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RESEARCH INTO TREMBLING FINGERS: A PERSONAL EXPERIENCE

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> The affection in question consists of a fine tremor, constantly present in typical cases during waking hours, voluntarily controlled for a brief time, affecting nearly all the voluntary muscles, chronic, beginning in very early life, not progressive, not shortening life, not accompanied with paralysis or any other disturbances of nervous function. It resembles to some extent the tremor of paralysis agitans, still more a simple neurasthenic tremor. A most striking feature is marked hereditary or family type, and its transmission along with other nervous diseases. Dana, 1887.[1]

One of Dana's patients was a watchmaker who had acquired the reputation of being the best craftsman in the district. Dana wrote—'I have myself seen him pick up a piece of delicate machinery of a watch in his forceps, carry it to the place where it should be fitted, the hand trembling like an aspen until just before it reached its destination, when it suddenly became firm and steady and deposited its burden just in the right place'.

The first professor of physiology in Glasgow was Andrew Buchanan who held the post from 1835 to 1862.[2] He was also a surgeon to the Glasgow Royal Infirmary from 1835 to 1862. He had a tremulous head and hand.

> As far back as the fifties, in the morning on which he had an operation to perform, he would keep his right hand supported in his buttoned coat, not even shaking hands with anyone till the operation was over.

Being born in 1798 and not dying until 1882 the tremor indeed did not shorten his life.

LITERARY REFERENCES

Acute emotion certainly causes tremor. In a biblical concordance under the headings 'tremble', 'trembled', 'trembles' and 'trembling' are numerous references.[3] In the first of these (Genesis XXVII, 33) is the account of how Jacob, on the instructions of his mother, impersonated his older brother Esau. Old and blind, Isaac was deceived into blessing Jacob, animals skins having been placed on Jacob's hand to mimic the hairiness of those of his brother. When the true Esau returned from hunting and the deceit became apparent, Isaac evidently became very angry

> Isaac trembled very exceedingly, and said, Who? where is he that hath taken venison, and brought it to me, and I have eaten of all before thou camest and have blessed him?

Similarly Shakespeare often referred to tremor and its association with acute anxiety. Under the heading 'tremble', 'trembled', 'tremblest' and 'trembling' there are again numerous references in a concordance.[4] One example occurs in Julius Caesar IV, 3, 38.

> Brutus—'Hear me, for I will speak. Must I give way and room to your rash choler? Shall I be frightened when a madman stares?'
> Cassius—'O ye gods, ye gods! must I endure all this'
> Brutus—'All this! ay, more: fret till your proud heart break; Go show your slaves how choleric you are, and make your bondmen tremble'.

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Horace Walpole described a painting by Hogarth[5] of a cruel jailer who had been extorting money from ragged prisoners. He was the warden of the Fleet prison, his crimes had been uncovered and in the painting he is being arraigned before a committee of the House of Commons:

> Villainy, fear and conscience are mixed in yellow and livid on his countenance, his lips are contracted by tremor, his face advances as eager to lie, his legs slip back as thinking to make his escape; one hand is thrust precipitately into his bosom, the fingers of the other are catching uncertainly at his button holes.

The word 'tremendous' comes from the Latin 'tremend-us' meaning 'that is to be trembled at, fearful, dreadful, frightful, terrible'. 'Tremulus' was used as a 'cognomen' by Romans in the name of Quintus, Marcius Tremulus, consul in 306 BC and victor over tribes of central Italy. I am indebted to Dr Arthur Kitchin for the following information.

> In early republican times the cognomen, was an unofficial nickname conferred on adults, laudatory or often pejorative, referring to some characteristic of the bearer. Later the cognomen was often passed down the generations and so did not necessarily characterise the individual. Tremulus was early, and is the only instance recorded of this name, so quite probably he was 'shaky' or became so.

According to the Oxford English Dictionary the word 'tremor' originally meant fear or terror, rather than its physical concomitant of shaking. This usage is apparent in one of Caxton's books, it was a translation from French, the 'boke of Enydos' (XXII, 81)

> Horrible dremes & cruel, comen to-fore her in hir mynde that tormente her in tremoure merueyllous.

Large tremors are associated with corresponding rhythmic discharges in the electromyogram but powerful inputs from descending motor tracts can take over the control of the motoneurones and transiently drive the activity in a tonic manner. The watchmaker and Professor Buchanan were, no doubt, holding their tremors in check, when they needed to by strong co-contraction of opposing muscle groups. In this way oscillations can be abolished and a tremorous limb held steady by muscular clamps. The rhythmic electromyogram has been replaced, temporarily, by a steady, fierce, discharge. As tonically contracting muscles cut off their own blood supplies the manoeuvre is effective only for a matter of seconds.

Richard, Coeur de Lion had a tremor

> Richard's outward aspect was imposing; he was wondered at for his height, his immense strength, held in check though it was by a constant recurring ague, 'which kept him, dauntless though he was, in a tremor as continual as the tremor of fear in which he kept the rest of the world; this made him a paladin of charity'.[6]

Oliver Cromwell suffered from tremor[7]

> The Venetian ambassador who saw him in 1655 observed that '. . . the hand holding his hat was trembling.

Two of his signatures have been reproduced. Finding the autograph when he was 41 unconvincing, I consulted two documents of 1648 held in the Scottish Record Office in Register House (PA. 7/23/2/58 & PA. 7/23/2/59). At that time Cromwell was 49. I found the calligraphy bold, rounded and without irregularities. However the illustration of his signature when aged 59 does suggest tremulousness.

ESSENTIAL AND PHYSIOLOGICAL TREMOR

The term 'essential tremor' is correct for otherwise healthy people who are clearly tremulous. There may or may not be a family history, the term covers both possibilities.

In communities which have been isolated for a long time it has been possible to study the genetics of hereditary tremor. In a Swedish parish 210 cases were investigated.[8]

> All but two could be traced back to four ancestral couples. The average age of onset was 50 in men and was somewhat later in women. Where hereditary factors are found there is usually evidence of an autosomal dominant. Penetration increases with age and is almost complete at 70 years.

As essential tremor does not threaten life there have been few autopsy reports. There is no known characteristic anatomical site or histological abnormality, so we may be dealing with subtleties of the 'wiring diagram'.[9]

> Large tremors are a nuisance but rhythmic movements of similar frequency can be useful. In the vibrato of violin players the fingertip is rocked on the string at an angle to its length without sliding along the string.[10] There is a regular oscillation at about seven cycles per second, changes in muscle length are minimal. After the overt vibrato rhythmic grouped muscular activity may still be detectable electrically.

THE ANATOMY OF TREMOR: MOTOR UNITS

Each muscle in the body is supplied with motor fibres, each of which controls a number of individual muscle fibres: the nerve fibre and its associated muscle fibres is known as a 'motor unit'. There are in most normal muscles a substantial number of different motor units each one of which thus contributes only a relatively small proportion of the total force. After nerve injury the remaining unaffected fibres may come to control many more of the muscle fibres and such giant motor units can make for very jerky contractions. Motor units increase in size in the elderly and this may contribute to unsteadiness, for instance, in handwriting. About 35 years ago I had working with me a technician who as a result of an attack of poliomyelitis had been left with a partial foot drop. I attached an accelerometer to his foot and when he attempted dorsiflexion a series of semi-rhythmic jerks occurred (Fig 1). Two examples are shown. The remaining motor fibres were few and had evidently sprouted.

FIGURE 1

Acceleration record of dorsiflexion of the foot showing effect of a giant motor unit as a result of poliomyelitis. Time marker—seconds.

Sometimes one hears a rumble in the ear due to activity of nearby muscles. Motor nerve fibres discharge at rates at which the mechanical forces are impulsive. It is possible with no special apparatus to be aware of this. Hold your index finger on the skin close to the lateral end of the eyelids, then gently contact the Orbicularis oculis. As the skin there is quite thin, you will be able to feel the

vibrations of the underlying muscle. With a piece of pressure tubing the sounds may be conducted to the ear and sound like those of a motor-bike engine. Muscles do not generate smooth postures and smooth movements, but discontinuities are minimised as the individual motor units are usually out of step with one another. They discharge at rates which vary slightly so that the ripple is reduced by averaging out, just as when soldiers marching over a bridge fall out of step to prevent the build up of damaging sways. The vibrations that are left constitute the basis of tremor.

Different motor units are influenced to some extent by the same factors, common inputs to the motoneurones. The asynchronicity is not complete. In one study[11]

> The cross-correlation between pairs of motor units showed a consistent tendency to synchronization in the hand as well as in the calf muscles. This synchronization was higher than could be expected from the random activity of asynchronously firing motor units. The amount of synchronization was correlated with the amplitude of physiological tremor, the stronger the tremor, the higher the synchronization coefficient.

Motor units vary in size and it is believed that the first to be activated normally are the smallest, this 'Henneman principle' minimises tremor. Excessive tremor may be expected to occur if there is abnormal synchronization of different motor units, or if motor units are unusually large. If in some people the Henneman principle was not obeyed, and large motor units were activated early, substantial tremor would result. This possible explanation for essential tremor does not appear to have been explored.

Tremors are mostly exhibited in the hands and fingers but may occur restricted to other muscle groups and to particular movements. A tremor may occur only on writing and drawing and there is an account of a professional golfer whose tremor in the left hand only appeared when he began his backswing.[12]

One study suggested that some tremors spread from a muscle or a muscular group to the other muscles of the limb.[17] The patients investigated suffered from diverse pathological conditions. The muscle in which the activity was believed to originate was called the 'inductor' or 'pace-maker'. Local anaesthesia of the inductor muscle lead to a cessation of the tremor; it was claimed that on occasions the relief lasted for several months.[13]

There are some grounds for believing that there are two types of essential tremor. The first is an exaggeration of physiological tremor. The second is much more serious, the oscillations are slower and larger and normal activities are disrupted.

A quite separate condition is 'orthostatic tremor:[14] there is an oscillation in the legs and trunk which only occurs on standing. The rate is quite rapid, clearly faster than that of essential tremor. It is at about 16 Hz and there is a quivering motion of the thigh muscles. The frequency sometimes halves to 8 Hz and the movements then become more vigorous with visible oscillation of the patella. The discharges in the right and left legs are synchronised. Standing after a short time may be impossible.

EXPERIMENTAL INVESTIGATIONS IN TREMOR

The first physiologist to measure tremor was Edward Sharpey Schäfer in one of his early studies.[15] Later he was to be for some 35 years professor of physiology

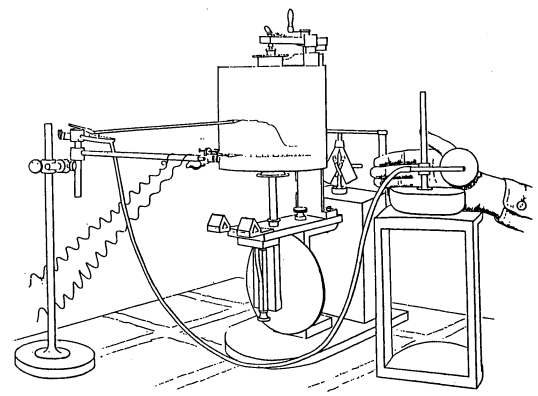

FIGURE 2

Schäfer's instrument for measuring tremor.

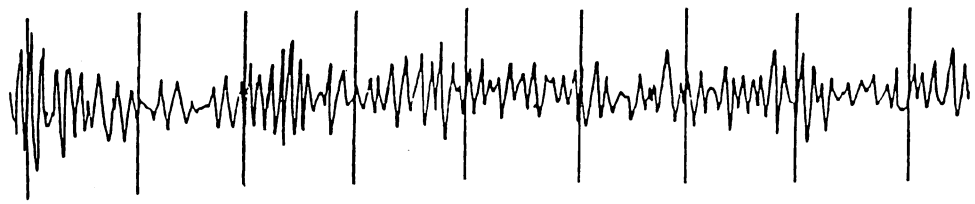

FIGURE 3

Record of tremor obtained with apparatus shown in Fig 2. The vertical lines correspond to seconds.

in the University of Edinburgh and was knighted. Schäfer's apparatus is shown in Fig 2. The older generation of physicians will recall making measurements of frog muscle contractions on a smoked drum and it was one of those splendid but simple, but now outdated, recording devices that Schäfer used. The drum was clockwork driven, the tambour applied to the thenar eminence picked up vibrations which were transmitted by an air-filled system to a straw with a writing point. A ripple at 8–10 oscillations per second occurred during muscular contractions. A record obtained during a continuing contraction is shown in Fig 3. Schäfer obtained an answer, now verified by others on numerous occasions, but his apparatus doubless had a low frequency resonance and his success seems to have come about by a mixture of good management and good luck.

Noninvasive methods of studying of tremor may provide information about the function of the neuromuscular system in health and disease. Tremor is the most frequently occurring movement disorder and I have been interested in instrumental investigations over a long period.[16,17]

For the study of the mechanisms of tremor[15] I devised an instrument where the weight of the hand was supported, and the momentary acceleration could be measured (Fig 4). At rest there was a low level vibration, partly caused by the mechanical events of the heart beat, but when the fingers were extended and the muscles became a little active there was a large increase (Fig 5).[18]

This physiological tremor was driven principally by muscle ripple but its frequency could be lowered by adding a bar of metal to the top of the device, the resonant frequency of the system having been lowered. The longer the bar

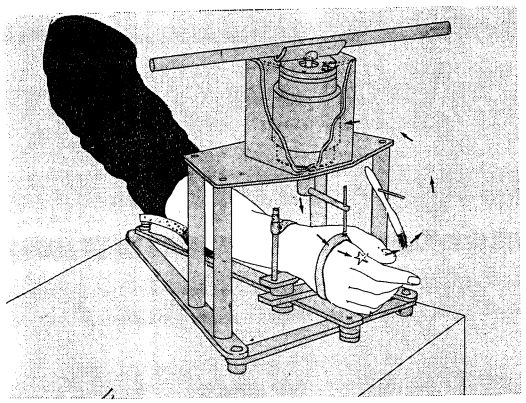

FIGURE 4

Apparatus for measuring tremor. The hand is suspended from a metal bar free to rotate and attached to a cylindrical angular accelerometer. Metal bars can be placed on the top of the instrument to change the amount of inertia into which the muscular system operates.

the lower the frequency. By contrast the rate of the tremor of Parkinsonism, evidently set by a central pace-maker, is insensitive to peripheral circumstances.[17] It is difficult to influence the rate of the tremor of paralysis agitans; although the amplitude may fluctuate widely the frequency usually remains almost constant.

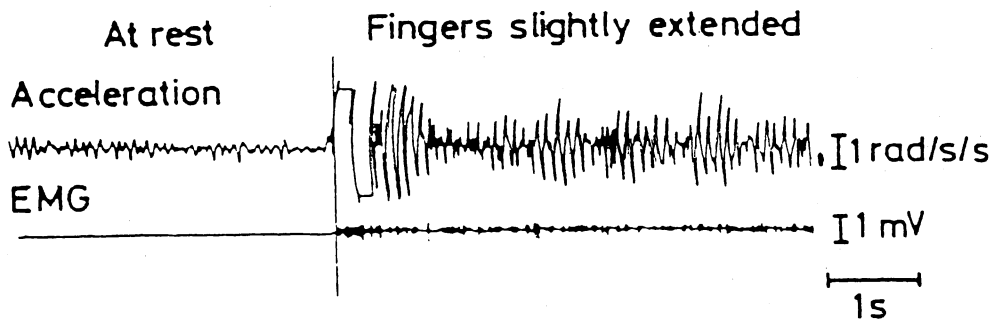

FIGURE 5

Record obtained using the 'hanging-hand tremorograph' shown in the last figure. There is an increase of finger tremor with the maintenance of a small change of posture necessitating slight muscular activity. The electromyogram becomes active.

When a blood pressure cuff is placed on the upper arm to occlude the arterial circulation physiological tremor is greatly reduced after, say, 2 minutes. This can be attributed to the ischaemia slowing the mechanical events so that the ripple produced by the muscle is less impulsive. It is apparent that the speed of muscular contraction is important in determining tremor level, the more sluggish the contractions the less the tremor.

Attached to the instrument was a small geared motor which could drive a paint brush to tap the hand every few seconds. With each trivial knock the hand

quivered with a series of oscillations which took several cycles to die away. There is a mechanical side to tremor; if the limb is tuned by its stiffness and inertia to a frequency close to the input from the muscles the oscillations will be conspicuous. It turns out that the natural passive resonance of the wrist is at about the frequency at which motor units discharge when there is a gentle or moderate contraction. It is this co-incidence which accounts, in large measure, for the peak seen on analysis at 10 Hz. Sometimes, as when pulling against a compliant spring or a spring with an attached weight, a violent tremor may build up in healthy people.[19]

TREMOR IN MEDICAL STUDENTS

Some authorities say that essential tremor is rare, others that it is common. In introducing first year medical students to the rudiments of neurological examination I have repeatedly observed that whilst most have stable fingers a significant minority exhibit conspicuous tremor. To investigate this further I clearly needed an appropriate measuring system. A very small silicon chip transducer taped to the middle finger recorded acceleration. The subject lifted the finger and the mean tremor over a five seconds epoch was displayed on a digital meter. Graphic records occasionally taken from those with conspicuous tremor were often similar to that obtained by Schäfer (Fig 3). The results show that the degree of tremor was distributed in a skew manner, with, as had been noted by eye, a minority of students having high levels.

When the same class was tested some months later the results were largely the same, most of those who had had high values in the first test also proved tremulous in the second. Some with high levels were unaware that their tremulousness was unusual. The instrumental measurements showed that all of the students had some tremor; anyone who denies tremor has only to point to a screen in a lecture theatre with a laser torch. With sufficiently sensitive instruments all parts of the human body show micro-oscillations; these are present even in anaesthetised, paralysed, patients. The vibrations are only abolished by death.

I had assumed that medical students, being young and presumably healthy, would be a good sample of a normal population, but when we tested a large number of people in a wide variety of walks of life the outcome suggested otherwise. Medical students in Edinburgh appear to be a very special group. When they were compared with school children attending a university open day and with silversmiths at the Edinburgh College of Art, the differences were highly significant. The values in the students were clearly higher ($p < 0{\cdot}001$).

A survey was therefore undertaken of tremor in a larger number of occupational groups. The data have been published in detail elsewhere.[20] A selection of the results is shown in Fig. 6.[20] The Edinburgh medical students had the highest values.

Tremor levels in other student groups and various categories of health workers are shown in Fig 7. Of the Edinburgh students the highest values were in males with home addresses in England, the median for the 33 such students being 70 cm/s/s. The eye surgeons had the lowest values.

In Stella Gibbon's *Cold Comfort Farm* a religious leader, Amos, is described, who by tales of hell fire and brimstone caused his brethren to 'quiver'. The origin of the name 'Quaker' is obscure but religious excitement can certainly give rise to tremor. There have been several sects with the name of 'Shaker'. The

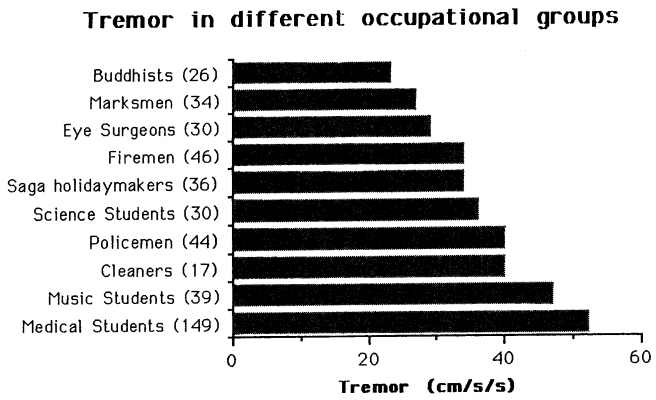

FIGURE 6

Tremor levels (median values) in medical students compared with other groups. The holiday makers were elderly people, mean age 65, on a fitness week in Dundee. The Buddhists were mostly British converts. The figures in brackets indicate the numbers tested in each population.

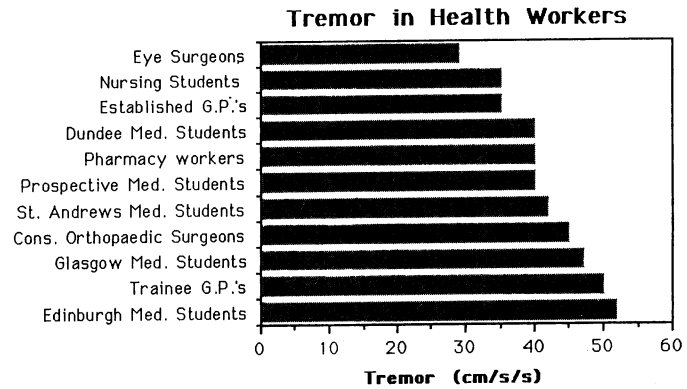

FIGURE 7

Tremor levels (median values) in medical students compared with other health workers.

Oxford English Dictionary states that the word "in the 17th century applied to various sectaries whose devotional exercises were accompanied by shaking . . ."

What is a normal population? I investigated groups of persons with known religious affiliations (Fig. 8). Young Unitarians on a weekend conference at St. Mark's Church, Castle Terrace, Edinburgh had values a little below those of the medical students. Church of Scotland ministers attending the General Assembly had lower values, as indeed did members of other congregations, the teaching nuns, and the Muslims. Almost the lowest values were found in Buddhists at the Samye Ling monastery on the Scottish borders. The lowest values of all were found in the Brahma Kumaris group. Male English medical students in their first year had values more than three times as high.

In a study using the Internal General Health Questionnaire a third of 300 fourth year medical students were estimated to have emotional disturbances.[21] The medical course is very demanding and first year university students are

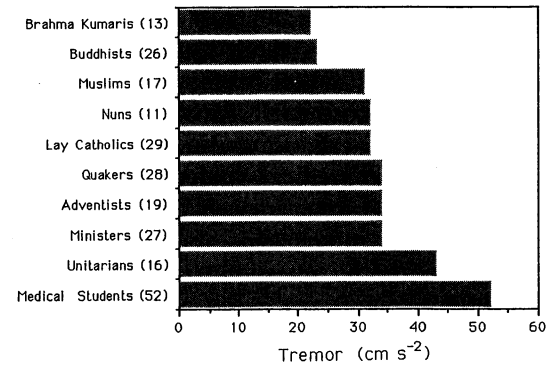

FIGURE 8

Tremor levels in Edinburgh medical students compared with people having known religious affiliations. Again the medical students have the highest values. Published first in the *Inquirer* (March 18th 1995) and reproduced by permission.

heavily stressed. Professor N. Kreitman in a memorandum to the Edinburgh Medical Faculty concluded

> There is reason to suspect that anxiety among our first year students is such as to inhibit their academic performance and to cause appreciable distress.

We do not at present know if the students having high tremor levels would show scores of anxiety on a general health questionnaire above the cut off level suggestive of psychiatric disability. Very high levels were however observed in a young man whose father had been publicly accused of very serious crimes. The surname was distinctive, and the case had widespread publicity in newspapers and on television.

ALCOHOL AND TREMOR

Alcohol induced delirium tremens may be associated with a dangerous degree of disorientation with hallucinations in which terrified patients have leapt from windows. An early account follows[22]

> The characteristic tremor is usually present from the first. It occurs only on movement, and is irregular, and considerable in range; it is most conspicuous in the arms, the face and the tongue, but is to be seen also in the legs when these are put into voluntary movement, especially if the patient attempts to stand. It is the more conspicuous, because the patient is usually in constant movement, picking at his bedclothes, searching for imaginary objects, attempting to get out of bed. This extreme restlessness is seldom absent. Often, in addition to the tremor on movement there are spontaneous slight, partial muscular twitchings, and in severe cases these may amount to considerable shock-like contractions and may occur in the muscles of the trunk as well as in the limbs.

The condition is precipitated by withdrawal from sustained heavy drinking and there is severe autonomic overactivity which can lead to fatal cardiac arrhythmias. Tremulous activity and elevated sympathetic drive is also experienced when morphine is no longer available to an addict. Plasma catecholamine levels are increased in these situations and significant benefit may be derived from treatment with β-blockers.[23] Calcium channel blockers seem to reduce the withdrawal symptoms from alcohol.

In moderate doses however in individuals who are only social drinkers, alcohol reduces tremor size.[24] There is a relationship between alcohol consumption and performance in activities where tremor would be a handicap such as snooker and playing musical instruments. Alcohol is banned in the Olympic modern pentathalon which involves shooting and fencing.

It is sometimes believed that medical students drink excessively and some physicians hearing of the results of these surveys have said 'of course its the beer'. I therefore sought to obtain some information about drinking habits.

I estimated the alcohol intake by questionnaire. The mean (±·SE) consumption for 94 men was 12·6±1·7 units per week and for 57 women was 7·2±1·1 units per week. This corresponds to only about a pint of beer per day for the men and half a pint for the women. There was no significant correlation between tremor level and estimated intake.

Some become chronic alcoholics because they find that drinking relieves the tremor, though the reduction is transient. It is often not the tremor *per se* which constitutes the problem but the social consequences of having conspicuous movements of this type and the comments engendered. Such subjects have found it embarrassing to have a haircut, speak in public or hold a cup of coffee. In situations where they would like to reduce the movements their anxiety commonly heightens them as Gowers wrote[22]: It frequently gives rise to grave misconception regarding the habits of the sufferer.

SENILE TREMOR

Gower gives this account:[22]

> In extreme old age slight tremor is often observed without the muscular weakness and rigidity that occur in paralysis agitans. At first it is noticed only on voluntary movement, and is generally influenced to a greater extent by movement than is paralysis agitans, ceasing or almost ceasing during rest, and always passing away during sleep. It usually commences in the arm, and often in both arms at the same time, but the head is affected much more frequently than in shaking palsy and occasionally the tremor begins in the muscles of the neck. The tremor is always fine, the range of movement being very small. After a time it occurs during rest as well as on movement. It is little influenced by treatment.

0Some older people have excessive tremor as a result of diverse neurological factors but this is not the norm. A sample of elderly people on a Saga holiday, had values well below those of the medical students (Fig 7). Only small changes were found in another study of subjects over the age of 65.[25] There is usually a slight lowering of the peak frequency.

TREMOR IN AEROPLANE PILOTS: METHODS OF STUDY

For some decades now it has been possible to put numbers to the increase of tremor with anxiety. Measurements of finger tremor have been made in airline pilots.[26] As with many sophisticated investigations of tremor the waveform was split instrumentally into its component frequencies. Fig 9 illustrates change in tremor under special circumstances. Gross finger tremor after touch down was usually associated with the persistence of an unresolved problem or the appearance of a problem of some magnitude during the final two miles of the approach. In Fig 9 the pilot before landing was given inaccurate information on cloud ceiling and there was standing water on the runway. The heart rate was accelerated. Another aircraft had taken off from a dusty runway during the final approach leading to very poor visibility on landing.

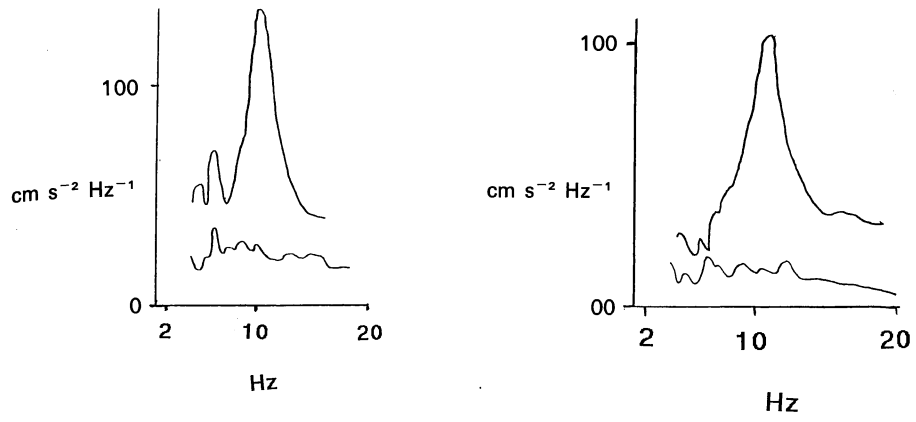

FIGURE 9

Two examples of tremor in airline pilots. In both examples a difficult landing was responsible for a large increase of tremor. The lower tracings are from control recordings.

The large peaks in these two figures, at about 10 Hz, verify Schäfer's conclusion about frequency, (vide supra).

Measurements of finger tremor were made in twenty-four cadets learning to fly with the East Lowlands Air Squadron in small single engined propeller planes known as 'Bulldogs'. The tremor increased by 58 per cent ($p<0·001$). The 95 per cent confidence limits were +29 per cent, +95 per cent.

BUNGEE JUMPING

To examine how far physiological tremor would rise under extreme stress, together with Dr A. S. Davies and Dr N. Powers, I measured physiological finger tremor in persons undertaking bungee jumping. In bungee jumping one end of an elastic rope is attached to the feet of someone prepared to jump from a great height—for example a platform, bridge or crane.[27] After several seconds free fall the exponent is momentarily brought to rest, upside down and fairly close to the ground. The person bounces up again almost regaining his initial height and then oscillates up and down several times, often also gyrating before coming to rest and being lowered to the ground.

Two sets of observations were made, one when students jumped in Edinburgh to raise money during 'Charities Week'. The other was organised commercially. The arrangements for both were the same. After being prepared for the jump the person entered a cage attached to a crane and was hoisted to some 50 meters (about 160 feet) above the ground. We made observations on 93 subjects just before jumping and as rapidly as possible after landing. In 33 instances we also made observations 10 minutes after landing. For 23 of the jumpers we also measured tremor some weeks later when they were not engaged in any athletic activity. They were aged 25·3±5·7 years (mean and S.D.) the range being from 18 to 50. There were 77 men and 16 women.

For the observations on jumping we used broader filtering than in the surveys summarised above. So, for comparability, we used the same instrument and procedure to measure tremor levels in 24 male and 22 female medical students during a practical class. On a day when they were not jumping the subjects' mean level of tremor was 59·0±21·8 cm s^{-2} ($n=23$). This did not differ

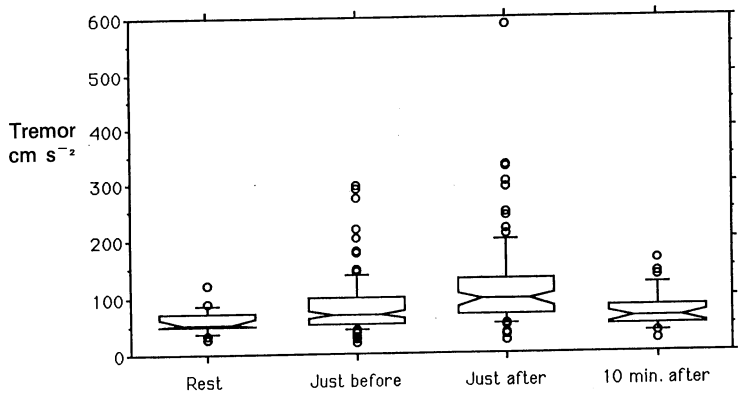

FIGURE 10

Bungee jumping, changes in tremor level with jumping Box plot representing the 10 per cent, 25 per cent, 50 per cent, 75 per cent and 90 per cent percentiles of the tremor. The notches indicate the 95 per cent confidence limits for the median. Values outside the 10 per cent and 90 per cent levels are plotted individually.

significantly from that of the medical students, the mean value for them being $63{\cdot}4 \pm 31{\cdot}1\ \mathrm{cm\ s^{-2}}$ ($n=46$). Just before the jump the mean value was raised, $84{\cdot}8 \pm 53{\cdot}9\ \mathrm{cm\ s^{-2}}$ ($n=93$). This difference from the rest value was highly significant ($p=0{\cdot}002$). Just after the jump the mean was even higher, $113{\cdot}71 \pm 80{\cdot}7\ \mathrm{cm\ s^{-2}}$ ($n=93$), $p=0{\cdot}0001$). Ten minutes after landing the values had fallen to $70{\cdot}7 \pm 34{\cdot}1\ \mathrm{cm\ s^{-2}}$ ($n=33$), figures which did not differ significantly from those before the jump. The results are summarised in Fig 10. As with tremors of different occupational groups the amplitudes are skew distributed. It will be seen that just before, and more particularly just after the jump, there were some quite unusually high values. Some of these may be the most conspicuous tremors ever recorded in healthy people. The highest value recorded was $588{\cdot}3\ \mathrm{cm\ s^{-2}}$. Had we been able to make recordings in the cage after it had been raised, and had not some time been lost after landing as the cords were being detached, even higher values would probably have been recorded. It will be seen however that in a small minority the tremor level was low, the stress of the event notwithstanding. They perhaps could quote Emily Brontë (1846)

> No coward soul is mine, No trembler in the world's storm-troubled sphere.

When the data for the men and women jumpers and the men and women medical students were examined no statistically significant differences were found.

The figures of the different subjects showed clear correlations on the different occasions. The results just before and just after the jump are shown in Fig 11, the correlation coefficient was 0·76. The correlation coefficient betwee the values just before the jump, and at rest was 0·78 ($n=23$), that before the jump and that 10 minutes after was 0·79 ($n=33$). It is evident that the people who had high tremors at rest are also likely to be those showing the highest values on the occasion of the jump.

Some of the increase observed is due to the anxiety of anticipation as the levels just before jumping were clearly higher than those at rest. Naturally had the participants been pushed off rather than jumped voluntarily the stress would

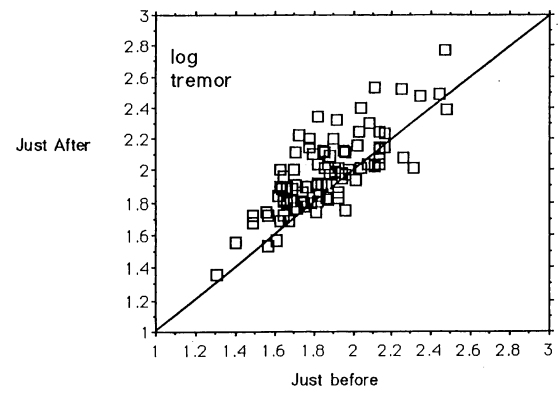

FIGURE 11

Bungee jumping. Mean tremor levels plotted on logarithmic scales. Data from just before and after the jump for the 93 participants.

have been of quite a different order of magnitude. A quotation from Chaucer (Troilus & Criseyde, V, 255) is apt

> And therwith-al his body sholde sterte,
> And with the sterte al sodeynliche awake,
> And swiche a tremour fele aboute his herte,
> That of the fere his body sholde quake;
> and therwith-al he sholde a noyse make,
> And seme as though he sholde falle depe
> ffrom heighe o-loft, and thanne he wolde weep,

It may be assumed that the jump and the anticipation of the jump gave rise, *inter alia*, to a massive liberation of adrenaline. It has long been known that this hormone may cause a conspicuous tremor. The half life of adrenaline in the blood stream is only some 1·5 minutes[28] a fact that may explain the clear drop in tremor level 10 minutes following landing.

People who undertake bungee jumping are a self selected group and usually pay about £50 for the experience. After the jump they commonly reported to us a feeling of exhilaration and a number were anxious to jump again and for a second jump the price may be reduced. The jump evidently induces a 'high'. Amongst the jumpers a number of leather clad motor cyclists were prominent, a group in which some may seek exciting experiences.

METABOLIC INFLUENCES ON TREMOR

Catecholamines, such as adrenaline shorten the contraction times of slow motor units but slow those that are fast. Each motor unit is constituted of muscle fibres having similar properties but, unlike the situation in some animals, human muscles contain motor units of mixed types. In maintaining a posture it will be the slow motor units in a muscle which are active and the action of adrenaline in generating tremor is thus understandable. Certain bronchodilator drugs, sympathomimetic amines, induce tremor by similar mechanisms. Adrenaline constricts skin vessels and increases the blood flow to the muscles. Both factors will raise muscle temperature, and this alone will increase tremor as the motor units will contract and relax more rapidly. In collaboration with Dr I. A.

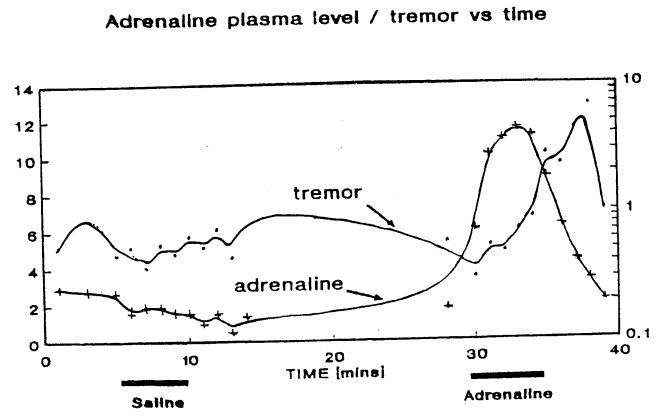

FIGURE 12

Observations with an infusion of saline showing no effect, followed later by an infusion of adrenaline with a large increase of tremor. The peak lagged behind that of the adrenaline plasma level. Left hand vertical scale—acceleration (cm s-2). Right hand vertical scale—adrenaline concentration plotted logarithmically (n mol/l).

MacDonald, of Nottingham, and with ethical approval, adrenaline was infused into volunteers and tremor measured. One example of the result is shown in Fig 12. There was a delay of a few minutes between the peak plasma level and the highest tremor level. This time lag is compatible with the view that the effect is determined, in large part, by temperature changes.

Caffeine and nicotine are known to increase plasma adrenaline and some people notice a tremor after drinking coffee or smoking but in an examination of these factors, drinking two cups of black coffee had no statistically significant effect on tremor level in fourteen volunteers. When two cigarettes were smoked there was a small transient increase. Twenty-five people were tested.

Hypoglycaemia may cause tremor. With ethical approval volunteers were infused with insulin whilst autonomic activity was monitored. As the plasma glucose fell out first, no changes were observed. At a certain critical level subjective effects and measurable changes developed almost explosively. When this threshold was reached the person started to sweat, the tremor rose, and the heart accelerated.

Tremor may be the first sign of hyperthyroidism.

> The tremor may, and usually does, affect the muscles of the lower limbs and of the trunk, as well as the muscles of the upper extremities. In many cases, the whole body can be felt to shake if the hand is placed upon the top of the head or upon the shoulder. Charcot states that this peculiar muscular tremor may be one of the first symptoms to be developed; and that it is of great diagnostic importance. In some of the imperfectly developed or rudimentary forms of the disease, in which there is no enlargement of the thyroid and no exophthalmos, but in which there is a notable and permanent fine, quick, rhythmical tremor confirms and greatly strengthens the diagnosis. Charcot directs special attention to the fact that in Graves' disease the individual digits do not tremble. In this respect, the tremor of exophthalmic goitre differs from alcoholic tremor and from the tremor of progressive general paralysis; in both of these affections, the tremor, as in Graves' disease, is a very rapid tremor (8 or 9 per second).[29]

Now that everything is measured and not just observed, it has not been confirmed that there is no finger, as opposed to wrist tremor, in hyperthyroidism.

The above quotation is from a work of Sir Byrom Bramwell, distinguished neurologist of the Edinburgh Royal Infirmary and founder of a medical dynasty in Edinburgh over one hundred years ago.[30] He was President of the Royal College of Physicians of Edinburgh (1910–1912) and his portrait hangs in the hall of the College. He was one of the first persons to obtain a graphic records of the tremor of thyrotoxicosis. In one study of this tremor, it was found that the amplitude appeared to correlate well with the severity of the condition.[31] The larger tremors were reported to be faster. This finding might repay re-investigation with the more accurate modern techniques; it is usual with tremors to find that increase of amplitude is associated with slowing. Many of the peripheral manifestations of thyrotoxicosis are similar to those produced by catecholamines, excess thyroid hormone evidently acting as a potentiator. Elevation of plasma triiodothyronine in rats speeds the contraction and relaxation of slow muscle fibres.[32] There is also a conversion of slow to fast muscle types. The physician may often have to decide whether a tremor is of nervous origin or indicates hyperthyroidism. It is unclear whether or not an instrumental differentiation may be possible.

TOXIC TREMORS

Many chemicals are neurotoxic and often an early, sometimes the only, sign of toxicity is the development of an exaggerated tremor. One example of tremor caused by toxicity was the 'hatters' shakes due to exposure to mercury.[22]

> A peculiar tremor, known among the workmen as the 'trembles' and medically as 'mercurial tremor' is the most common and characteristic symptom. It is at first occasional, occurring only when the patient is excited, and is always increased by emotion. It usually begins in the face and tongue and then invades the arms, and afterwards the legs. At first the tremor occurs only on movement but ultimately it may become constant. During sleep, the tremor usually ceases, but in extreme cases may only lessen. It interferes much with articulation, rendering the speech stammering and hesitating when considerable it may render the movement of the arms so unsteady that the patient cannot feed himself, and his gait become affected.

Workers in the fur, felt and hat industry suffered from exposure to mercury nitrate.

A tale that has been passed down in the felt-hat industry about the origin of this use of mercury is of some medical interest.[33]

> The felting process began with camel hair in what is now a part of Turkey. The hair of camels was made into tough felt material for tents. It was discovered that the felting process was accelerated with the urine of the camel. The art was brought back to Western Europe by the followers of the Crusades. It became the habit for the workers to urinate on the fibres before felting them. The story goes that one particular workman was being treated with mercury for venereal disease. It was noticed that his fibres, after the treatment mentioned above felted quicker and better than that of his more healthy comrades.

Some drugs are noted for their tremorogenic properties.[34] Thus 'tremorine' is appropriately named, its properties came to light during the routine screening of a number of compounds in mice.

A cat was anaesthetised with nitrous oxide and halothane and the lateral movements of the left forepaw measured. The tremor that resulted was certainly not reduced as a result of a stereotaxic lesion of the ventro-lateral nucleus of the thalamus (Fig 13).

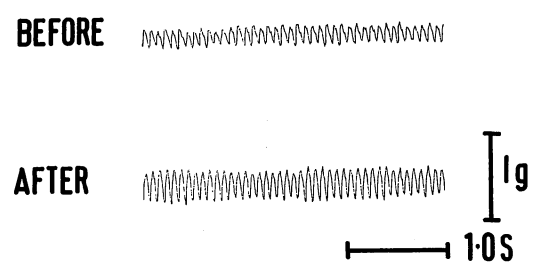

FIGURE 13

Tremor of paw of a cat caused by tremorine. The rate, about 15 Hz, is clearly faster than vigorous human tremors. The tremor clearly persisted following a lesion of the ventrolateral nucleus of the thalamus, a procedure which is often effective in abolishing some forms of human tremors.

Another compound, Harmaline, is a short acting monoamine oxidase inhibitor used to produce tremors in animals; the cerebellum and parts of the brain stem become rhythmically active.

One outbreak of an epidemic of tremor resulted from the exposure of people to an insecticide, chlordecone

> In July 1975, a 33 year old male chemical worker from a small factory in Hopewell, Virginia was examined by his family physician. He complained of headache, tremors and irritability. It was not for the first time that he had sought medical attention for these problems. In the past no specific diagnosis had been made and tranquilizers had been prescribed.[35]

A blood sample showed enormous amounts of chlordecone, the only product made by the patient's employer, and led to the uncovering of an ecodisaster. The chemical had been discharged into the James River and many residents in the immediate vicinity had evidence of chlordecone intoxication. Chlordecone, alias kepone, had given rise to 'Kepone Shakes'. Kepone is a polycyclic chlorinated hydrocarbon. Due to lack of adequate industrial safety measures, workers in the small factory (it was a converted petrol filling station) were exposed to large amounts of this toxic material for many months. Tremor developed in 76 of the 148 exposed workers. Visible trembling of the hands, trunk and legs occurred. There was mild instability that widened the station and slowed the gait. Eventually the constant, progressive trembling impaired dexterity for handling small tools, fastening clothing, drinking from containers or eating with utensils.

PARKINSON'S DISEASE

At first the tremor of Parkinsonism may be difficult to distinguish from other conditions for the onset is ingravescent and there may at first be no other signs or symptoms of the disease. Parkinson[36] wrote

> So slight and nearly imperceptible are the first inroads of this malady, and so extremely slow is its progress, that it rarely happens, that the patient can form any recollection of the precise period of its commencement. The first symptoms perceived are, a slight weakness, with a proneness to trembling in some particular part; sometimes in the head, but most commonly in one of the hands and arms. These symptoms gradually increase in the part first affected; and at an uncertain period, but seldom in less than twelve months or more, the morbid influence is felt in some other part.

A contaminate of illicit drugs, methyl-phenyl-tetrahydropyridine 'MPTP', is known to be a cause of Parkinsonism.[37] In the first recorded case

> In 1976 a 23 year old American addict manufacturing his own pethidine analogue took a synthetic shortcut and injected himself daily ... On the third day he developed a pure and severe Parkinsonian syndrome which responded dramatically to levodopa but persisted (with some spontaneous improvement) until his suicide 18 months later.

Drugs may induce Parkinsonian type tremors. Forty-nine psychiatric patients who had been treated with phenothiazine or butyrophenone drugs 14 (28 per cent) had unusual levels of low frequency tremor.[38] In an age matched control of 154 people the incidence was 3·2 per cent.

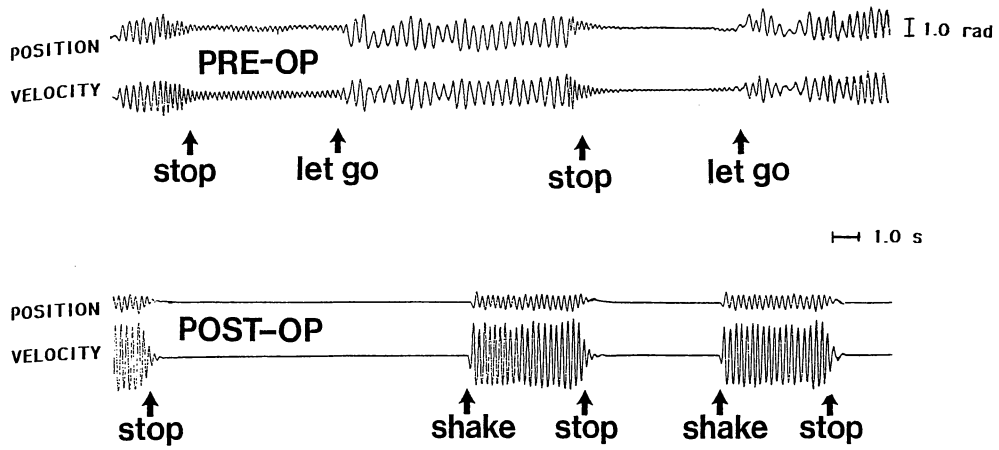

FIGURE 14

Parkinsonism. Upper—recording from the wrist showing continuous tremor which is lessened in amplitude and increased in frequency by attempts of the patients to cause it to cease. Lower—after stereotaxic operation the tremor is abolished and rapid voluntary flexion and extension movements can be made and stopped instantly.

The tremor of Parkinsonism is often temporarily suspended during voluntary movement. I studied a patient with this condition before and after a stereotaxic operation. A part of the ventrolateral nucleis and globus pallidus was coagulated by diathermy. Before the operation there was continuous low frequency tremor of the hands, on attempting to stop this it became smaller and faster. After the operation there was no tremor. When the hands were flapped to mimic the previous movement the motion could at once be halted (Fig. 14). Sterotaxic surgery has a place too in the treatment of severe essential tumour.[39] Lithium, given for the treatment of depression, is also liable to produce a tremor.

INTENTION TREMOR

Voluntary movements are sometimes obviously erratic in their velocity. If the reader raises and lowers his hand he may find that at a certain rate on the way down the motion is almost in a series of steps. The discontinuities in healthy people are however normally comparatively small. They can be investigated by the use of a tracking task. The person sits in front of a large screen cathode ray tube which has two beams. One of the spots is driven by a wave form generator,

the other is controlled by movements of his wrist. Arrangements can be made to display the difference in the position of the two beams. The person is instructed to move the spot under his control to be accurately below that of the other. If the waveform provides a jump of the spot from one side of the screen to the other at an unpredictable time the person can only respond after a 'reaction time'. Apart from this delay normal people can with fair accuracy match the two movements. An example of such an experiment is shown in Fig 15.

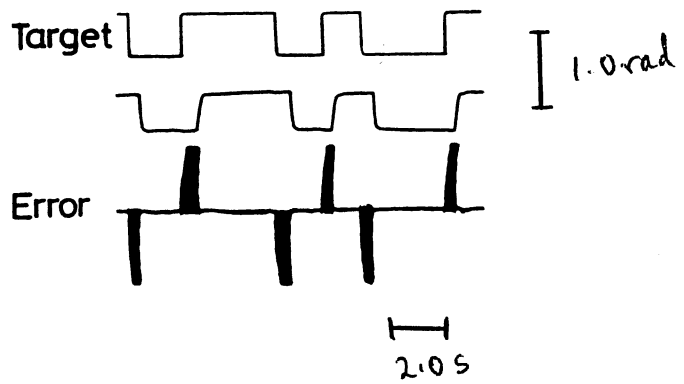

FIGURE 15

Top—movements of oscilloscope spot driven by a waveform generator from one side to the other at an unpredictable time. Middle—movements of the spot controlled by the subject's wrist. Lower—error, there is at first a large difference before the person reacts, but the final positions of the spots are essentially the same, typical of the responses of a well coordinated person.

With intention tremor, such as is found with cerebellar lesions, the velocity of the motion throughout may be quite irregular and the variations become greater as towards the end of the motion the target is being approached in a series of oscillations.

In a rapid movement such as the tracking task the limb is controlled by a triphasic sequence. The prime mover muscle at first accelerates the limb, the motion is then checked by the antagonistic muscle and finally the prime mover comes in again. This sequence is preprogrammed and its correct execution evidently depends on the integrity of the cerebellum.

HEAD TREMOR

The head may show a tremor. Sometimes as in severe Parkinsonism this is merely one aspect of a generalised tremor, however it is not uncommon for the head to be the sole, or main affected part. The head is stabilised by the vestibular apparatus but when the function of this is lost bilaterally there is normally no head tremor. When streptomycin was first introduced for the treatment of tuberculosis many patients, as a result of the very high doses used initially, became unstable and could not walk satisfactorily but there was no head tremor. The small muscles of the neck are very rich provided with muscle spindles and possible it is to their malfunction that isolated head tremor may be attributed.

I studied one patient with a severe head tremor and a tremor of the left hand of unknown origin. He had been treated with diazepam (Valium). When however 10 mgm were given intravenously the tremor was greatly increased (Fig 16). By contrast brandy largely suppressed the movements (Fig 17).

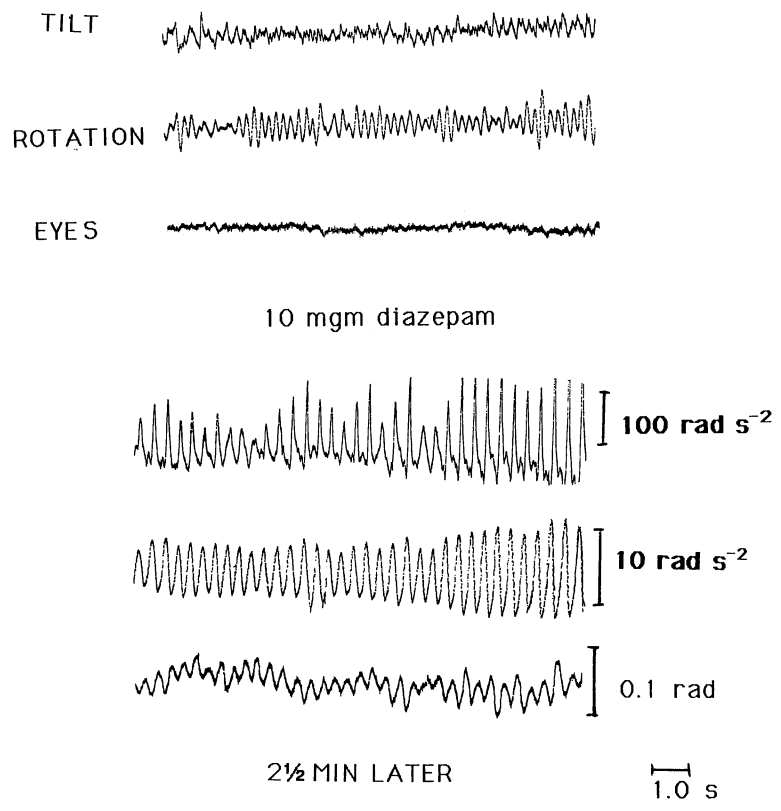

FIGURE 16

Top—control. Records of lateral tilt of the head, axial rotation of the head, and lateral movements of the eyes recorded by electro-oculography. Bottom—an injection of diazepam was followed by a slowing and large increase of tremor.

THE EFFECT OF COLD

The temperature of a limb is very important. Healthy volunteers immersed the forearm in warm (44°C) or cold (11°C) water for 4 minutes. The mean tremor level in the range 7–12 Hz was $63{\cdot}5 \pm 47{\cdot}5\ \mathrm{cm\,s^{-2}}$ before and $109{\cdot}7 \pm 39{\cdot}3\ \mathrm{cm\,s^{-2}}$ after warming ($n=22$). With cooling the figures were $50{\cdot}7 \pm 39{\cdot}3\ \mathrm{cm\,s^{-2}}$ before and $21{\cdot}6 \pm 19{\cdot}5\ \mathrm{cm\,s^{-2}}$ afterwards ($n=27$). The differences were highly significant ($p<0{\cdot}001$ and $p<0{\cdot}001$). Later a further five normal subjects were tested and the data displayed by spectral analysis. Typical results are shown in Fig 18.

Cooling[40] diminishes tremor as may be achieved, for instance, by holding the forearm under a running cold tap. Sixteen normal people and the same number of patients with essential tremor were investigated, the muscles of the forearm being subjected to moderate cooling in water. In both groups cooling produced a profound long lasting decrease in tremor of the corresponding hand. The results with a patient drawing an Archimedes spiral is shown in Fig 19. The effect could last for, say 40 minutes, and might be therapeutically useful for someone who,

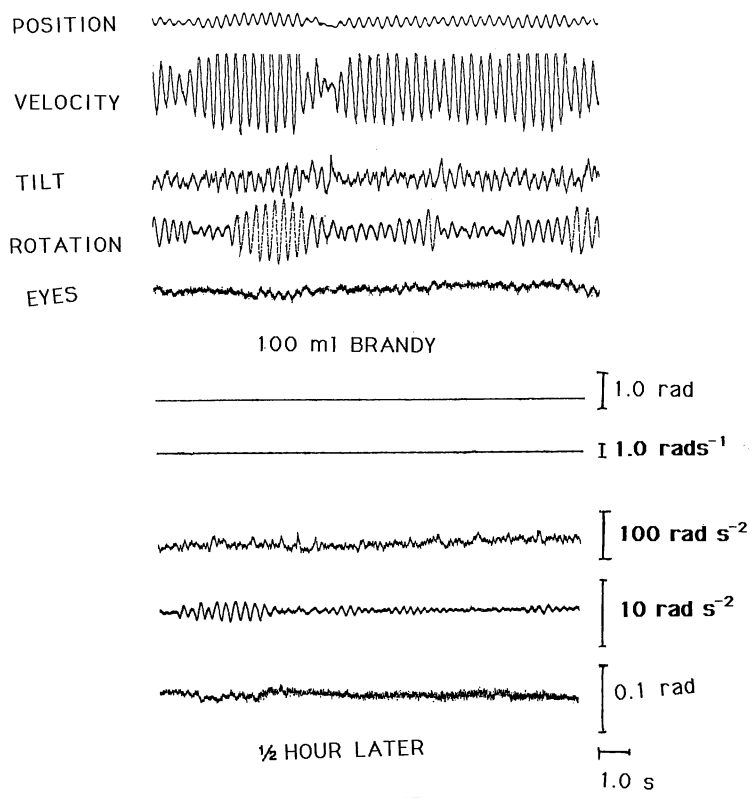

FIGURE 17

Top half—control. Lower half after drinking brandy. In each the upper two traces are recordings of tremor of the left hand, the next two of head movements and the last of eye movements. The head and eye recordings were similar to those in the previous figure.

for instance, had difficulty in signing cheques. There is thermostatic control of the core temperature of the body but not of the extremities, and the arm, having been cooled, stays cool for a considerable period. Biologists and surgeons now use microdissection extensively. One limitation to these skills is the level of physiological tremor.[41] Cooling here too may have its place.

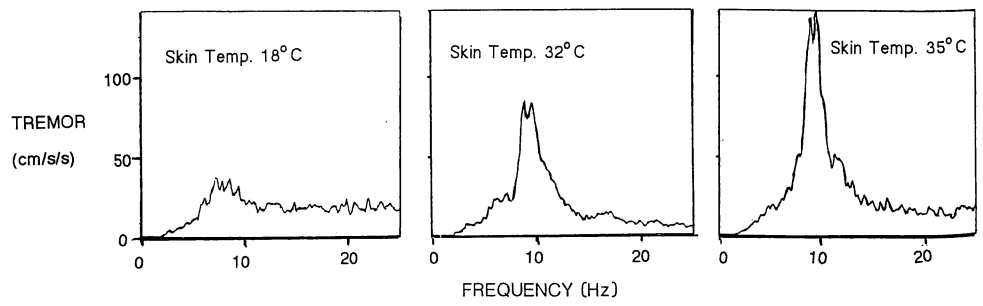

FIGURE 18

The peak of tremor activity at 10 Hz is clearly reduced by cooling and increased by warming.

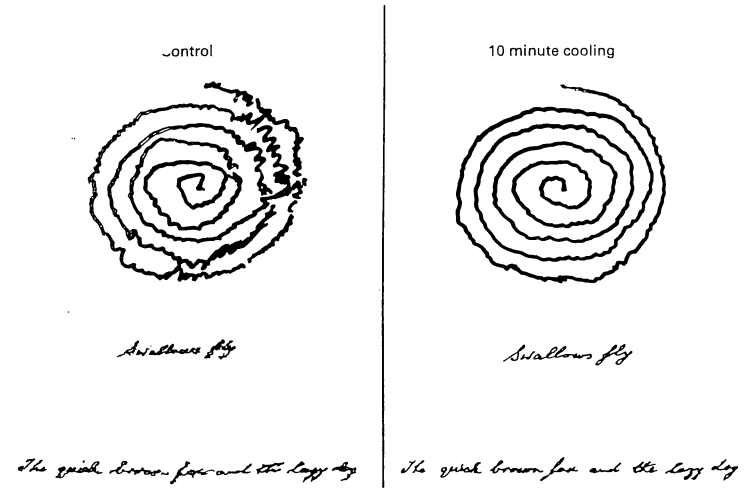

FIGURE 19

Improvement in dexterity produced by cooling in a patient with essential tremor. The patient was a man of 70 with a 40 year history of essential tremor. Drawing and writing were much improved by 10 minutes cooling at 10°C.

CONCLUSION

Tremor is simple to observe, and now its vigour and frequency can be measured with comparative ease. The observations open a window onto muscle function and motor control. It is said[42] that

> the price of freedom of movement, in a system having continuous forcing is a certain amount of instability.

If tremor is small it is like noise in an electrical system, merely an inevitable byproduct of the operation of the body's equipment.

ACKNOWLEDGEMENTS

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CONSENSUS CONFERENCE ON AUTOLOGOUS TRANSFUSION*

FINAL CONSENSUS STATEMENT

People of the UK have been and continue to be well served by their National Blood Transfusion Services. The panel emphasises the need to utilise good surgical techniques which minimise blood loss and recognises the importance of efforts to limit the use of blood to clinical necessity.

Notwithstanding the safety of allogeneic blood transfusion, a number of questions have been raised internationally, particularly in North America and the European Union, suggesting that the supply of blood can be supplemented by autologous transfusion techniques.

It is recognised that all blood transfusions carry risks. Screening of donated blood, however, has greatly reduced the potential risks of transfusion-transmitted diseases. There remains a degree of uncertainty on the immunological effects of allogeneic transfusion.

When used as the sole source of transfused blood, the principal advantage of autologous blood transfusion is the avoidance of the risks of transmitting infectious agents and potential immunological side effects of allogeneic transfused blood.

The panel notes the paucity of controlled randomised trials in the evaluation of these procedures and recognises the need to develop appropriate methodology and outcome measures to determine risk benefit and cost effectiveness.

Provision of services, present and future, should take account of the rights, interests and requirements of patients. Good medical practice requires the disclosure of alternatives as well as risks and benefits.

Preoperative Autologous Donation (PAD)

At the present time, in the UK there is a low degree of public interest, although the facility of PAD is potentially widely available. In Centres which offer this facility, the present take-up is low compared to take-up rate in America of up to 10 per cent accounting for 5 per cent of the total blood usage.

Not all patients are suitable and patients must be carefully selected on medical grounds. Eligible patients who undergo elective orthopaedic surgery are the primary target of PAD and it is possible to achieve exclusive use of autologous blood in at least 75 per cent of cases.

A current disadvantage is the difficulty of guaranteeing non-cancellation of routine surgery within the NHS. Other disadvantages include the possibility of cardiovascular accidents following donation. A further concern is that the operation has to be scheduled to allow usually for 1–4 donations at approximately weekly intervals. In some patients this could be a disadvantage. Although there are practical difficulties associated with the general introduction of PAD in the UK, we foresee that this practice may become more widespread provided that appropriate resources are made available.

*Held in the College on 4–5 October 1995.