A new method for the measurement of tremor at rest

by

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(4 figures)

Summary

This paper establishes a standard method for measuring human tremor at rest. The new electronic instrument described is an application of this method. It solves the need for an effective and simple tremor-measuring instrument fit for wide distribution. This instrument consists of a piezoelectric accelerometer connected to an electronic circuit and to a device displaying the results. The signal was analysed both using this method and also by a computer after accelerometer analogic/digital conversion. The tremor of 1079 healthy subjects was studied. Spectral analysis showed frequency peaks between 5.85 and 8.80 Hz. However the variations of the amplitude of tremor at rest was the most interesting parameter in relation to the subjects' neurological condition. Adrenaline, nicotine, and caffeine can increase the tremor at rest. On the contrary, a relaxation session decreased tremor at rest significantly in healthy subjects ($P<0.01$). This new tremor-measuring method opens new horizons in the understanding of physiological and pathological tremor, stress, anxiety and in the means to avoid or compensate them.

Résumé

Nous décrivons une méthode standardisée pour la mesure du tremblement humain au repos. Le nouvel instrument électronique que nous décrivons pour la mise en application de cette méthode répond au besoin d'un instrument facilement utilisable auprès d'un large public. Ce système est composé d'un accéléromètre piézoélectrique relié à un circuit électronique et à un système d'affichage du résultat. Le signal issu du capteur a été analysé à la fois en appliquant cette méthode et par ordinateur après conversion analogique/digital. Le tremblement de 1079 sujets sains a été étudié. L'analyse spectrale a montré un pic de fréquences entre 5,85 et 8,80 Hz. Cependant les variations de l'amplitude du tremblement se révèlèrent être le paramètre le plus intéressant en rapport avec l'état neurologique des sujets étudiés. L'adrénaline, la nicotine et la caféine peuvent augmenter le tremblement au repos. Par contre une séance de relaxation diminue le tremblement au repos des sujets sains de manière significative ($P<0,01$). Cette nouvelle méthode de mesure ouvre de nouveaux horizons pour la compréhension du tremblement humain physiologique et pathologique, de l'anxiété, du stress et pour l'étude des moyens de les prévenir et de les soigner.

Introduction

Tremor has been defined as rhythmic oscillations produced by involuntary contractions of antagonist muscles which may be alterning or synchronous (KOLLER, 1984). Even at rest, humans and animals are subject to barely perceptible movements : tremor, due to unconscious muscular contractions. Some forms of tremor can be physiological, but other forms can be pathological, as in Parkinson's disease : Tremor is a frequent cause for neurologic consultation. In past studies on humans and animals, tremor was most often evaluated either by self-evaluation of patients (ZDONCZYK *et al*., 1988), or by simple eye-observation of animals (STERN *et al*., 1985). Tremors are recognized clinically by the movements they produce, and can be recorded by piezo-electric transducers such as accelerometers. Specific apparatus for quantifying tremor has sometimes been used (KOLLER *et al*., 1986; TYRER & BOND, 1974*a*; LEHTINEN & GOTHONI, 1985), but a precise, reproducible standard method for quantifying human tremor has not yet been developed on a large scale. Currently, tremor is separated into two types (i) tremor at rest (ii) kinetic tremor (tremor due to dynamic movements of the limbs). The existing tremor registering methods do not distinguish between tremor at rest and kinetic tremor.

This paper presents a new, simple and non-invasive method for the measurement of tremor at rest. Our experiments using this method concerned general data (influence of age and sex on tremor) and the tremorogenic effects of some environmental parameters : coffee-drinking, cigarette-smoking, alcohol, stress.

Material and methods

The instrument developed, consists of an accelerometer, connected to an electronic circuit and to a displaying system (LCD, voltmeter, or computer). Several piezo-electric accelerometers, with sufficient precision, are already available for the measurement of tremor. However, they are not suitable for large scale distribution because : (i) these accelerometers are fragile and can be easily damaged by mechanical shocks (for example, if the operator happens to drop the captor on the floor). A system fit for wide distribution must be shock-proof and (ii) the price of these captors is very high. (iii) there existed no standard measuring position and no tremor reference scale previously.

The use of the standard measuring method described, has enabled us to develop a new accelerometer, fit for wide-scale fabrication and with satisfactory technical characteristics for the measurement of human tremor. We have tested and propose a standard measuring position (SMP), as well as a tremor reference scale associated to this SMP.

The technical characteristics of the captor have been tested by fixing the captor on a vibrating platform with known and adjustable amplitude and frequency. The technical

characteristics of the described captor (Figure 1) are shown on Figure 2. The precision is ± 1 %.

FIG. 1. *High-technology, precise, robust, piezo-electric accelerometer.*

One end of the piezo-electric element is linked to a mobile 1.3 g mass (2). The microscopic movements of the mass generated by tremor are limited by stops (3) in order to avoid damage to the captor in case of mechanical shock. The signal is collected by the wires (4) soldered on both sides of the piezo-electric element (1).

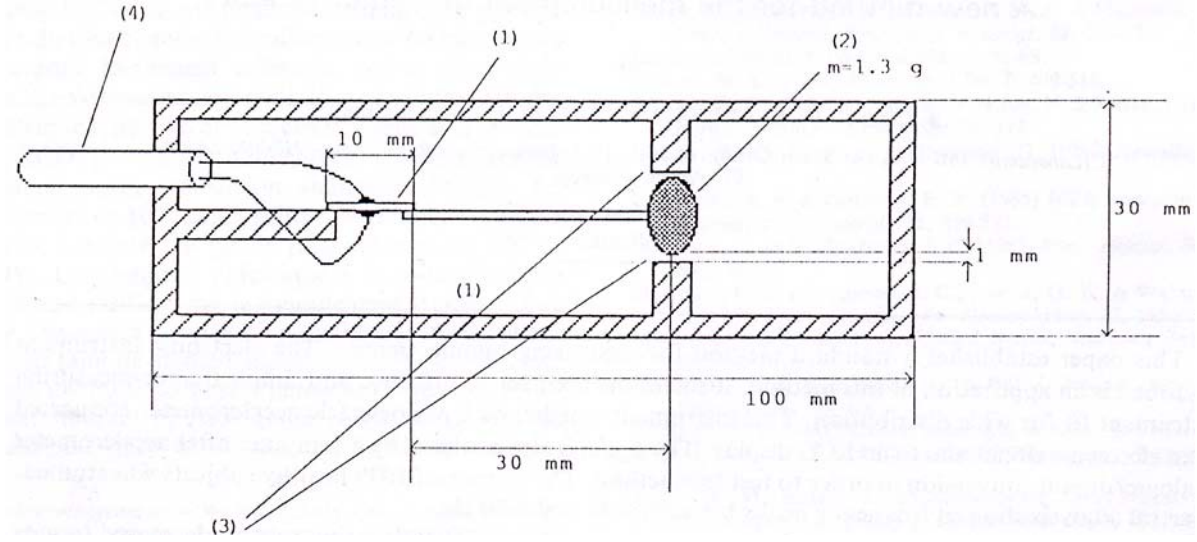
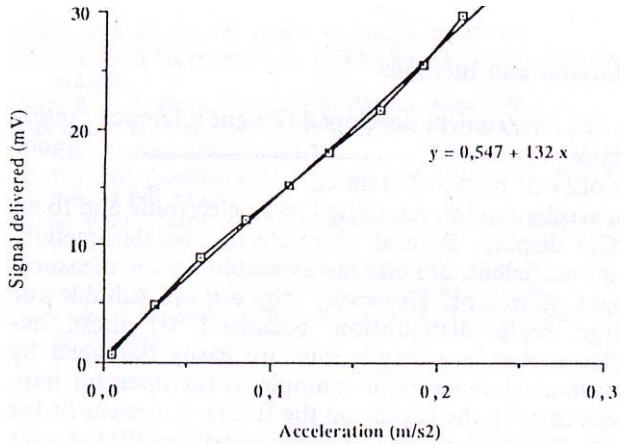


FIG. 2. *Signal in Volts delivered by the described accelerometer as a function of the acceleration.*

The accelerometer was placed on a platform vibrating sinusoïdally at a known frequency (f) with an adjustable displacement amplitude (A). The amplitude of acceleration is then given by $[d^2x/dt^2]=A \times (2 \quad f)^2$. The signal delivered by the captor (in mV) was simply measured by an electronic circuit with a voltmeter. The graph obtained is linear with a 1 % precision between 0 and 0.25 m/s^2. The acceleration of hand tremor in the described standard position is usually inferior to 0.1 ms^{-2}. This authorizes the use of such an accelerometer for the measurement of human tremor with a 1 % precision.



Signal analysis

In order to determine the characteristics of the tremor and work out an adequate treatment of the signal, a spectral analysis of the signal must be done. Our spectral analysis was done by *Compaq* 286 PC computer equipped with a Data Translation DT 2808 A/D interface (*Data Translation Inc*., 100 Locke drive, Marlboro, MA, USA), after amplification of the signal and analog/digital conversion. The sampling frequency was 100 Hz.

In order to quantify tremor, we define a tremor index, expressed in ms^{-2} by the following formula :
Tremor index = $k \, . \, A_{corr}$ where $1/k = 6.66 \times 10^{-4}$ and A_{corr} is the amplitude of acceleration in ms^{-2} during the period of measurement, after elimination of undesired parasites. Thus the tremor index is proportional to the amplitude of the acceleration of tremor at rest, and all undesirable signals are eliminated. From a physiological point of view, this tremor is generated by the transformation of metabolical energy into mechanical energy by the muscular cells. This energy creates the tremor and is dissipated in the form of viscosity and friction in the muscles. This measurement method eliminates the kinetic tremor induced by small involuntary muscular movements, which deliver a much higher amplitude signal not in relation with the tremor at rest.

This new instrument has been tested by analyzing the signal delivered by the captor simultaneously with a simplified electronic circuit and with a computer after analog/digital conversion.

Tremor measurement

One thousand and seventy nine healthy subjects (507 male and 572 female) measured their tremor after answering a written questionnaire on the following points : age, sex, average cigarette and tobacco consumption (in cigarette equivalents), average coffee consumption (in cups/day equivalents), average alcohol consumption (in g of alcohol/24 h), regular use of tranquilizers or not, date and time of measurement. The mean age of the group was 42.4 years.

The subjects were male and female volunteers who measured their hand tremor following our instructions for a standard measuring position (SMP) : the subject stands with both feet

on the ground, holding the captor in the dominant hand (right for right-handed and left for left-handed subjects), palm upwards, fingers slightly abducted, upper arm vertical and fore arm inclined downwards at a 45 % angle from vertical. This is a comfortable standard position which is easy to maintain without muscular movements during the measurement. The captor is held in the hand with moderate pressure, not clenched. Small variations around this standard position do not have much effect on the amplitude of tremor (±5 %). The subject is asked to keep his eyes open, look straight ahead and to avoid speaking, clenching the captor, and moving during measurement. Speaking, clenching the captor, and voluntary muscular movements induce a tetanization tremor (clenching) or kinetic tremor (speaking or moving) of much higher amplitude than tremor at rest. However, the tremor induced by small involuntary movements will be eliminated by the electronic treatment of signal and will not affect the result.

In order to have a reproducible measure of tremor, it is necessary to fix the duration of the measurement. We tested measures from 1 s to 10 min duration, and opted for a standard measure duration of 20 s, because tremor at rest (A_{min}) is reached in usually in less than 15 s. Tremor index was classified as "low and normal" when below 25, "moderate" between 25 and 50, and "high" over 50. The subjects were asked to make a self-evaluation of their psychological stress-level : low-stress, moderate stress or high-stress and the self-evaluations were compared to the objective measurements of the tremor index.

Tremor was also measured in a group of 17 subjects, 8 males and 9 females, aged 19 to 73 before and after participating in a 30 min guided relaxation session. On arrival, the subjects sat down for 10 min. They were then told that they were participating in a scientific experiment and instructed how to use the tremor measuring instrument. Their tremor was measured immediately before (pre-session tremor) and after the relaxation session (post-session tremor). Subjects were asked to keep calm and not to speak during the experiment, until the post-session measurements were finished.

Statistical analysis

Results are expressed as mean values ± SEM. Non-parametric statistical tests were used. A *P*-value < 0.05 was considered significant while a *P*-value <0.01 was considered highly significant.

Results

Spectral analysis of tremor

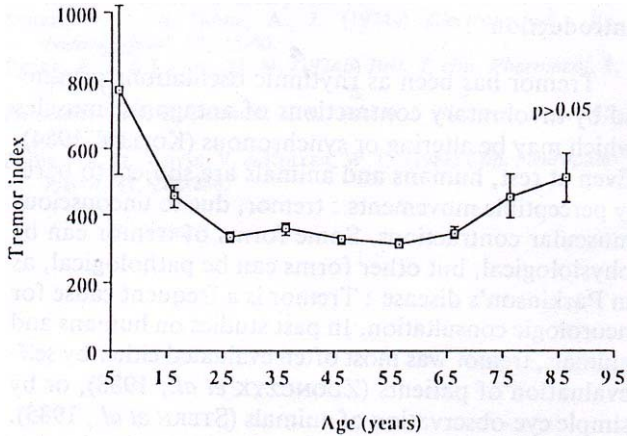
Spectral analysis of human tremor showed that human tremor had a frequency peak (or sometimes several peaks) located between 5.85 and 8.80 Hz. The position and shape of the frequency peaks did not differ significantly from one subject to another or over time. Most often, the tremor seems to be located in the same frequency range (3 to 20 Hz) and variations in the spectrum are not easily explainable by their frequencies, and do not appear to be clearly correlated with the subject’s neurological condition. No significant results were obtained by using the location of the peak frequency as a tremor indicator. This led us to quantify the amplitude of the signal rather than to locate the frequencies.

Environmental factors and tremor

Statistical analysis of the tremor index showed that the average tremor of the group was 37.1 ± 0.9.
The difference between male (35.2 ± 1.1) and female (38.6 ± 1.2) tremor index was not significant. The tremor index as a function of age (Fig. 3) showed that tremor was relatively stable from above 15 years to under 65 years. Below 15, and over 65 years, tremor was significantly higher ($P < 0.05$) and reached 55.1 ± 8.1 in octogenarians.

FIG 3. *Influence of age on tremor.*

Tremor is significantly higher in senile subjects above 65 years of age and in children below 15 years of age.

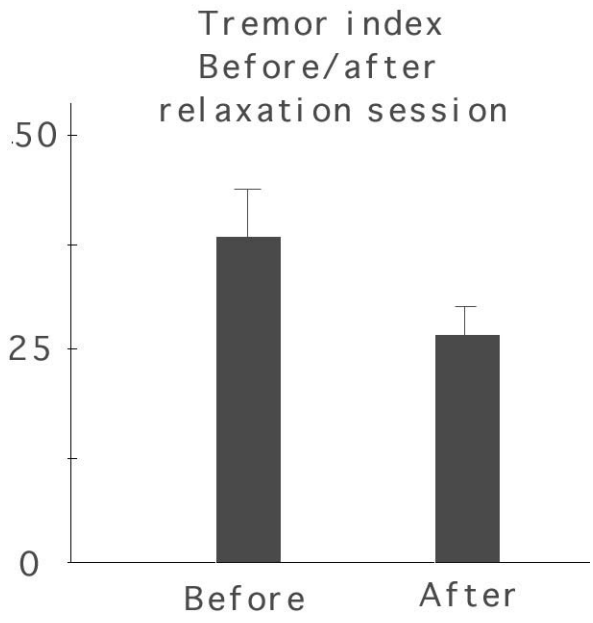


Among the subjects studied, 7.2 % were not able to self-evaluate their stress. Self-evaluations of the stress levels were in concordance with the tremor index in 83.6 % of the other subjects ($P<0.0l$).

The tremor index decreased significantly ($P<0.0l$) after a relaxation session (38.3 ± 5.5 before *versus* 26.4 ± 3.7 after the session). Of the 17 subjects participating, 13 subjects had a post-session tremor lower than pre-session tremor (Fig. 4).

The variations of tremor due to the consumption of tobacco, coffee and alcohol in this study were not significant (see discussion below). The tremor of subjects using tranquilizers was significantly higher (43.6 ± 2.8) than the tremor of subjects not using tranquilizers (36.3 ± 0.9).

FIG. 4. *Tremor and relaxation* Tremor has been measured in a group of 17 volunteer subjects participating to a 30 minute relaxation session. Tremor level of the subjects was measured before and after the session. Tremor measurements were significantly lower after the session.



$P < 0.01$

Discussion

Several techniques were proposed by previous authors for the measurement of tremor at rest or with loads (ZAHALAK & CANNON, 1983; FOKKENS *et al*., 1982; ROELS *et al*., 1983). But these measurements were very seldom used until today in clinical practice and never used by the general public because : (i) there was no simple tremor measuring instrument available until recently, and the very few available accelerometers were very expensive and fragile, (ii) in addition to the accelerometer, a precise measurement of tremor until today required complex electronic equipment and personnel training, to proceed with the measurements, with sufficient scientific knowledge to operate these instruments, in the rare cases when they were available (iii) the tremor data obtained even with adequate equipment requires special numerical treatment to eliminate parasite signals, otherwise the measurements are useless or very imprecise. No standard and simple instrument for measuring tremor has yet been commercialized. MURRAY (1981) emphasizes the need for an effective instrument measuring subjective and objective aspects of tremor. The lack of such a standard, optimized and easy-to-handle instrument has limited both the number and the quality of publications on tremor until now.

This paper establishes a standard method for measuring human tremor (standard measuring position and standard reference scale as defined above), and the electronic instrument described solves the need for an effective and simple tremor-measuring instrument. The technical characteristics of this system is well adapted for the measurement of human tremor at rest. It is shock-resistant and financially viable for large scale medical and/or public distribution. We have used acceleration of tremor rather than its integral (velocity) or the integral of velocity (displacement). There are arguments for using acceleration (MARSHALL & WASLH, 1956), velocity (MARSDEN *et al*., 1969) and displacement (REDFEARN, 1957) in the measurement of tremor. It is likely that all three are equally valid. Acceleration was chosen because an accelerometer is technically simpler. The choice of a one-axis

accelerometer is acceptable, because, in the standard measuring position as described, the tremor is approximately isotropic, that is the three components of the amplitude of tremor, A_x, A_y, A_z are similar. This justifies the use of a one-axis accelerometer indifferently oriented in space. The kinetic tremor is eliminated by the electronic circuit. This is important, since kinetic tremor often has a very high amplitude in the same range of frequencies as tremor at rest.

Earlier studies (KOLLER, 1984; TYRER & BOND, 1974*a*) and our own measurements have shown that human tremor is mainly concentrated in the 3 to 20 Hz area. This is the reason for filtering out the frequencies below 3 and above 20 Hz. The pattern of frequencies do not seem to have much physiological significance, and may be due to electromagnetic parasites from other electrical devices (50 Hz) or to mechanical resonances of the accelerometer. It is important to note that much of the research until now on tremor has not taken into account the possibility of mechanical resonance due to the piezoelectric captor, which can lead to false interpretation of results, since the resonance frequencies of accelerometers may be in the 3 to 20 Hz range (LEHTINEN & GOTHONI, 1985). In our system, the mechanical resonance frequency of the accelerometer was rejected at 45 Hz, in order to avoid interference with the measurement.

Voluntary muscular movements generate tremor due to muscular contractions. We define "Tremor at rest" as the tremor which remains in the absence of voluntary muscular activity. A simple integration of the amplitude of the signal would reflect both tremor at rest and kinetic tremor. The frequencies of tremor at rest and kinetic tremor are in the same range. So it is not possible to isolate the latter from the former by filtering out specific frequencies. How can one separate the smallest but most interesting component of the signal (tremor at rest), from kinetic tremor which is of much higher amplitude and has the same frequency range ? The problem is partially solved by adopting a standard position which includes "standing still" in the instructions given to the subject. However, some kinetic tremor still remains which is of much higher amplitude than tremor at rest. Therefore, a special electronic treatment of the data is made to make sure that the undesirable parasite tremors are not taken in consideration. Thus, even some muscular movements during the measurement does not modify the result. Tremor measurements by this method do not have to be longer than 20 s in duration. Another advantage of this system is that if the subject is disturbed during measurement, the result will not be affected. This permits measurements in non-quiet areas, such as hospital rooms, or at home, which is very important for a self-measure by the patient. Any temporary disturbance or movement of the subject during measurement will not affect the result as long as the subject respects the SMP (standard measuring position).

The peak frequency of human tremor was found between 5.85 and 8.80 Hz. This is coherent with some authors' results (KOLLER, 1984; TYRER & BOND, 1974*a*), which showed frequencies in a range of 6 to 11 Hz for physiological arm tremor, but slightly lower than others (BIARY & KOLLER, 1987; SHAHANI & YOUNG, 1974), who located physiological tremor in the 8 to 12 Hz area.

Pathological tremor such as essential tremor and parkinsonian tremor can be quantified by the described method, because they affect mainly the hands and because their frequencies are located between 6 and 12 Hz (KOLLER, 1984).

The higher tremor observed on subjects over 65 years of age confirms the existence of the clinically well-known senile tremor and also demonstrates that the proposed method is adequate for its quantification. Measurements of elderly tremor at home, without hospitalization, could enable fo1low-up of tremor under specific medical treatments and to observe the effect on tremor of environmental factors such as fatigue, smoking, diet... The higher tremor observed in children below the age of 15 may be explained by (i) artifacts due to the protocol, because children will not always maintain the standard position during 20 s as instructed, or (ii) the existence of a higher tremor in children, which could be due to an immaturity of the nervous system. Only one publication previously mentioned the existence of a higher tremor in children.

Nicotine often induces hand tremor (TYRER & LADER, 1974*b*; STIFFMAN *et al.,* 1983), and it potentiates the tremorogenic effect of alcohol-withdrawal (GOTHONI & IKOLA, 1985). Nicorette, a nicotine gum sometimes recommended to help patients stop smoking, can, in some instances, induce tremor (STEUFFER *et al,* 1986). Caffeine is also known to induce arm tremor within minutes after injection in humans. Such tremor is significantly higher than the tremor induced by injection of a placebo (GOTHONI & IKOLA, 1985; STEUFFER *et al.,* 1986; FOLEY *et al.,* 1967; SHIRLOW & MATHERS, 1985; CHAIT & GRIFFITHS, 1983). In contrast, Koller reports that caffeine does not always induce tremor (KOLLER *et al.,* 1987). Our negative results concerning the influence of nicotine and caffeine on tremor are surprising in regard to the literature (LEHTINEN & GOTHONI, 1985; FOLEY *et al,* 1967; SHIRLOW & MATHERS, 1985; CHAIT & GRIFFITHS, 1983) and confirm Koller's doubts (KOLLER *et al.,* 1987). However, one must distinguish between the effect of chronic consumption and the immediate effect (GOTHONI & IKOLA, 1985). Our results are concordant with all other results if we consider that caffeine and nicotine have an immediate, momentary, and sometimes quite important tremorogenic effect after ingestion. Such a temporary effect did not appear in our protocol because measurements were not undertaken immediately or shortly after ingestion. The subjects were asked what is their usual average consumption of coffea or tobacco, not if they had or not absorbed these substances shortly before the measurements. Measurements of tremor made immediately before and after consumption of caffeine and nicotine clearly show an immediate but temporary tremorogenic effect of caffeine and nicotine (unpublished observations).

The ingestion of small doses of alcohol usually reduces tremor amplitude (KACHI *et al.,* 1985) within 15 min (GROWDOWN *et al.,* 1975). However, the most spectacular effects of alcohol on tremor appear with the withdrawal : the symptoms of alcohol withdrawal often include strong tremor (DERR & DERR, 1986; GOTHONI & IKOLA, 1985). This withdrawal tremor occurs in some cases after a short period such as a single night's sleep following a few days of alcohol consumption. The alcohol-withdrawal tremor has the characteristics of enhanced physiologic tremor, which makes it measurable by our method. A permanent tremor is sometimes observed in chronic alcoholics (KOLLER, 1984). It is not determined, however, whether this tremor is caused by a direct effect of ethanol which would enhance a coexisting essential tremor, or whether it is due to peripheral nerve disease. Ethanol withdrawal increases the tremorogenic effect of harmine (GOTHONI, 1985) and also potentiates nicotine-induced tremor (GOTHONI & IKOLA, 1985). Most of the subjects in our experiments were not addicted alcoholics. The chronic consumption of small doses of alcohol did not appear to influence tremor. However, it may be that, as for nicotine and caffeine, the immediate effect is different from the chronic effect. It may be also that the effect on tremor of reasonably small doses of alcohol is inexistant while only doses above a minimum amount of ethanol produce a modification in tremor, or that tremor modifications

are both ways (increase or decrease of tremor) depending on the individual, or that some types of alcohol (such as that in wine) may decrease tremor while distillated alcohols could increase tremor (unpublished observations seem to confirm this phenomenon).

There is considerable evidence that psychological stress increases tremor amplitude. It is well-known for example that physiological tremor increases in states of anxiety or during emotional stress (HAIDER *et al.,*1983), during which an increase in release of catecholamines from the adrenal medulla takes place, and ß-b1ockers are often successful in relieving such tremor (KELLY, 1978). KOLLER *et al* (1987) observed that examination stress is often accompanied by whole body microvibrations relieved by propanolol. Mental stress can not only induce tremor in healthy subjects (HAIDER *et al*, 1983), but also exaggerate the pathological tremor of patients suffering from essential (GINGO *et al*, 1986) and parkinsonian tremors (ROELS *et al*, 1983). Panic attacks often observed in anxious patients generate tremor, which is also relieved by ß-blockers (KELLY, 1978). Tremor can be experimentally produced in human subjects by injections of stress-hormones such as adrenaline (injections of 10 µg/min) (FOLEY *et al*., 1967). This effect is almost systematic : adrenaline injections (l8 µg/min) produced a significant increase of tremor within minutes following injection on 17 out of 18 patients tested by stimulating adrenergic receptors by adrenaline injections (MARSHALL & SCHNEIDEN, 1966). This adrenaline induced tremor is almost back to normal 15 min after injection. Our results concerning the impact on tremor of a relaxation session and the correlation between measured tremor and self-evaluated stress, both confirm the link between psychological stress (subjective "stress" or "nervousness") and tremor (objectively quantified).The significantly higher tremor observed in subjects using tranquilizers can be explained as follows : (i) subjects using tranquilizers have higher tremor because they are more exposed or more sensitive to stressful situations than other subjects, (ii) the action of the tranquilizers does not suffice to lower their tremor.

The latency of tremor due to stress, adrenaline injections or ingestion of caffeine and nicotine seems quite short. Tremor usually appears within the first minute after stress or adrenaline injection and the duration of such tremor is approximately 15 min (MARSHALL & SCHNEIDEN, 1966). This short latency time could be used for prevention and educational purposes, with measures made immediately before and after smoking and/or drinking coffee. Confronted with measurements showing the neurotoxic effect of his daily habits, the subject could then be encouraged to stop smoking or drinking coffee.

Conclusion

The method described is simple and non-invasive. It can be used to quantify tremor at rest, to evaluate and to follow physiological or pathological tremors such as tremor due to psychological stress, senile, essential and parkinsonian tremors. The new measuring method and instrument opens new horizons to the understanding of physiological and pathological tremor, stress, anxiety and to the means to avoid or compensate them. The effect on tremor of various environmental parameters such as professional stress, cigarette-smoking, or coffee-drinking habits can be quantified. The effects of various stress-control methods such as medical treatments (*ß*-blockers) or relaxation sessions can also be quantified.

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