STUDIES ON MINOR TREMOR*
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Jasper and Andrews (1938) observed that the tremor of the parts of the human body had the frequency of 8-12 c/s., mixing with that of 17-30 c/s., corresponding respectively with the α and β waves of electroencephalogram. Schwab and Cobb (1939), studying in paralysis agitans, could not find any correlation with the brain wave. Lindqvist (1941) also studied in the relation between the tremor and α rhythm and found no constant relation between them. Ditchburn (1953) observed the tremor of 30-80 c/s. in the extra ocular muscle.

Rohracher (1952) found by using a special pickup that the body surface of warm-blooded animals is constantly vibrating and that this phenomenon cannot be observed in cold-blooded animals. Since this specific vibration in warm blooded animals was enhanced in the fevered condition and inhibited during hibernation, Rohracher supposed that it might be caused by the action of autonomic nervous system which controls body temperature. On account of the finest amplitude of vibration, he called it “Mikroschwingung, microvibration”. Since 1955 the authors have been studying this fine tremor. The present investigation was undertaken to elucidate the physiological meaning of the tremor and its originating mechanism more precisely. The authors call this fine tremor the “Minor tremor” (MT). This “minor” means invisible. In this connection, the tremor in parkinsonism which is visible may be called the major or gross tremor, but in our concept these two phenomena may be explained similarly from the point of originating mechanism.

METHOD

Cats and rabbits were used as experimental animals. Occasionally human volunteers were subjected to the test. MT in the human being was led from the left thenar eminence, when the subjects lay on their back keeping quiet, and the both arms were streched parallel to the body axis, the palms being abducted to face upward.

A soft cushion was spreaded under the arm. Light anesthesia with phenobarbital in cats or with urethane in rabbits was applied in the physiological study, whereas principally no anesthetic was used in the pharmacological study.
MINOR TREMOR

MT in the animal was led usually from the depilated skin surface of a hind limb. As MT is a fine displacement of body surface, it is better to use pickup with as little inertia as possible.

Halliday (1956) led the tremor with photolight and this method is good in lineality but inconvenient (i.e., it needs a dark room). Two types of pickup were used. One is a Rochelle salt pickup with a round pointed needle. The frequency characteristic of this pickup changes by the weight of a needle. In case of a needle of 1 gram, acceleration amplitude characteristic is 3 to 50 cycles, having a contact area of 1 mm².

Another type of pickup is a special one with the vacuum tube RCA 5734, which feels the vibration on the weight which hangs on the plate pin. It has a wide contact area of 2 × 5 cm² and a weight of 20 g. (fig. 1). The sensitivity of the vertical oscillation to the horizontal is a ratio of 3:1. This pickup was generally used in the experiment of human subject.

The frequency characteristic of the vacuum tube pickup is 0.5 to 40 cycles.

Though the contact pressure of pickup does not alter the wave form of MT in our experiment, touching as light as possible is desirable for the purpose of faithful recording. The pickup was connected to the electroencephalographic equipment and the amplified MT was recorded on the inkwriting oscillograph paper. In order to avoid noise, higher frequencies above 30 cycles were cut down in the amplifier.

In case of analyses of MT, automatic E.E.G. frequency analyzer was used and the coefficient of appearance of seven frequency bands such as 1–2 c/s, 2–4 c/s, 4–8 c/s, 8–13 c/s, 13–20 c/s, 20–30 c/s, and 30–60 c/s. were calculated.

RESULTS

MT in the normal condition

The frequency of MT led from the surface of a hind limb was 8–12 (most frequently 11) cycles per second in the cat and 6–14 (mostly 8) in the rabbit. In the human being the frequency of MT from the thenar eminence was 8–12 cycles, though individual differences ranged from 5 to 13 cycles (fig. 2). The amplitude of MT showed a great variability (1–10 micron) according to the places where pickup was attached. In general, MT at a distant place from muscles was small in amplitude. In normal subjects, the amplitude of MT was
FIG. 2. Analysis of normal minor tremor. MT is a original record. The tracings from the second to the 8th show the analyzed pattern of each frequency band. The vertical deflections indicate the integrated pattern of each band.

1-2 micron, 1 micron corresponding to 1 milivolt in our pickup. MT was led from the flexor side of a forearm when the arm and hand were bent, the amplitude of MT was decreased in parallel with the intensity of muscle contraction, whereas MT led from the extensor side did not change significantly or increased slightly. In normal subjects, MT was recorded every five minutes during a complete rest for 30 minutes. A gradual decrease in MT was observed (fig. 3). The frequency distribution of MT was analysed by the automatic analyzer, and the appearance of not only 8-13 c/s. band but also 4-8 c/s. and 13-20 c/s. bands and others were well noted before resting. After 5 minutes rest, the frequency of 8-13 c/s. band increased in most experiments, that of 4-8 c/s. band and 13-20 c/s. decreased moderately and that of 1-4 c/s. and 20-60 c/s. decreased remarkably. The increase in 8-13 c/s. band which corresponds to the alpha rhythm of the brain waves

FIG. 3. The gradual decrease of amplitude in minor tremor during rest.
FIG. 4. The frequency distribution soon after (O') and 5 minutes after taking rest on bed.

FIG. 5. Two examples of the effect of overbreathing on minor tremor.
A: control
B: immediately after 3 minute breathing
C: 5 minutes later

and the characteristic changes in the other bands have a very important significance to study the origin of MT, as will be discussed later. Figure 4 shows the histogram of frequency distribution of MT immediately after taking rest and after 5 minutes. The frequency band of 8-13 c/s. is below 30% at first, but after 5 minutes it is above 30%, while that of 4-8 c/s. and 13-20 c/s. are decreased or unchanged.

The environmental thermal change also influences MT. The amplitude of MT was increased by dipping the limb of a rabbit into the warm water at the temperature of 50 °C., whereas it was decreased in cold water of 0° C. Upon administration of pyrogens, the frequency and amplitude of MT increased. The amplitude of MT was increased by 3 minute hyperventilation in normal subjects and patients (fig. 5). Though subjects were forced to breathe after 1 minute rest when a decrease in amplitude was expected, the amplitude was raised, indicating that the effect of overventilation overcame the natural decrease.

Relation between MT and other rhythms in the organism

The possibility that other rhythmical movements in the body might be the origin of MT was excluded as follows: Respiratory movements are definitely low in frequency so that they cannot be considered to have any relation to MT. In order to investigate the relation between MT and heart rate, the heart of a rabbit was extirpated while MT was recorded from a limb. The amplitude of MT was gradually reduced but the frequency of MT did not change until the complete cessation of MT was observed 30 minutes after the extirpation.
of heart.

A pickup was placed on the exposed intestine of a urethanized rabbit and the vibration of intestine was recorded. The frequency was found to be only 1-5 cycles per second, apparently lower than that of MT. Acetylcholine injected intravenously in a dose of 0.01 mg/kg. enhanced the intestinal vibration, whereas MT was not significantly affected by this drug.

The skull of an animal was trephined and a needle pickup was attached to the dura surface. The vibration of brain was synchronous with the heart rate and usually avoid of the 10 cycles rhythm. From the above experiments, the relation between MT and other rhythms in the organism was not given and only the connection with the rhythm of EEG was remained.

**Regional difference in frequency**

It is very important to know the frequency difference in localities, because this explains whether the origin of MT is based on the stretch reflex or not. Generally speaking, where the muscles are small, higher frequencies (β band) are prevailing and on the parts with large muscles the frequency abounds with α and θ band.

**Influence of peripheral stimulations on MT**

When the ear of an anesthetized cat was held by clip, MT was inhibited strongly, and after the inhibition had continued for a while, the amplitude of MT began to increase remarkably. In case of a light anesthesia, the amplitude of MT was rather high. A remarkable influence on MT was observed by a strong oppression of ear. When the air was blown to the ear, a slight change was also seen. In case of holding the nose, the inhibition of MT was observed but not so significant, and in the forefoot and tail it was not clear. When the smoke of tobacco was blown to the nose of cats, the inhibition was also shown.

In human subjects, these effects were not so noticeable as was seen in cats, but the increase in amplitude of MT was sometimes shown. In the photic stimulation of 10 cycles by stroboscope, the alpha band was sometimes influenced, and the detailed results will be reported in near future.

**Influence of the central and peripheral nervous system on MT.**

When the sciatic nerve of a cat was cut, the MT from the region of its innervation was enhanced temporarily and then decreased markedly. The decrease in amplitude lasted for a long time and did not recover. The MT from the other side on which the sciatic nerve was left intact, remained unchanged. The electric stimulation of the peripheral cut end of sciatic nerve with the low intensity which produced no jerk increased the amplitude of MT as long as the stimulation was continued. All unilateral dorsal roots of spinal cord below the thoracic level were cut in a cat. The amplitude of MT led from the ipsilateral hind limb was increased at first, followed by a gradual diminution and became hardly recognizable after one hour. MT from the contralateral hind limb remained unchanged. When aminocordin (nikethamide) was injected intravenously in this preparation, MT of both sides was accelerated slightly. When all unilateral ventral roots of spinal cord below the thoracic
level were cut, MT from the ipsilateral limb was completely inhibited, whereas contralateral MT was not influenced. Intravenous injection of aminocordin in this preparation enhanced the contralateral MT but did not activate the depressed MT of ipsilateral limb. When the one side of labyrinth is broken, the decrease in amplitude of MT of ipsilateral hind limb was discovered.

The motor area of the left cerebral hemisphere in a cat was removed while MT was recorded from bilateral hind limbs. The amplitude of MT led from the right side was slightly inhibited whereas that of the left was unchanged or increased. The asymmetry of MT following this preparation was diminished after one day or two.

Non-convulsive electroshock was given through the electrodes inserted into the both ears in a cat for three minutes. The frequency and amplitude of MT were markedly increased not only during the electric stimulation but also after the shock. In other experiments, the depressed MT by the intravenous injection of Amytal sodium was restored by the electro shock. At the same time EEG was shifted to the arousal pattern and E.M.G. also increased the spike discharges.

By the mere application of an electric current to the cranium, it is difficult to decide what places are stimulated. The application of the electrical stimulation to motor area increased MT of the opposite side hind limb clearly. Though it was not definite, a narrow inhibitory area located behind the motor area.

The inhibition of MT was observed by the application of electric stimulation to the fronto-orbital and auditory areas. In the cerebellum, both the inhibitory and facilitatory area are located, and complicated.

Stimulating electrodes were implanted permanently in various places of the cat’s brain, through them the stimulation was applied, and the change in MT in the opposite side of hind limb was studied. The effect of central stimulation on MT was studied. If we cite an instance, the results are as follows: MT was inhibited by the stimuli of hypothalamus during stimulation, and was restored immediately or augmented after the interruption. The long inhibition (about 3 minutes) was observed by stimulation of N. hypothalamus ventromedialis.

The hypothalamus was noted to have an strong influence on MT, and it is very interesting to consider the close connection between the emotion of human being and MT as will be discussed later, since hypothalamus is the site of emotion. MT was accelerated later than the beginning of stimulation, or in some cases after the interruption.

In any cases, the inhibition was not shown in the caudate nucleus. The marked inhibition was observed in the stimuli of the inferior colliculus, and the acceleration in the internal capsule.

Pharmacological and clinical studies
It will be helpful to guess the origin of MT to know how MT is modified by various drugs. Table 1 shows the effects of drugs on MT in cats (table 1).
In human being, several drugs were tested. Metrazol also increases the amplitude and frequency of MT. MT is accelerated by the hyperventilation and metrazol as though the brain wave is enhanced by them. Especially, this effect is significant when MT is led from the eyelid, or in epileptic patients. Intravenous administration of mephenesin 3.3 mg/kg reduced the amplitude of MT in all cases, at the same time the frequency of the wave other than a band reduced remarkably and a band occupied 70% of the whole. From this fact, it is suggested that the effect of resting on MT illustrates the muscle relaxation, and the waves other than a band, if a band is analogically considered as the a wave of EEG, will express some active elements.

Alcohol is a muscle relaxant, and after drinking alcohol, MT changed significantly. Intramuscular injection of chlorpromazine inhibits MT, but by the oral administration of a large dose, it increases the amplitude of MT from an early stage. A detailed analysis of frequency has not been done but the fluctuation of a mean period is not so remarkable. It was found that the increase in the amplitude of MT is growing gradually before the muscle rigidity was appeared as a reaction to chlorpromazine.

Tremor of parkinsonism is a gross and visible tremor, and it is influenced and modified by the central nervous system above the spinal cord, and explained by the same mechanism as MT. The amplitude of MT was decreased

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Dose (per Kilogram)</th>
<th>Acceleration</th>
<th>Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminocordin</td>
<td>25 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Thérapique</td>
<td>10 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Metrazol</td>
<td>0.2 mg.</td>
<td>±</td>
<td></td>
</tr>
<tr>
<td>Hexabarbital</td>
<td>20 mg.</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Pentothal</td>
<td>20 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Urethane</td>
<td>100-500 mg.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>5 mg.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>1-5 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Barium chloride</td>
<td>5 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Magnesium sulphate</td>
<td>25-100 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Calcium chloride</td>
<td>25 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Curare</td>
<td>0.1 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Mephenesin</td>
<td>15 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Tetraethyl ammonium bromide</td>
<td>5-10 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Cs. Cr</td>
<td>1-5 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Nicotine</td>
<td>0.02-0.05 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Procaine</td>
<td>5-10 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Xylocain</td>
<td>2-5 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Adrenalin</td>
<td>0.001-0.01 mg.</td>
<td>+ → +</td>
<td></td>
</tr>
<tr>
<td>Acetylcholine</td>
<td>0.05-0.01 mg.</td>
<td>± ← → +</td>
<td></td>
</tr>
<tr>
<td>Atropine</td>
<td>0.2 mg.</td>
<td>+ ← →</td>
<td></td>
</tr>
<tr>
<td>Pilocarpine</td>
<td>0.2 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Eserin</td>
<td>0.01 mg.</td>
<td>+ ← →</td>
<td></td>
</tr>
<tr>
<td>Vagostigmin</td>
<td>0.25-0.5 mg.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Ergotamine</td>
<td>0.05 mg.</td>
<td>± ← → +</td>
<td></td>
</tr>
<tr>
<td>Bentylimidazoline</td>
<td>5 mg.</td>
<td></td>
<td>+</td>
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</table>
and the frequency restored to 10 cycles by the intramuscular or intravenous administration of Diethazine hydrochloride. It had a high amplitude of 5–7 cycles before the prescription (fig. 6). It will be suggested from this fact that the abnormal interference from the extra pyramidal system above spinal cord may modulate the normal MT. The tremor of 6 cycles, spike and wave type, was recorded in the Wilson’s disease, and it may be the abnormal interference from the above extrapyramidal system centering around the corpus striatum. Though the authors have not many example of the tremor of Basedow’s disease, the frequency of MT is increased, and it is imagined that it will have some connection with the basal metabolism.

The relation between emotion and MT is frequently observed clinically. When the patient who had received electroshock treatments was fixed with the electrodes of EEG on the head, then the large amplitude of MT was observed. The patient felt the uneasiness of electroshock through electrodes, and when the electrodes were taken off in this case, MT was restored to normal. When the patient is put into a state of hypnosis, and under experimentally induced stress situations, for example, having an experience of bitter taste, sprinkling hot water producing a burn, or inspiring fear as if fallen from a cliff, then the amplitude and frequency of MT are increased, and when he is in a tranquil mind or comfort condition, the frequency of MT decreases and the wave of $a$ band becomes superior. It is possible to change MT by a suggestion of coldness or warmness hypnotically. The frequency and amplitude of MT decrease in the drowsy state, and increase in the awakening.

DISCUSSION

Several studies were achieved on the fine tremor of body surface, and very few of them made a full discussion on its mechanism. The first conception is that a part of body has the tendency to resonate in special frequency. If so, however in case of loading, the frequency must change, but no change was observed experimentally, and the idea of the mechanical factors does not hold
good. Marshall (1956) has objected to the theory that MT is caused by the feedback of stretch reflex, showing that the tremor is independent of a distance from the spinal cord, changes by the age, or appears by the section of dorsal roots. These facts are contrary with our experiments. (MT is inhibited markedly by the section of dorsal roots).

They considered that the muscle is a kind of low pass filter as possible reasons and that the discharges of below 15 cycles in motor fibers may change into mechanical oscillation, and higher discharges will be filtered. Harmoen et al. (1958) reported that in a large muscle the frequency of MT is slower than in a small one. This seems to explain the low pass filter theory. However, these have no evidence theoretically. The most appropriate idea is that MT will be caused by the autorhythmicity of motor neuron, spinal cord or stretch reflexes. The concept that the origin of MT is located in muscle fiber is supported by several experimental data in the present study as discussed in the experimental results. Although the vibration originates in muscle, the nerve innervating the muscle and the spinal cord connecting with this nerve undoubtedly play important roles in the development of MT. This idea is indicated by the above mentioned data.

Another important fact found in the present study is that the section of dorsal roots markedly inhibits MT. This fact, together with the inhibition of MT by the section of ventral roots, indicates that MT is accomplished by the spinal reflex. Thus the circuit for MT is considered as follows: -spinal cord- ventral root- efferent nerve- muscle fiber- afferent nerve- dorsal root- spinal cord.

Now that MT is likewise observed in the static state of muscle, the impulses to produce MT should pass through the small motor nerve system and through the afferent nerve from the muscle. In our experiment of cats, the oppression given to the ear caused an acceleration of MT, followed by a marked inhibition, or an augmentation from the first.

According to Granit, the pinna reflex has a strong element of gamma system, and when the ear is touched, the afferent impulse from the gamma motor system, muscle spindle, is influenced markedly, but has no effect on muscle contraction frequently. From this fact, it is suggested that MT has a close connection with the gamma motor system. The gradual decrease in amplitude and frequency of MT by the resting shows that MT has some relation to muscle relaxation and muscle tonus.

For the purpose to interpret the mechanism of rhythmical nature of MT, there have been only few serviceable observations. Denny-Brown (1929) reported that discharges of 5-8 cycles per second appeared in neuromuscular unit following the extension of soleus muscle, and irregular discharges combined by the strong extension. Morita (1956) also observed discharge of 10 cycles appearing reflexly in muscle of spinal rabbit. These periodic impulses may cause periodic contraction of muscle spindle, as is confirmed by Kōketsu et al. (1956), and this contraction of 10 cycles seems to be the source of MT. The last problem why the impulses are interrupted with the rhythm of 10 cycles may be explained by the refractory period of a motor neuron. Although MT is
MINOR TREMOR

produced fundamentally by the spinal reflex, many experimental data suggesting that the higher center influences MT were shown.

The neurological connection of brain with the small nerve system has been evidenced by the recent study. The proprioceptive impulses of muscle reach the cerebral cortex is well known. Eldred et al. (1953) reported that internal capsule has a facilitatory and inferior colliculus has an inhibitory influence on the small motor nerve system. Furthermore, according to Granit and Kaada (1953), the discharges from gamma motor system are influenced by the central nervous system.

For example, the facilitatory areas locate in the brain stem, diencephalic reticular system, and also in motor cortex, anterior lobe of cerebellum, pyramidal tract, caudate nucleus and the inhibitory areas in bulbo-reticular system, cerebellum, motor cortex, orbito-frontal area and amygdala. In our experiment, it was found that the hypothalamus has a strong effect on MT, and further the parts of N. caudatus, cerebellum, and motor area, the inferior colliculus, fronto-orbital area, and motor area have trng effects on MT. A close relation was observed between the effects of central stimulation on the gamma motor system as Granit and Kaada had reported and those on MT. MT becomes abnormal by the neurological disorders, such as Parkinsonism and Wilson's disease. Although it may be the influence of higher central structures, but that of gamma system is also undeniable.

That MT is influenced by emotion was proved by the experimental hypnosis. Accordingly, MT will be helpful as the guide to express the emotional state. It will be useful psychiatrically and psychophysiological and also to study the muscle tonus. The authors have no experience, but Halliday (1956) reported that no tremor has been observed in tabetic patients. This fact indicates that the origination of MT is on stretch reflex.

The relation between MT and E.M.G. has been studied by Sugano (1957), Hiroishi and Kawaoka (1957), Marshall (1956) and Lippold et al. (1957), although Hiroishi and Lippold et al. observed the parallel change, whereas Marshall denied it. Sugano sometimes observed the coincidence with E.M.G., but no definite relation was established between MT and E.M.G. Whereas Gordon et al. (1948) reported that the action potential and mechanical movement are parallel in the upper eyelid. The idea that MT is the result of delay in stretch reflex as was derived from the detail analysis of E.M.G. by Lippold (1957) is reasonable. MT is observable all over the body surface, though its amplitude is variable according to the localities. Rohracher (1955) supposed that MT might be concerned with the control of body temperature, because MT was observed in warm-blooded animals and not in cold-blooded. The reason why MT is absent in cold-blooded animals may be explicable with the anatomical difference in the proprioceptive structures. Namely, the differentiation between the large and small motor nerve fibers in cold-blooded animals is so incomplete that no independent impulse in the small motor nerve system exists. The possibility, however, that cold-blooded animals have a kind of MT of which frequency and amplitude are too low to be recorded, is undeniable.

Because the facts that MT is inhibited by cold stimulation is against the
purpose to control the body temperature. If MT were useful for the production of heat, coldness would increase MT in order to keep the body temperature. But on this point, further studies will be required.

Since the inhibition of MT is induced by the central nervous depressants, recording of MT may be an useful indicator of the depth of anesthesia. In this meaning MT appears to be superior to EEG, because the leading of MT from the body is more simple and the change due to the anesthetics is more sensitive than EEG.

Application of MT to the diagnosis of neurological or neuromuscular disease will be possible. Individual difference of MT (i.e. male and female) might be useful to the diagnosis of human character or constitution. Clinical application of MT is now under investigation by the authors, Rohracher (1958), and Denier (1957). Since alcohol has the marked influence on MT, the degree of intoxication may be decided. The effect of fatigue and age on MT will be reported in future.

SUMMARY

Minor tremor (MT), the phenomenon that the body surface of the warm-blooded animal is constantly vibrating, was led with the special pickup. The present investigation was to elucidate the meaning of MT and its originating mechanism.

1) The rhythm of MT was principally 10 cycles per second, and its amplitude was 1-10 micron. MT was influenced by the resting, temperature and hyperventilation. All other possible origins of the rhythm were excluded.

2) The originating mechanism of MT was discussed and it was suggested that the spinal reflex, especially gamma motor system, may be responsible to the production of MT. The evidences are as follows:
   a) relation between the pinna reflex and MT,
   b) relation between the electrical stimulation of central nervous system and MT,
   c) the effect of drugs on MT.

3) Application of MT to the diagnosis of certain diseases will be possible in future.

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LITERATURE