Acta physiol. scand. 1964. 61. 331—347

From the Nobel Institute for Neurophysiology, Karolinska Institutet, Stockholm 60, Sweden

The Effects of Extensor Muscle Spindles and Tendon Organs on Homonymous Motoneurones in Relation to γ-Bias and Curarization

By

ROBERTO BIANCONI,[1] RAGNAR GRANIT and DONALD J. REIS[2]

Received 7 December 1963

Abstract

BIANCONI, R., R. GRANIT and D. J. REIS. *The effects of extensor muscle spindles and tendon organs on homonymous motoneurones in relation to γ-bias and curarization.* Acta physiol. scand. 1964. *61.* 331—347. — The ventral root L 7 is divided into a peripheral and central stump. The former is used for contracting the gastrocnemius-soleus muscle by a brief tetanus supra-threshold for the γ fibres. The latter records the monosynaptic test response by which the autogenetic excitability of the gastrocnemius-soleus motor nuclei is measured during and immediately after contraction. There are three major aims behind these experiments: (i) to discover whether at any time in or after contraction and stretch the spindle secondaries can be given a functional task, (ii) to provide a basis of comparison with similar experiments in flexors (subsequent paper) in which the spindle secondaries have autogenetic effects of opposite sign, (iii) to define autogenetic excitability during contractions in terms which are sufficiently precise to provide a basis for further work aiming at distinguishing between pre- and postsynaptic components of inhibition.

The old question of how sense organs measuring length and tension in the muscles contribute to reflex autogenetic control of their own muscles was clarified for extensors in general outlines fourteen years ago (Granit and Suursoet 1949, Granit 1950, Hagbarth and Naess 1950, McCouch, Deering and Stewart 1950, Granit and Ström 1951, Hunt 1952). The reason for returning to it now is the improved knowledge of the anatomy of the muscle spindles (Cooper 1959, 1960, 1961, Swett and Eldred 1960, Barker and Gidumal 1961, Barker and Cope 1962, Boyd 1962) which poses fresh problems. This paper will deal with limb extensors, a second paper (Bianconi, Granit and Reis 1964)

[1] Fellow of the Consiglio Nazionale delle Ricerche-Istituto di Fisiologia Umana, Università di Parma, Italy.

[2] Visiting Special Fellow, National Institute of Neurological Diseases and Blindness.

with flexors. In both papers the principal method used is monosynaptic testing of a cut ventral root whose peripheral portion is used for stimulating extra- and intrafusal muscle to contract. An essential part of the problem is a comparison between extensors and flexors. The autogenetic reflexes from the latter have not been receiving the same amount of attention as those of the former.

A large number of authors have contributed to the establishment of some generally accepted correlations between fibre diameter, conduction velocity and reflex effects of the muscular end organs. In analysis of reflexes the following generalizations are permissible in the sense that they are statistically valid: the large primary afferents in extensors cause autogenetic excitation. These derive from muscle spindles and are often termed Ia afferents. The Ib afferents include both fast and somewhat slower fibres and belong to tendon organs. Their reflex effect is autogenetic inhibition. The smaller or group II spindle afferents also cause autogenetic inhibition. The evidence for these conclusions inasmuch as fibre diameters, conduction velocities and reflex effects are concerned cannot here be reviewed in detail but some major contributions are; with regard to fibre diameters (Eccles and Sherrington 1930, Lloyd and Chang 1948, Rexed and Therman 1948, Hagbarth and Wohlfart 1952); correlating velocities with reflex effects (Lloyd 1943 *a*, *b*, Brock, Eccles and Rall 1951, Laporte and Lloyd 1952, Hunt 1954, Laporte and Bessou 1957, 1959, Bessou and Laporte 1962). For application of the intracellular technique to these problems, see Eccles, Eccles and Lundberg (1957 *a*, *b*).

The new knowledge of the anatomy of the muscle spindles implies that the large primary afferents (cat extensors) possess terminals on both nuclear bag and nuclear chain fibres while the small secondary afferents chiefly have terminals on nuclear chain fibres though some are located on the myotube region of the nuclear bag fibres. Thus, assuming the muscle spindles to be excited by stretch or by their own motor supply, then, unless stretch be small, primary excitatory and secondary inhibitory afferents will always be excited together. If the spindle is made to discharge by intrafusal contraction elicited by stimulation of its motor fibres in the ventral roots, both end organs will again discharge together because technical limitations prevent separate stimulation in the roots of nuclear bag and nuclear chain fibres in such studies. Furthermore, assuming that in the life of the organism nuclear chain motor fibres could be excited separately, the primary afferents would nevertheless be stimulated at the same time by their terminals on them.

From such considerations arose a fresh problem: how can the nuclear chain secondaries ever exercise their inhibitory effect against excitation from the primaries which in the same spindle have at their disposal both types of intrafusal muscles, NB (nuclear bag) and NC (nuclear chain) fibres. Reformulating the question in terms of our experiments: do constellations occur with stretch and contraction as natural stimuli in which the inhibitory effect of the spindle secondaries can be demonstrated? The major experimental complication is

obviously tension which mobilizes inhibitory tendon organs which have to be eliminated or otherwise excluded.

In contraction our experimental reply to this question is based on the discovery by Cooper (1959, 1961), since repeatedly confirmed (Lundberg and Winsbury 1960, Harvey and Matthews 1961*b*, Bianconi and Van Der Meulen 1963), to the effect that the phasic component of the spindle discharge is insignificant or absent in secondaries. When contraction is over they resume firing at the previous rate (Harvey and Matthews 1961*a*, Bessou and Laporte 1962), while primaries often pick up their original discharge rate slowly and a large number of them early on the downstroke of contraction fire a burst followed by a second pause (Granit and Van Der Meulen 1962). Thus it is at the end of contraction that one should expect secondaries to dominate over primaries.

Methods

A. General principle of analysis. The method has been used in previous studies from this laboratory (e. g. Granit 1950). In brief, it is based on the fact that changes in the afferent discharge from spindle and tendon organs will vary depending on the length and tension of the muscle as well as on the rate of change of these parameters during stretch or contraction and thereby alter the net balance of excitatory and inhibitory impulses arising from the muscle to converge on its own motor neurones. A monosynaptic test of reflex excitability of these same motor neurones at any instance during manipulation of the muscle (allowing a few milliseconds for conduction and synaptic delays) will therefore by the size of the test response reflect the net balance of excitation and inhibition of muscular origin. Variabilities in spindle organ sensitivity resulting from variations in γ motor excitation of the intrafusal muscles are eliminated by section of the ventral roots. Ventral rhizotomy permits initiation of contraction by electrical stimulation of the peripheral end of the cut ventral root and also, by varying stimulus intensity, to excite γ as well as α motor fibres in different proportions. In addition it serves to eliminate recurrent effects on motoneurones resulting from the conditioning stimulus.

B. Specific techniques. Cats were anesthetized with Nembutal (40 mg/kg) but occasionally spinalized by sharp section either at T12 while under Nembutal or at C1 after ether anesthesia, and then maintained on artificial respiration. The left hind limb and hip were denervated in the usual way. Further denervation was later performed if ventral root stimulation resulted in contraction of hip or paraspinal muscles. In some animals the contralateral limb was also denervated. Ventral roots L7 and S1 were sectioned about 1 cm from entrance into the spinal cord. The animals were placed in a frame, body temperature maintained at 37—38° C, and the left leg fixed by drills in the head of the femur and tibial crest and the ankle rigidly clamped. The tendons of gastrocnemius and soleus were freed and attached by a stiff hook, either separately or together, to a strain-gauge myograph mounted on a hydraulically regulated pulling device which allowed accurate and reproducible setting of muscle length. Bipolar stimulating electrodes of silver wire with interelectrode distances of 3—4 mm were placed on the distal portion of the cut ventral root for the conditioning stimulus, cathode towards the muscle. Selection of either the L7 or S1 ventral root for the conditioning stimulus was determined by the maximal size of the contraction elicited by stimulation of the root. As a rule this was obtained from L7. The monosynaptic test stimulus was delivered through electrodes placed on the gastrocnemius nerves in the popliteal fossa with the cathode upwards. The monosynaptic response was recorded from the central stump of the ventral root

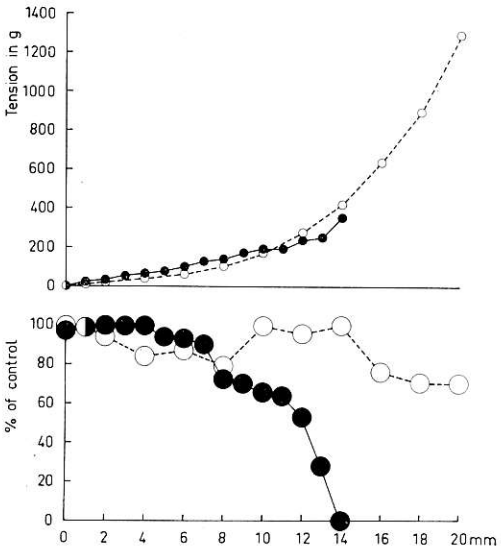

Fig. 1. Different patterns of changes in excitability of gastrocnemius-soleus motoneurones during static stretch of deefferented gastrocnemius-soleus. Extension in mm. Two cats. Nembutal anesthesia. *Upper graph:* Muscle tension at different extensions in the two animals. *Lower graph:* Monosynaptic excitability at different extensions. Lines in full and broken lines in each graph corresponds to the same animal.

whose peripheral portion had been chosen for stimulation of the muscle. Paraffin oil was used to cover exposed tissues.

The conditioning tetanus for the peripheral stump of the cut ventral root lasted 19 msec and consisted of a train of shocks of 0.8 msec duration delivered at a frequency of 500/sec. Tetanic stimulation was used in order to produce a sufficient degree of intrafusal contraction when wanted. Occasionally motor twitches were studied.

The test stimulus to the gastrocnemius nerves consisted of a single shock of 0.9 msec duration set at an intensity which produced a monosynaptic test response of about 50 % of maximum.

Muscular contraction was recorded by a strain-gauge myograph with a maximum sensitivity of 0.75 g/mm deflection. Muscle length and tension are referred in the paper to that found at 'zero length' which is defined as that length of muscle at which the myograph at high sensitivity senses an increment of tension when the slack is taken off the muscle by pull on the tendon. This zero length was frequently checked during the course of the experiment.

In order selectively to block extrafusal contraction without affecting intrafusal contraction two techniques were used. The first was an attempt to block the α motor fibres by anodal blockade in a manner similar to that described by Kuffler and Vaughan Williams (1953), by adjusting interelectrode distance, shock strength and duration for the electrodes on the cut ventral root. It actually proved possible on occasion to demonstrate that intrafusal contraction, as deduced from increased discharge of single spindle afferents, was proceeding with little or even no contraction of extrafusal fibres. This dissociation between extra- and intrafusal contraction was seen for both primary and secondary spindle afferents and from ankle flexor and extensor muscles. This result proved to be highly variable, however, and success or failure in selective blockade depended on a number of critical factors which excluded regular use of anodal blocking. Because of this inconstancy this approach was abandoned in favour of selective blockade by Flaxedil. It is mentioned here because as far as we know, it is first the time the method has been applied to the mammalian preparation with some success.

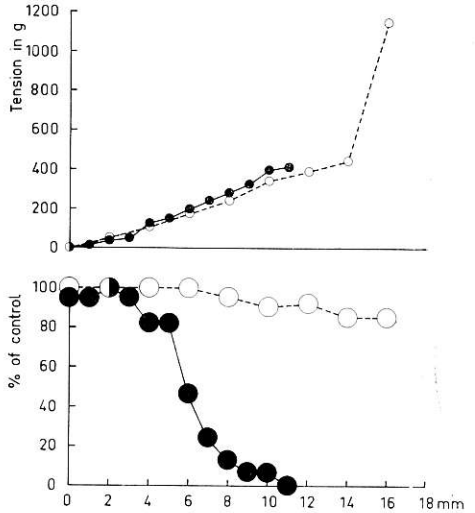

Fig. 2. Spinal cat (Th 12). Changes in the excitability of gastrocnemius-soleus motoneurones during static stretch of de-efferented gastrocnemius-soleus. Extension in mm. Single and double monosynaptic test shocks. *Upper graph:* Muscle tension at different extensions in two trials with single (line in full) and double (broken line) test shocks. *Lower graph:* Monosynaptic excitability at different lengths with single (line in full) and double (broken line) test shocks.

Blockade of extrafusal contraction was successfully accomplished by the intravenous administration of Flaxedil which in low doses may eliminate extrafusal contraction but leave intrafusal contraction unimpaired (Granit, Homma and Matthews 1959). Doses of Flaxedil of 1.5—2.0 mg/kg given in a single intravenous injection predictably resulted in almost complete attenuation or total disappearance of all extrafusal contraction within 3 min after the injection. This state persisted for 15—30 min while the animal was maintained on artificial respiration. With this dose of Flaxedil the monosynaptic control did not change and the discharge of single spindles elicited by supramaximal stimulation of ventral roots was preserved.

Results

Effects of static stretch on monosynaptic reflex excitability

It has been shown previously (Granit 1950, Granit and Ström 1951, Henneman 1951, Hunt 1952) that static stretch of the ankle extensors usually, but not invariably, will result in an inhibition of the monosynaptic reflex elicited from the homonymous and heteronymous muscle nerves. These experiments have been repeated in order to evaluate the effect of steady stretch of ankle extensors at different extensions, and hence at different tensions, on the monosynaptic test response elicited homonymously. All observations were made 20—30 sec after the muscles had been stretched to a given length and the monosynaptic test response had stabilized.

In general, plots of the monosynaptic reflex excitability against both extension and passive tension led to curves which fell into two broad groups illustrated in Fig. 1 by two representative experiments. The two curves are derived from two different animals both anaesthetized with Nembutal, and whose passive tension curves (upper graph) are almost identical. In the first type (Fig. 1,

solid line) the monosynaptic test response either started at or reached its maximal response within the first 3—4 mm of stretch during which the tension in the muscle rarely exceeded 50 g. With further stretch the monosynaptic test response became reduced with a tendency for the diminution of the response to increase progressively with each further mm of stretch until it disappeared completely. The onset of the downward break in the curve was more consistently observed at tensions of 50—100 g than at any constant length.

In the second type of response (Fig. 1, broken line) monosynaptic excitability was not reduced by more than some 30 % by stretching the muscle, even beyond the physiological range. In some instances, no reduction of the monosynaptic test response was seen at all.

It was found possible to convert the first type of curve (exhibiting sensitivity to inhibition) to that of the second type by doubling the monosynaptic test shock. An example of this is illustrated in Fig. 2. Initially, the monosynaptic excitability to a single test shock (Fig. 2, solid line) was progressively reduced by increasing stretch after exceeding a threshold at about 50 g of tension and hence progressed to complete inhibition at 11 mm of stretch when the tension was 400 g. By then adjusting the intensity and duration of the test shock so that the test response was doubled and only the (summated) second shock resulted in a monosynaptic test response (Fig. 2, broken line), the monosynaptic response was only inhibited by 15 %, even at extreme lengths and high tension.

Comment. These experiments confirm earlier work (Granit and Ström 1951, Henneman 1951, Park, Teasdall and Magladery 1951, Hunt 1952, Buller and Dornhorst 1955, Libet, Feinstein and Wright 1959) and demonstrate inhibition to stretch except when double shocks are used whose synaptic potentials sum to levels beyond those that can be prevented by inhibitory repolarization. It is likely that both tendon organs and spindle secondaries contribute their share to such inhibitions as have been seen here during static stretch with tensions of over 50 g which is the beginning of the range for stimulation of tendon organs. Such tensions represent extensions well beyond the threshold for secondary spindle organs and strongly suggest that in the circumstances inhibition from secondaries requires the support of the tendon organs to exceed the concealed state. The different types of curve obtained are best explained by the settings of spinal internuncial control, as determined by supraspinal and other sources. Such factors have been studied by Job (1953), R. M. Eccles and Lundberg (1959), Holmqvist and Lundberg (1959), Holmqvist, Lundberg and Oscarsson (1960), Hufschmidt (1960, 1961).

Effects of contraction on monosynaptic reflex excitability

It is convenient for the purpose of relating the changes in monosynaptic reflex excitability to changes in the afferent input arising from the contracting muscle to divide the events from stimulus to contraction into four phases (see Fig. 8) as follows: *I*, a pre-contraction phase consisting of the period from the

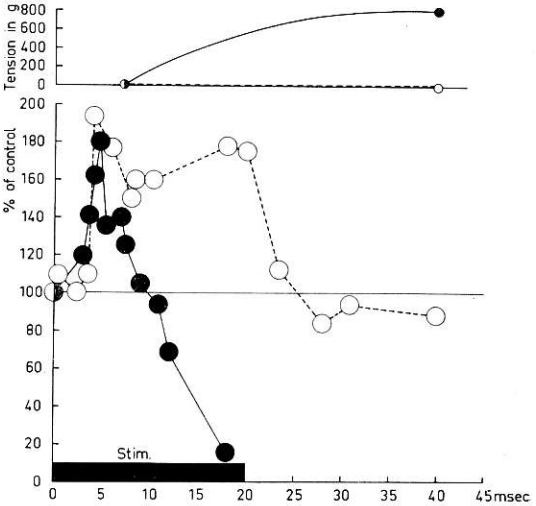

Fig. 3. Cat, Nembutal anesthesia, before and after Flaxedil. Excitability of gastrocnemius motoneurones and muscular response conditioned by tetanization of distal end of cut ventral root L7. Muscle extended 2 mm. Stimulus 10 × threshold for extrafusal contraction. Timing in msec begins with onset of tetanization. *Upper graph:* Muscle tension before (line in full) and after (broken line) Flaxedil (2.0 mg/kg i. v.). *Lower graph:* Monosynaptic excitability before (line in full) and after (broken line) Flaxedil.

onset of ventral root stimulation to the earliest observable contraction of the muscle as recorded by the myogram set at moderate or high gain, *II*, a phase of tension rise which begins at the moment of earliest observable contraction, as above, up to and through the plateau of maximal tension occurring during a tetanic stimulation. *III*, a phase of declining tension beginning at the first fall-off of muscle tension from its peak value during relaxation and terminating when muscle tension has returned to its pre-contraction level, *IV*, a late or post-contractile phase beginning at the termination of any recorded tension. The changes that occur in monosynaptically tested excitability during these events will now be described for each phase separately.

I. Pre-contraction phase. The presence of facilitation of the monosynaptic test response beginning 3—4 msec following a supramaximal conditioning stimulation of the cut ventral root and prior to the onset of contraction was demonstrated by Granit (1950) and confirmed by Hagbarth and Naess (1950). In this study a similar early facilitation of the monosynaptic test response was commonly observed. This exhibited a latency from the onset of a tetanus as brief as 3 msec and persisted during the stimulus train until the beginning of the muscle contraction. Then it rapidly declined or disappeared. Markedly reducing or totally abolishing extrafusal muscle contraction by the administration of intravenous Flaxedil did not alter the magnitude of it. After significant reduction or elimination of contraction by this technique, the early facilitation persisted until several milliseconds after termination of stimulation of the ventral root, as illustrated in Fig. 3. It should be noted that although the fall of the reflex excitability precedes the onset of observed contraction by 2 msec, the possibility of some contraction preceding its registration by the myograph is real. In this

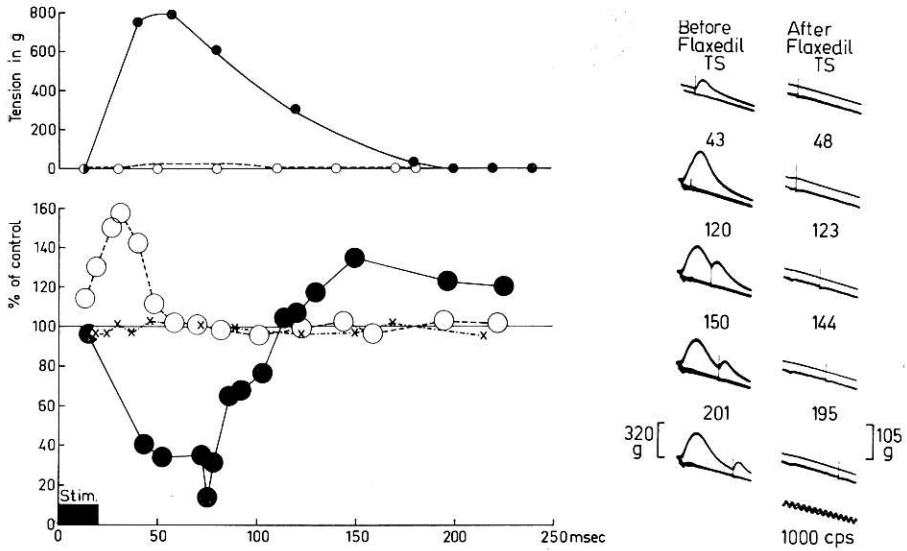

Fig. 4. Spinal cat (C 1) before and after Flaxedil. Excitability of gastrocnemius motoneurones and muscular response as conditioned by tetanization of distal end of cut ventral root L7. Resting length of muscle 10 mm. Stimulus at 3.2 × threshold for extrafusal contraction. Timing in msec begins with onset of tetanization. *Upper graph:* Muscle tension before (line in full) and after (broken line) Flaxedil. *Lower graph:* Monosynaptic excitability before (line in full), after Flaxedil (broken line), and after section of muscle nerve (crosses). *Inset:* Samples of original records of myogram (upper line) and monosynaptic test response (lower line) with test shock (TS) alone with conditioning shocks at times marked above them. Tests after Flaxedil begin at 4 min after injection of 2.0 mg/kg i. v. Note, that Phase I is not included in the figure.

instance the latter was set at a moderate sensitivity. As a rule the fall of reflex excitability ran parallel with the rise of muscle tension.

It appears therefore that the decline of the Phase I facilitation is due to the alteration in input to the spinal cord from muscle receptors and is dependent on contraction. The mechanism of Phase I facilitation of the monosynaptic test response, its relationship to the early discharge and its implications with regard to α motor innervation of the muscle spindles have been discussed in detail by others (Granit, Pompeiano and Waltman 1959, Hunt and Perl 1960, Bessou, Emonet-Denand and Laporte 1963). The present study has not been designed critically to examine this particular problem. However the persistence of Phase I facilitation after paralytic doses of Flaxedil makes its dependence wholly on tensile or ephaptic excitation of afferents from the massed muscle action potential unlikely.

II. Phase of increasing and maximal muscle tension. This, as we have seen, is accompanied by a considerable fall of excitability, in Fig. 4 beginning in spite of maintained supramaximal stimulation of the ventral root. These observations confirm those previously made in this laboratory (Granit and Suursoet 1949, Granit 1950, Granit and Ström 1951, Hagbarth and Naess

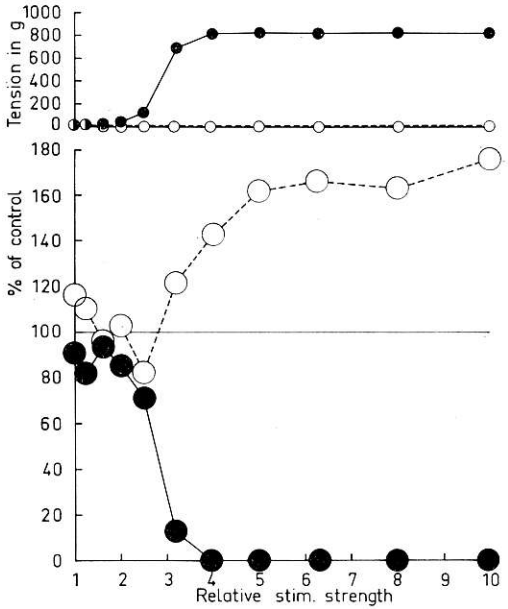

Fig. 5. Same cat as Fig. 4, before and after Flaxedil. Changes in excitability of gastrocnemius motoneurones at different intensities of conditioning tetanus to distal end of cut ventral root L7. Intensities in multiples of threshold intensity for extrafusal contraction. Interval between onset of conditioning tetanus and test shock 42 msec. Resting length 10 mm. *Upper graph:* Maximal recorded tension of gastrocnemius during contraction before (line in full) and after (broken line) Flaxedil (2.0 mg/kg i. v.). *Lower graph:* Monosynaptic excitability before (line in full) and after (broken line) Flaxedil.

1950). Curarizing by Flaxedil so as to remove tension while retaining for a while intrafusal sensitivity to motor impulses led to the striking change, seen in Fig. 4. Phase II inhibition reverted to a facilitation which gradually approached zero. The late facilitation belonging to a later phase (see below) disappeared. The duration of the Phase II facilitation under Flaxedil varied from case to case; maximally it lasted up to 220 msec into Phase III and increased with increased resting length. It should be noted that no observations in Fig. 4 refer to Phase I. The experiments generally ended with severance of the motor nerve to prove that the effects noted were muscular.

Stimulus strength and extension determine the magnitude of the motor effect on intrafusal fibres and so, for Fig. 5, we have selected the moment of near-maximum facilitation (as determined after Flaxedil) for a study of the effect of the intensity of stimulation at an extension of 5 mm, empirically found to be sufficient for good spindle activation. The interval between onset o ventral root tetanus and test shock was 42 msec at that moment. The abscissae in Fig. 5 represent stimulus strength in multiples of threshold for extrafusal contraction.

It is seen in the figure that before Flaxedil inhibition by our test essentially ran parallel with contractile tension but that, after Flaxedil leading to removal of tension, the remaining facilitation required stimuli of a strength near the extrafusal maximum in order to appear at all and that it continued to increase when the stimuli became stronger (5 $\times$ threshold). This, of course, is as would

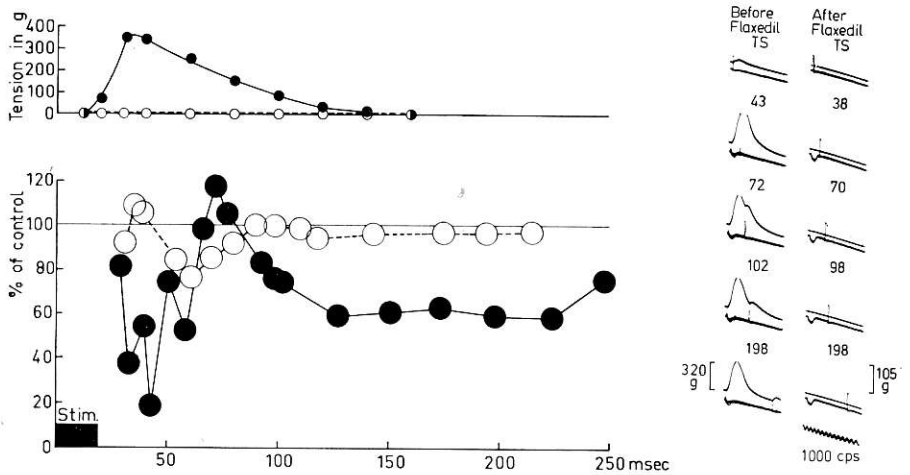

Fig. 6. Spinal cat (C 1), before and after Flaxedil. Excitability of gastrocnemius motoneurones and muscular response as conditioned by tetanization of distal end of cut ventral root L7. Zero resting length of muscle. Stimulus 10 × threshold for extrafusal contraction. Timing in msec begins with onset of tetanization. *Upper graph:* Muscle tension before (line in full) and after (broken line) Flaxedil. *Lower graph:* Monosynaptic excitability before (line in full) and after Flaxedil (broken line). *Inset:* Samples of original records of myogram (upper line) and monosynaptic test response (lower line) with test shock (TS) alone and with conditioning shocks at times marked above them. Tests after Flaxedil begin at 4 min after injection of 2.0 mg/kg i. v.

be expected from present knowledge of the role of the γ fibres for spindle primaries and thus indirectly for their reflex effects (see e. g. Granit 1955)

Such experiment as a rule ended with controls in which either procaine block or nerve section was used to demonstrate that the ventral root stimuli actually had activated the intrafusal muscle fibres of spindles in the ankle extensors.

It is of interest that although intrafusal contraction initiated by stimulation of γ motor fibres is well known to result in increased discharge from excitatory primary and inhibitory secondary spindle endings, facilitation uniformly dominated after Flaxedil paralysis. This indicates that the net result of augmenting spindle discharge by this method of γ motor fibre stimulation will always be to produce more 'primary' than 'secondary' effects, no matter what the initial muscle length or tension, and this holds good even in animals of the type showing failure of inhibition to extreme stretch. The regularly occurring inhibition during this phase of contraction also provides further documentation in support of the view that autogenetic inhibition during contraction is the dominant effect of tendon organs rather than merely the result of withdrawal of autogenetic facilitation by spindle unloading. Supramaximal tetanic stimulation should maintain some spindle activity within the pause (Hunt and Kuffler 1951 *a*).

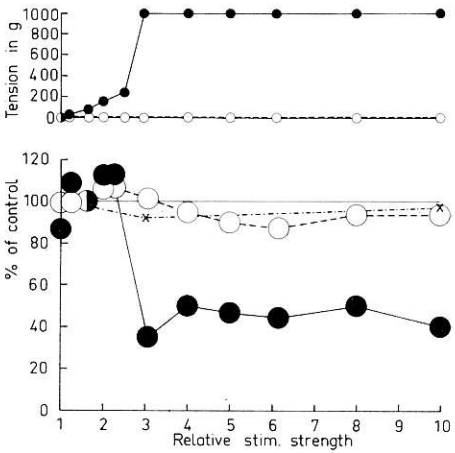

Fig. 7. Same cat as Fig. 6, before and after Flaxedil. Changes in excitability of gastrocnemius motoneurones at different intensities of conditioning tetanus to distal end of cut ventral root L7. Intensities in multiples of threshold intensity for extrafusal contraction. Interval between onset of conditioning tetanus and test shock 100 msec. Resting length zero. *Upper graph:* Maximal recorded tension of gastrocnemius during contraction before (line in full) and after (broken line) Flaxedil (2.0 mg/kg i. v.). *Lower graph:* Monosynaptic excitability before (line in full) and after (broken line) Flaxedil.

III. Phase of excitability during declining tension. During the period of decline from the peak tension, excitability usually begins to increase. Though the change in the curve temporally corresponds to the onset of decline of peak tension, its rate of return to control levels is faster than that of muscle tension (Fig. 6). Frequently this effect has the character of a transient facilitation which occurs when the muscle tension has fallen to 1/2 or 1/3 of its peak tension (see Fig. 4 and 6). This transient facilitation has been previously noted (Granit 1950). Its relationship to the time course of relaxation of the muscle is identical with that of the small contraction seen during the period of declining tension of the tendon jerk, the so-called 'myotatic hump' (Creed, Denny-Brown, Eccles, Liddell and Sherrington 1932) or 'myotatic appendage' (Ballif, Fulton and Liddell 1925) and it would thus appear to be the neuronal basis of that mechanical event. Despite loss of tension the late facilitation usually ends with reversal to inhibition (see Fig. 6). Less frequently facilitation persists (Fig. 4). Following the administration of Flaxedil the transient Phase III facilitation disappears completely while the Phase II facilitation which occurs during and immediately following the tetanic stimulation still is seen, indicating that the absence of the response after small doses of Flaxedil is due to something caused by variations of muscle tension. The transient Phase III facilitation may be seen with the muscle at any initial length although it generally tends to be accentuated by greater lengths.

In some instances with prolonged inhibition the Phase III facilitation may be concealed and only appear as a transient reduction in inhibition. The onset of this transient rise in excitability also coincides with the moment at which the 'myotatic hump' occurs.

IV. Post-contraction phase. Changes in the amplitude of the test response are usually seen to persist following the return of the muscle to its control length and

tension. Most commonly during this period there is marked inhibition which may continue up to several hundred milliseconds after muscle tension has disappeared and hence, unlike the inhibition found during Phase II of contraction, is independent of tension. Nevertheless, following administration of Flaxedil this persistent late inhibition entirely disappears. This is illustrated in Fig. 6.

The relationship of the late, persistent inhibition of Phase IV to the stimulus intensity is illustrated in Fig. 7, plotted as Fig. 5. The curves have been obtained from the same animal as illustrated in Fig. 6 and the interval between the onset of the conditioning tetanus and the test shock is chosen to be 100 msec which is well within the late persistent inhibition. It is seen that both the reflex inhibition (Fig. 7, lower graph, solid line) and the muscular contraction (upper graph, solid line) reach their plateaus at similar stimulus intensities — 3.2 × threshold — although the threshold for the onset of the monosynaptic reflex inhibition is somewhat higher than that for contraction. Following the elimination of extrafusal contraction by Flaxedil (Fig. 7, upper graph, broken line) both contraction and monosynaptic inhibition (Fig. 7, lower graph, broken line) disappear, an effect which also follows section of the muscle nerve.

The long-lasting Phase IV inhibition may also follow a twitch contraction of the ankle extensors elicited by a single shock to the ventral root at the threshold for maximal extrafusal contraction. It is seen with muscles at any initial length or tension, although occasionally its magnitude may diminish at greater initial lengths.

On occasion a late persistent facilitation of monosynaptic reflex excitability has been found (Fig. 4) which then appears as a continuation of the facilitation that develops in Phase III with the fall off from peak tension in the relaxing muscle. This, too, usually disappears following Flaxedil although in one instance when the muscle was stretched to 10 mm it persisted after Flaxedil blending into the facilitation that occurred during and immediately following the tetanic conditioning stimulus.

Reversal of a Phase IV facilitation to inhibition was seen in one animal anaesthetized with Nembutal following spinalization at T12 later in the experiment. In another experiment Phase IV facilitation following a conditioning tetanus at 3.2 × threshold for extrafusal contraction reverted to inhibition when the intensity of the conditioning stimulus was raised to 10 × threshold, without any observed change in the magnitude or duration of the muscle contraction. This reversal with increased conditioning stimulus intensities was an exception for in all other instances no significant alteration in the late response was observed for conditioning stimuli greater than those required for maximal extrafusal contraction.

It would appear therefore that Phase IV inhibition in some way depends on contraction. It is independent of tension and evidently its genesis is not fundamentally caused by prior excitation of γ motor fibres because it also occurs after a motor twitch.

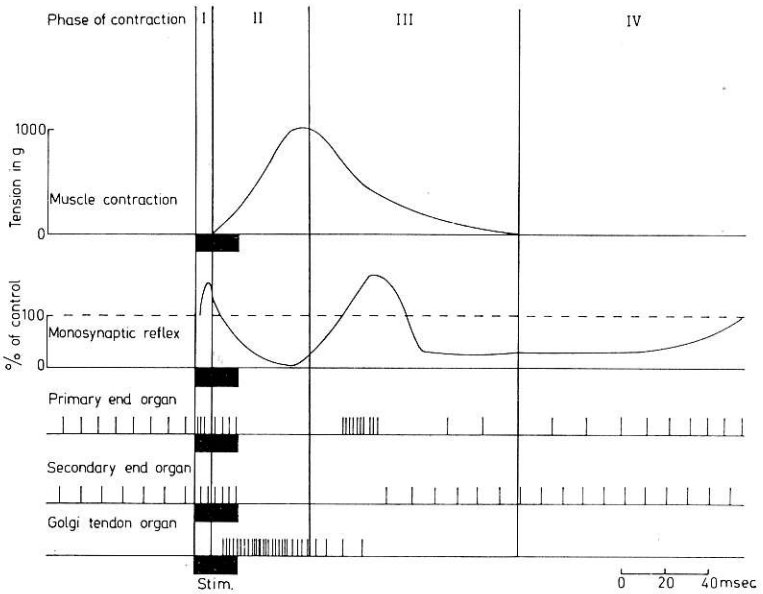

Fig. 8. Schematic representation of temporal relationship between spindle and tendon organ response, excitability of ankle extensor motoneurones, and contraction of ankle extensors initiated by tetanic stimulation of distal half of cut ventral root. The muscle is assumed extended to about 5 mm and peak contraction is about 1,000 g. The stimulus intensity is over 5 × threshold for extrafusal contraction. The phases of contraction (I—IV) are as described in text. Monosynaptic reflex is in relative magnitude of control. Receptor activity represented as discharge of single afferent units.

Discussion

Fig. 8 summarizes our results and relates the four phases described to probable events in the end organs which measure muscle length and muscle tension during tetanization of the root (generally L 7) at strengths exceeding what is required for the γ fibres. The behaviour of spindles during such circumstances is reasonably well known and so the literature before 1955 need not be specifically quoted (summarized by Granit 1955). Autogenetic excitability of the motoneurones is plotted below the curve for contraction.

Phase I. The early phase of facilitation, which represents a kind of positive feedback mechanism helping the muscle to start, was described by Granit and Suursoet (1949) and by Granit (1950). When ventral roots are stimulated there occurs a well known sensory 'backresponse' (e. g. Lloyd 1941, 1942, Leksell 1945) which Hunt and Kuffler (1951 *b*) called the 'early discharge' having analyzed it in terms of single spindle and tendon organ afferents. They ascribed it to mechanical events preceding recordable contraction. Granit et al. (1959) proved that the earliest part of it is due to ephaptic stimulation, as

Lloyd and Leksell had surmised. This effect can hardly be avoided in extensors with shocks to the ventral roots and so, in the present experiments, it must initiate Phase I facilitation. Succeeding ephaptic stimulation in extensors and, likewise in flexors were ephaptic effects are negligible, spindles fire before γ impulses have had time to influence them (Granit et al. 1959) and do so also in response to reflex stimulation (Rutledge and Haase 1961). Granit et al. (1959) failed to find satisfying correlations with tension and extension and therefore suggested that there would be α innervation of some spindles, as since shown to exist by Bessou, Emonet-Denand and Laporte (1963) in the digital muscles where sufficient isolation of individual components can be obtained. "The functional significance of fast spindle activation ... is independent of whether the α fibres concerned go to spindles alone, to extra- and intrafusal muscle, or only to nearby extrafusal fibres to which spindles are inserted so as to receive a brief twitch while the full force of the extrafusal contraction later is neutralized" (Granit et al. 1959, p. 416).

Phase II. As pointed out above, early spindle effects are neutralized during rising tension, partly by the pause of the spindles, but definitely also by inhibition sensitive to tension and hence arising in tendon organs. Thus, at this stage, brakes are applied (negative feedback).

Phase III. The transient facilitation on the falling phase of contraction which corresponds to the 'myotatic appendage' or hump of the tendon jerk (see above) has a natural explanation in the fact that a considerable number of spindle primaries deliver a high-frequency burst at the moment of drop in tension (Granit and Van Der Meulen 1962). Therefore it is — and should be — absent when contraction is removed by Flaxedil.

Phase IV. Of great interest is the late inhibition which demonstrates that the balance between primaries and secondaries is shifted in favour of the latter because tension now is negligible. After an isometric contraction those primaries which possess a transient burst in Phase III are silent for a while afterwards before they again pick up their discharge (Matthews 1933, Harvey and Matthews 1961 *a*, Bessou and Laporte 1962). A large number of the others start firing gradually. This is probably an expression of their great phasic sensitivity to small variations of length (Granit and Henatsch 1956), non-existent in the large majority of secondaries (Bianconi and Van Der Meulen 1963). After an isometric contraction the latter fire at the rate determined by the degree of extension (Bessou and Laporte 1962, see expecially their Fig. 9). In this situation (Phase IV) the inflow from the secondaries dominates over that of the primaries, as illustrated in Fig. 8, and for this effect it is of little significance whether contraction is caused by a shock or by a tetanus.

This being so, Flaxedil by removing the contraction and thus the cause of the post-contractile depression of the discharge from the primaries, must also remove the inhibition recorded in Phase IV, as demonstrated above (Figs. 6 and 7).

The idea, launched by Boyd (1962), that the nuclear chain-fibres dominated by secondaries are activated by slower γ fibres (γ_2) than the nuclear bag-fibres (γ_1) made us suspect that there would be more of the late inhibition, the stronger the stimulation of the ventral roots. This occurred only once (see above) and so we cannot say that our experiments have offered any evidence in favour of Boyd's notion. Indeed, none of the other inhibitions we have seen have ever been increased by increasing stimulus strength to the ventral root so as to bring in the smallest γ fibres. Spinalization, however, which balances the spinal cord towards the flexor reflex and increases its sensitivity to extensor inhibitions (Job 1953, R. M. Eccles and Lundberg 1959, Holmqvist and Lundberg 1959, Hufschmidt 1960, 1961), was found to emphasize concealed or weak inhibitions.

Perusal of the descriptive sections will show that in every instance after Flaxedil when γ fibres were brought in by stimulation in excess of that needed for maximal contractions, the autogenetic reflex excitability behaved as if primaries alone had been activated. If this be due to the unphysiological mode of stimulation, the more important it seems that natural dominance of the secondaries in Phase IV is a consequence of extrafusal contraction. If this explanation of our finding is correct, a consequence of autogenetic facilitation in flexor secondaries is that Phase IV must be excitatory in them. This is actually the case, as our second paper will demonstrate (Bianconi, Granit and Reis 1964) and the opposite effects in extensors and flexors in Phase IV would seem to exclude after-effects of engagement as such (see our second paper).

Thus, for the first time, a functional role of these elusive organs, the spindle secondaries, has been found with natural stimuli, because extrafusal contractions can hardly be regarded as unnatural howsoever caused. They must belong to the arsenal of behavioural patterns.

Summary

1. In cats under Nembutal the nuclei of the ankle extensors have been conditioned by a contraction elicited from the cut peripheral stump of the appropriate ventral root by rief tetani above γ threshold. The excitability of the nuclei has been studied by monosynaptic testing along the course of the contraction.

2. Flaxedil has been used to remove contraction while leaving the effect of the γ efferents on the intrafusal muscles practically intact.

3. The results are summarized and related to the contraction and the discharge of spindle primaries, secondaries and tendon organs in Fig. 8.

4. The pause of reduced excitability of the extensor centre after contraction is ascribed to the spindle secondaries.

5. The results should be compared with those obtained in similar experiments on the flexor centre in the subsequent paper.

This work has been supported by the Swedish Medical Research Council and the Rockefeller Foundation.

References

BALLIF, L., J. F. FULTON and E. G. T. LIDDELL, Observations on spinal and decerebrate knee-jerks with special reference to their inhibition by single break-shocks. *Proc. roy. Soc. B.* 1925. *98.* 589—607.

BARKER, D. and M. COPE, The innervation of individual intrafusal muscle fibres. In *Symposium on muscle receptors.* Editor D. BARKER Hong Kong Univ. Press. 1962. pp. 263—269.

BARKER, D. and J. L. GIDUMAL, The morphology of intrafusal muscle fibres in the cat. *J. Physiol.* (Lond.) 1961. *157.* 513—528.

BESSOU, P., F. EMONET-DENAND and Y. LAPORTE, Occurrence of intrafusal muscle fibres innervation by branches of slow α motor fibres in the cat. *Nature* (Lond.) 1963. *198.* 594—595.

BESSOU, P. and Y. LAPORTE, Responses from primary and secondary endings of the same neuromuscular spindle of the tenuissimus muscle of the cat. In *Symposium on muscle receptors.* Editor D. BARKER Hong Kong Univ. Press. 1962. pp. 105—119.

BIANCONI, R., R. GRANIT, and D. J. REIS, The effects of flexor muscle spindles and tendon organs on homonymous motoneurones in relation to γ-bias and curarization. *Acta physiol. scand.* 1964. *61.* 348—356.

BIANCONI, R. and J. P. VAN DER MEULEN, The response to vibration of the end organs of mammalian muscle spindles. *J. Neurophysiol.* 1963. *26.* 177—190.

BOYD, I. A., The structure and innervation of the nuclear bag muscle fibre system and the nuclear chain muscle fibre system in mammalian muscle spindles. *Phil. Trans. B.* 1962. *245.* 81—136.

BROCK, L. G., J. C. ECCLES and W. RALL, Experimental investigations on the afferent fibres in muscle nerves. *Proc roy. Soc. B.* 1951. *138.* 453—475.

BULLER, A. J. and A. C. DORNHORST, Autogenetic inhibitory impulses from human muscle. *J. Physiol.* (Lond.) 1955. *128.* 20P.

COOPER, S., The secondary endings of muscle spindles. *J. Physiol.* (Lond.) 1959. *149.* 27—28P.

COOPER, S., Muscle spindles and other muscle receptors. In *Structure and function of muscle.* Editor G. H. BOURNE Academic Press, New York and London, 1960. vol. I. pp. 381—420.

COOPER, S., The responses of the primary and secondary endings of muscle spindles with intact motor innervation during applied stretch. *Quart. J. exp. Physiol.* 1961. *46.* 389—398.

CREED, R. S., D. DENNY-BROWN, J. C. ECCLES, E. G. T. LIDDELL and C. S. SHERRINGTON, *Reflex activity of the spinal cord.* Clarendon Press. Oxford. 1932.

ECCLES, J. C., R. M. ECCLES and A. LUNDBERG, Synaptic actions on motoneurones in relation to the two components of the group I muscle afferent volley. *J. Physiol.* (Lond.) 1957*a*. *136.* 527—544.

ECCLES, J. C., R. M. ECCLES and A. LUNDBERG, The convergence of monosynaptic excitatory afferents onto many different species of alpha motoneurones. *J. Physiol.* (Lond.) 1957*b*. *137.* 22—50.

ECCLES, J. C. and C. S. SHERRINGTON, Numbers and contraction-values of individual motor-units examined in some muscles of the limb. *Proc. roy. Soc. B.* 1930. *106.* 326—357.

ECCLES, R. M. and A. LUNDBERG, Supraspinal control of interneurones mediating spinal reflexes. *J. Physiol.* (Lond.) 1959. *147.* 565—584.

GRANIT, R., Reflex self-regulation of muscle contraction and autogenetic inhibition. *J. Neurophysiol.* 1950. *13.* 351—372.

GRANIT, R., *Receptors and sensory perception.* Yale Univ. Press, New Haven 1955.

GRANIT, R. and H.-D. HENATSCH, Gamma control of dynamic properties of muscle spindles. *J. Neurophysiol.* 1956. *19.* 356—366.

GRANIT, R., S. HOMMA and P. B. C. MATTHEWS, Prolonged changes in the discharge of mammalian muscle spindles following tendon taps or muscle twitches. *Acta physiol. scand.* 1959. *46.* 185—193.

GRANIT, R., O. POMPEIANO and B. WALTMAN. The early discharge of mammalian muscle spindles at onset of contraction. *J. Physiol.* (Lond.) 1959. *147.* 399—418.

GRANIT, R. and G. STRÖM, Autogenetic modulation of excitability of single ventral horn cells. *J. Neurophysiol.* 1951. *14.* 113—132.

GRANIT, R. and V. SUURSOET, Self-regulation of the muscle contraction by facilitation and inhibition from its proprioceptors. *Nature* (Lond.) 1949. *164.* 270.

GRANIT, R. and J. P. VAN DER MEULEN, The pause during contraction in the discharge of the spindle afferents from primary end organs in cat extensor muscles. *Acta physiol. scand.* 1962. *55.* 231—244.

HAGBARTH, K. E. and K. NAESS, The autogenetic inhibition during stretch and contraction of the muscle. *Acta physiol. scand.* 1950. *21.* 41—53.

HAGBARTH, K. E. and G. WOHLFART, The number of muscle-spindles in certain muscles in cat in relation to the composition of the muscle nerves. *Acta Anat.* 1952. *15.* 85—104.

HARVEY, R. J. and P. B. C. MATTHEWS, Some effects of stimulation of the muscle nerve on

afferent endings of muscle spindles, and the classification of their responses into types A1 and A2. *J. Physiol.* (Lond.) 1961*a*. *156*. 470—497.

HARVEY, R. J. and P. B. C. MATTHEWS, The response of de-efferented muscle spindle endings in the cat's soleus to slow extension of the muscle. *J. Physiol.* (Lond.) 1961*b*. *157*. 370—392.

HENNEMAN, E., Excitability changes in monosynaptic reflex pathways of muscles subjected to stretch. *Trans. Amer. neurol. Ass.* 1951. 194—196.

HOLMQVIST, B. and A. LUNDBERG, On the organization of the supraspinal inhibitory control of interneurones of various spinal reflex arcs. *Arch. ital. Biol.* 1959. *97*. 340—356.

HOLMQVIST, B., A. LUNDBERG and O. OSCARSSON, Supraspinal inhibitory control of transmission to three ascending spinal pathways influenced by the flexion reflex afferents. *Arch. ital. Biol.* 1960. *98*. 60—80.

HUFSCHMIDT, H.-J., Wird die silent Period nach direkter Muskelreizing durch die Golgi-Sehnenorgane ausgelöst? *Pflüg. Arch. ges. Physiol.* 1960. *271*. 35—39.

HUFSCHMIDT, H.-J., Bausteine motorischer Regelung. *Schweiz. Arch. Neurol. Psychiat.* 1961. *87*. 260—280.

HUNT, C. C., The effect of stretch receptors from muscle on the discharge of motoneurones. *J. Physiol.* (Lond.) 1952. *117*. 359—379.

HUNT, C. C., Relation of function to diameter in afferent fibers of muscle nerves. *J. gen. Physiol.* 1954. *38*. 117—131.

HUNT, C. C. and S. W. KUFFLER, Further study of efferent small-nerve fibres to mammalian muscle spindles. Multiple spindle innervation and activity during contraction. *J. Physiol.* (Lond.) 1951*a*. *113*. 283—297.

HUNT, C. C. and S. W. KUFFLER, Stretch receptor discharges during muscle contraction. *J. Physiol.* (Lond.) 1951*b*. *113*. 298—315.

HUNT, C. C. and E. R. PERL, Spinal reflex mechanisms concerned with skeletal muscle. *Physiol. Rev.* 1960. *40*. 538—579.

JOB, C., Über autogene Inhibition und Reflexumkehr bei spinalisierten und decerebrierten Katzen. *Pflüg. Arch. ges. Physiol.* 1953. *256*. 406—418.

KUFFLER, S. W. and E. M. VAUGHAN WILLIAMS, Properties of the 'slow' skeletal muscle fibres of the frog. *J. Physiol.* (Lond.) 1953. *121*. 318—340.

LAPORTE, Y. and P. BESSOU, Etude de sous-groupes lent et rapide du groupe I (fibres afferentes d'origine musculaire de grand diamètre) chez le chat. *J. Physiol.* (Paris) 1957. *49*. 1025—1037.

LAPORTE, Y. and P. BESSOU, Modifications d'excitabilité de motoneurones homonymes provoquées par l'activation physiologique de fibres afférentes d'origine musculaire du Groupe II. *J. Physiol.* (Paris) 1959. *51*. 897—908.

LAPORTE, Y. and D. P. C. LLOYD, Nature and significance of the reflex connections established by large afferent fibres of muscular origin. *Amer. J. Physiol.* 1952. *169*. 609—621.

LEKSELL, L., The action potential and excitatory effects of the small ventral root fibres to skeletal muscle. *Acta physiol. scand.* 1945. *10*. Suppl. 31.

LIBET, B., B. FEINSTEIN and E. W. WRIGHT, Tendon afferents in autogenetic inhibition in man. *EEG Clin. Neurophysiol.* 1959. *11*. 129—140.

LLOYD, D. P. C., Centripetal discharges in dorsal and ventral roots following stimulation of muscle by ventral root volleys. *Proc. Soc. exp. Biol.* (N. Y.) 1941. *47*. 44—47.

LLOYD, D. P. C., Stimulation of peripheral nerve terminations by active muscle. *J. Neurophysiol.* 1942. *5*. 153—165.

LLOYD, D. P. C., Neuron patterns controlling transmission of ipsilateral hind limb reflexes in cat. *J. Neurophysiol.* 1943*a*. *6*. 293—314.

LLOYD, D. P. C., Conduction and synaptic transmission of reflex response to stretch in spinal cats. J. *Neurophysiol.* 1943*b*. *6*. 317—326.

LLOYD, D. P. C. and H.-T. CHANG, Afferent fibers in muscle nerve. *J. Neurophysiol.* 1948. *11*. 199—207.

LUNDBERG, A. and G. WINSBURY, Selective adequate activation of large afferents from muscle spindles and Golgi tendon organs. *Acta physiol. scand.* 1960. *49*. 155—164.

MCCOUCH, G. P., I. D. DEERING and W. B. STEWART, Inhibition of knee jerk from tendon spindles of crureus. *J. Neurophysiol.* 1950. *13*. 343—350.

MATTHEWS, B. H. C., Nerve endings in mammalian muscle. *J. Physiol.* (Lond.) 1933. *48*. 1—53.

PARK, A. M., R. D. TEASDALL and J. W. MAGLADERY, Certain effects of brief stretch. *Bull. Johns Hopkins Univ. School Med.* 1951. *88*. 549—561.

REXED, B. and P.-O. THERMAN, Calibre spectra of motor and sensory nerve fibres to flexor and extensor muscles. *J. Neurophysiol.* 1948. *11*. 133—140.

RUTLEDGE, L. T. and J. HAASE, Flexor muscle spindles and reflex firing of early discharging units. *J. Neurophysiol.* 1961. *24*. 182—192.

SWETT, J. E. and E. ELDRED, Comparisons in structure of stretch receptors in medial gastrocnemius and soleus muscles of the cat. *Anat. Rec.* 1960. *137*. 461—473.