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SYNCHRONIZED IMPULSE DISCHARGES FROM RECEPTORS IN THE DEEP TISSUES IN RESPONSE TO A VIBRATING STIMULUS

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In the present paper a series of experiments is described dealing with the effect of mechanical vibrations on the receptors in the deep tissues of animals.

It has been found that when a vibrating tuning-fork is applied to the bones or tendons of an animal, rhythmical discharges of impulses synchronized to the stimulation frequency can be recorded from the nerves of the neighbouring muscles. These discharges come from the "stretch" receptors.[1]

With this technique it has been possible to investigate the "stretch" receptors' response to stimulation at different frequencies. The response at high frequencies appears similar to that obtained in the auditory nerve and its mode of production seems analogous (after Wever & Bray's [1930] hypothesis).

In a brief preliminary note it was suggested [Echlin & Fessard, 1937] that the synchronized discharges described might be concerned in vibratory sensibility. This is of course a purely theoretical supposition, but is considered in detail in the final discussion, where the possible effect of the pattern of peripheral afferent discharges on central interpretation is mentioned.

General remarks on the problem of vibratory sensibility

Although the present paper deals with peripheral afferent discharges that may or may not give rise to any sensation, we are forced to speak of vibratory sensibility if we are to discuss the work of most past authors who have studied the effect of vibrations on sensory receptors: for before the advent of modern electrical methods sensation was an unavoidable intermediary and usually the only sign of peripheral activity in sense organs. It is not our

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[1] "Stretch" receptors—those receptors in muscle and tendon which respond to stretch. See Matthews [1931 *a*].

intention, however, to give a detailed account of the literature on vibratory sensibility, as this is most extensive and in many cases too vague to allow of concise analysis; but rather to record briefly some of the views relating to its origin and to draw what conclusions we feel to be justified.

Any one who is acquainted with the literature on vibratory sensibility will be aware of the wide divergence of opinions as to the receptors responsible for its appreciation.

Some of the earlier workers [Rumpf, 1899; Weber, 1846; Treitel, 1896–7] were of the opinion that skin receptors probably are the most important in vibratory sensibility, but their evidence is entirely inadequate. Later von Frey [1915] and D. Katz [1923] gave definite evidence that the skin receptors are stimulated by vibrations, and came to the conclusion that they only are concerned in the appreciation of vibrations. They differ, however, as to the type of end organ involved, Katz believing it to be a specialized one and von Frey a pressure receptor. Adrian, Cattell & Hoagland [1931] have shown that single cutaneous receptors in the frog will respond at the same rate as a vibrating stimulus.

In opposition to the above beliefs, Head [1920], Déjerine [1914], Egger [1908], Neutra [1905], Piéron [1919], Symns [1917], Frank [1921], Bing [1905], Gordon [1936], Pollock [1937] and many others (which includes most neurologists) concluded that deep receptors certainly take part in the appreciation of the vibrations of the base of a tuning-fork. Most of the latter group of experimenters have felt that this method of stimulation affects largely the deep receptors, but some admit that those in the skin also participate. Many of them disagree, however, as to which deep end organs are responsible for the sensation.

Piéron [1919] feels that vibratory sensibility is evoked from any receptor either superficial or deep, and Bonnier [1898] likewise inclines to this view. Goldscheider [1904], although he admits the importance of deep sensibility, favours the cutaneous origin.

Head was firm in his opinion that only those receptors concerned in the appreciation of position and passive movements were involved, and remarks "the tuning-fork produces rapidly repeated movements of small range; these can be recognized, provided the appreciation of passive movements is shown to be normal". Egger and Déjerine, however, were equally convinced that receptors in the periosteum and possibly in the immediately neighbouring attachments (but not in the muscles) were peculiarly sensitive to vibrations. The evidence for this belief is supported mainly by the clinical observation that a tuning-fork produces its maximum effect when its base is placed upon a bone or joint, and little, if any, sensation of vibration results when it is applied to the belly of a muscle. This evidence, however, is not sufficient to rule out the possibility that the tendon and muscle receptors may respond; for most authors on the subject have pointed out that the bone is a particularly good medium for the transmission of vibrations. Neutra [1905] has suggested that these vibrations are reflected into the muscles which, he believes, contain the receptors for vibration, and Minor [1904] and Symns [1917] found that the response to a tuning-fork was unimpaired over bones that had been grossly affected by fractures or disease.

Apparently the only clinical objection to Neutra's suggestion is Egger's and Symns's observation that in certain cases of severe muscular atrophy, vibration sense was found to be normal. In fact, Egger showed that in some cases of unilateral atrophy, vibratory sensibility lasted longer in the atrophic than in the normal limb, "proof that the muscle is not the site of the perception of vibration". This objection can be disposed of, as Sherrington [1894] found that the muscle spindles ("stretch" receptors) are not affected by the muscular atrophy following section of the peripheral motor neurons, and by Batten [1897] and others who have shown that the muscle spindles are normal in cases of extreme muscular atrophy in man (i.e. acute poliomyelitis, progressive muscular atrophy, myopathies). Sherrington estimates that in the muscles of the limbs from one-half to one-third of the fibres in the muscular nerve branches are sensory and that most of these sensory fibres end in the muscle spindles. These fibres, as is well known, in part end in the cerebellum and in part pass forward by way of the median fillet to end in the cerebrum.

It would appear, therefore, that there is no clinical or experimental proof to eliminate the possibility that receptors in muscles and tendons participate in vibratory sensibility, and this appears more than likely from Head's conclusion that "Thus from a developmental point of view vibrations and changes in posture are closely associated together and I believe that even in man they evoke the same physiological consequences." This possibility is also strengthened by Cohen & Lindley's [1936] observation that with increased muscle tonus there is a rise in the threshold to vibrations.

There is, however, a theoretical objection to the participation of these end organs, connected with the central effect of peripheral afferent discharges in response to a vibrating stimulus. This is: How could the discharges from a slowly adapting receptor, such as the "stretch" receptor (should they produce any conscious effect at all), give rise to other than a perfectly continuous sensation? We know that variations in frequency of afferent discharges from different receptors are interpreted centrally as changes of intensity. But we also know that variations in frequency can be recognized as such when a vibrating stimulus is used. Possible mechanisms that might be involved in this central discrimination have been theoretically considered and discussed by Wever & Bray for audition, Adrian [1935], Piéron [1935] and others for cutaneous vibration sense, and by us in the final discussion for deep vibratory sensibility.

Technique

In the present investigation we have used cats, rabbits and frogs. The mammals were anæsthetized with dial intraperitoneally and then placed in a steam heated box with a glass front, where the dissection was carried out. One of the animal's legs was fixed by means of a clamp about the foot and a nail driven through the suprapatellar ligament. Various nerves in a hindlimb were exposed and placed upon the electrodes which led to a condenser coupled amplifier. The nerve impulse discharges were recorded by a Dubois' oscillograph. The presence of a loud-speaker in the output circuit was of considerable value in distinguishing when synchronization of the impulse discharges occurred.

The same recording apparatus was used in the experiments with frogs. The preparations (the whole limb, the gastrocnemius muscle, or toe-muscle preparations) were fixed by pins driven through the bones in a small ebonite Ringer-containing chamber, the nerve extending on to electrodes in a separate compartment. The whole arrangement was similar to that used by Matthews [1931*a*]. Records were taken from various nerves in the hindlimb. For a single unit preparation, that described by Matthews [1931*a*] in the toe muscle was employed.

Tuning-forks of various sizes and frequencies (85–530 vibrations per sec.) were used for stimulation throughout. To insulate these, rubber was placed around the shaft and the base painted with shellac. Owing to this precaution, mechanical artefact rarely occurred, but when it did, was easily recognized by the sinusoidal type of wave which it produced in the records. This type of stimulation has disadvantages; at high frequencies the amplitude of vibration is extremely small and rapidly damped. In cats we have not obtained an impulse response to frequencies above 530 per sec., and are unable to tell whether this is due to the low amplitude of vibration or to the fact that the receptors or nerve fibres are incapable of producing discharges above this rate. We have attempted to use various types of electrically driven vibrators, but so far have been largely unsuccessful either on account of electrical interference or due to the inadequacy of the type used.

Preliminary experiments

In order to determine whether receptors in the deep tissues of animals will respond to intermittent stimulation, we applied vibrating tuning-forks in different ways to the lower limbs of cats, while recording from the sciatic, femoral, or common peroneal nerves. The skin was at first left intact below the knee and the base of the tuning-forks of 100–440 vibrations per sec. applied to all portions of the limb. We found that, on recording from the sciatic or common peroneal nerve, when the base of the tuning-fork was pressed against the tibia, the anterior surface of the ankle or on other bony points, a faint sound of the same pitch as the tuning-fork came from the loud-speaker. When using the peroneal nerve, if the animal's foot was plantar flexed so as to stretch the anterior tibial group of muscles, the sound increased in loudness but diminished usually or disappeared completely if the foot was dorsi flexed. This increase in loudness of the sound on stretching the tendons was especially marked when using a large fork of 100 vibrations per sec.

In many places where cutaneous innervation was intact, as demonstrated by light stroking of the hairs, application of the base of the smaller forks gave no synchronized response. However, if the vibrating prongs of the tuning-forks were brought in contact with these areas, very loud sounds of the same pitch as the fork were heard.

On crushing the nerve between the tissues and the electrodes, further stimulation failed to elicit a response, giving evidence that the sounds described were due to nerve impulses. Records of the discharges produced (Fig. 1A) showed complex waves of high amplitude which were regular in rhythm and synchronized to the same frequency as that of the tuning-forks employed.

After removing the skin from the cat's leg, the same type of discharge was obtained when stimulating either with the base (see Fig. 1B) or prongs of the forks, and similar increases in the responses were present when the appropriate tendons were stretched. In the experiments where the base of the fork was used, the discharges appeared to be of equal loudness and amplitude both before and after the skin was removed, but in those in which we stimulated with the prongs somewhat greater responses seemed to be present with the skin intact. To avoid interference when employing the prongs of the tuning-fork, the cat's skin was kept dry, and insulating tape or dry cotton bound around the limb when the skin had been removed. The bases and shafts of the forks were of course insulated as described under "Technique".

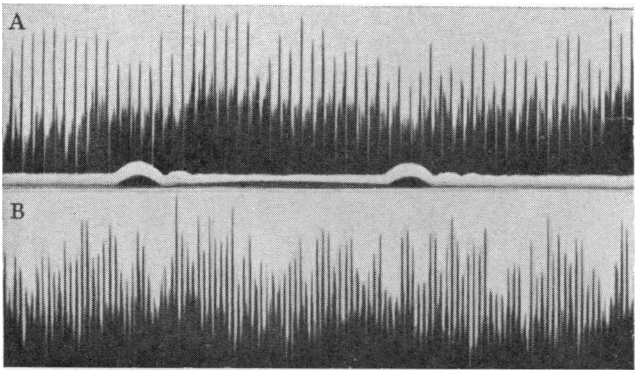

Fig. 1. Cat. Synchronized sensory discharges recorded from the peroneal nerve. A, stimulation with the base of a tuning-fork (freq. 128) applied to the ankle. Skin intact. Time marker 1/5 sec. B, base of a tuning-fork (freq. 240) applied on a bone (tibia). Skin removed from the whole leg. Same time-scale.

The above observations showed that deep receptors are stimulated by the vibrations of a tuning-fork, and the fact that the responses increased during stretch of a tendon suggested that the "stretch" receptors might play an important role in the production of these discharges. Experiments were accordingly carried out to see if this were true.

Synchronized impulse discharges from the "stretch" receptors in muscles and tendons

Since the work of Adrian [1926], Adrian & Zotterman [1926], and Matthews [1931*a*, *b*, 1933], it is well known that if a tendon to a muscle be stretched there occurs in the nerve to the muscle a complex asynchronous discharge of nerve impulses as a result of the stimulation of many "stretch" receptors. In order to see whether these receptors would respond synchronously to a vibrating stimulus, a string was tied to the tendon of the gastrocnemius muscle in a frog and, while this was being held under a fixed tension, the prongs of a vibrating tuning-fork were applied to it. Immediately in the loud-speaker the noise of the asynchronous discharge in the sciatic nerve, due to tension, was replaced by a loud sound of identical frequency to that of the tuning-fork.

A large number of similar experiments were done on cats and frogs with the same result. The records obtained when forks of 85–530 vibrations per sec. were used on cats (or 85–440 vibrations per sec. on frogs) show regular discharges of respective frequencies, but the height of the individual composite waves in the discharges varies (Fig. 2). This variance in wave height appears to depend mainly upon the amplitude of the vibration, provided the tension remains constant; for if a large fork is struck hard and immediately placed against the string, most of the asynchronous discharge disappears and the height of the individual waves in the synchronous one are of high amplitude (Fig. 3 B). When stimulating the frog gastrocnemius muscle in this manner, the asynchronous discharge is at times completely replaced by the synchronous one (Fig. 3 A). As the fork begins to vibrate with less amplitude, however, the waves in the rhythmic discharge become smaller (Fig. 4) and at the same time a more abundant background of asynchronous impulse discharge appears, if the steady tension applied is strong enough. Neither adaptation nor fatigue is responsible for the main features of this, for the experiment can be repeated over and over with the same result. Also when the same fork is struck very lightly or applied when its vibrations have become of low amplitude, the beginning of the resulting discharge appears like the end

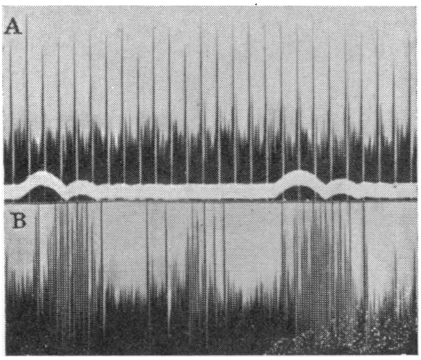

Fig. 2. Cat. Tibialis anticus muscle. Prongs of a tuning-fork applied on a string attached to tendon. The graphs show instances of responses A to low frequency (82 per sec.) and B to high frequency (530 per sec., near the upper limit) stimulations. Time marker 1/5 sec.

of the other, that is, it is composed of a rhythmic series of waves of low amplitude superimposed on an asynchronous discharge. This same feature is evident in the discharges from high-frequency, low-amplitude forks. It follows of course from these findings that the duration of the discharge also depends upon the length of time the vibrations remain above a certain amplitude, and this is for only a fraction of a second with the highest frequencies, the fork being quickly dampened by the contact of the string.[1]

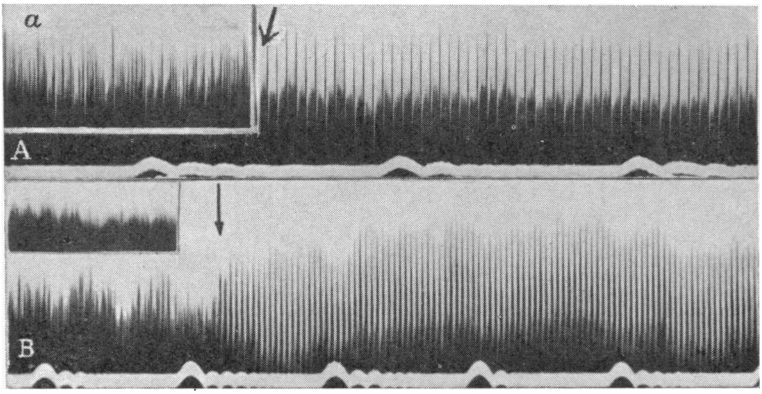

Fig. 3. Frog. Gastrocnemius muscle. A, B, asynchronous afferent discharge in response to a strong tension (100 g.) replaced from the arrow by a synchronized discharge when a tuning-fork was applied to the tendon. Time marker 1/5 sec. In B the left upper corner record shows irregularities of base-line at rest, and in A inset *a* shows the response to stretch—see text.

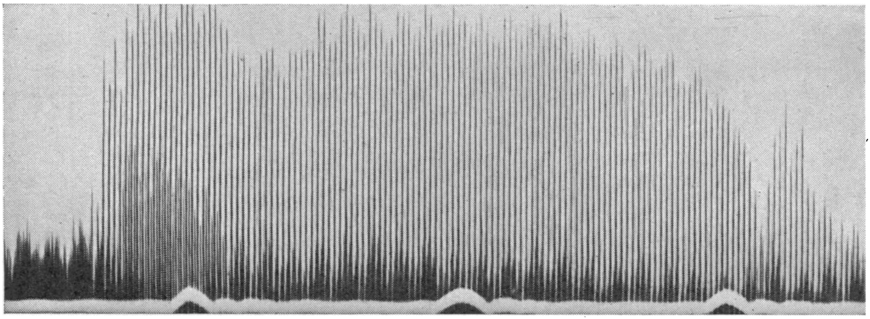

Fig. 4. Cat. Peroneus longus muscle. Synchronized impulse discharge from "stretch" receptors in response to stimulation with prongs of a tuning-fork applied to a string attached to the tendon. Frequency of stimulation 240. At the beginning, some receptors respond twice at each vibration. Time marker 1/4 sec.

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[1] Using an electrically driven vibrator, the frequency of which could be varied rapidly, it was possible to record a "tune" from the nerve.

Interpretation. That the discharges described above are due to the "stretch" receptors is evident from the fact that those resulting from constant stretch on the tendon largely disappear and are replaced by synchronous waves of high amplitude.

Since no evidence of synchronous discharge remains in some of the records from frogs' gastrocnemius muscles, it means also that all the "stretch" receptors in these particular cases are participating in the formation of the synchronous discharge, i.e. that all those which are stimulated by the stretch are capable of responding to a vibrating stimulus. The high amplitude of the individual waves in the discharges is, of course, the result of the summation of the individual impulses from many receptors. As fewer and fewer receptors respond synchronously when the amplitude of the fork vibrations diminishes toward the end of a single stimulation, the height of the individual waves accordingly decreases and the asynchronous background increases.

The discharges from "stretch" receptors in response to a vibrating stimulus applied to bone

Knowing that the "stretch" receptors are so sensitive to a vibrating stimulus, a number of experiments were performed to see if and how they would react when the stimulation was applied to a neighbouring bone. From the preliminary experiments we felt fairly sure that the "stretch" receptors would react, but the proof was still lacking.

After completely removing the skin from one leg of cats or rabbits, the experiments mentioned under "Preliminary experiments" were repeated in more detail and the same findings obtained.

The tendons were now divided about the ankle and a string attached to each. The strings were passed over a pulley, where they could be loaded with different weights and the impulse response to combined stretch and tuning-fork stimulation studied. With the base of a large tuning-fork of 100 vibrations per sec. on the tibia, little or no synchronized discharge appeared in the common peroneal nerve until one of the anterior tibial group of muscles was stretched. The best response could be obtained from stretch of the tibialis anticus when recording from the nerve to this muscle (Fig. 5). Even the slightest stretch (a few grams) on this muscle produced some synchronized discharge, at least at the beginning of the stretch, and this increased as more and more tension was used. The maximum synchronization occurred when between 50–100 g. were placed on the string. Weights greater than this also gave prolonged synchronized responses, but these did not always come on immediately.

The reason for this latent period will be discussed in some detail later. With the base of the tuning-fork on the upper insertion of the gastrocnemius the results were the same, synchronization of the response usually occurring only during stretch of the tendon.

In one cat, the peroneus longus muscle was completely removed from the animal, leaving the nerve attached to the muscle. Its upper insertion was fixed to a wax block and a string attached to the tendon. The whole preparation was kept warm by cotton soaked in warm Ringer, and before it died several experiments performed. It was found that on applying a vibrating tuning-fork to the string on the tendon, the usual synchronized discharge resulted. Also when the base of a large tuning-fork (100 vibrations per sec.) was placed on the wax, similar discharges appeared whenever the tendon was stretched. The results were the same when isolated preparations of the gastrocnemius muscle in the frog were used.

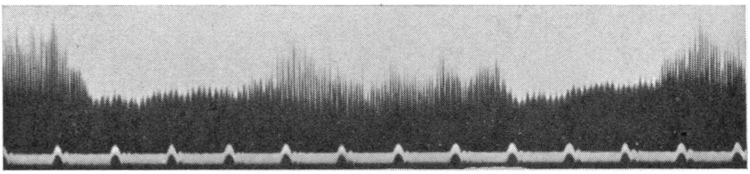

Fig. 5. Cat. Skin removed from leg. Base of a 100 D.V. tuning-fork applied on a bone. Sensory discharges during alternations of stretch and release of the tendon of tibialis anticus. A.C. main disturbances in the intervals. Time marker 1/5 sec.

Discussion. The above experiments provide conclusive evidence that "stretch" receptors in the frog, cat or rabbit are stimulated by the vibrations of the base of a tuning-fork applied to bone and that, like bone, any solid object (wax block) under similar conditions can serve in the capacity of transmitting medium for vibration. Stimulation of apparently all the deep tissues of the leg gave no definite evidence that any other receptors respond to the vibration of the *base* of a tuning-fork, and if they do (i.e. if they take part in the meagre synchronized responses occurring without tension being applied to the tendons) we have found no evidence that the discharges from them are comparable to the massive response from the "stretch" receptors. We feel that the feeble synchronized discharges resulting from stimulation of the bone, when the neighbouring muscles are relaxed, may all come from "stretch" receptors closely applied to the bone, for it will be remembered in what intimate contact the tibialis anticus (and other muscles) are with the bones. Negative evidence, however, is not always trustworthy, and it is entirely probable that other receptors in the deep tissues (such as the Pacinian corpuscles) will respond to a vibrating stimulus (if the amplitude be sufficiently large), and hence they may contribute in small part to the discharges described.

The responses from single "stretch" receptors

There are a number of problems of some interest which the above findings suggest, but little can be learnt concerning them unless single receptor preparations are used in their study.

The first problem is to determine whether the synchronized responses, which occur when a tendon is stretched during stimulation of the bone with a tuning-fork, are due mainly to the fact that the vibrations can more easily reach the receptors when the muscle is transformed into a rigid medium by the stretch, or whether other important factors are also involved.

For a single unit preparation, that in the toe muscle of a frog was used. It was set up in an ebonite chamber as described, tension being applied to the muscle through a string tied to the tendon. The vibrations were transmitted to the preparation by applying the base of a large tuning-fork of 100 vibrations per sec. to the side of the ebonite chamber. It was found that no impulses resulted on this type of stimulation until tension was put on the tendon. When the tension was gradually applied, no synchronized response appeared until it reached about 1–3 g. If it was now increased more or less rapidly so that the normal discharge from the receptor reached a considerably higher level than the rate of the vibrating fork, synchronization again disappeared. Below and above a certain frequency, therefore, the rate of discharge is determined by the stretch rather than by the vibrations of the fork.

The base of the vibrating fork (100 per sec.) was again placed on the ebonite chamber, and, 1 sec. after its application, weights of various sizes applied to the string on the tendon and photographs taken of the resulting discharges. As nearly as possible the fork was struck with the same force and the weight applied at approximately equal rates in each experiment. Naturally variables entered here, but they were partly eliminated by doing a large number of experiments. A mechanical apparatus for striking the fork with equal force each time was tried, but caused too much base-line fluctuations to be practical. Photographs were now taken of the normal response of the receptor to the above weights without any simultaneous stimulation from the tuning-fork. Five minute intervals were allowed for recovery of the receptor between all experiments, and during these intervals the preparation was irrigated with fresh Ringer.

The results show that if the tendon be stretched by a weight of about 1–3 g., the receptor's discharge is not synchronized with that of the fork, except at the beginning of its response, when its rate of discharge approaches that of the fork, i.e. 100 per sec. With heavier weights (8–30 g.) the reverse effect is found, the discharge becoming synchronized to the rate of the fork only after a short interval. In this interval the receptor fires off at a higher rate than the tuning-fork. As adaptation to the stretch brings about a slowing in the rate, the frequency of the discharge suddenly becomes that of the fork, and for some time continues at this level (Fig. 6*a* and *c*), the duration depending mainly upon the amount of stretch and amplitude of the fork. After an interval, however, the impulse rate falls below that of the fork. Of course this latter effect is partly due to the decreasing amplitude of the fork vibrations; but if the fork is applied at varying intervals after stretch has commenced, it can be determined at what time, and at what frequency of discharge, synchronization no longer appears, or is replaced, as frequently observed, by synchronization at submultiple frequencies (Fig. 6*d*).

Discussion. The above experiments reveal that a "stretch" receptor is much more likely to respond at the same rate as a vibrating stimulus if, due to stretch, its own discharge rate approaches that of the stimulus frequency. In other words, if a receptor is already discharging at a rate close to that of a vibrating stimulus, it requires only a minute amount of vibration to synchronize its response to the vibration frequency. This behaviour can, therefore, partly explain the great sensitivity of the "stretch" receptor to a vibrating stimulus such as a high-frequency tuning-fork.

Another factor which apparently plays a role in the production of the synchronized discharges observed during stretch is probably that the stretch in transforming the muscle into a more rigid structure provides a better transmission medium for the vibrations. However, it has been shown that this is not the dominant mechanism, since in a muscle made quite rigid by the stretch of several hundred grams, no evident synchronization of the discharge occurs on stimulation with the base of a large 100 per sec. fork until a considerable interval has elapsed. During this interval the frequency of discharge from most receptors remains too high for synchronization to occur. Naturally, however, the length of this interval can be shortened by using vibrations of greater amplitude.

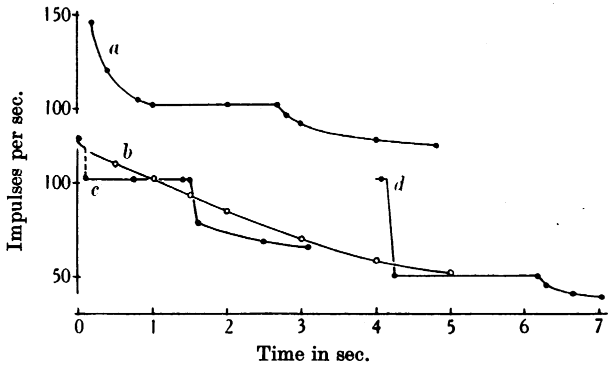

Fig. 6. Frog (single "stretch" receptor in toe muscle). Adaptation curves. In *a*, a steady tension 10 g., superimposed vibratory stimulation at 100 per sec. In *b*, steady tension 2 g., without vibratory stimulation; *c*, same preparation with tuning-fork applied; *d*, a little later, in response to a new application of the tuning-fork at full strength.

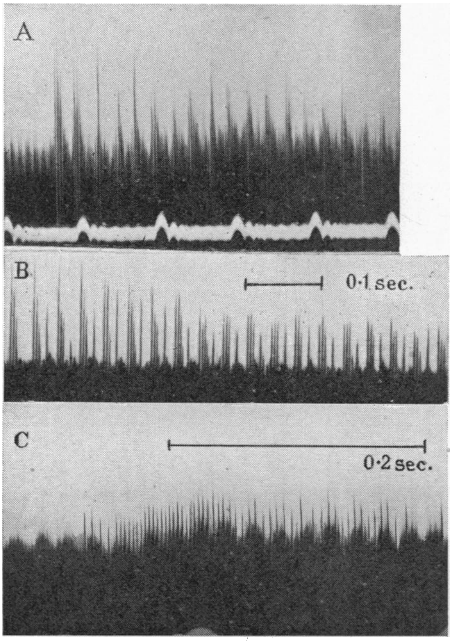

Fig. 7. A, Cat. Tibialis anticus muscle. Shows the impulse response of many receptors on stretching the tendon 25 times a sec. Recording from nerve to tibialis anticus. Time marker 1/5 sec. B, Frog. Toe muscle with several receptors. An instance of grouped impulses in response to a low frequency stimulation (32 per sec.). Average frequency in each group of three impulses: about 300 per sec. C. Shows the impulse response from a single stretch receptor in a frog on stimulation at 330 per sec. Time marker 1/5 sec.

Some observations relating to low-frequency stimulation of "stretch" receptors

So far nothing has been said concerning the type of discharge resulting from very low frequency stimulation of the "stretch" receptors. For this type of stimulation, we used a large strip of steel fixed firmly at one end, and free to vibrate at the other, where the string from the tendon of a muscle was attached. The frequency of the vibrating end could be varied by adjusting a load at different lengths along the strip. The main features of the discharge obtained by this method were the same from either frog's gastrocnemius muscle or from any of the anterior tibial group of muscles in the cat. The frequencies used varied from 5 to 32 per sec. As seen in Fig. 7 A the discharge is composed of a rhythmic series of composite wave potentials occurring at the stimulation frequency. The composite nature of each individual wave is much more evident than in the higher frequency discharges, where the waves are often formed by a single rather than a group of spikes. This difference is undoubtedly due to the fact that with the lower frequency stimulation the vibrations were of comparatively long duration and large amplitude, and hence caused a series of impulses to be discharged from the individual receptors at each stimulation (see Fig. 7 B).

Observations on high frequency stimulation of "stretch" receptors

Adrian *et al.* [1931] have shown that in response to an interrupted air jet directed against the skin of a frog, impulse discharges occur from single receptors at the same frequency as the stimulation rate. Even though the rate be raised to 250–300 per sec., the frog shows no sign of discomfort. This finding, as they point out, is extremely convincing evidence that the "touch" receptors in the frog cannot give rise to a sensation of pain no matter how they are stimulated.

We have found the same type of evidence in regard to the stretch receptors. Matthews [1933] suggested that high-frequency discharges from these receptors might give rise to a sensation of pain. Our evidence comes from the following experiments. If instead of tying a string to the tendon of a single unit toe-muscle preparation (frog), the tendon is left attached to the phalanges of the skinned foot and these allowed to hang in the air outside the ebonite chamber, a frequency in the nerve as high as 330 per sec. (at 22° C.) can be produced by bringing the prongs of a vibrating tuning-fork against the toe. This frequency is apparently close to the upper limit at which a "stretch" receptor can respond, and is comparable to that resulting from a rapid strong stretch, i.e. 316 per sec. at 22° C. obtained by us and 290 per sec. at 14° C. by Matthews [1931*a*]. Similar frequencies must occur in the nerves of an intact frog if its toes are stimulated when hanging in the way described. There is no way in which the messages from these receptors could be further intensified, yet if this is done to a normal frog it usually pays little or no attention to the stimulation.

The evidence in cats on this problem is not as yet complete but seems definite. It is, as shown, that composite rhythmic discharges from many "stretch" receptors occurred at frequencies up to 530 per sec. when the prongs of a tuning-fork were applied to a tendon or at 440 per sec. when the base was placed on a bone. Frequencies over 240 per sec. have not been recorded from single receptors, but only two of these preparations have been studied, and in each case the receptor had a high threshold to stretch and was probably of the A_2 or B type described by Matthews [1933]. It is not surprising, therefore, that they were not stimulated by the feeble vibrations of a high-frequency fork. However, when one considers that a single muscle spindle in a frog will respond at 330 per sec., it seems hard to believe that there are not many "stretch" receptors in cats that will do so at 500 or over. Since the upper frequencies for stretch and for response to vibrations are so similar in the frog, it would appear more than likely that it is the same in the cat. In any case the cat shows no sign of pain if the base of a tuning-fork (or many tuning-forks) of any frequency is applied to a bony point or if the vibrating prongs are brought in contact with the tendons in its ankle or toes.

Discharges at submultiples of the stimulation frequency

The fact that the composite potential waves in the discharges in response to the higher frequencies of stimulation, like those in the eighth nerve, occur at the same frequency as the stimulation, suggests a comparison between the two phenomena. Adrian [1935] has already discussed a similar parallelism between the synchronized discharges in frog cutaneous nerves in response to intermittent stimulation and the impulses in the auditory nerve.

As is well known, the eighth nerve can transmit regular series of waves at frequencies of 1000 per sec. or over. It seems unlikely that a single fibre would conduct at this rate, and the current opinion [see Wever & Bray, 1930; Adrian, 1935] is that these high-frequency discharges, formed of composite potential waves, are probably the result of many fibres each conducting at a submultiple of the stimulus frequency.

Good evidence in support of this theory has been offered by Adrian, Bronk & Phillips [1931]; for they found that the eighth nerve was still capable of carrying these high frequencies, when the refractory period of the fibres had been increased to about three or four times its normal length, by either covering the petrous bone and auditory nerve, in cat, with crushed ice, or packing ice in the tympanic bulla of the guinea-pig. Evidence along the same lines has been found in the present investigation. It is as follows:

A. In the first place, as already mentioned, the highest frequency obtained from a single "stretch" receptor in a frog by intermittent stimulation was 330 per sec. at 22° C., which agrees fairly closely with Matthews's upper limit to stretch of 290 at 14° C. When working with frogs' muscles containing many receptors, however, frequencies of 440 per sec. at 17° C. have been obtained with ease on intermittent stimulation. Even after irrigation of these preparations with iced Ringer for a short time (30 sec.) frequencies of 440 have still been recorded, but on continuing the irrigation the receptors failed to respond to the fork.

B. Single "stretch" receptor preparations from frogs were set up as usual and stimulated by placing the base of a large vibrating tuning-fork (100 per sec.) on the walls of the ebonite chamber while maintaining a constant stretch on the tendon. As described above the records from this type of stimulation show that the discharge frequency becomes synchronized to the vibration rate when the response due to stretch approaches 100 per sec. When adaptation, due to maintained stretch, brings about a fall in the frequency, however, the discharge rate often suddenly becomes a half or a third that of the fork, i.e. 50 or $33\frac{1}{3}$ per sec. (see Fig. 6*d*). Also if the preparation is subjected to stretch alone and the frequency of the discharge allowed to fall to 40 per sec., application of the fork (100 per sec.) will often cause a sudden rise of the rate to 50 per sec. From these experiments it would certainly seem that the receptor, under normal conditions, can respond at submultiples of the stimulation frequency.

C. Our final evidence comes from experiments on frog toe-muscle preparations containing two receptors. The experiments undoubtedly prove that "stretch" receptors will respond at submultiples of the stimulation frequency and that the composite discharge from a number of these receptors will, at the same time, reproduce the stimulation frequency through a process of alternation.

Preparations containing two receptors were selected. Just before stimulation with a vibrating tuning-fork (232 per sec.), a steady tension was applied to the muscle. In Fig. 8, part 1, an example is shown where tension alone produced a discharge of 185 impulses per sec. from one receptor (*a*) and 165 per sec. from the other (*b*), the composite response being therefore completely irregular: then, as soon as the tuning-fork was allowed to exert its action (at *S*), each receptor took on the frequency of the stimulation and the complex discharge was abruptly replaced by one of double amplitude at 232 per sec. In part 2, after some adaptation to stretch had been allowed to occur ((*a*) 155 per sec., (*b*) 118 per sec.), the tuning-fork (232 per sec.) was again applied. In this case the result was a synchronized discharge at 116 per sec. From the height of the response it is obvious that each receptor was discharging at 116 per sec.

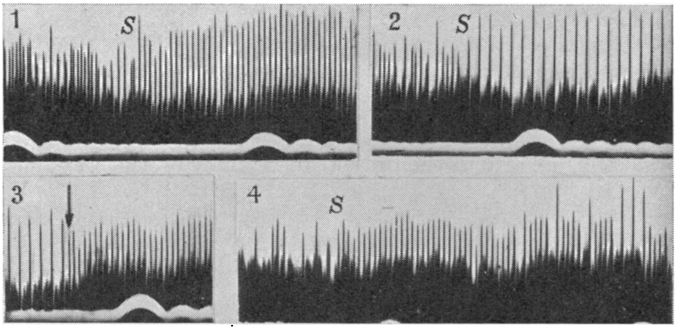

Fig. 8. Frog. Toe muscle under steady tension (10 g.) with superimposed vibratory stimulation (at *S*) during the course of adaptation. Two receptors. Example of responses at full (1) or half (2, 3, 4) frequency. Alternation can be seen in 3 (from the arrow) and 4 (from *S*). Time signal 1/5 sec.

In other records (parts 3, 4) it is seen that each receptor may be firing at half the stimulation rate but the total response be of the same frequency as the tuning-fork, each receptor responding to alternate vibrations. The amplitude of the waves in these cases is, of course, that of a single impulse.

Responses at submultiple rates are often preceded by transitional stages in which the response from one of the receptors keeps the normal rate while the other begins to show signs of deficiency. Such signs are of two kinds: first a progressive shift of the response from the second receptor, showing its tendency not to keep exactly in phase with that from the first and to be somewhat delayed with respect to it; and secondly, an occasional dropping out of an impulse from the second receptor's response. This may occur more and more frequently until every second impulse is dropped, i.e. the second receptor firing then only at half the stimulation frequency. After each of these dropped impulses, the receptor may recover more completely and the shift mentioned above disappear, so that good synchronization of the discharge from the two receptors occurs. An analysis of a typical record is given in Fig. 9.

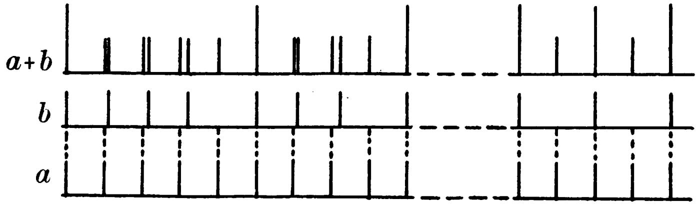

Fig. 9. Schema drawn from an actual record on 2 units. One of them (*a*) responds exactly in phase with the stimulation, the other (*b*) with some shift and failures until a rhythm at half frequency is obtained.

DISCUSSION

Before entering into a theoretical discussion of the possible central effects of the discharges described in this paper, it seems advisable to review briefly some of the facts we have presented.

In the first place it has been shown that if a vibrating tuning-fork is applied in different ways to the limb of an animal, discharges from "stretch" receptors will result, and these will be synchronized to the rate of the stimulating vibrations.

Also, we have seen that, at least in most cases, the bones played a role of passive transmitters of these vibrations to the receptors in tendons and muscles, as originally suggested by Neutra [1905], and that vibrations had little effect upon the receptors if the muscles were flaccid. When some tension was applied to the tendons, however, discharges synchronized to the rate of the tuning-fork occurred in the corresponding nerves. The effect of the tension in these cases was apparently twofold. First by changing the muscle and its tendon into a more rigid structure a better transmission medium for the vibrations was provided. Secondly it was shown that the receptors became extremely sensitive to vibrations when they were placed in a state of activity by the stretch; for the nearer the discharge rate of a receptor approached that of the stimulating fork, the more likely was it to become synchronized to the vibration rate, i.e. the receptor's threshold to vibrations was lowered.

In the experiments, of course, this stretch (tension) had to be applied mechanically as the muscles were in a flaccid state, due either to the effect of the anæsthesia or to severance of nerves or tendons. In an intact animal, however, the conditions would be quite different, for here, due to normal muscular tone, there would always be some stretch on the tendons and this would also be present on the muscles during extension. Matthews [1931*b*, 1933] has shown that in mammals many of the "stretch" receptors in tendon or muscle are active both during extension (stretch) and contraction. Therefore, in the normal animal, there would apparently always be many receptors discharging in any muscle (except perhaps during sudden relaxation or contraction of a muscle as in the "silent" period of reflexes), and hence in a condition to respond to vibrations. The impulse response to a vibrating stimulus would, however, vary with different tensions on a muscle.

So far in this paper nothing has been said of how the vibrations of a bone are transmitted to a muscle or tendon. It seems likely to us that the vibrations are not usually transmitted directly into the mass of a muscle, but stimulate many of the receptors, both in the muscles and tendons, by minute stretches of the tendinous attachments. These attachments are not only formed by the large tendons but are, of course, present along the whole length of most long bones, where they are in the form of thousands of tiny tendons.

The central problem

Peripheral aspects. So much for the facts. When one considers the possible effect of these discharges on the central nervous system, the ground is not quite so secure. It is known that postural tonus is a reflex from the sensory endings in muscle [Liddell & Sherrington, 1923]. When a vibrating tuning-fork is applied to a human bone, however, it evokes only a sensation of vibration, and usually no observable reflex effect on posture or tone. Yet, if our observations on animals can be applied to man, we must assume that it is causing massive discharges from the "stretch" receptors. The volume of these discharges will, as pointed out, vary with the state of the muscle tone, and this might explain why vibratory sensation fluctuates during contraction and relaxation of muscles.

Should these discharges produce no sensation it would mean that only deep receptors such as the Pacinian and Golgi Mazzoni corpuscles are concerned in the registering of the fine and complicated movements. This seems hardly likely, for they are apparently neither sufficiently numerous nor suitably placed to do so. It is more than likely that such receptors take a part in vibratory sensibility, but we have not been able to identify their discharges and hence these must be small compared to the massive responses from "stretch" receptors.

As to the cutaneous receptors, the possibility that these play a role in vibratory sensibility, as explored clinically in man with the *base* of a tuning-fork, is not ruled out by our experiments on animals. In fact it seems probable that they do, especially in regions where the skin is more or less tense and richly innervated; for we know that they certainly respond to some kinds of vibratory stimuli [Adrian, Cattell & Hoagland, 1931; von Frey, 1915; Piéron, 1935, etc.], and it has been shown that they are stimulated by the vibrating prongs of a tuning-fork. However, true as this may be, they are apparently less sensitive to the vibrations of the *base* of a tuning-fork than the deep receptors, as Head has already suggested.

The possible effect of the pattern of peripheral afferent discharges on central interpretation

If discharges from "stretch" receptors give rise to any sensation whatsoever, and we take into account the present state of knowledge concerning central mechanisms, theoretical assumptions can be made which fairly support the view that the synchronized discharges under discussion are interpreted centrally as an intermittent stimulation.

To begin with, we need no assumption to say that, taken as a whole, the complex afferent discharges described offer special patterns that no other external stimulation than a vibratory one could produce, and as such might give rise to a specific sensation. But we can be less vague than this as soon as we admit that the ordinary fate of afferent series of impulses is to be smoothed out in the centres [see Adrian, 1935], so giving rise to a steady sensation; for a vibratory sensation may then be regarded as due to circumstances in which the smoothing effect is checked in some way resulting in large regular oscillations of the central excitatory state.

Adrian [1935] has pointed out that the discharge from a single slowly adapting receptor, such as the "stretch" receptor, cannot very well give rise to a sensation of vibration; for a constant stimulus to one of them will produce a rhythmical series of impulses (as it will at times from a touch receptor), the frequency of which is not interpreted as such, but rather as degrees of intensity, and any resulting sensation could only be continuous in nature.

However, at low-frequency stimulation it has been shown that, as expected, the response to vibrations of each single "stretch" receptor often occurs in small groups of a few impulses separated by intervals of rest. Similar results have been obtained by Cattell & Hoagland [1931] working with skin receptors stimulated by intermittent puffs of air. It is quite obvious that such a response will result in regular fluctuations of the central excitatory state in each of the corresponding centres. Very distinct intervals of rest between groups are not necessary, and any uneven distribution of impulses, provided the fluctuations occur with regularity, certainly produces periodical variations in centres that may be interpreted as rapid modulations in intensity, i.e. vibrations.

All that has been said before concerns events that are supposed to occur in single receptors or centres. Such a simplification is rarely found in natural conditions. At any rate, even if a stimulation does occasionally affect a single cutaneous receptor, it seems hardly likely that this could ever be true of "stretch" receptors, for there are apparently always many of these end organs active in any muscle (except perhaps during sudden relaxation or twitch).

As is well known, the normal composite response to a steady stimulation of a group of either cutaneous or deep receptors is completely asynchronous. The sensation resulting, like the discharge, is a continuous one which rises and declines in intensity according to the number of receptors stimulated and the frequency of their individual discharges. When intermittent stimulation is applied to these receptors, however, a very different type of discharge is produced, at least from the "stretch" receptors (and "touch" receptors if the vibrations be strong enough); for here, as soon as the receptors feel the effects of the vibrations, the discharge from each one will become synchronized to the stimulation frequency (sometimes at submultiples of it) and the composite discharge will be a rhythmical copy of the stimulating vibrations. It seems hard to believe therefore that these discharges, so different from those resulting from steady stimulation, do not have a specific effect on the centres.

Synchronization of impulses as we have seen is not always quite perfect, and we must admit some spread during conduction toward the centres due to differences in velocities. These differences must be small, however, since only one type of impulse is concerned. In any case the impulses are undoubtedly distributed around a modal value, so that synchronization is relatively preserved (at least in the form of emerging crests in overlapping bursts of impulses) when the composite discharge reaches the centres. Obviously these periodical bursts of impulses counteract the smoothing effect if some central convergence is present. For then several impulses, meeting in the same place at approximately the same time, would be capable of mutual reinforcement of their effects upon the centres.

Integration is a common feature of higher central mechanisms, and there seems to be no good reason why it should not occur in this case. Some experimental evidence of it being true, at least for the motor centres, is found in the observations made in man by Hoffmann [1919] and by Preisendorfer [1919]. These authors have shown that the normally asynchronous mass of impulses from the motor centres in a voluntary contraction can be transformed into large composite waves of the same frequency as that of the stimulus when strong vibrations are applied to tendons and muscles.

If the impulses in the discharges under discussion are integrated in their effect, a large fluctuation in central excitatory state should occur when each individual composite wave in the synchronized discharge arrives at the adequate centres. The separate fluctuations, if they give rise to any sensation whatsoever, could only, it would seem, be interpreted as fluctuations in tension or movements (or as contact in the case of the "touch" receptors), and deep vibratory sensibility would then be the appreciation of rapidly repeated minute passive movements.

This is just what Head has already visualized, for he says: "The tuning-fork produces rapidly repeated movements of small range" and "from the periphery to the cortex vibration and passive movements evoke sensation or are abolished together—in both of them sensation is evoked by afferent impulses caused by a series of minute passive movements."

By different methods then we have come to the same conclusions as Head. We wish it clearly understood, however, that our interpretation of the findings, as concerns vibratory sensibility, is a purely theoretical one, and it still remains possible that the discharges we have described never reach consciousness.

What pathways these high amplitude synchronized discharges follow in the C.N.S. and whether synchronization is maintained above the reflex level in the spinal cord could probably be determined by exploration of the C.N.S. with concentric needle electrodes and possibly by recording from the sensory cortex.

SUMMARY

1. The vibrations of a tuning-fork will stimulate the "stretch" receptors in muscle and tendon if the base of the fork be applied to a neighbouring bone, or its prongs be brought in contact with a tendon.

2. In response to this type of stimulation the "stretch" receptors give rise to afferent discharges composed of rhythmic series of composite waves synchronized to the rate of the vibrating stimulus.

3. The individual composite waves are the result of the summation of impulses from many receptors. Within certain limits the number of receptors participating rises with an increase in the amplitude of the stimulating vibrations (tension remaining constant).

4. When the stimulus rate reaches a certain level, a "stretch" receptor produces a single impulse in response to each vibration, up to a certain high-frequency level.

5. The impulse discharge from a "stretch" receptor is much more likely to become synchronized to the stimulation rate if, due to stretch or contraction of the muscle, its rate already approaches the vibration frequency. Under these conditions its threshold to vibrations is lowered, and this explains in part the extreme sensitivity of "stretch" receptors to tuning-fork stimulation.

6. Bone serves as a transmitting medium for vibrations and causes many of the tendons fastened to it to be stretched sufficiently to stimulate the receptors in muscle and tendon at each vibration. By tendons we mean tendinous attachments which are present along the greater part of most long bones, as well as the larger tendons.

7. Evidence presented strongly suggests that discharges from "stretch" receptors are incapable of giving rise to a sensation of pain.

8. In response to intermittent stimulation, two "stretch" receptors may each respond at half the frequency of stimulation, yet the composite discharge be synchronized to the stimulation rate. Thus a proof that a high-frequency discharge may occur in a nerve when the separate fibres are carrying discharges only at submultiples of this frequency is offered.

9. It is suggested that the synchronized discharges from "stretch" receptors, produced by tuning-fork stimulation, might be largely responsible for deep vibratory sensibility. A theoretical discussion in support of this hypothesis is presented.

10. If this be true, then the same end organs are concerned in deep vibratory sensibility and the appreciation of changes in posture.

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