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ELECTRICAL AND MECHANICAL FACTORS IN THE ADAPTATION OF A MAMMALIAN MUSCLE SPINDLE

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Sensory nerve endings usually respond to maintained stimulation by the generation of a train of impulses declining in frequency with time. In some receptors, for instance the Pacinian corpuscle (Hubbard, 1958) and receptors in the skin of the frog (Loewenstein, 1956), adaptation largely depends upon mechanical factors. In these instances adaptation is rapid, and the impulse frequency falls abruptly to zero; the muscle spindle behaves differently in that its response consists of two phases—an initial high-frequency burst, followed by a steady discharge (Matthews, 1931, 1933; Katz, 1950; cf. Eyzaguirre & Kuffler 1955).

It seemed likely that the rapid first phase in the discharge of the muscle spindle was analogous to the quickly adapting response of the Pacinian corpuscle, and was therefore also due to mechanical factors. If the electrical properties of the membrane of the nerve terminals were responsible for the adaptation, then one would expect that electrical polarization applied to the nerve terminals themselves would also produce such an adaptation in two phases. If polarization does not give the two phases which are produced by stretch, then the difference might be due to mechanical adaptation.

We have recorded from a single mammalian muscle spindle and have compared the effects of electrical and mechanical stimulation on the same ending.

METHODS

Preparation. In all experiments the tenuissimus muscle was dissected from a cat or kitten previously anaesthetized with sodium pentobarbital 40 mg/kg (Abbott Laboratories) injected intraperitoneally. We used the central part of the muscle, which contains 5–10 stretch receptors arranged in series longitudinally down the middle (Boyd, 1956). The isolated preparation was mounted in Krebs's solution of composition (mM): NaCl 115, KCl 4·6, $NaHCO_3$ 24·1, $CaCl_2$ 2·46, $MgSO_4$ 1·15, KH_2PO_4 1·15, glucose 8·85. A mixture of 95% O_2 and 5 % CO_2 was bubbled through the bath. The bath contained 15–20 ml. Krebs's solution, which was changed at frequent intervals. The temperature could be maintained at any desired level, usually 37° C. The muscle was clamped at one end by a pair of forceps (insulated

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from earth) on a rack and pinion so that the resting length could be varied. The other end of the muscle was tied to a rod through which it could be given step-wise or sinusoidal stretches. The square-wave mechanical displacement was produced by an electromagnet or a vacuum-operated bellows. The sinusoidal displacement, of variable frequency or amplitude, was applied by means of a cam and slider system. The resulting movement of the muscle was displayed on one beam of an oscilloscope by means of a transducer (RCA 5734).

Recording. The recording of afferent activity was made from single spindles. Single afferents were obtained at first by the laborious process of splitting down the main nerve trunk to the muscle. A far more convenient method was to make use of the anatomical features of the preparation, which are shown in Fig. 1. The small twigs usually contained one or two afferent fibres from muscle spindles, in addition to motor fibres. Single-fibre preparations were obtained by dividing these twigs. Responses from single spindles could be recorded up to 36 hr after the dissection. The preparation would also survive for many hours immersed in liquid paraffin.

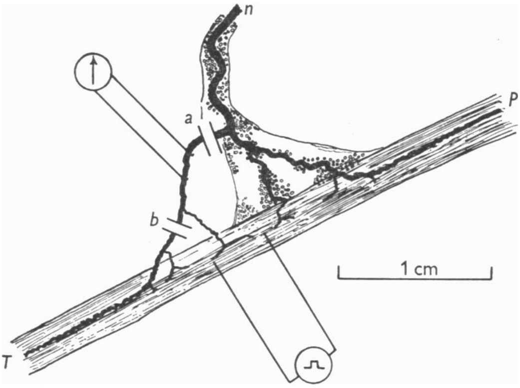

Fig. 1. Diagram showing tenuissimus muscle of the kitten with nerve supply (n) and position of recording and stimulating electrodes for polarization experiments. P is the pelvic end and T the tibial end. Cuts have been made at (a) and (b) leaving only the twig for recording.

The nerve was placed on the wick of a non-polarizable electrode which consisted of an Ag–AgCl wire dipping into an agar-saline bridge. Electrodes were arranged either for dipolar recording from the nerve, or with one electrode on the muscle (Katz, 1950). The nerve, and in some cases the whole preparation, could be raised into a layer of liquid paraffin for recording purposes. A cathode-follower input stage fed into either an a.c. or a d.c. amplifier connected to a cathode-ray oscilloscope. Grid current was less than 10^{-11} A. Polarizing electrodes were of the same form as the recording electrodes and were placed on the muscle on each side of the supposed position of the nerve ending; in some cases one electrode was put on the nerve twig itself (Edwards, 1955).

Square waves were produced by a circuit giving pulses of variable duration, polarity and voltage, balanced about earth; a swamping resistance of 4·7 MΩ in series with the preparation was used to eliminate the effects of changes in resistance of the preparation.

It was necessary to ensure that the applied current was polarizing the nerve terminals and not producing its effects by direct stimulation of the nerve trunk or the muscle. The following precautions were taken: the muscle was raised into paraffin and blotted to remove saline and so prevent current spread; it was carefully observed under the microscope so that current strengths could be kept well below those which caused twitching of individual fibres; curare 5×10^{-6} (w/v) was used as an additional safeguard, although with the stimulus strengths used there was no evidence that large or small motor fibres were being excited. Only if considerably stronger stimuli were used did spikes from other fibres appear in the recording. The criteria for assuming that the spikes produced by the polarizing current were due to an effect on the ending, rather than on the whole nerve trunk, were (*a*) the effects of the current and stretch of the muscle would summate, (*b*) pinching the nerve within the muscle as close to the receptor as possible abolished the effect, (*c*) the position of the electrodes was critical to within 1 mm, (*d*) the effect was not obtained by simply stimulating the nerve, and (*e*) when current flowing in one direction increased the rate of firing, then reversing the flow decreased it.

RESULTS

Polarization of the nerve endings

In a slightly stretched muscle, showing a discharge from the spindle, the application of a direct current through a cathode near the receptor increased the frequency of firing. If the muscle was relaxed, and there was no discharge, then a train of impulses was initiated. If the polarity was reversed with the anode near the receptor, the frequency was reduced or firing was abolished (Fig. 2).

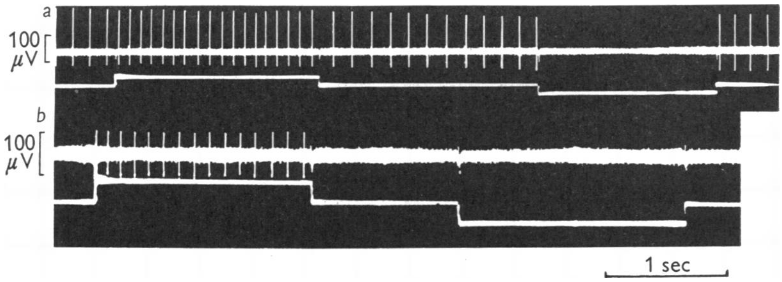

Fig. 2. *a*, Effect of d.c. on steady discharge due to stretch. Upper record, action potentials from single muscle spindle; lower record, current flowing through preparation, upwards spindle −ve, downwards spindle +ve. Depolarization causes increase in frequency; hyperpolarization stops the discharge. *b*, Effect of d.c. on relaxed spindle. Only depolarization causes a discharge.

The alteration in frequency was closely related to the applied d.c. (Fig. 3), as in the frog (Edwards, 1955). The relationship did not hold when the d.c. produced twitching or stopped the discharge completely.

The discharge produced by d.c. was regular, and the frequency remained constant during the entire period of depolarization (Figs. 2 and 4). In Fig. 4 it can be seen that the frequency was 27/sec when the d.c. was applied and was still the same after 1·3 sec. At threshold, d.c. either initiated a regular train of impulses or none at all. In a few spindles there was a gradual decline in frequency of a few impulses per second during the course of polarization, but this never amounted to more than 10 % of the initial frequency. There was an upper limit to the frequency which could be obtained by depolarization, because if the voltage was too high stimulation of the muscle fibres interfered by producing a contraction. If the muscle was observed to twitch with these high voltages a high-frequency burst of firing was often seen, presumably as a result of intrafusal contraction. Only voltages well below twitch threshold were used in our experiments.

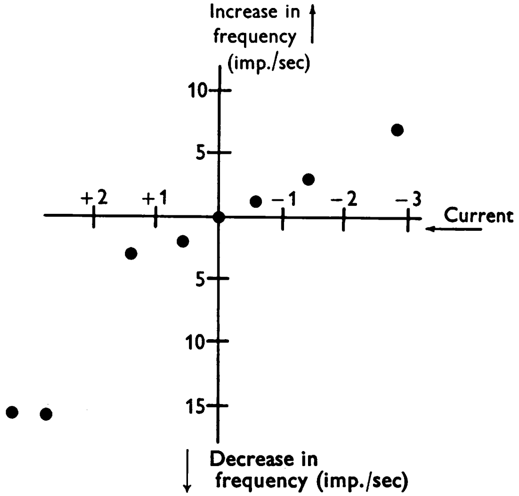

Fig. 3. The relationship between change in firing frequency (ordinate) and applied d.c. in relative units. Current flow through muscle less than 4 μA. Muscle slightly stretched to give a steady discharge of 16/sec, hence points corresponding to −16/sec indicate that polarizing current has stopped the discharge.

The effect of stretch

At 37° C the spindles were silent when the muscle was relaxed. The effect of mechanical stretch was quite different from that of d.c. The response occurred in two phases, an initial burst of impulses at a high frequency followed by a maintained discharge at a much lower frequency (Matthews, 1931, 1933; Katz, 1950).

In Figs. 4 and 5 the effects of stretch and depolarization on the same muscle spindle are shown. With the stretch response the firing frequency in the initial burst was 92/sec and fell to 25/sec in 0·3 sec. It remained at about 25/sec for a further 1 sec. This is in contrast with the constant frequency of 27/sec maintained during the entire period of electrical stimulation. This difference was found in all twenty fibres.

In contrast again with the effect of d.c. on the endings, a threshold stretch produced only the first phase. If the initial tension on the muscle was increased, the same increment of stretch now gave both phases. A tension between these gave the first burst, followed by only a few impulses of the second phase (Fig. 6). If the same experiment was done using d.c.

instead of added stretch (i.e. initial length was altered and a given d.c. pulse was used each time) the spindle responded with a train of impulses at constant frequency or not at all.

Spindles damaged, either during dissection or deliberately, had quite different responses. The threshold was higher, firing was irregular, sometimes in rhythmical bursts and often of high frequency. All such fibres were rejected.

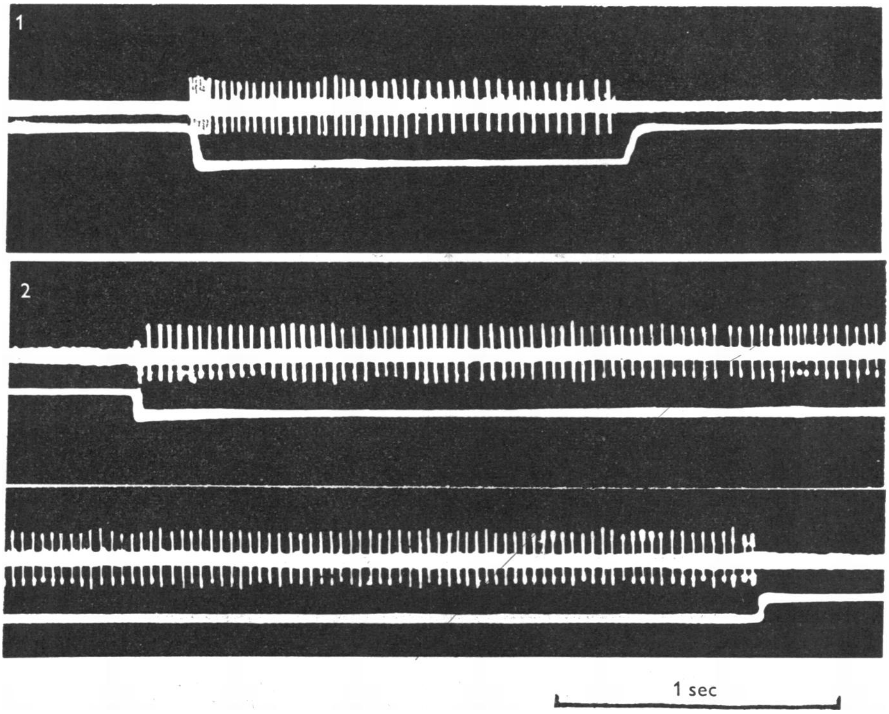

Fig. 4. The effect of stretch (1) and d.c. (2) on the same muscle spindle. In (1) lower beam records displacement; there is a high-frequency burst initially, followed by a steady discharge. In (2) depolarization (lower beam) gives rise only to a maintained discharge. The bottom records are the continuation of the middle ones.

The receptor potential

The receptor potential recorded during mechanical stretch, after procaine (0·01 %), also showed two phases. It was largest during the initial stretch and then declined (Fig. 7). The frequency of firing was proportional to the magnitude of the receptor potentials. On relaxation of the muscle after a stretch there was frequently an 'off effect' which consisted of a brief hyperpolarization. This was previously found in the frog (Katz, 1950).

These receptor potentials were distinguished from movement artifacts

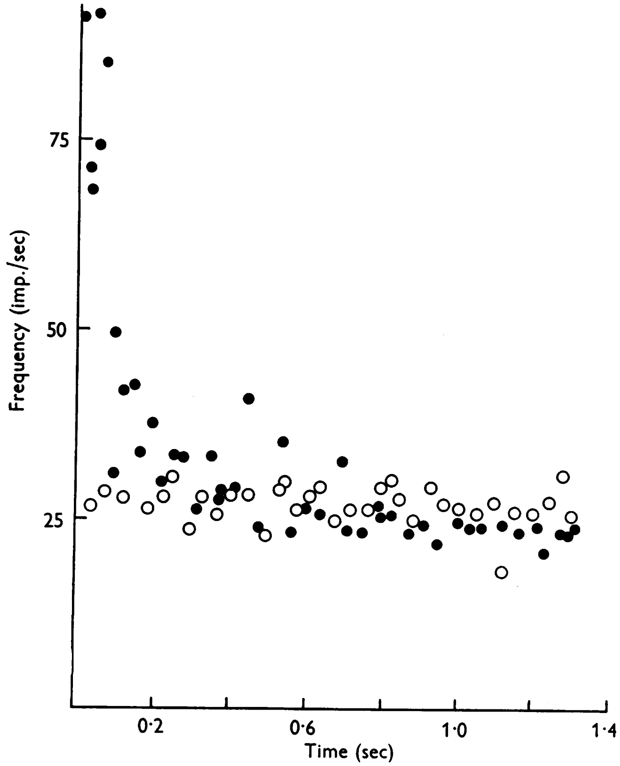

Fig. 5. Relationship between frequency of firing and time after stretch (●) and d.c. (○) applied at time 0 to a single spindle.

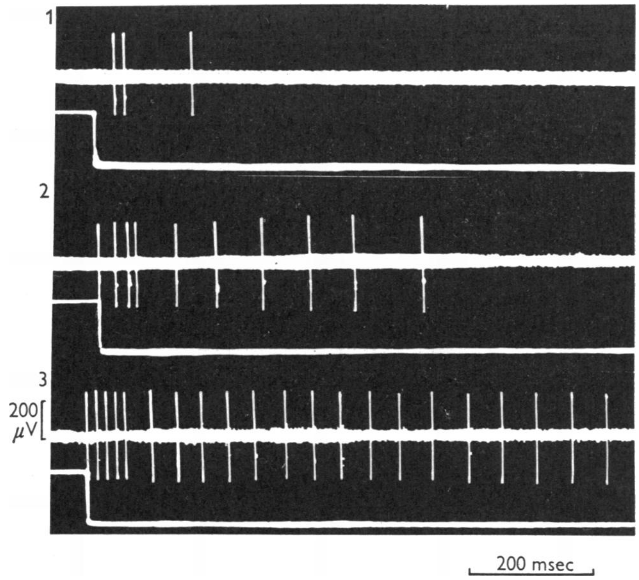

Fig. 6. The effect of a stretch of 1 mm on a muscle (1) completely relaxed, (2) held at 5 % greater length, (3) at 10 % greater length.

in the usual way. If the nerve was placed in contact with muscle surface, then electrotonic spread was short-circuited, and the receptor potentials disappeared. Pinching the nerve had a similar effect. Furthermore, if the recording interface was near enough to the ending, changes in the shape of the action potential could be observed even without procaine. The action potential was of longer duration and was preceded by a gradually increasing depolarization (Lippold, Nicholls & Redfearn, 1960).

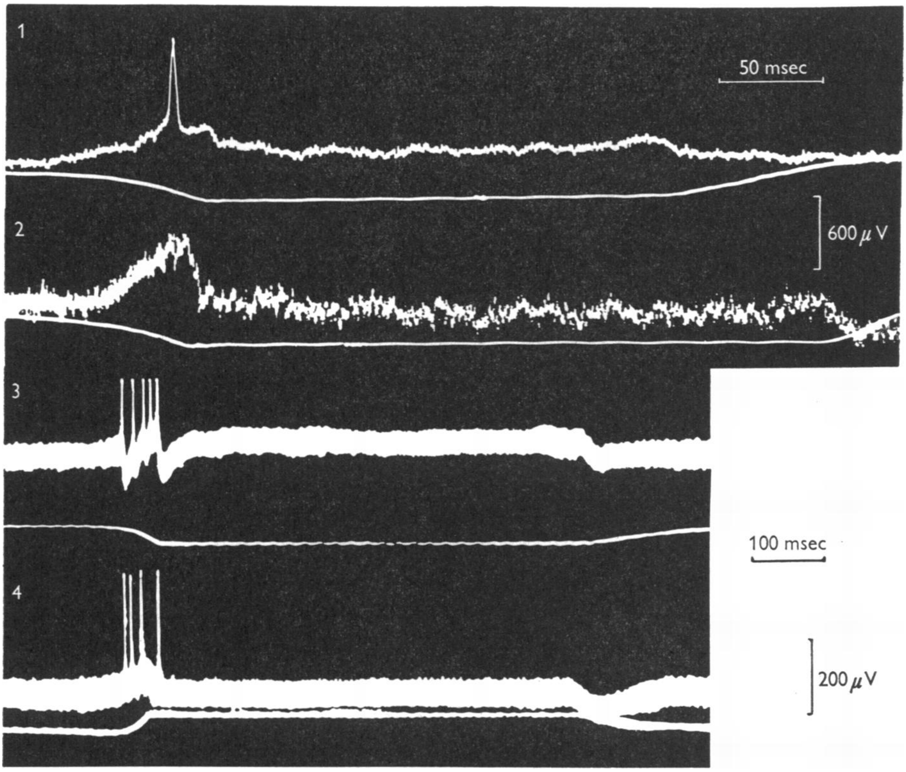

Fig. 7. Receptor potentials (upper beam) recorded from two different spindles when stretched (lower beam): (1) shortly after procaine 0·01 % showing one spike followed by decline in receptor potential; (2) 15 min after procaine, pure receptor potential (gain increased 3 ×); (3) and (4) another fibre shortly after procaine showing receptor potential and 'off effect'. In (4) stretch is signified by an upward deflexion of the lower beam.

DISCUSSION

When a muscle is stretched, its muscle spindles give a discharge initially of high frequency (the 'dynamic phase'), the peak value of which depends upon the rapidity of the stretch; subsequently the discharge rate falls to a lower frequency (the 'static' phase) which is related to the degree of extension of the muscle. This decline in the discharge rate during a maintained stretch is the adaptation of the sensory mechanism. Theoretically it could be due entirely to the physical properties of the linkage between the sensitive nerve terminal and the tendon which is being stretched. It could also be due to the behaviour of the nerve membrane, which might introduce a differential component in its electrical response to an undistorted mechanical input.

On the basis of previous work in the frog it might have been predicted that both mechanical and electrical factors were operative in the process of adaptation. First, Katz (1950) showed that the receptor potential had an overshoot during the dynamic phase of a rapid stretch. Secondly, Matthews (1931) found that the discharge from spindles in the frog's toe muscle declined with time when the nerves were artificially depolarized by the passage of a constant current through them. However, the frog stretch receptor differs greatly from that in the mammal both in structure and in function, and further experimental evidence is needed to make a clear distinction between the operation of the two factors.

Our experiments indicate that adaptation in the mammalian spindle occurs as a result of the physical characteristics of the spindle and extrafusal muscle. When a rectangular mechanical pulse is used to stretch the muscle, the resultant receptor potential is distorted. It is not rectangular but has a 'hump' which coincides with the instant of application of stretch and the magnitude of this hump varies with the rate of stretching. This is the effect to be expected if the terminal membrane were sensitive to the mechanical stress within the muscle and if this stress were proportional to the first differential of the applied strain.

From rough estimates in experiments such as that of Fig. 7 it does appear that no additional adaptation is introduced by a non-linearity in the relation between firing frequency and receptor potential during the dynamic phase of the stretch (cf. Katz, 1950). We have verified this directly by producing a depolarization of the terminal with an applied current. A rectangular current pulse initiates a non-adapting train of impulses, whose frequency is roughly proportional to the current. There is never an initial burst of impulses at a high frequency when the polarizing current is first applied. Matthews (1931) described, in the toe muscles of the intact frog, a certain amount of electrical adaptation to heavy polarizing currents, but it is fairly clear that he was forced to use high current densities in his muscles, which led to difficulties with electrode polarization and contraction of intrafusal and perhaps extrafusal muscle fibres. Edwards (1955), on the other hand, did record in isolated frog muscle a non-adapting discharge from the muscle spindles when he put a voltage across them.

This comparison between the response to mechanical stretch, which produces 'overshoot' in the receptor potential (and thus the initial dynamic phase in the discharge), and that due to polarization of the nerve endings, which gives rise to an unvarying discharge, is clear evidence that no adaptation occurs in the membrane itself. It is therefore the result of physical processes involved in the transmission of forces from the tendon to the nerve ending. Adaptation can be pictured as a physical deformation in the region of the terminals which is exaggerated when a muscle is stretched rapidly, followed by restitution to a lower or 'adapted' level determined by the degree of stretch.

A further possibility is that an undistorted mechanical displacement is transmitted to the nerve terminal and that the conversion of this to a depolarization is non-linear. Nothing is known about this transducer system and it does not seem profitable to speculate about its possible role at present.

SUMMARY

1. The adaptation of muscle spindles has been studied in the isolated tenuissimus muscle of the kitten.

2. The effects of mechanical stretch and of depolarization with applied direct current have been compared in the same single muscle spindle. There is no adaptation to direct current but there is a pronounced initial fall in frequency of the discharge due to stretch, which corresponds to a decline in the receptor potential.

3. On the basis of this difference it is concluded that adaptation in the mammalian muscle spindle is mechanical in origin or occurs during the generation of the receptor potential.

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