2\pi\sigma^2)^{-\frac{1}{2}}\int_0^\infty \nu \exp\left(-\frac{\nu^2}{2\sigma^2}\right) \mathrm{d}\nu = (2\sigma^2/\pi)^{\frac{1}{2}} \approx 0\cdot8\sigma. \qquad (2)$$

If we consider the average wave form at a time when the single unit always adds an amplitude a, the net voltage $\bar{\nu}$ will be

$$\begin{aligned} \bar{\nu} &= (2\pi\sigma^2)^{-\frac{1}{2}}\left[\int_{-a}^\infty (\nu+a)\exp\left(-\frac{\nu^2}{2\sigma^2}\right)\mathrm{d}\nu + \int_a^\infty (\nu-a)\exp\left(-\frac{\nu^2}{2\sigma^2}\right)\mathrm{d}\nu\right] \\ &= (2\pi\sigma^2)^{-\frac{1}{2}}\left[2\int_a^\infty \nu\exp\left(-\frac{\nu^2}{2\sigma^2}\right)\mathrm{d}\nu + \int_{-a}^{+a}(\nu+a)\exp\left(-\frac{\nu^2}{\sigma^2}\right)\mathrm{d}\nu\right] \\ &= (2\sigma^2/\pi)^{\frac{1}{2}}\left[\mathrm{e}^{-\frac{1}{2}u^2} + u\int_0^u \mathrm{e}^{-\frac{1}{2}w^2}\,\mathrm{d}w\right] \qquad (3) \end{aligned}$$

where $u = a/\sigma$ and $w = \nu/\sigma$. In Fig. 2C, the interrupted lines show the contribution to the rectified average expected from rectification alone (eqn. (2)), and from the e.m.g. measured in the unrectified average alone. The continuous line above these is the summation predicted by eqn. (3). Note that very little summation occurs at the two extremes of amplitude. This can be shown mathematically from eqn. (3) since for small values of u

$$\bar{\nu} \approx 0\cdot8\sigma\,(1+\tfrac{1}{2}u^2),$$

while for u greater than about 3, $\bar{\nu} \approx a$. The maximum summation (when $\alpha = 0\cdot8$) is only 30 %, and the increase in area due to summation (the shaded portion above the interrupted lines) can be computed for any wave form using eqn. (3). With the waveform of Fig. 2B the summation is only 9%.

In Fig. 7 the rectified surface e.m.g. was further filtered before analysis using a third-order low-pass Paynter filter (time constants = 10 msec; cut-off frequency ≈ 16 Hz) as described by Gottlieb & Agarwal (1970).

Spectral analysis. In addition to these analyses in the time domain, computer programmes were available to calculate as a function of frequency (1) the spectrum of the force record, (2) the spectrum of an impulse train, (3) the cross-spectrum between the force record and an impulse train, and (4) the best-fitting linear frequency response function for the force related to the impulse train. This is obtained by dividing the cross-spectrum by the spectrum of the impulse train (Bendat & Piersol, 1966). For our purposes the shape of the impulses was not of interest. Therefore, the programmes treat the trigger pulses as Dirac δ-functions filtered appropriately for the frequency band considered. These programmes, including their assumptions and limitations for the analysis of neural data, have been described in detail elsewhere (French & Holden, 1971*a*, *b*, *c*).

RESULTS

Fig. 3 shows the results of averaging the force correlated with the impulses from single motor units. The predetection facility of the tape recorder was used together with a delay so that approximately 10 msec of the force record is seen before the occurrence of the impulses from the motor units. In Fig. 3A the force record begins to rise sharply after a latency of a couple of msec, and reaches a maximum of 0·7 g at a time 45 msec after the beginning of the impulses. The time interval for the force to decline from the peak to half its maximum value (half-relaxation time) is 25 msec. As seen in the lower part of this figure, subsequent impulses only occurred during this time on about 10% of the sweeps, so most of the force changes observed represent the largely unfused twitches produced by this motor unit. A small degree of fusion is indicated by the fact that the tension from preceding impulses had not decayed completely (note the slow decline of tension before the occurrence of the triggered impulses).

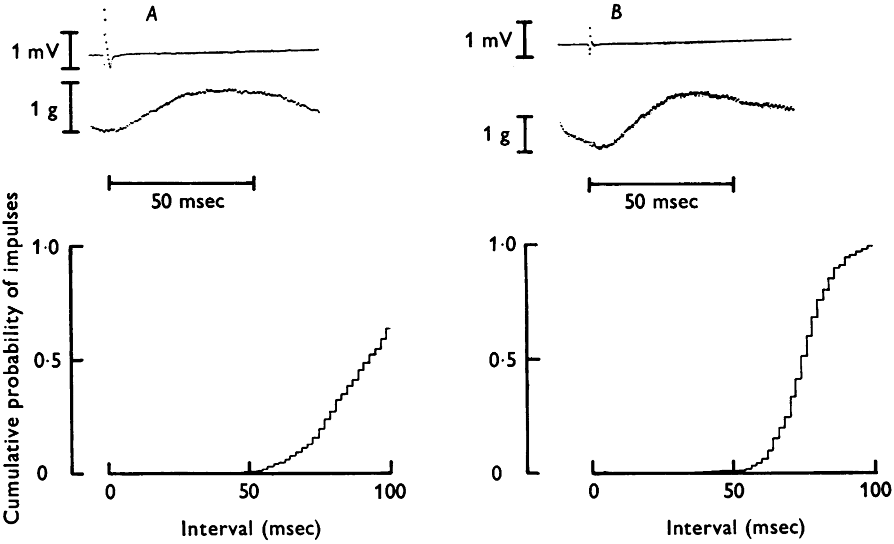

Fig. 3. Average responses correlated with the discharge of single motor units. Shown from top to bottom are the average wave form of impulses recorded by a bipolar needle electrode, the average force correlated with the occurrence of these impulses, and the cumulative probability of impulses occurring within the intervals indicated following the impulses at 0. The two parts *A* and *B* were recorded from different subjects and show units which were firing with different mean rates (10·5 and 13 impulses/sec).

Sometimes the discharge could not be maintained at low rates and the average force had a more fused appearance (Fig. 3*B*). The tension from preceding impulses was still decaying quite markedly before the occurrence of the triggered impulses. Subsequent impulses occurred commonly after an interval of about 60 msec, so the falling phase of the tension record is slowed and does not reach the half-relaxation point. However, the somewhat higher force (1·5 g) and somewhat briefer contraction time (40 msec) are easily measured. In order to check that these values did not vary markedly with the rate of discharge from single motor units, the contraction time and maximum force were measured at two different rates in fourteen motor units (typically about 7 and 10 impulses/sec). The arithmetic mean ratio of the contraction times at the higher rate to that at the lower rate was 1·022 ± 0·027 (mean ± S.E.) while the ratio of the tensions was 1·35 ± 0·14 (mean ± S.E.). The geometric mean for the ratios of maximum tension was 1·26. These values are not significantly different from unity so that measurements of contraction time and twitch tension generated by the motor units do not appear to depend strongly on firing rate, despite some degree of fusion.

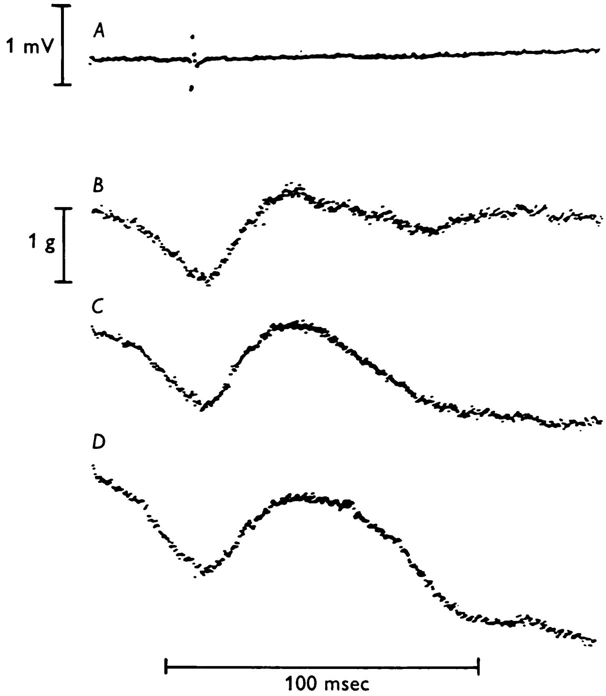

Fig. 4. Average forces correlated in time with the discharge of the single motor unit shown in *A* (same unit as in Fig. 3*B*). No limitation of rate was imposed in *B*. In *C* and *D* impulses which occurred with preceding and succeeding intervals shorter than 65 and 70 msec respectively, have been excluded using the rate limiter (Fig. 1). Further explanation in text.

Rate limitation. Occasionally, the discharge rate was high enough that even the peak tension was unclear. In order to measure the twitch tensions and contraction times for such units, and to measure the half-relaxation times for units such as shown in Fig. 3*B*, it was desirable to select out those portions of the discharge where the motor unit was firing at a lower rate. A circuit is described in the Methods for selecting only those impulses where the preceding and succeeding impulses occurred at an interval greater than T msec. This effectively limits the analysis to those portions of the record where the rate of firing is being maintained at below $(1000/T)$ impulses/sec. This rate limiter was of considerable value in analysing motor units from subjects who had no previous experience in controlling the discharge of single motor units, and for analysing those motor units, even in experienced subjects, which could not be maintained for several minutes at a low rate.

The effect of selecting increasingly long minimum intervals is shown in Fig. 4*B–D*, using the same unit as in Fig. 3*B*. In Fig. 4*B*, no limitation was used, and the trace is similar to Fig. 3*B* except that the duration of the sweep was twice as long. Generally, a value of T could be selected (Fig. 4*C*) where (1) the tension fell well below the maximum value before the occurrence of later impulses, and (2) the tension preceding the triggered impulses was not significantly altered. In this way accurate values for the contraction time and twitch tension could always be obtained. The values of the half-relaxation time (30 msec in Fig. 4*C*) were more difficult to obtain (see also *Stimulation* below).

A further difficulty is illustrated by the bottom trace (Fig. 4*D*) in which an increased negative slope is observed even *before* the triggered impulses occurred. This trace was obtained from the fraction of impulses where both the preceding and succeeding intervals were longer than 70 msec. Spontaneous slow fluctuations in force were generally seen and the longest intervals were apparently more common when the mean force level was slowly declining (see also Clamann, 1970). Because of these difficulties half-relaxation times could only be measured in a fraction of the units studied.

The observation of trends in the data with extreme rate limitation raises the general question of the effect other motor units have on the average values measured for a given motor unit. To demonstrate that these average values represent the contractile properties of single motor units, one must show that *the impulses from other motor units did not tend to occur grouped together in time with those from the single motor unit being studied* (*synchronization*). Therefore, we examined the degree of synchronization between motor units in this muscle under the conditions of our experiments in three ways by (1) stimulation experiments, (2) averaging the total activity recorded with the surface e.m.g. which was correlated in time with the impulses from a single motor unit, and (3) measuring the cross-correlation between the firing times of two motor units recorded simultaneously by separate needle electrodes. These results will be examined in turn in the next three sections.

Stimulation. In several experiments the needle electrode was carefully positioned so as to record the largest possible signal from a single motor unit. The average force correlated with the impulses from the motor unit was measured in the usual way (Fig. 5*B* and *C*). Then the bipolar needle electrode was connected to a stimulator and stimuli having a duration of 0·1 msec were applied. Such brief stimuli tend to excite nerve branches rather than single muscle fibres. As the intensity of the stimulus was increased, all-or-none increments were recorded by the surface e.m.g. which were similar in size to motor unit potentials recorded during voluntary contractions. Sometimes a small all-or-none twitch could also be seen by careful observation of the skin over the muscle. The response to stimulation at a low rate (less than 2/sec) could be averaged and the time course of the tension changes produced by the stimuli could be measured (Fig. 5*A*). In the absence of observable e.m.g. responses no average tension changes were found. The average tension produced by stimuli strong enough to generate the first increment in the e.m.g. repre-

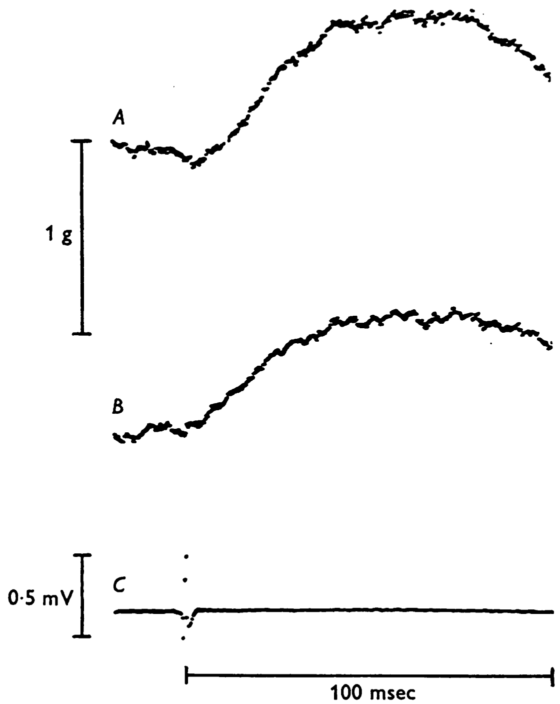

Fig. 5. Comparison of the average twitch *A* produced by stimulating a single unit and the average force *B* correlated with the impulses from a single unit *C* recorded at the same location in the muscle. The traces have been aligned so that the stimuli producing *A* occurred at the same point in the trace as the recorded impulses in *C*. Evidence is presented in the text that a single unit was being stimulated.

sents the twitch tension produced by a single motor unit (Buchthal & Schmalbruch, 1970; Sica & McComas, 1971). Note the similar size and time course of the twitch tension evoked by stimulating a single motor unit and the average tension correlated with the spontaneous discharge of a motor unit in the same location in the muscle. On several occasions when stimulation was attempted, good agreement with the twitch tensions measured during a voluntary contraction was obtained (as in Fig. 5). On other occasions the stimulated twitch did not agree with the average tension which was correlated with the discharge of motor units recorded at that site by the electrode during voluntary contractions. This variation in different experiments was expected since the nerve branch closest to the electrode may be the one going to the motor unit being recorded or it may merely pass by the electrode to innervate a motor unit some distance away. However, if the average during voluntary contractions actually measured the tension produced by the nearly synchronous discharge of several motor units, the twitches produced by stimulating single units should often have been markedly smaller. No such difference between stimulation and voluntary activation was observed.

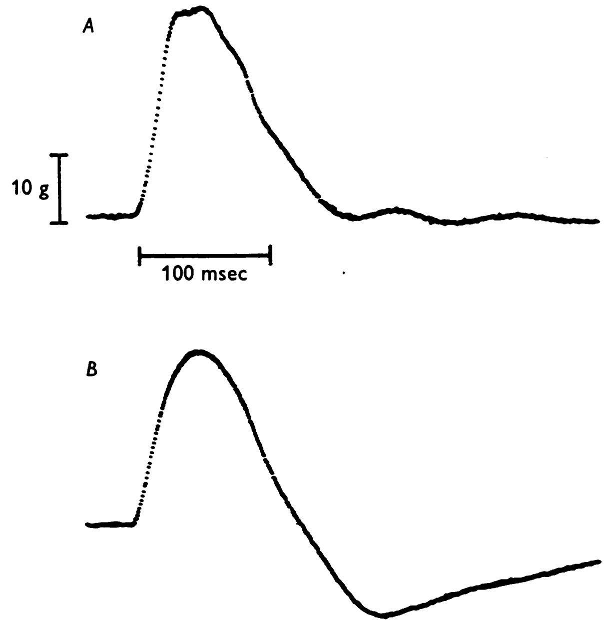

Fig. 6. Comparison of the average tension produced by stimulating at 1·7 sec before *A* and during *B* a voluntary isometric contraction of 350 g. Note the more rapid relaxation and undershoot in *B*, the left edge of the time scale indicates the time of stimulation.

With further increases in the stimulus, other all-or-none increments could be seen. Fig. 6*A* shows the response to stimulating a small number of motor units when there was a minimal voluntary contraction. Fig. 6*B* gives the response to the same stimulus applied during a voluntary contraction of 350 g. The contraction time and the twitch tension are similar, but relaxation occurs more rapidly. The falling phase in Fig. 6*B* extends below the base line before slowly returning to the original level. This phenomenon is probably a reflex effect as will be discussed later. Evidence that it was not purely mechanical in origin is presented in Fig. 7. The top trace shows that stimulating a few motor units in another subject also produced a contraction, then a relaxation below the previous level, followed by an oscillatory return to this level. The surface e.m.g. was also being recorded in this experiment and is shown in the middle trace after rectification and filtering (see Methods). The two sharp peaks in the e.m.g. (which actually go off scale) represent the stimulus artifact and the direct response to the stimulus. This response produced a small additional force of just over 2 g with a contraction time of about 40 msec. Each successive maximum or minimum in the tension follows a corresponding maximum or minimum in the surface e.m.g. with a similar latency. The results shown in Figs. 5–7, irrespective of their interpretation, suggest (1) the values of twitch tension and contraction time obtained during voluntary contractions are reliable measures of the twitches obtained from single

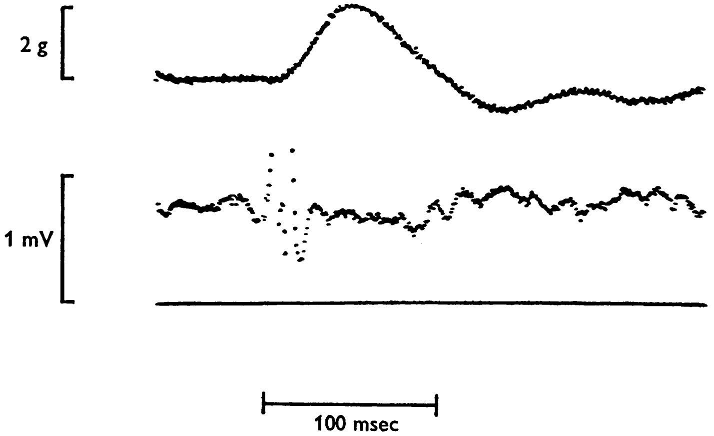

Fig. 7. Average tension (top trace) and average rectified surface e.m.g. (middle trace) produced by stimulation of a few motor units during a voluntary contraction of 400 g. The bottom trace is a reference zero for the rectified e.m.g. Note the 10 Hz oscillations produced in both the tension and the e.m.g. following a contraction of only 2 g. Further explanation in text.

motor units, and (2) the measured values for half-relaxation time during voluntary contractions may underestimate the true values.

Correlation with the surface e.m.g. Although the stimulation studies above suggest that the early time course of the force generated by single motor units can be measured simply by averaging, the results are not conclusive. In fact, the oscillations produced by stimulation (Fig. 7) represent a slight tendency toward synchronization in the discharge of motor units. Therefore the correlation was measured during voluntary activity between the timing of impulses from single motor units and of impulses from the whole population of motor units recorded by surface electrodes. Typical results from two subjects are shown in Fig. 8. The wave forms recorded with surface electrodes (second traces from top in Fig. 8) were of longer duration than those from needle electrodes (top traces) as commonly observed. In Fig. 8*A* the peaks in the rectified (third) trace were coincident with and agree in magnitude with the occurrence of the waveform in the unrectified trace (see also Fig. 2 in Methods). However, for all six units of another normal subject (Fig. 8*B*) a period of increased activity was evident in the rectified e.m.g. extending approximately 10 msec before and after the occurrence of activity in the unrectified trace. This indicates a tendency for other motor units to discharge near the time of impulses from the motor unit being studied. The force correlated with the discharge of single

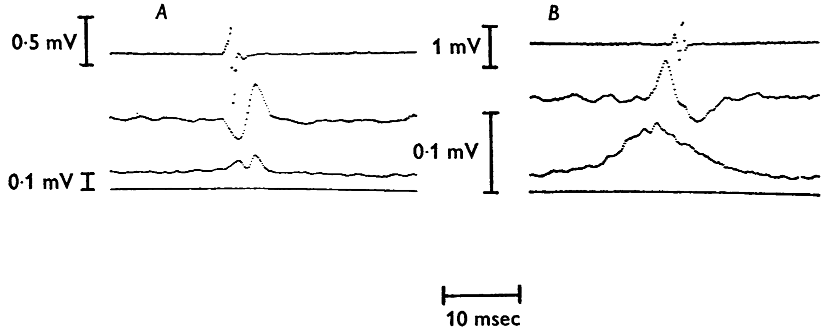

Fig. 8. Surface e.m.g. associated with the impulses recorded by a bipolar needle electrode. The traces from top to bottom show (1) the average impulse from a single motor unit recorded by a needle electrode, (2) the average unrectified surface e.m.g. associated with the impulses, (3) the average rectified surface e.m.g., and (4) a reference zero for the rectified signal. *A* and *B* are typical records from two different subjects. Note that the rectified surface e.m.g. in *B*, but not in *A* remains higher for about 10 msec before and after the occurrence of the impulses in the unrectified trace. This indicates that other motor units were tending to fire more often during this period in synchrony with the discharge of the motor unit recorded by the needle electrode.

motor units in this subject was also several times larger at all force levels than in any other subject.

For forty-five units from six subjects we measured the area in the rectified e.m.g. trace (see dotted area in Fig. 2) which was (1) above the steady level due to the ongoing activity of other motor units, and (2) above the voltage levels found in the unrectified trace. This extra area was expressed as a percentage of the area measured for the single unit on the unrectified trace (see Fig. 2*B*). In most of the subjects this extra area was minimal (well within the limits ($< 10\%$) expected from partial summation according to Fig. 2). However, for the subject shown in Fig. 8*B*, the extra area was two or more times the area due to a single unit in five of the six units studied. We must conclude that in this subject there was a definite grouping of motor unit activity during normal isometric contractions. One other subject might have had a slight tendency for grouping of motor units. The extra area measured for eleven motor units in this subject was $19 \pm 3\%$ (mean ± S.E. of the mean) which is somewhat higher than expected from partial summation.

Cross-correlations between motor units. The surface e.m.g. and stimulation studies reported above indicate strongly that in most subjects the impulses from single motor units are remarkably independent of those from other units in the muscle. In other individuals who can be identified by recording the surface e.m.g., several motor units may tend to discharge more or less synchronously. To get further insight into the mechanisms involved in this synchronization, the cross-correlations between motor units recorded on two separate bipolar needle electrodes were measured (see Methods). This was done for eleven pairs of units in two subjects, one of whom had shown evidence of synchronization from the surface e.m.g. recordings (Fig. 8*B*). A typical histogram for the cross-correlations between impulses from two units in this subject is shown in Fig. 9 (*A vs. B*) together with the autocorrelation histograms for each unit separately. The autocorrelation histograms are often helpful in interpreting any periodicities observed in cross-correlation histograms (Moore *et al.* 1970). The successive peaks in the autocorrelation histograms of Fig. 9 merely indicate the times at which the next and subsequent impulses occurred most commonly, measured from the time at which an impulse occurred to start the sweep. The cross-correlation histogram on the left of Fig. 9 is flat except for the obvious increase in a few bins just around zero time. Such an increase was observed in all five pairs of units examined from this subject, and again indicates the tendency for motor units to fire more or less synchronously. The implications of this result will be considered in the Discussion.

The second subject showed no significant correlations between the six pairs of units examined (using a test of significance described by Holmes &

Houchin, 1966), although a small tendency for a peak near zero was observed in one or possibly two pairs of units (Fig. 9*C vs. D*).

Frequency response. Another important property of motor units and whole muscles is their ability to respond to fluctuating signals which are found in normal behavioural movements and in tremor. The simplest way to predict the response of a linear system to signals of various frequencies is to take the Fourier transform of the response to a brief stimulus (impulse response). For a muscle the response to an impulse is the twitch, and the Fourier transform of the twitch can now be conveniently obtained using the Fast Fourier Transform algorithm (Cooley & Tukey, 1965). However, muscles show well known non-linearities, such as a fused response to high (tetanic) rates of stimulation. Therefore, the frequency response obtained from the twitch may not be applicable to more natural conditions, where the motoneurone is producing a somewhat irregular series of partially

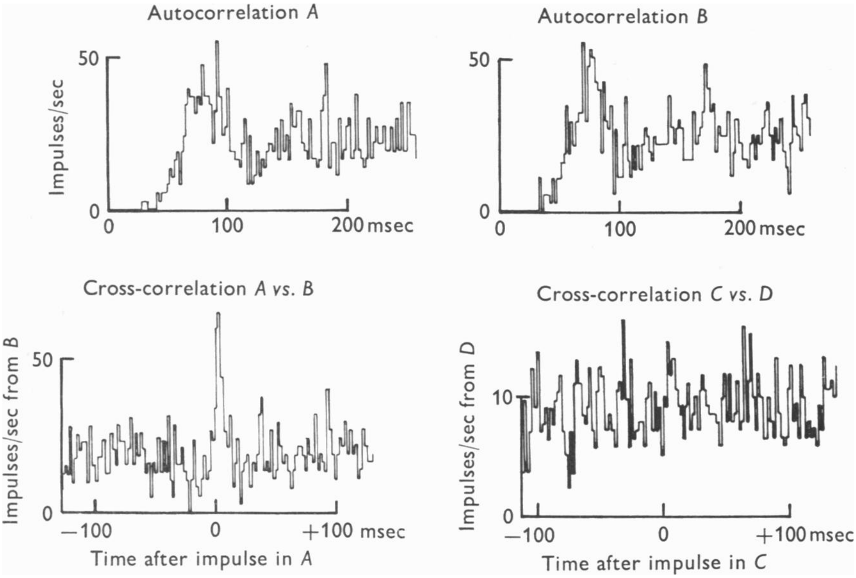

Fig. 9. Autocorrelation and cross-correlation histograms for pairs of units recorded simultaneously on separate needle electrodes. The autocorrelation histograms for units *A* and *B* have peaks at intervals where the next and subsequent impulses are generated following the impulses which begin the sweeps. The prominent peak near zero time in the cross-correlation histogram for these units indicates a tendency for impulses in the two motor units to occur nearly synchronously. Data from the same subject as in Figs. 8*B* and 9*B*. The cross-correlation histogram from another subject (units *C vs. D*) showed, at most, a statistically insignificant peak near zero time. Further explanation in text.

fused contractions. Nonetheless, at various physiological rates of activity, linear models have been shown to account for most of the data obtained in experiments where muscles are stimulated with sinusoidally varying (Rosenthal, McKean, Roberts & Terzuolo, 1970) or randomly varying stimulus trains (Stein *et al.* 1972). The train of impulses produced naturally by a single motor unit during voluntary contractions contains a wide range of frequencies, and it is possible by spectral analysis to measure that part of the tension in the muscle which is linearly related to each frequency component contained in the train of impulses (see Methods). Therefore, the linear frequency response provides another way to compare at least the linear behaviour of motor units during stimulation and voluntary activity.

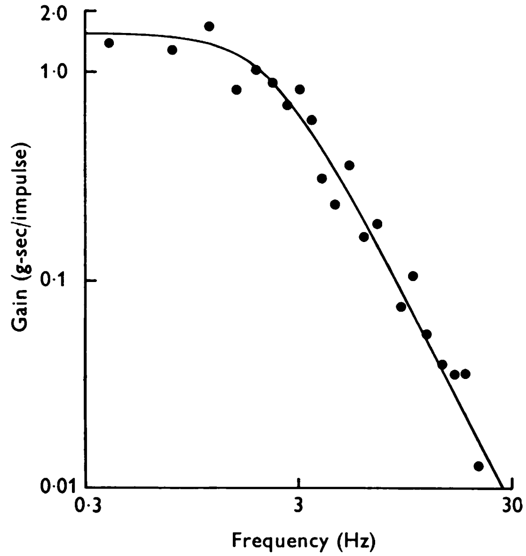

Fig. 10. Frequency response for a single motor unit during a voluntary isometric contraction. The gain measures the change in g for each impulse/-sec modulation in firing rate of the motoneurone at the frequency indicated. The continuous curve is the gain expected for a critically damped, linear, second-order system with a low frequency gain of 1·6 g-sec/impulse and a natural frequency of 3 Hz (D'Azzo & Houpis, 1966).

Fig. 10 shows the amplitude of the frequency response (often referred to as *gain*) for a single motor unit measured by spectral analysis on a log-log plot. The continuous line is the curve expected for a critically damped, second-order linear system (e.g. a suitably chosen mass, spring and dashpot would be an example of such a system). Three parameters which characterize a simple second-order system are its gain at low frequencies, G_0, its natural frequency, f_n, and its damping ratio, ζ (this ratio is 1 for a critically damped system). The other fitted values are given in the caption of Fig. 10. Note that the response amplitude falls off sharply beyond the natural frequency, even on a log-log plot. For a second-order system the slope on such a plot approaches -2, which indicates that the response amplitude falls off as $1/f^2$ at high frequencies. The gain is already reduced by more than an order of magnitude at a frequency of 10 Hz. These results indicate that the contractile properties of human motor units will be a strong factor in limiting the component of physiological tremor near this frequency (Schäfer, 1886; Hammond, Merton & Sutton, 1956; Lippold, 1970).

For twelve units recorded during voluntary activity the mean natural frequency was 2·4 Hz (individual values ranged from 1·4 to 5 Hz), and the mean damping ratio was 1·2 (values ranged from 1·0 to 2·0). In ten experiments one or more motor units were stimulated, and the frequency response was obtained from the Fourier transform of the twitch. The damping ratios were similar (mean 1·2, range 1·0–1·5), but the natural frequencies measured during stimulation were generally higher (mean 5·6 Hz, range 4–7 Hz). Both methods contain possible errors and limitations, so the significance of this difference is uncertain. It will be considered further in the Discussion.

DISCUSSION

The results presented here confirm the suggestion (Stein *et al.* 1972) that simply by averaging the force correlated in time with the discharge of single motor units, the early time course of contraction produced by the motor unit can be determined in many human subjects. In a few experiments (Fig. 5) we have been able to compare the average force associated with voluntary activation of a motor unit and the force produced by stimulation of a motor unit via the same needle electrode. Stimulation has been the only previous method (Buchthal & Schmalbruch, 1970; Sica & McComas, 1971) whereby the contractile properties of single motor units could generally be measured. Extreme care must be taken (unpublished observation) to ensure that only a single motor unit is being stimulated, whereas recording the electrical activity of single units is a well known and routine procedure.

Stimulation has the advantage that the full time course of a twitch can be studied, although when stimulation was superimposed on a voluntary contraction, an undershoot in tension was observed (Fig. 6). Determination of the time course by averaging voluntary activity is restricted by the minimum rates of firing normally generated (5–10 impulses/sec). The twitches are therefore partially fused, and it is often not possible to measure the half-relaxation time of the twitch. However, the contraction times and twitch tensions measured were rather insensitive to the rate of firing over the range of rates examined. We have also noted (unpublished observations) that these parameters are not appreciably affected using stimulation of motor units at rates up to about 10 Hz. Those periods where the rate of discharge was slower than a preset value could be selected automatically (*Rate limitation*) to obtain a more complete twitch tension curve. However, rate limitation must be used with caution, because the slowest rates of firing tend to occur when the force in the muscle is slowly declining (Clamann, 1970). Therefore, with extreme rate limitation the twitch is superimposed on a downward-sloping trace (Fig. 4*D*).

Averaging the force correlated in time with the impulses of a motor unit during voluntary activity has the important advantage that the function of a motor unit can be associated with its contractile properties. However, this association can only be made if the impulses from one motor unit are not synchronized to those of other motor units. A strong one-to-one synchronization of motor units has only been reported in certain disease states (Lenman & Ritchie, 1970). However, a weaker tendency for the impulses of motor units to occur in a group has been noted under various conditions (Buchthal & Madsen, 1950; Lippold, Redfearn & Vučo, 1957, 1960; Person & Kudina, 1968). Taylor (1962) could find no evidence that this grouping was due to mechanisms which synchronized the impulses of motor units. He could account for the observed grouping from the probability that various independent motor units might fire within a given time interval.

Using more stringent tests under the conditions of our experiments, the impulses from different motor units in most subjects were generated remarkably independently of one another. However, one subject showed a definite degree of synchronization, which was evident as a broad peak lasting ± 10 msec, when the discharge of one motor unit was correlated with that of a second motor unit (Fig. 9) or with the whole population recorded by the surface e.m.g. (Fig. 8). A brief increase around zero time would be expected in the cross-correlation histogram between two units if the units shared substantial common excitatory inputs (Moore, Segundo, Perkel & Levitan, 1970), for example, from higher centres or from muscle spindles. The second suggestion is consistent with the recent finding (Mendell & Henneman, 1971) that all motoneurones in a muscle may receive excitation from each muscle spindle afferent. Shared inhibition from Golgi tendon organs or from Renshaw cells would tend to produce a much broader peak in the cross-correlation histogram (Moore *et al.* 1970). The relative lack of secondary peaks at the times of the peaks in the autocorrelation histogram also excludes the possibility that one unit was synaptically driving the other.

In other subjects, an undershoot in tension and e.m.g. activity was observed, often followed by oscillations at about 10 Hz, when stimuli were applied which produced a contraction of even a few grams. This could also be a reflex effect due to an unloading of muscle spindles by the extra contraction. However, the role of Golgi tendon organs or Renshaw feed-back cannot be discounted in the stimulation experiments. Marsden, Merton & Morton (1972) have recently shown that reflex gain does vary systematically with the level of voluntary contraction. One possible explanation of our results is that there are marked differences in the reflex gain used by different subjects doing the same task. High reflex gain would be desirable to maintain a given position accurately, but carries the risk of producing damped oscillations at about 10 Hz such as occur in tremor (Lippold, 1970). An absence of tremor and associated synchronization of motor units would be desirable for producing a finely graded, smooth voluntary contraction. The magnitude of the tremor component near 10 Hz is well known to vary in different subjects and to depend on the level of voluntary effort (Sutton & Sykes, 1967).

The frequency response of motor units studied both during voluntary contraction and by stimulation was well fitted by a linear, second-order model, although differences in natural frequency were observed using the two methods. A second-order model also fits the data obtained from stimulating soleus muscle of the cat (Stein *et al.* 1972), and the natural frequency declines and the damping ratio increases in that preparation as the mean rate of stimulation is increased under isometric conditions. Thus, the difference in rate during voluntary activity (5–10 impulses/sec) and during stimulation (1·7/sec) might account for the observed difference. The frequency response obtained from recording single units measures the extent of the linear correlation between the train of impulses and the tension in the muscle at various frequencies. However, the method cannot distinguish cause and effect. It will measure linear correlations in tension produced by the motor units, *and* any fluctuations in the firing rate of the motor unit which are linearly correlated with the general fluctuations in tension of the muscle. Even though a motor unit does not become entrained to high-frequency fluctuations in tension, its rate of discharge may vary with low-frequency fluctuations. Such an effect could explain the differences observed in the frequency response functions obtained by stimulation and by voluntary activation of motor units.

Using either method, the response of the contractile elements to fluctuations in neuronal firing rate with frequencies near 10 Hz was already about an order of magnitude lower than the response to low-frequency fluctuations. This should be a powerful mechanism for limiting the component of physiological tremor near 10 Hz. Studies on neuronal models in which subthreshold inputs decay exponentially with time (Rescigno, Stein, Poppele & Purple, 1970) indicate that in the absence of neuronal variability, the discharge of neuronal models will always become entrained to cyclic inputs, and show a discharge pattern that will repeat indefinitely. The presence of neuronal variability (Stein & French, 1970; Stein, 1970) tends to disrupt these patterns, but the simplest pattern (i.e. where one impulse is generated per cycle of oscillation) is the most resistant to disruption. Motor units fire steadily over a limited range of rates (approximately 5–20 impulses/sec in our experience). Motor units firing at rates very different from 10 impulses/sec will not easily become entrained to these oscillations. However, motor units firing close to this rate may become entrained. The magnitude of physiological tremor near 10 Hz would then be determined by the number of motor units firing at appropriate rates and the strength of reflex effects. The magnitude would be limited by the resistance of motor units firing at other rates to entrainment by the reflex effects, and the low gain of the contractile elements in muscle at the frequencies found in normal tremor. Further work is required to determine the relative importance of these factors in normal postural tremor.

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