

Neuronal Mechanisms Underlying Physiological Tremor

J. H. J. ALLUM, V. DIETZ, AND H.-J. FREUND

Department of Neurophysiology, University of Freiburg, Freiburg, West Germany

SUMMARY AND CONCLUSIONS

1. Tremor force was recorded during stationary isometric contractions of intrinsic hand muscles of normal subjects. Subjects maintained a steady force level between their thumb and forefinger for 30 s. The force level varied from weak (0.2 kg) to strong contractions (7 kg). These experimental conditions were the same as those in two preceding studies, where single motor-unit activity (14) and the correlation between the discharges of two simultaneously recorded motor units and physiological tremor (11) have been investigated.

2. Two alterations of the power spectra were observed at successively stronger contractions: increase of tremor amplitude and changes in the shape of the power spectrum. At all force levels, the power spectra of tremor force show the well-known decay of tremor amplitude from the lower to the higher frequencies with a local peak at 6–10 Hz. This peak does not show a significant change with respect to frequency when the force level is varied. It is shifted toward lower frequencies in a pathological condition (Parkinsonism) where the recruitment firing rates of the motor units are significantly lower than in the normal.

3. Higher frequencies (greater than 20 Hz) are barely present in the power spectrum during the very weak contractions. They become significant as the contractions become stronger.

4. The steep decay of the power spectrum toward higher frequencies has a similar slope (–43 dB/decade) as the reduction in amplitude of the unfused part of the muscle contractions with increasing stimulus rates (–38 dB/decade). The cutoff of the power spectrum above 25 Hz parallels the achievement of total fusion of muscle twitches above this rate.

5. The results are consistent with the hypothesis that the power spectrum over the range of 6–25 Hz is mainly caused by the unfused

parts of the twitch contractions of motor units firing between recruitment (6–8/s) and total fusion of the twitches (25–30/s). The decline of the power spectrum toward higher frequencies can be explained by mechanical damping, which results from increasing fusion of the twitch contractions. The low-frequency part of the power spectrum is assumed to be the result of the slow force deviations produced by changes in the net output of the motoneuron pool.

6. These assumptions were supported by additional animal experiments where the number and rate of force-producing elements could be controlled. Bundles of ventral root filaments innervating cat soleus and gastrocnemius muscles were stimulated synchronously and asynchronously at a number of different rates. The force output of the strain gauge was recorded, filtered, and analyzed in the same way as the human force records.

7. Stimulation of one nerve bundle at one fixed frequency led to a sharp peak in the power spectrum at that frequency plus peaks of decreasing height representing the harmonics of the stimulation frequency. The height of the peaks decreased at –37 dB/decade.

8. Asynchronous stimulation of nerve bundles at a fixed rate revealed the same peaks and harmonics observed with synchronous stimulation, but their amplitude was reduced as power spread to harmonics and submultiples of the asynchronous frequency.

9. When the rate of synchronous stimulation was increased, the fundamental and harmonic peaks in the power spectrum decreased in amplitude. The fundamental peak decreased with rate at –34 dB/decade. This is consistent with the decrease in individual twitch tensions caused by increasing fusion. Both this decrease and that due to the harmonics alone are approximately equal to the decrease of the human physiological tremor spectrum.

10. Slow modulations in the rate of stimulation caused a smoothing and broadening of the power spectrum, particularly into frequencies lower than the stimulation rate.

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11. These experimental results suggest that the neural and contractile parameters of muscle are reflected in the power spectrum precisely according to the assumptions underlying the hypothesis about the generation of human physiological tremor. Physiological tremor is, therefore, regarded as representing the mechanical envelope of motor-unit activity in the tremor-producing muscle. The presence of physiological tremor in muscles without any synchronization between their motor units (11) shows that synchronization is not the basic mechanism underlying the generation of physiological tremor.

INTRODUCTION

The mechanisms underlying physiological tremor are still a matter of controversy. Several investigators favor the hypothesis that tremor is the result of a rhythmic modulation of the activity of several motor units caused by a servo-loop oscillation in the stretch reflex arc (19, 20, 22, 23, 26, 27, 38, 39, 45, 47). The arguments against this explanation are that tremor rates do not depend on the length of the reflex arc (31–33), that tremor is still present after deafferentation (28, 30) and, as described in this article, that physiological tremor does not consist of one dominant frequency but has a broad spectrum of 1–25 Hz. Only a local peak at approximately 6–10 Hz is imposed on the decline of the force amplitude over frequency. The servo-loop hypothesis implies that there is a synchronization of motor units at one preferred frequency. This has, however, never been shown. Some authors were unable to demonstrate more than chance synchronization between independently discharging units (24, 49). Others observed only a weak synchronization which differed between subjects (34, 35) and seemed to be related to tremor amplitude (17). If present, the synchronization between units is not restricted to a distinct frequency, but is present for the whole range of discharge frequencies (11). Synchronization is restricted to a very short time span (± 3 ms) and has, therefore, been attributed to a common input into the motoneuron pool (46).

In the experiments described here, the tremor force generated mainly by the first dorsal interosseus and adductor pollicis brevis muscles during isometric contractions of different strength was spectrally analyzed. The aim of the present study was to relate findings from the analysis of tremor force to those obtained on the neuronal activities under the same experimental conditions (11, 15). This combined approach applied to tremor generation under natural conditions provides new insights into the

peripheral mechanisms of physiological tremor. For example, motor units in the first dorsal interosseus muscle are recruited with discharge rates of 6–8/s (15). Correspondingly, the local peak of the physiological tremor power spectrum invariably occupies the range 6–10 Hz.

On the basis of this and other similarities between the firing range and fusion properties of motor units and the shape of the power spectrum of tremor force, we propose the hypothesis that the spectrum of tremor force between 6 and 25 Hz represents the mechanical result of the partially fused twitches of motor units. The detailed spectral analysis of tremor force reported in this article is directed toward substantiating this hypothesis. Spectral analysis of tremor force produced at various force levels has been reported by Sutton and Sykes (47). Their data were, however, confined to the frequency range between 0.256 and 12.5 Hz and, therefore, did not reveal all the spectral information.

Experiments were also performed on cats in order to test the hypothesis stated above in a situation where the number of active motor units and their firing rates could be controlled. In addition to substantiating our assumptions, the cat data show that for a steady contraction, frequency components lower than 6/s in the tremor spectrum can be produced by small changes in the firing rates and number of active units.

Our results on the spectral content of tremor force and their relation to the motor-unit properties of the force-generating muscle support the suggestions of Marshall and Walsh (33). They regarded physiological tremor to be the inevitable result of the asynchronous discharge of motor nerve fibers "converted to mechanical ripples by the muscles."

METHODS

Human experiments

Physiological tremor during isometric contractions was recorded from seven normal subjects (six male, one female). Subjects sat, with relaxed arm muscles, in a comfortable chair with arm rests. Attached to the front of the right arm rest were two brackets whose outer surface (3 cm apart) were gripped by subjects between the thumb and forefinger while the rest of the hand was supported. Two synergistic muscles, first dorsal interosseus and adductor pollicis brevis, are the main force generators in this situation.

The force exerted on the forefinger bracket was measured with a DC strain-gauge bridge whose working range was 0–10 kg. The output of the bridge was DC amplified and displayed

to the subjects by means of a voltmeter. Subjects were instructed to maintain a particular voltmeter reading during each trial of 30 s, thus controlling the isometric force level. Recordings were taken at force levels of 0.2–7 kg, with at least a minute's pause between each recording to avoid the effects of fatigue. The maximum force, within a tolerance of 0.2 kg, that each subject could maintain for 30 s, was also recorded. Average maximum force for six subjects was 6.8 kg, standard deviation 0.6 kg. A seventh subject had a maximum well outside this range, 9.5 kg.

A second parallel DC signal from the strain-gauge bridge was high pass filtered (a second-order filter with asymptotic break points at 4.5 and 14 Hz) and amplified to improve resolution of tremor force oscillations in the range 5–30 Hz. Both the filtered signal and the DC signal were stored on FM magnetic tape for later analysis.

Cat experiments

Experiments were performed on six adult cats (2.0–3.0 kg). Initial surgery was performed under halothane anesthesia. After surgery the animals were deeply anesthetized with pentobarbital (35 ml/kg injected intravenously).

The lumbosacral segments L₆–S₂ of the spinal cord were exposed by laminectomy and the animals mounted in a rigid frame immobilizing the spinal cord. The dura was opened and the ventral roots of these segments were cut close to the spinal cord and arranged into small filament bundles. Exposed tissue was covered with mineral oil kept at 36–38°C. Heating pads were used to keep body temperature constant throughout the experiment.

Special clamps were used to fix the femoral bone in order to avoid movements of the hindlimb. The gastrocnemius and soleus muscles were carefully freed from surrounding tissues, leaving the blood supply and the nerves intact. The Achilles tendon was attached in series with a strain gauge (working range 0–1 kg) by a short steel hook. Prior to each experiment the muscle was stretched until the resisting force was 100 g.

Four S₁ ventral root filament bundles in the distal nerve stump were isolated and placed on four pairs of bipolar silver electrodes. Their electrical stimulation elicited small contractions of the gastrocnemius or soleus muscles. Each bundle was independently stimulated via an isolation unit. Stimulation pulses were rectangular, 0.2 ms duration, and occurred at controlled rates between 1 and 30/s. Stimulus strength at 1 Hz was usually adjusted to achieve a twitch amplitude of 30 g.

The force output of the strain gauge was recorded, filtered, and analyzed in the same way as the human force records.

Data analysis

Records of high-pass filtered tremor force were transferred from FM magnetic tape to a digital computer (IBM 1130) via an analog to digital converter set to sample every 5 ms. To determine the force amplitude at each of a number of frequencies, sections 18.5 s long from the force records were Fourier analyzed with the digital computer for their spectral content. The procedure for Fourier analysis was as follows:

1) Line-frequency noise and FM-tape noise in the data were removed by passing it forward and backward in time through a Butterworth digital low-pass filter (18). Over the forward pass the filtering order is taken successively at points $t = 0, t = \Delta t, \dots, t = n\Delta t$, and over the backward pass the order is $t = n\Delta t, t = (n - 1)\Delta t, \dots, t = \Delta t, t = 0$; where Δt is sampling interval. The rationale for the two time passes is to cause zero phase shift yet double the magnitude response of the filter. The digital filter gain was flat until 30 Hz, at which point the gain was down 0.92 dB, at 50 Hz attenuation was –39.6 dB.

2) The power spectra were calculated at integer frequencies of 0.054 Hz from the autocorrelation function of the filtered data with mean removed. For this purpose the following relationship (4) was used:

$$\hat{G}_x(f) = \frac{1}{f_c} \left[\hat{R}(0) + 2 \sum_{r=1}^{m-1} \hat{R}(r\Delta t) \cos\left(\frac{\Pi r f}{f_c}\right) + \hat{R}(m\Delta t) \cos\left(\frac{\Pi m f}{f_c}\right) \right]$$

Where $\hat{G}_x(f)$ is an estimate of the true power spectral density function and is defined for integer frequencies ($n\Delta f$, where Δf is 0.054 Hz) in the range DC to an upper limit dictated in the current experiments as 30 Hz. In the equation above $\hat{R}(r\Delta t)$ is the estimate of the autocorrelation function at lag r , m is the maximum lag number (400 was used), and f_c is one-half of the sampling frequency, i.e., 100 Hz. The signals analyzed by the computer were a set of samples of finite duration, i.e., a truncated data series. Thus, the estimate of the autocorrelation function is also truncated and $\hat{G}_x(f)$ is indirectly affected. An estimate of this artifact is gained from an examination of the true value of $\hat{G}_x(f)$ for a sine wave which is an impulse function at the sine wave's frequency. Truncation of the data yields a broadened pulse (or main lobe) for $\hat{G}_x(f)$ at the sine-wave frequency and adds an infinite number of smaller side lobes. Half of these side lobes are negative and introduce an erroneous power spectrum result (or leakage) equal, at the maximum, to about one-fifth of the height of the main lobe. To suppress this artifact the autocorrelation esti-

mates were multiplied in the time domain by a function known as a Tukey window (6). The effect of this data window on the spectrum is to increase the bandwidth of a theoretical impulse in the frequency domain to 0.0606 Hz while leakage due to side lobes is attenuated -21 dB with respect to the main lobe (21).

A typical power spectrum which results from our high-pass filter technique is shown in Fig. 1. Increased resolution in the range 5–30 Hz is observed; for comparison, a spectrum of the same tremor recording without high-pass filtering is illustrated.

RESULTS

Human experiments

CHARACTERISTICS OF TREMOR FORCE DURING STEADY ISOMETRIC CONTRACTIONS. All tremor records were obtained while the subjects tried to maintain a constant isometric force level by pressing against a force transducer arranged between their thumb and forefinger. When this force is measured with high-

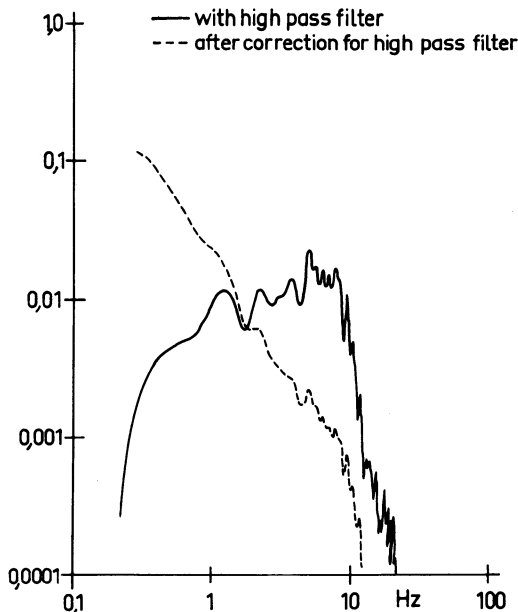


FIG. 1 Effect of high-pass filter on a power spectrum. The solid line shows a spectrum of a single record of physiological tremor at 0.7 kg after high-pass filtering. Increased resolution of frequencies above 6 Hz is evident. The ordinate for this plot gives amplitude squared at each frequency in arbitrary units. The spectrum obtained without the filter is shown by the dotted line. For this plot units are arbitrary units of amplitude normalized with respect to the filtered data at 7.0 Hz. The amplitude plot falls off at approximately -30 dB/decade between 1 and 10 Hz. A similar falloff was obtained by Sutton and Sykes (47).

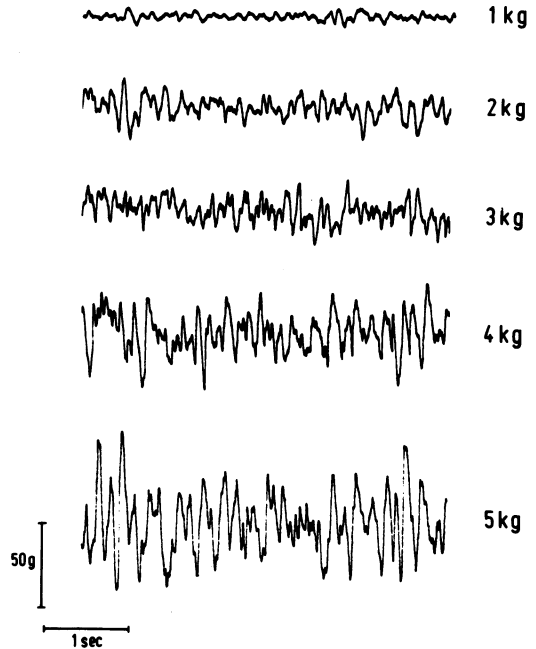


FIG. 2 Examples of physiological tremor recordings at five different force levels. An increasing amplitude of tremor in the successive traces as force increases can be observed from top to bottom.

gain AC amplification, force deviations are seen which show the same characteristics as position tremor or other tremor forms.

Some examples of tremor force deviations during isometric contractions of increasing strength are shown in Fig. 2. The amplitude of the tremor increases at successively stronger contractions. No single regular frequency is represented in these waveforms, but a number of frequencies. The spectral content of the records, such as shown in Fig. 2, is plotted in Fig. 3 for five force levels. The spectrum shows that tremor has a broad frequency distribution between 1 and 25 Hz and a local peak which remains between 6 and 10 Hz over all force levels. Each of the spectra shown in Fig. 3 falls off steeply above 10 Hz, leaving negligible power in the spectrum above 25 Hz. The spectral content of tremor force produced in our experimental conditions resembles closely that measured during complex hand (47) or position tremor (19).

Because tremor frequencies and motor-unit firing rates in the range 6–25 Hz are of current interest, most of our tremor spectra are shown with linear abscissa (Fig. 3) rather than the normal logarithmic abscissa (Fig. 1). A logarithmic scale would unduly compress the meaningful range of interest. In addition, averaged data were used to reveal the trends in ampli-

tude and spectral content more clearly than the individual tremor spectra.

INFLUENCE OF ISOMETRIC FORCE ON TREMOR AMPLITUDE. Tremor amplitude increases with increasing isometric force. Figure 2 shows that this is the case for the original waveforms, and Fig. 3 shows this effect more clearly after records from several subjects were spectrally analyzed and averaged. When the amplitude at the peak of power spectrum is examined it increases at an approximately linear rate with force. The change of tremor amplitude squared with isometric force is shown in Fig. 4B for a fixed frequency in the power spectrum (7.5 Hz). The best power-law relationship between amplitude squared and force has an exponent of 1.3 ($r = 0.85$). This suggests that tremor amplitude is almost linearly related to isometric force. A linear relationship between twitch tension of motor units and their isometric threshold force of recruitment has been observed by Milner-Brown and co-workers (36). A similarity to underlying mechanisms is implied by these findings, namely that tremor amplitude is correlated with the twitch amplitude of newly recruited units.

The amplitude variability between subjects,

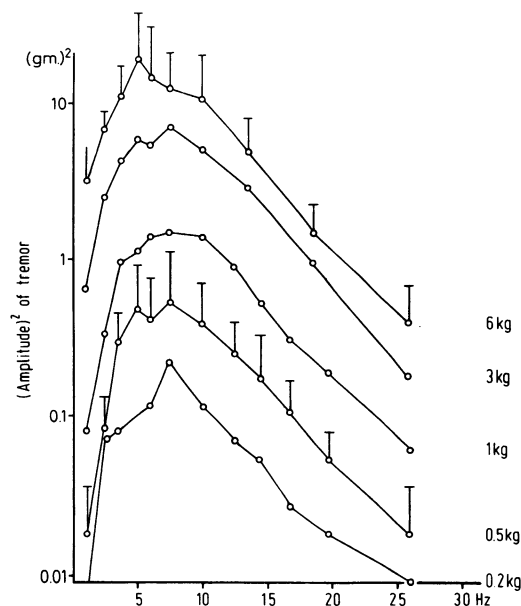


FIG. 3. Average tremor spectra at five different force levels. Single spectra at each force level shown were taken from six subjects of approximately equal physical strength (average maximum maintained force 6.8 ± 0.6 kg) and then averaged. Every plotted point represents an average value for a frequency bin whose edges were placed equidistant between the plotted points. Standard deviations of tremor (amplitude)² are shown by vertical bars for 6 and 0.5 kg.

as measured by the standard deviation at each frequency, is marked by vertical bars in Fig. 3 for two force levels. Standard deviations of the size shown normally allow a significant separation between average spectra at force levels 2 or 3 kg apart. Because the tremor experiments on one subject were not completed on the same day, day to day variations in tremor amplitude were examined. The standard deviations for repetitive measurements of single subjects were calculated from the tremor records taken on seven successive days. These standard deviations are approximately 50% smaller than those measured between subjects, even at high force levels.

INFLUENCE OF ISOMETRIC FORCE ON DOMINANT TREMOR RATE. The dominant tremor rate is represented by the local peak in the power spectrum. With respect to the remainder of the spectrum, the peak is not prominent (Fig. 1). The frequency dependence of this peak on the strength of the contractions is shown in Fig. 4A. The tendency for a slight shift of the peak to lower frequencies with increasing force is not significant ($t = 0.68$). This has already been observed in previous studies (7, 8, 19, 20, 26, 27, 31, 47). The relative stability of the dominant tremor rate stands in contrast to the increase in the discharge rates of motor units as force increases. According to our hypothesis, the peak of the power spectrum is produced by the motor units with the largest unfused twitches and with discharge frequencies close to recruitment frequencies. The largest units are the most recently recruited motor units, and their onset firing rates are approximately the same irrespective of their threshold force of recruitment (15, 36, 37). Further evidence for this correspondence between motor-unit recruitment frequencies and the frequency of the power spectrum peak comes from a pathological condition. It has recently been observed that in Parkinson's disease the motor units start firing at rates of 3–5/s, which are significantly lower than in normals (13). Correspondingly, the dominant tremor rate of 3–5 Hz for these patients is abnormally low, as shown by the example of a Parkinsonian tremor spectrum in Fig. 5. Also, the peak in this spectrum is considerably larger than the peak in normals, and reflects pathologically greater synchronization (12).

INFLUENCE OF ISOMETRIC FORCE ON SPECTRAL CONTENT OF TREMOR. The power spectra of tremor force recorded for weak contractions of 0.2 and 0.5 kg from six normal subjects have no power greater than 0.04 g^2 (Fig. 3) above 15 Hz. During stronger contractions (3 and 6 kg, for example) the spectra show successively greater amplitudes of the high-

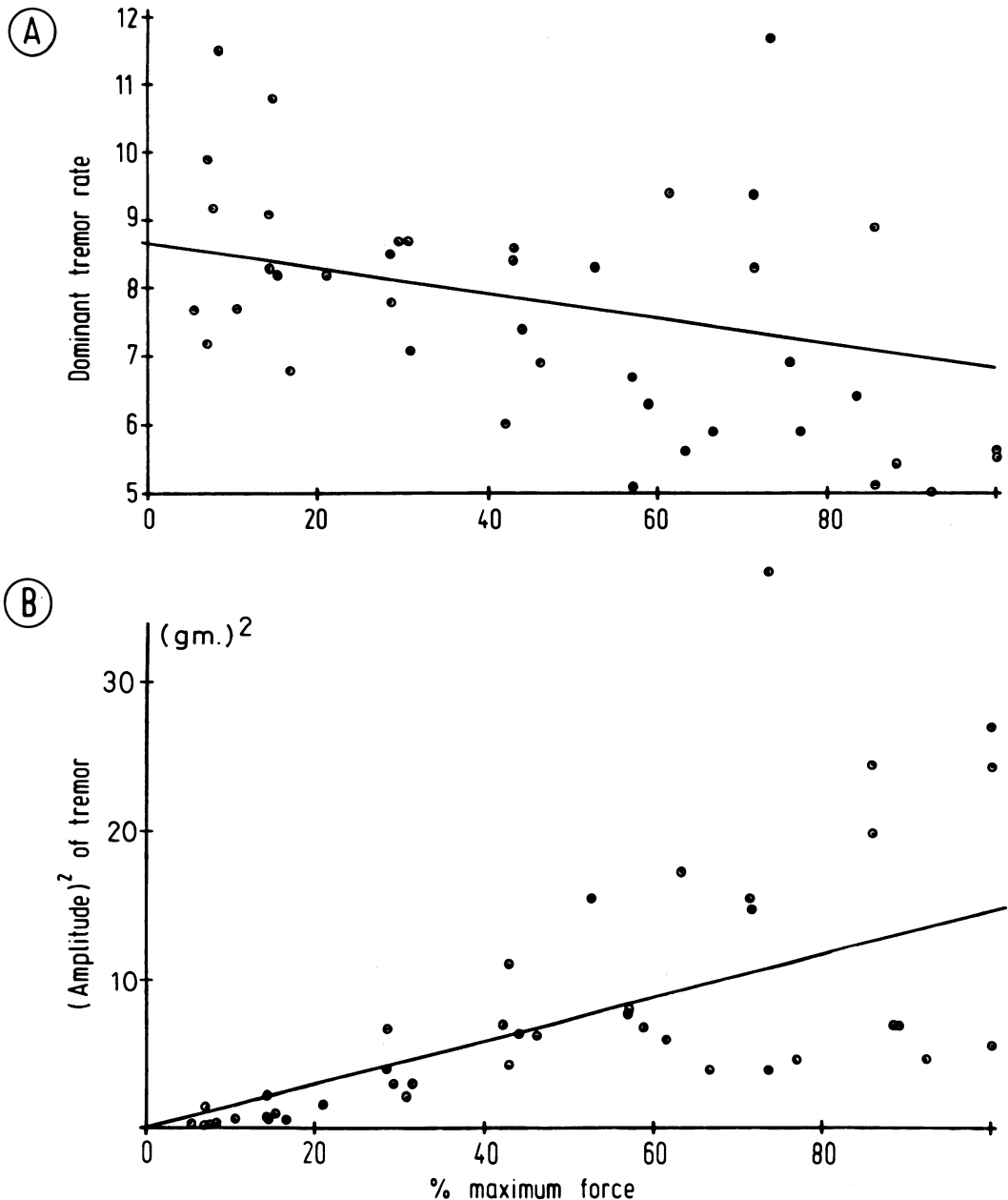


FIG. 4. Influence of force on dominant tremor rate and amplitude at 7.5 Hz. *A*: plot of dominant tremor rate versus isometric force level expressed as a percentage of the maximum isometric force. The dominant tremor rate was taken as the peak of the power spectrum. The straight line is the best linear fit to data points. A slight but insignificant decrease in the dominant rate occurs as force increases ($r^2 = 0.104$). The average dominant tremor rate at 50% maximum force is 7.8 Hz. *B*: relationship between the amplitude squared of tremor at 7.5 Hz and force is shown. A power curve regression yields an exponent of 1.3 ($r = 0.85$) and indicates a near-linear relationship between tremor amplitude and force (exponent 1.14).

frequency components. The difference in amplitude at 6 and 0.2 kg is somewhat larger (41%, expressing differences as a ratio) for higher frequencies (ca. 15 Hz) than for lower frequencies (ca. 8 Hz). This slight increase in the

high-frequency components at higher force levels is much less pronounced than one might expect from the marked increase in the number of motor units firing at higher rates when force increases.

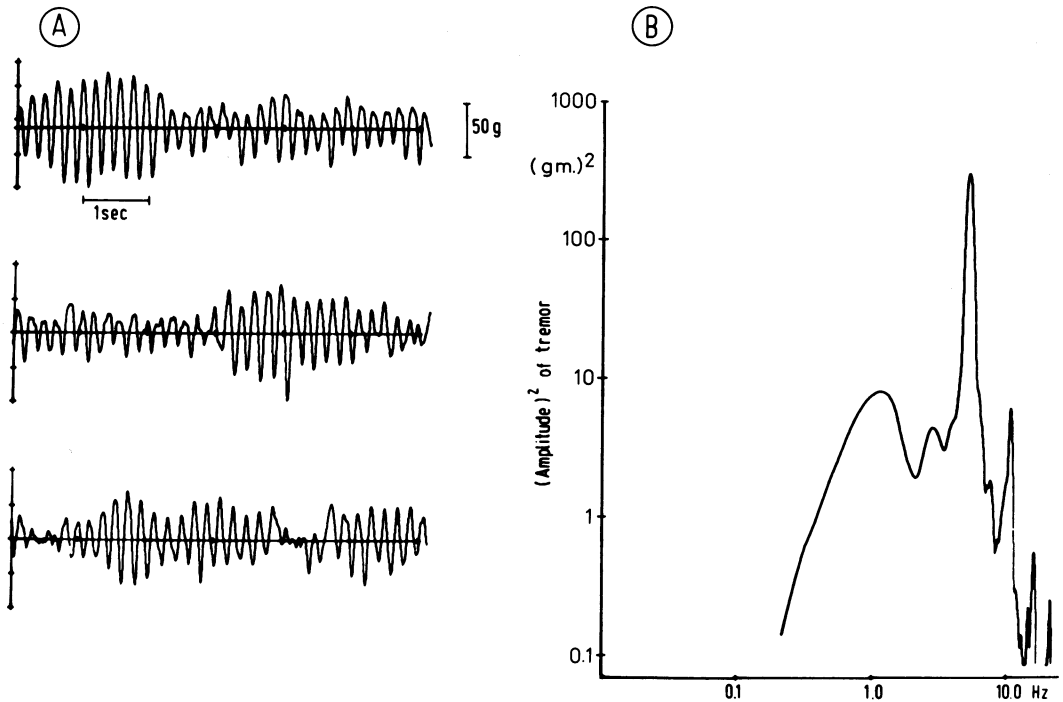


FIG. 5. Tremor recorded from a Parkinsonian patient. *A*: force recorded in three traces, each continuous with the trace above. A consistent beating at 5 Hz is observed. The spectrum for the record is shown in *B*. Peaks at 5 Hz and harmonic frequencies thereof are present. Isometric force level was 3 kg.

Negligible power is observed in the power spectra of Fig. 3 above 20 Hz, even though during strong contractions more units fire at higher than at lower rates. The reflection of this tendency to higher firing rates in the frequency analysis of the contractile force will be obscured by the decreasing amplitude of the twitch contractions, that is, by mechanical damping (Fig. 6). This tendency is also limited by the maximum firing rate of motor units, 25/s (15); 25 Hz is also the limit beyond which high firing rates are totally obscured in the

tremor spectrum as only the unfused parts of twitch contractions can contribute to the high-frequency part of the spectrum. The frequency-response characteristics of muscle fibers to sinusoidal stimulation of ventral root fibers also show this mechanical damping (3, 29, 44).

To examine the extent to which the decay of the power spectrum of tremor force can be attributed to mechanical damping characteristics in our experimental condition, force records for the same muscles used for our tremor experiments were examined during supramaximal elec-

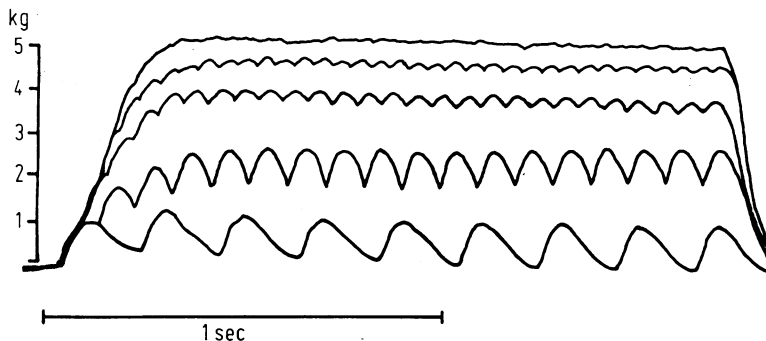


FIG. 6. Twitch contractions of first dorsal interosseus and adductor pollicis brevis muscles. Each contraction curve was obtained by supramaximal stimulation of the ulnar nerve at rates of 5, 10, 16, 20, and 25/s. As stimulation rate increases the individual twitch contractions become more fused.

trical stimulation of the ulnar nerve at different rates. Figure 6 shows that the contractions become more fused at higher stimulation rates as the amplitudes of individual twitches decline. The same is true for stimulation of single human motor units (9, 35). The decrease in amplitude of the unfused parts of the twitch contractions has a slope of -38 dB/decade for stimulation rates between 10 and 16/s (average of four subjects), and closely resembles the decline of the power spectrum in this frequency range, -43 dB/decade (average of six subjects). This latter value has been corrected for the effect of our high-pass filter, uncorrected the decline is -29 dB/decade. The mechanical effects of twitch contractions were examined in the cat with similar results. A falloff of -34 dB/decade is observed in the range between 10 and 20/s (see below).

Stimulation of the whole muscle is only a rough estimator of the twitch contraction properties of single motor units. This is because the motor units of the first dorsal interosseus muscle show almost a threefold range of contraction times (36). Although the negative correlation between contraction times and the threshold force of recruitment for motor units is only weak (36), these alterations in fusion properties will differentially influence the damping characteristics at each force level. Correspondingly, this could partially account for changes in the decay of tremor power spectra with force. This factor can only be relevant, however, for weak efforts where the number of units recruited varies considerably with the force level. Since 85% of the units are already active at 20% of the maximal voluntary effort, the differences in contraction times will be of little impact for stronger contractions since the force increase is mainly achieved by firing-rate modulation (5, 15, 37). It was, therefore, assumed that the error introduced by different fusion properties of motor units, because contraction times change with force, is minimal for the force range of interest.

Once the effect of mechanical damping on the power spectrum is known, other factors contributing to its shape can be explored. After subtracting the mechanical damping falloff of -38 dB/decade, the power spectrum has a less steep appearance (Fig. 7). In contrast to the original power spectrum, this frequency distribution provides a better estimate of the proportion of units active at particular firing rates. For example, in the range of 15–20 Hz, the corrected power spectrum for 5 kg tends to rise slightly with respect to that for 3 kg. This is an indication that the number of units with firing rates in this range have proportionally increased. Similarly, if the curves are examined between 6 and 10 Hz, the 5-kg corrected spec-

trum falls off more rapidly than the 3-kg spectrum in accordance with decreased number of units recruited at higher force levels. Thus, the corrected power spectrum slopes change with force, as would be expected from the recruitment and rate-coding properties of human motor units (15, 36).

To obtain a measure of the change in the power spectrum slope as isometric force increases, we compared the slopes of each subject's power spectrum in a low firing rate domain (5.5–8.5 Hz) and a high firing rate domain (11.5–15.5 Hz). The results are shown in Fig. 8. The two slopes show trends with increasing force, which would be expected if power spectra contain information about units entering the high-frequency domain and leaving the low-frequency domain. That is, the low firing rate domain slope becomes steeper and the high firing rate domain slope becomes flatter with increasing force. After correction for our high-pass filter and the mechanical effect of fusion, the slopes always fall off, i.e., have negative values. Figure 8 implies changes in the rate modulation of already recruited units and in the number of newly recruited units with increasing force, which are in agreement with similar observations in cat muscles (10). The consistent finding is, however, the persistence of the decay from low toward high frequencies at all force levels, even after correction for mechanical damping. This implies that another force-generating mechanism may be involved. A description of this mechanism will be pursued in the discussion.

In order to obtain supplementary evidence as the question of whether or not motor-unit activities are reflected in the muscle force power spectrum as the mechanical envelope of twitch contractions, thus confirming the assumptions made for the human tremor data, additional experiments were performed on cat muscles. In these experiments the number and rates of the force-producing elements could be controlled.

Cat experiments

STIMULATION OF BUNDLES OF VENTRAL ROOT FILAMENTS OF CAT TRICEPS SURAE MUSCLES AT SAME RATE. Stimulation of a bundle of ventral root filaments at a low rate produces unfused or partially fused twitch contractions. When a series of twitch contractions are Fourier analyzed it is to be expected first, that the fundamental peak amplitude in the spectrum at the stimulation frequency has a value representative of the twitch contraction amplitude and second, that harmonics of the stimulation frequency also appear in the spectrum (Fig. 9A). The harmonics represent the non-sinusoidal aspects of the twitch contraction.

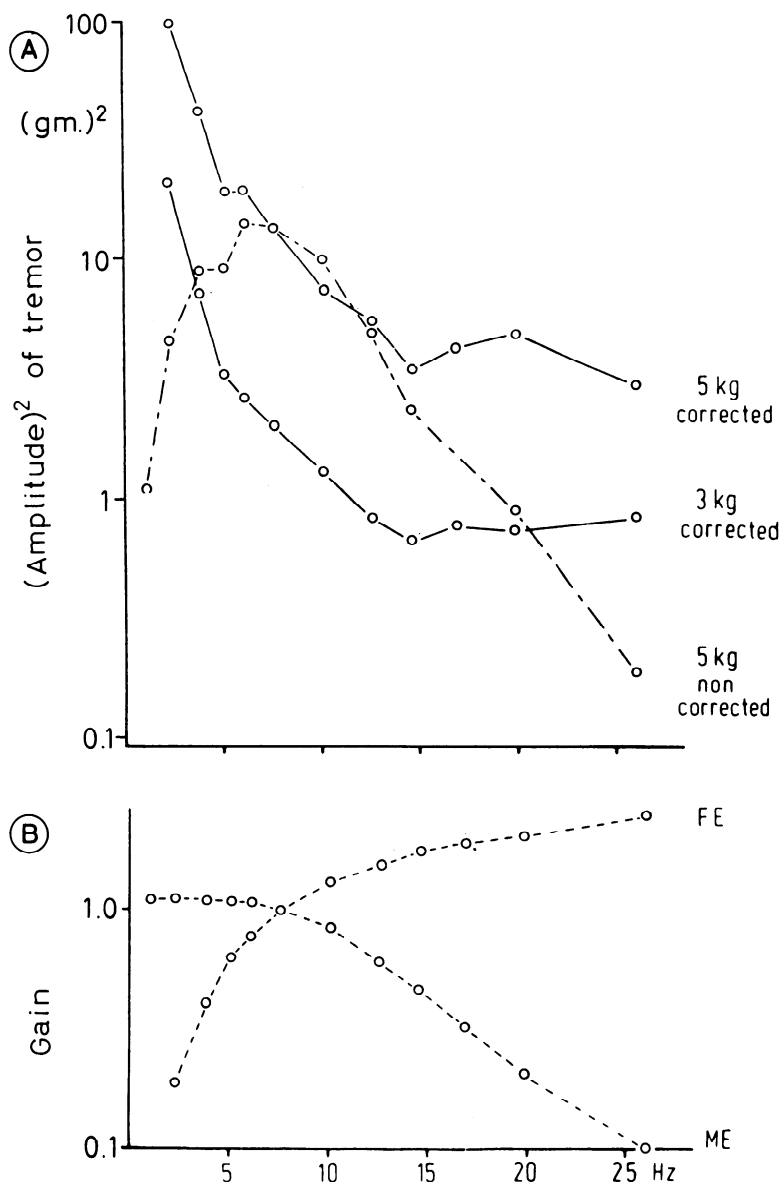


FIG. 7. Tremor plots corrected for the mechanical damping of motor units. A: two plots labeled 5 and 3 kg corrected, show physiological tremor after correction for high-pass filtering and the mechanical reduction in twitch amplitudes as a unit's firing frequency increases. These plots thus more nearly reflect the proportion of units firing at different frequencies. Another plot shows the original average spectra (seven recordings from the same subject over 7 successive days) and is labeled 5 kg uncorrected. B: curve labeled ME shows the effect of mechanical damping. To obtain the amplitudes required for this plot four subjects were stimulated using the identical procedure by which Fig. 6 was obtained. Measurements were taken when the twitch-contraction amplitudes remained constant, and then measurements were normalized to the value at 7.5/s. The gain curve for the high-pass filter is shown by the curve FE; again values are normalized to that at 7.5 Hz.

As the stimulation rate is increased the twitch contractions become more and more fused and have smaller amplitudes. This falloff of peak amplitude with the forced firing rates of the units has a slope of -34 dB/decade. This result is inevitable from the frequency response charac-

teristics of the cat triceps surae muscles, which decline according to a second-order system (29, 44). The slope is similar to the slope observed for physiological tremor spectra (-43 dB/decade) over the corresponding frequency range.

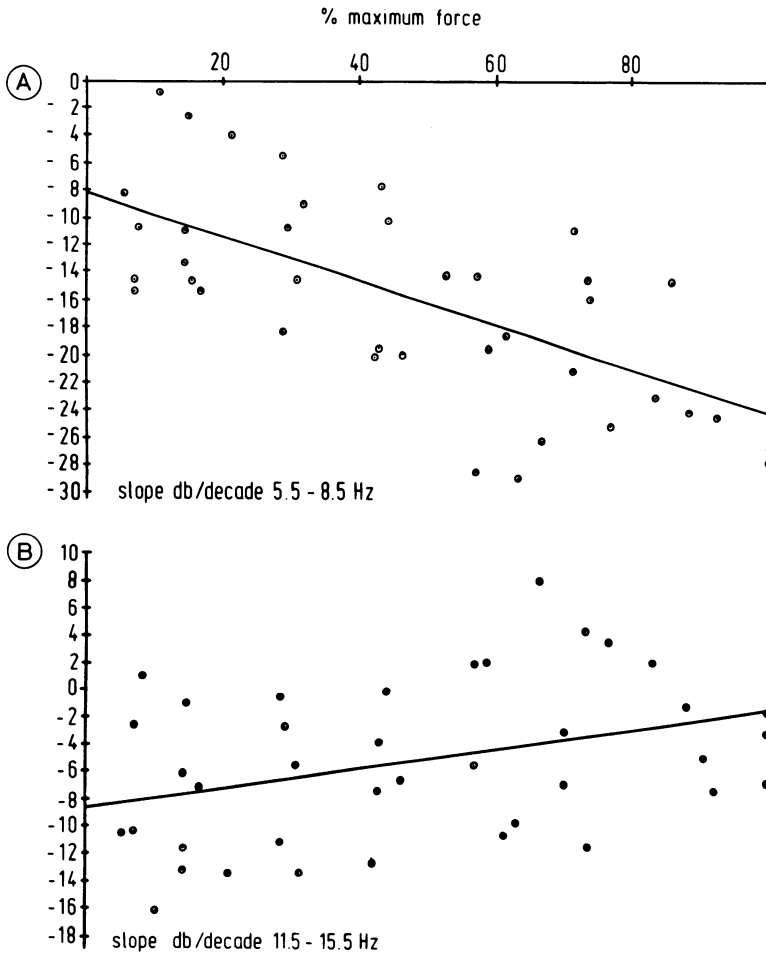


FIG. 8. Influence of force on tremor spectrum slopes in low-frequency and high-frequency domains. From the tremor spectra the slope (in decibels per decade) was measured in a low-frequency domain, 5.5–8.5 Hz (A), and in a high-frequency domain, 11.5–15.5 Hz (B). The change in these two slopes is plotted against percentage maximum force for six subjects. Straight lines in each graph represent the best linear trends through data. In A the correlation coefficient is 0.69 (significant at the 0.1% level) and in B, the coefficient is 0.4 (significant at the 1% level).

Of interest is the falloff of the harmonics with increasing rate of stimulation. The falloff has a slope of -37 dB/decade, again almost parallel to the physiological tremor slope. When the stimulation rate is increased, the slope of the harmonics is marginally steeper; however, their amplitudes decrease in conjunction with the decrease in the amplitude of the fundamental frequency.

Asynchronous or distributed stimulation of several nerve bundles has been used to smooth the ripples in the force record due to individual twitch contractions (42). To obtain the same effect, four nerve bundles previously stimulated synchronously were stimulated asynchronously at the identical rate and magnitude. During the asynchronous stimulation a slow modulation of

the force record occurs as a consequence of variations in chance synchronization between stimulation channels (Fig. 9B, upper part). These low-frequency effects are reflected in the power spectrum (Fig. 9B). The spectra shows a clear spread of power into frequencies below the units' stimulation rates as the power of the fundamental peaks and harmonics is reduced.

STIMULATION OF BUNDLES OF VENTRAL ROOT FILAMENTS AT VARYING RATES. In natural conditions, the firing rates of motor units vary slightly even during steady isometric contractions (17, 24). In order to examine the influence of such variations on the force power spectrum, the stimulus rate of one filament bundle was kept constant at 5.2/s, while the stimulation frequencies of the other three bundles were

slowly varied by approximately 3/s about their mean rates. Thus, the mean rates of 7.2, 11.6, 16.1/s were changed 4 and 10, 8 and 14, and 13 and 19/s, respectively. The result for records which have been high pass filtered and Fourier analyzed are shown in Fig. 9C. The 5.2-Hz peak due to the one filament bundle with constant rate is preserved in the figure while peaks due to the mean rate of the other bundles are smoothed. In addition, there is a prominent increase in other frequency components when the stimulus rate is varied. The total increase in the low-frequency components is, however, obscured by our high-pass filter technique. When a DC record is Fourier analyzed, the enhancement of low-frequency components is clearer (Fig. 9D). An even greater augmentation of

the low-frequency part of the spectrum can be obtained by switching the stimulation to one filament bundle on and off, imitating a change in the number of active units in a muscle.

Although only four partially fused twitch contractions produced the power spectrum shown in Fig. 9C, there is a resemblance (Fig. 7) to the power spectrum of tremor force obtained during steady voluntary contractions of human hand muscles.

DISCUSSION

On the basis of the results obtained, we propose the hypothesis that the power spectrum of physiological tremor originates from two different force-generating mechanisms of muscle;

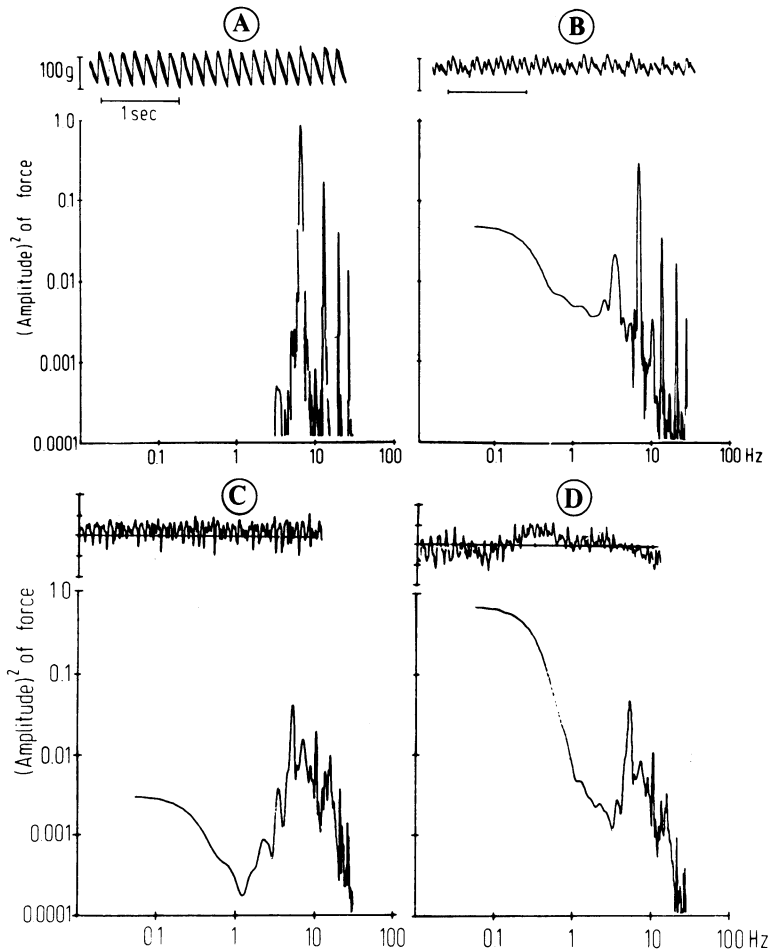


FIG. 9. Power spectra of the force produced by stimulation of four ventral root bundles. In A, all bundles were stimulated synchronously at 6.5/s, and in B the four bundles were stimulated asynchronously at the same rate. For asynchronous stimulation, additional components below 6 Hz are seen. The spectrum shown in C results from stimulating bundles at 5.2, 7.2, 11.6, and 16.1/s, with a 3/s modulation imposed on the latter three rates. In D the same record as C was analyzed but without the force record being high pass filtered. Part of each force record spectrally analyzed is shown above the respective spectrum.

one associated with low frequencies, the other with high frequencies.

The low-frequency part (below 6 Hz) of the power spectrum is produced by the slow force variations. We assume that these slow changes of the net activity of the whole motoneuron pool involve two processes. First, slow changes in firing rate and second, changes in the number of active units. These two processes produce more force than the unfused parts of the twitch contractions of single motor units. (Compare low- and high-frequency parts of the 5-kg trace in Fig. 7.) This has also been shown for the force records obtained when efferent nerve bundles are stimulated (Fig. 9D).

The high-frequency part (above 6 Hz) of the power spectrum is produced by the unfused parts of the twitches of motor units firing at different rates. This frequency range of the power spectrum corresponds to the range of firing rates between recruitment (6–8/s) and obvious fusion of the twitch contractions of the motor units (>25/s). The sharp falloff and low amplitude of the power spectrum at about 25 Hz corresponds to the fusion frequency of the motor units and indicates that higher firing rates, if they exist, are not functionally important for stationary isometric contractions.

The crucial assumption underlying this hypothesis is that the net changes of the motor-unit pool activity and of the single-unit twitch contractions really lead to the appearance of corresponding spectral components in the power spectrum. Evidence for this was presented by the cat experiments.

The first assumption to be tested in the cat experiments was that the rate of the motor-unit twitch contractions can be recognized from the appearance of a corresponding frequency component in the power spectrum. This was confirmed from the results for stimulation of a single ventral root filament bundle. The power spectrum of the corresponding force record always showed a sharp peak at the frequency of stimulation.

Our second assumption implied that the decay of the physiological tremor power spectrum over the normal firing range of motor units, 6–30/s, predominantly results from the decreasing amplitude of each motor-unit's twitch contraction as mechanical fusion becomes increasingly effective. The power due to harmonics decreases with frequency at approximately the same rate as that due to the mechanical effects of fusion.

Physiological tremor power spectra do not contain several individual peaks, but a single broad peak. Our third assumption postulated that asynchronous firing of motor units would cause part of this broadening. Whereas the peaks representing the stimulation frequency

and the harmonics thereof are evident in both conditions of synchronous and asynchronous stimulation, it is over the remainder of the spectrum that differences are observed. Corresponding to asynchronous stimulation, a smoothing of the force record and slow force modulations occur. These are represented by the appearance of significant amplitudes below 6 Hz in the tremor spectrum.

Our last assumption, basing the shape of tremor spectra on the normal firing characteristics of motor units, referred to small rate modulations of already active units. These modulations were assumed to cause large alterations in the low-frequency part of the spectrum (below 6 Hz). When three of four already asynchronously stimulated ventral root bundles are given small rate modulations, large, low-frequency amplitudes appear in the spectrum.

For these cat experiments only four ventral root bundles were stimulated, producing four summated twitch contractions. Human physiological tremor spectra have a smoother profile than we were able to produce because of the large number of asynchronously discharging units with a range of twitch-contraction amplitudes. Nevertheless, by examining the effect of stimulation rate, synchrony, modulation of basic rate, and the number of twitch contractions applied to cat triceps surae muscle, we have shown that each of these effects contribute in a characteristic way to the shape of the power spectrum. This "mimicking" of neural and contractile events in the force output of a muscle occurs according to the assumptions underlying our hypothesis on the generation of physiological tremor.

Once such a relationship between neural activities and their appearance in the power spectrum is established, the hypothesis that the same relationship underlies human physiological tremor can be tested as described in the RESULTS section. The changes of amplitudes and spectral content of the power spectrum associated with rising force levels were described. These changes showed a close correspondence to those of the motor-unit activities.

In our experiments on human tremor there was always an increase of tremor amplitude with rising force. This increase was consistently more pronounced for the higher frequency components (>15 Hz). This relative gain of the higher frequencies was clearly disclosed when the power spectra were corrected for mechanical damping (Fig. 7). The changes of the power spectra with rising force indicate that tremor force is generated by an increasing number of motor units that fire at higher rates.

Additional weight to the assumed correspondence between firing rates and the shape of the

tremor power spectrum is given by data from a pathological condition, Parkinson's disease, in which the peak of the tremor spectrum and motor-unit firing rates at recruitment occur at lower frequencies than in physiological conditions. Further evidence comes from observations of eye muscles for which both motor-unit discharge and tremor rates are strikingly different from those of skeletal muscles. In the cat, eye motor units commence firing at about 70/s and achieve fusion at rates above 150/s (25). Human eye muscles have motor units with similar firing rates (43, 50). It is, therefore, to be expected from our hypothesis that the tremor rates are correspondingly higher. The microtremor of human eye muscles is indeed in the range 70–150 Hz (1, 2).

An exact determination of the relationship between the neural activities and their reflection in the physiological tremor power spectrum is not possible for two reasons. The first is the lack of information about the actual motor-unit parameters in a particular experimental condition: contraction amplitudes, contraction times, number of units active, motor-unit firing rates. The second is our lack of knowledge about the power generated by each of the two tremor-generating mechanisms.

The changes in the number of units active and in the firing rates of the units already recruited are assumed to represent the neural basis for slow force variations generating the low-frequency part of the spectrum. It is probable that this low-frequency mechanism extends beyond 6 Hz, but with low power. In this case, physiological tremor in the frequency range above 6 Hz would be produced by the two mechanisms. The local peak above 6 Hz then represents the frequency beyond which the second mechanism is added to the first. This is schematically illustrated in Fig. 10. The low-frequency force generator is represented by the hatched area, and the high-frequency force generator, representing the unfused parts of the motor-unit twitch contractions, is represented by the dotted area. This scheme only serves to illustrate the basic principle and does not provide any information about the actual power provided by each of the two mechanisms.

Such an overlap of the two mechanisms could also explain why the local peak at 6–12 Hz is preserved at strong contractions. Even after correction for mechanical damping, the power spectra still show a decay from low toward high frequencies. This contrasts with the larger proportion of motor units firing at higher rates if the contractions are strong. The overlap of the two tremor-generating mechanisms illustrated in Fig. 10 could account for this decay.

The results on asynchronous ventral root stim-

ulation (Fig. 9B) confirm that some power is also spread from the high-frequency generator into the low-frequency range. This is not shown in Fig. 10.

In addition to the reasons discussed above, two other factors contribute to the preservation of the 6- to 10-Hz peak with rising force even when most units fire at higher rates: 1) the increase of the twitch-contraction amplitude with the recruitment threshold of the unit (9, 35)—the fewer units recruited at higher force levels produce a much larger amount of force as compared to the greater number of low-threshold units; 2) the poor firing rate modulation of the high-threshold units (5, 15, 40, 41, 48)—this implies that the units contributing the largest twitch contractions remain in a firing range close to that of recruitment for a considerable force range.

The power spectrum of physiological tremor appears to be the direct result of motor-unit activity and does not depend on the presence of any synchronization between motor units. The amplitude at a particular frequency relative to that of other frequencies is, however, determined by the synchrony of motor-unit discharges. For physiological tremor, controversial results have been obtained with respect to the question as to whether synchronous discharges are a relevant tremor-generating mechanism or not. Taylor (49)

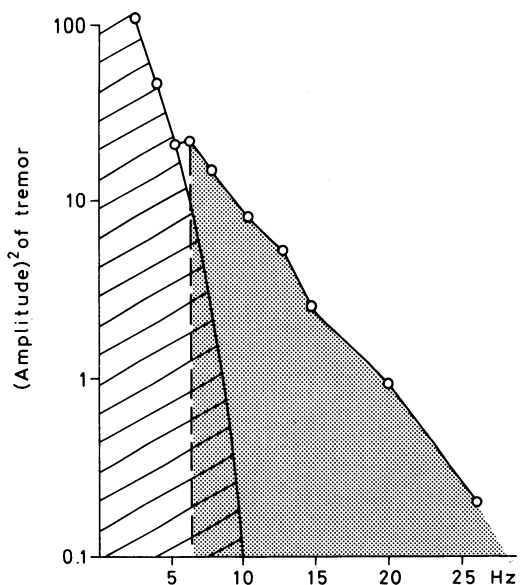


FIG. 10. Schematic illustration of the tremor-generating mechanisms. The hatched area represents the part of the power spectrum which is produced by the force variations due to changes of the net activity of the whole motoneuron pool. The dotted area is produced by the unfused parts of the twitch contractions of single motor units.

has concluded that tremor is the result of chance synchronization of randomly discharging units. Kranz and Baumgartner (24) did not observe a more than random synchronization between units. More than random synchronization was observed in some normal subjects but was not found in others (11, 35). Subjects with trained muscles always produced more than random synchronization (34). Dietz and co-workers (11) observed a significant positive correlation between the amount of synchronization and tremor amplitude.

If synchronization between motor units is present, it extends only over a very short time span (± 3 ms) (11). A similar "short-term synchronization" has been observed in respiratory muscles of the cat, which was attributed to a common input into the motoneuronal pool (46). This assumption is further supported by the observation that the synchronized discharges were present between the units irrespective of their firing rates (11). Therefore, there is no evidence for motor units to follow a preferred "oscillation frequency." This lack of a preferred frequency when units are synchronized has also been observed by Elble and Randall (14).

The presence or absence of synchronous discharges changes the amplitude and shape of the power spectrum of tremor but does not determine the presence or absence of tremor itself.

Physiological tremor is a necessary byproduct of muscle activity. As demonstrated in a preceding study, subjects with weak physiological tremor do not show any synchronization at all (11). Nevertheless, they do have physiological tremor. If synchronization is present, it is only a weak short-term synchronization, which is not restricted to a certain range of firing rates. This short-term synchronization is compatible with the hypothesis of a common input into the motoneuron pool, but is not compatible with an oscillation at a preferred frequency. However, oscillation at one frequency is clearly the characteristic feature of pathological tremor.

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Present address of J. H. J. Allum: Institute for Brain Research, University of Zürich, CH-8029 Zürich, Switzerland.

Present address of H.-J. Freund: Dept. of Neurology, University of Düsseldorf, D-4 Düsseldorf, West Germany.

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