

REFLEX SELF-REGULATION OF MUSCLE CONTRACTION AND AUTOGENETIC INHIBITION

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THE DEVELOPMENT that followed upon Sherrington's original discovery of the lengthening reaction (45) and P. Hoffmann's demonstration of the silent period in the electromyogram accompanying the knee jerk (28) may be well known but so much time has now elapsed since these problems were the subject of active experimentation that it is necessary, in reopening the field, to begin by surveying the ground in the light of recent research in order to show where we stand and why again reasonably some progress may be expected.

Sherrington pointed out that the lengthening reaction in the quadriceps muscle was accompanied by Philipsson's reflex of crossed extension as well as by ipsilateral flexion, thereby giving autogenetic inhibition a functional status within the framework of reciprocal innervation. The silent period was held by Denny-Brown (9), on similar evidence, to be but an expression of autogenetic inhibition. It was hypothetically localized to the annulo-spiral afferent system and shown to require a strong synchronous efferent volley, set up by a tap on the tendon or by an electrical shock to the motor root. Hoff *et al.* (27) found a silent period in one extensor after excitation of another only when the former had discharged owing to facilitation.

At that time it was necessary to preserve intact efferent supply in order to study the silent period by means of silver pins stuck into the muscle. We have since learned that strong synchronous stimuli—at least electrical ones—set up a centripetal 'back-response' due to electrical cross-excitation in the muscle (34, 30) as well as back-responses from artificial synapses formed by severed nerves, especially in the unanaesthetized decerebrate preparation (23) used by Denny-Brown. Such back-responses are particularly strong in the afferents. If, as found by him, the silent period requires strong synchronous efferent volleys, we are entitled to conclude from his work that the motoneurons may have been tested by combined synchronous afferent and efferent (antidromic) back-responses, to which they responded by setting up positive after-potential and subnormal excitability. Of this the silent period would have been a consequence.

The last conclusion was, in fact, suggested by Gasser (18) who, having demonstrated the correlation between the late positive phase of the cord potential and inhibition (18, 20, 29), explained the silent period as the result of such subnormal excitability. My own work on the retina had at about the same time led to the conclusion that excitation and inhibition were associated with potential changes in the electroretinogram of opposite sign (see *e.g.* summary, 22). Then followed the demonstration by Eccles and Pritchard

(14) that an antidromic volley delivered into a motor root elicits a root potential of the same general shape as that of the superior cervical ganglion (10), an initial negative phase accompanied by hyperexcitability followed by a positive phase and consequent subnormality. In 1939 (12) Eccles pointed out that orthodromic stimulation of dorsal roots sets up a similar type of potential change on the ventral side and finally (13) he published a very complete analysis of this ventral root potential (the well-known phenomenon discovered by Umrath (46) and studied by Barron and Matthews (2)). In this work it was ultimately proved that no internuncial excitation was required for the ventral root potential so that it legitimately could be called the synaptic potential of the motoneurons.

The general line of thinking, inaugurated by Gasser and followed by Bremer and Bonnet (4, 5) in important work, would seem, indeed, to have settled, once and for all, the question of the silent period, the more so as Bernhard (3) showed that a shock to the afferent gastrocnemius nerves was followed by a depression of the ensuing monosynaptic volley to a second shock and accompanied by a positive change in the root potential. In this work, however, the conditioning shock was strong and therefore Lloyd's (35) high-threshold group II and group III fibres were not excluded. In addition, the positive component of the root potential was held to be something peculiar for extensor motoneurons whilst the silent period is seen in the flexors also (9).

Problem and principle of analysis

In coming to the conclusion that the silent period need be no more than an interesting physiological artefact due to a subnormal phase following a synchronous normal orthodromic volley in monosynaptic stretch-afferents, we have successfully done away with true autogenetic inhibition. We would then be compelled to explain Sherrington's lengthening reaction as an ordinary nociceptive response inducing the flexion reflex whilst inhibiting the extensors. This does not seem very likely in view of Cooper and Creed's (7, 8) demonstration of highly complex facilitatory effects of synergistic and inhibitory effects of antagonistic muscles turning up in muscles subjected to stretch or induced to contract. Neither does it seem likely that the single-shock technique can uncover all the essential features in the normal interplay of reflexes to stretch and contraction which arise from a minimum of five sense organs in the muscle. In returning to the work of the Oxford school, to the papers mentioned as well as to those of Liddell and Sherrington (32) and of Fulton and Pi-Suñer (17), we can take advantage of the fact that a great many questions today can be simplified by testing directly the state of excitability of a given set of well-defined motoneurons subjected to afferent influences from the muscle. It is no longer necessary to try the devious route over the silent period in the electromyogram and to keep the complicating efferent supply intact.

The method developed (26) is based on Lloyd's (36) important demon-

stration that the monosynaptic reflex of Eccles and Pritchard (14) runs in the largest afferents from the muscle and back again through the efferents of the same muscle. The monosynaptic response from the severed ventral root may therefore be used as a test of the excitability of a particular set of motoneurons destined for a given muscle. Since it is faster than any other reflex volley through the cord, it will gauge their level of excitability, as determined by any given amount of preceding afferent influx from stretch or contraction, without the complication of the additional impulses set up by the contraction initiated by the test volley itself (see Fig. 1).

The full theoretical significance of the analysis by means of the monosynaptic volley should not be missed. If, for instance, the test shock finds the motoneurons inhibited, then by whatever synergistic muscle this inhibition has been produced and independently of how many synapses it has traversed, this inhibition has ultimately by some central mechanism been applied on to the motoneurone itself. The monosynaptic test volley, running a non-stop course to the motoneurone, cannot itself have been held up by clashing with internuncial refractoriness or subnormality. An inhibition shown by the monosynaptic test will always be genuine and can be due to post-excitatory subnormality of the tested motoneurone, only when this has discharged, for instance, when stimulated from the muscle supplying the afferents for the monosynaptic test volley itself. The internuncial mechanism can come in at a pre-motoneurone level only if the inhibitory impulses succeed in stopping a facilitatory background discharge which is assumed to be necessary for maintaining the excitability of the motoneurone.

TECHNIQUE

Most animals were in light dial anaesthesia, 0.3–0.4 cc./kg. Some, in addition, were made spinal by a section at or just above Th12. Some decerebrate cats were used but the 'tonic' changes were found to be too much of a complication at this stage of the analysis. The ventral roots from L5 downwards were severed, the long L7 and S1 often in the middle, leaving a central stump for recording and a peripheral stump for neuromyal stimulation of the muscle by the conditioning shock (see Fig. 1). The leg to be used was denervated, leaving only the medial and lateral gastrocnemius nerves for stimulating electrodes buried between the muscles in the closed wound. This stimulus, which below is usually referred to as the test shock (for the monosynaptic volley), was triggered about every 5 seconds by the synchronizing circuit of the electrical system. In some experiments the nerve to the quadriceps muscle was preserved also. In such experiments ileopsoas was cut, together with the muscles around the hip joint. In addition, the rectus component of the quadriceps was removed. The conditioning shock sometimes stimulated muscles around the spine to contract. Further sectioning of muscles was then carried out at the beginning of the experiment, the effect being checked by stimulation until gastrocnemius alone contracted. The muscle contracted isometrically and tension was recorded by the Brown-Shuster myograph to which were fitted two crossing coils, one fixed and fed by a high-frequency current, the other movable with the myograph lever. The capacitative changes, caused by the slight myograph excursions, were amplified and transmitted to the lower beam of a double cathode-ray oscillograph. The monosynaptic volley was recorded on the upper beam (Fig. 1). When the muscle afferents were to be stimulated by stretch the myograph was pulled upon by a string running over a pulley to the middle of a lever (on the floor), the free end of which was provided with a rotating circular disc. To the axis of a cogwheel driven by a motor was fixed a bar with a handle that pressed on the disc about every fifth second, triggering the sweep circuit by a microswitch. The myograph return to zero was speeded up by rubber bands. The onset of stretch, as recorded by the myograph, is not

accurate to the millisecond. Two flip-flop stimulators, triggered by a delay circuit, and a condenser-coupled amplifier completed the electrical outfit. Time was recorded by a Philips sound generator.

Sources of error. The monosynaptic response often varies in size. This difficulty could be overcome by taking a sufficient number of readings, often up to 10, for each position of the test shock and checking less accurate experiments by more accurate ones. The points in the curves are averages of all the readings for a given position. The effects to be described are of a very large order and the main findings confirmed by several modifications of the experimental conditions. In particular stretch can be—and actually was—used to

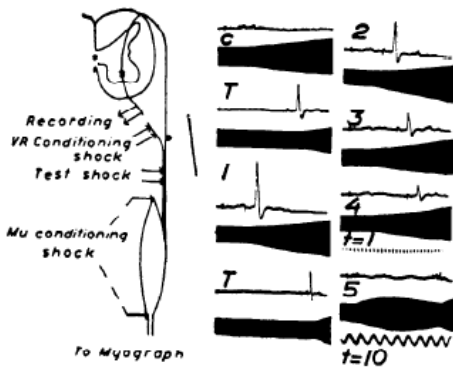


FIG. 1

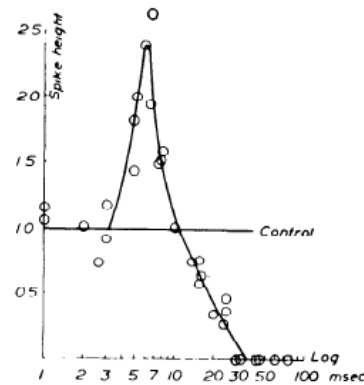


FIG. 2

FIG. 1. Excitability of gastrocnemius motoneurons during contraction of gastrocnemius. *Left.* Diagram illustrating experimental arrangement. *Right.* c, conditioning shock alone, its discharge above, its myogram below; T (upper) test shock with its myogram; 1–4, both together at different time intervals ($t=1$ msec.). T (lower) test shock alone at $t=10$ msec.; 5, together with conditioning shock at $t=10$ msec.

FIG. 2. Variation of spike height relative to monosynaptic control = 1.0 plotted against interval between conditioning and test shock in experiment such as that of Fig. 1. Conditioning shock on ventral root L7, test shock on med. and lat. gastroc. nerves. Initial tension 250 gm. Conditioning shock elicits contraction of 550 gm.

confirm the findings obtained by setting up muscle contractions. This provided a check on sources of error such as stimulus escape to the spinal cord. Besides, the motor fibres are large and of low threshold so that strong stimulation of the roots is by no means necessary. The question of peripheral refractoriness in the nerve used for the test shock is another source of error which is dealt with in Section 6.

RESULTS

1. *Motoneurone excitability during contraction and stretch.* To the right in Figure 1 are some records from an experiment in which the muscle is contracting in response to a shock to the peripheral stump of the ventral root, a fast time base being used for c (conditioning shock alone), for test shock alone (T, upper) and the combined responses 1–4 whilst a slow time base is used for record 5 which illustrates complete inhibition at a long interval between conditioning shock and test shock, the latter being placed as in the control (T, lower). Figure 2 is a complete analysis of the excitability changes in the same experiment, the size of the control being given by the line 1.0. It should be noted that the interval between conditioning and test shock is given in logarithmic units. The muscle contraction is fully developed within 25–30 msec. The illustrated sequence of changes—facilitation-inhibition—is typical for most cats. Facilitation is rarely absent in a good preparation; the depth and extent of inhibition varies a great deal

from animal to animal. The same result was obtained by stimulating the muscle directly.

In Figure 3 a similar experiment has been performed with the root stimulated by a slowly rising current in order to exclude direct cross-excitation by a synchronous muscle action potential. The form of the stimulating current is shown in record 1, 2 is the muscle contraction set up by this

FIG. 3. As in Fig. 1 but stimulation of ventral root S1 by slowly rising current recorded in 1; 2, myogram of conditioning stimulus alone; 3, monosynaptic control together with its myogram; 4-9, conditioning stimulus and test shock together; 10, monosynaptic control and time 100 Hz. Modest initial tension.

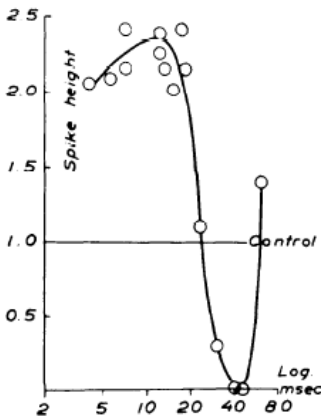
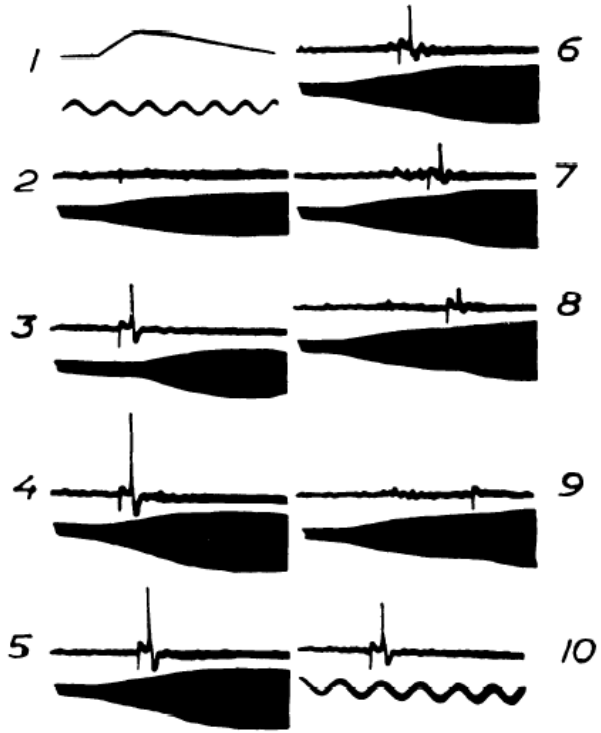


FIG. 4. Spinal cat. Analysis of effect of stretch of gastrocnemius muscle on its monosynaptic response. Ordinates, spike height in terms of control 1.0; abscissae, time from beginning of visible stretch of, in all, 4 mm. at modest initial tension. Note: Stretch increasing during the time shown.

stimulus by itself (conditioning stimulus), 3 the monosynaptic response of the test shock alone, and 4-9 the combined responses at increasing time intervals. The test shock is repeated in 10. Clearly the same sequence, early facilitation followed by inhibition, is obtained. Similarly, in some experiments with the flexor tib. ant. the same type of curve was obtained.

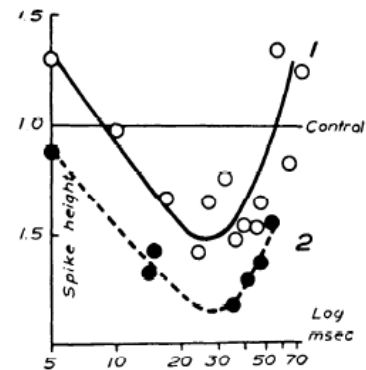
Finally, in Figure 4, there is a complete analysis of the results obtained by triggering the sweep and stimulating the muscle under light tension by a 4 mm. stretch. Some actual records from another experiment are given in Figure 10. The stretch is slow compared with the contractions, its maximum

being reached within a time of 80–100 msec. The initial phase of facilitation accordingly is longer. The phase of inhibition in Figure 4 appears contracted on account of the logarithmic time scale. In this experiment it is succeeded by a second facilitation appearing before the final level of stretch has been reached. Sections 5 and 6 will be devoted to effects of stretch.

Conclusion. The muscle action is aided by a central reflex mechanism of self-regulation, first speeding up, then damping its activity. Primary governors are the end organs recording muscle tension. Autogenetic inhibition is thus no physiological artefact but, on the contrary, facilitation and inhibition are aspects of a physiological integration incorporated in the normal performance of the muscle machine.

2. *Size of test shock and effect of initial tension.* Maximal or supramaximal test shocks have generally been used for the monosynaptic volley in order to overcome refractory phenomena in the nerve and excessive fluctuation in

FIG. 5. Experiment, plotted as in Fig. 2, to show effect of size of monosynaptic control on autogenetic inhibition. Initial tension 250 gm. Curve 1, maximal monosynaptic volley eliciting contraction of 275 gm. Curve 2, small monosynaptic volley eliciting contraction of only 50–75 gm. Conditioning shock to ventral root S1 elicits 150 gm. tension.



the size of the monosynaptic response. Figure 5 shows that a diminution in the strength of the test shock (half maximum instead of maximum response) may deepen and expand the inhibitory trough in the curve. This is what one would expect.

Muscle tension is the most important factor in determining the form of the excitability curve of the motoneurons under proprioceptive firing. There are great differences from preparation to preparation. Some animals have actually given a definite phase of inhibition to stimulation of the root—as in Figure 2—despite no initial tension whatever. This is perhaps not surprising in view of the fanlike organization of the gastrocnemius muscle fibres around longitudinal septa of fascicular tissue which makes it difficult to predict how and where tensile stress occurs. There may also be a low-threshold component of cross-excitation in some muscles with consequent subnormal phase of refractoriness in the motoneurons. Inhibition at zero initial tension is shown in Figure 6 (circles). At the other extreme, in the same figure, an initial tension of 700 gm. (black squares) produces a much heavier inhibition. In this experiment, at 700 gm. tension, stimulation was afterwards shifted to the muscle. The slightest contraction sufficed to give strong inhibition; indeed, it proved difficult to make the stimulus sufficiently weak so as to obtain the curve of Figure 7 with the phase of depressed excitability still above the zero line. The inhibitory phase was succeeded by a

second facilitation. Secondary facilitations are very common (cf. Fig. 4, to stretch) but these phenomena will not be treated in the present paper.

Whilst, in general, the greater the initial tension, the better marked the inhibition, there have been exceptions in the sense that certain preparations are prone to give facilitations alone or merely a relative depression in an excitability curve running entirely above the line of control in the figures (see below, section 4, concealed inhibition). Drs K. E. Hagbarth and K. Naess,* working with the same apparatus, have found it possible to obtain more inhibition by combining stretch with contraction. In one of their experiments stretch and contraction by themselves merely gave facilitation. A slight contraction added in the midst of a stretch set up inhibition.

FIG. 6. As in Fig. 2 to show effect of initial tension on autogenetic inhibition. Conditioning shock to ventral root S1 and maximum mono-synaptic response.

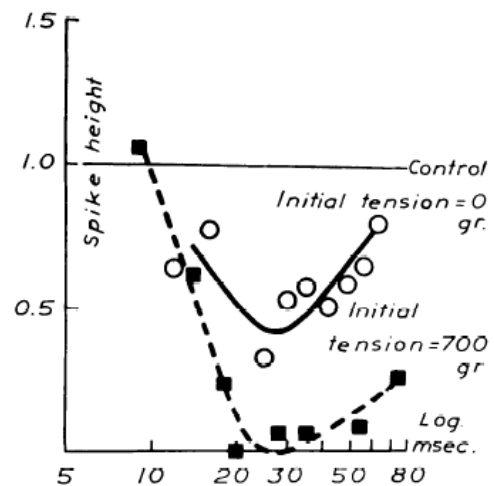
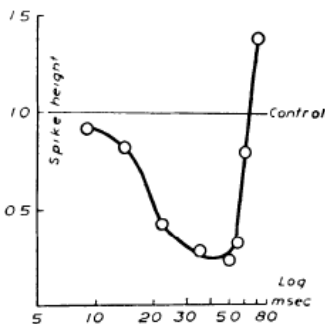


FIG. 7. Same experiment as in Fig. 6 but conditioning shock shifted to gastrocnemius muscle, still at 700 gm. initial tension. Very weak conditioning shock. Note: Rise after inhibition.

Within narrow limits facilitation also is favoured by an increase of tension, but important receptors, setting up facilitation, must have very low thresholds. In favourable preparations it is sometimes quite easy to obtain facilitation alone at low initial tensions and inhibition succeeding it after a slight increase in tension. In order to demonstrate the effect of tension it is by no means necessary to use extremes as in Figure 6. The full inhibitory effect is generally obtained below 300 gm. of initial tension. The facilitatory phase is hardly ever missing. When strong, it may occlude or greatly postpone inhibition. Initial tension has the same effect upon the response to stretch as on that to contraction. High initial tension should be used with great caution because the stretch reflex (32), as well as the afferent discharge (39), is known to suffer from it. This may explain why in Denny-

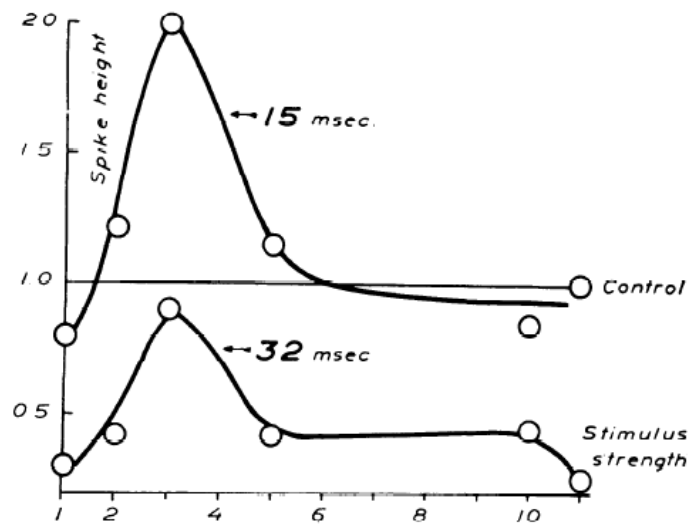
* Private communication from work to be published in *Acta physiol. scand.*, 1950.

Brown's work (9) the silent period was absent at very high initial tensions. Having investigated the effect of tension, I used modest or, whenever possible, low initial tension in the work that followed.

Conclusion. Increase of initial tension, within limits, may augment the excitatory phase of the excitability curve but has a fairly regular and relatively greater effect on the inhibitory trough which deepens and expands.

3. *Effect of strength of stimulus eliciting contraction.* This experiment introduces an interesting new aspect of the problem because of Leksell's (30) important observation that selective stimulation of the small efferent

FIG. 8. Effect of strength of conditioning shock for gastrocnemius muscle from ventral root S1 on size of monosynaptic response at intervals 15 (upper) and 32 (lower) msec. between conditioning and test shock. Abscissae, stimulus strength in multiples of threshold strength. Modest initial tension.



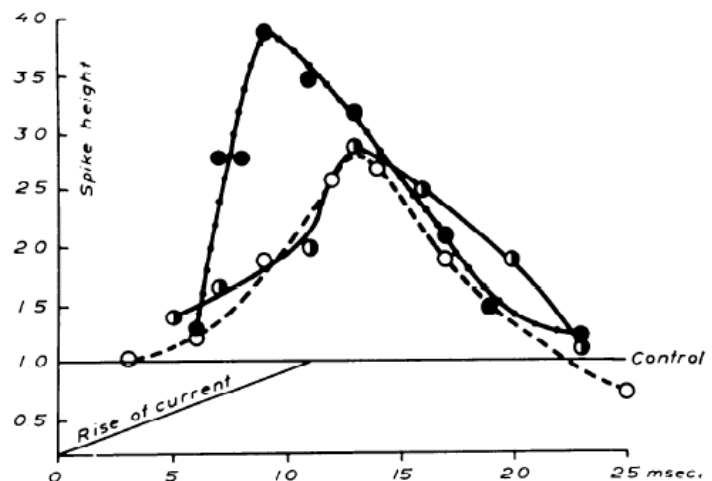
fibres in the ventral roots does not add to the muscle tension but discharges afferent fibres, provided that the muscle is under some initial tension. His so-called gamma efferents (cat) became activated at about three times the threshold for the motor alphas and the gamma maximum generally appeared around 15 times the alpha threshold. The alpha maximum was completed at about three times the threshold value. This region of stimulus strength therefore represents the degree of stimulus strength at which further increase does not add to the contraction of the muscle but introduces gamma activity with consequent increase of afferent input into the cord. On Leksell's evidence (to be compared with Barker's (1) recent histological work on the muscle spindles), the gamma efferents supply the muscle spindles in addition to larger motor fibres of the alpha class. It is thus clear that, on gradually increasing stimulus strength to the root, one is approaching a region, around thrice the threshold of the motor units, in which a second afferent outburst occurs owing to gamma activation of the muscle spindles. From this strength upwards the muscle contraction remains constant (until the shock is strong enough to excite repetitive firing or spread to the spinal cord) whilst the afferent input increases.

In order to study the effect of this afferent secondary discharge on inhibition it is necessary to place the test shock in such a position relative to

the muscle contraction that the monosynaptic response remains well above zero in the inhibitory phase. Otherwise, on increasing stimulus strength, it soon disappears owing to complete inhibition, with the consequence that this inhibition itself cannot be gauged. Facilitation is less important in this connexion because it is maximal at such low stimulus strength that it is difficult to know whether the secondary contraction of the muscle spindles has added to it or not and, also, because we need hardly doubt that muscle spindles can originate it.

In Figure 8 a single shock to the peripheral stump of the ventral root was applied in the usual fashion and two positions, 15 and 32 msec., were chosen for the interval between conditioning and test shock. There is clearly a low-threshold inhibition, due to motor alphas; facilitation then gets the upper hand with further increase in the muscle contraction up to about thrice the threshold for the motor alphas. The 15 msec. curve is facilitated and passes above the control line; for the 32 msec. curve the excitability remains depressed, though less so than before. Beyond this strength of

FIG. 9. Concealed inhibition. Conditioning stimulus is the slowly rising current of record 1 in Fig. 3, stimulating gastrocnemius muscle to contract from motor roots S1 and L7. Plotted as Fig. 2 but time linear. Part of sensory L7 cut across for control of test shock from the gastrocnemius nerves. Plateau strength of current of constant rising time varied. Strength: 1.0, half-filled circles; 1.6, filled circles; 4.0, open circles. Good initial tension.



stimulus, inhibition increases in spite of the fact that the contraction did not alter. Facilitation, however, had not disappeared. Tests at shorter intervals between conditioning and test shock showed that facilitation still was present, even at maximum stimulus strength, but its duration had shortened so that it no longer extended to the 15 msec. shock interval. This experiment is interesting because both the motor alpha primary and the motor gamma secondary discharge from the afferents could be shown to have an inhibitory component. In many experiments the former low-threshold inhibition is completely absent or covered by facilitation, the latter high-threshold inhibition is present in most cases. When stimulus strength is gradually augmented, it is occasionally possible to show very clearly that inhibition continues to increase beyond the moment when the muscle contraction has reached its maximum. This effect, however, is not always demonstrable and the experiment suffers from the difficulty that the results cannot be checked by stretch.

Conclusion. The experiment suggests that gamma efferents going to the muscle spindle, by setting up a discharge from this organ, have initiated inhibition and thus indicates that autogenetic inhibition can be obtained from the muscle spindles.

4. *Concealed inhibition.* In preparations which, to all appearance, give pure facilitation there may nevertheless be concealed inhibition. Figure 9 is from an animal with a small monosynaptic response which increased a great

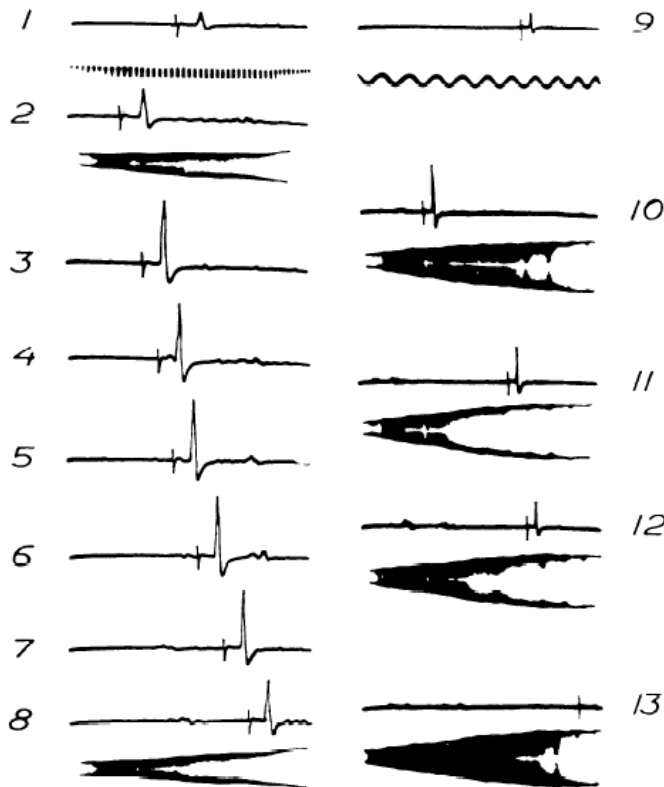


FIG. 10. Spinal cat. Effect of stretch of gastrocnemius muscle on its own monosynaptic response, shown as control in 1 and 9 together with times 1000 and 100 Hz respectively; 2-8, test shock shifted in early phase of stretch of which myographic controls, to save space, have been left only in records 2 and 8; 10-13, same stretch of 3 mm. recorded with the slower sweep circuit of record 9. In record 13 complete inhibition. Modest initial tension. (With increased tension more inhibition was noted.)

deal when the muscle was stretched or made to contract. The stimulus was the slowly rising current of constant duration (*cf.* Fig. 3, record 1) applied to the peripheral stump of ventral root S1. The currents of relative plateau strength 1.0 and 4.0 gave the two lower curves whilst the large rise of facilitation was obtained with relative current strength 1.6.

It seems that, at plateau strength 4.0 for the stimulating current to the root, new end organs in the muscle must have been activated by the contraction and also that the new afferent fibres concerned cannot have had very much slower conduction rates than the excitatory fibres, previously activated, since otherwise there would have been an initial rise of facilitation followed by a drop when the current increased from 1.6 to 4.0. As it is, inhibition sets in early enough to suppress part of the initial facilitation to current strength 1.6 without succeeding in doing away with it completely. It is evident that, in rising to plateau strength 4.0, the current must have traversed the value 1.6. End organs with considerable inhibitory effects,

represented among the fast fibres, must have been slightly excited at or somewhat below current strength 1.6 to be able to come in so definitely when, owing to a further increase in current strength, the muscle spindles (or other muscle fibres) were induced to contract more strongly.

Conclusion. The phenomenon of concealed inhibition, when seen with slowly rising currents, may be employed to show that there are some end organs with greater inhibitory effects than others.

5. *Observations on stretch.* In a number of animals light stretch of the gastrocnemius muscle merely induces facilitation; heavy stretch also induces inhibition. Thus the threshold, in terms of tension caused by stretch, is higher for inhibition than for excitation. In such preparations it is easy to see how, as the stretch increases, suddenly a point is reached where inhibition appears. If facilitation is very prominent it may be difficult to obtain good inhibition. On the hypothesis of motoneurone subnormality this is difficult to understand. Why do the motoneurons refuse to become subnormal? The records of Figure 10 show the effect of stretch of the gastrocnemius on the monosynaptic volley from its own nerves. An analysis of another similar experiment was given in Figure 4.

Tension and length of stretch are interchangeable in the sense that good inhibition may be obtained by slight stretch at high tension or, alternatively, by heavy stretch in a muscle at low initial tension. A certain amount of tensile stress is therefore necessary for inhibition. It cannot be explained as a necessary consequence of preceding facilitation. The inhibition can increase without increase of facilitation. We have never gone beyond 6 mm. stretch which, after all, is less than a third of what muscles can do easily (32).

Conclusion. By increasing stretch or initial tension it can be shown that inhibition increases without an increase of facilitation, or even in spite of diminished facilitation, a fact very difficult to explain without assuming that there are separate inhibitory end organs.

6. *Effect of stretch of one extensor upon another.* In several cases afferent control of the test shock was included in order to find out whether part of the inhibition might not be peripheral, due to refractoriness in the nerve which would diminish the size of the test volley. Such an effect was occasionally seen but not with good monosynaptic responses. In order to avoid this complication entirely but also in order to study the central distribution of autogenetic facilitation and inhibition, the stretch was set up in the quadriceps muscle or in one component of the divided gastrocnemius muscle whilst the monosynaptic volley was elicited from the gastrocnemius nerve—in the latter case not the half that was stretched. Thus the motoneurons tested were in the first case not at all, in the second perhaps only to some extent, identical with those receiving the impulses from tension organs in the muscle through the monosynaptic arc.

Figure 11 is an analysis of an experiment with the divided gastrocnemius muscle and the test shock on the severed lateral nerve to the gastrocnemius.

There is the usual sequence of facilitation-inhibition in response to stretch of the medial component that had its afferent nerve intact. According to Lloyd (37) there should be monosynaptic direct facilitation across the two

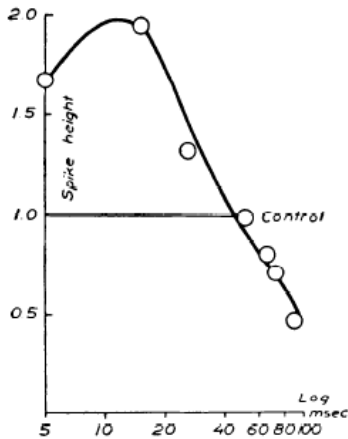


FIG. 11. As Fig. 4. Lateral and medial components of gastrocnemius muscle separated. Test shock for monosynaptic response to severed lat. nerve, medial component in good initial tension stretched 4-5 mm.



FIG. 12. Spinal cat. Effect of 4 mm. stretch of quadriceps muscle at light initial tension on monosynaptic volley elicited from the severed gastrocnemius nerves. 1 and 7, monosynaptic controls at times 1000 and 100 Hz respectively. 2-6, early phase of stretch analyzed with faster sweep and stretch control included in 2; 8-10, later phase of stretch with slower sweep. Note: Recovery from full inhibition in 10.

gastrocnemius nerves, tested by the single shock technique. Figure 12 shows the effect of stretch of quadriceps (in all experiments lacking the rectus component) on the gastrocnemius monosynaptic volley. The curve is of the characteristic type, facilitation succeeded by inhibition at a certain degree

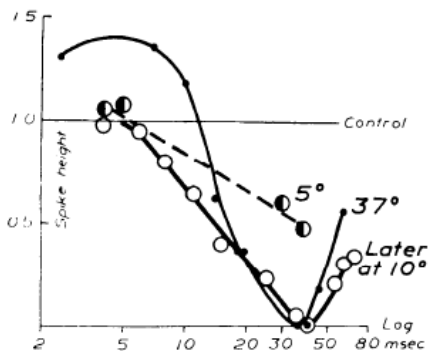


FIG. 13. Quadriceps in light initial tension stretched 4 mm.; gastrocnemius motoneurons tested by volley from their severed motor axons. Thermode on quadriceps nerve. Plotted as in Fig. 4. Full explanation in text.

of stretch. Records of this type have been analysed in Figure 13, curve marked 37°.

There has been inhibition in all the experiments in which the effect of stretch of quadriceps was tested on the gastrocnemius monosynaptic volley. There has been facilitation also but not as marked as in the experiments

kept within the gastrocnemius system. Thus, for instance, in the experiment of Figure 10 the gastrocnemius monosynaptic control was 5 times increased by stretching the gastrocnemius muscle. The stretch was then shifted to the quadriceps which gave an optimal facilitation of only 1.34 times the monosynaptic control. All facilitations from the quadriceps field upon the gastrocnemius motoneurons have remained below 50 per cent. In one of the experiments pure facilitation was obtained by slight stretch of a quadriceps at low initial tension, good inhibition as soon as the initial tension had been increased. However, all these differences are differences of degree rather than of kind. This is evident when comparing Figures 4, 10, 11, 12 and 13.

Conclusion. The autogenetic facilitation and inhibition from one extensor upon its own motoneurons is reflected in synergistic leg muscles. Hoff *et al.* (27) have shown that the effect of one extensor upon another led to a silent period only when it succeeded in discharging its motoneurons; it now remains to be investigated whether inhibition to stretch can occur without preceding facilitation of the inhibited motoneurons.

7. *Independent fibres for excitation and inhibition.* It is, of course, perfectly clear (see *e.g.* 45, 37, 6, 24) that there are inhibitory fibres in the muscles but what remains to be proved is that there are special inhibitory fibres from end organs responding to *stretch* or increase of tension. Warming of nerves is a method for selective activation of small fibres, as established by C. von Euler (15), and by this method it was shown (24) that warming of the gastrocnemius nerves in a decerebrate animal causes slight excitation succeeded by complete inhibition of the tension maintained by the static postural stretch reflex. However, these fibres may be the pain fibres (*cf.* 31, 21) and they are at or below the delta range because these are the largest afferents stimulated by warming (15, 24).

In order to find out whether there are special tension end organs for inhibition of synergistic muscles the following types of experiment were performed. (i) A U-shaped thermode was placed on the quadriceps nerve cooling a length of 1 cm. while the test shock to the gastrocnemius nerves was shifted between facilitatory and inhibitory positions during stretch of the quadriceps. In Figure 13 is shown the original excitability curve with the quadriceps nerve at 37°. Then water was passed through the thermode (the nerve and the thermode itself were covered with cotton pads soaked in paraffin) and it is seen that facilitation almost disappeared while part of the inhibition still was left. The nerve was cooled for some time until the supply of cold water in the tank had run out when the water temperature, measured by a thermo-couple just outside the animal, had risen to 10°. In this slightly damaged nerve there was only pure inhibition left. (ii) Pressure is known to attack the fibres of greatest diameter first (19). In the experiment of Figure 14 the quadriceps muscle was stretched while its nerve was compressed between thumb and forefinger of the experimenter. The monosynaptic test volley came from the severed popliteal nerve. Initially a position of facilitation (F-p) and one of inhibition (I-p) were chosen, as shown in

the uppermost row of control records before pressure. Then pressure was applied and, when (vertical row, left) the facilitation had disappeared, the test shock was quickly shifted over into the inhibitory position. There was still strong inhibition. The test shock was shifted back into the facilitatory position. Facilitation was still absent (lowermost record). The nerve quickly recovered and the middle row of records was obtained in the same fashion.

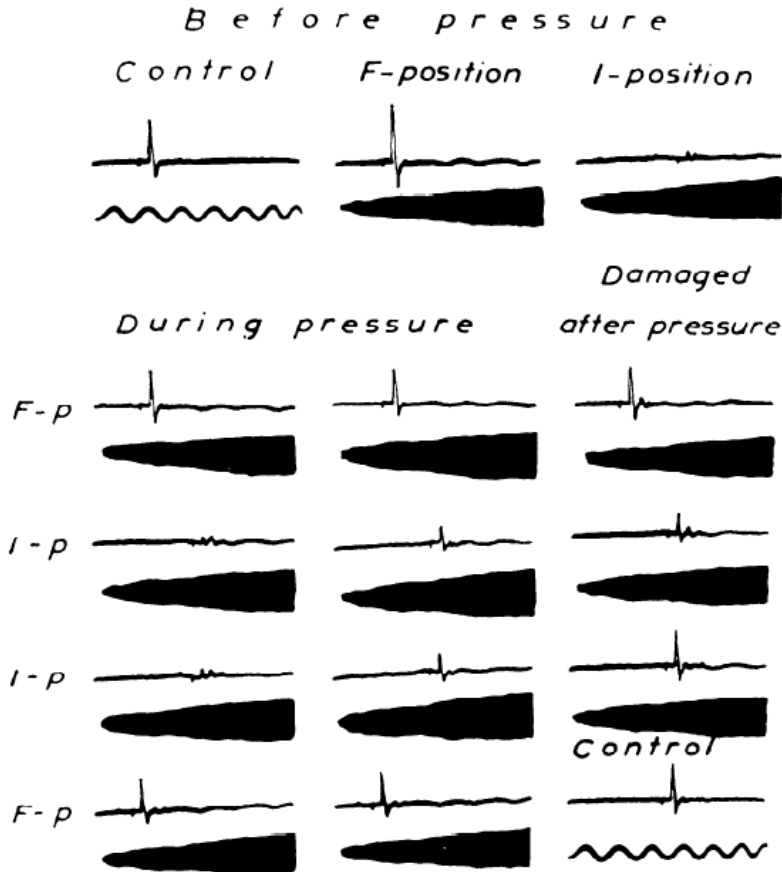


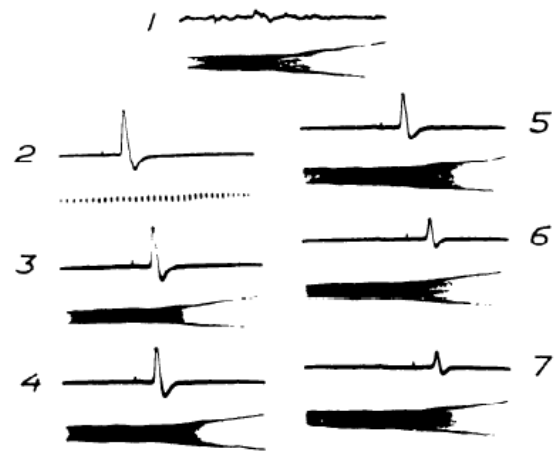
FIG. 14. Quadriceps in light initial tension stretched 4 mm. and test shock on popliteal nerve. Effect of pressure upon quadriceps nerve, as fully explained in text. Time 100 Hz.

This time part of the inhibition disappeared, too. The nerve still recovered a couple of times from repeated exposures to pressure but ultimately a steady state was reached in which all facilitation was lost and only part of the inhibition remained, variable in amount and not as great as before (vertical row, right). In this, just as in the experiments on cooling, the excitatory fibres in the long run proved more sensitive to interference than the inhibitory ones, perhaps merely because the latter were better represented in the centre concerned. In other similar experiments the margin between disappearance of excitation and of inhibition was still narrower, if it was present at all.

The same nerve could not be used for both test shock and pressure because the slight pull, on touching it, augmented facilitation, sometimes to such an extent as to occlude inhibition, or, at any rate, so as to make the controls unreliable. Also, on pressing or cooling the nerve, artificial synapses tended to arise (23, 25) as well as excitability changes spreading electrotonically to adjacent regions (23). These sources of error proved to be very disturbing. Accordingly this type of experiment was soon given up in favour of the one employed above.

Conclusion. Since the excitatory component of the excitability curve can be separately removed, without concomitant changes in the inhibitory component, inhibition cannot be due to post-excitatory subnormality in the tested motoneurons which show no signs of having been activated.

FIG. 15. Effect of gastrocnemius contraction on quadriceps motoneurons. Contraction of gastrocnemius muscle elicited from ventral roots L7 and S1. Test shock for monosynaptic volley on severed nerve to quadriceps. 1, at high amplification, shows effect on recording leads (L6) of gastrocnemius contracting to conditioning shock; 2, test shock and time 1000 Hz; 3-7, combined responses. Inhibition did not increase later in the contraction. Spinal cat.



Inhibition must arise in some other manner and in this sense the remaining fibres are true inhibitory fibres.

8. *Relative size of excitatory and inhibitory fibres.* There was so little facilitation from the large quadriceps field upon the smaller field of the gastrocnemius motoneurons that it seemed reasonable to expect that no facilitation would be left if the situation was reversed, *i.e.*, if the quadriceps motoneurons were tested by the monosynaptic volley and stimulated from the smaller gastrocnemius system. This proved to be true. Actually Brooks and Eccles (6), by the single shock technique, found no facilitation when conditioning and test shock were applied respectively to gastrocnemius and quadriceps nerves. (They do not mention ever having tried reversing conditioning and test shock.)

In the experiment of Figure 15 contraction was used instead of stretch in order to obtain a better measure of time intervals. It is thus a repetition of the experiment of Figure 1, but this time with the monosynaptic test shock applied to the severed quadriceps nerve instead of to the gastrocnemius nerves. The leads are on L6 and the gastrocnemius muscle is made to contract by a shock to the severed motor roots L7 and S1. No other muscle contracted in response to this stimulus. Record 1, at higher amplification

than the others, shows that the conditioning shock to the root elicited a muscle contraction and, after 6 msec., a very small response in L6. This response should be compared with the monosynaptic control at half maximum size and low amplification in record 2. We can never know with absolute certainty whether the small response of record 1 is from an artificial synapse, or is due to cross-excitation in the gastrocnemius muscle or to mechanical stimulation of its tension receptors. But, considering that the latent period of the monosynaptic test response is of the order of 3 msec., it is clear that

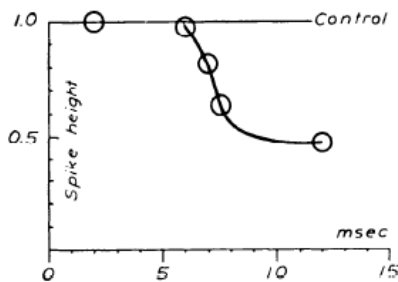


FIG. 16. Experiment of Fig. 15 analyzed as in Fig. 2 but time between conditioning shock and test shock linear.

the conditioning volley which perhaps has travelled about thrice this distance in 6 msec. must have been conducted in very fast fibres. At the moment (6 msec.) when this volley appeared at the leading-off electrodes the test shock was discharged into the quadriceps nerve. When its volley arrived into the spinal cord it just escaped inhibition; when discharged between 0.5 and 1.0 msec. later it fell into the early phase of inhibition as shown by the complete analysis of the experiment in Figure 16. If the receptors setting up inhibition from the gastrocnemius nerves had discharged through fibres very much smaller than those setting up the stretch reflex (and facilitation), a result like this would have been impossible. In this experiment, however, it is possible that direct and indirect inhibition are mixed. Brooks and Eccles (6) have found the inhibition of gastrocnemius upon quadriceps to be so early as to suggest that it is direct. We cannot ascertain the moment of initiation of the afferent discharge and therefore must be content with these approximations. They suggest, as did the previous experiments, that the conduction time of excitatory and inhibitory impulses is of much the same order of magnitude and therefore that the fibres are of much the same size. When inhibition survived excitation in the experiments of the last section the most probable interpretation would seem to be that the inhibitory fibres had a very much better peripheral or central representation than the excitatory ones.

The experiment was finally carried out with tetanic conditioning stimulus which gave a long-lasting complete inhibition to zero level. Figure 17 compares a single shock with tetanic stimulation.

Conclusion. Fibres from excitatory and inhibitory end organs in the muscle are both represented among the large and rapidly conducting fibres.

DISCUSSION

Skeletal muscle is provided with nervous governors for facilitation and inhibition which are pitted against one another in the spinal centre. In the normal mode of operation of the muscle machine the contraction is first

speeded up by facilitation, then damped by inhibition. The greater the initial tension or the more (in stretch) the muscle is stretched, the more important become the inhibitory brakes. Special sense organs exist in the muscle for excitation and for inhibition, both being represented among the large and rapidly conducting fibres (smaller ones not excluded). The effect of inhibitory sense organs is probably reinforced by motoneurone refractoriness

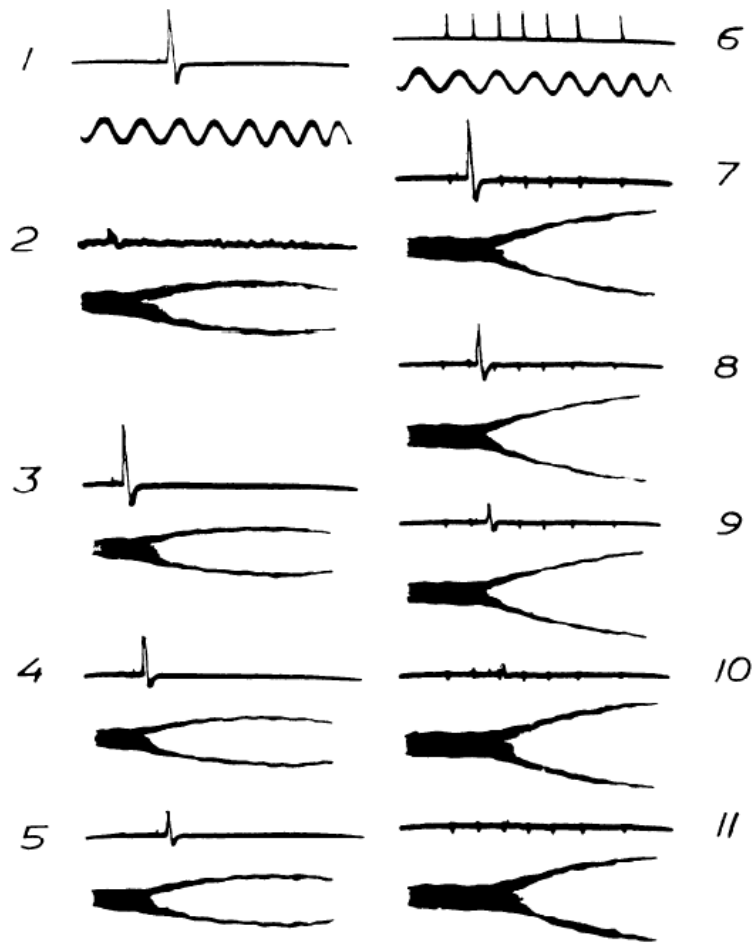


FIG. 17. Same experiment as in Fig. 15 but recorded somewhat later and with slower sweep speed in order to compare single conditioning shock (left) and tetanic conditioning shock (right). 1, quadriceps monosynaptic control; 2, effect of conditioning shock alone at high amplification; 3-5, combined responses; 6, form of tetanic stimulus; 7-11, combined responses showing complete inhibition that lasted within the visible range of the tetanic gastrocnemius contraction, whilst with the single shock (left) inhibition nowhere in the contraction went below minimum illustrated in record 5. Time 100 Hz.

following strong synchronous afferent excitation of the kind that plays a less important rôle in normal muscle activity. In the leg extensor system (analyzed in detail above) fibres are distributed from both excitatory and

inhibitory end organs to allied muscles across one joint to the next joint. Excitatory end organs have a more restricted central distribution than inhibitory ones. Yet some facilitation and a great deal of inhibition are shared by extensors capable of synergistic co-operation—for instance, while maintaining posture of the limb. The inhibitory fibres are, of course, only inhibitory in the sense that they represent autogenetic inhibition. They may well be excitatory on antagonists (9, 45).

On the evidence obtained, the self-regulation of the muscle contraction (stretch, also, would—if the ventral roots were intact—induce contraction) can be discussed from two points of view: (i) its central mechanism, (ii) nature of end organs concerned.

Central mechanism. Since the gastrocnemius motoneurons are inhibited by stretching the quadriceps muscle, and, since in this case monosynaptic transfer seems unlikely (37), the process is probably carried across internuncials. This process may be some kind of blocking of the facilitatory internuncial bombardment of the motoneurone (its so-called general background activity) leading to a drop of motoneurone excitability sufficient to prevent activation by the monosynaptic system. To be as efficient and fast as it is, the blocking process would have to be localized to the immediate neighbourhood of the motoneurons. Actually there is no reason whatever to assume that the mechanism for indirect autogenetic inhibition differs in the least from that of the direct immediate inhibition of Renshaw (40) and Lloyd (33). It is an unexplained effect at the level of the motoneurone. Brooks and Eccles (6) stress the significance of specific positive focal potentials. The question as to whether this process merely acts by removing facilitatory background or by active anodal polarisation of the cell membrane of the motoneurone is hardly ripe for discussion. The time relations of the autogenetic inhibition, as well as the fact that it attacks the motoneurons of synergistic muscles across a joint without evidence for preceding facilitation, seem to exclude the idea of motoneurone refractoriness. Motoneurone refractoriness and subnormality due to positive afterpotential must play a rôle with large synchronous afferent volleys (silent period).

Nature of end organs. Ruffini (42, 43) and Sherrington (44) agreed in placing the fibre sizes at the level of the end organ in the following order: annulo-spirals, Golgi tendon organs—both relatively large as compared with the flower spray endings. Barker's (1) recent work suggests the same conclusion. But there is a missing link in the histological evidence; the relative fibre sizes are not known in the nerve stem itself. On our evidence there could be inhibitory fibres smaller than the largest excitatory ones, provided that there are some very large inhibitory fibres too, and this view does not disagree with Lloyd's demonstration that the monosynaptic myotatic afferents would have to be the largest ones. These, on Matthews' (39) evidence would have to be the A2 or the B endings, the former assumed by him to be the annulo-spirals, the latter the Golgi tendon organs. Either of the two would have to be inhibitory for synergistic muscles. The lower mechanical

threshold of the A2 endings is in favour of their being excitatory for their own muscle. The facilitation may be supported by A1 endings which run in smaller fibres and were assumed to be the flower spray endings (39). It is difficult to ascribe inhibition to them because they are of the "in parallel" type, first postulated by Fulton and Pi-Suñer (17) and then found by Matthews. These are silenced in twitch, silenced in tetanic contraction, and the more effectively the greater the initial tension. They are thus silent under conditions when inhibition is at its very best.

When Matthews ascribed the silent period to the Golgi tendon organs, his B organs, he based his conclusion on experiments (9) which could be satisfactorily explained by motoneurone subnormality. For this no special inhibitory end organs are needed. Our results, as they stand at the moment, are best explained by assuming the annulo-spirals (A2) to be excitatory and the Golgi tendon organs (B) inhibitory. This presupposes that the latter have higher mechanical thresholds though not necessarily as high as one is led to assume from Matthews' results with a few selected samples. Our experiments with pressure applied to nerve cannot differentiate A2 from B endings because there are fibre properties which are not distributed in proportion to fibre size (see *e.g.* 16).

Inhibitory end organs, on our evidence, are likely to exist in the muscle spindles also. Actually Sherrington (44) pointed out that there are Golgi tendon organs also in the tendons of some muscle spindles. Barker (1) states that they "frequently occur in association with muscle spindles." These could be responsible for the low-threshold inhibition to contraction and the secondary inhibition in the experiments varying stimulus strength to the ventral roots (Section 3). Motoneurone refractoriness may also provide an alternative explanation of the low threshold inhibition in slack muscles which was demonstrated only in experiments on contraction. We also know from Ruffini's (42, 43) work that the Golgi tendon organs often are associated with special types of Pacini corpuscles and, in addition, there are free nerve endings in the muscle spindles. The latter seem to represent small fibres (1) and may be pain receptors. Next to the ear, the eye, etc., the muscle spindle, according to Ruffini, is the most highly developed sense organ in the body and clearly more detailed information is needed about its physiology.

Rexed and Therman (41) as well as Lloyd and Chang (38) agree in finding three definite groups in the calibre spectra of muscle afferents. These have not yet been correlated with the types of endings in the muscle. It is obvious, too, that some development on the afferent side of the type of analysis used in this work still can add a great deal more to the specification of the properties of the end organs responsible for autogenetic inhibition.

SUMMARY

In experiments on acutely de-efferented cats the monosynaptic reflex response from the gastrocnemius nerves has been used to test the excitability

of the gastrocnemius motoneurons during contraction or stretch of the muscle. Whatever the mode of stimulating the tension end organs, by making the muscle contract by a conditioning shock or a slowly rising current from electrodes on the motor root, from electrodes in the muscle itself, or by merely stretching it, there is first an increase of excitability of its motoneurons followed by a depression, as gauged by the size of the monosynaptic test volley.

Contraction or stretch of the synergistic quadriceps muscle (deprived of its rectus component) causes the same sequence of excitability changes in the gastrocnemius motoneurons, first facilitation, then inhibition.

The facilitatory component can be selectively removed by cooling the quadriceps nerve or by compressing it gently, leaving the inhibitory component intact, and thus indicating that inhibition is initiated by separate tension receptors. These can also be isolated directly by testing with the quadriceps monosynaptic volley and making the gastrocnemius muscle contract. There are thus for synergistic extensors separate inhibitory fibres responding to stretch and they have been shown to conduct almost as rapidly as the fibres causing facilitation of the motoneurons.

Inhibition is favoured by an increase of initial tension of the muscle and it is found to possess a slightly higher mechanical threshold than facilitation.

In conclusion it is pointed out that the muscle machine is working under self-regulation from autogenetic governors, first aiding it to contract, then damping the discharge from its motoneurons; also that the inhibitory brakes are put on with greater efficiency, the more the damping becomes necessary owing to increase of tensile stress.

The results are discussed from the points of view of the central mechanisms concerned and the receptors engaged as governors.

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