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OSCILLATION IN THE STRETCH REFLEX ARC AND THE ORIGIN OF THE RHYTHMICAL, 8–12 C/S COMPONENT OF PHYSIOLOGICAL TREMOR

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SUMMARY

1. A brief downward, stepwise displacement applied to the outstretched finger gives rise to a train of approximately sinusoidal movements of it, lasting often more than 1 sec. The frequency of these waves is the same, in any one subject, as that of physiological tremor.

2. The oscillations are regular in form, and bear a constant phase relation to the applied displacement; they can be summated using an averaging computer (Biomac 1000) triggered by the mechanical stimulus.

3. The oscillations are altered in the same way as is physiological tremor by a number of factors. Cooling the arm before recording lowers the frequency, warming raises it, while the application of an arterial cuff decreases the amplitude and tends to elevate the frequency. These factors have effects of similar magnitude on both the oscillations and the tremor.

It thus appears highly likely that the waves produced by a mechanical input and physiological tremor waves are due to the same process, namely oscillation in an underdamped servo-system.

4. The oscillation is not due simply to the mechanical, die-away resonance of the finger, because bursts of muscle action potentials can be recorded in phase with the finger movements both in the wave train evoked by the mechanical displacement and during normal tremor.

5. It is concluded that physiological tremor in the 8–12 c/s band is due to oscillation in the stretch reflex servo-loop.

INTRODUCTION

The hypothesis that the tremor of normal, voluntary, muscular contraction in the 8–12 c/s band is due to oscillation in the stretch-reflex loop is based largely on the effects of interruption of the afferent nerves from a limb. Dorsal root section in the experimental cat (Lippold, Redfearn & Vučo, 1959) abolished the 12 c/s peak; in most tabetic patients the

rhythmical component of physiological tremor is absent (Halliday & Redfearn, 1958). Moreover, muscle action potentials can be recorded in well defined groups which are synchronous with tremor, and on cooling a limb both action potentials and tremor occur at a lower frequency (Lippold, Redfearn & Vučo, 1957*b*).

Recently, a number of authors have questioned the servo-loop hypothesis for tremor. Marsden, Meadows, Lange & Watson (1967) studied one patient whose right arm had been totally deafferented surgically. They found a well defined 9·5 c/s tremor peak in both the deafferented and the normal limb and concluded 'that physiological tremor arises independently of sensory feed-back and that the tremor peak is not solely the result of inherent delay in operation of the stretch-reflex mechanism'.

Yap & Boshes (1967) obtained 'average patterns' of normal finger tremor, ballistocardiogram and the electrocardiogram, which they found, using a computer of average transients, to be related. They drew the conclusion that cardiac action is the origin of normal finger tremor. Observations made on experimental animals led Van Buskirk & Fink (1962), Brumlik (1962), Brumlik, Mier, Petrovick & Jensen (1964), and Wachs (1964) to dispute the neuromuscular basis of normal tremor since they claimed that it persisted in the anaesthetized state and despite various surgically produced lesions of the spinal cord and roots.

The following experiments are an attempt to resolve this controversy and to throw further light upon the mechanisms underlying physiological tremor.

It is possible to investigate the action of servo-mechanisms in two ways. First, a step-function perturbation can be introduced into the closed loop. In an overdamped or critically damped system, oscillation does not occur but in an underdamped condition the loop will oscillate in predictable phase relation with the input. Secondly, the parameters of the loop itself can be manipulated; for instance, if the loop gain can be reduced below unity, oscillation will cease, or if the delay is changed, the frequency of oscillation will alter correspondingly. Experiments of this nature, upon the human stretch reflex, will be described in this paper and their results should indicate, unequivocally, whether or not oscillation can occur in the reflex arc and be responsible for physiological tremor.

A demonstration of these experiments has been given (Lippold, 1969).

METHODS

Subjects

The subjects were seventy-three normal volunteers, of both sexes, ranging in age from about 17 to 45 yr. They were free from any obvious neurological abnormality which could be detected on a cursory examination. They sat upright on a chair with

the left forearm resting horizontally on a foam rubber mat. In one series of experiments the arm was, in addition, held rigidly in a heavy framework which effectively immobilized the arm, wrist and elbow joint.

Tremor recording

Records of finger tremor were made in two ways: (*a*) by recording force of contraction, and (*b*) by recording finger displacement.

(*a*) Clamped rigidly to the framework holding the arm was a strain gauge assembly which recorded the force of extension of the forefinger or middle finger, as it was maintained in the raised position against a predetermined, isometric load. It is well established that the amplitude of tremor is directly proportional to the force of voluntary contraction in a muscle (Hammond, Merton & Sutton, 1956; Sutton, 1956, 1957) and it is therefore important to monitor and control the contraction strength. The subject was able to maintain a predetermined tension in his own finger by observing the oscilloscope trace of the output of the bridge circuit of the strain gauge, using direct coupling throughout. A calibrated bias, applied to the trace, enabled any desired tension to be held; usually records were made at a tension of 50 g (Fig. 1*a*).

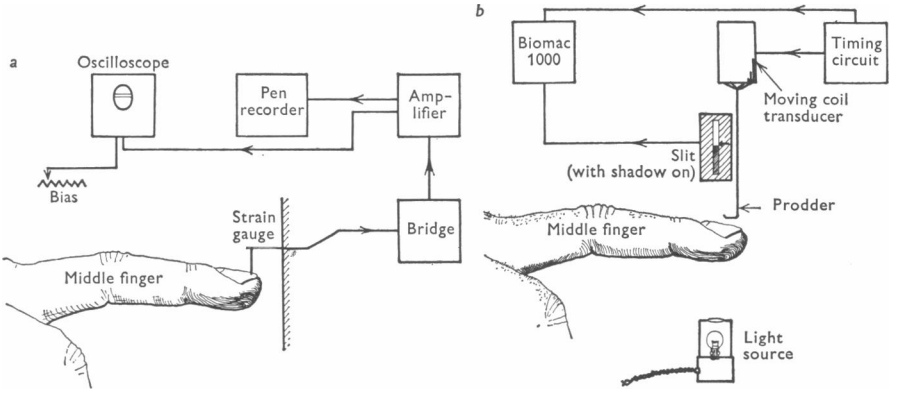

Fig. 1. Methods for recording tremor. (*a*) Force of contraction. (*b*) Displacement.

(*b*) The freely extended middle finger was arranged to interrupt a parallel beam of light directed at a phototransistor mounted behind a vertical, ground-glass slit (Fig. 1*b*). Subjects were asked to keep the shadow of the finger-nail as close as possible to a fiducial mark halfway down the slit. The arm and wrist were supported. The method is a modification of that first described by Eagles, Halliday & Redfearn (1953) and Redfearn (1956).

Electrical recording

In addition to the DC channel, a parallel amplifier, using an over-all T.C. of either 4 sec or 1 sec and an H.F. filter set with its 3 db point at 250 c/s, fed a hot-stylus pen-recorder (Sanborn, type 320) and either a Mnemotron CAT 400B computer or a Biomac 1000 computer. The computer output was written out on an X–Y plotter. The whole system was calibrated with time-locked mechanical pulses each of 10 msec duration and 100 μ amplitude applied to the recording strain gauge by means of a piezo-electric crystal driven by a square-wave generator, or the mechanical stimulator (q.v.) was used with 30 msec pulses of 2 mm amplitude to calibrate the optical system.

Mechanical stimulation

The finger was prodded by means of a moving coil transducer driven by a power amplifier. The amplitude of the stepwise displacement was kept constant at 2 mm (measured with a dissecting microscope). The subject, in maintaining the position of his finger, as described above, kept it about 0·5 mm lower than the off-level of the prodder.

Thus normal tremor could be recorded, as well as the oscillations resulting from a prod, the finger at all times being free and unloaded. The duration of the prod was usually 30 msec. The experiment was cycled using a crystal-controlled oscillator.

Warming and cooling

In the experiments involving the effects of temperature on tremor, and on the oscillations produced by prodding, all records were made with the hand, forearm, and as much of the upper arm as possible immersed in a Perspex water-bath. The prodder was in the bath. Some difficulty was experienced with scattering of the light beam by bubbles forming on the inside of the Perspex with hot water, and condensation on the outside with cold water. Records made in the water-bath could not be compared with those in air since the weight of the part is different and the water itself has a damping effect.

Frequency analysis

Baseline-cross interval analysis was used, care being taken to ensure that the wave form measured was smooth (e.g. not admixed with 50 c/s pick-up). Intervals were measured using a d.c. level detector which gave an output pulse each time the recorded wave form attained a pre-set potential level. Interval histograms were plotted either with the Biomac 1000 or by hand.

Action potential records

Conventional EMG methods were used. Surface electrodes were applied over the extensor muscle of the middle finger, as delineated by palpation when forced extension of the finger was made (see Lippold, 1952; Bigland & Lippold, 1954*a*, *b*; Edwards & Lippold, 1956 for details of the techniques).

RESULTS

Introducing a step-function perturbation into the loop

(*a*) *Single recordings.* When 30 msec prods were delivered to the freely extended left middle finger, a train of between 5 and 20 approximately sinusoidal waves resulted from each one. Figure 2 shows the effect in a subject having considerable resting tremor, while Fig. 3 shows the same response in a subject having relatively little resting tremor. It was always found that the oscillations were of the same frequency as the normal tremor in any one subject. Usually the amplitude was of the same order of magnitude (but slightly larger than found in spontaneous tremor). These records are typical responses; in subjects with much resting tremor, the latter was

found to continue throughout the experiment, being synchronized and increased in amplitude by each prod. In subjects with little resting tremor, each prod would produce a train of waves, sometimes as few as three or four in number, in the form of a heavily damped sinusoidal oscillation. It was often possible to transform the tremor in subjects of the second type to that of the first by the performance of fatiguing contractions of the extensor muscle which increased the resting tremor in it.

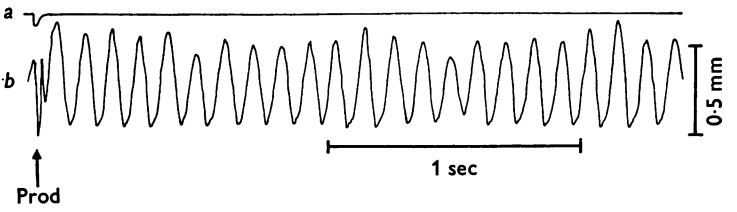

Fig. 2. Oscillation produced by prodding finger (= 30 msec stretch delivered at arrow): trace (*a*) is a record of the mechanical displacement; trace (*b*) is the record of the movement of the outstretched, unloaded, left middle finger recorded by method (*b*) of Fig. 1. The left middle finger in many individuals gives better tremor records than the forefinger. Subject shown has marked resting tremor of about 0·5 mm amplitude.

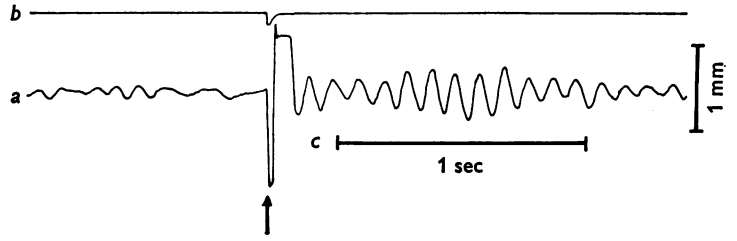

Fig. 3. The effect of prodding the finger in a subject with less resting tremor than the one shown in Fig. 2. Experimental conditions similar. (*a*) Record of finger displacement (downward movement is shown as a downward deflexion). (*b*) Prod delivered at signal. (*c*) Time trace (1 sec). (In this record, the flat part of the trace is due to the finger rebounding to hit the stationary prodder.)

(*b*) *Averaged recordings.* It was clear from the records obtained that the pattern of the mechanical response of the finger to each prod was stereotyped. Averaging of these responses with the computer showed that the wave form would truly summate; in other words the amplitude of each wave in the summed result of n sweeps was about n times the amplitude in a single sweep. A control record of n sweeps taken without stimulation showed no summated waves. These findings are shown in Fig. 4.

The fact that these waves produced by a stepwise displacement of the

finger can be shown to summate, indicates that they are phase-locked to the mechanical stimulus and must represent oscillation in an under-damped system, either mechanical or neurological in origin.

It is known that the mechanical, die-away resonant frequency of the finger is at about 25–30 c/s (Halliday & Redfearn, 1956; Randall & Stiles, 1964; Stiles & Randall, 1967). The frequency of the waves in the experiments of Fig. 4 was about 8 c/s and in all subjects was the same as that of their individual normal physiological tremor. The records of Fig. 4 were obtained by delivering the prod to the finger 80 msec before the commencement of recording. Because the initial components of the response were large and exceeded the capacity of the computer store if sufficient resolution

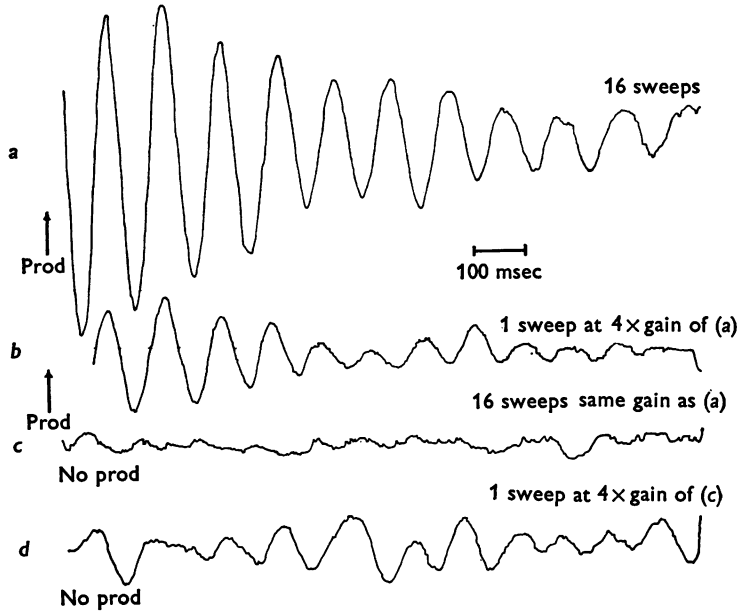

Fig. 4. In normal subjects the finger can be made to oscillate by itself, 5–20 times, by prodding it once. A brief (30 msec) stretch given 80 msec before the arrows gives a phase-locked damped train of waves of the same frequency as normal tremor. Recording method (*b*) of Fig. 1. Trace (*a*) Sum of 16 sweeps; 256 counts per address. (*b*) One sweep; 64 counts per address (i.e. at 4 × the gain of (*a*)). (*c*) Control. No prodding. Average of 16 sweeps; 256 counts per address. (*d*) Control. No prodding. 1 sweep. 64 counts per address.

was required to examine adequately the remainder of the sweep, the first 80 msec of the response was omitted. However, in Fig. 10, taken for other purposes, the mechanical record does show these early waves and it can be seen that there are initially two or perhaps three oscillations which have a frequency of about 27 c/s superimposed on the recording. These faster waves represent the purely mechanical response of the finger.

The effects of temperature

It is now necessary to show that the oscillations produced by prodding are of the same nature and origin as physiological tremor. In each subject the frequency of both was the same and the response to cooling and warming was the same.

(*a*) *Upon the oscillations.* Figure 5 shows the results of an experiment in which the arm and forearm were immersed in the water-bath, (*a*) with the

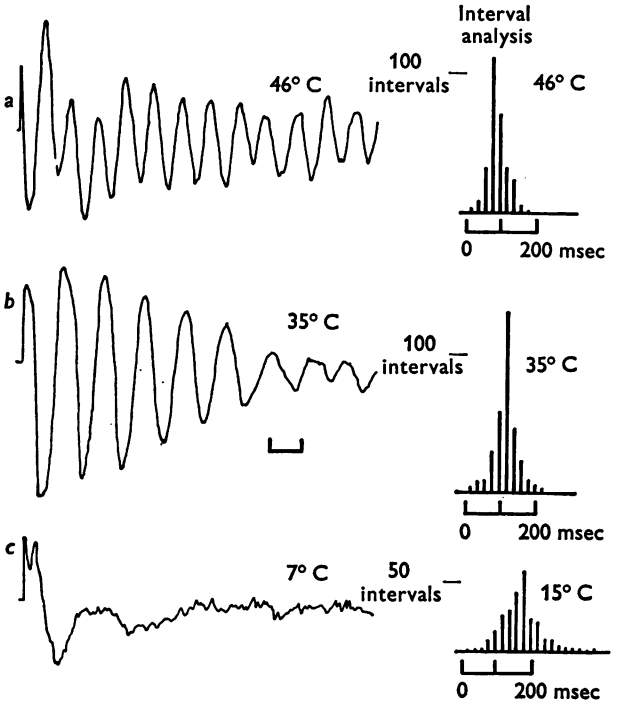

Fig. 5. Arm temperature and frequency of oscillation. Warming the arm raises the frequency; cooling lowers it. (*a*) Arm immersed in bath at 46° C. Record obtained as in Fig. 4, line (*a*). (*b*) Arm in bath at 35° C. (*c*) Arm in bath at 7° C. (the interval analysis was made at 15° C because the record was too irregular at 7° C). On the right are shown baseline-cross interval histograms. Prod in (*a*), (*b*) and (*c*) given 80 msec before commencement of trace. 16 sweeps each.

temperature of the water at 46° C, (*b*) at 35° C, and (*c*) at 7° C. The records are computer averages of 16 sweeps each, triggered by the prod.

It can be seen from inspection of the records, and from the baseline-cross interval analysis, that warming raises the frequency whilst cooling lowers it.

(*b*) *Upon tremor.* Figure 6 shows the results of an experiment upon the same subject as demonstrated in Fig. 5, made under identical conditions, with the sole exception that normal tremor of the outstretched unloaded finger was recorded by means of a single sweep, randomly triggered and at 16 times the gain of the records in Fig. 5. There was no prodding.

It can be seen that the frequency of tremor and the frequency of the oscillation due to prodding are both altered in the same way and to the same extent by changes in temperature of the water-bath.

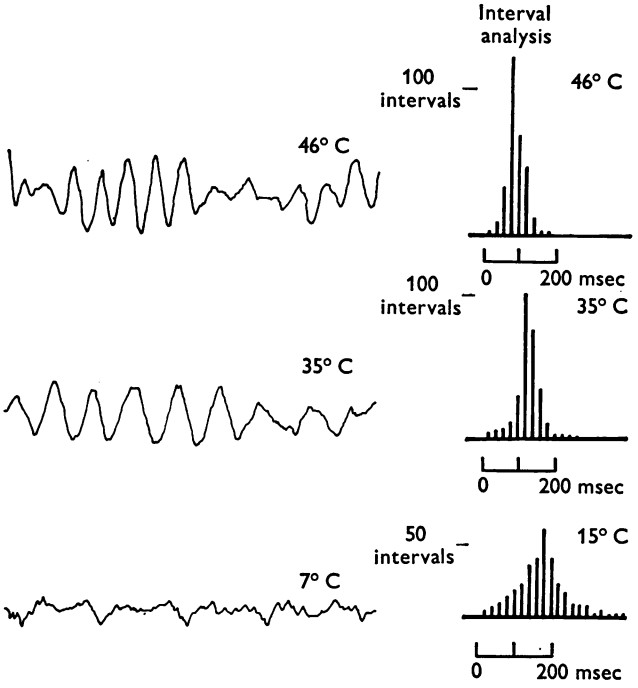

Fig. 6. Arm temperature and tremor. Warming and cooling change tremor frequency to the same degree as shown for the oscillations due to prodding in Fig. 5. Records obtained under identical conditions as Fig. 5 but only 1 sweep at 64 counts/address (i.e. at four times the gain), no prodding.

The effects of ischaemia

The effects of ischaemia on finger tremor were first described by Halliday & Redfearn (1954). A sphygmomanometer cuff, just above the elbow, inflated to between 150 and 200 mm Hg, resulted in the depression of all frequencies of normal tremor within about 1–2 min. In many subjects tremor was abolished after 3 or 4 min. When the cuff was removed, tremor returned within 1 min and attained the control amplitude after usually less than 5 min.

Figure 7 shows a recording of physiological finger tremor made whilst an arterial cuff was inflated (at the arrow). At the instant of inflation it was usual to find that a momentary increase of normal tremor occurred, presumably as a result of readjustments in posture, etc., made by the subject. After 1–2 min, the record shows a continual decline in the amplitude and measurement shows a small increase in frequency of the 8–12 c/s waves.

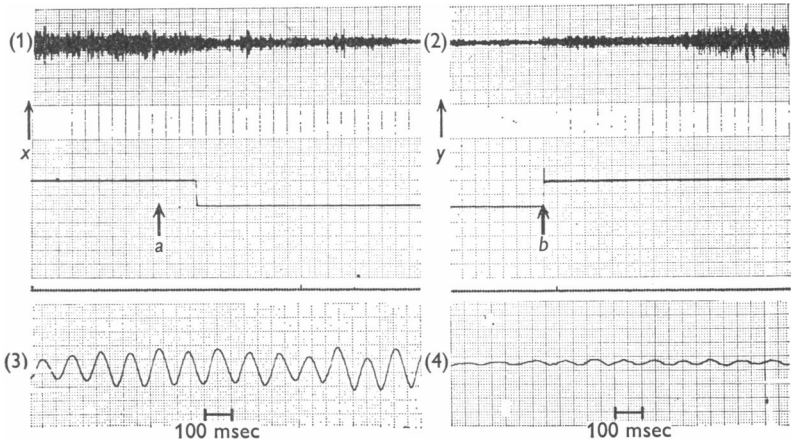

Fig. 7. (1) Recording of normal tremor by method (*b*) of Fig. 1. At (*a*) an arterial cuff at 200 mm Hg was inflated (taking 12 sec) on the upper arm. (2) At (*b*) cuff was released. At arrow (*x*) about 1 sec of tracing was taken and shown at (3). At arrow (*y*) tracing (4) was taken. Time scales: for (1) and (2) each heavy graph line is 5 sec apart, for (3) and (4) each heavy line is 50 msec apart. Gain of mechanical trace adjusted for 1 large square = 0·1 mm excursion of finger.

It appears that all frequencies of tremor are affected by ischaemia. There are no changes in stretch-reflex threshold during the first 4–5 min of ischaemia and the maximum force of a voluntary contraction is unaltered (until ischaemic paralysis develops after a longer interval).

The reduction in tremor does not occur if a venous cuff (i.e. one inflated to a pressure of 60–70 mm Hg) is applied; in fact this procedure, if anything, tends to increase tremor amplitude. Neither is it found on compression of the radial nerve above the elbow, long enough to produce numbness and weakness of the finger extensor muscles. Figure 8 shows amplitude–duration diagrams of the separate physiological tremor waves recorded from a subject before and during a period of arterial cuff application, illustrating these findings.

Halliday & Redfearn (1954) did not hazard any explanation for the effects of ischaemia upon tremor, but in view of the facts that (*a*) the twitch itself is unaffected,

(*b*) a venous cuff does not have any effect, and (*c*) nerve block is ineffective in altering tremor, it seems likely that the muscle stretch receptors themselves are implicated. Matthews (1933) found, in the anaesthetized cat, that any impairment of the normal blood supply to a muscle resulted in the muscle spindles within it giving a sustained, high frequency discharge with a concomitant reduction in sensitivity to stretch. Observations made during other experiments on mammalian muscle spindles (Lippold, Redfearn & Vučo, 1958; Lippold, Redfearn & Nicholls, 1960*a*, *b*) lend support to the view that cessation of the circulation to a muscle spindle will, in fact, almost abolish its response to stretch.

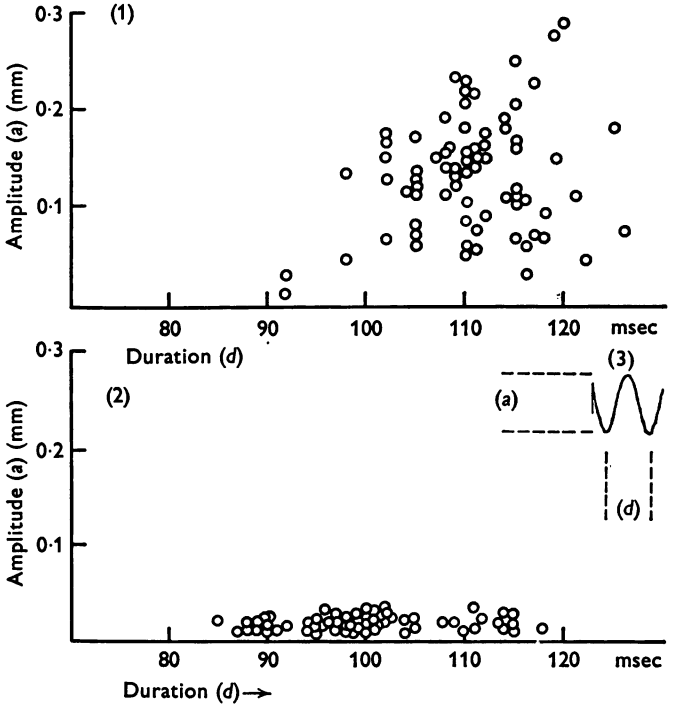

Fig. 8. Amplitude–duration relationship of tremor waves recorded before (1); during (2) a period of 5 min application of an arterial cuff as shown in Fig. 7. The slight increase in tremor frequency and the reduction in amplitude can be seen during ischaemia. Measurements made as shown in inset (3) from X–Y plotter and Biomac 1000. Single sweeps, random triggering. Time course = 4 sec. (This method overcomes any distortion due to pen recording.)

If the foregoing assumptions are true, the imposition of ischaemia in a limb and its resultant effects on the spindles are equivalent to altering the loop gain at its peripheral part. Reduction of tremor results because the loop gain is reduced towards or below unity and if the spindles become insensitive to stretching, the situation is equivalent to the opening of the

loop at this point. Tremor then disappears. Whatever the mechanism whereby tremor is affected by ischaemia, the fact that a peripheral manoeuvre, such as applying a pressure cuff to an extremity, can profoundly modify its wave amplitude, is evidence in favour of the oscillating servo-loop theory.

It was found that ischaemia had similar effects to those described above upon the oscillations produced by prodding. Figure 9 shows the diminution of the response to prodding following application of an arterial cuff. In most experiments similar changes occurred; additionally, before tremor was abolished the frequency usually rose by 1 or 2 c/s; so did the frequency of the oscillations due to prodding. This is further evidence that the oscillations and normal tremor waves have the same origin.

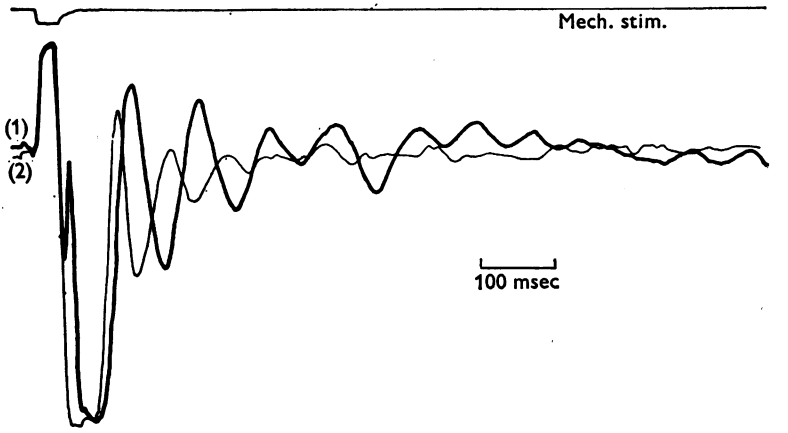

Fig. 9. The diminution of the response to prodding which occurs during ischaemia (records tracings of originals). Prodding resulting in oscillations (recorded in same way as Fig. 4, line (*a*)). Prod given 80 msec before start of trace. (1) Thick line: taken immediately before cuff inflation. (2) Thin line: taken 3 min following application of arterial occluding cuff at 200 mm Hg on the upper arm.

Action potential recording

In order to show that the processes of tremor do involve neural mechanisms and are not simply the result of mechanical resonance of the finger, it is possible to record muscle action potentials responsible for the contraction maintaining the raised finger. In the case of spontaneous tremor, it has already been shown in many different accessible muscles in the human body that groups of action potentials occur with a frequency of 8–12 c/s and that they do synchronize with tremor (Lippold, Redfearn & Vučo, 1957*b*).

Figure 10 is taken from a subject who had surface electrodes on the skin of the forearm over the extensor digitorum communis to provide the top recording of each pair, the bottom being the simultaneously recorded displacement of the finger following a single prod, given at each arrow. The top pair is representative of the majority of experiments made upon this and other subjects. The prod produces, as usual, a damped train of oscillations lasting for 9 cycles (a downward deflexion represents depres-

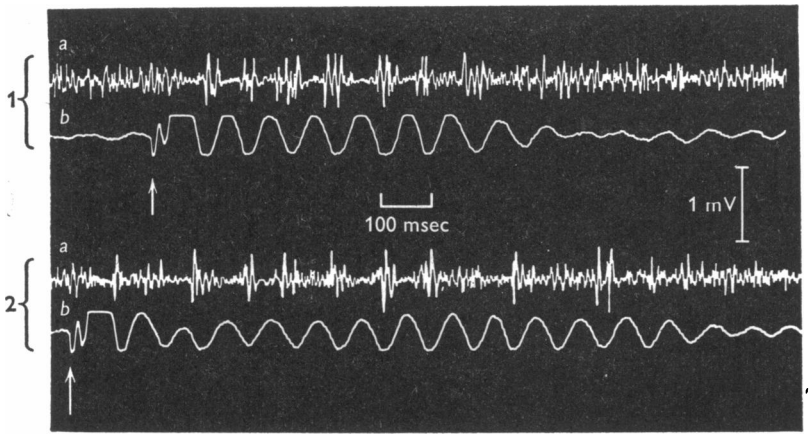

Fig. 10. The oscillations following prodding are in phase with groups of muscle action potentials. Recordings (*a*) are obtained from surface electrodes over the extensor digitorum communis. Recordings (*b*) displacement of finger, recorded by method (*b*) of Fig. 1 following a prod given at arrow. (1) Record showing usual configuration of response. (2) Record showing increase in response amplitude after first few waves (see text).

sion of the freely extended middle finger; wrist firmly supported). At the time of the prod, the mechanical trace shows a downward, sharp finger movement about 0·3 mm in excursion. This is followed by a second smaller downward peak, about 30 msec later, almost certainly representing the mechanical die-away response of the finger (i.e. 30 c/s is its resonant frequency in the unloaded flaccid state). The top of the first tremor wave is flattened because the shadow of the finger-nail has overlapped the upper limit of the slit. The next six waves continue without decrement and then the oscillation dies away.

The trough of each of these waves is in alignment with a burst of action potentials in the top trace. It was not possible to pick out groups to correspond with the two or three fast waves at the start of the response. In all these experiments such bursts could be made out but Fig. 10 was one of the best results. Groups also accompanied normal tremor waves in the absence of prodding.

The bottom pair of traces, from the same subject, is included because it shows, after the seventh wave, an increase in amplitude of the oscillation lasting for the next five waves before the activity tends to die away. This must indicate that energy is being fed into the system at the appropriate frequency and phase. The waves, after the seventh, cannot therefore be due to simple mechanical resonance. One may look upon this record (and that shown in Fig. 3) as showing the oscillations merging into true tremor. This type of response to a prod occurred considerably less often than that shown in the top pair of traces, but nevertheless could be seen in the records of the majority of subjects on at least one or two occasions.

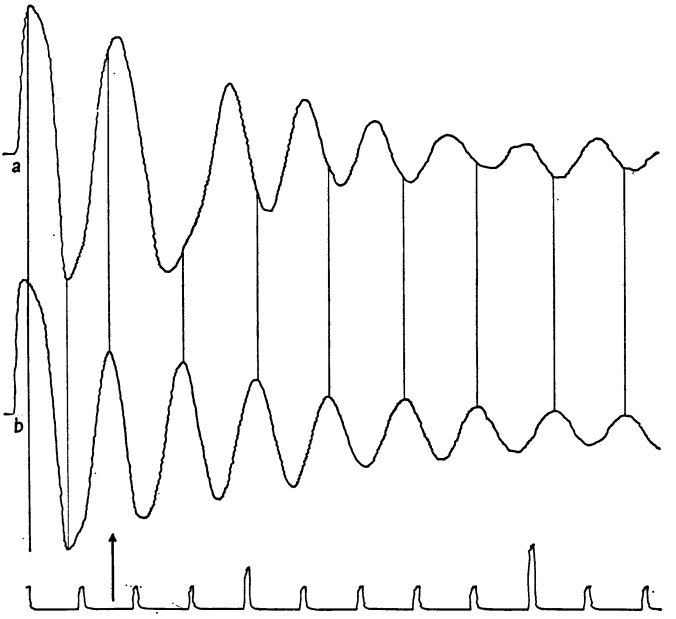

Fig. 11. The effect of a double stimulus (32 sweeps; Biomac 1000). (*a*) 80 msec before arrow, 30 msec prod given. 205 msec after prod, electric shock (0·05 msec duration; 7·5 V amplitude) delivered to skin over ext. dig. comm. (*b*) as in (*a*) but no shock given. Time trace: 100 and 500 msec. Note approximately 180° phase shift in (*a*) which follows the electric shock.

Ancillary experiments

(*a*) *Double prodding.* It was suggested by A. F. Huxley that a second prod, timed to be 180° out of phase with the first, and three cycles later, should stop the oscillation. It proved difficult to obtain this result mainly because of trouble encountered in adjusting the amplitude of the prods. It was easy to demonstrate that an anti-phase prod would alter the phase of the oscillations by 180° but not to stop them.

In order to overcome this difficulty, an electrical stimulus (0·05 msec duration, 5–10 V amplitude) delivered to the skin over the extensor muscle was substituted for the second prod. Figure 11 shows thirty-two mechanical responses averaged. 205 msec after the prod the shock was given and resulted in a 180° phase reversal. This indicated that the strength of the electrical stimulus was too great since it generated its own train of waves, 180° out of phase with the preceding waves.

If the strength of the electrical stimulus was turned down, it proved possible to achieve a balance so that the oscillations were almost abolished (Fig. 12). Without altering any of the other parameters of the experimental

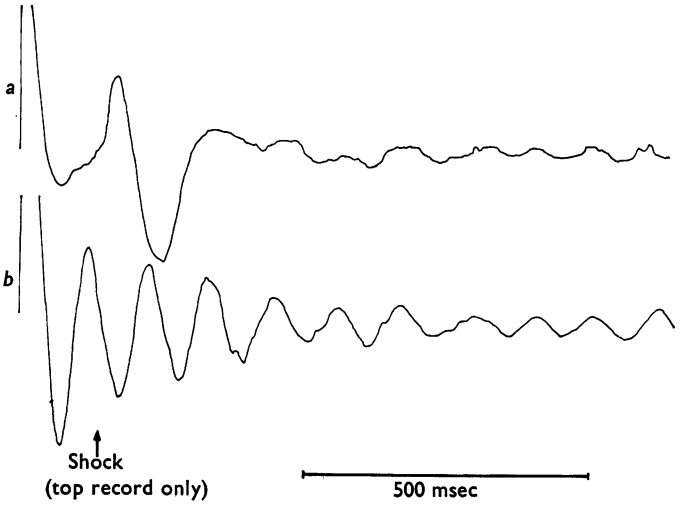

Fig. 12. Same experiment as Fig. 11. (*a*) Electric shock (2·5 V) given 205 msec after prod. (*b*) Control; no shock (tracing). Note diminution of oscillations which occurs after shock. Shock given 80 msec before arrow.

procedure, when the electrical stimulus was retarded by a further half wave-length, summation occurred. In other words, the response to the shock was itself much larger and the waves following it remained in phase and were enhanced.

(*b*) *Random prodding and normal tremor.* By the same reasoning as above, it should be possible (if the servo-loop theory of tremor is true) to halt normal tremor by applying a mechanical prod to the finger at the appropriate instant, and in the appropriate phase. In subjects having more or less continuous tremor it proved easy to demonstrate this point.

If the prodder is activated at random (or at long) intervals and a large number of recordings are obtained, a selection can be made according to the phase of the tremor wave where the stepwise displacement is imposed.

It is clear (Fig. 13) that tremor is stopped for several cycles when the prod is in antiphase; when it is in phase tremor is enhanced. It is rather difficult to explain findings such as these except on the basis that tremor is the result of either mechanical or neurological oscillation.

(*c*) *Pulse rate and tremor.* It is difficult to reconcile the results of experiments on the servo-loop with those purporting to show that tremor is due to cardiac action (for references, see Introduction) except perhaps on the basis that each pulse wave causes any limb to swell, thereby stimulating stretch receptors within its muscles. Tremor, however, is at 8–12 c/s whereas the heart normally beats at about 1 c/s. The experiments already described above, in which the arm was firmly clamped to prevent transmitted vibration from the cardiovascular system from reaching the finger and in which an arterial cuff excluded the pulse, are relevant here. Inflating the cuff had no immediate effect on tremor (see Fig. 7), therefore the heart cannot be involved in generating normal physiological tremor.

To demonstrate this in another way, several subjects were invited to run up and down a flight of stairs in order to raise the heart rate. In no case could any change in frequency of tremor be detected.

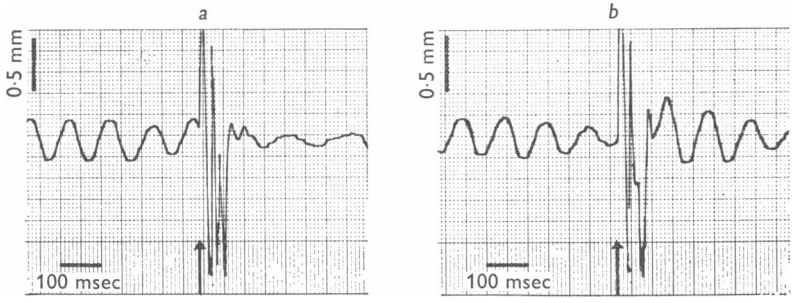

Fig. 13. Tremor is stopped (or greatly reduced) for several cycles when the prod is given out of phase with it (at arrow trace (*a*)). It is enhanced when given in phase (at arrow trace (*b*)). Note that a downward prod is here shown as an upward deflexion. Time bar = 100 msec. Calibration = 0·5 mm.

The influence of visual feed-back

Sutton & Sykes (1967) found that depriving a subject of visual information about the position of his limb abolished or greatly reduced the amplitude of the 9 c/s component of physiological tremor. Their experimental arrangements were totally different from the ones used in this investigation and it was therefore of considerable interest to know how tremor of the outstretched free finger would be affected by closing the eyes.

Subjects found it simple to maintain the required position of the outstretched finger with closed eyes, and under the conditions of these experiments no significant differences could be detected in frequency, amplitude or general wave form of tremor as recorded with the eyes open or closed.

Figure 14 shows a record of normal tremor, recorded using the photocell

method, taken before and during eye closure (the black bar shows the time at which the eyes were closed). This is a typical recording and no obvious differences can be detected.

Figure 15 shows the averaged mechanical responses to a prod, given 80 msec before the arrow, line (*a*) with the eyes open and line (*b*) with the

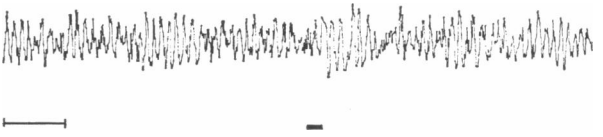

Fig. 14. Recording of tremor, middle finger extended, held free, wrist supported. The finger's position was under visual control of the subject, since he was instructed to maintain the shadow of his finger-nail at a fiducial mark on the recording phototransistor. Time bar = 1 sec.

At the black mark his eyes were closed. A typical recording, this shows little change in the pattern of the tremor. A few subjects consistently exhibited a slightly increased amplitude of tremor after eye closure. Frequency was not determined in these experiments but casual inspection revealed no obvious difference.

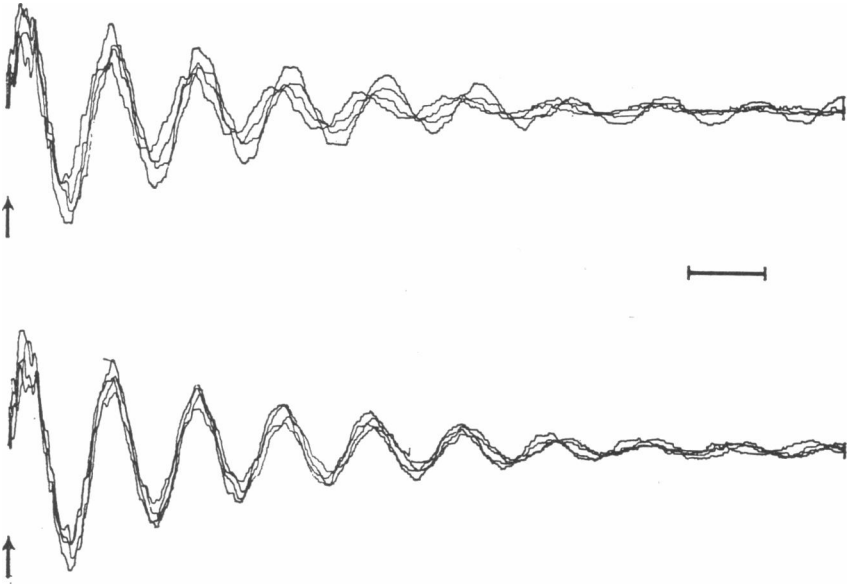

Fig. 15. Averaged recordings of the mechanical response to a prod obtained as in Fig. 4, trace (*a*). Top: four superimposed records with eyes open. Bottom: the same, but with eyes closed. Time bar = 100 msec.

Sixteen sweeps averaged; 256 counts per address. Sweeps at 1953 msec intervals. Prod 80 msec before arrow. Records were taken consecutively, those when the eyes were shut alternating with those having the eyes open.

eyes closed. Each is four superimposed computer write-outs of the sum of sixteen sweeps following the prod, given at 1953 msec intervals.

It can be seen that there is no systematic difference in the mechanical response to a prod with the eyes open or with the eyes closed. These are typical records. Most subjects appeared to have slightly smoother and more closely superimposed records when the eyes were closed, a fact which might be taken to indicate that visual control of finger position tends to disrupt a little the pattern of the oscillations produced by the prod.

In these experiments, it was noted that the overall magnitude of tremor could be to some extent affected by voluntary control exerted by the subject. Various closed loops could be demonstrated involving, for instance, the auditory system (the sound of the recording pen-writer when this was used at high gain), and receptors in skin and bone (the subject could easily judge the position of the finger by the force with which the prod hit it).

DISCUSSION

Definition of physiological tremor

It is clear that considerable confusion exists with regard to the definition of normal physiological tremor. For the purposes of this paper, it has been confined to the ripple which is superimposed upon normal voluntary muscular contraction. This then means that limb movements due to the pulse, vibration resulting from passing traffic, and voluntary movements of a corrective nature made in the course of undertaking a tracking task are excluded. Physiological tremor is distinguished from the tremor of Parkinson's disease by the appearance of the frequency analysis, the former having a peak between 8–12 c/s and the latter, one at about 5 c/s. Parkinsonian tremor has an entirely different origin from normal tremor (Lance, Schwab & Peterson, 1963; Calne, 1968; Walsh, 1969) and it is important that experimental findings in the one are not indiscriminately used as evidence in support of theories attempting to explain the other.

The disappearance of tremor on opening the servo-loop

Any feed-back loop containing a delay will go into oscillation if the loop gain is above unity. Reduction in the loop-gain will decrease the amplitude of oscillation and opening the loop, i.e. reducing the loop-gain to zero, will abolish it. The mechanism producing the rhythm of physiological tremor (at 8–12 c/s) has generally been thought to be of this oscillatory nature because deafferentation abolishes tremor (in tabes dorsalis: Halliday & Redfearn, 1958; in the anaesthetized cat: Lippold *et al.* 1959).

The work of Marsden *et al.* (1967) challenges these facts on two counts. First, in one patient, surgical deafferentation has not abolished tremor. Secondly, it is stated that the examination of a series of tabetic patients did

not confirm the finding that the 8–12 c/s tremor peak was reduced or absent in such cases. As far as the first point is concerned, one possibility to account for the continued tremor after surgical intervention might be that the deafferentation was incomplete. It has already been suggested (Lippold, 1969) that C4 might supply the median nerve in this patient; this root was not divided surgically. Concerning the second point, no details of the experiments on the tabetics are given. Tabetic patients can be divided into two groups: those who have no 8–12 c/s rhythm and those with an abnormally large rhythm at this frequency. Halliday & Redfearn (1958) clearly demonstrated that the absence of the 8–12 c/s peak was well correlated with the degree of the deafferentation as determined by clinical testing. The less severely deafferented patients showed an increase in physiological tremor, a fact which could well be due to the working of the remaining small number of intact reflex arcs at a much higher loop-gain (by increased gamma activity) in order to attempt compensation for the proprioceptive loss.

The experimental evidence for the effect of deafferentation on tremor is now being questioned. It therefore has been the purpose of the experiments presented here to examine the mechanisms underlying physiological tremor in another way.

The demonstration of oscillation in the servo-loop

These experiments show that the outstretched finger can be made to oscillate, for quite long periods, by introducing a brief mechanical displacement. Moreover, these oscillations are phase-locked to the stimulus and hence must involve either mechanical or neurological feed-back. Since muscle potentials can be recorded in constant phase relation to the oscillations, these must also be occurring in the motor nerve supply to the muscle (and within the motoneurone pool). A purely mechanical origin is ruled out additionally by the observation that the amplitude of such a train of induced oscillations often increases over a period of time, thus indicating an input of energy (apart from the initial displacement applied) into the system. The mechanical resonant frequency of the finger studied in these experiments is about 30 c/s and confusion between this and servo-loop oscillation should not arise.

It only remains to demonstrate similar cyclic activity in the afferents from muscle spindles. This cannot at present be achieved in the intact human but previous work in the anaesthetized cat is relevant here (O. C. J. Lippold, J. G. Nicholls & J. W. T. Redfearn, unpublished). Figure 16 is taken from this work and shows activity in a single afferent fibre from an annulo-spiral ending within the gastrocnemius muscle which is being sinusoidally stretched at about 10 c/s. A peak-to-peak amplitude of the applied stretch of less than 1 % of the total possible physiological excursion of the muscle would produce this response. In twenty-five human subjects it was found

(O. C. J. Lippold, unpublished) that the amplitude of normal tremor varied between 0·1 and 2 % of the normal range of movement of the finger. Thus it is highly likely that physiological tremor will also involve stretch receptor activation in phase with it.

Oscillation in the servo-loop and tremor

It is of course impossible to prove conclusively that the oscillation induced by a mechanical input and the waves of physiological tremor have the same origin. However, they have a similar wave form, are always of the same frequency in any one subject, and are altered in the same way

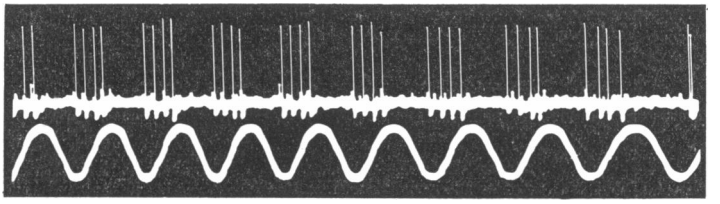

Fig. 16. Response to sinusoidal stretching of a single annulo-spiral ending in gastrocnemius of anaesthetized cat. Top trace: action potentials recorded from single dorsal root fibre, ventral roots intact. Bottom trace: mechanical displacement of tendon (stretch upwards). Unpublished work by O. C. J. Lippold, J. G. Nicholls & J. W. T. Redfearn. Frequency approx. 10 c/s. Stretch is 1 % of resting length of muscle. Amplitude of spikes about 1 mV.

by a number of factors such as warming and cooling, so it is reasonable to infer that the two phenomena represent the operation of the same mechanism. Perhaps most convincing is the way in which the oscillations merge into normal tremor. Also, the fact that it is possible to stop or greatly to reduce normal tremor by giving a mechanical stimulus which is out of phase with the ongoing wave form is fairly conclusive evidence and rather difficult to explain satisfactorily on any other basis.

Visual feed-back modifying tremor

It is clear that the feed-back systems controlling muscle length and tension are complex in nature and that the loops activated by muscle spindles are but one example of many which can be called into play during various kinds of limb movement and during different experimental conditions. It is, furthermore, likely that these loops, in some circumstances, may exhibit oscillation when their parameters approach critical values in terms of the Nyquist stability criteria.

Despite the fact that delays in some of these loops may be from $\frac{1}{4}$ to $\frac{1}{2}$ sec (e.g. visual reaction time), it is still possible for the loops to oscillate with a period shorter than the delay itself. An oscillatory condition will occur in any system of closed connexions where the total phase shift is a

multiple of 360° and the total magnitude ratio is unity. If a longer closed loop, such as one involving visual feed-back, is active and showing a tendency to oscillate at a subharmonic of the stretch reflex frequency, oscillation in the latter may well be stimulated to occur at about its own fundamental frequency.

Thus Sutton & Sykes (1967) found that removal of visual cues (i.e. opening the visual feed-back loop) abolished or greatly reduced the 9 c/s tremor in a manual task. This involved the relatively strong contraction of several muscles (total force was 2·3 kg) in a tracking task which cannot be directly compared with the experimental method used in this paper. Further work by Dymott & Merton (1968) indicated that the influence of visual feed-back depended rather critically on the detailed conditions of the experiment. The degree of flexion of the wrist determined whether or not the 9 c/s tremor peak was affected by visual information.

Merton, Morton & Rashbass (1967) showed that visual pathways were involved in the production of tremor by the elegant method of introducing additional delays into the visual loop, between the subject and the display of his arm displacement that he was watching. This gave rise to peaks in the power spectral analysis of tremor, at frequencies other than 9 c/s, which were related to the magnitude of the extra delay. Again, however, this result appears to be rather critically dependent on the experimental set-up and it must be emphasized that visual pathways are by no means always active in producing tremor. For instance, in the experiments reported in this paper, visual pathways were not involved, since closing the eyes did not alter either tremor of the free extended finger or the oscillations due to prodding.

Other hypotheses for tremor

It is relevant to consider other possible hypotheses to account for tremor in the light of the experiments reported in this paper.

(*a*) *Normal tremor is of cerebral origin.* For a long time, since the alpha rhythm was first described in the normal human subject by Berger (1929), it has been obvious that the wave form and frequency of alpha waves and muscular tremor are alike. Moreover, the two phenomena are altered in much the same way by a number of factors (Jasper & Andrews, 1938) and vary with age similarly (see Hill, 1963; Marshall & Walsh, 1956). It is usually stated that no direct phase correspondence can be found between the pre-central alpha rhythm and any peripheral muscular tremor and also that whilst overbreathing alters the frequency of alpha rhythm, it does not affect tremor (Lindqvist, 1941). It might be pointed out, however, that the latter conclusion is hardly supported by the evidence given in the paper quoted, and that it would be worthwhile repeating these experiments with

the more refined techniques now available. The only possible solution which would accord with the results in this paper would involve a feedback loop including the cortex (or subcortical motor systems) as well as the muscle itself. On the whole this seems unlikely since tremor can still be observed at about 10 c/s when the cut peripheral end of the spinal cord is electrically stimulated at a wide range of frequencies.

(*b*) *Tremor is of spinal origin.* It is possible that the motoneurone pool has some inherent rhythmical tendency, due either to the properties of motoneurones themselves or to the synaptic and interneuronal organization of the pool.

A number of motoneurones firing independently but at similar frequencies exhibit periods of apparent synchronization and desynchronization. Taylor (1962) puts forward the theory that the grouping of action potentials in the electromyogram of normal muscles arises in this way. It is not possible satisfactorily to explain the effect on frequency of the grouping brought about by warming and cooling in terms of Taylor's theory (this paper; Lippold *et al.* 1957*b*). Because only the muscle itself is cooled, it would be necessary to postulate, in addition, some afferent, temperature-sensing pathway from it to the motoneurone pool. Furthermore, a different hypothetical pathway would have to exist, this time proprioceptive in nature, to explain the results of prodding the finger.

(*c*) *Tremor arises purely in the muscle.* Muscle is pictured as acting like a low-pass filter in the hypothesis first put forward by Marshall & Walsh (1956). Action potentials, at more or less random intervals, will only result in discrete, obvious movements of the muscle if their frequency is lower than tetanic fusion frequency. Any motor units firing at about 10 c/s will give tremor; above this rate they will produce a fused and smooth tetanus. The main objections are that factors altering fusion frequency, for example fatigue which lowers it considerably, should also alter tremor frequency. Fatigue does not slow tremor. It, in fact, increases the amplitude markedly and slightly raises the frequency (Lippold, Redfearn & Vučo, 1960).

The results given in this paper are also incompatible with this theory. One would not expect to find the close correspondence between muscle action potentials in groups and tremor waves, while the phase-locked wave train following a brief displacement cannot be explained in terms of a muscle-filtering effect. Stimulation of a muscle through its nerve at increasing frequency shows progressive smoothing of the response without any increase in tremor at 9 c/s (Lippold *et al.* 1957*a*).

Why does a voluntary contraction exhibit tremor?

If we do accept the servo-loop hypothesis for tremor, at first sight it seems surprising that a control mechanism of this nature and degree of

sophistication should be allowed to suffer the inaccuracies springing from its uncontrolled oscillation. The oscillation in a feed-back loop can be removed by increasing the damping in the system. This is customarily introduced in man-made control systems by applying a term in the transfer function of the system proportional to the first derivative of the misalignment. In the reflex arc this corrective action occurs mainly at the muscle spindle, whose response to stretch contains both displacement and velocity sensitive components (Matthews, 1931, 1933; Katz, 1950; Eyzaguirre & Kuffler, 1955; Lippold *et al.* 1960*a*).

Excessive damping of this nature must lead to slowness in response to a stimulus. There is therefore a necessary compromise between, on the one hand, speed of response, and, on the other, output error in the form of tremor. It would appear that in most individuals a certain amount of tremor, sometimes as much as 2% of the physiological range of a muscle contraction, can be tolerated in the interests of achieving speed of response.

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