PLASTIC CHANGES OF THE SIMPLEST RESPONSES OF THE MAMMALIAN CENTRAL NERVOUS SYSTEM

By

R. A. WESTERMAN

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Owing to the nature of the experimental procedures used, most of the research reported in this Thesis has been performed in collaboration with other members of this Department.

However, all operative procedures, histological work and the section on limb thrusts during walking, are entirely my own work.

The following papers have appeared or have been submitted for publication:-

Eccles, Rosamond, M and Westerman, R.A. (1959)
Enhanced Synaptic Function Due to Excess Use.
Nature Lond. 184, 460-461.

.....

Kozak, W., W.V. Macfarlane and R.A. Westerman
(Submitted for publication)
Slow Changes in the Reflex Responses of Chronic Spinal Cats to Touch, Heat and Cold.

.....

Kozak, W. and R.A. Westerman (Submitted for publication)
Plastic Changes of Spinal Monosynaptic Responses from Tenotomized Muscles in Cats.

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Roderick A. Westerman.

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Section I. GENERAL INTRODUCTION AND HISTORY OF THE PROBLEM

In his Sidney Ringer Memorial Lecture, J.Z. Young (1946) said "Probably every one of our tissues - blood vessels, muscles, bones, ligaments, skin, glands, nerves, and brain is being modified day by day through the use we make of them."

On examination, numerous examples present themselves to support his contention, ranging from the calloused skin of a labourer's hands, to the wasting of Quadriceps femoris muscles following immobilisation in bed. It is more difficult to present clear examples of such changes within the central nervous system, but this is the subject of the present investigation - how overuse and disuse affect central synapses.

An introduction to the discussion of plastic changes at the simplest levels of the central nervous system demands first an examination in general terms of both structure and function of these levels.

With the advancing knowledge of central nervous structure in the latter half of the nineteenth century, work of His (1886), Forel (1887), Kolliker (1893), van Gehuchten (1897) and Cajal (1904) demonstrated the discontinuity of afferent fibres, intercalated neurones, and motor cells. This led to the clear formulation of the neurone theory by Waldeyer (1891), and made possible this generalised concept of neurone behaviour. The opposing reticular theory, championed by Gerlach (1872) and supported by Golgi (1910) postulated that nerve cells were connected with each other by a diffusely anastomosing fibrillary network. The issue was resolved first by work of Held (1895, 1897) and Auerbach (1897) and then by the classical work of Cajal (1908, 1909, 1911) who finally established the neurone theory against all

opposition when they demonstrated the 'end feet' on the surface of the nerve cell and its dendrites. This naturally led on to a concept of the synapse, developed physiologically by Sherrington (1897), which proved to be of central importance in understanding the organization of the central nervous system.

According to our present views, each nerve cell functions as a unit, and acts in an excitatory or an inhibitory manner by means of the intimate synaptic connections which its branches make with other nerve cells. Transmission from the receptor sites (synaptic endings upon the cell) to its own synaptic endings (effector sites) is propagated by an all-or-nothing impulse. The character of this impulse has been precisely defined in peripheral fibres (Hodgkin and Huxley, 1952; Tasaki, 1953; Hodgkin, 1958), and all available evidence suggests that impulses within the central nervous system are essentially similar.

If we examine the organization of the central nervous system with particular reference to the way in which its individual units are linked together, we see that histologically neurones are organized in complex and specific patterns (Cajal, 1909, 1911; Lorente de No 1934a, 1934b, 1938). Physiologically the convergence of excitatory and inhibitory synaptic actions onto any one neurone results in algebraic summation of opposing actions - depolarization and hyperpolarization of the membrane, respectively. The firing of an impulse occurs only if the net depolarization exceeds the critical threshold level (Coombs, Curtis and Eccles, 1957a, b). With the convergence of many excitatory paths onto one neurone, it is possible to see how patterned behaviour can occur, when summation of excitatory

synaptic actions can make that neurone fire an impulse, and so in turn exert its own synaptic action on the neurones involved in the next stage of that pattern (Eccles, 1957; Coombs et al, 1957a,b; Sherrington, 1925, 1929; Lloyd, 1946). One neuronal unit in such a pattern requires approximately one millisecond to operate, so fractions of a second suffice for the creation of countless diverse and complex spatio-temporal patterns. Within this frame of reference there is sufficient explanation for the immense variety and complexity of animal behaviour. To explain the phenomena of learning and memory, Konorski (1948), among others, has invoked the concept of plasticity of central synapses - relatively enduring changes of structure and function as opposed to more transient changes. For example, post-activation potentiation has a much longer duration than synaptic facilitation (Lloyd, 1949). There are two major hypotheses, not mutually exclusive, the first of which states that learning is a is a dynamic process dependent upon the enduring circulation of patterned impulses in reverberating circuits (Hilgard and Marquis, 1940; Householder and Landahl, 1945; Rashevsky, 1938). While this mechanism may operate in the nervous system for the responses to some sensory inputs, it does not explain memory surviving deep anaesthesia, coma, or convulsive seizures, and probably only operates over relatively brief intervals after the presentation of the initial conditioning stimulus.

The alternative hypothesis, which does not exclude the first mechanism as being partly responsible for learning, suggests that patterned activation of synapses brings about some enduring morphological changes, which increase the efficacy of the synapses so activated.

(Cajal, 1911; Eccles, 1953, 1958; Hebb, 1949; Toennies, 1949; Jung, 1953). It is very likely that a specific patterned activation of central neurones follows the presentation of any given sensory input (Eccles, 1959).

If the synapses initially activated were thereby rendered more effective, subsequent re-presentation of the same stimulus would be more likely to activate the same neural pathway, with yet further reinforcement, etc. Hebb (1949) and Gerard (1949) envisage a combination of the two mechanisms in their concept of learning and memory.

The first evidence that more enduring changes of central synapses do occur, comes from the classic demonstration by Larrabee and Bronk (1947) of prolonged potentiation following repetitive stimulation in sympathetic ganglia. Subsequent work (Lloyd, 1949, 1950, 1952; Eccles and Rall, 1951; and Eccles and Krnjevic, 1959) has defined the essential features of this phenomenon. The functional significance of this enhancement of a single presynaptic volley subsequent to a burst of repetitive activity in the same presynaptic fibres should not be underestimated because of its relatively short duration (minutes). Prolonged repetitive firing of many proprioceptive afferent fibres probably occurs under natural conditions (Matthews, 1933; Granit, 1955), and the normal level of synaptic efficacy may be maintained by this continuous presynaptic bombardment. At the neuromuscular junction Liley (1956b) and Hubbard (1959) provide evidence that the presynaptic impulse has a dual effect. It produces the brief synchronous release of transmitter seen as the endplate potential, and also causes mobilization of further transmitter which is indicated by an increase in the frequency of discharge of the spontaneous miniature endplate potentials.

Indirect support for the hypothesis of similar plastic changes occurring at central synapses comes from the electron microscopic studies of De Robertis and Franchi (1956) who found that synaptic vesicles of retinal rods and cones were considerable reduced in size after prolonged total darkness. They further found that in the acoustic ganglion agglutination and lysis of synaptic vesicles occurred soon after destruction of the organ of Corti (De Robertis, 1956). In the adrenal medulla the population of synaptic vesicles in the presynaptic terminals underwent considerable changes after synaptic activation by electrical stimulation of the splanchnic nerve (De Robertis and Ferriera, 1957). This suggested a physiological role for the synaptic vesicles in transmission of the nerve impulse across synaptic junctions, and lent more meaning to the previously observed structural changes.

More direct evidence for the plastic behaviour of central synapses was provided by the investigations of the monosynaptic reflex. Motoneurones were activated monosynaptically by proprioceptive impulses in the primary afferent fibres from annulospiral endings of muscle spindles. The postulated deleterious effect of a prolonged period of disuse on synaptic efficacy was first examined in this way by Eccles and McIntyre (1953).

To secure total disuse they sectioned dorsal roots L6,7,8, extradurally, just distal to the ganglion in order to preserve the central pathway of these fibres from degenerating. Testing some weeks later they found a depression of monosynaptic reflexes relative to the control side. The depressed reflexes from previously cut dorsal roots showed a greater degree of post-tetanic potentiation than the

corresponding control reflexes, and also displayed after a tetanus some residual enhancement lasting several hours. Although there was some shrinkage of fibres histologically, the evidence of the slower time course of the post-tetanic potentiation and the prolonged residual potentiation suggested that an additional factor was operating, namely, disuse. These authors concluded that the lack of normal proprioceptive afferent activity in presynaptic fibres brought about the observed depression of monosynaptic reflexes. These findings were confirmed in analogous experiments (Eccles, Krnjevic and Miledi, 1959) in which monosynaptically induced excitatory postsynaptic potentials were recorded intracellularly from motoneurones. Disuse was effected by severing the nerve to one muscle of a synergic group, the other one or more nerves providing controls. Results for the disused paths obtained intracellularly were directly comparable with the previously described study, except that no residual potentiation was observed.

Such operative procedures in which disuse is secured by sectioning afferent fibres, have the disadvantage that some shrinkage and deficiency of dorsal root fibres occurs (Eccles and McIntyre, 1953; Eccles et al, 1959). This shrinkage may extend right to the terminals, and could at least partly account for the observed reflex depression.

From the postulate that prolonged disuse reduces synaptic efficacy, it follows that excess use is likely to lead to an enduring enhancement of synaptic function above the normal level. At present there is a little experimental evidence for this latter postulate. One example would be monosynaptic reflexes in the segment immediately adjacent to chronically inactivated segments (Eccles and McIntyre, 1953), and possibly another would be the recovery of synaptic function which

accompanies nerve regeneration some four to five weeks after the nerve has been severed (Eccles et al, 1959).

It is clear from the foregoing, that there is an obvious need for the rigorous testing of such postulated synaptic changes by simple quantitative experiments. This requires the simplest possible situations. For this reason the monosynaptic reflex has provided the test system for both major lines of investigation. In this thesis the results of three series of investigations will be presented, each directed at one aspect of the problem of plasticity in the central nervous system.

The first section deals with the question of disuse. The afferent input of monosynaptic paths in the spinal cord was altered by operatively subjecting the animals to tenotomy. After a survival period, spinal reflexes were found to be enhanced by tenotomy, but this could be prevented by transecting the spinal cord between T10 and T11 at the time of tenotomy.

The second section presents the results of an analysis of reflexes from skin nerves in chronic spinal cats, and an explanation of the exaggerated flexor reflexes shown by chronic spinal animals.

The third section covers the problem of excess use of central synapses. By an operative procedure involving nerve sections followed by exercise, spinal monosynaptic reflexes were significantly enhanced. This effect was not prevented by transecting the spinal cord at the time of initial operation.

MATERIALS AND METHODS

1. Operative Methods.

All surgical procedures other than the final acute experiments were carried out as follows:-

Anaesthesia was induced with intraperitoneal pentobarbitone sodium in a dose of 40 mg/Kg.

Full aseptic and antiseptic precautions and accepted surgical techniques were used throughout.

Careful postoperative supervision was given.

2. Experimental Methods, including Sources of Error.

Since the principal method used here to assess plastic changes in the central nervous system entails a comparison between responses of the normal side of an animal and those of the experimentally treated side, attention was paid to the elimination of extraneous variables, or at least their equalisation on the two sides. This assessment of relative change allowed the pooling of all results from a number of animals treated in the same manner at all stages.

The more important considerations are listed below:-

(1) Animals of both sexes were used, with a wide range of ages and body weights.

(2) There was a random choice of the control and experimental sides.

(3) Anaesthesia was standardized and was induced with intraperitoneal pentobarbitone sodium in a dose of 40 mg/Kg of body weight. Then the spinal cord was exposed following laminectomy. Skin wounds above the level of section were infiltrated with 1% procaine hydrochloride solution.

(4) The preparation of the peripheral nerves for stimulating or recording was performed by one operator when possible, both legs being opened and given pairs of nerves prepared consecutively. Care was taken during the preparation to obtain equal lengths of nerves, and to minimise damage to their blood supply by dissecting with blunt, fine glass hooks in preference to cutting, and using warmed Ringer-Locke solution to keep all tissues moist. Full preparation required tying cotton loops at the proximal cut end of each nerve for its subsequent attachment to stimulating electrodes.

(5) Care was exercised during the laminectomy to avoid any trauma to the spinal cord, and the dura was covered with Ringer-soaked sheets of fascia to prevent desiccation.

(6) Temperature, circulation and respiration of the animals were maintained as nearly normal as possible by the use of a heated table, light anaesthesia, and, when necessary, the continuous infusion of sterile Dextran at a rate of 3 - 5 drops per minute.

(7) The preparation of the ventral roots was the final part of the operative procedure. After their identification, the roots were severed just short of their dural penetration. Cotton loops were tied at their proximal cut ends so that they could readily be mounted on the recording electrodes. The preparation of ventral roots required the utmost gentleness in order that asymmetrical responses should not be caused by root injury on either side.

Routinely before all the monosynaptic testing described below, the spinal cord was transected between T10-L2 segmental levels depending on the requirements of the experiment, so as to eliminate possible reflex inequality caused by tonic asymmetrical

discharges of suprasegmental origin.

The animal was then placed in the frame in which fixation was achieved by clamping an upper lumbar or lower thoracic vertebral body, the iliac crests, and a mid-lumbar vertebral body through slits in the lumbodorsal muscles. The skin of the incisions in the back and both legs was raised by sewing to the frame so as to contain pools of warmed mineral oil maintained by heaters between 35 -38° C. The nerves in both leg pools and the ventral roots in the back pool were mounted on bipolar platinum electrodes for stimulation and recording. Placement of stimulating and recording electrodes on nerve and roots was identical for the two sides and interpolar distances were made equal. The experimental arrangement of a cat in the frame is shown in Figure 1. Stimuli were condenser discharges delivered through an isolation transformer, and the reflexes were monophasically recorded through AC amplifiers, displayed on a double beam Cathode Ray Oscilloscope screen, and photographed.

(8) During the experiment, testing the thresholds of nerve stimulation provided a check on the condition of the nerves. Monitoring the ingoing afferent volleys from the cord dorsum during the experiment, and recording monophasically from the dorsal roots at the conclusion of the experiment were useful guides to the state of both the peripheral nerves and the dorsal roots.

(9) In the case of monosynaptic reflex responses, equality of responses from the control muscle nerves was the best guide to the state of the spinal cord and the ventral roots of the two sides of the animal. Skin nerves as well as control muscle nerve responses

were used when recording the spinocerebellar tract responses and mass discharges in order to assess equality and condition of the spinal cord halves.

(10) Many records of each reflex were taken so that the mean values for the two sides could be compared. Testing the degree of post-tetanic potentiation of reflexes gave a sensitive measure of relatively small changes in synaptic efficiency.

(11) At the conclusion of the experiment all muscles in both hindlimbs were dissected, and wet weights determined on a Mettler K balance whose accuracy was $\pm$ 0.05 gram.

(12) Appropriate nerves were dissected and their lengths measured for the calculation of conduction velocities.

(13) Histological examinations were carried out when necessary.

NOTE: For the sake of convenience and brevity, throughout the text that hindlimb which had been subjected operatively to experimental manipulation will be henceforth termed the operated side. The hindlimb subjected only to a dummy operation is termed the normal side.

3. Statistical Treatment of Results.

Standard statistical methods were used to assess the significance of differences in reflex amplitudes, latencies, muscle weights, etc. This involved the calculation of the arithmetical mean, standard deviation, and standard error of the mean. The student t-test (paired method) was applied to gauge the significance of differences between two means. Whenever a difference in means is termed significant in the text, the value of t has been 2.5 or more, thus using 1% confidence limits.

4. Histological Techniques.

(a) Nerves, dorsal and ventral roots from the animals in the Nerve Section - Excess Use series were impregnated with 1% osmic acid and embedded in paraffin. Sections were cut at 6 - 10μ and micro-photographed, then fibre diameters were measured on a photographic enlargement. Histograms of fibre spectra were prepared.

(b) Specimens taken at the level of cord transection from the chronic spinal animals were fixed in 10% neutral formol-saline and embedded in paraffin. Longitudinal sections were cut at 5 - 7μ thickness and stained by the Palmgren method of silver impregnation, then microscopically examined for evidence of regeneration.

5. Calculation of Results.

(a) Conventions used in measuring latencies. See Figure 2.

(b) Use of spike height as a measure of reflex size.

The monosynaptic reflex response (see Figure 2) to stimulation of a muscle nerve recorded as a monophasic spike from an appropriate cut ventral root is the integral of the responses of individual active cells in the motoneurone pool. The spike area is thus a function of the number of active cells in the pool, and the total duration of the spike response is a measure of the degree of asynchronism of motoneurone activity.

By printing on photographic paper, cutting out and weighing the areas under the spikes, the areas of a graded series of monophasically recorded spike responses could be determined, and were poltted against spike height. (see Figure 3.)

The observed linear relationship shows that the spike height is directly proportional to the area under the spike and therefore to

the number of motoneurones in a pool which are activated by the test volley.

(c) Reasons for comparing ratios of corresponding reflexes from the two sides of each animal. These are twofold.

(1) The first reason is purely a statistical one. Consider a series of similar experiments in a number of animals. The size of monosynaptic reflexes recorded from ventral roots in response to single volleys in peripheral nerves supplying the corresponding muscle in each cat, will depend upon a number of factors: the size of the group Ia afferent volley from that muscle; the excitability of the motoneurones supplying the muscle pool; the depth of anaesthesia; the physiological state of the ventral root; etc. If all the reflex responses thus obtained are expressed in terms of absolute potential recorded (i.e. in mV), there is a very wide variation. Analysis of results from a large number of animals would be required before differences between all responses of the two sides become significant. However, more uniform results from different animals are obtained if one calculates the corresponding reflexes recorded from the two sides in a given animal as the ratio (size of reflex from the operated side) / (size of corresponding reflex from the normal side.) The scatter of results is reduced and hence significant results are obtained with fewer experiments.

(2) The second reason relates to the distribution of segmental supply of any particular muscle.

Most of the muscles whose nerves are tested, receive their innervation from at least two spinal segments. Smaller

reflex responses are often recorded (see Figure 4) from ventral roots of larger diameter (e.g. L7 VR is larger than S1 VR).

A comparison of reflexes between animals on the basis of the spike size in mV introduces statistical variations due to the heavy weighting by larger reflexes representing smaller roots. Greater variations arise if there is asymmetry of reflexes in corresponding roots induced by the experimental procedures. The ratio of reflex spikes in corresponding roots statistically assigns equal weight to reflexes occurring in different roots, and thus partly compensates for the described variations.

SECTION II

A. TENOTOMY SERIES - DISUSE.

Introduction: The test systems used in this series of experiments have been monosynaptic pathways.

(a) In the monosynaptic reflex arc described histologically by Cajal (1909) and experimentally established by Lloyd (1943a,b), motoneurones are monosynaptically activated by impulses in the large afferent fibres from the annulospiral endings of muscle spindles (see Figure 5). In testing this system with electrical stimulation, volleys applied to cut muscle nerves are supramaximal for group Ia fibres. The monosynaptic reflex responses of motoneurones innervating those muscles may be recorded monophasically from the cut ventral roots, and are a measure of the excitability of the motoneurone pool thus activated.

(b) The spinocerebellar tracts, both dorsal (uncrossed) and ventral (crossed), have cells of origin in nuclei shown diagrammatically in Figure 6. Clarke's column cells are known to occupy the dorsomedial aspect of the dorsal horn over segments L4 upwards, (Rexed, 1954) and send their axons rostrally as the uncrossed dorsal spinocerebellar tract (D.S.C.T) ascending in the dorsal part of the ipsilateral lateral column. The nucleus of the ventral spinocerebellar tract (V.S.C.T) has been recently located (Hubbard and Oscarsson, in print) in the dorsolateral part of the ventral horn over segments L4 - 5. Axons from these cells ascend as the V.S.C.T. in the crossed lateral column.

The afferent connections of V.S.C.T are entirely group Ib fibres, but the D.S.C.T while receiving largely Ia connections,

also received some Ib afferents. The Dorsal and Ventral Spinocerebellar tract neurones are thus activated monosynaptically by volleys of suitable strength in peripheral muscle nerves. The tract responses may be recorded as mass discharges from the spinal cord, hemisected after the removal of dorsal funiculi. This method of preparation is fully described by Rudin and Eisenman (1951, 1954) and Laporte, Lundberg and Oscarsson (1956).

In order to test the postulated adverse effects of disuse on synaptic function, unilateral tenotomy was chosen as the method of reducing afferent activity from stretch receptors, and was applied in several different procedures to be described. It was assumed that tenotomy would prevent the development of active tension, and would also reduce the tension passively produced by limb movements. It was further assumed that tenotomized muscles thus contracting under isotonic rather than isometric conditions would provide a much smaller prioceptive afferent input to their central synaptic connections than the corresponding intact muscles in the other hindlimb. In series (1) of this section, the plaster of Paris immobilization was provided in order to reduce further the effects of passive stretching of tenotomized muscles, but, as will be shown, it proved to be unnecessary. Unilateral tenotomy would therefore be expected to produce a situation in which the central synaptic connections of stretch-afferent fibres from tenotomized muscles were subjected to relative disuse during the survival period between tenotomy and the final testing of reflex activity. This testing was accomplished by comparing the reflex responses from nerves to tenotomized muscles

with those from corresponding intact muscles in the control hindlimb.

Methods: In Section A, several experimental techniques were employed, each consisting of an initial aseptic operation followed by a survival period of between 1 - 5 weeks before final testing using the monosynaptic systems described above. The various operative procedures may be listed as follows, and will be discussed below:

(1) Unilateral tenotomy of ankle and toe extensor muscles together with plaster of Paris immobilization of the tenotomized hindlimb;

(2) Unilateral tenotomy of ankle and toe extensor muscles;

(3) Unilateral tenotomy of ankle and toe extensors with transection of the spinal cord at the T10-11 level.

(1) Unilateral tenotomy and plaster immobilization.

Methods: At initial aseptic operations, the 20 animals in this group were subjected to unilateral tenotomy by excising about 1 cm from the tendo Achilles (medial and lateral gastrocnemius, plantaris and soleus muscles) and the flexor digitorum longus and flexor hallucis longus tendons. Dummy operations were performed on the contralateral hindlimbs, which provided controls. Further controls were provided by muscle groups such as hamstring and peroneal muscles which were intact in both hindlimbs. Plaster of Paris immobilization of toes, ankle, and knee in a position of moderate flexion were carried out on the tenotomized hindlimb immediately after operation. After periods of survival ranging from 3 - 4 weeks, the final acute experiments were performed according

to the methods described previously (pp. 8 - 11).

Results: (a) All muscle groups as depicted in Figure 7 showed wasting in the hindlimb subjected to tenotomy and plaster immobilization. This was most marked for the two tenotomized groups ankle and toe extensors, and for the knee extensors. Their mean percentages of wasting were 43.8%, 24.2% and 19.1% respectively, which were all significant (see Table 1). There was less wasting of other groups, but it was also significant, $P < 0.01$.

(b) Actual records of monosynaptic reflexes recorded monophasically from out ventral roots in one typical experiment, as shown in Figure 8. There is approximate symmetry between the levels of reflex responses evoked by maximal group 1a volleys in the control nerves (Hamstring and Peroneal). (Figure 8; B1, P1). By contrast the reflexes evoked from nerves to tenotomized muscles are significantly greater than the responses from corresponding nerves on the normal side (Figure 8; G1, F1). The maximum post-tetanic responses after the standard conditioning tetanus of 400 impulses per second had been applied for 10 seconds still showed symmetry between the control nerves of both hindlimbs (Figure 8; B2,P2). Under such conditions the increase of responses from tenotomized groups was much less obvious (Figure 8; G2,F2). The means of monosynaptic reflex responses from all animals in this series are summarised in Table 2, and are displayed on a histogram in Figure 9.

The summary in Table 2 shows that the mean pretetanic

levels of responses from nerves to tenotomized muscles are significantly increased relative to the control hindlimb. This reflex enhancement is much smaller when post-tetanic reflexes from corresponding nerves are compared. Mean reflexes from control muscle nerves showed no significant deviation from symmetry both before and after tetanic conditioning.

(c) Central latencies for this series of experiments are summarised in Table 3(a). There is a mean shortening of central latency by 0.13 msec. in the tenotomized group, and this was statistically significant.

Conduction velocities shown in Table 3(b) however showed no significant differences between tenotomized and control groups.

Discussion: In retrospect, it becomes clear that by combining in this series unilateral tenotomy and plaster immobilization there are two experimental variables. Since the results obtained by unilateral tenotomy alone are so closely similar (see Sub-Section (2)), the results from the two groups will be discussed together on pages 30 - 33.

(2) Unilateral tenotomy alone.

Methods: The 21 animals in this series were initially subjected to aseptic operations. The procedure used was identical to that just described in Section A (1), except that tenotomized hindlimbs were not immobilized in plaster of Paris.

After periods of survival between one and five weeks, reflexes were tested at final acute experiments by the methods detailed on pp. 8 - 11 of this thesis.

Results:

(a) As with tenotomy and plaster immobilization, all muscle groups in the tenotomized hindlimb showed wasting, which is detailed in Table 4, and summarised in Figure 10. Wasting was significant for the two groups of tenotomized muscles, viz. ankle extensors 24.9%, toe extensors 18.0%, and will be discussed later.

(b) Records of monosynaptic reflexes, recorded in ventral roots from one typical experiment, are shown in Figure 11. The results are closely similar in essential features to those described for the previous series with tenotomy and plaster immobilization. Pretetanic and maximum post-tetanic reflex levels for control nerves (Hamstring and Peroneal Nn.) of both hindlimbs, are symmetrical. There is a significant increase of pretetanic reflexes from nerves to tenotomized muscles. This reflex enhancement is much reduced if the maximum post-tetanic levels of reflexes are compared.

The results from all 23 animals in this series are summarised as a histogram in Figure 12, and are detailed in Table 5 (a). There is symmetry of control reflexes, within the limits of experimental variability and it is statistically significant. The average increase of reflexes from nerves to tenotomized muscles varies from group to group, but the pattern remains quite constant. There is a significant 60 - 110% enhancement of monosynaptic reflexes elicited by maximal group Ia volleys in nerves to tenotomized muscles, when compared with their corresponding paired controls.

The maximum post-tetanic levels of response from the nerves to tenotomized muscles showed an increase relative to the paired control muscles, but this enhancement was much reduced (25 - 69%) and was not significant within the 1% confidence limits employed.

This post-tetanic trend toward reflex symmetry is possibly attributed to the existence of a smaller subliminal fringe with the motoneurones of the tenotomized muscles, which would arise on account of their more powerful excitatory activation by the group Ia afferent volleys.

The effect of varying the frequency of the testing volley (Lloyd, 1957) was investigated, and the pooled results from five animals are presented in Figure 13. As can be seen, both sets of points lie close to the same curves. There was a decrease in the size of reflexes evoked by maximal testing volleys as the frequency of testing increased and there was no significant difference between nerves to tenotomized and normal muscles in respect of this effect.

The time course of post-tetanic potentiation was studied in all cats for reflex paths from the normal and tenotomized muscles. Figure 14 shows actual records of pre and post-tetanic reflexes for nerves to both control and tenotomized muscles, and demonstrated the absence of significant differences in the time course of post-tetanic potentiation for the two groups. The observed time courses of post-tetanic potentiation are comparable with those obtained by other investigators using similar parameters of stimulation: Lloyd, (1949); Eccles and McIntyre (1953).

Figure 15 contains the pooled results from four cats, for each nerve tested, and shows clearly the absence of significant differences in time course of potentiation over the short interval plotted. Recovery from the later phase of P.T.P was followed for up to 15 minutes in three cats and showed no significant differences between the tenotomized and control sides.

(c) Central Latencies were calculated for nerves to both tenotomized and normal muscles, and these results are summarised in Table 6 (a). There was a significant shortening, by 0.11 msec. of the central delay for pathways from the tenotomized muscles.

Conduction Velocities were also calculated, and the summarised results in Table 6 (b) indicate that there was no significant difference of conduction velocity between the normal and tenotomized groups.

The absolute and relative refractory periods of afferent paths from both normal and tenotomized muscles were determined in a number of animals and the means showed no significant differences for the two groups.

(d) Results from testing the reflex responses of the other monosynaptic system, namely the spinocerebellar tracts, are shown in detail in Table 5 (b) and summarised in Figure 17.

Typical records are shown in Figure 16. Symmetrical responses from both dorsal and ventral spinocerebellar tracts were evoked by stimulating the control nerves to hamstring and peroneal muscles. Good symmetry in respect of ipsilateral tract responses were obtained for the cutaneous nerve, sural, and for the mixed nerve, deep tibial. Nerves to tenotomized muscles did

not show significant differences in the size of their V.S.C.T potentials, but a significant 45 - 55% enhancement of their D.S.C.T responses, evoked by maximal group Ia volleys, was found.

Although of smaller size, this increase was in good agreement with the enhancement of monosynaptic reflex responses of nerves to tenotomized muscles as recorded in the ventral roots. It was surprising, however, that the cells of Clarke's column nucleus, which have a powerful synaptic linkage with primary afferent fibres (Szentagothai and Albert, 1955) and therefore display only a small subliminal fringe by conventional facilitation tests (Lloyd and McIntyre, 1950; McIntyre, 1951), should give give such a relatively large increase. On the other hand, potentiation of the D.S.C.T response of between 20 - 50% has been demonstrated following tetanic conditioning (Oscarsson, 1957). The results described thus indicate a more powerful enhancement of synaptic efficacy following tenotomy than would appear at first sight.

(e) The symmetry of the afferent input provided by the maximal group Ia volleys was tested at the conclusion of the experiments by monophasically recording volleys from the dorsal roots severed close to the spinal cord. Typical records obtained by this procedure are displayed in Figure 18, and show the good symmetry which was usually obtained. In the few cases where some asymmetry existed, it was tempting to apply a correction factor on the basis of relative volley size, to the reflex levels obtained. This course was rejected because there should be a random incidence

of such inequality from nerves to either tenotomized or normal sides. The pooled reflex results presented in the tables therefore contain no corrections.

The afferent connections of D.S.C.T are largely group 1a rather than 1b (Laporte et al, 1956) while those of V.S.C.T are exclusively from group 1b afferent fibres (Oscarsson, 1957). Since there is enhancement of D.S.C.T reflex responses but not of V.S.C.T reflexes, the results suggest that probably the group 1a primary afferents are responsible for the enhancement of both the ventral root and D.S.C.T monosynaptic responses.

(f) This unexpected result that tenotomy results in enhancement of monosynaptic responses raised a number of considerations which pointed to the need for some direct experimental analysis of proprioceptor function in tenotomized muscles. First, it is merely an assumption that tenotomy results in reduced afferent discharges from affected muscles. Further, although no functional regeneration of tendons per se was found after the intervals used, one noticed frequently during final experiments that the central ends of the severed tendons had become firmly adherent to the overlying skin and subjacent deep fascia. This occurred in one case as early as one week postoperatively, and while not constituting effective regeneration, yet might enable the muscle to develop sufficient tension to provide stress on the muscle receptors, instead of contracting isotonically as would be the case immediately after tenotomy. However, the progressive nature of the wasting of tenotomized muscles makes it less likely that any effective tension is developed during the survival periods up to 3 - 4 weeks.

Finally, past evidence that prolonged disuse has adverse affects on synaptic function (Eccles and McIntyre, 1953; Eccles et al, 1959) casts doubt on the initial assumption that tenotomy results in a diminished discharge from stretch receptor afferents (Cf. Beranek and Hnik, 1959).

A preliminary attempt was made to analyse the afferent activity from chronically tenotomized muscles, using a method described by Matthews (1933). In this procedure, recording was carried out directly from the distal segment of muscle nerves, cut 2 cm from their entry into the muscles. Afferent spike discharges of up to 50μV could be recorded in this way. In order to make valid comparisons of the activity of corresponding normal and tenotomized muscles, the temperatures of the pools were kept equal and minimum disturbance of muscle blood supply was ensured by leaving the skin over the calf muscles intact. The hindlegs were fixed symmetrically on the frame and interpolar distances between recording electrodes were equalised, as was the position of electrodes on the nerve relative to the muscle.

Figure 19 illustrates with typical records, the results obtained from testing, in this manner, 50 nerves in ten animals. Since the frequency of the afferent discharge could not be affected by variations in application of recording electrodes, it was considered important to compare frequency rather than amplitude of discharge for normal and tenotomized muscles.

A summary of all results is given in Table 16 (a). This shows that there was an average increase of 22% in the afferent discharge frequency recorded from tenotomized muscles by comparison with corresponding normal muscles.

By a simple frame and pulley system, a 1.0 Kg. pull could be halved and applied simultaneously to the tendons of corresponding muscles in both hindlimbs. The frequency of discharge with 500 g stretch was still significantly 11.7% higher from tenotomized muscles than from paired normal muscles.

Although the results obtained by this method of recording are open to certain objections, the figures appear to be significant. A possible explanation might be found in the muscle wasting which results from tenotomy. It has been demonstrated that primary afferent receptors in muscle are extremely sensitive to changes in length of the order of microns, particularly if the muscle tension is low (Lundberg and Winsbury, 1960). It is not unreasonable to suppose that spindles in a wasted muscle may be more susceptible to the effects of passive squeezing and deformation during movements of the tenotomized hindlimb. This could result in an increased group Ia discharge from tenotomized muscles, and provides a possible explanation of the observed phenomena.

The relative amount of wasting of different muscles varies with the duration of the postoperative survival interval. Figure 20 summarises these results obtained for control and tenotomized muscle groups in fifteen cats. The control muscles waste initially with almost the same rapidity as tenotomized muscles, but from the tenth postoperative day show a reversal and gain weight until they return to their original weight by about five weeks. Wasting of tenotomized muscles continued after the tenth day and had not ceased by five weeks. The average wasting

of quadriceps femoris, typefying the control muscle groups, is shown plotted against postoperative days in Figure 21. In the tenotomized hindlimbs there was more wasting of this knee extensor group than other intact muscles. This is quite analogous to the quadriceps wasting which results from immobilization of sick persons in bed. This wasting of quadriceps began to regress after the sixteenth day, and recovery of original weight was achieved after five weeks. By contrast, Figures 22 and 23 provide results for the two groups of tenotomized muscles, triceps surae, ankle extensors, and the flexor digitorum longus group of toe plantar flexors, respectively. These show a progressive wasting even up to five weeks, there being a roughly linear weight loss with identical slopes for the two muscle groups. There is evidence given by Helander (1957, 1958) that wasting of muscles due to different causes (e.g. denervation, tenotomy, and immobilization) involves in each case the loss of different types of muscle protein constituting muscle fibres. It is interesting to speculate whether the intrafusal muscle fibres are involved in the loss of substance, and if so, what effect this has on the afferent function of spindles. Further investigation of proprioceptor activity in tenotomized muscles is desirable.

Meanwhile the available evidence leads to the conclusion that tenotomy of muscle results in increase of the monosynaptic reflexes evoked by group Ia volleys. The results of part (3) will be presented before the final discussion.

(3) Unilateral tenotomy, with spinal transection.

Methods: In this series of eight cats the procedure of initial

unilateral tenotomy conformed to that already described, but in addition the spinal cord was exposed and transected at T 10-11 level, immediately prior to the tenotomy. The animals were kept for postoperative intervals of 2 - 5 weeks, after which reflexes were tested in the manner already described.

Results: (a) As shown by Figure 24 and Table 7, there was muscle wasting of all hindlimb muscle groups in this series, but it was smaller in amount than that seen in animals of series (1) and (2). The degree of wasting was significant for several muscle groups, viz. ankle extensors and flexors, and both extensors and flexors of toes. It is interesting that significant additional wasting still results from tenotomy after spinal cord transection, because the latter is known to induce considerable wasting if applied without tenotomy (Hnik, 1960).

(b) The monosynaptic reflex responses were recorded from ventral roots as described, and Figure 25 comprises typical records from one experiment. There was the usual symmetry of control reflexes from the two sides. In contrast to previous results, nerves from tenotomized muscles now yielded reflex responses which did not differ significantly in size from their control counterparts.

The same reflex symmetry was seen between maximum post-tetanic levels of response from paired nerves to corresponding control and tenotomized muscles. A summary of results for all animals in this series appearing in Table 8 (a) and Figure 26 provides the same clear results. In these animals with both tenotomy and spinal cord section, there was no increase of ventral root monosynaptic reflexes.

(c) The behaviour of spinocerebellar tract responses under these conditions is in good agreement with the previously stated result. This may be seen from the sample records in Figure 27 where there are no significant differences between dorsal or ventral spinocerebellar tract responses from nerves to tenotomized muscles compared with normal controls. The summary Table 8 (b) shows average tract responses for all animals in the series, and agrees in all respects with results just described. It is apparent that T 10-11 spinal cord transection prevents any increase of monosynaptic reflexes from nerves to tenotomized muscles.

(d) Further, it is seen from Table 9 that central latencies do not differ significantly between nerves to normal and tenotomized muscles.

(e) The results of the analysis of afferent spike discharge from five cats in the series are presented in Table 16 (b). Symmetry between corresponding normal and tenotomized muscles, may be seen in the records of Figure 28. The mean discharge frequency from tenotomized muscles was 3% smaller than that from normal muscles, but this difference was not statistically significant.

One can summarise these results by stating that spinal cord section at T10 level, performed at the time of unilateral tenotomy prevents the occurrence of all changes induced by tenotomy alone.

Section A - Discussion.

In this section the results of three tenotomy procedures have been presented.

There are some reports of reflex effects in the nervous system caused by immobilization of limbs (Nasledov, 1957; Spiegel, 1927; Thomsen et al, (1942 1946). However, in these reports, limbs were fixed in extreme flexion or extension, and none deals with the effects of immobilizing a limb in the position of rest, as was carried out in this study. Further, the reflex changes were assessed by observing behaviour and reactions to tactile stimuli, and noting the postural effects of cortical ablations. It is doubtful whether the plastering procedure used with tenotomy in Section (1) could have contributed to the reflex changes observed. For purposes of discussion, the most relevant results are those obtained in Section (2) with unilateral tenotomy alone, and one feels justified in treating the plaster group with this series.

The observed effects of unilateral tenotomy, or tenotomy with plaster immobilization, are to enhance spinal monosynaptic excitations of two types. There are no detectable changes of the afferent path, in particular conduction velocity, refractory period, or time course of post-tetanic potentiation; hence this increase of reflex responses from nerves to tenotomized muscles indicates an enhancement of the synaptic excitatory action. As a consequence more motoneurones would be activated by single maximal volleys to peripheral nerves, and there would be greater synchrony of their discharge. A further consequence would be the observed shortening of central latency and the

reduction of the relative enhancement after tetanic conditioning. It is of interest that Beranek and Hnik (1959) independently provide results for the monosynaptic reflexes recorded in ventral roots, differing only quantitatively from those described. Differences in technique could account for the greater enhancement which they observed in reflex responses from tenotomized muscles.

In the absence of any knowledge of the afferent behaviour of chronically tenotomized muscle, it is difficult to explain the observed enhancement on grounds of hypersensitivity resulting from disuse of central synaptic connections. We cannot assume that the muscle receptors are silenced by tenotomy, because there is good evidence that even isolated muscle spindles of frog striated muscle discharge spontaneously (Buchthal and Jahn, 1957), and certainly the mechanical deformation of tenotomized muscles during walking would be enough to cause group 1a discharges on the basis of findings by Lundberg and Winsbury (1960a). However, the group 1b impulses from Golgi tendon organs have a much higher threshold, and do not respond as well to phasic stretch (Hunt and Kuffler, 1951a,b; Lundberg and Winsbury, 1960b) and so should be greatly reduced or silenced by tenotomy.

With evidence that there is little or no convergence of 1a and 1b excitatory activation onto the same D.S.C.T neurones (Lundberg and Winsbury, 1960b) the observed 40% enhancement of D.S.C.T response could be due to a relatively larger enhancement of D.S.C.T neurones activated only by group 1a afferents over those activated by 1b afferents. In the latter case, there should be a parallel enhancement of responses from V.S.C.T neurones which are entirely 1b activated, but this is not observed. There is

thus some evidence to suggest that this effect of tenotomy on the monosynaptic systems described, is brought about through their group Ia connections.

Before further postulates were made, it was necessary to have some indication of the afferent activity from chronically tenotomized muscles. Accordingly, the preliminary analysis was performed in the simple manner described, and the results suggested that chronically tenotomized muscles give increased afferent discharges. This requires confirmation using the more precise methods of single fibre recording (Hunt, 1951, 1954; Kuffler, Hunt and Quilliam, 1951).

This result provides one attractive explanation of the observed effects of tenotomy: that increased discharges of group Ia impulses from chronically tenotomized muscles, with consequent increased use of their central synapses, leads to an enduring enhancement of synaptic efficacy.

There are strong arguments against the alternative hypothesis that the observed reflex enhancements result from some form of disuse hypersensitivity.

Firstly, there is no evidence that reduction of afferent activity from tenotomized muscles resulting in disuse of their central synaptic connexions does occur: the present results suggests the reverse. Secondly, it has been shown that spinal cord section (at T10-11 level) at the time of unilateral tenotomy prevents the occurrence of all reflex changes induced by tenotomy alone, and prevents the increase of afferent activity from tenotomized muscles. Since the interruption of descending pathways by cord

transection can only increase the number of "disused" synapses on motoneurones, the effect of cord section in preventing these changes induced by tenotomy, cannot be explained in this way.

There are a number of supraspinal sources of control of the gamma motoneurones (Granit, 1957). Spinal cord section just prior to tenotomy would remove these sources of gamma activation. Tenotomy, with release of muscle tension, would lead to deloading of spindles, but normally gamma motoneurones might be reflexly activated as a consequence of tenotomy and thus cause contraction of intrafusal fibres, and consequent increased spindle discharge.

If the development of the increased discharge from tenotomized muscles depended upon this action of the gamma-loop mechanism, the removal of supraspinal sources of gamma activation could reduce gamma efferent activity sufficiently to prevent this increased spindle discharge; hence the observed absence of reflex enhancement under such conditions.

Lack of evidence precludes further speculation and leads one to a simple and more general conclusion. Tenotomy of muscles results in an increase of the monosynaptic responses evoked by group Ia afferent volleys. There is some evidence that this effect is brought about by increased discharges of group Ia impulses from chronically tenotomized muscles, i.e. that it is due to an enhancing effect which accompanies increased use of their central synapses. The effects are prevented by spinal cord section (T10 - 11) immediately prior to tenotomy.

SECTION B. CHRONIC SPINAL CATS - CUTANEOUS REFLEXES.

(1.) It has been known since Sherrington's experiments (1899, 1910) that animals whose spinal cords are transected, sometimes demonstrate exaggerated flexion responses. It seemed that this preparation could provide an opportunity to confirm the presence of such overactive flexor tone and study its effects upon spinal polysynaptic reflex pathways. In this section a comparison has been made between the reflex activity of chronic spinal cats, and normal cats which were rendered spinal at varying intervals prior to testing. As a preliminary to the electrophysiological analysis which follows, careful observations were made of the evolution of spinal reflexes following spinal transection, and of the patterns of reflex behaviour exhibited by chronic spinal animals whose spinal cords had been severed at least six months before.

The animals used in this study fell into two groups, (a) Chronic spinal kittens which, after spinal cord transection during the first week of life, were reared until 6 - 9 months old. (b) Normal kittens of the same age whose spinal cords were cut at the age of 6 - 9 months.

For both the week-old kittens and older animals, the same procedure was followed at initial aseptic operation. Ether anaesthesia was used, and a laminectomy was performed at the chosen level, over only 1 - 2 segments, which gave sufficient exposure for section of the spinal cord.

The spinal cord was transected with scissors after opening the dura mater. Upon complete division of the spinal cord and dura, there was retraction of up to 5 mm of the severed ends

of the spinal cord, rendering any excision of spinal cord unnecessary. (The spinal cords from all cats were ultimately examined histologically, and no evidence of regeneration was found).

The spinal sections were performed at one of two levels - high thoracic T2 - 3 level, or low thoracic, T12 - L2. Unless otherwise states, all results in this section have been obtained on animals with low thoracic transection.

The postoperative management of these spinal animals was tedious rather than difficult. Catheterization was sometimes necessary in the first 3 - 4 days, but after that, urine could be manually expressed. Occasionally enemas were necessary during the first 1 - 2 weeks. The animals were kept in cages whose floors consisted of 2" deep trays, filled with sawdust. By careful cleaning, pressure sores and perineal ulcers were largely avoided. The young kittens were left with the mothers and consequently required less attention during the first 3 - 4 months up to weaning. Animals were fed daily with minced meat and milk ad libitum.

By four months or more after thoracic spinal section, the isolated distal segment of these cats is highly excitable (Sherrington, 1906a; Clark, 1940) and a variety of reflex responses may be elicited with ease.

These have been classified as follows:

(A) Exteroceptive Reflexes
1. Protective Reflexes.
2. Cleaning Reflexes.
3. Sexual Reflexes.

(B) Interoceptive Reflexes. 4. Excretory Reflexes.

5. Vasomotor Reflexes.

(C) Proprioceptive Reflexes. 6. Postural Reflexes.

(These are also exeroceptive in part)

It would be appropriate at this point to deal with these in turn, in further detail, but the reflex behaviour of spinal animals has been extensively described by numerous authors including Clark (1940), Macht and Kuhn (1948), Sahs and Fulton (1940), and in the most extensive manner by Sherrington (1900, 1906a, 1906b, 1910). Only mention will be made of the reflex responses which are fully developed in the chronic spinal amimal, with special attention to three types of reflexes not well described in previous studies. These are thermokinetic (flexion) responses to heat and cold, toe-fanning, and an abnormal contralateral type of scratch response.

(A) Protective Reflexes.

The observations here in no way differed from previously well-established observations that the responses of spinal animals generally to noxious stimuli are in effect withdrawals (Sherrington, 1910). The actual movements executed depend on the area to which the noxious stimuli are applied (Sherrington, 1910; Hagbarth, 1952) and also depend upon the position of the stimulated area and limbs in relation to the rest of the animal (Sherrington, 1910). Overactive tonic flexion was never seen in these animals, and the level of all flexion responses was never more than that found in the normal animals (c.f. electrophysiological findings).

The following withdrawal responses have been demonstrated in the hindlimbs of all chronic thoracic spinal cats, and have been previously described.

Ipsilateral flexion responses, with and without crossed extension (Sherrington, 1910; Lloyd, 1943b) and ipsilateral extension (Hagbarth, 1952, 1960). Bilateral extension in response to pinching the skin of the belly in the midline, and direct withdrawal movements of the tail have also been seen.

Thermokinetic Reflexes. These are reflex responses of the hindlimb to heat and cold stimuli, which are worth reporting in detail as only one author has previously described these (Macht and Kuhn, 1948; Macht, 1943) and the present observations are at some variance with these reports.

There are quite characteristic responses of chronic high thoracic spinal cats to thermal stimuli provided by immersion of the hind toes in water at a certain temperature above or below the skin temperature of the immersed limb. Immersion of hind toes in iced water at 1°C evoked an immediate kicking or jerking with ipsilateral hindlimb withdrawal and accompanied by very strong flexion at hip, knee and ankle. Then followed a vigorous shaking of the limb by rapid alternating flexions and extensions. There were contralateral extensor thrusts and tail circling. The toe movements alternated between a persistent wide toe-fanning with dorsiflexion, or a marked plantar flexion response. The latency of withdrawal was almost always less than 1 second. The responses to hind foot immersion in water at 50°C were equally characteristic, and quite similar to the withdrawal responses to cold. The differences seen were firstly, a relatively longer latency of up to 10

seconds. This was followed by the same violent kicking movements and withdrawal in the most extreme flexion. In this withdrawal, all joints of the immersed hindlimb were flexed to their mechanical limit. Toe-fanning was never seen. Macht and Kuhn found these responses in chronic decerebrate, bulbospinal and high thoracic spinal cats, being most pronounced in the spinal preparation. These responses could be repeatedly elicited in every one of the seven chronic animals tested in this manner. It was apparent that there were thresholds for these thermokinetic responses to cold and heat, above or below which, respectively, no withdrawal could be evoked.

The threshold of the response to cold averaged 28.5°C based upon repeated testing of both hindlimbs of seven spinal animals. This varied only slightly from individual to individual. The threshold for cold was related to the skin temperature of the immersed limb. The response was dependent upon a gradient between the temperature of water and skin temperature. Macht and Kuhn suggested with little evidence that the receptors involved were probably Krause's end bulbs. In the case of water at temperatures above body temperature, the threshold for withdrawal was found to average 48.5°C and was relatively constant being independent of body temperature.

That this response was not dependent upon tactile stimuli was demonstrated in two ways:

(i) By application of $\frac{3}{8}$" diameter metal rods as thermodes, to various points over the hindparts of these high thoracic spinal cats below the level of section. The temperatures of the rods applied were 1°C, 55°C or 37°C, the latter being close to the skin

temperature found in hindlimbs of all seven cats.

Without exception, the application of thermodes at 37°C failed to evoke any response whatsoever. Withdrawal reflexes to cold (1°C) could be elicited from the skin of hindpaws and toe pads, and the perianal skin for about 2 cms around the anus. Such withdrawal consisted of the ipsilateral flexion as described.

Withdrawal responses to heat were more generalised, and could be elicited from almost any skin areas below the level of section with no particularly sensitive zones. Without exception, application of thermodes at 37°C failed to evoke any response whatsoever. This observation together with the presence of clear temperature thresholds for the responses to hot and cold immersion, provided good evidence that these thermokinetic responses were not tactile in nature.

(ii) Macht and Kuhn (1948) examined the behaviour of normal cats to hot and cold stimuli and described similar withdrawal responses to those found in spinal animals. They concluded that such ipsilateral flexion, withdrawal and shaking of hindlimb in normal cats were evoked by tactile stimulation, because the response was not influenced by the temperature of the water within the range 1 - 45°C. One could confirm their results using the same technique of holding an animal and immersing the hind toes by lowering the animal towards the water.

By using a different technique, however, clear thresholds could be determined for responses of normal animals to both heat and cold stimuli. The animals stood with one hindlimb in a thin plastic tray and water of the desired temperature was poured

into the tray and allowed to rise slowly over the toes, its temperature being taken near the hind foot.

The threshold for withdrawal responses to cold determined in this manner averaged 12°C, and for heat 49°C. These thresholds determined for each cat were constant and repeatable. Without exception, there were no ipsilateral withdrawal responses to water at or near body temperature, applied in this manner.

One concludes that there may be a tactile component in the response to hindlimb immersion in water, depending on the method used. Regardless of this, at temperatures above or below the threshold for response, the thermokinetic reflexes as described are evoked, and are yet another manifestation of the prepotent protective flexion response.

(h) Reflex Stepping and Mass Reflexes. Stepping movements involving rhythmically alternating flexion and extension can often be provoked in these chronic spinal animals. The genesis of these movements is dealt with by Sherrington (1913). Descriptions have been given of mass reflexes in spinal man by Head and Riddoch (1917), and in spinal cats by Clark (1940). Such movements have been repeatedly observed in 11 chronic thoracic spinal cats. Almost any cutaneous stimulus, sometimes requiring several repetitions, would initiate the mass response which spreads, and then continues without further stimulation. A mass reflex begins with tail lashing, a crossed extensor or scratch response, and then spreads to involve more and more muscle groups, until finally the trunk twists vigorously, legs jerked clonically in a position of flexion, and urination and sometimes defaecation occurs. Such

mass discharges sometimes last as long as 15 minutes. A distended bladder, rectum, or stomach all greatly increase the ease with which such a mass reflex can be elicited.

2. Cleaning Reflexes.

(a) Perineal Cleaning. Tactile stimulation of the skin over the posterior aspect of the thigh, ischial region, perianal or perivulval areas, the perineum and lower abdomen, evoke characteristic reflex movements. These consist of ipsilateral hip flexion, with extension of the hindlimb at the knee and ankle joints. This posture is maintained continuously during the uninterrupted application of a tactile stimulus to the reflexogenous area, and relaxes on the cessation of the stimulus. This spinal reflex movement produces a posture resembling that adopted by normal animals for licking and cleaning the hindparts. It has therefore been classified as a cleaning reflex.

(b) Toe-fanning Response. This reflex could be readily elicited from the hindpaws of every chronic spinal cat with both high or low thoracic section. The response consists of an ipsilateral dorsiflexion of the toes, with separation of the digits, fixation of the foot in a dorsiflexed position, and the leg in a semiflexed posture. It is illustrated diagrammatically in Figure 29. An adequate stimulus for this response is touching or rubbing the fur and skin between the toes, and it is more readily evoked from the plantar than the dorsal surface, and also sometimes from the ventral aspect of the foot for a short distance. Continuance of the stimulus leads to uninterrupted maintenance of the response for periods of up to several minutes, after which the response fades

and the limb relaxes. Thus this reflex does demonstrate fatigue in the Sherringtonian sense, a feature shared by other responses (e.g. scratch reflex) which are subordinate to the prepotent flexion reflex. Facilitation is also shown by this toe-fanning response. As mentioned, during a maintained initially adequate stimulation, the toe-fanning reflex grows weaker, or disappears, and may then be replaced by withdrawal of the foot in which the limb is flexed at all joints. A painful stimulus (e.g. pinprick) then applied to the reflexogenous zone facilitated the subsequent eliciting of a strong reflex once more, by the tactile stimulation which had become inadequate owing to fatigue. This spinal toe-fanning response may play a role in the normal animal's reaction to tactile or painful stimulation of the skin between the toes. Such stimuli would be encountered when a flea, stone, thorn, mud, etc. irritated the reflexogenous zone between the toes. Following such stimuli, an immediate cleaning and licking normally occurs after the preliminary movement - the toe-fanning response - has exposed the affected area. This would explain the frequent occurrence of the reflex as part of the withdrawal response to cold, and also the facilitating effect of painful stimuli applied to the receptive field of this reflex. A very full account of the sign of Babinski has been given by Fulton and Keller (1932) and one feels that this observation in no way contradicts their concept that the Babinski sign displayed by primates is the vestigial remnant part of a protective flexion response. This toe-fanning seen in chronic thoracic spinal cats would seem to be more than part of a protective flexion response and has been

categorised as a cleaning reflex.

(c) Scratch Reflexes. These are fully described in the classical studies of Sherrington (1906a, 1906b). However, in all the chronic high thoracic spinal cats investigated, an abnormal type of crossed-scratch response could be elicited. Some features of this are illustrated diagrammatically in Figure 29. The classical scratch response as described by Sherrington was elicited from a saddle shaped area, just below the section which was quite narrow dorsally, being only 2 - 3 cms wide, but extending caudally some 8 - 10 cms on the ventral surface of the animal. The rostral end of this area abutted the skin innervated from above the level of section. The entire skin area below the level of section was mapped in detail for four chronic spinal cats, testing with both mechanical and electrical stimulation, to obtain a map of the reflexogenous zone for the contralateral scratch response. This is shown diagrammatically in Figure 29. The reflex movements themselves need only be described as containing all the features of the normal ipsilateral scratch response but appears in the hindlimb contralateral to stimulation. It was sometimes possible for areas caudal to the saddly shaped zone described, to elicit both ipsilateral and contralateral scratch responses. This phenomenon was quite variable and its occurrence could not be related to anything. However, the contralateral scratch response could be elicited so readily by the lightest touching of most of the hindparts (Figure 29) that it is remarkable that it has not been previously described.

The remaining types of reflexes listed in the

classification, namely, sexual, excretory, vasomotor and proprioceptive reflexes have been dealt with by Sherrington (1900), Fulton (1943), Denny-Brown and Robertson (1935), Sherrington (1906a) and Sahs and Fulton (1940), and require no description. Similarly, the phenomena of spinal shock, and the evolution and return of spinal reflexes after transecting the spinal cord have been fully described by various authors (Sahs and Fulton, 1940; Sherrington, 1906a, 1906b; Mc Couch, 1924; Fulton and Sherrington, 1932). In the latter context it is of interest only to mention that weak thermokinetic reflexes are seen in cats, from the second day after high thoracic section. Weak toe-fanning responses do not appear until about one week has elapsed after cord section.

The pattern of reflex behaviour in these chronic spinal animals indicates that the isolated part of the spinal cord is hyperexcitable, and most of the reflex responses are enhanced. For comparison with the clinical observations, the electrophysiological results from these animals are presented.

(2) Electrophysiological analysis of the cutaneous reflexes of chronic spinal cats was undertaken in order to further evaluate these changes in reflex patterns observed in chronic spinal animals.

Animals used fell into two groups.

(a) 7 acute low thoracic spinal animals. These were adult cats whose spinal cords were transected between T12 and L2 at the start of the final experimental testing. Five of these animals were decerebrated at the intercollicular level under ether anaesthesia, using the method of Bazett and Penfield (1922).

Testing of reflexes commenced not less than four hours after the cessation of ether, to allow time for removal of

most of the drug. The remaining two cats had their spinal cords sectioned under ether anaesthesia on the day prior to the experiment. They were not anaesthetised for the final experimental procedure, all manipulations being carried out below the level of spinal section. Animals were kept warm, were petted frequently, and given meat and milk when required. By such care, and by keeping a loose black woollen stocking over the animal's head, they remained quiet and rarely showed any distress. By this method it was hoped to avoid the depressant effects of anaesthetics upon the polysynaptic reflexes (Hagbarth and Naess, 1950; Petersen, 1952).

(b) 7 chronic low thoracic spinal animals. Five of these were subjected spinal cord transection between T12 and L2 during the first week of life, and two were rendered spinal at the age of four months. All were used when not less than nine months of age. Final experimental testing was carried out without anaesthesia and followed the procedure described above.

Dissection of both hindlimbs in each animal was routinely undertaken. For all animals, the hindlimb dissections and the preparation of cutaneous and muscle nerves was performed according to the description given on pages 8 - 11.

The following four cutaneous nerves were used for conditioning:

sural nerve, saphenous nerve, superficial peroneal nerve, (after removing the component supplying peroneus brevis and tertius) and tibial nerve, including only the medial and lateral plantar nerves without removing their contributions to flexor digitorum

brevis and the interossei.

For recording reflex discharges nerves were chosen supplying muscles with relatively simple modes of action.

Nerve to Quadriceps - Supplying vastus lateralis, medialis and vastocrureus, which are knee extensors. Nerve to rectus femoris (hip flexor) was omitted.

Nerve to Triceps Surae - Supplying medial and lateral heads of gastrocnemius and soleus, which are all extensors of the ankle, and plantaris (plantar-flexes the toes) i.e. all are physiological extensors.

Nerve to Biceps-Semitendinosus - Supplying the biceps femoris (except the nerve to anterior biceps, a hip extensor, was omitted) and semitendinosus. These muscles are knee flexors.

Peroneus Profundus Nerve - Supplying tibialis anticus and extensor digitorum longus. Both are ankle dorsi-flexors and the latter dorsiflexes the toes.

Nerve - Supplying flexor digitorum longus and flexor hallucis longus, which plantar-flex the toes, tibialis posterior, which plantar-flexes the foot. i.e. all are physiological extensors.

The stimulating and recording arrangements are illustrated in Figure 30 and described in the legend.

The standard procedure followed in all experiments included both ipsilateral and contralateral conditioning of each cutaneous nerve in turn. With graded stimulation of various strengths from threshold to 100V, the reflex discharges into each muscle-nerve

were recorded in turn.

Unsuccessful attempts were made to integrate electrically the entire polysynaptic reflex discharge into muscle nerves which was evoked by stimulation of cutaneous nerves.

Comparisons between reflex responses of the two groups of animals have been made on the basis of the latency, amplitude and duration of the reflex discharges. Responses in muscle nerves were grouped as reflexes to flexor or extensor groups of muscles and were tested in both ipsilateral and contralateral groups. Attempts have also been made to relate the characteristics of the reflex to the type of afferent fibres which are active, by comparing the reflex spike discharge into muscle nerves with the form of the afferent volley set up by a range of stimulus strengths suprathreshold for each type of afferent fibre in turn.

The following results were obtained:

Results: Volleys in four hindlimb cutaneous nerves, namely, sural, saphenous, superficial peroneal and tibial - evoked polysynaptic reflex discharges into all the muscle nerves tested both ipsilaterally and contralaterally. Certain general statements can be made concerning these reflexes from both acute and chronic spinal animals.

(1) The characteristics (particularly latency, maximum amplitude, and duration) of the reflex discharge into a particular muscle nerve evoked by volleys in each of the cutaneous nerves, show very little variation. Figure 31, A, B, C, D illustrates this with typical records of the reflex discharges into biceps-semitendinosus nerve set up by stimulating each of the four cutaneous nerves.

(2) Reflex discharges into nerves to flexor muscles (Figure

31, E, F) have a shorter latency, greater amplitude, and at high stimulus strengths a longer duration than those in nerves to extensor muscles (Figure 31, G, H). However, in the nerves to toe plantar flexors, flexor digitorum longus and flexor hallucis longus (Figure 31, H), much larger reflex discharges were obtained than those into gastrocnemius (Figure 31, G) or quadriceps nerves. The same results were seen with contralateral testing (Figure 31, I, J, K, L).

(3) What seems to be an exception to both the foregoing statements is found in the case of reflex responses evoked in nerves to extensors by stimulation of the cutaneous nerve which supplies the skin overlying the muscle. In this case the reflex discharges in the nerve to the extensor muscle may be relatively large (Hagbarth, 1952). Examples are given by the reflexes into gastrocnemius nerve from stimulation of the sural nerve, and reflex discharges into the tibialis posterior and flexor digitorum longus nerve from saphenous nerve stimulation.

(4) Ipsilateral reflex discharges into flexors always have shorter latency, greater maximum amplitude and longer duration than the corresponding contralateral reflex discharges at the same stimulus strengths relative to their respective thresholds. (Figure 31, E, F, compared with I, J).

(5) Complementary to this generalisation is the frequent finding that reflex discharges in nerves to extensors are generally of larger amplitude and longer duration in response to stimulation of the contralateral than the ipsilateral cutaneous nerves. (Figure 31, K, L, compared with G, H).

In all the records of reflex discharges there were a number of recognisable components having different latencies and thresholds. Attempts were made to correlate the afferent fibre components of the reflex discharges, but it proved most difficult to achieve monophasic recording of the afferent volley even with the recording and stimulating arrangements described in Figure 30, and the use of cocaine or potassium to kill the distal end of the cutaneous nerve. Fow statements can therefore be made in this regard. Quite clearly on several occasions however, a component having high threshold and long latency was found, which on the basis of the stimulus required (more than 20-50 V) and the calculated conduction velocity of the fibres o.2 - o.5 m/sec was probably caused by activity in the C fibres. The appearance of this component corresponded quite well with the amount at which the prolonged reflex discharge began to appear. This prolonged discharge always appeared at strength of stimulation greater than 20X threshold of the reflex discharge (which corresponds to δ threshold) and usually only at stimulus intensities of more than 20 V. Such repetitive discharge was seen on only two occasions in the afferent volley recorded from the distal portion of the nerve with the stimulating cathode distal relative to the spinal cord.

All the reflex discharges evoked in the various groups of muscle nerves by volleys in the four cutaneous nerves tested in each leg have been pooled and grouped together. The results have been expressed in terms of latency, duration, and maximum amplitude of the reflex discharges and are given in detail in Table 17 (a), (b), (c) respectively. Histograms A, B, C, in Figures 33 and 34

illustrate the essential features of these results graphically. The average latencies of the four groups of muscles given in Table 17 (a) have been confirmed electromyographically in these animals before the acute experiments. A hammer used to elicit tendon jerks and withdrawal responses, triggered the oscilloscope sweep, and records were photographed.

At the lower stimulus intensities (illustrated in the Tables by results at 1.2 and 2.0 X threshold) there were only minor differences in respect of latency, duration or maximum amplitude of corresponding reflex discharges, between acute or chronic spinal animals. None of the differences was statistically significant. However, higher stimulus intensities (of more than 20 X threshold) greatly prolonged the duration of reflex discharges in all groups of nerves, but notably in the nerves to ipsilateral flexor muscles (see Figure 34, D). This prolonged discharge was significantly longer in the chronic spinal animals for all groups of nerves. Reflex discharges were up to 5 x longer in the case of ipsilateral flexors of chronic spinal compared with acute spinal animals and in some instances lasted up to 2 sec. averaging 520 msec. in duration.

There was only one other difference between the two groups of animals which should be mentioned, but to which little weight should be attached. There was an overall 20% reduction in thresholds for reflex discharges in nerves to flexor muscles in chronic spinal animals compared to acute spinal animals.

Discussion: It is profitable to first consider the useful generalisations made concerning reflex discharges for both acute and chronic spinal animals.

The first finding is that comparable volleys in the various cutaneous nerves evoke comparable reflex discharges in any particular muscle nerve. This is compatible with the observations of convergence of excitatory and inhibitory actions onto motoneurones (Eccles et al, 1957) and interneurones (Kolmodin and Skoglund, 1954; Kolmodin, 1957) and suggests that largely the same sets of interneurones are activated by volleys in the various cutaneous nerves.

Hagbarth (1952, 1960) has clearly demonstrated that ipsilateral extensor activity can be evoked by stimulation of nerves innervating the skin overlying the extensor muscle. Such extensor activity occurs as a withdrawal response forming part of the group of protective flexion reflexes. Skin areas supplied by the various hindlimb cutaneous nerves in cat have been described in detail by Sherman, Tigay, Arieff and Schiller (1949) and have been used in assessing the results. The findings here described in this third generalisation, namely, that the reflex discharges evoked in nerves to extensor muscles by stimulation of the cutaneous nerve supplying the skin overlying those muscles was larger than those evoked by other ipsilateral cutaneous nerves, agree with the cited observations of Hagbarth (1952), and also with the second general observation that reflex activity in nerves to flexor muscles is much greater than that into extensor muscle nerves. This electrophysiological evidence for the increased flexor reflex activity in both acute and chronic spinal cats supports the contentions of numerous observers (Sherrington, 1906; Sherrington and Sowton, 1915; Head and Riddoch, 1917; Creed, Denny-Brown,

Eccles, Liddell and Sherrington, 1932; Fulton, 1943; Wright, 1945; Whitteridge, 1948) that spinal animals and man show increased flexor reflex activity. The observations on reflex behaviour of the chronic spinal animals did not suggest that there was any increase of tonic flexion, but all protective responses were exceedingly active; and noxious stimuli leading to flexion responses were most efficacious in giving rise to mass reflexes of long duration.

The apparent discrepancy in the second generalisation, namely, that reflex discharges into flexor digitorum longus nerves were much larger than those to other extensors, quadriceps and gastrocnemius may be explained by the clinical observations made on the chronic spinal animals. Depending on the nature of the stimulus, and the site of application, most flexion withdrawal responses of the hindlimbs were found to show flexion at all joints. This included plantar-flexion of the digits.

Although in relation to weight bearing and antigravity action, the flexor digitorum longus and flexor hallucis longus have been very rightly classed as physiological extensors (Sherrington, 1906) plantar-flexion is the reaction of the toes during withdrawal of the hindlimb and the participation of these muscles in the flexion reflex is borne out by the electrophysiological findings here.

The fourth observation, that ipsilateral flexion reflex discharges are larger than those into contralateral nerves to corresponding flexor muscles, bears out the observed behaviour of these animals during withdrawal reflexes and all the previous descriptions (Sherrington, 1906, 1910) of such flexion responses.

Relatively powerful noxious stimuli usually evoke ipsilateral flexion with crossed-extension and there is little activity in contralateral flexors unless stepping ensues. The final general statement that reflex activity is greater in contralateral extensor muscle nerves complements the preceding one and also accords with the known reflex behaviour of spinal animals.

With regard to the described differences between the results for acute and chronic spinal animals, the decrease of the flexor reflex threshold in the latter group is hardly likely to be of much significance. One reason for this is the use of ether anaesthesia and decerebration for five of the seven animals in the first group while no anaesthetic was administered to the chronic spinal animals or the remaining two acute spinal animals. Reflex thresholds depend on so many factors that a much larger series of animals would be required before much significance could be attached to such threshold differences.

The other and more striking difference between the two groups is however significant. Such prolongation of reflex discharges can be due to continuous activity in chains of interneurones, but might also be explained by repetitive activation of afferent fibres in the cutaneous nerve by enormous stimulus strengths (20 - 100 V) applied giving rise to recurrent loops and the repetetive firing of fibres. This is unlikely in view of the brief duration of the stimulus (less than 0.4 msec at 100 V) and most unlikely in face of the finding that such prolonged discharge did not occur in the cutaneous nerve activated by centrifugally directed volley and recorded from the distal cut end of the cutaneous nerve. One

cannot however, fully exclude the possibility of repetitive discharges of afferent fibres.

Allowing that such reflex discharges of up to 2 sec in nerves to ipsilateral flexor muscles are probably due to interneuronal activity, the difference between responses in acute and chronic spinal animals is quite significant. This provides confirmation and an explanation for the enhanced excitability of the reflexes in chronic spinal animals using clinical tests. However, there is some suggestion that it is only the highest threshold slow conduction velocity component of the afferent discharge which gives rise to such prolonged reflex discharges. Laporte and Böer (1955), Laporte and Bessou (1957), and Voorhoeve, Laporte and Bessou, (1959), have shown that ipsilateral flexor reflexes may be provoked by stimulation of non-medullated C fibres in the cat. Their records illustrate the same degree of prolonged discharge with maximal C fibre stimulation that has been found with high intensities of stimulation in acute spinal animals.

Repetitive discharge of gamma motoneurones has been described (Hunt and Paintal, 1958) and the most striking effects arise from cutaneous afferents. It is possible that fusimotor neurone activity is largely responsible for the prolonged reflex discharges observed. The removal of supraspinal control by spinal cord section has obvious immediate effects on the spinal reflexes (R.M. Eccles and Lundberg, 1959), but some of the immediate effects resulting from the release of supraspinal inhibition may be partly obscured over a short period by the depressing effects of spinal shock with disturbances of blood supply.

Holmqvist, Lundberg and Oscarsson (1960) have shown that descending inhibitory influences arising from a centre of the medulla impinge on the spinal neurones involved in the flexor reflex. Spinal transection has been shown to cause the immediate release of the flexor reflex from inhibition, with consequent enhancement of the mass discharges ascending the spinal cord in the flexor reflex tracts. It is now apparent from the results described that there are also slower changes following spinal transection involving an increased excitability of flexor reflex interneurones to stimuli arising in the highest threshold afferent fibres. Such slow progressive enhancement of excitability resulting from spinal transection can explain in part the observed reflex behaviour of chronic spinal animals.

McCouch, Austin, Liu and Liu (1958) describe non-specific sprouting of new afferent terminals as a possible cause of spasticity. Their histological evidence of sprouting is good and such new growth of terminal fibres occurring in these chronic spinal animals could also explain in part the slow changes in reflex excitability which follow cord transection. This cannot be excluded.

All the results presented in this section indeed bear out Sherrington's observation in his Marshall Hall Prize Lecture (1899) where he states: "My own experience leads me to think that the condition of a spinal cord isolated by a spinal transection is often more normal a few hours after the transection than it is when long periods of weeks and months are allowed to elapse".

Summary: Observations which extend previous descriptions of the patterns of reflex behaviour of chronic spinal animals have been

made. An electrophysiological analysis has been made of the polysynaptic reflex discharges into muscle nerves evoked by stimulation of various cutaneous nerves. This has enabled certain useful generalisations to be made, and displays one striking difference in the reflex activity of chronic spinal cats compared with acute spinal animals, namely, prolonged reflex discharges into ipsilateral flexors from high intensity cutaneous afferent stimulation. In spite of this, one concludes that such polysynaptic reflex pathways do not provide a system on which the effects of use or disuse may be assessed in a very precise manner.

SECTION C. Nerve Sections - Excess Use.

This section presents the results of attempts to give excess use to the synapses of some monosynaptic pathways through the spinal cord. Other monosynaptic paths were kept as controls. Animals were subjected to an initial aseptic operative procedure that was designed to provide increased mechanical stress on some muscles, with a consequent increased activity of proprioceptors, and overuse of their central synapses. If all the muscles but one of the synergic group of muscles are denervated, there should be overuse of that innervated muscle. Synergic groups of extensor muscles, both of ankles and toes, were chosen because they have antigravity action during standing and walking and are therefore subjected to much stretch during use of the hindlimb. The animals were exercised daily over a 3 - 4 week survival period in order to accentuate the mechanical stress on the remaining innervated muscle. The other hindlimb which was subjected to only a dummy operation provided controls.

The same monosynaptic test systems previously described were used to assess the reflex changes, and the results obtained are presented and discussed in Section (1).

In a later refinement, an alternative apparatus for providing exercise was devised in order to give a measure of the actual thrusts of each leg during the to and fro walking of the animals across a strain gauge platform. In this way, the pressures during walking exerted by the normal hindlimb could be determined, relative to those of the hindlimb containing denervated muscles. The changes of hindlimb thrusts relative to postoperative survival

time and other factors, will be dealt with in Section (2).

The final section (3) will describe the reflex changes induced in monosynaptic pathways due to the nerve section procedure when there was, in addition, spinal transection at the level between T10 and T11 at the time of nerve section.

(1) Nerve Sections - Excess Use.

Methods: The initial aseptic operations in this series of 20 cats were performed using methods described in the early sections. Two alternative operative procedures were employed, and these are shown diagrammatically in Figure 35. In one hindlimb, nerves to all ankle and toe extensor muscles, except one in each synergic group, were cut and capped in order to prevent regeneration. The muscles spared were flexor digitorum longus, and either the medial or the lateral head of gastrocnemius, all other ankle and toe extensor muscles being denervated. The contralateral hindlimb was used to provide controls, and was subjected to a dummy operation which was identical in every respect but omitted the nerve sections and capping.

A survival period of between three and five weeks was allowed. During this time the animals were exercised continuously for one or two half-hour periods daily according to individual tolerance either in a simple treadmill or on the strain gauge apperatus to be described later. The final acute experiments were performed at the completion of the given survival period. The methods for these differed in no way from the methods described on pp. 8 - 11.

Note: Throughout the following text, when reference is made

to the muscles in the synergic groups of denervated muscles, whose innervation was left intact, these have been termed the spared muscles.

Results: (a) The average muscle wasting in the hindlimbs was calculated for each of the muscle groups listed in Table 10. The results are summarised in the form of a histogram in Figure 36. A significant degree of wasting occurred in those denervated muscles of the ankle extensor and toe extensor groups, averaging 43% and 42% respectively. This degree of wasting or more, following denervation, has been reported by a number of authors in the past. (Eccles, 1944; Helander, 1957).

Small amounts of wasting, not statistically significant, were found for the other muscle groups on the operated side. The spared muscles, flexor digitorum longus and medial or lateral gastrocnemius, showed negligible amounts of wasting. On the other hand, although one has postulated that these muscles are overused during exercise in the postoperative survival period, there was no evidence of any hypertrophy of these spared muscles.

(b) There were characteristic changes in the monosynaptic reflex responses evoked from the nerves to spared muscles by maximal group Ia volleys. Actual records, typical of the monosynaptic reflex responses obtained, are shown in Figure 37. Reflexes from the nerves to control muscle groups (biceps-semitendinosus and peroneal muscles) are seen to be approximately symmetrical. This symmetry of control reflexes obtains both before and after tetanic conditioning at 400 impulses / second for 15 seconds. (Figure 37, BA, T; PA, T). On the other hand,

nerves to the spared muscles flexor digitorum longus, and either medial or lateral gastrocnemius, provided monosynaptic reflex responses which were significantly 100% or more larger than those from the corresponding contralateral controls. (Figure 37, GA, FA).

After tetanic stimulation with the standard parameters, there is only about 30% enhancement of monosynaptic reflex responses from nerves to the spared muscles. (Figure 37, GT, FT). This was considerably smaller than the increase in the pretetanic levels of reflexes from the nerves.

Table 11 gives a detailed statistical summary, for all 20 animals in the series, of the monosynaptic reflex responses obtained from all groups of nerves tested. These results are displayed as a histogram in Figure 38. In approximately half the animals in this series, operative procedure A was employed while B was used in the remainder (see Figure 35). There are therefore both lateral and medial gastrocnemii as spared muscles, but never from the same animal. Nerves supplying the bilateral control muscle groups, biceps-semitendinosus and peroneal muscles, gave surprisingly consistent results for the tested monosynaptic reflex responses. Reflexes from control nerves in the operated hindlimb were always slightly larger than those reflexes from corresponding nerves in the normal hindlimb. The significance of this relatively small enhancement was not readily apparent from the results in any one experiment. In the pooled results, however, on the operated side, the reflexes from peroneal nerve show a 11% enhancement significant with 1% confidence limits. The 9% enhancement of biceps-semitendinosus reflexes is significant if 5% confidence limits are used.

This small but significant change will be discussed later. After tetanic conditioning, the relative increase in reflex responses from the nerves to control muscle groups on the denervated side, was reduced below a significant level.

By contrast with the small relative increase in reflexes of control groups just described, the monosynaptic reflex responses evoked from nerves to spared muscles on the operated side showed a very significant 113% - 157% average increase relative to reflexes from corresponding nerves in the normal limb. This degree of increase of reflexes from nerves to spared muscles was seen prior to tetanic conditioning. After tetanic stimulation, there was still a significant relative increase in reflexes from spared muscles, but this had been reduced to between 20% - 39%.

It is worth mentioning that reflexes were obtained from the nerves which had been sectioned, but these were always very small, variable, quite late in onset and slow to peak. In fact, all the changes described by Eccles, Libet and Young (1958), for chromatolysing motoneurones as seen using microelectrode techniques, could be observed in the ventral root monosynaptic responses of severed nerves. (cf. Downman, Eccles and McIntyre, 1951; Eccles and McIntyre, 1953; McIntyre, Bradley & Brock, 1959)

(c) Central Latencies were determined for the monosynaptic reflex responses of the various nerve groups tested. These have been pooled, and all the means for both the control groups and the spared group in each hindlimb, are given in Table 12 (a).

There is a statistically significant average shorten-

ing by 0.14 msec. of the central latencies of reflexes from nerves to spared muscles. The shortening of central latency shown by enhanced reflexes in this series of experiments is comparable to that central latency reduction seen for the enhanced reflexes from nerves to tenotomized muscles.

(d) Spinocerebellar Tract Responses. Attempts were made to compare the mass discharges of spinocerebellar tracts for the different groups of nerves. Good responses of both DSCT and VSCT were always obtained from nerves to biceps-semitendinosus and peroneal muscles. However, the nerve to one head of gastrocnemius muscle gave responses which were usually too small to measure. Similarly, the nerve to flexor digitorum longus alone gave very small spinocerebellar tract responses. It thus proved impossible to obtain sufficient measurable responses from important group of nerves to spared muscles. No statistical analysis was possible, and the results were quite inconclusive.

(e) Conduction Velocities and Absolute Refractory Periods of the various groups of nerves were calculated, and are listed in Table 12 (b). There were no statistically significant differences in conduction velocity of nerves to the different muscle groups, or of their absolute refractory periods.

(f) The effect upon reflex height of altering the frequency of the testing volley. This has been determined and Figure 39 shows the combined results from four animals. There is increasing depression of reflex height with increasing frequency of testing volley up to 10 per second. This is in good agreement with the findings of Lloyd,Hunt&McIntyre (1955); Lloyd (1957) and

Jefferson and Schlapp (1953). There is no significant difference between the reflexes evoked from nerves to spared or corresponding normal muscles. For each different reflex, both sets of points are scattered about the same line.

(g) Time course of Post-tetanic Potentiation.

Typical records to display the reflex changes after tetanic stimulation are reproduced in Figure 40. The time courses of post-tetanic potentiation are displayed graphically in Figure 41. There are no significant differences between corresponding nerve groups in the two hindlimbs shown during the recovery from potentiation. When followed in several cats over longer periods up to 15 minutes, there were no differences found, and at all times the curves of reflex heights from corresponding groups of nerves in both hindlimbs ran a parallel course.

The essential features of these changes induced by the nerve section procedure may be summarised as follows:

Nerves to spared muscles evoke reflexes which are significantly increased by 113% - 157% relative to their contralateral controls. A significant shortening of central latency, averaging 0.14 msec. occurred with these enhanced reflex responses. These are taken to indicate a greater potency of the monosynaptic innervation of motoneurones innervating spared muscles.

There were no demonstrable changes in the afferent fibres. Conduction velocity, refractory period, effects of varying the frequency of the testing volley, and the time course of post-tetanic potentiation did not differ significantly for the two groups. It was therefore concluded (Eccles and Westerman, 1959)

that changes in the excitatory synapses were responsible for the increased gastrocnemius and flexor digitorum longus monosynaptic reflexes. The change could be either at the presynaptic terminals of the group Ia fibres or on the postsynaptic membrane. This hypothesis supposed that excess use of the synapses involved in these pathways leads to an enduring increase of synaptic efficacy. Various possible mechanisms by which the presumed excess proprioceptor afferent activity could make synaptic action more efficient have been presented (Eccles and Westerman, 1959).

Before speculating further about possible mechanisms involved it was important to examine the question of excess synaptic usage from two directions. The first of these was to investigate whether the remaining spared muscles of each synergic group actually do bear more than their normal share of weight during exercise in the postoperative phase. A test is thus provided for the supposition that they are subjected to more stretching and thus give an increased afferent input relative to the normal side. Secondly, if the observed results are due to excess synaptic use, it would be predicted that the reflex enhancement from the spared muscles would be decreased or abolished if the postoperative exercising of the denervated limb is prevented. The latter was dealt with by performing a spinal cord transection between T10 and T11, at the time of nerve sections. The results of this will be presented in Part (3) of this section.

The first question raised concerning the hindlimb activity and weight-bearing will be dealt with at this point.

(2) Pressures exerted by legs during walking.

Methods: The apparatus used to measure the thrusts exerted by

the limbs during walking consisted of a wire-sided corridor 4 inches wide and three feet long. Let into and flush with the floor near the centre of the corridor was a 2" square pressure platform. This moved quite freely in a vertical plane, with negligible lateral travel. Pressure applied to the platform was thus transmitted with minimal losses to a Grass force-displacement transducer. The 0 - 1 Kg range of the latter was used, and the strain gauge was included in a resistance bridge circuit, followed by an amplifier and pen recorder. A block diagram of the circuit is shown in Figure 43. The instrument was calibrated in 100g steps up to 1 Kg at the commencement of each trial, and gave accurate readings to within 2%. The system had a frequency response such that with rapidly applied pressures such as occurred during fast walking, there were losses of no more than 10% in the recorded force. Six animals in all were subjected to the nerve section procedure B (see Figure 30) described. These animals were mobilised from the second day postoperatively but could only be induced to stand for short periods and to walk with considerable difficulty. After the first four or five days these animals lost much of their reluctance to walk, and quickly learned to walk up and down along the corridor to receive rewards of food. Stepping on the 2" square platform occurred only by chance and made difficult the recording of a suitable number of pressures during a given trial. The animals could be induced to step on the platform each time they passed by the simple expedient of covering the floor surrounding it with $\frac{1}{4}$" thick Estafoam. This latter, the cats refused to walk upon. Of the two alternative

courses - jumping across all the Estafoam, or adjusting their gait to use the platform in a "stepping-stone" fashion - they usually chose the latter. The dimensions of the Estafoam were adjusted until there was no discernable disturbance of the animal's normal walking pace or stride. After a number of trials using the Estafoam and rewarding only hits on the platform with food, the foam could be dispensed with. Only one cat (W106) proved to be an exception, and rarely stepped on the platform in the absence of the Estafoam. For each cat at every trial, about 20 pressures of each limb were recorded, and the mean pressures calculated.

By three weeks postoperatively, the animals had lost almost all traces of limp and would run and jump without obviously favouring the hindlimb in which nerve sections had been performed.

As a result of the operation, certain changes in the distribution of body weight are found.

Unfortunately, there are yet too few figures obtained with normal cats to present definite evidence as to the distribution of the support of body weight during walking. From a limited number of observations, it appears that at any instant during walking, the body weight is equally supported by one hindlimb and the contralateral forelimb.

Results: The main features to be seen in the actual records obtained by this method are illustrated in Figure 44 and described in the legend.

During the first few days there is a general shift

of body support towards the forelegs and this is shown in Figure 45. This almost certainly occurs as a result of the pain and disability from the wounds of both hindlimbs (nerve sections in one hindlimb and dummy operation in the other).

The most important finding in all cats is shown in Figure 46. The pressure exerted by the operated hindleg during walking expressed as a % of that exerted by the normal hindleg, shows an approximately exponential increase from 50% to 90% when plotted against postoperative days. When the same figures are plotted against a logarithmic scale in Figure 47 the exponential nature of the change is shown. The main body of the exponential (b) has a half time of 20 days, but this curve is distorted during the first five days and follows a second line (a) with a half time of five days. The likely explanation of this early distortion is to be found in the pronounced limping walk seen during the first few days and mentioned previously. Separate plotting of results shows that on the second postoperative day both hindlimbs exert only 50% of foreleg pressures (as in Figure 46). The hindlimb pressures, relative to those exerted by forelimb, increase with postoperative interval up to 80% on the sixth day and 90% of the forelimb pressures by the twenty-fifth day.

It can be shown that the use of Estafoam to encourage stepping on the strain gauge platform does not introduce any serious artifact into the results. In Figures 48 and 49, absolute pressures of fore and hindlimb, in grams, are plotted against postoperative interval. Cat W108 did not require the use of Estafoam to encourage stepping on the platform, while Estafoam was used with W106 from the fourteenth postoperative day onwards.

There appear no essential differences in the course of recovery with time using the absolute limb pressures as a criterion.

The final Figure 50 shows that the operated hindlimb bears an increasing percentage of the body weight during post-operative recovery. The exponential character of the change is distorted over the first 5 -6 days as a result of the artifact introduced by the "limping walk" mentioned above. After the thirty-seventh day the curve flattened out when 45% of the total body was borne by the operated hindlimb during walking.

Conclusions: The distribution of the body weight undergoes characteristic changes following the described nerve section procedure. In the six animals used for this study, all the ankle extensor muscles (L.G, S., Pl.) were denervated with the exception of the medial head of gastrocnemius.

This spared muscle always represents about one third by weight of the total synergic group. Analysis of the triceps surae muscles in 18 normal cats showed that medial gastrocnemius occupies between 32% - 38% by weight of the whole synergic muscle group and averaged 34.6% (Standard Error $\pm$ 0.4).

During the readjustments and compensatory shifts of body balance which follow the operative procedure, the operated hindlimb pressures relative to those of the normal hindlimb, increase steadily from their initial postoperative level of 50% up to 90% by four weeks. This indicates that during walking and weight bearing, the one spared ankle extensor (medial gastrocnemius) now exerts 90% of the force exerted by the entire synergic group of the other hindlimb. Presumably this is achieved by an increase in the number of active fibres in the muscle, and means an increase

of 160% in the work performed by this muscle on the basis of the proportion between the volume of medial gastrocnemius and the whole synergic group. The force required to support an animal weighing 2 Kg at any instant is only 1 Kg exerted by each hind-limb and the contralateral forelimb. There are many figures (Eccles and Sherrington, 1930; Cooper and Eccles, 1931) which indicate that the maximum tetanic twitch tension exerted by one head of gastrocnemius muscle can be as high as 12 - 15 Kg in large cats. It is clear that during weight-bearing these extensor muscles have a large reserve of power, and are exerting only a small percentage of their maximum tetanic tension. It is thus relatively easy for the one spared ankle extensor muscle to assume the entire weight-bearing role formerly carried out by all the synergists acting in concert. Nothing is known about the afferent activity from the spared muscles under these conditions, but it is reasonable to postulate that, after operation, the spared muscles must be stretched more by the body weight than postoperatively. The proprioceptive bombardment from these muscles is increased accordingly. As the spared muscles must contract more strongly during walking, the activity of their spindle afferents could diminish with increased muscle contraction, but this is in turn dependent upon the supraspinal activation of gamma motoneurones. It is always the latter which set the level of activity within the system and it is clear that since the spared muscles contract more strongly there is more control than just that exerted by the γ loop. Some evidence of the major role of supraspinal control in bringing about the functional readjustment of spared muscles

is found in the action of ethyl alcohol in these animals. Ethyl alcohol given as single doses, 1 ml per Kg by mouth, 3 - 4 weeks after the operation resulted in a reduction of the operated hindlimb pressure by 20% - 25% lasting for several hours. The action of this drug which leads to depression of higher centres (Sollman, 1957), has therefore been to remove partially the compensating mechanisms responsible for the increasing proportion of weight borne by the spared muscles during the postoperative phase of functional readjustment. In relation to these results interesting functional readjustments resulting from tendon transplants have been described (Close and Todd, 1959). Although muscular hypertrophy may result from increasing work done from an increased initial length with increasing force of contraction during shortening (Rarick, 1960) the spared muscles in these experiments show no significant increase in weight (Table 10).

The results of this series of experiments suggest that supraspinal influences may be important in bringing about the remarkable postoperative recovery and readjustment of muscle activity in the operated hindlimb. There is likely to be enhanced gamma activation of muscle spindles during weight bearing in the post-operative recovery phase when the spared muscles are contracting more strongly. This should result in increased proprioceptor discharge, and is in accord with the explanation of the monosynaptic reflex enhancement on the basis of increased synaptic usage (Eccles and Westerman, 1959).

Further understanding of the processes involved in bringing about these changes is made possible by the results of the

subsequent investigations.

(3) Nerve section procedure with spinal transection.

In this final section the effect on reflexes, of spinal transection at the time of unilateral nerve section was tested in seven animals. It was postulated that, if the reflex enhancement observed following the nerve section procedure was due to excess synaptic use, prevention of post-operative exercising of the limb should decrease or abolish the reflex enhancement from nerves to spared muscles.

The Methods employed followed closely those described for subsection (1). The procedure at the initial aseptic operations in the seven animals used was that in which the medial gastrocnemius and flexor digitorum longus muscles were spared (Procedure B in Figure 35), their remaining synergists being denervated. At the outset of the operation however, the spinal cord was exposed and transected at the level of T10 - 11. The contralateral limb provided controls and was subjected to a dummy operation. Survival times between three and five weeks were permitted, and during much of this time the animals were completely flaccid below the transection.

Limb and tail movements evoked during manual expression of urine were seen only after a fortnight, but there were very few reflex movements of the hindlimbs, and every effort was made to keep the animals as still as possible.

Plaster of Paris immobilization of the operated hindlimb was carried out in two animals, but as the results did not

differ appreciably, all have been grouped for the purposes of discussion.

Results: (a) The average muscle wasting for each of the several hindlimb muscle groups is shown in Table 14. The results are summarised in histogram form as Figure 51. A significant degree of wasting occurred in those denervated muscles of the ankle extensor and toe extensor groups, averaging 15.6% and 26.5% respectively. This is superimposed on the background wasting of all muscles in both hindlimbs, resulting from the spinal transection (Hnik, 1960). The spared muscles medial gastrocnemius and flexor digitorum longus, showed minimal wasting which was not significant.

(b) The monosynaptic reflex responses evoked by maximal group Ia volleys to nerves from spared muscles, showed the characteristic enhancements described in subsection (1). In fact, the results of this section are almost identical to those described for the nerve section procedure alone. Actual records, illustrating the typical monosynaptic reflex responses obtained are shown in Figure 52. Reflexes from the nerves to control muscle groups (biceps-semitendinosus and peroneal muscle groups) are seen to be approximately symmetrical. (Figure 52; B1, 2, P1, 2). By contrast, nerves to the spared muscles, flexor digitorum longus and medial gastrocnemius, gave rise to monosynaptic reflex responses which were significantly 100% or more greater than those from the corresponding contralateral controls. (Figure 52, G1, F1.). After tetanic stimulation enhancement of reflexes from nerves to the spared muscles persists to a reduced degree being only 30% - 60%. (Figure 52, G2, F2.)

A detailed summary of monosynaptic responses of all cats is given in Table 14. These results are summarised in the form of a histogram as Figure 53.

It is seen that with the exception of the nerve to quadriceps femoris which provided symmetrical reflexes, nerves to the control muscle groups biceps-semitendinosus and peroneal muscles gave monosynaptic reflex responses which were enhanced by 15% and 20% respectively on the operated side. This enhancement was statistically significant in the case of peroneal group and an explanation of these changes will be provided in the discussion.

Nerves to spared muscles evoked reflex responses which were significantly increased by an average 109% in the case of medial gastrocnemius, and 152% from flexor digitorum longus compared to corresponding reflexes from the normal side. These results should be compared with those obtained in subsection (1), which they resemble closely.

(c) Central Latencies of monosynaptic reflexes were calculated for all groups of nerves, and the pooled results are given in Table 15. There is a statistically significant 0.11 msec average shortening of central latencies of the enhanced reflexes from nerves to spared muscles. There is no significant difference of central latency for control reflexes from the two sides.

Discussion:

The reflex enhancements and latency changes found in this series are almost identical to those observed for reflex responses from the same nerves in the series of animals with the nerve section procedure alone. From these results it is clear that the spinal cord transection, to which the animals in this group

were subjected, has had no obvious effect upon the reflex changes induced by the nerve section procedure.

Before discussing these changes an explanation must be provided for the small statistically significant enhancement of monosynaptic reflexes from control nerves on the operated side.

In a series of histological investigations of dorsal roots and ventral roots from five animals in which the nerve section procedure had been carried out 3 - 5 weeks previously, the following results were obtained. Photomicrographs of 10 sections of osmic acid fixed specimens were taken and used for fibre counts, the measurement of fibre diameters, and for the calculation of the relative cross sectional areas of corresponding dorsal and ventral roots from both sides of the same animal.

(i) The cross sectional area of dorsal roots S1 and L7 is reduced by an average of 13.3% on the side of nerve sections.

(ii) The areas of cross section of ventral roots S1 and L7 were reduced by an average of 9.5% on the side of the nerve sections.

(iii) The total fibre count of ventral roots (based on over 10^5 fibres) was reduced by an average 7.3% on the side of the nerve sections. From this latter it can be seen that there must be a small overall reduction in the average fibre diameter of those fibres in ventral roots of the operated side.

(iv) This latter observation is well borne out by the fibre diameter spectrum which was calculated for one pair of

ventral roots, and is shown in Figure 54. This shows a slight shift to the left for the ventral root on the side of nerve sections. This indicates a reduction of fibres with larger diameter, and an increase of smaller diameter fibres. This result is in good agreement with those of other observers (Hammond and Hinsey, 1945; Sanders and Young, 1946).

One explanation for the enhancement of reflexes from control nerves on the operated side, can now be offered. This is based upon the shrinkage of ventral roots shown to occur as a result of the nerve section procedure (see Figure 55).

For a cylindrical ventral root of cross sectional area A, the electrical resistance of a given length of ventral root is inversely proportional to A. The action potential recorded with a fixed interelectrode distance will depend upon the resistance of the active fibres compared to the resistance of inactive fibres and extracellular space through which the action current flows. In a pair of ventral roots under comparable conditions, it may be calculated that a 10% reduction in the cross sectional area of one root, such as is demonstrated to occur, will result in a 12% enhancement of the actional potential recorded from that root (see Figure 55). This calculated reflex increase is within the range of that recorded from nerves to control muscles on the operated side.

It therefore appears that shrinkage of the ventral roots S1 and L7 on the side of nerve sections, with the consequent more efficient recording of the reflex discharge could provide an

attractive explanation of the observed enhancement of control reflexes from this side. This would also contribute in part to the reflex enhancement seen from nerves to spared muscles.

Very little shrinkage of L6 ventral roots results from the nerve section procedure described. There was no enhancement of reflex responses evoked from the nerve to quadriceps which appears in L6 ventral roots, and not in S1 and L7. These facts support the postulated explanation of the small 10% - 20% enhancement of reflex responses evoked from control nerves on the operated side.

Consider now the reflex changes in spared nerves following the nerve section procedure. Since there was no demonstrable changes of afferent fibres of the reflex arcs tested in these series of experiments, the synapse must be the site at which the observed reflex changes are brought about. There are three possible mechanisms by which this increased cell excitability or increased synaptic potency can occur.

(i) An increased synaptic efficacy due to excess use of the synapses has been postulated (Eccles and Westerman, 1959). This may be brought about by increased mobilization of transmitter (Eccles, 1959). There is some evidence in this situation to support this postulate. Alterations in the numbers and/or dispositions of synaptic vesicles at the presynaptic terminals have been shown in electronmicroscopic studies to occur under various conditions of synaptic usage (De Robertis, and Franchi, 1956; De Robertis, 1956; De Robertis and Ferriera, 1957). Furthermore, Hubbard (1959 and personal communication) provides evidence that activated neuromuscular synapses show increased miniature epp

frequency even during repetitive stimulation. This suggests more efficient manufacture and/or mobilization of transmitter, together with a greater availability of transmitter for release by activated synapses.

It is surprising that spinal transection which almost abolishes hindlimb movement during the post-operative recovery phase, does not alter the course or magnitude of the reflex enhancement from spared muscles, However, in view of the extreme sensitivity of the muscle spindles to mechanical stimuli (Matthews, 1933; Hunt and Kuffler, 1951; Kobayashi, Oshima and Tasaki, 1952; Granit, 1955) one cannot exclude the possibility of excess synaptic usage resulting from increased spindle discharge from spared muscles. Such increased proprioceptor discharge may also result from an excess gamma activity as a consequence of the nerve section procedure, even after the removal of supraspinal gamma activation by spinal cord section. This postulate is not in conflict with the limited knowledge of the behaviour of the gamma system (Hunt and Paintal, 1958; Hunt and Perl, 1960) and provides an interesting contrast to the situation with tenotomy where spinal transection abolishes the increased afferent activity and the reflex enhancement. Suprasegmental influences are thus most important in the tenotomy situation but have no appreciable role in the reflex enhancements resulting from the nerve section procedures. This explanation of the results depends upon the presence in any particular pathway of inhibitory afferent connections from its synergic muscles ending on its fusimotor neurones. Nerve sections with removal of heteronymous (synergic) gamma inhibition would thus lead to increased

gamma activation with its attendent consequences. Further investigation of the proprioceptive afferent activity from spared muscles after this nerve section procedure would be necessary to confirm these postulates.

(ii) Another possible explanation lies in the evidence of McCouch, Austin, Liu and Liu (1958), that degenerating nerve fibres within the spinal cord stimulate adjacent fibres to generate collateral sprouts. Such sprouting is non-specific, and little is known of the functional state of any synaptic connections made by such collateral sprouts (Murray and Thompson, 1957). However, the presence of degenerating afferent fibres, but not chromatolysing motoneurones, occurring in the close proximity of the intact synergic afferent fibres and motoneurones could well result in sprouting and formation of new terminals (Murray and Thompson, 1957; McCouch et al, 1958). The results of Eccles and McIntyre (1953) in which dorsal roots adjacent to those severed gave enhanced reflex responses compared to the contralateral control side could be explained on the basis of sprouting, since intraspinal sprouting from intact spinal sensory neurones by adjacent dorsal root section has been demonstrated (Liu and Chambers, 1955). The alternative explanation proposed by Eccles and McIntyre (1953), suggested that more mechanical stress was placed on the remaining stretch receptors of the weight-bearing extensor groups which had undergone partial deafferentation. As a consequence, increased activity of these synapses led to enhancement of synaptic function.

Further evidence that such sprouting may develop aberrant connexions with functional significance is given by a recent

investigation (Eccles, Eccles and Magni, 1960) of monosynaptic excitatory actions on motoneurones regenerated to antagonistic muscles. In these experiments nerves to antagonistic muscles (Peronei to medial gastrocnemius) were cross-united and some months later intracellular recording of the monosynaptic EPSPs provided a sensitive measure of the development of aberrant synaptic connexions to motoneurones with inverted function. There were large increases (over tenfold) of aberrant connexions between motoneurones of inverted function and afferents from their former antagonists. For a number of reasons these authors attributed the changes mainly to the development of a changed surface specificity of these motoneurones with the selective attraction of sprouts from adjacent fibres, but they were unable to exclude the effects of non-specific sprouting which could provide a partial explanation of the observed changes.

The observed enhancement of monosynaptic reflex responses from nerves to spared muscles could be partly explained by the occurrence of such non-specific sprouting of the intact afferent terminals adjacent to those terminals of severed afferent lines which are undergoing degenerative changes. The formation of new homonymous synaptic connexions to motoneurones would give a greatly enhanced synaptic efficacy to Ia excitatory volleys. Hence there would be an enhancement of reflexes from these pathways. This should cause spreading of excitation to the non-synergic muscles, but this was only found to a very small extent. Very little degeneration of intramedullary afferent terminals is likely to follow such peripheral nerve section in the adult (Hess, 1957). Both

these facts argue against this explanation.

(iii) Denervation hypersensitivity has been recognised (Cannon and Haimovici, 1939; Cannon and Rosenblueth, 1949, Teasdale and Stavraky, 1953) but the changes occurring in denervated cells have been imperfectly understood. The recent well-controlled investigations by Axelsson and Thesleff (1959) and Miledi (1960) of the hypersensitivity of denervated muscle, shows that the whole surface of the denervated fibres becomes sensitive to the transmitter acetylcholine - i.e. there is an increase in the size of the receptor area. Such a phenomenon has not been suggested to occur with motoneurones in previous accounts of 'denervation hypersensitivity' (Teasdale and Stavraky, 1953; Cannon and Rosenblueth, 1949). The situation here is quite different, but one can postulate that a similar phenomenon could occur, and in the intact cell upon which degenerating fibres end, degeneration of excitatory synaptic connexions would cause the post-synaptic membrane to become hypersensitive, and that there would be, by analogy with the denervated muscle fibres, an extension of the sensitive subsynaptic receptive membrane. Thus excitatory volleys in homonymous afferent paths ending on the intact cell would be far more effective in exciting spike generation and firing the cell. This increased excitability of such motoneurones supplying spared muscles would result in increase of their monosynaptic reflex responses as tested by maximal volleys in their peripheral nerve.

The excitatory synaptic connexions of Ia afferents from the synergic muscle groups tested in this study are extensive, and on the quantitative basis of species differences in Ia receptiveness

(Eccles et al, 1957), this postulate explains how there is a different mean % of enhancement for reflexes from each different nerve. It further explains why the nerve section procedure induces almost the same degree of reflex enhancement for each nerve after spinal cord transection, as occurred without cord section.

Evidence against such a hypersensitivity has been obtained in the experiments of Eccles et al (1959) when the monosynaptic actions of normal afferent lines were tested onto normal cells whose synergist afferent collaterals would have been degenerating from peripheral nerve section. There was no evidence of 'denervation hypersensitivity' or increased synaptic efficacy using the relatively sensitive techniques of microelectrode recording. Mc Couch et al (1958) also found no evidence of denervation sensitization of motoneurones. In the case of muscle, the spread of transmitter-sensitive receptor sites into region of intact synapses on muscle does not occur (Miledi, 1960) and has only been shown to occur with degeneration (Axelsson and Thesleff, 1959). There is no evidence to support this third alternative explanation of the reflex enhancement.

Summary:

The described procedure in which all muscles but one of the synergic group were denervated has resulted after 3 - 5 weeks interval in enhanced monosynaptic reflex responses from the spared muscles compared to the corresponding contralateral reflexes. Spinal transection prior to nerve sections, quite surprisingly, did not affect the course or magnitude of the induced change. In the absence of definite evidence, there is more to commend an explanat-

ion of this reflex enhancement in terms of increased proprioceptive afferent bombardment, and excess synaptic use with enhanced synaptic efficacy. This explanation is not incompatible with the results of Section A.

FINAL DISCUSSION and SUMMARY.

In considering the results of these investigations attention should be paid first to those more precise results from the simpler systems studied in Sections A and C.

The problems involved in relating synaptic function to learning have been discussed by McIntyre (1953) and Eccles (1959), as have the effects of use and disuse on synaptic function in this context. (Eccles, 1959).

The properties of "plasticity" of synapses at higher levels of the central nervous system postulated to explain the phenomena of learning and of conditioned reflexes, have been shown in this investigation to occur at synapses in the simplest pathways of a mammalian central nervous system.

From the results of experiments discussed above (Eccles & McIntyre, 1953; McIntyre, 1953; Eccles et al 1959), it appears likely that prolonged disuse has a harmful effect on the efficiency of synaptic action. In Section A, attempts are described, to produce disuse of central synapses by reducing discharges of impulses from muscle spindles by tenotomy procedures. The results obtained suggest at first sight that the reverse occurs. Figure 56 summarises the positive findings obtained in that series of investigations, viz. reflex responses from tenotomized muscles were enhanced in two monosynaptic pathways and this effect was prevented by spinal transection. This suggested that the gamma system reset itself at a higher level of activity following tenotomy and caused increased spindle discharges with consequent overuse of the monosynaptic Ia connexions. If this is so, there is experimental support for the

hypothesis that excess use leads to enduring increase of synaptic efficacy. Some evidence for this has been cited in respect of post-tetanic potentiation at neuromuscular junctions, where there is an increased frequency of the miniature end-plate potentials (Brooks, 1956; Liley, 1956; Hubbard, 1959), which represent quantal emission of chemical transmitter from presynaptic terminals (Katz, 1958). However, this is only for a few minutes and may be irrelevant to the long enduring changes.

DiGiorgio (1943, 1947) describes postural and reflex asymmetries which were induced in dogs by cerebellar lesions and which persisted up to nine days after spinal transection. In these experiments, she subjected dogs and rabbits to resection of the lobus ansa paramedialis of the cerebellum permitting survival for varying intervals up to 25 days before mid-thoracic spinal cord section was performed. Asymmetry both of reflexes and tonus appeared within 7 - 9 hours for rabbits and two days for dogs. Her techniques were of necessity imprecise, and the observations not quantative. However, there was a suggestion that an enduring increase in excitability of the spinal reflexes resulted from the prolonged asymmetrical barrage of descending impulses due to the unilateral cerebellar lesion. A more convincing demonstration of lasting changes in synaptic organization due to excess use is provided by Morrell (1959). He produced continuous neuronal bombardment, via the corpus callosum, of an area of cerebral cortex, by placing a primary epileptogenic lesion in the symmetrical area of the contralateral cortex. Finally, after several weeks, the removal of the primary focus did not alter the increased excitability of the

previously normal cortex subjected to continuous neuronal bombardment. The development of hyperexcitability and seizure in this area could be prevented either by section of corpus callosum, or by a subpial partial isolation of the area before or within the first 24 hours after production of the primary epileptogenic lesion in the contralateral cortex. He further demonstrated histological changes of the ribonucleic acid distribution in cell populations subjected to continuous synaptic bombardment, so supporting previous results (Hamberger and Hyden, 1949; Brattgard and Hyden, 1952).

In attempting to explain the results of tenotomy, a possible hypothesis depends upon the activation of annulospinal endings by impulses in the gamma afferent fibres (Leksell, 1945; Hunt, 1951; Kuffler et al, 1951; Granit, 1955). Furthermore, these primary endings are extremely sensitive to mechanical stimuli and certainly could not be silenced by tenotomy or plaster (Matthews, 1933; Hunt and Kuffler, 1951; Kobayshi et al, 1952; Granit, 1955; Lundberg and Winsbury, 1960a and b).

Possibly the tenotomy reflexly produces an increased discharge from gamma motoneurones, with as a consequence an increased discharge from the annulospinal endings, even though they have much mechanical stress removed by the tenotomy. However, the actions of the gamma system under conditions of chronic spindle deloading or overloading are not well understood, and a detailed knowledge of the afferent activity of spindles under such conditions is necessary before definite conclusions may be drawn from such investigations.

Section B describes investigations of changes in

reflex activity in polysynaptic systems, produced by chronic spinal transection. Changes in the patterns of reflex behaviour have been observed in chronic spinal animals and an electrophysiological analysis has been made of the cutaneous reflexes into various muscle nerves. From these results a number of generalizations emerge which hold for both acute and chronic spinal animals. Descriptions of flexion reflexes provoked by stimulation of non-medullated C fibres in the cat have been given (Voorhoeve, Laporte and Bessou, 1959; Laporte and Bessou, 1957; Laporte and Böer, 1955) and it is of interest that the only striking difference between the reflexes of the acute and chronic spinal animals is the very prolonged duration at higher stimulus intensities, of the discharges particularly to ipsilateral flexors. Two explanations, not mutually exclusive, are provided for the slow onset of the reflex changes after spinal section, including the enhanced discharges to ipsilateral flexors in respect of the highest threshold components of the reflex discharge. This may be attributed either to slow changes following release from supraspinal inhibitory influences or the growth of new connections. It appears that the effects of use and disuse on synaptic function are not readily investigated with even the simpler polysynaptic pathways such as the flexor reflex.

The results described in the final section may be summarised as a histogram (Figure 57). Denervation of all but one of a group of synergic hindlimb muscles, results in marked ehhancement of the ventral root monosynaptic reflex evoked from the nerve to the spared muscle, by comparison with the corresponding contralateral

reflex. The degree of reflex enhancement is unaltered by lower thoracic spinal transection at the time of hindlimb nerve sections. The results have been fully discussed, and three alternative explanations of the observed changes have been proposed.

The first suggests that the nerve sections lead to increased gamma activation of stretch receptors in the remaining innervated member of the synergic muscle group during activity. This results in increased proprioceptive bombardment and consequent excess use of synapses. Synaptic efficacy is enhanced by this excess use, resulting in enhancement of the monosynaptic reflex responses.

The second proposed that degenerative changes in the fine central terminals of severed afferent pathways probably caused non-specific sprouting of adjacent fibres resulting in the formation of new synaptic connexions between intact afferent terminal sprouts and homonymous as well as heteronymous motoneurones. Increased synaptic potency resulting from the formation of new synapses on their motoneurones results in enhancement of monosynaptic reflexes evoked by nerves to spared muscles.

There is nothing to recommend the final postulate which depended upon the development of hypersensitivity of the post-synaptic membrane of motoneurones innervating spared muscles.

The first two mechanisms may operate singly or in combination and in the absence of definite evidence the first of these alternatives is most likely. In spite of the surprising result of prior spinal transection, it is most attractive to postulate that the nerve section procedure leads to increased gamma activity, with

consequent increases in afferent discharge from spared muscles. This accords with the clear results of Section A, that increased synaptic usage results in enhanced synaptic efficacy with larger monosynaptic reflexes from these pathways. Gamma overactivity is common to the explanation of both the first and final section results. Further experimental testing is essential to support this postulate. It has been shown that the effects of overuse and disuse of central nervous synapses are best studied in the simplest nervous pathways. It is important to avoid complications introduced by operative interruption of these pathways. The simplest levels of the mammalian central nervous system have been shown here to demonstrate a remarkable degree of plasticity of function and structure. Such plasticity can no longer be regarded as a special property of the higher levels of the central nervous system.

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REFERENCES

AUERBACH, W. , (1897) Neurologisches Centralblatt n.10 .

AXELSSON, J. and THESLEFF, S. (1959) J.Physiol. 147, 178-193.

BAZETT, H.C. and PENFIELD, W.G. (1922) Amer.J.Physiol. 134, 177-185.

BERANEK, R. and HNIK, P. (1959) Science. 130, 981-2 .

BRATTGAARD, S.O. and HYDEN, H. (1952) Acta Radiol. (Supp.94) 1-48.

BROOKS, V.B. (1956) J.Physiol. 134, 264-277.

BUCHTHAL, F. and JAHN, U. (1957) Acta physiol. scand. 42, Supp.145, 25-27

CAJAL, S.R. (1904) Textura del sistema nervioso del hombre y de los vertebrados. Madrid, 1904.

CAJAL, S.R. (1908) Arch. Fisiol. 5. 'Neuron theory or reticular theory'. Translation by Purkiss and Fox , Madrid. 1954.

CAJAL, S.R. (1909) 'Histologie du système nerveux de l'homme et des vertebres' Vol.I Paris: Maloine, 1909.

CAJAL, S.R. (1911) op. cit. Vol.II , 1911.

CANNON, W.B. and HAIMOVICI, H. (1939) Amer.J.Physiol. 126, 731-740.

CANNON, W.B. and ROSENBLUETH, A. (1949) 'The supersensitivity of denervated structures,' Macmillan: New York.

CLARK, G. (1940) Amer. J. Physiol. 130, 712-722 .

CLOSE, J.R. and TODD, F.N. (1959) J. Bone and Joint Surg. 41A, 189-208.

COOMBS, J.S., CURTIS, D.R. and ECCLES, J.C. (1957a) J.Physiol. 139, 198-231.

COOMBS, J.S., CURTIS, D.R. and ECCLES, J.C. (1957b) J.Physiol. 139, 232-249.

COOPER, S. and ECCLES, J.C. (1930) J.Physiol. 69, 377-385.

CREED, R.S., DENNY-BROWN, D., ECCLES, J.C., LIDDELL, E.G.T. and SHERRINGTON, C.S. (1932) 'Reflex activity of the spinal cord.' Oxford Univ.Press, London

DENNY-BROWN, D. and ROBERTSON, E.G. (1935) Brain. 58, 256-310.

DE ROBERTIS, E. (1956) J.Biochem. Biophys. Cytol. 2, 503-513.

DE ROBERTIS, E. (1957) J.Biophys. Biochem. Cytol. 3, 611-614.
and FERRIERA, A.V.

DE ROBERTIS, E. and FRANCHI, C.M. (1956) J.Biophys. Biochem.Cytol.2, 307-318.

DI GIORGIO, A.M. (1943) Arch.Fisiol.43, 47-63.

DI GIORGIO, A.M. (1947) Arch.Fisiol.47, 254-261.

DOWNMAN, C.B.B., ECCLES, J.C. and McINTYRE, A.K. (1951) Proc. Univ. Otago med. School. 29, 45.

DOWNMAN, C.B.B., ECCLES, J.C. and McINTYRE, A.K. (1953) J.comp.Neurol.98, 9-36.

ECCLES, J.C. (1944) J.Physiol. 103, 253-266.

ECCLES, J.C. (1953) The Neurophysiological Basis of Mind: The Principles of Neurophysiology. Oxford, Clarendon Press.

ECCLES, J.C. (1957) The Physiology of Nerve Cells . The Johns Hopkins Press , Baltimore,

ECCLES, J.C. (1958) Perspectives in Biology and Medicine. 1, 379-394.

ECCLES, J.C. (1959) C.I.O.M.S. Symposium on Brain Mechanisms and Learning. Montevideo , 1959. To be published 1961, C.I.O.M.S.

ECCLES, J.C., ECCLES, R.M. and LUNDBERG, A. (1957) J.Physiol. 137, 22-50 .

ECCLES, J.C., ECCLES, R.M. and MAGNI, F. (1960) J.Physiol. In Press

ECCLES, J.C. and KRNJEVIC, K. (1959) J.Physiol.149, 274-287.

ECCLES, J.C., KRNJEVIC, K. and MILEDI, R. (1959) J.Physiol.145, 204-220.

ECCLES, J.C., LIBET, B. and YOUNG, R.R. (1958) J.Physiol.143, 11-40.

ECCLES, R.M. and LUNDBERG, A. (1959) J.Physiol.147, 565-584.

ECCLES, J.C. and McINTYRE, A.K. (1953) J.Physiol.121, 492-516.

ECCLES, J.C. and RALL, W. (1951) J.Neurophysiol. 14, 353-376.

ECCLES, J.C. and SHERRINGTON, C.S. (1930) Proc.Roy. Soc.106B, 326.

ECCLES, R.M. and WESTERMAN, R.A. (1959) Nature, Lond.184, 460-1

FOREL, A. (1887) Einige hirnanatomische Betrachtungen und Ergebnisse. Arch.f.Psychiatrie u.Nervenkrankheiten . Bd XVIII , 1887.

FULTON, J.F. (1943) Physiology of the Nervous System . Oxford University Press , London.

FULTON, J.F. and KELLER, A.D. (1932) THE SIGN OF BABINSKI . A Study of the evolution of cortical dominance in primates. Charles C Thomas, Baltimore.

FULTON, J.F. and SHERRINGTON, C.S. (1932) J.Physiol. 75, 17-22.

GEHUCHTEN, V. (1897) La structure des centres nerveux: La moelle epiniere. Anatomie du systeme nerveux de l'homme 2nd. ed. -L'anatomie fine de la cellule nerveuse. Louvain.

GERARD, R.W. (1949) Amer.J.Psychiat. 106, 161-173.

GERLACH, J.von (1872) The Spinal Cord . In : S.Stricker, "A manual of histology ." (English Translation) London: New Sydenham Society, 1872.

GOLGI, C. (1910) Atti Soc. ital. progr. sc. 3rd.réunion.

GRANIT, R. (1955) Receptorsand Sensory Perception. New Haven: Yale University Press. 1955

GRANIT, R. (1957) Premier Congres International des Sciences Neurologiques. Brussels. 21-28 Juillet . Premiere Journee Commune , pp63-80.

HAGBARTH, K.E. (1952) Acta physiol. scand. 26, Supp.94, 1-58.

HAGBARTH, K.E. (1960) J.Neurol. Neurosurg.Psychiat. 23, 222-227.

HAGBARTH, K.E.and NAESS, K.(1950a) Acta physiol. scand. 21, 336-361.

HAMBERGER, C.A.and HYDEN, H. (1948) Acta Oto-Laryngol. 17

HAMMOND, W.S.and HINSEY, J.C. (1945) J.comp. Neurol. 83, 79-89.

HEAD, H. and RIDDOCH, G. (1917) Brain. 40, 188-263.

HEBB, D.O. (1949) The organization of behaviour. New York: John Wiley & Sons.

HELANDER, E.(1957) Acta physiol. scand. 41, Supp.141.

HELANDER, E.(1958) Nature, Lond. 182, 1035.

HELD, H (1895-1897) Beitrage zur struktur der nervenzellen und ihrer Fortsatz Arch. f. Anat. u. Physiol. Anat. Abt. 1895 et1897.

HESS, A. (1957) Biol. Rev. 32, 250 .

HILGARD, E.R.and MARQUIS, D.M.(1940) Conditioning and Learning . New York: Appleton-Century-Crofts.

HIS, W. (1866-7). Zur Geschichte des menschlichen Ruckenmarks und der Nervenwurzeln. Oktober, 1886.

HNIK, P. (1960). Experientia. 16, 326 - 327.

HODGKIN, A.L. (1958). Proc.Roy.Soc. London. B 148 : 1.

HODGKIN, A.L. & HUXLEY, A.F. (1952). J.Physiol. 117, 500.

HOLMQVIST, B., LUNDBERG, A. & OSCARSSON, O. (1960). Arch.ital. Biol. 98, 60 - 80.

HOUSEHOLDER, A.S. & LANDAHL, M.D. (1945). Mathematical Biophysics of the Central Nervous System, Bloomington. Principia Press.

HUBBARD, J.I. (1959). Nature. London, 184] 1945 - 1947.

HUBBARD, J.I. & OSCARSSON, O. J. Physiol. In Press.

HUNT, C.C. (1951). J. Physiol. 115, 456 - 469.

HUNT, C.C. (1954). J. Gen. Physiol. 38, 117 - 131.

HUNT, C.C. & KUFFLER, S.W. (1951a). J. Physiol. 113, 283 - 297.

HUNT, C.C. & KUFFLER, S.W. (1951b). J. Physiol. 113, 298 - 315.

HUNT, C.C. & PAINTAL, A.S. (1958). J. Physiol. 143, 195 - 212.

HUNT, C.C. & PERL, E.R. (1960). Physiol. Rev. 40, 538 - 579.

JEFFERSON, A.A. & SCHLAPP, W. (1953) in: Ciba Foundation Symposium on the Spinal Cord. London - Churchill, J.& A. pp.99 - 117.

JUNG, R. (1953). in: Handbuch der innieren Medizin. Berlin, Gottingen & Heidelberg - Springer.

KATZ, B. (1958). Bull. Johns Hopkins Hosp. 112 (b), 275 - 295.

KOBAYASHI, Y., OSHIMA, K.& TASAKI, I. (1952). J.Physiol. 117, 152 - 171.

KOLLIKER, R.A. von. (1893). Handbuch der Gewebelehre des Menschen, Bd.2; Nerven system des Menschen und der Thiere. Leipzig

KOLMODIN, G.M. (1957). Acta Physiol. Scand. 40, Supp. 139.

KOLMODIN, G.M. & SKOGLUND, C.R. (1954). Experientia (Basel) 10, 505-506.

KONORSKI, J. (1948). Conditioned reflex and neuron organization. Cambridge: Cambridge University Press.

KUFFLER, S.W., HUNT, C.C. & QUILLIAM, J.P. (1951). J.Neurophysiol. 14, 29 - 54.

LAPORTE, Y. & BESSOU, P. (1957). J. Physiol. Paris. 49, 1025-1043.

LAPORTE, Y. & BOER, A (1955). C.R. Soc. Biol., Paris. 149, 808-810.

LAPORTE, Y., LUNDBERG, A. & OSCARSSON, O. (1956). Acta Physiol. Scand. 36, 175 - 187.

LARRABEE, M.G. & BRONK, D.W. (1947). J. Neurophysiol. 10, 139-154.

LESKELL, L. (1945). Acta. Physiol. Scand. 10, Suppl. 31, 1 -

LILEY, A.W. (1956b). J. Physiol. 133, 571 - 587.

LIU, C.N. & CHAMBERS, W.W. (1955). Amer. J. Physiol. 183, 640 - 641.

LLOYD, D.P.C. (1943). J. Neurophysiol. 6, 111 - 120.

LLOYD, D.P.C. (1943b). J. Neurophysiol. 6, 293 - 316.

LLOYD, D.P.C. (1943c). J. Neurophysiol. 6, 317 - 328.

LLOYD, D.P.C. (1946). J. Neurophysiol. 9, 421 - 438.

LLOYD, D.P.C. (1949 - 1950). J. Gen. Physiol. 33, 147 - 170.

LLOYD, D.P.C. (1952a). Electrical Manifestations of action in neurones. In: The biology of mental health and disease, 135-161. New York - Hoeber, P.B.

LLOYD, D.P.C. (1957). J. Gen. Physiol. 40, 435 - 450.

LLOYD, D.P.C., HUNT, C.C. & MC INTYRE, A.K. (1955). J. Gen. Physiol. 38, 307.

LLOYD, D.P.C. & MC INTYRE, A.K. (1950). J. Neurophysiol. 13, 39 - 54.

LORENTE de NO, R. (1934). J. Psychol. Neurol. Lpz. 45, 381.

LORENTE de NO, R. (1934). J. Psychol. Neurol. Lpz. 46, 113-177.

LORENTE de NO, R. (1938) in: Physiology of the nervous system.

London - Fulton, J.F. Oxford University Press.

LUNDBERG, A. & WINSBURY, G. (1960a). Acta. Physiol. Scand. 49, 155 - 164.

LUNDBERG, A. & WINSBURY, G. (1960b). Acta. Physiol. Scand. In press.

MACHT, M.B. (1943). Fed. Proc. 2, 32.

MACHT, M.B. & KUHN, R.A. (1948). Arch. Neurol.Psych. 59, 754.

MATTHEWS, B.H.C. (1933). J. Physiol. 78, 1 - 33.

MILEDI, R. (1960). J. Physiol. 151, 1 - 23.

MORRELL, F. (To be published 1961). CIOMS Conference on Brain Mechanisms and Learning - Montevideo Uraguay, Aug.1959.

MURRAY, J.G. & THOMPSON, J.W. (1957). Brit. Med. Bull. 13, 213

MC COUCH, G.P. (1924). Amer. J. Physiol. 71, 137.

MC COUCH, G.P., AUSTIN, G.M., LIU, C.N. & LIU, C.Y. (1958). J. Neurophysiol. 21, 205 - 216.

MC INTYRE, A.K. (1951). Proc. Univ. Otago Med. School. 29, 16.

MC INTYRE, A.K. (1953). 19th International Physiological Congress. Montreal.

MC INTYRE, A.K., BRADLEY, K. & BROCK, L.G. (1959). J. Gen. Physiol. 42, 931 - 958.

NASLEDOV, G.A. (1957). Sechenov J. Physiol. 43, 1040-1049.

OSCARSSON, O. (1957). Acta. Physiol. Scand. 42, Supp. 146.

OSCARSSON, O. (1960). Acta Physiol. Scand. 49, 171 - 183.

PETERSEN, I. (1952). Acta Physiol. Scand. 26, Supp..96.

RARICK, G.L. (1960). in: Science and medicine of exercise and sport. New York.- Harper Bros.

RASHEVSKY, N. (1938). Mathematical Biophysics. Chicago - University

of Chicago Press.

REXED, B. (1954). J. Comp. Neurol. 100, 297 - 379.

RUDIN, D.O. & EISENMAN, G. (1951). Science. 114, 300.

RUDIN, D.O. & EISENMAN, G. (1954). J. Gen.Physiol. 37, 505 - 538.

SAHS, A.L. & FULTON, J.F. (1940). J. Neurophysiol. 3, 258 - 268.

SANDERS, F.K. & YOUNG, J.Z. (1946). J. exp. Biol. 22, 203 - 212.

SHERMAN, I,, TIGAY, E., ARIEFF, A., & SCHILLER, M. (1949). J. Neurophysiol. 12, 1 - 15.

SHERRINGTON, C.S. (1897) in: Foster's textbook of physiology. London - Seventh edition. 3, 929.

SHERRINGTON, C.S. (1899). Medico - Chirurgical Transactions. 82, 449 - 477.

SHERRINGTON, C.S. (1910). J. Physiol. (Lond). 40, 28 - 121.

SHERRINGTON, C.S. (1913). Proc. Roy. Soc. 86B, 233-261.

SHERRINGTON, C.S. (1925). Proc. Roy. Soc. London B 97, 519 - 545.

SHERRINGTON, C.S. (1929). Proc. Roy. Soc. London B 105, 332-362.

SHERRINGTON, C.S. & SOWTON, S.C.M. (1915).J. Physiol. 49, 331.

SHERRINGTON, C.S. (1906b). J. Physiol. 34, 1 - 50.

SHERRINGTON, C.S. (1906a). The integrative action of the nervous system (Silliman Memorial Lectures). London - Constable & Co. Ltd.

SHERRINGTON, C.S. (1900). In: Schafer, Textbook of Physiology. 2, 782-883.

SHERRINGTON, C.S. & SOWTON, S.C.M. (1911). Proc. Roy. Soc. 83B, 435 - 446.

SOLLMANN, T. (1957). A manual of pharmacology and its applications to therapeutics and toxicology. 8th Edition. Philadelphia - W.B. Saunders & Co.

SPIEGEL, E., (1927). Der tonus skelettmuskulatur. Berlin.

SZENTAGOTHAI, J. & ALBERT, A. (1955). Acta. Morphol. 5, 43 - 51.

TASAKI, I. (1953). Nervous Transmission. Springfield, Ill. - Thomas, C.C.

TEASDALE, R.D. & STAVRAKY, G.W. (1953). J. Neurophysiol. 16, 367 - 375.

THOMSEN, P., ALTAMIRANO, M. & LUCO, J.V. (1942). Medicina (Buenos Aires) 3, 67.

THOMSEN, P. & LUCO, J.V. (1946). Proc. Soc. Exper. Biol. and Med. 60, 381 - 382.

TOENNIES, J.F. (1949). Arch. Psychiat. 182 : 478.

VOORHOEVE, P.E., LAPORTE, Y. & BESSOU, P. (1959). Acta. Physiol. Pharm. Neerl. 8, 299.

WALDEYER-HARTZ, H.W.G. (1891). Deutsche Med. Wchnschr. 17, 1213, 1244, 1287, 1331, 1352.

WHITTERIDGE, D. (1948). In: Winton, F.R. & Bayliss, L.E. Human Physiology (3rd Edition). London - Churchill, J. & A.

WRIGHT, S. (1945). Applied physiology. London - Oxford University Press.

YOUNG, J.Z. (1946). The Lancet. 2, 109 - 113.

Table 1. Muscle Wasting.

(Unilateral Tenotomy and plaster immobilization - 20 cats)

The figures quoted are the mean % wasting of the muscle groups in the tenotomized hindlimb, relative to those of the normal hindlimb. Standard Errors of the means are in parenthesis. Figures asterisked * are statistically significant with 1.0% confidence limits.

Hindlimb Muscle Groups	% Wasting of Tenotomized side Mean	(± S.E)
Quadriceps Femoris	* 19.1%	(± 2.6)
Adductor Femoris and Adductor Longus.	-	-
Biceps Femoris, Semitendinosus, Semimembranosus.	7.0%	(± 2.4)
Medial and Lateral Gastrocnemius, Soleus, Plantaris (Tenotomized)	* 43.8%	(± 3.1)
Peroneal Muscles	5.0%	(± 1.8)
Extensor Digitorum Longus and Tibialis Anterior	5.5%	(± 2.8)
Tibialis Posterior, Flexor Digitorum Longus and Flexor Hallucis Longus. (Tenotomized)	* 24.2%	(± 3.9)

Table 2. Summary of Monosynaptic Reflexes.

(Unilateral tenotomy and plaster immobilization - 20 cats)

The figures quoted are the mean of the ratios of corresponding reflexes from tenotomized side / normal side for the given muscle nerve. Thus 1.00 indicates symmetry of corresponding reflex responses. The figures in parenthesis are Standard Errors of the means, and those results asterisked * differ significantly from 1.00 with 1.0% confidence limits.

Nerve	Monosynaptic Reflex Spike		Post-tetanically Potentiated Spike	
	Mean	(± S.E)	Mean	(± S.E)
Biceps Semitendinosus (Control)	1.15	(±0.106)	1.11	(±0.055)
Peroneal (Control)	0.97	(±0.085)	0.85	(±0.090)
Medial and Lateral Gastrocnemius (Tenotomized Group)	* 1.89	(±0.184)	*1.44	(±0.104)
Plantaris (Tenotomized Group)	* 1.88	(±0.200)	1.24	(±0.096)
Flexor Digitorum Longus, Flexor Hallucis Longus and Tibialis Posterior (Tenotomized Group)	* 1.69	(±0.194)	1.30	(±0.130)

Table 3 (a) Central Latencies

(Unilateral Tenotomy and plaster immobilization series)

Figures are mean central latencies in msec. with Standard Errors of the means in parenthesis.

Nerves	Normal Side Mean (± S.E)	Tenotomized Side Mean (± S.E)
	msec	msec
Control Group (Biceps Semitendinosus and Peroneal)	0.96 (±0.034)	0.98 (±0.034)
Tenotomized Group (Gastrocnemii, Plantaris, Flexor digitorum longus and hallucis longus)	1.00 (±0.031)	0.87 (±0.036)

In the tenotomized group the shortening of central latency by 0.11 msec. is statistically significant with 1.0% confidence limits.

Table 3 (b) Conduction Velocities

Figures are mean conduction velocities in m/sec with Standard Errors in parenthesis.

Nerves	Normal Side Mean (± S.E)	Tenotomized Side Mean (± S.E)
	m/sec	m/sec
Control Group (as above)	89.3 (± 4.4)	89.6 (± 4.8)
Tenotomized Group (as above)	92.7 (± 2.8)	93.9 (± 2.9)

Differences of conduction velocity between the tenotomized muscles and the corresponding intact muscles are not significant at a 50% level.

Table 4. Muscle Wasting.

(Unilateral Tenotomy alone - 21 cats)

The description of this Table is the same as that heading Table 1.

Hindlimb Muscle Groups	% Wasting on Tenotomized side Mean	(± S.E)
Quadriceps Femoris	7.4%	(± 2.7)
Adductor Femoris and Adductor Longus	6.9%	(± 2.5)
Biceps Femoris, Semitendinosus, Semimembranosus	6.8%	(± 2.2)
Medial and Lateral Gastrocnemius, Soleus, Plantaris (Tenotomized)	* 24.9%	(± 3.8)
Peroneal Muscles	6.3%	(± 5.3)
Extensor Digitorum Longus and Tibialis Anterior	11.4%	(± 2.0)
Tibialis Posterior, Flexor Digitorum Longus and Flexor Hallucis Longus (Tenotomized)	* 18.0%	(± 4.7)

Table 5 (a) Summary of Monosynaptic Reflexes.

(Unilateral tenotomy series - 21 cats)

The description of this Table is the same as that heading Table 2.

Monosynaptic reflexes recorded monophasically from ventral roots				
Nerve	Monosynaptic Reflex Spike Mean	(± S.E)	Post-tetanically Potentiated Spike Mean	(± S.E)
Biceps Semitendinosus (Control)	1.25	(±0.15)	1.08	(±0.06)
Peroneal (Control)	1.02	(±0.06)	1.05	(±0.05)
Medial and Lateral Gastrocnemius (Tenotomized Group)	* 1.59	(±0.22)	1.25	(±0.18)
Plantaris (Tenotomized Group)	* 1.76	(±0.32)	1.56	(±0.29)
Flexor Digitorum Longus Group (Tenotomized Group)	* 2.14	(±0.29)	1.76	(±0.17)

Table 5 (b) Summary of Spinocerebellar Tract Responses

(Unilateral tenotomy series - 21 cats)

Figures quoted are the means of the ratios of corresponding spinocerebellar tract responses from the tenotomized side / normal side, for the given muscle nerve. Thus 1.00 indicates symmetry of corresponding tract reflex responses. The figures in parenthesis are Standard Errors of the means, and those results asterisked * are significant with 1% confidence limits after application of the Student t-test.

Spinocerebellar Tract responses recorded from hemisected spinal cord.				
Nerve	D.S.C.T. Reflex (Ipsilateral) Mean	(± S.E)	V.S.C.T. Reflex (Contralateral) Mean	(± S.E)
Biceps Semitendinosus and Semimembranosus (Control)	1.14	(±0.24)	0.95	(±0.21)
Peroneal (Control)	1.14	(±0.19)	0.93	(±0.14)
Sural (Control)	1.05	(±0.11)		
Medial and Lateral Gastrocnemius and Plantaris. (Tenotomized Group)	* 1.47	(±0.10)	0.94	(±0.09)
Flexor Digitorum Longus and Flexor Hallucis Longus (Tenotomized Group)	* 1.55	(±0.19)	0.98	(±0.09)

Table 6 (a) Central Latencies

(Unilateral Tenotomy Series)

Figures are mean central latencies in msec. with Standard Errors of the means in parenthesis.

Nerve	Normal Side Mean (± S.E)	Tenotomized Side Mean (± S.E)
	msec	msec
Control Group (Biceps Semitendinosus and Peroneal)	0.86 (±0.031)	0.86 (±0.031)
Tenotomized Group (Gastrocnemii, Plantaris, Flexor digitorum longus and hallucis longus)	1.03 (±0.043)	0.92 (±0.032)

In the tenotomized group the shortening of central latency by 0.11 msec. is statistically significant with 1% confidence limits.

Table 6 (b) Conduction Velocities

Figures are mean conduction velocities in m/sec. with Standard Errors.

Nerve	Normal Side Mean (± S.E)	Tenotomized Side Mean (± S.E)
	m/sec	m/sec
Control Group (as above)	96.0 (± 3.9)	95.4 (± 4.2)
Tenotomized Group (as above)	95.9 (± 4.4)	94.2 (± 4.1)

Differences of conduction velocity between the tenotomized muscles and the corresponding intact muscles are not significant at a 50% level.

Table 6 (c) Absolute Refractory Periods - Tenotomy Series

Figures give absolute refractory periods in msec. with Standard Errors in parenthesis.

Nerve	Normal Side Mean (± S.E)	Operated Side Mean (± S.E)
	msec	msec
Control Group (Biceps Semitendinosus and Peroneal)	0.68 (±0.04)	0.65 (±0.04)
Tenotomized Group (Gastrocnemii, Plantaris, Flexor digitorum longus and hallucis longus)	0.64 (±0.04)	0.66 (±0.05)

There are no significant differences for the two groups on each side.

Table 7. Muscle Wasting.

(Unilateral Tenotomy with Spinal cord transection - 8 cats)

The figures quoted are the mean % wasting of the muscle groups of the tenotomized hindlimb relative to those of the normal hindlimb. Standard Errors of the means are in parenthesis. Figures asterisked * are statistically significant with 1.0% confidence limits.

Hindlimb Muscle Groups	% Wasting on Tenotomized side Mean	(± S.E)
Quadriceps Femoris	2.6%	(± 1.7)
Adductor Femoris and Adductor Longus	2.9%	(± 2.7)
Biceps Femoris, Semitendinosus, Semimembranosus.	7.0%	(± 3.0)
Medial and Lateral Gastrocnemius, Soleus, Plantaris (Tenotomized)	*13.5%	(± 5.7)
Peroneal Muscles	12.5%	(± 4.4)
Extensor Digitorum Longus and Tibialis Anterior	8.0%	(± 1.9)
Tibialis Posterior, Flexor Digitorum Longus and Flexor Hallucis Longus (Tenotomized)	*20.5%	(± 3.6)

Table 8 (a) Summary of Monosynaptic Reflexes.

(Unilateral tenotomy with spinal cord transection - 8 cats)

The description of this Table is the same as that heading Table 2 except that no variations of figures from 1.00 are statistically significant at even a 10% level.

Monosynaptic reflexes recorded monophasically from ventral roots

Nerve	Monosynaptic Reflex Spike Mean	(± S.E)	Post-tetanically Potentiated Spike Mean	(± S.E)
Biceps Semitendinosus (Control)	0.98	(±0.075)	0.99	(±0.075)
Peroneal (Control)	1.06	(±0.077)	1.06	(±0.041)
Medial and Lateral Gastrocnemius and Plantaris (Tenotomized Group)	0.98	(±0.061)	0.99	(±0.054)
Flexor Digitorum Longus and Flexor Hallucis Longus (Tenotomized Group)	1.07	(±0.107)	1.04	(±0.037)

Figure 8 (b) Summary of Spinocerebellar Tract Responses.
(Unilateral tenotomy with spinal cord transection - 8 cats)

The description of this Table is the same as that heading Table 5 (b) except that no variations of figures from 1.00 are statistically significant at even a 10% level.

Spinocerebellar tract responses recorded from hemisected spinal cord.				
Nerve	D.S.C.T. Reflex (Ipsilateral) Mean	(± S.E)	V.S.C.T. Reflex (Contralateral) Mean	(± S.E)
Biceps Semitendinosus and Semimembranosus (Control)	1.14	(±0.68)	1.24	(±0.30)
Peroneal (Control)	0.85	(±0.27)	1.19	(±0.27)
Medial and Lateral Gastrocnemius and Plantaris (Tenotomized Group)	1.20	(±0.43)	1.37	(±0.35)
Flexor Digitorum Longus and Flexor Hallucis Longus (Tenotomized Group)	0.91	(±0.87)	0.91	(±0.76)

Table 9. Central Latencies.

(Unilateral tenotomy with spinal cord transection - 8 cats)

Figures are mean central latencies in msec. with Standard Errors of the means in parenthesis.

Nerve	Normal Side Mean (± S.E)	Tenotomized Side Mean (± S.E)
	msec	msec
Control Group (Biceps Semitendinosus and Peroneal)	1.06 (±0.041	1.08 (±0.050)
Tenotomized Group (Gastrocnemii, Plantaris, Flexor digitorum longus and hallucis longus)	1.04 (±0.032)	1.07 (±0.033)

Differences between central latencies of nerves to normal and tenotomized muscle groups are not statistically significant at the 10% level.

Table 10. Muscle Wasting.

(Nerve Section Series – 20 cats)

The figures quoted are the mean % wasting of the muscle groups in the operated hindlimb relative to those of the normal side. Standard Errors of the means are in parenthesis. Figures asterisked * are statistically significant with 1.0% confidence limits.

Hindlimb Muscle Groups	% Wasting on the operated side Mean	(± S.E)
Quadriceps Femoris	2.6%	(± 1.3)
Adductor Femoris and Adductor Longus	0.8%	(± 2.2)
Biceps Femoris, Semitendinosus, Semimembranosus.	4.0%	(± 1.3)
(Medial and Lateral Gastrocnemius, Soleus, Plantaris) Denervated (L.G., S., PL.)	* 43.6%	(± 3.5)
Spared (M.G.)	1.3%	(± 1.1)
Peroneal Muscles	7.3%	(± 0.8)
Extensor Digitorum Longus and Tibialis Anterior	4.1%	(± 1.1)
(Tibialis Posterior, Flexor Digitorum Longus and Hallucis Longus) Denervated (F.H.L & T.P)	* 41.5%	(± 6.4)
Spared (F.D.L)	0.3%	(± 2.2)

Table 11. Summary of Monosynaptic Reflexes.

(Nerve Section series - 20 cats)

The figures quoted are the means of the ratios of corresponding reflexes from the operated side / normal side for the given muscle nerves. Thus 1.00 indicates symmetry of corresponding reflex responses. The figures in parenthesis are Standard Errors of the means, and those results asterisked * differ significantly from 1.00 at the 1% level.

Monosynaptic reflexes recorded monophasically from ventral roots				
Nerve	Monosynaptic Reflex Spike Mean	(± S.E)	Post-tetanically Potentiated Spike Mean	(± S.E)
Biceps Semitendinosus (Control)	1.09	(±0.062)	1.03	(±0.041)
Peroneal (Control)	* 1.11	(±0.048)	1.07	(±0.004)
Quadriceps Femoris (Control)	Insufficient figures to analyse.			
Lateral Gastrocnemius (Spared Group)	* 2.13	(±0.27)	* 1.39	(±0.16)
Medial Gastrocnemius (Spared Group)	* 2.57	(±0.30)	1.20	(±0.10)
Flexor Digitorum Longus (Spared Group)	* 2.21	(±0.19)	* 1.35	(±0.10)

Table 12 (a) Central Latencies.

(Nerve Section series - 20 cats)

Figures give mean central latencies in msec. with Standard Errors of the means in parenthesis.

Nerves	Normal Side Mean	(± S.E)	Operated Side Mean	(± S.E)
	msec.		msec.	
Control Group (Biceps Semitendinosus, Peroneal and Quadriceps)	1.08	(±0.07)	1.08	(±0.08)
Spared Group (Medial /or Lateral gastrocnemius and Flexor digitorum longus)	1.10	(±0.08)	0.96	(±0.08)

The shortening of central latency by 0.14 msec. in the group of spared muscles is significant at the 1% level.

Table 12 (b) Conduction Velocities

Figures give mean conduction velocities in m/sec with Standard Errors of the means in parenthesis.

Nerves	Normal Side Mean	(± S.E)	Operated Side Mean	(± S.E)
	m/sec		m/sec	
Control Group (as above)	83.1	(± 4.4)	83.3	(± 4.6)
Spared Group (as above)	83.6	(± 5.9)	83.1	(± 6.7)

The differences of conduction velocity between the two sides is not significant at the 50% level.

Table 12 (c) Absolute Refractory Periods - Nerve Section Series

Figures are absolute refractory periods in msec. with Standard Errors in parenthesis

Nerves	Normal Side Mean	(± S.E)	Operated Side Mean	(± S.E)
	msec		msec	
Control Group (Biceps Simitendinosus, Peroneal and Quadriceps)	0.66	(±0.01)	0.65	(±0.04)
Spared Group (Medial / or Lateral gastrocnemius and Flexor digitorum longus	0.70	(±0.03)	0.70	(±0.04)

There are no significant differences for the two groups on each side.

Table 13. Muscle Wasting

(Nerve Section Series, with spinal cord transection - 7 cats)

The description of this Table is the same as that heading Table 10.

Hindlimb Muscle Groups	% Wasting of operated side Mean	(± S.E)
Quadriceps Femoris	*9.7%	(± 3.8)
Adductor Femoris and Adductor Longus	2.5%	(± 1.3)
Biceps Femoris, Semitendinosus, Semimembranosus.	1.1%	(± 2.4)
Medial and Lateral Gastrocnemius, Soleus, Plantaris) Denervated (L.G., S., PL.)	*15.6%	(± 7.4)
Spared (M.G) Weight gain	+ 8.8%	(± 3.5)
Peroneal Muscles	2.4%	(± 4.2)
Extensor Digitorum Longus and Tibialis Anterior.	8.5%	(± 3.8)
(Tibialis Posterior, Flexor Digitorum Longus and Hallucis Longus) Denervated (F.H.L & T.P)	*26.5%	(± 5.9)
Spared (F.D.L)	0.4%	(±11.2)

Table 14. Summary of Monosynaptic Reflexes.

(Nerve Section Series, with spinal cord transection - 7 cats)

The description of this Table is the same as that which heads Table 11.

Monosynaptic reflexes recorded monophasically from ventral roots				
Nerve	Monosynaptic Reflex Spike Mean	(± S.E)	Post-tetanically Potentiated Spike Mean	(± S.E)
Biceps Semitendinosus (Control)	1.15	(±0.095)	1.02	(±0.055)
Peroneal (Control)	* 1.20	(±0.060)	1.10	(±0.040)
Quadriceps Femoris (Control Group)	0.99	(±0.010)	0.99	(±0.010)
Medial Gastrocnemius (Spared Group)	* 2.09	(±0.18)	1.60	(±0.25)
Flexor Digitorum Longus (Spared Group)	* 2.52	(±0.37)	* 1.65	(±0.18)

Table 15. Central Latencies

(a) (Nerve Section series, with spinal cord transection - 7 cats)

Figures are mean central latencies in msec. with Standard Errors of the means in parenthesis.

Nerves	Normal Side Mean (± S.E)	Operated Side Mean (± S.E)
	msec	msec
Control Group (Biceps Semitendinosus, Peroneal and Quadriceps)	1.04 (±0.11)	1.03 (±0.10)
Spared Group (Medial gastrocnemius and Flexor digitorum longus)	1.24 (±0.07)	1.13 (±0.06)

The shortening of central latency by 0.11 msec. in the group os spared muscles is significant at the 5% level.

Table 16. Summary of Afferent Spike Discharges Recorded from the Distal Segments of Severed Muscle Nerves.

Corresponding muscles from both hindlimbs were used for recording. The figures, obtained from all muscles of all cats in each series, indicate the mean number of spike discharges per sweep (of 10 msec. duration). Standard Errors of the means are in parenthesis. Figures asterisked * indicate significance with 1.0% confidence limits.

(a)	Unilateral Tenotomy Series (10 cats)	Normal Muscles	Tenotomized Muscles	% Change from Tenotomized Muscles
	Resting Activity (Muscles not stretched)	11.0 (±0.28)	13.4 (±0.27)	22% increase *
	Muscle Stretched (0.5 Kilo pull)	18.8 (±0.38)	21.0 (±0.33)	11.7% increase *
(b)	Unilateral Tenotomy with Spinal Transection (5 cats)	Normal Muscles	Tenotomized Muscles	% Charge from Tenotomized Muscles
	Resting Activity (Muscles not stretched)	13.0 (±0.32)	12.6 (±0.27)	3% decrease

Table 17. The reflex discharges evoked in the various groups of muscle nerves by volleys in the cutaneous nerves tested, (sural, saphenous, superficial peroneal and tibial nerves) in each leg have been pooled, and grouped together.

Reflex discharges into various muscle nerves have been grouped as subserving either flexion (Biceps-semitendinosus nerve and Peroneus profundus nerve) or extension (nerve to Triceps surae, nerve to Flexor digitorum longus and nerve to Flexor hallucis longus).

A further subdivision was required because both ipsilateral and contralateral conditioning was employed.

Although conditioning stimuli to cutaneous nerves were graded in strength up to 100 - 200 X threshold, the results for only three strengths are presented in this table (1.2X threshold, 2.0X threshold, 20X threshold).

The results have been tabulated in three parts:

Table 17 (a) Latency of reflex discharge.

Table 17 (b) Duration of reflex discharge.

Table 17 (c) Maximum amplitude of discharge.

Table 17 (a)

This table presents the mean latencies of reflex discharges for all animals in both the acute acute and chronic spinal groups. The figures are mean latencies in msec: Standard errors have been calculated but are omitted for simplicity.

Nerves to	Type of Animal	Discharge Latencies in msec.		
		Strength of Conditioning Stimulus		
		1.2X Threshold	2.0X Threshold	20X Threshold
Ipsilateral Flexors	Acute Spinal	6.3	6.0	6.0
	Chronic Spinal	6.3	5.8	5.7
Ipsilateral Extensors	Acute Spinal	7.7	7.5	7.6
	Chronic Spinal	7.9	7.9	7.8
Contralateral Flexors	Acute Spinal	8.4	8.7	8.1
	Chronic Spinal	8.8	8.4	8.4
Contralateral Extensors	Acute Spinal	10.8	10.2	-
	Chronic Spinal	11.0	11.0	-

Table 17 (b)

The mean duration of reflex discharges are shown for all animals in both the acute and chronic spinal groups. The figures give mean duration in msec : standard errors have been calculated and are in parenthesis. The figures asterisked * are significant at the 1% level.

Nerve to	Type of Animal	Discharge Duration in msec.		
		Strength of Conditioning Stimulus.		
		1.2X Threshold	2.0X Threshold	20X Threshold
Ipsilateral Flexors	Acute Spinal	3.9 (±0.08)	8.3 (±0.46)	*111 (± 19)
	Chronic Spinal	3.5 (±0.15)	9.3 (±0.42)	*520 (±138)
Ipsilateral Extensors	Acute Spinal	5.5 (±0.28)	8.5 (±0.16)	69.0 (±9.5)
	Chronic Spinal	4.9 (±0.45)	8.4 (±0.26)	85.0 (±15.6)
Contralateral Flexors	Acute Spinal	5.0 (±0.29)	9.4 (±0.27)	*22.0 (±2.4)
	Chronic Spinal	4.6 (±0.26)	9.7 (±0.27)	*50.0 (±8.6)
Contralateral Extensors	Acute Spinal	6.0 (±0.31)	10.0 (±1.80)	23.0 (±3.0)
	Chronic Spinal	4.9 (±0.24)	7.1 (±0.44)	40.0 (± 5.2)

Table 17 (c)

The maximum amplitudes of the reflex discharges are shown for all animals in both the acute and chronic spinal groups. The figures are mean maximum amplitudes in mV. The standard errors have been calculated, but are omitted for simplicity.

Nerves to	Type of Animal	Maximum amplitude of reflex discharge in mV.		
		Strength of conditioning tetanus		
		1.2X Threshold	2.0X Threshold	20X Threshold
Ipsilateral Flexors	Acute Spinal	0.15	0.41	0.72
	Chronic Spinal	0.14	0.37	0.54
Ipsilateral Extensors	Acute Spinal	0.08	0.12	0.17
	Chronic Spinal	0.06	0.11	0.16
Contralateral Flexors	Acute Spinal	0.06	0.13	0.10
	Chronic Spinal	0.11	0.16	0.13
Contralateral Extensors	Acute Spinal	0.12	0.16	0.25
	Chronic Spinal	0.12	0.17	0.24

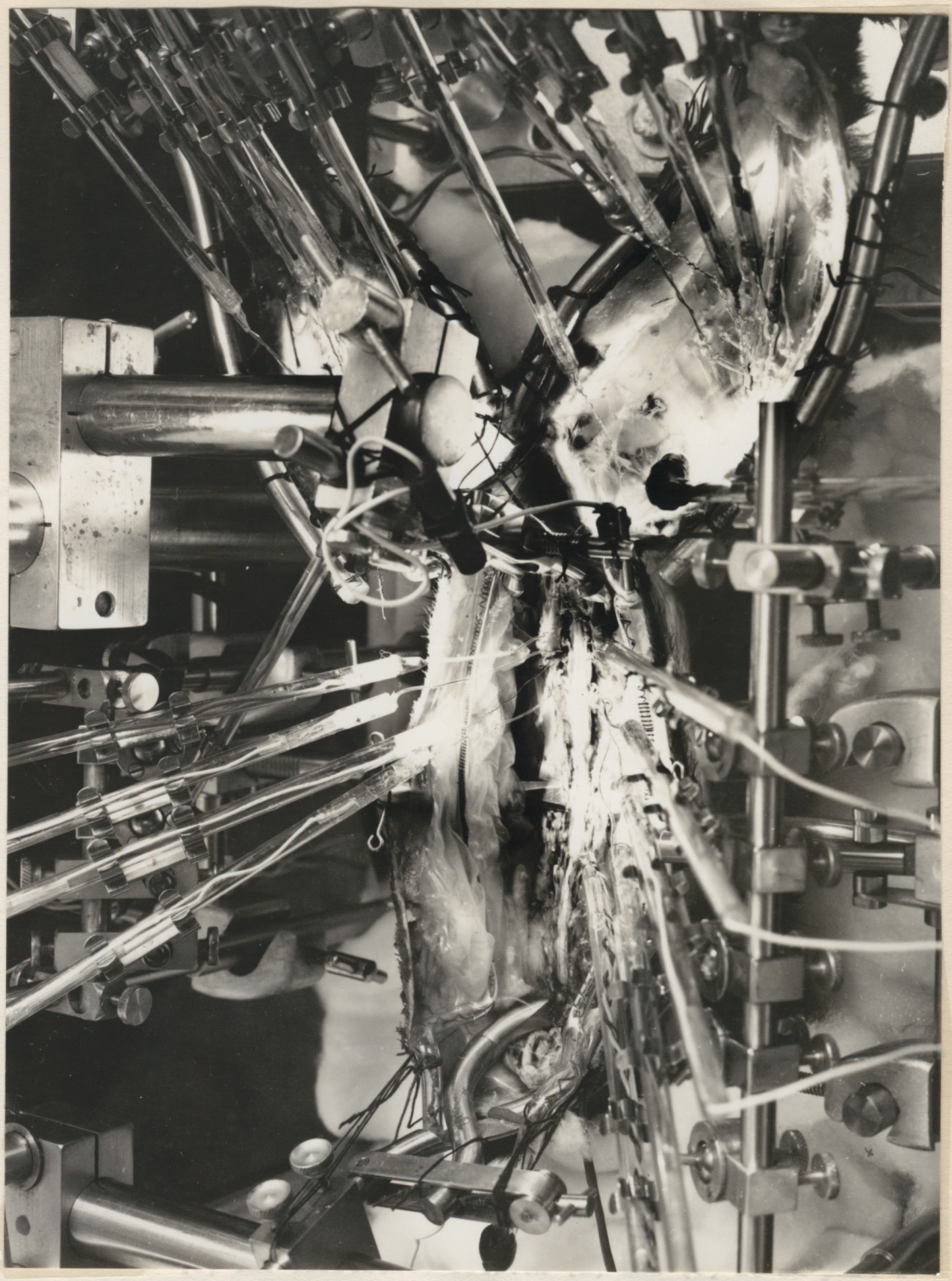

Figure 1. Illustrates the experimental arrangement of a cat in the frame. The hindlimb and back pools may be clearly seen. Nerves for stimulation are seen in the electrodes in the near leg pool, while L6 and L7 ventral roots on the near side are mounted on recording electrodes.

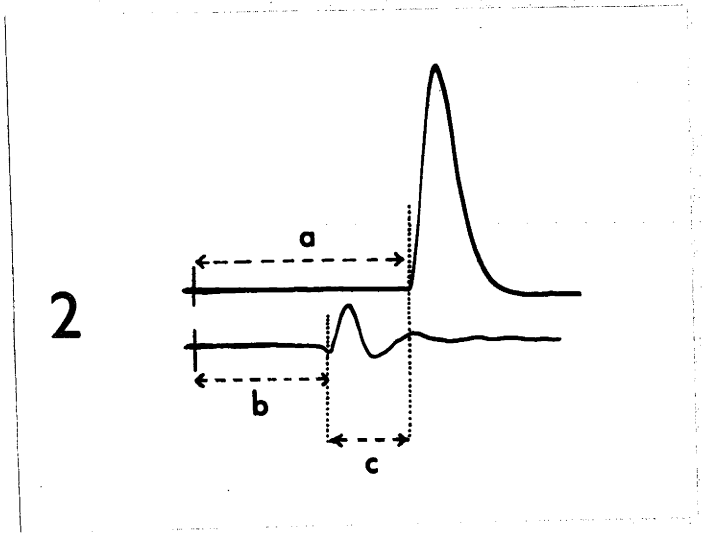

Figure 2.

The conventions used throughout this thesis for latency measurements are shown in 2.

(a) Latency of reflex is measured from the stimulus artifact to the first point of ascent on the spike's rising phase.

(b) Latency of triphasic volley is measured from the stimulus artifact to the peak of the first positive (downward) deflection.

(c) The difference between (a) and (b) is in part a measure of the central synaptic delay, and has been termed the central latency.

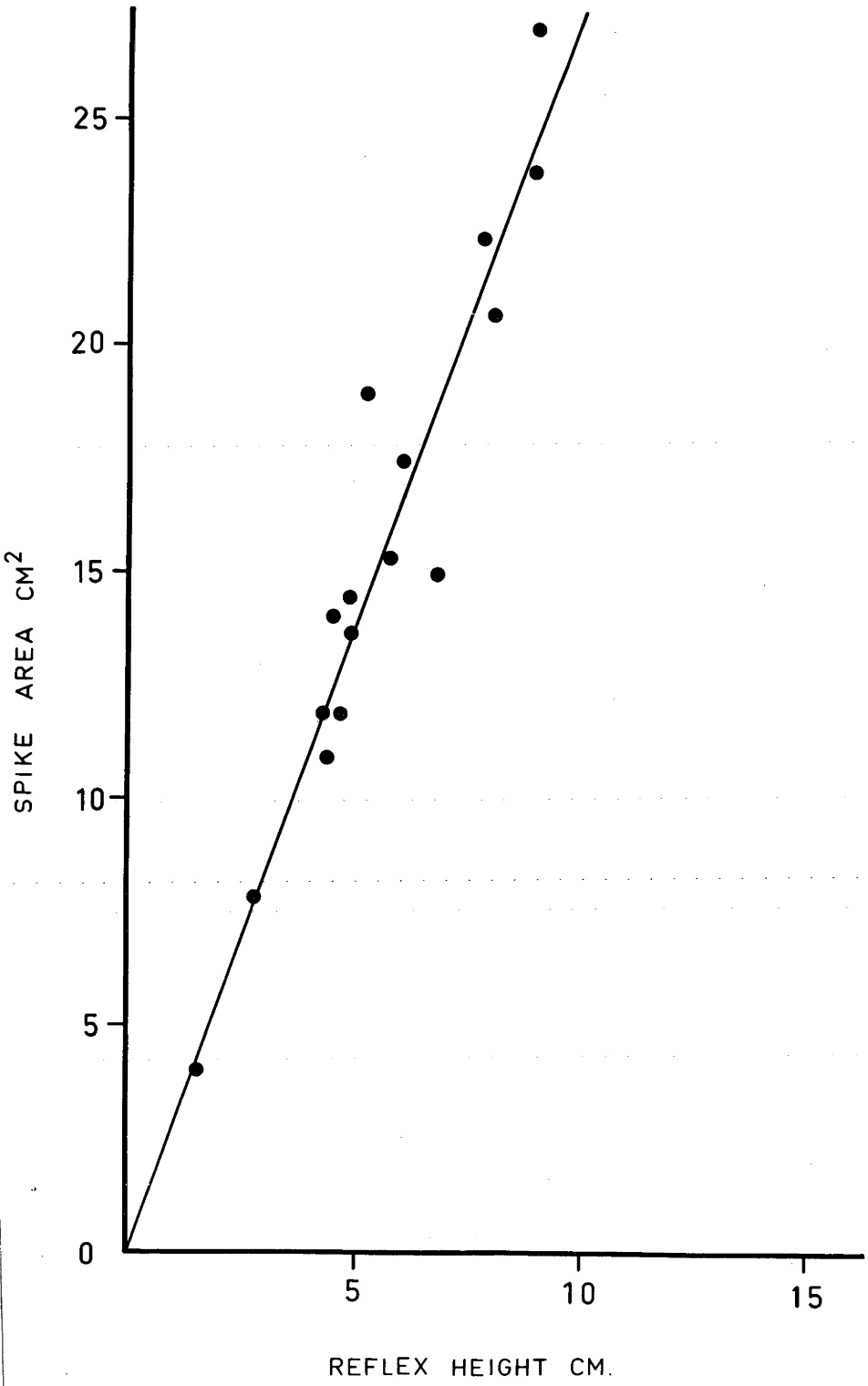

Figure 3.

Ordinate represents the area under the monophasic spike in cm^2. Abscissa represents the height of the monophasic spike in cm.

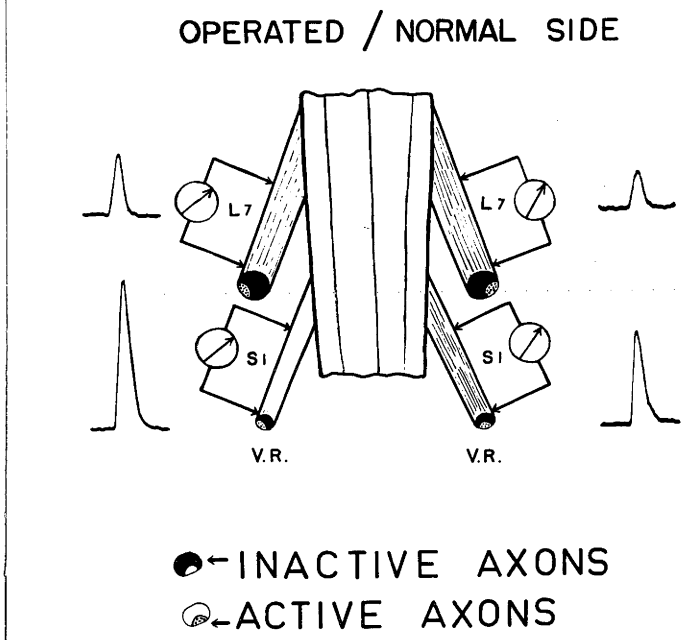

Figure 4. Shows the reflexes evoked in S1 and L7 ventral roots by maximal group Ia volleys in nerves to gastrocnemius. As depicted, although the reflexes in both the S1 ventral roots are larger than the reflexes in corresponding L7 roots, there are more active fibres in the latter. This is due to the greater shunting resistance of the larger ventral root in reducing the recorded action potential. There is depicted an enhancement of reflex responses on the operated side relative to those of the normal side, such as was found with reflexes evoked from nerves to tenotomized muscles.

DIAGRAM OF MONOSYNAPTIC REFLEX CONNECTIONS

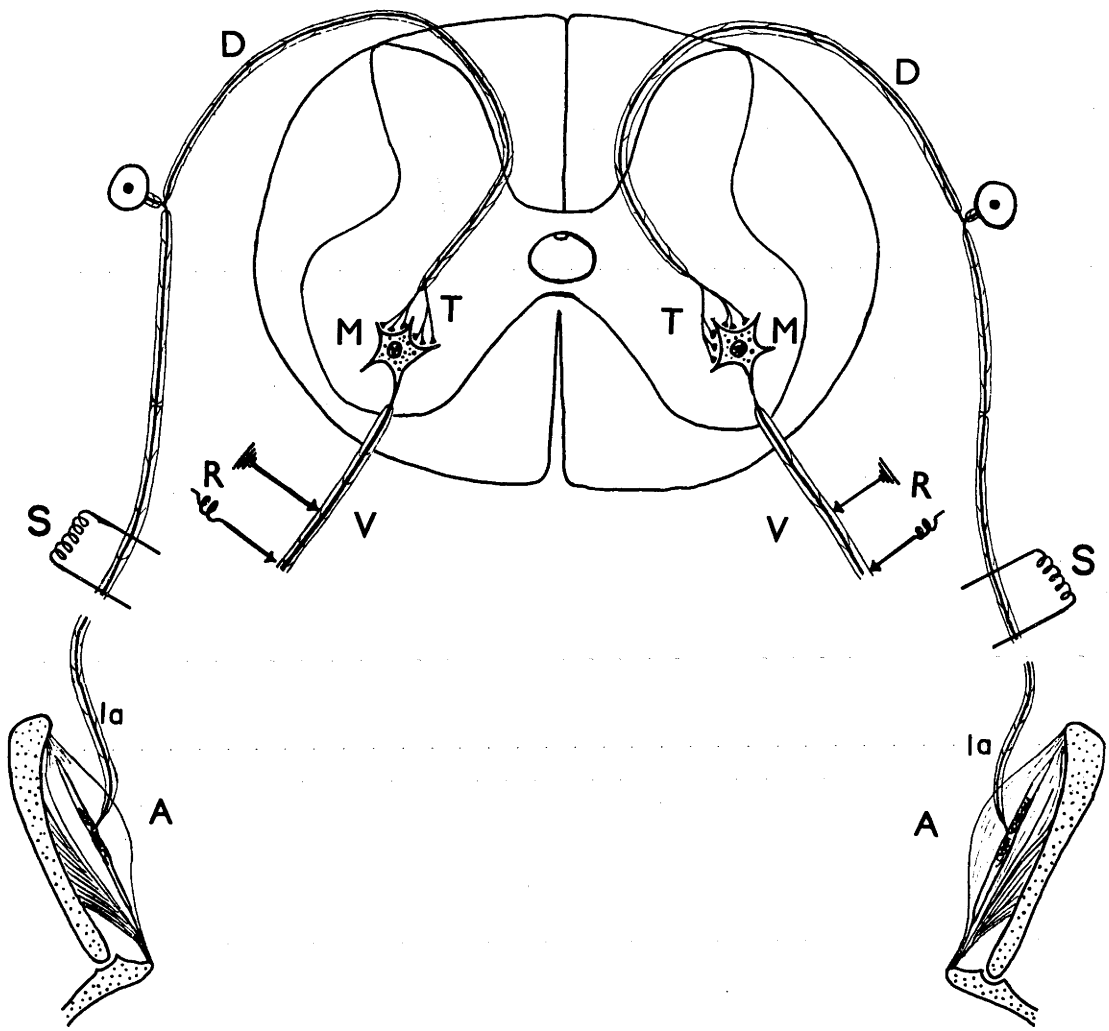

Figure 5. Represents diagrammatically the monosynaptic reflex arc. Proprioceptive afferent fibres of group Ia, from primary (annulospiral) endings from a given muscle make monosynaptic connections T in the ventral horn with motoneurones M whose axons innervate that muscle. Thus stimulation at S evokes a reflex response of motoneurones, recorded at R in ventral roots V.

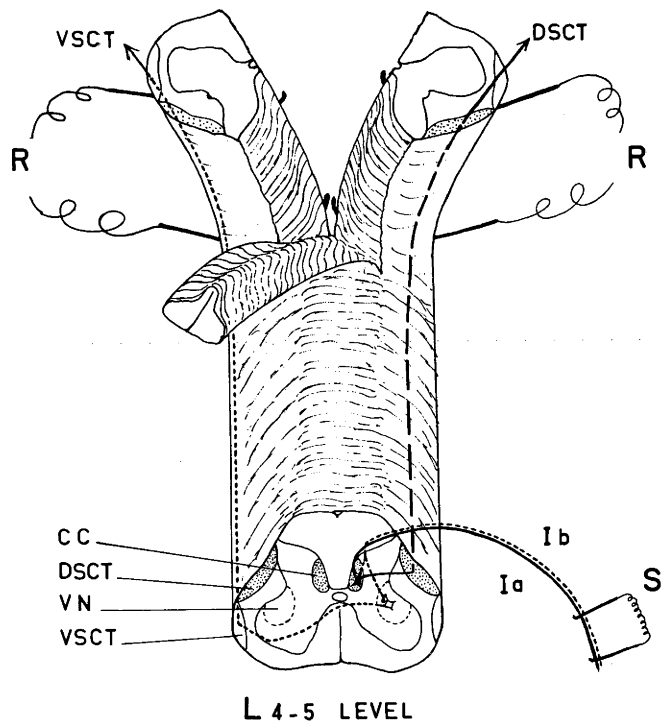

Figure 6. This figure illustrates diagrammatically the mono-synaptic connections of the spinocerebellar tracts, and the methods of recording from the hemisected spinal cord.

C C = Nucleus of Clarke's Column. (origin of dorsal spinocerebellar tract)

DSCT = Dorsal spinocerebellar tract axons ascending in the dorsal part of the ipsilateral lateral column.

V N = Nucleus of ventral spinocerebellar tract.

VSCT = Ventral spinocerebellar tract axons ascending, after crossing, in the ventral part of the contralateral lateral column.

S = Stimulating electrodes on hindlimb muscle nerve.

R = Recording electrodes placed under halves of spinal cord following removal of dorsal funiculi, and hemisected.

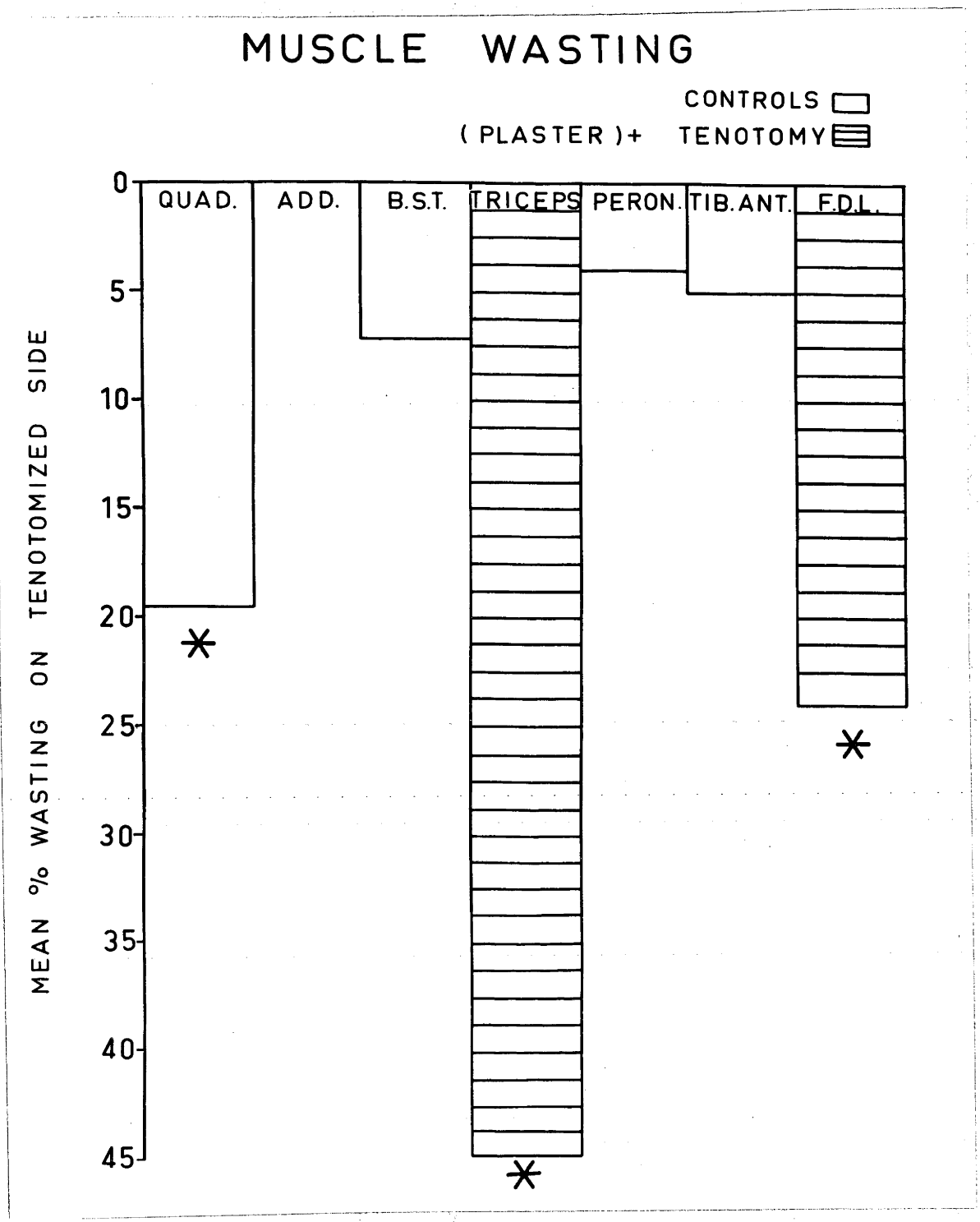

Figure 7. Muscle wasting with unilateral tenotomy and plaster of Paris immobilization.

The results in this histogram are presented in detail as Table 2. The ordinate represents the mean % wasting of muscle groups on the tenotomized side relative to corresponding muscle

P.T.O

Figure 7. Legend Continued.

The abscissa shows the various muscle groups tested, whose abbreviations are as follows:

Quad. - Knee extensors and includes Rectus femoris, vastus lateralis, intermedius and internus.

Add. - Adductors of hip.

B.S.T. - Knee flexors, i.e. Biceps femoris and Semitendinosus, and hip extensor, semimembranosus.

Triceps - Ankle extensors, i.e. medial and lateral gastrocnemius, Soleus and a plantar-flexor of toes - Plantaris.

Peron - Ankle flexors and evertors, i.e. Peroneal muscles Peroneus longus, Peroneus brevis and Peroneus tertius.

Tib.Ant.- Anterior tibial group of muscles which are ankle flexors, and dorsi-flexors of toes - Tibialis anterior and Extensor digitorum longus.

F.D.L. - Toe plantar flexors, i.e. Flexor digitorum longus and Flexor hallucis longus.

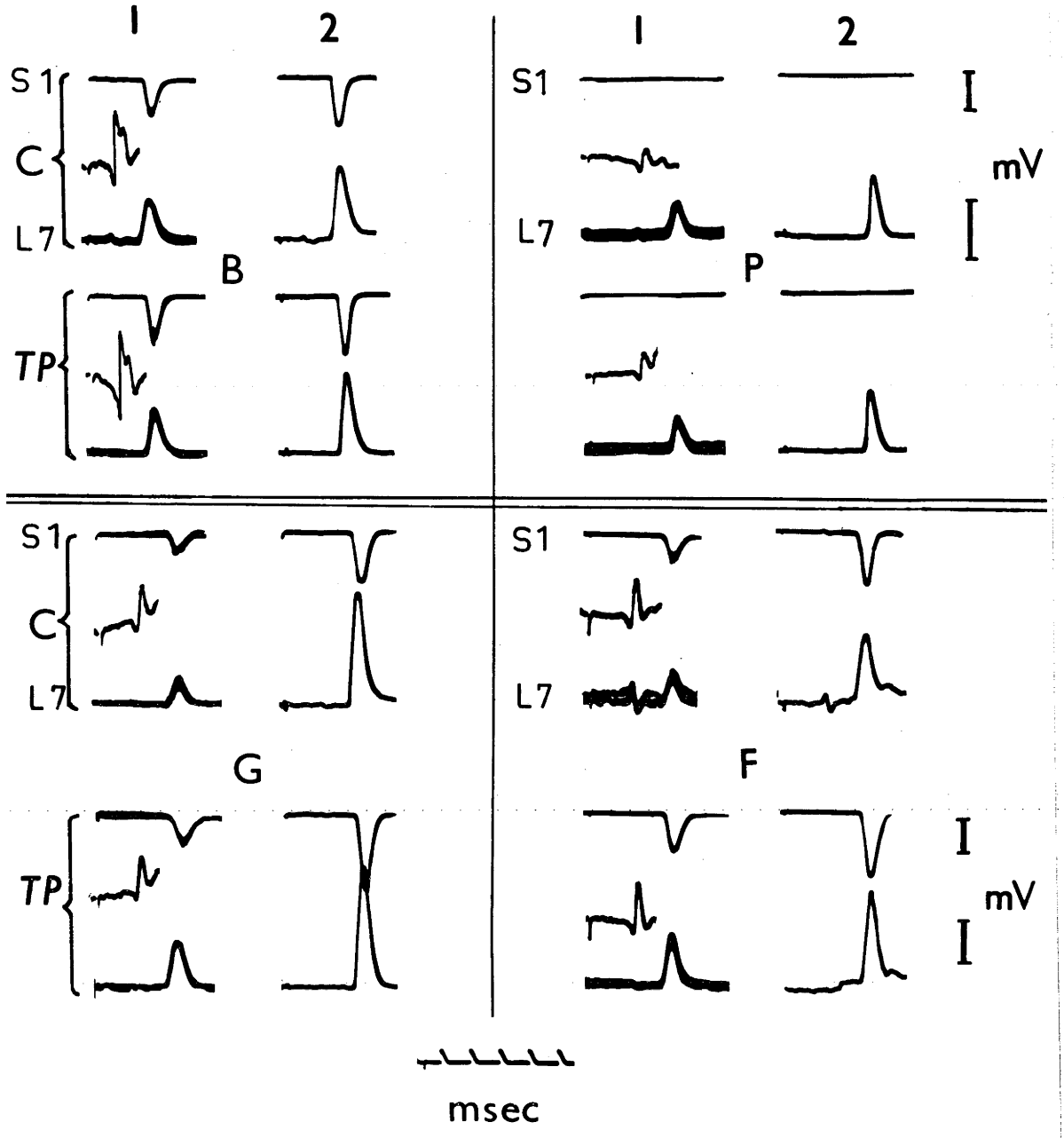

Figure 8.

The records in this figure from one typical experiment illustrate the results obtained in the series tenotomy plus plaster immobilisation. Reflexes for each nerve are recorded in two ventral roots simultaneously, S1 ventral root on the upper beam, L7 on the lower beam. The afferent ingoing dorsal root volley is inset between the two beams.

P.T.O

Figure 8. Legend Continued.

C = Monosynaptic reflex responses from nerves in the control hindlimb while T.P = reflexes from nerves in tenotomized and plastered limb.

All responses in vertical columns 1 before and 2 after tetanic conditioning at 400/sec for 15 sec.

Each quadrant of the figure shows reflex responses from one given muscle nerve of both hindlimbs.

Upper two groups Biceps semitendinosus (B) and Peroneal (P) are bilateral controls and show symmetry of afferent volleys and of reflex responses both before and after tetanic stimulation.

Both the lower two groups, Gastrocnemii (G) and Flexor digitorum longus (F), compare reflex responses (C) from contralateral control nerves with those (T P) from nerves to tenotomized muscles (T P).

There is a relative increase of reflexes from the nerves to tenotomized muscle groups. Afferent volleys still show symmetry.

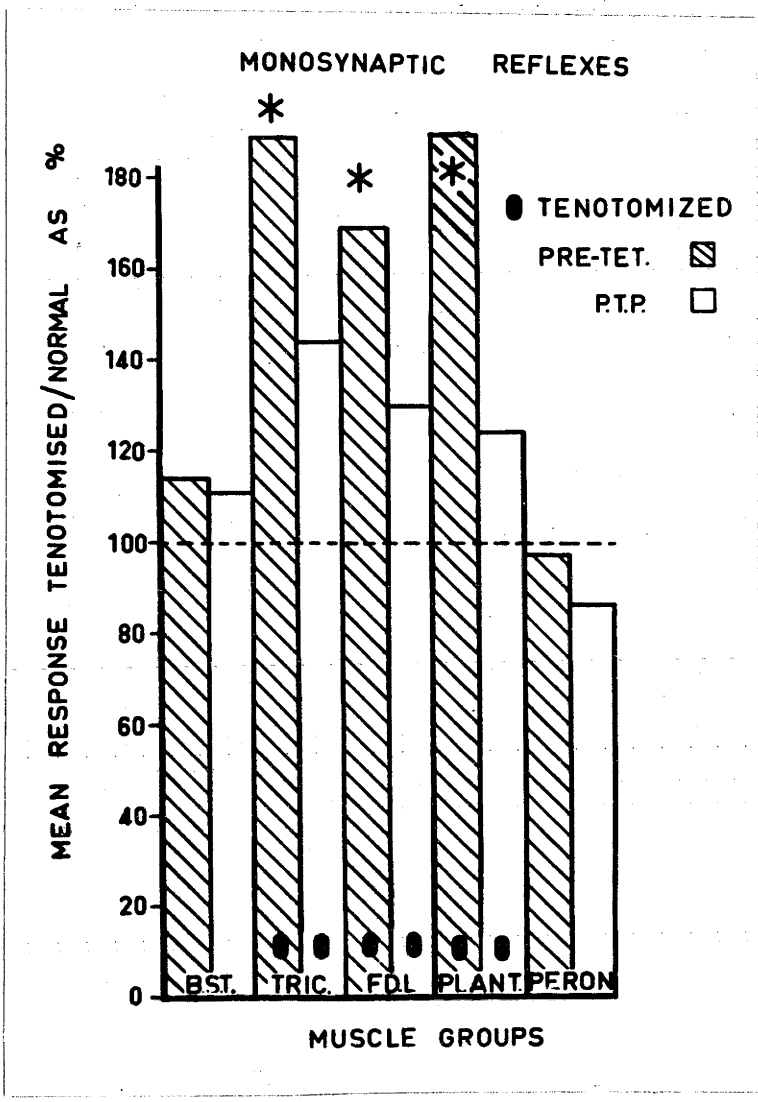

Figure 9.

This figure shows the results detailed in Table 2, for monosynaptic reflexes from all animals in the series displayed as a histogram.

P.T.O

Figure 9. Legend Continued.

Cross-hatched columns indicate mean monosynaptic reflex responses, before tetanic conditioning, while open columns show maximum levels of post-tetanic responses. Tenotomized muscle groups are indicated by a black spot, the remainder being controls. Those columns asterisked * indicate that the increase is statistically significant at a 1% level.

The ordinate represents the ratio of mean reflex responses from tenotomized side / corresponding reflex from normal side expressed as a percentage. 100% represents symmetry of responses from the two sides. The abscissa represents nerves to the following muscle groups denoted by the symbols:

B.S.T. - Nerve to Hamstring muscles.

Tric. - Nerve to both heads of Gastrocnemius muscles.

F.D.L. - Nerve to Flexor digitorum longus and Flexor hallucis longus.

Plant - Nerve to Plantaris.

Peron - Nerve to Peroneal group.

Quad. - Nerve to Quadriceps femoris.

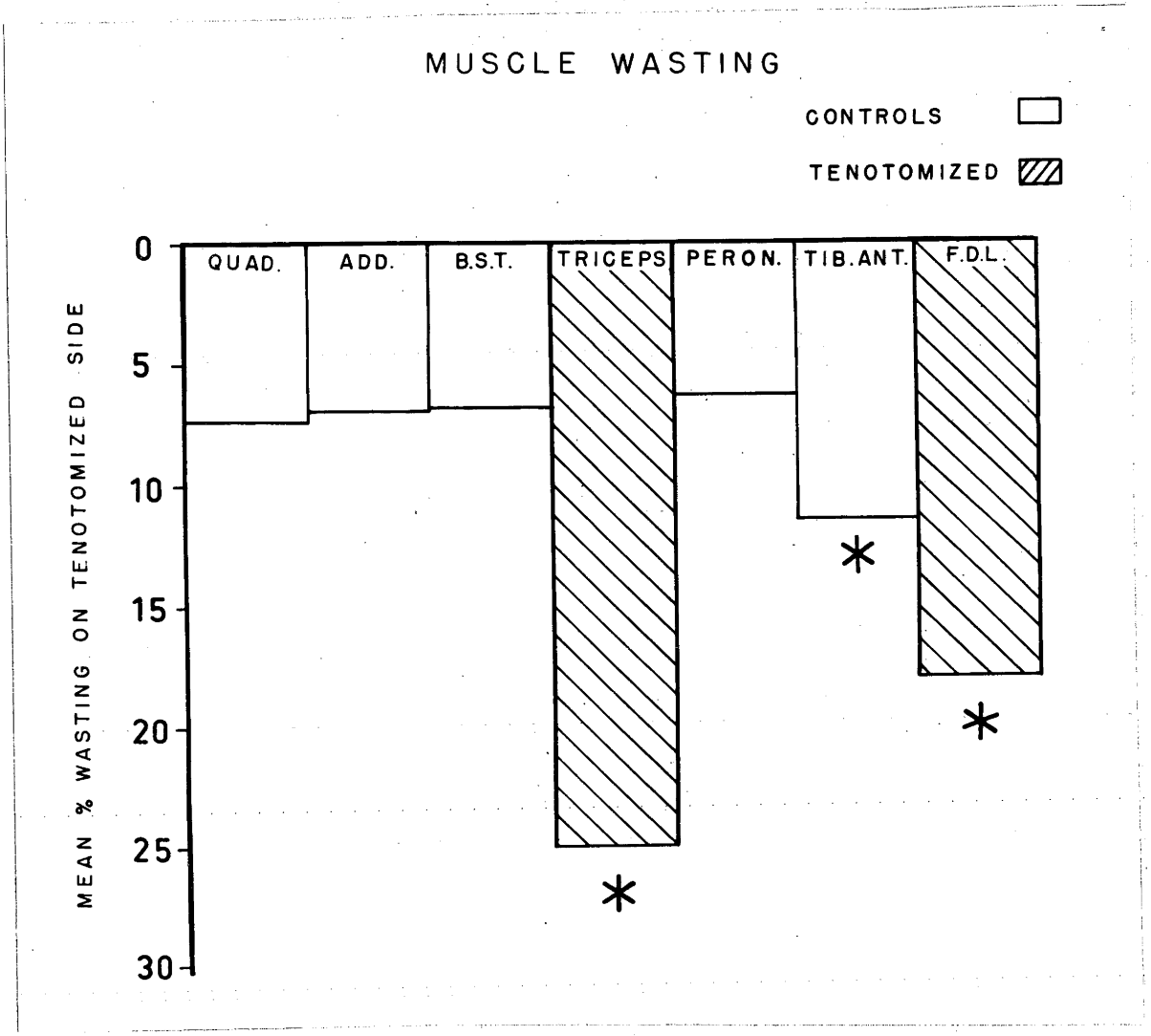

Figure 10.

Muscle wasting with unilateral tenotomy alone.

The ordinate represents the mean % wasting of the muscle groups on the tenotomized side.

The abscissa shows the various muscle groups, whose symbols are identical with those in Figure 7.

Those results asterisked * are statistically significant at the 1% level.

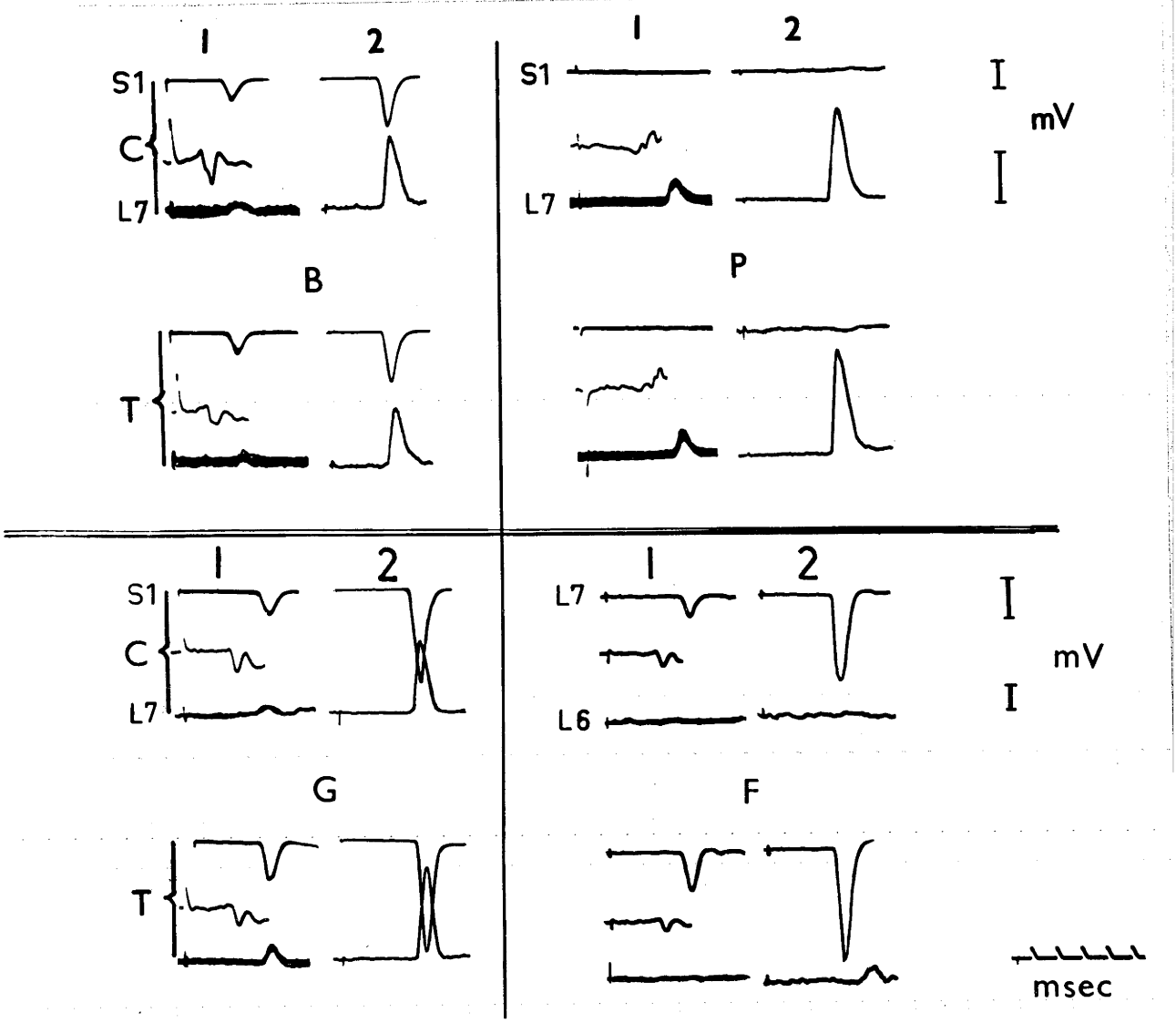

Figure 11. These monosynaptic reflex responses are actual records from one typical experiment from the series of animals with only unilateral tenotomy.

The arrangement of the figure and its nomenclature are identical to that used in Figure 8, except that the horizontal rows T represent the responses from various nerves in the tenotomized hindlimb, while C represents those responses from the normal side of the animal. As in Figure 8, there is symmetry of bilateral controls and significant enhancement of reflexes from

P.T.O

Figure 11. Legend continued.

nerves to tenotomized muscles, both before, 1, and after, 2, standard tetanic conditioning.

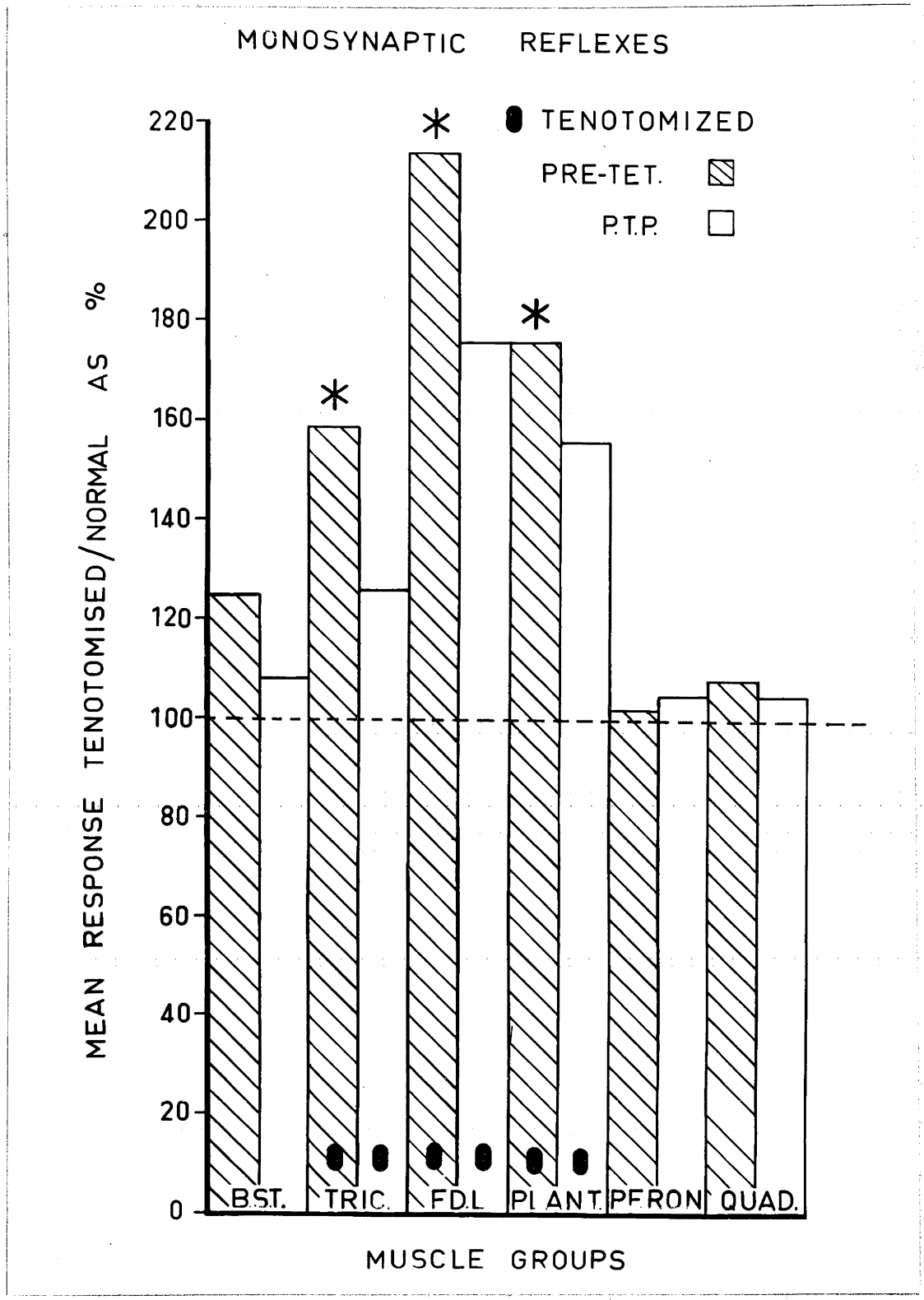

Figure 12.

This histogram displays the results detailed in Table 5 (a) of monosynaptic reflexes from the unilateral tenotomy series. The description of this figure is identical to that for Figure 9.

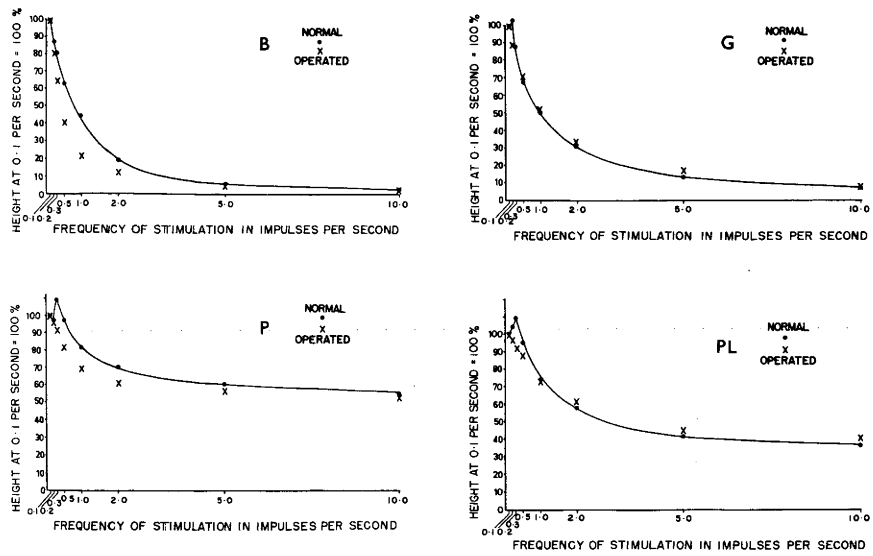

Figure 13. In this figure the ordinates represent the reflex height as a percentage, 100% being arbitrarily chosen as the reflex height at a conditioning frequency of 0.1 impulses per second. Abscissa denote frequency of conditioning volleys in impulses per second.

Symbols: B - Nerve to Hamstring muscles.

P - Nerve to Peroneal muscles.

G - Nerves to Gastrocnemii.

Pl - Nerve to Plantaris.

The filled circles represent the heights of reflexes from nerves to muscles in the control hindlimb, while crosses represent reflex heights for the nerves from the tenotomized hindlimb. Each point is the mean of results from three different animals.

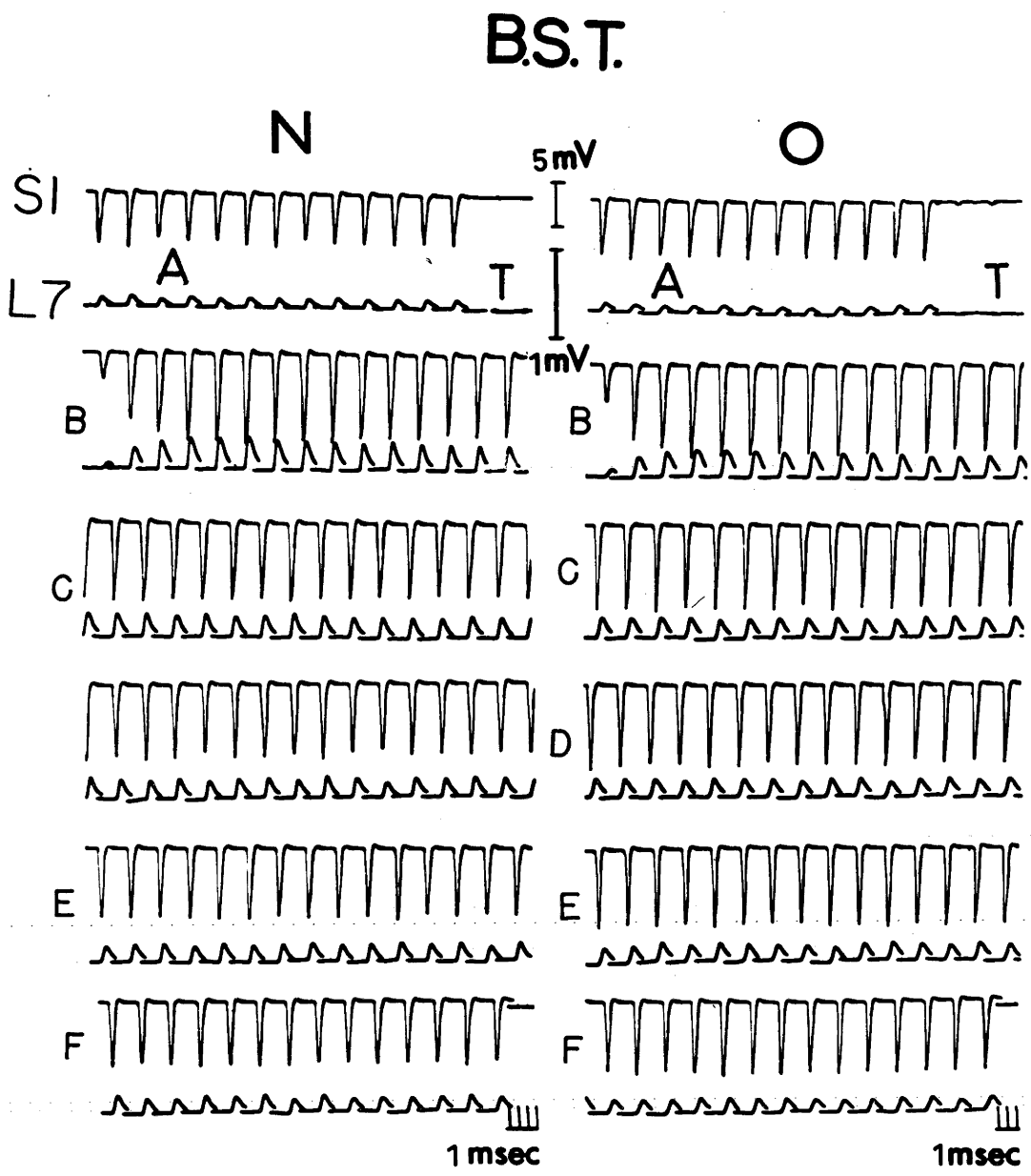

Figure 14.

These records from the nerves to Biceps semitendinosus in one typical experiment illustrate the time course of post-tetanic potentiation. Records were obtained by photographing responses on moving film with the Cathode Ray Oscilloscope screen masked except for a 2cm. gap. Frequency of testing volley 0.3/sec.

Note the symmetry of reflexes from nerves of both the normal and operated hindlimbs. This reflex symmetry is evident

P.T.O

Figure 14. Legend Continued.

both before (A) and after (B - F) tetanic conditioning with the standard tetanus. See also Figure 40.

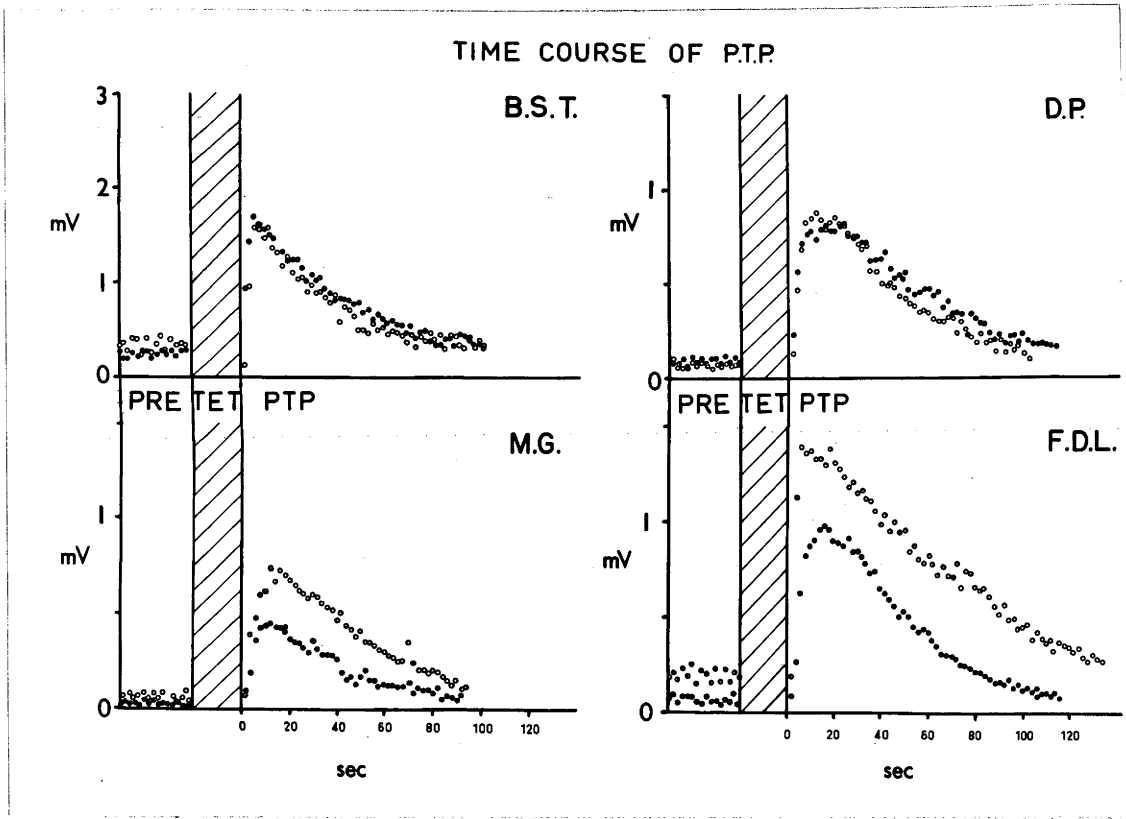

Figure 15.

This figure shows the time course of post-tetanic potentiation for nerves to control (filled circles) and tenotomized (open circles) muscles from a single experiment.

Ordinate represents reflex heights in mV. Abscissae represent time.

The pretetanic reflex heights are denoted by the symbol PRE, the standard conditioning tetanus of 400 impulses per second for 15 seconds occupies the cross-hatched area TET. The series of post-tetanic reflexes are shown as PTP.

Testing volleys in this case 1 per 2 sec.

Symbols denote the following:

B.S.T. - Nerve to Hamstring muscles.

D.P. - Nerves to Peroneal muscles.

M.G. - Nerve to medial gastrocnemius muscle.

F.D.L. - Nerve to Flexor digitorum longus and Flexor hallucis longus.

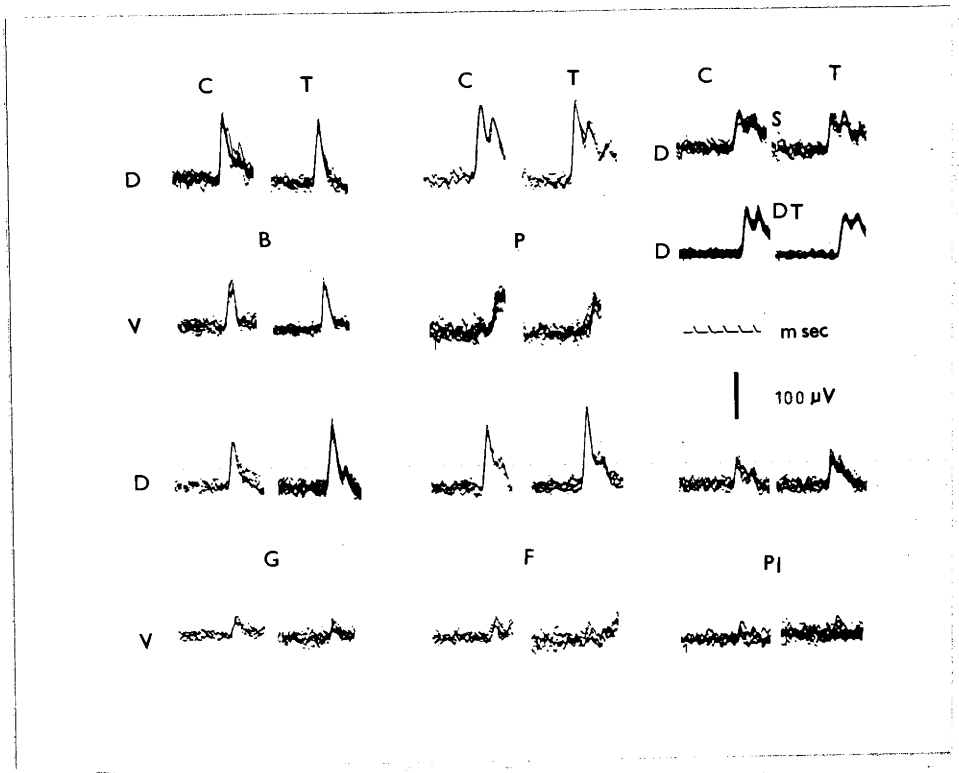

Figure 16. This figure shows actual records of Dorsal and Ventral spinocerebellar tract responses from one typical experiment.

The symbols are as follows:

D = Dorsal spinocerebellar reflex.

V = Ventral spinocerebellar reflex.

C = Responses evoked from nerves to control hindlimb.

T = Responses evoked from nerves to tenotomized hindlimb.

B = Nerves to Hamstring group of muscles all together.

P = Nerves to Peroneal group of muscles all together.

G = Nerves to both heads of Gastrocnemius, and to Soleus.

F = Nerves to Flexor digitorum longus and Flexor hallucis longus together.

Pl = Nerve to Plantaris

S = Sural (skin) nerve.

DT = Deep Tibial (mixed) nerve.

Note the symmetry of all VSCT responses from corresponding nerves and the DSCT responses from bilateral control nerves (B., P., S., D.T.). Nerves to tenotomized muscles (G., F., Pl.) show significant enhancement of DSCT responses.

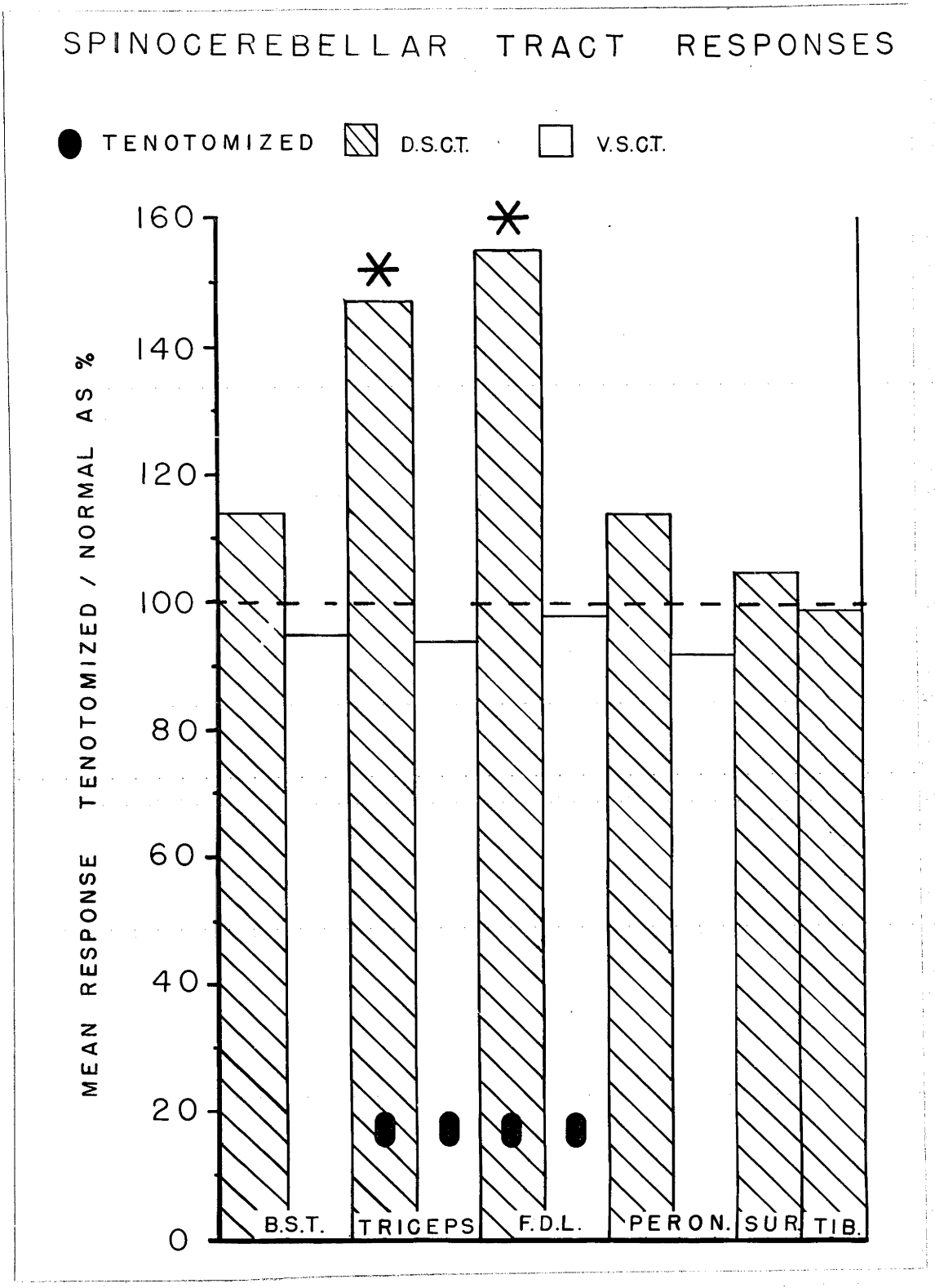

Figure 17. This histogram shows spinocerebellar tract responses detailed in Table 5 (b). The ordinate represents the mean of the spinocerebellar tract responses from the tenotomized side / corres-

P.T.O

Figure 17. Legend Continued.

ponding response from normal side, the ratio being expressed as a percentage. 100% thus represents symmetry of responses on the two sides.

The abscissa represents the various muscle nerves tested, the abbreviations used being:

B.S.T. – Whole Hamstring nerve including nerves to Biceps femoris, Semitendinosus, Semimembranosus.

Triceps – Whole Triceps surae nerve including nerves to Medial and Lateral gastrocnemius, Soleus and Plantaris.

F.D.L. – Toe extensor group including Flexor digitorum longus and Flexor hallucis longus.

Peron – Peroneus profundus nerve.

Sur – Sural nerve, both branches.

Tib – Deep Tibial nerve.

Filled spots designate those nerves to tenotomized muscles. Cross-hatched columns indicate DSCT responses and open columns represent VSCT responses.

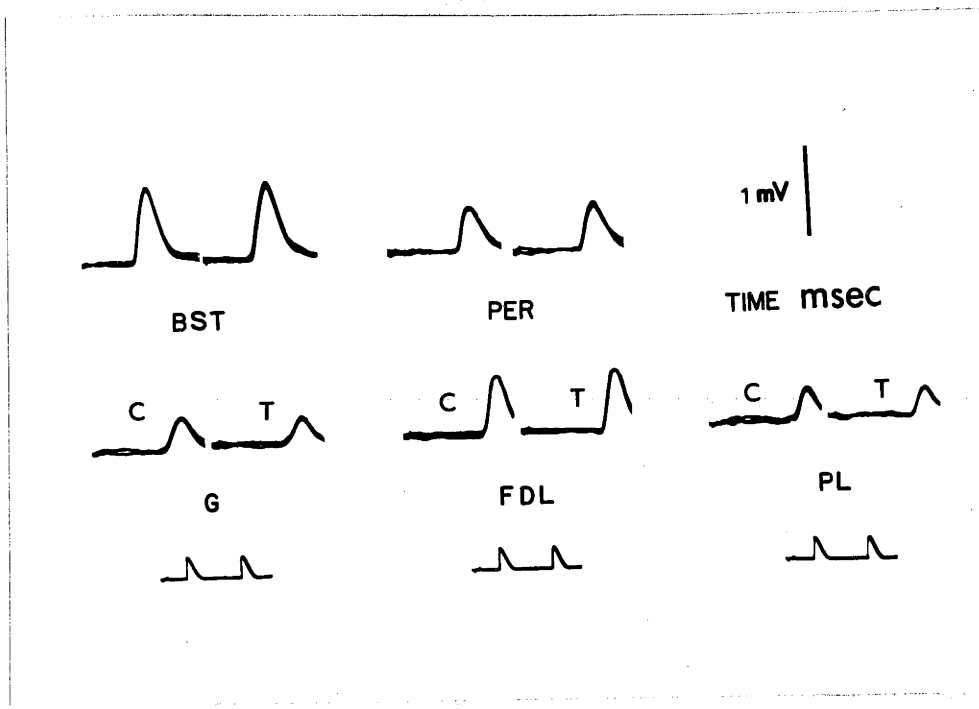

Figure 18. Afferent Volleys.

Records obtained from one typical experiment are shown in this figure. Volleys recorded monophasically from cut dorsal roots at the conclusion of the experiment were evoked by stimulation of the various muscle nerves denoted by the following abbreviations:

B.S.T.	-	Nerve to Hamstring muscles.
Per.	-	Nerve to Peroneal and anterior tibial groups of muscles.
G	-	Nerve to Gastrocnemii - Soleus.
F.D.L.	-	Nerve to Flexor digitorum longus and Flexor hallucis longus.
PL	-	Nerve to Plantaris.

Ten responses evoked from each nerve from control hindlimb C and tenotomized hindlimb T are superimposed in these records. Note the good symmetry between volleys from corresponding nerves.

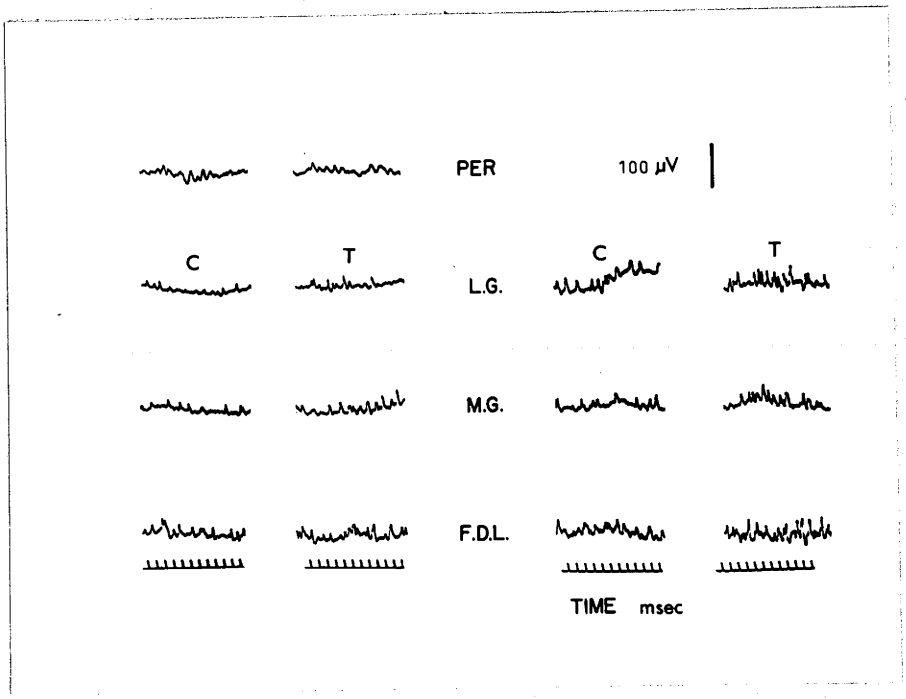

Figure 19.

This figure shows actual records from two different animals of the afferent discharges recorded from the cut nerves of non-stretched muscles in both hindlimbs.

Columns C denote responses from muscles of the normal hindlimb, while those in column T are from the tenotomized hindlimb.

Muscles denoted by the following symbols:

PER	–	Deep Peroneal muscles. (controls – intact in both hindlimbs)	
L.G	–	Lateral head of Gastrocnemius	Tenotomized in one hindlimb.
M.G	–	Medial head of Gastrocnemius	
F.D.L.	–	Flexor digitorum longus	

Note the symmetry of controls in respect of discharge frequency and the increased frequency of discharge from tenotomized muscles.

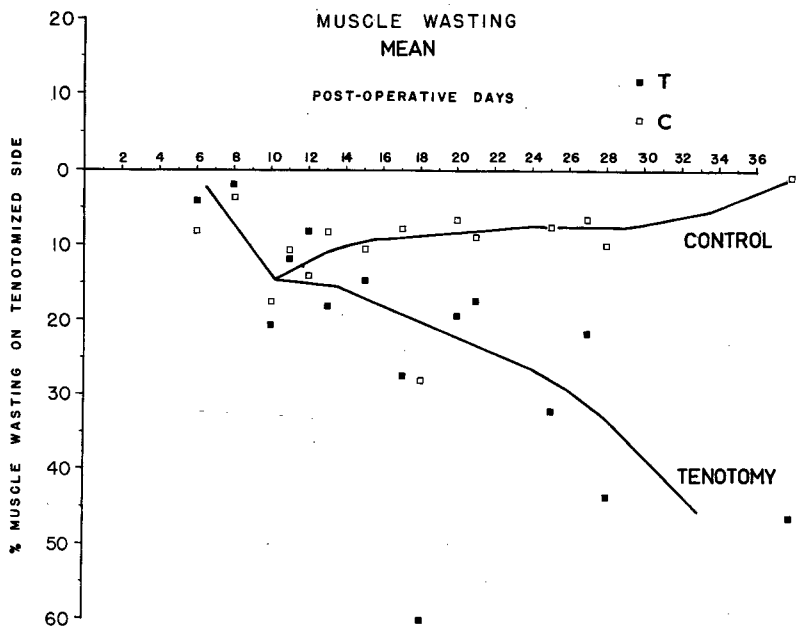

Figure 20.

Time Course of Muscle Wasting with Unilateral Tenotomy.

All muscle groups in the tenotomized hindlimb show some wasting.

Filled squares each represent the mean amount of wasting for all tenotomized muscles from a single animal. Open squares represent the mean amount of wasting for all control muscles from a single animal. This latter group comprises all intact muscles in the tenotomized hindlimb.

The ordinate represents % wasting of muscles in tenotomized hindlimb compared to the corresponding muscles in the normal hindlimb.

Abscissa represents postoperative days of survival.

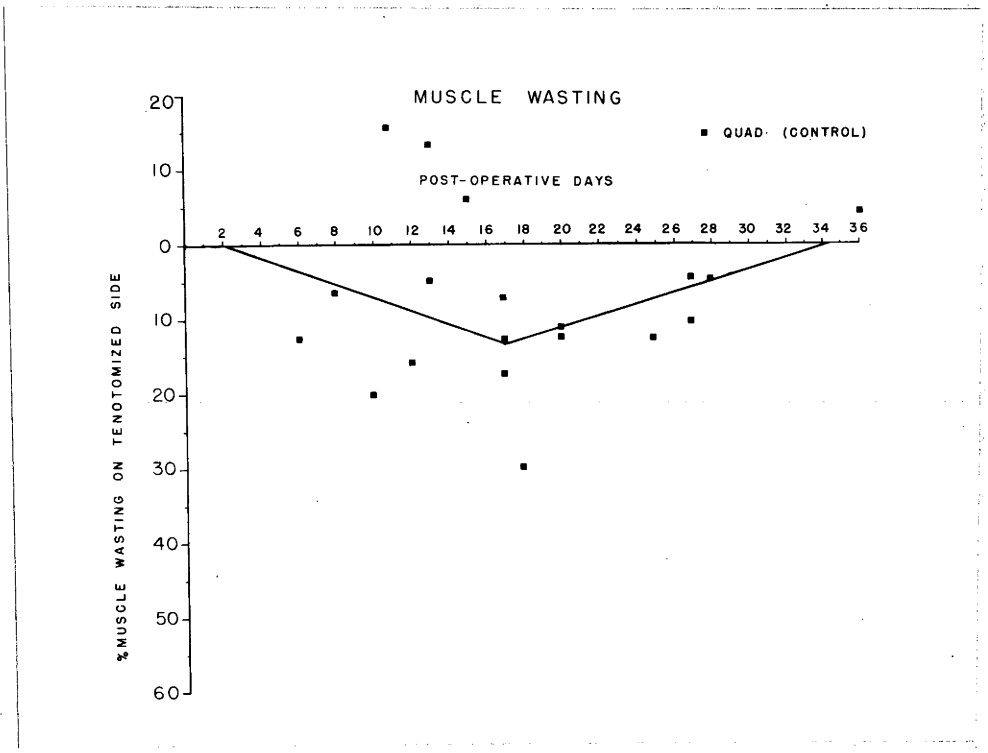

Figure 21.

Time Course of Muscle Wasting for one Group of Nontenotomized Muscles.

Each filled square represents the mean amount of wasting for the quadriceps femoris muscles of the tenotomized hindlimb of all animals.

Ordinate shows % muscle wasting of Quadriceps on the tenotomized side, relative to the corresponding muscle group from the normal side of each animal.

Abscissa represents postoperative days of survival.

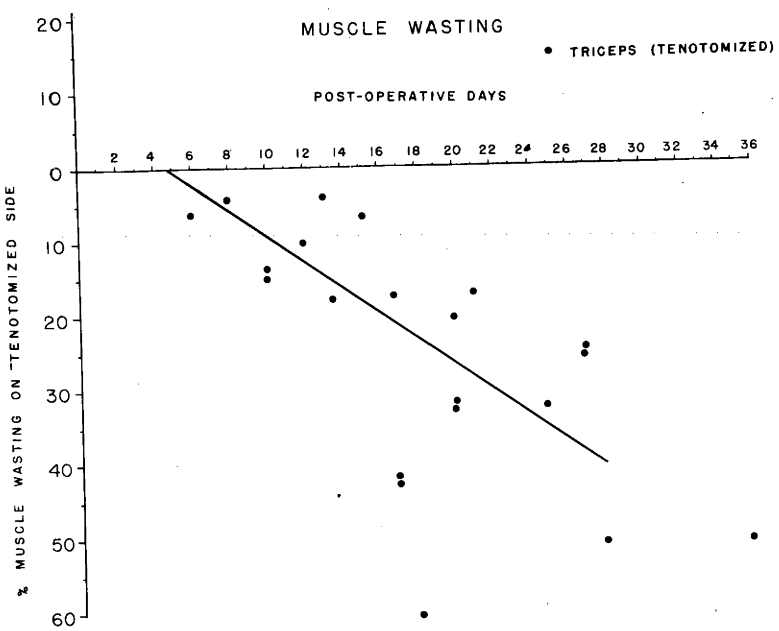

Figure 22.

Time Course of Muscle Wasting for one Group of Tenotomized Muscles.

Each filled circle represents the mean amount of wasting for the Triceps surae muscles from the tenotomized hindlimb of all animals.

Ordinate shows % muscle wasting of Triceps on the tenotomized side, relative to the corresponding muscle group from the normal side of each animal.

Abscissa represents postoperative days of survival.

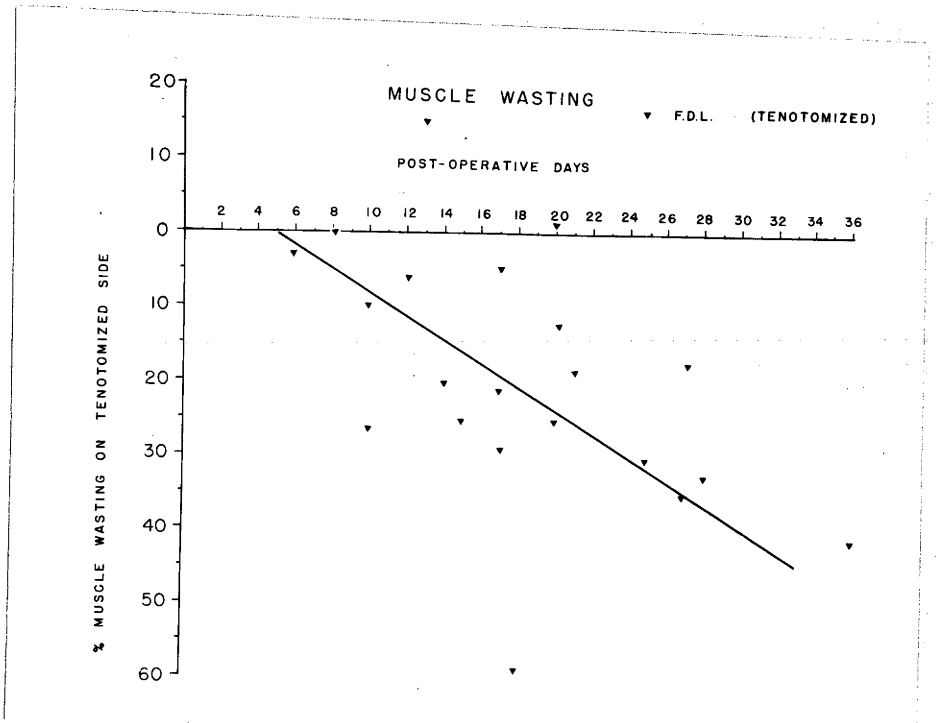

Figure 23.

Time Course of Muscle Wasting for a Second Group of Tenotomized Muscles.

Each filled triangle represents the mean amount of wasting for the Flexor digitorum longus group of muscles from the hindlimb of all animals.

Ordinate shows % muscle wasting of F.D.L. groups on the tenotomized side, relative to the corresponding muscle group from the normal side of each animal.

Abscissa represents postoperative days of survival.

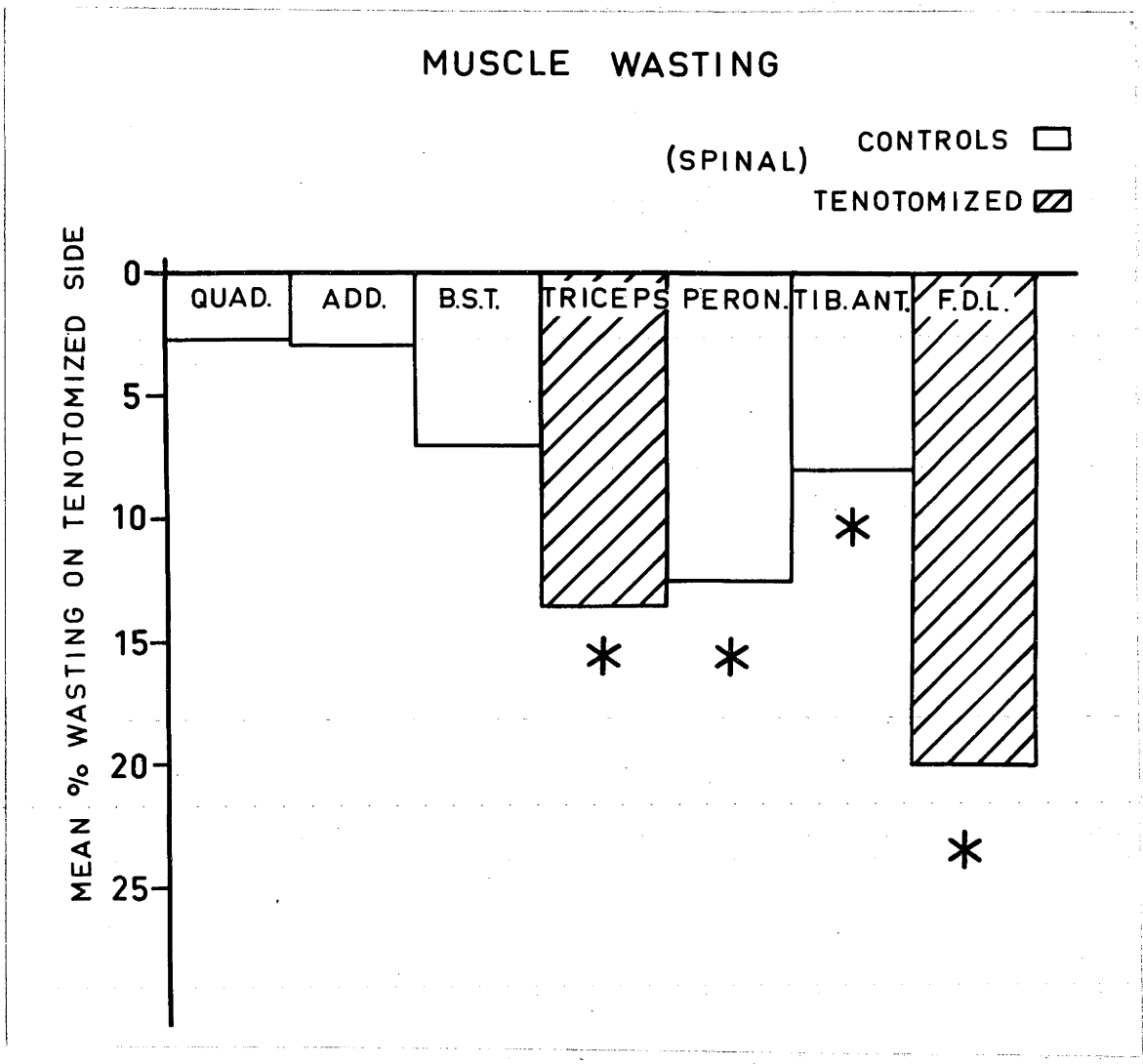

Figure 24.

Muscle Wasting with Unilateral Tenotomy and Spinal Cord Transection.

The ordinate represents the mean % wasting of the muscle groups on the tenotomized side.

The abscissa shows the various muscle groups, whose symbols are identical to those in Figure 7.

Those results asterisked * are statistically significant at the 1% level.

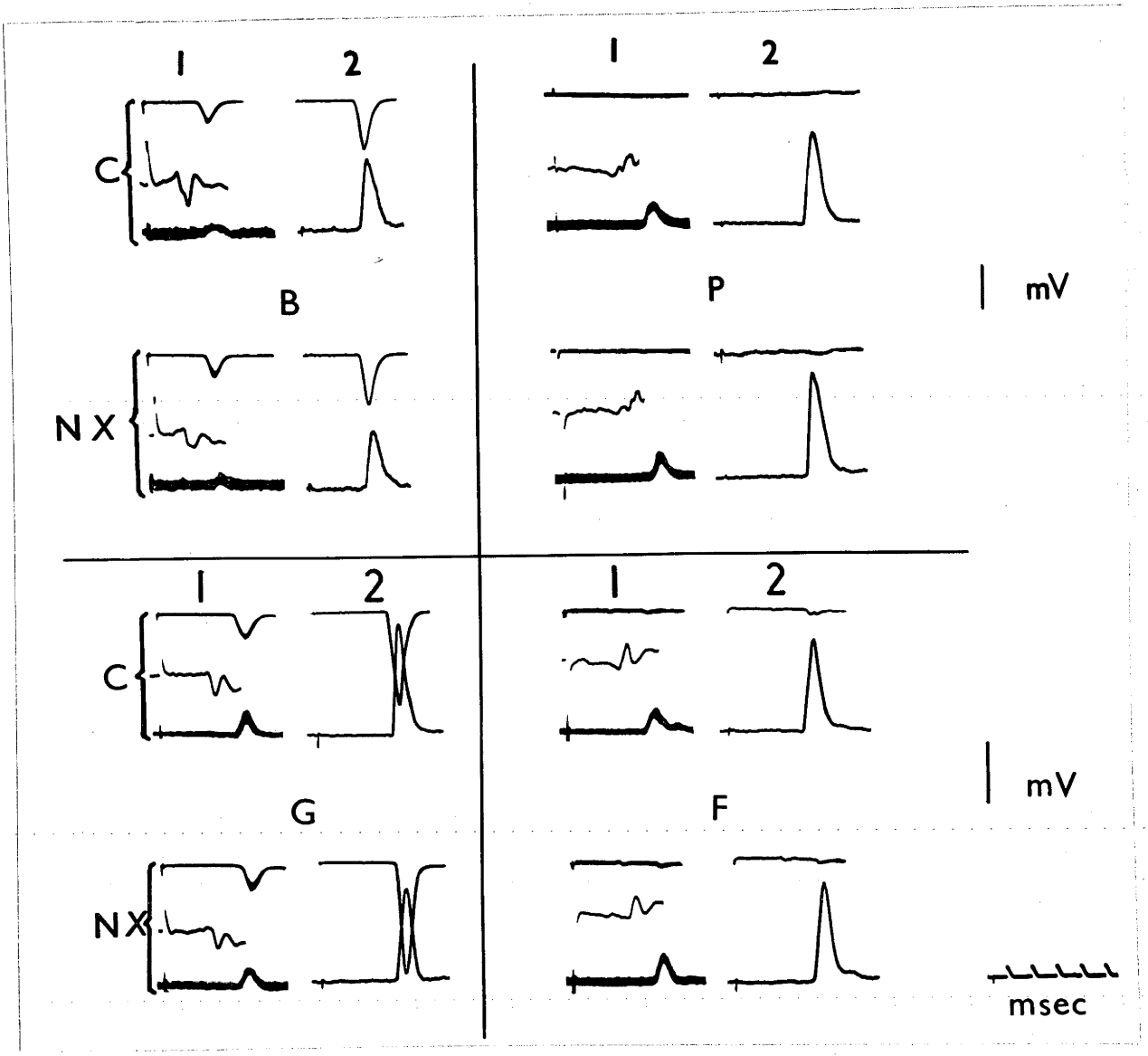

Figure 25. These monosynaptic reflex responses are actual records from one typical experiment from the series unilateral tenotomy plus spinal transection. The arrangement of the figure and the abbreviations used are identical to those in Figures 8 and 11, except that horizontal rows NX represent the responses from the various nerves in the tenotomized hindlimb, while C represent those from the normal side of the animal.

Note the symmetry of all reflex responses from corresponding nerves, both before, 1, and after, 2, standard tetanic conditioning.

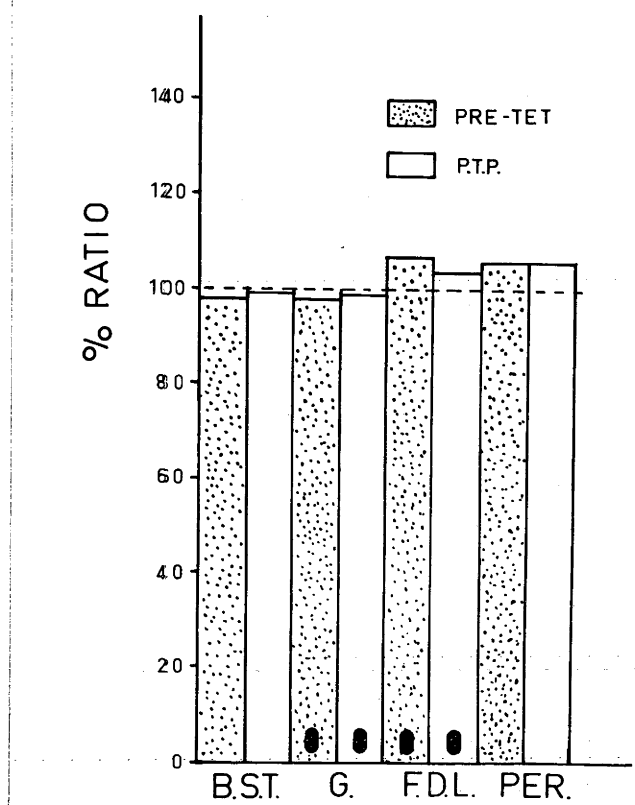

Figure 26.

The results from the series of tenotomy plus spinal transection summarised in Table 8 (a) are presented here in the form of a histogram. For the description and symbols, reference should be made to the legend for Figure 9.

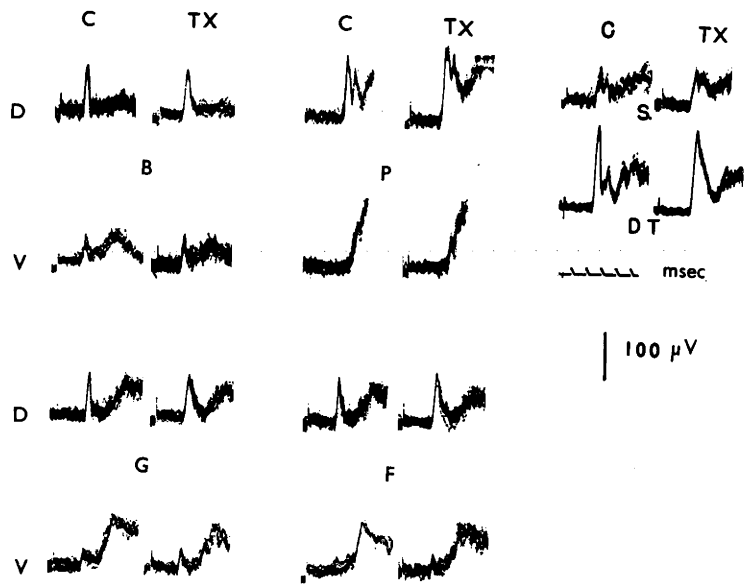

Figure 27.

These spinocerebellar tract responses are actual records all taken from one typical experiment from the series of animals with unilateral tenotomy and spinal transection. The arrangement of the figure and abbreviations used are identical to those in Figure 16 except that vertical columns TX denote responses from nerves to the tenotomized hindlimb.

Note the near symmetry of all reflex responses from corresponding nerves in both hindlimbs.

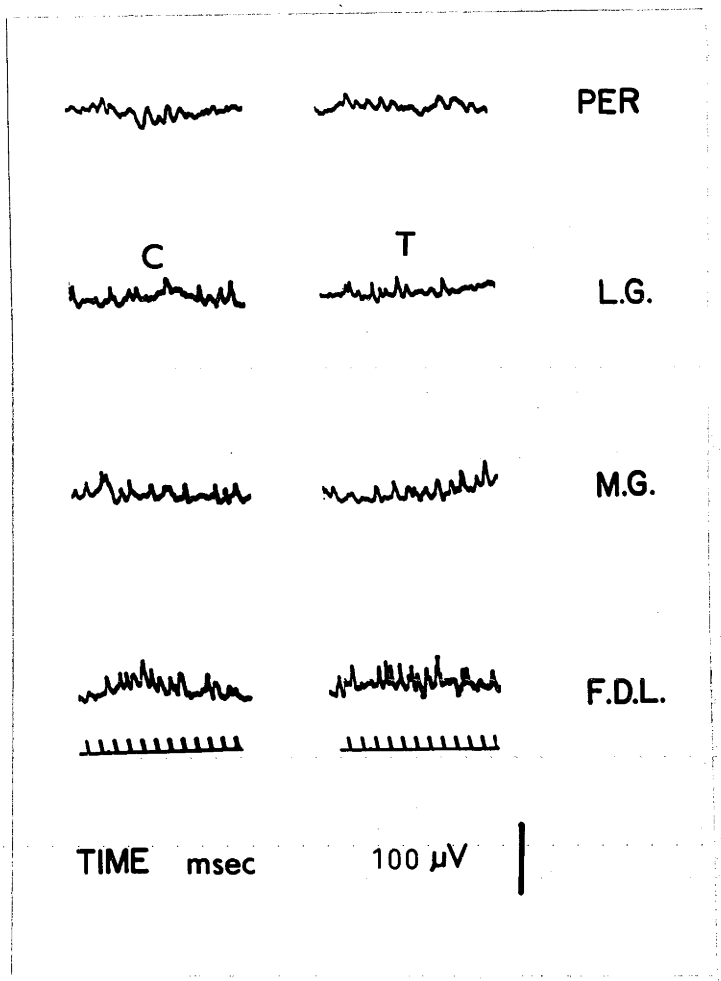

Figure 28.

These are actual records of the afferent discharges recorded from the cut nerves of non-stretched muscles in both hindlimbs. They are typical of the results obtained for all animals tested in the series unilateral tenotomy with spinal transection. Abbreviations are identical to those in Figure 19.

Note symmetry of all nerves in respect of their discharge frequency.

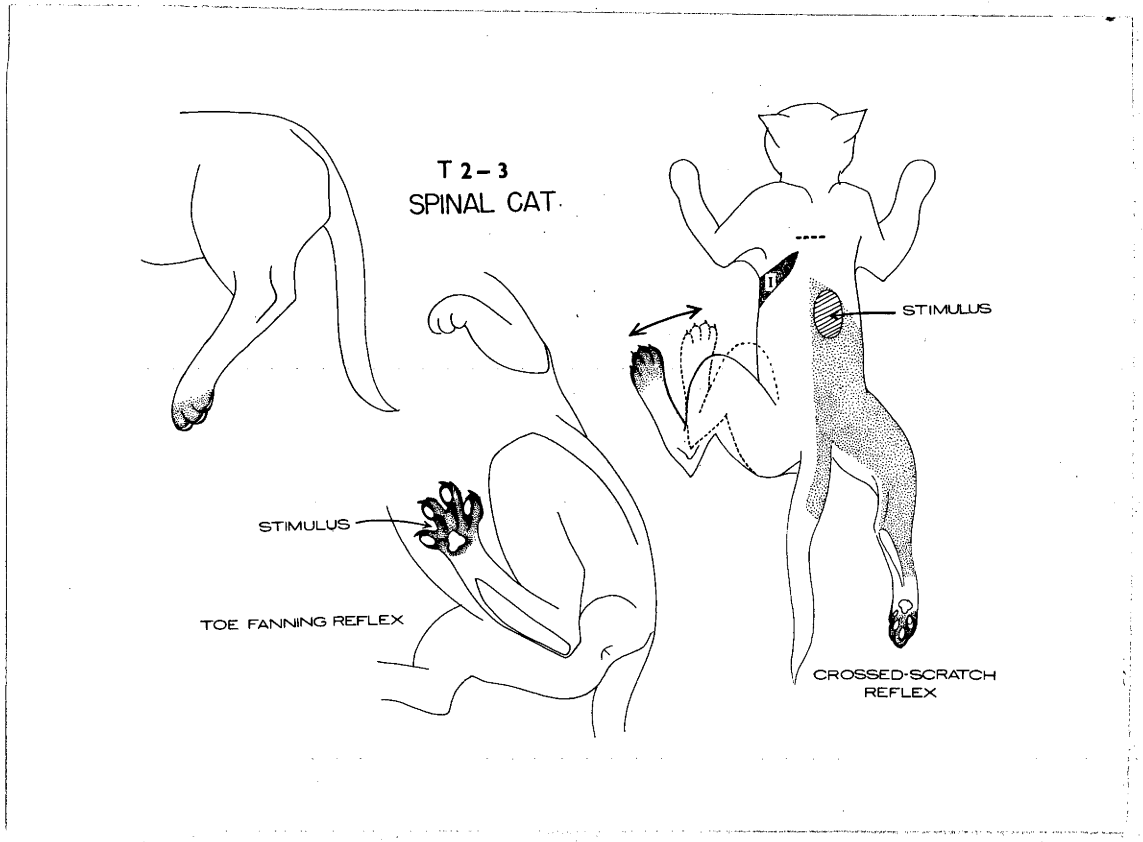

Figure 29.

This figure shows several important features of the reflex behaviour of chronic high thoracic (T2 - 3) spinal cats. (a) Toe fanning reflex described in the text is shown, its reflexogenous zone being dotted in. Note the characteristic position of fixation of the limb in partial flexed during the reflex.

(b) The scratch responses which may be elicited from these animals take one of two forms described in the text. Ipsilateral scratch responses may be elicited from the darkly stippled area 1 adjacent to the section level. Crossed-scratch movements are easily evoked by tactile or electrical stimulation of the skin over a wide receptive field (- lightly stippled) and it is the contralateral hindlimb which responds.

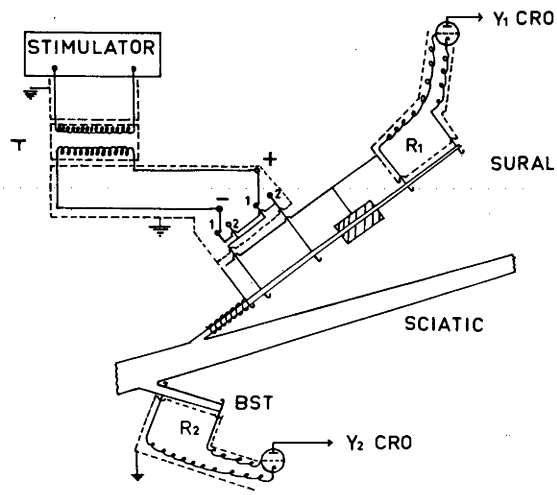

Figure 30.

This diagram illustrates the stimulating and recording system used for minimal artifact when stimulating by up to 100 V, and recording from nerves peripherally. Stimuli were thyratron discharges, transformer-isolated, and were applied to a cutaneous nerve, e.g. Sural. Reflexes in muscle nerves, B.S.T. elicited by volleys in cutaneous nerve sural, were recorded at R2. The afferent volley was monitored by electrodes at R1 separated by a 5 mm wide earthed plate from the stimulating electrodes. So that there was always cathodal stimulation of nerve nearest to recording point, a switch device was used. All recording electrodes were screened to within 5 mm of the nerve, and all screening was connected to a common earth. With stimuli of 100 V, the artifact recorded was less than 0.1 mV.

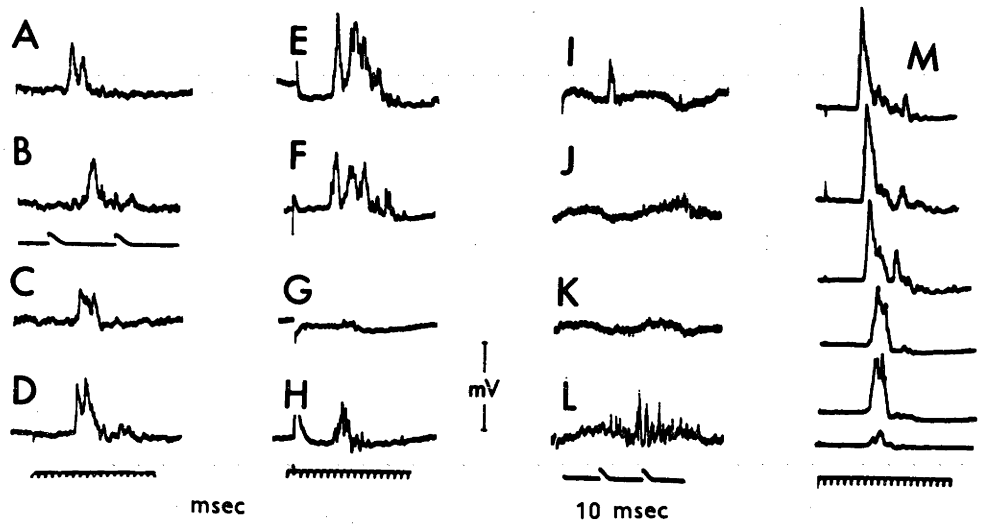

Figure 31. This figure shows some of the typical features of cutaneous reflexes evoked in muscle nerves of chronic spinal animals. A, B, C, D, show the reflex responses evoked in the biceps-semitendinosus nerve by volleys in the ipsilateral sural, saphenous, tibial and superficial peroneal nerves respectively. Stimulus strength is 25 X threshold in each case. Note that the reflex discharges to all nerves have almost the same latency and show relatively small variations in size and shape.

P.T.O

Figure 31. Legend Continued.

E, F, G, H, show the reflex discharges evoked by maximal volleys (50xT) in the left tibial nerve. Ipsilateral reflex discharges are seen in biceps-semitendinosus nerve, E, deep peroneal nerve, F, gastrocnemius nerve, G, and flexor digitorum longus nerve, H. Note that the reflex discharges into nerves supplying flexor muscles (E, F) are larger than those in nerves to extensors (G, H) and that the former have shorter latencies.

Reflex discharges in the corresponding contralateral muscle nerves are shown in I, J, K, L, evoked by maximal volleys in the left tibial nerve. Note that all contralateral discharges are smaller than the corresponding ipsilateral reflexes, and that the former have longer latencies.

Column M depicts the progressive increase in both maximal amplitude and duration of reflex discharges into biceps-semitendinosus nerve evoked by volleys in tibial nerve. Stimulus strengths from below upwards, relative to threshold, are 1.1, 2.5, 5, 10, 25, 100.X threshold of reflex.

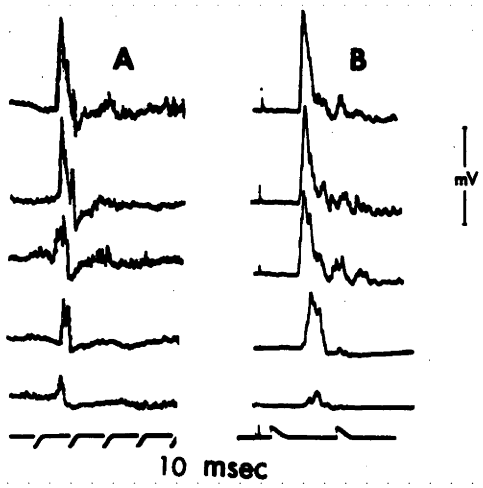

Figure 32. Records in columns A and B of this figure show the ipsilateral reflex discharges into the biceps-semitendinosus nerve of a chronic and acute spinal animal respectively. These reflex discharges are evoked by volleys of graded strength applied to the tibial nerve. Reading from below upwards, the stimulus strengths relative to threshold are 1.1, 1.2, 2.0, and 25 X threshold.

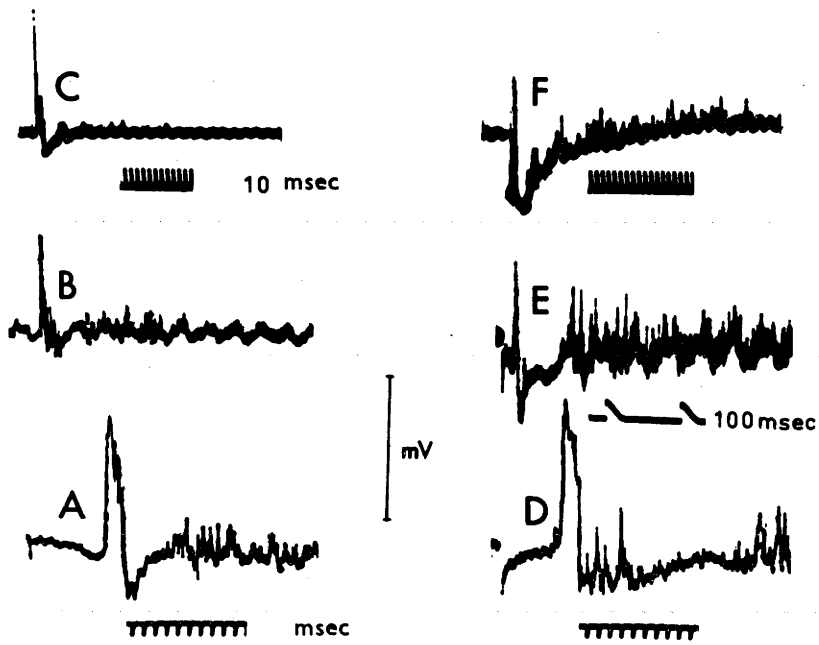

Figure 32 (a) Records show ipsilateral reflex discharges into the biceps-semitendinosus nerves of an acute and chronic spinal animal evoked from the tibial nerve. Records were obtained with a slower sweep velocity than in the previous figure, with the stimulus 100 X threshold, in order to show the prolonged reflex discharge into the ipsilateral biceps-semitendinosus nerve. In records (D,E,F) from the chronic spinal animal this discharge is longer than 400 msec. duration but the corresponding reflex discharge (A,B,C) is much less prolonged in the acute spinal animal.

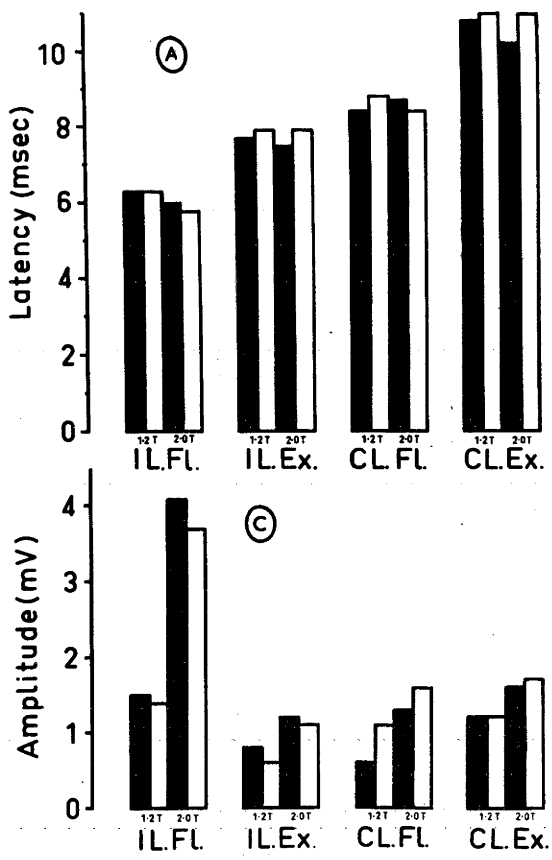

Figure 33. This figure displays as histograms A and C part of the results of reflex latencies and amplitudes given in detail in Tables 17 (a) and 17 (c) respectively. The results are means from all nerves tested in the two groups of animals, and are pooled in the manner described in the introduction to Table 17.

There are no significant differences of latency or maximum amplitude of reflex discharges between acute (filled columns) and chronic (open columns) spinal animals.

The abbreviations are as follows:

Il. Fl = Ipsilateral Flexors.

Il. Ex = Ipsilateral Extensors.

Figure 33. Legend Continued.

CL. Fl = Contralateral Flexors.

CL. Ex = Contralateral Extensors.

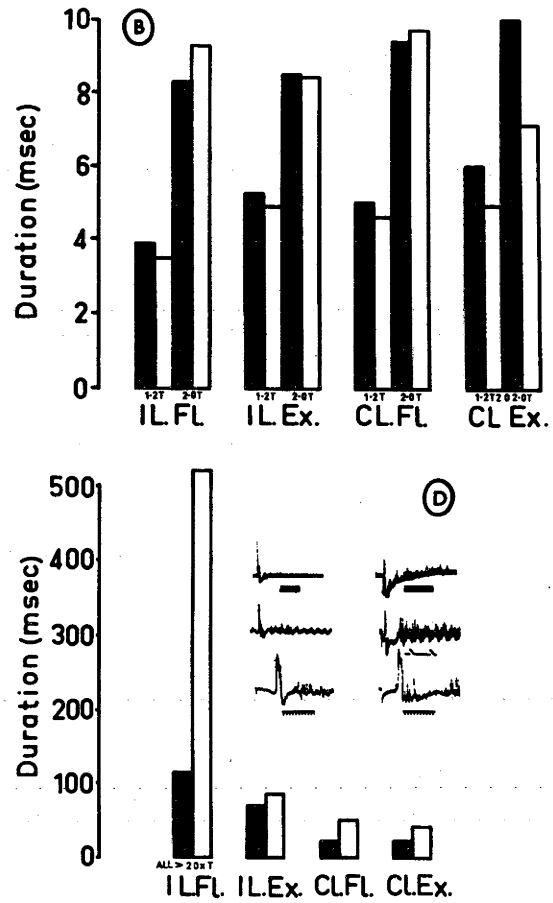

Figure 34. The histograms B and D depict the results shown in Table 17 (b) for the duration of the reflex discharges into muscle nerves evoked by cutaneous nerve stimulation. The results are the means from all nerves tested in the two groups of animals, and are pooled in the manner described in the introduction to Table 17. At the lower strengths of cutaneous nerve stimulation used in B, there are no significant differences in the duration of the reflex discharges evoked in the various muscle nerves between the acute (filled columns) and chronic (open columns) spinal animals. Histogram D shows the very prolonged reflex discharges evoked in

Figure 34. Legend Continued.

nerves to flexors by stimulating the ipsilateral cutaneous nerve at strengths greater than 20X threshold. The durations of such reflex discharges in nerves to ipsilateral flexors of chronic spinal animals were five times longer than the corresponding reflex discharges in acute spinal animals (see also the inset).

There is a less significant prolongation of the reflex discharges evoked in the other groups of muscle nerves of chronic spinal animals compared to the acute spinal group.

The inset shows, for the two groups of animals, actual records of the reflex discharges evoked in nerves to biceps-semitendinosus by stimulation of the ipsilateral tibial nerve.

The abbreviations used in this figure are the same as those in the preceding figure.

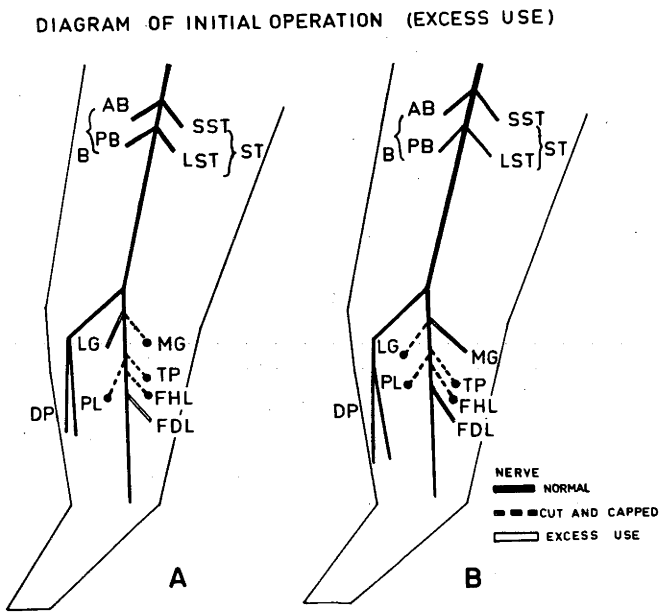

Figure 35.

This illustrates diagrammatically the two alternative procedures employed in the initial operative surgery. The abbreviations for various muscles are as follows:-

B	=	Biceps femoris (comprising Anterior head of Biceps and Posterior Biceps).
S.T.	=	Semitendinosus (comprises short and long Semitendinosus muscles).
L.G.	=	Lateral head of Gastrocnemius together with Soleus.
M.G.	=	Medial head of Gastrocnemius.
T.P.	=	Tibialis posterior muscle.
F.H.L.	=	Flexor hallucis longus.
F.D.L.	=	Flexor digitorum longus.
D.P.	=	Peroneal and anterior tibial group of muscles.

In Procedure A, L.G. and F.D.L. are spared, while M.G, T.P., F.H.L., PL., are denervated. In the alternative Procedure B, M.G. and F.D.L. are the spared muscles while L.G., T.P., F.H.L., PL nerves were cut and capped.

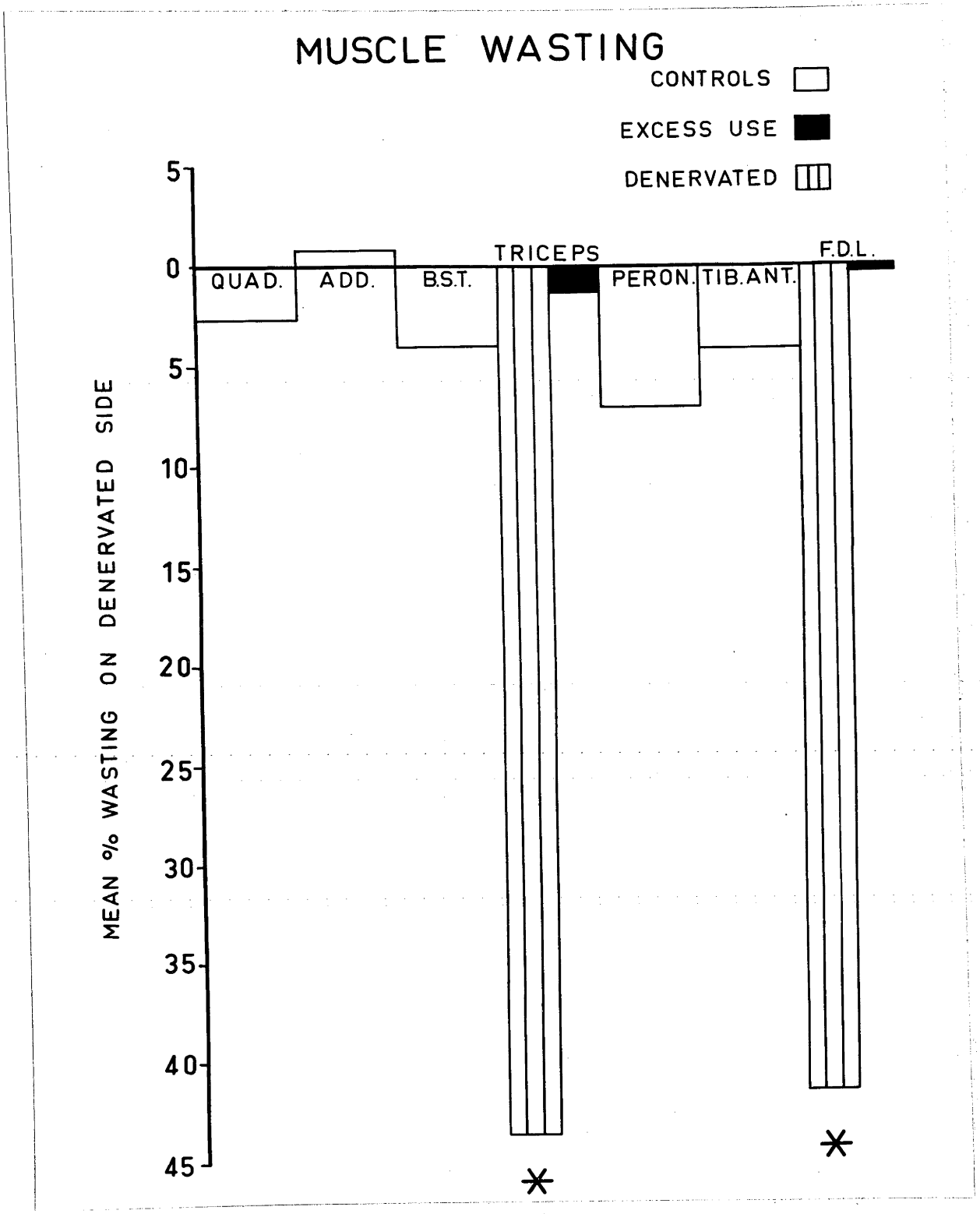

Figure 36. Muscle Wasting with Nerve Section Procedure.

The ordinate represents the mean % wasting of the muscle groups on the tenotomized side. The abscissa shows the various muscle groups, whose symbols are identical with those in Figure 7. The results asterisked * are significant at the 1% level.

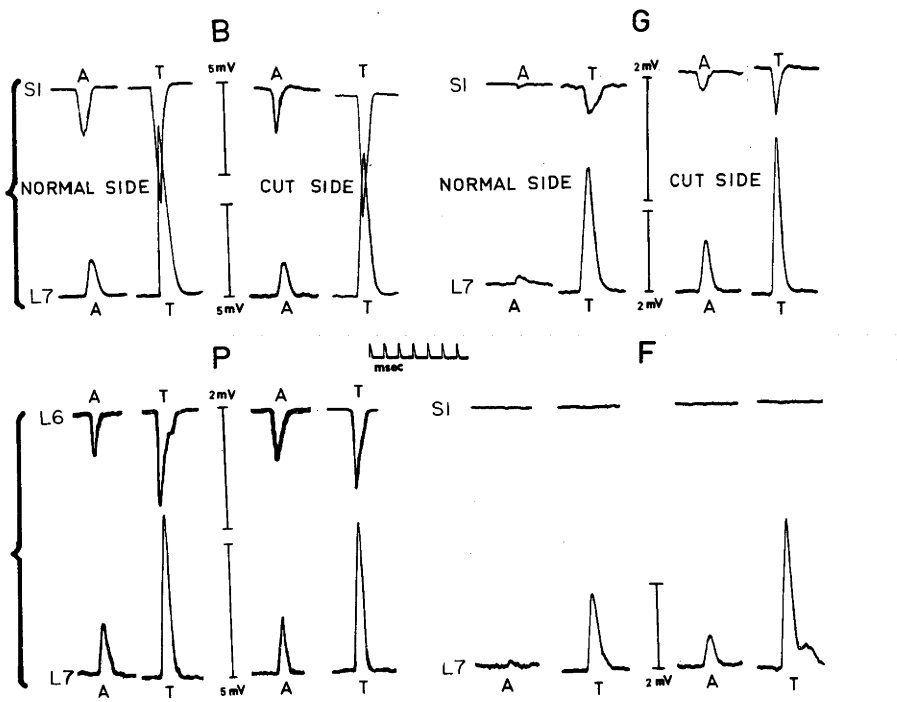

Figure 37.

These monosynaptic reflex responses are taken from one typical experiment in the series of animals subjected to the nerve section procedure.

Nerve abbreviations - B - Biceps Semitendinosus nerve.
P - Deep Peroneal nerve.
G - Nerve to Gastrocnemius (spared).
F - Flexor digitorum longus nerve.

Ventral roots are labelled. Vertical rows A indicate levels of reflexes before and rows T after tetanic conditioning with the standard tetanus. Note that reflex responses of bilateral controls (B & P) are symmetrical, while those from the nerves to spared muscles (G & F) are much enhanced relative to the corresponding nerve on the normal side.

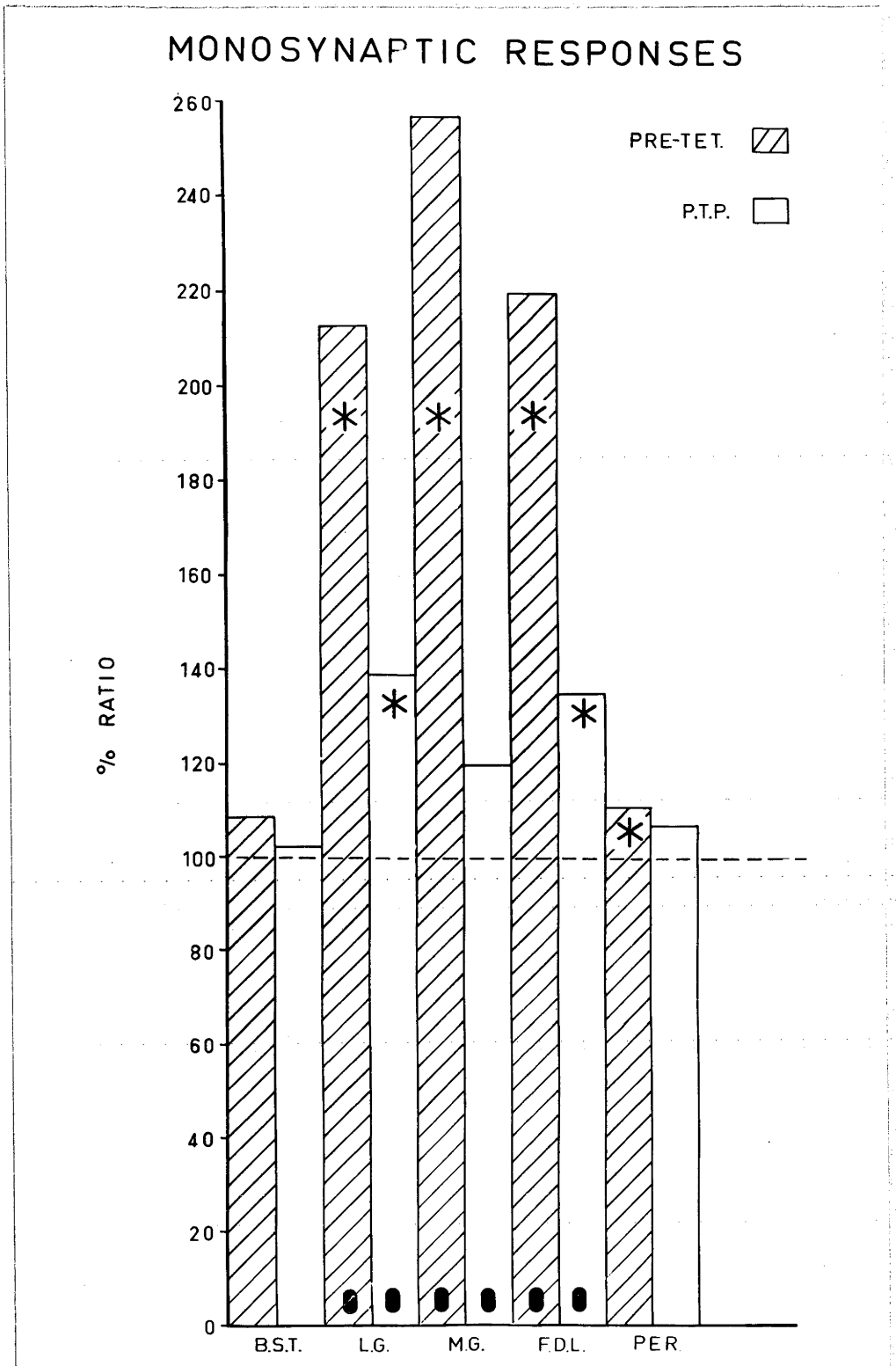

Figure 38. Monosynaptic Reflexes - Nerve Section Procedure.

This histogram displays the results shown in Table 11 of monosynaptic reflex responses from the series of animals with the nerve section procedure. The ordinate, abscissa and description of this figure are identical to those for Figure 9.

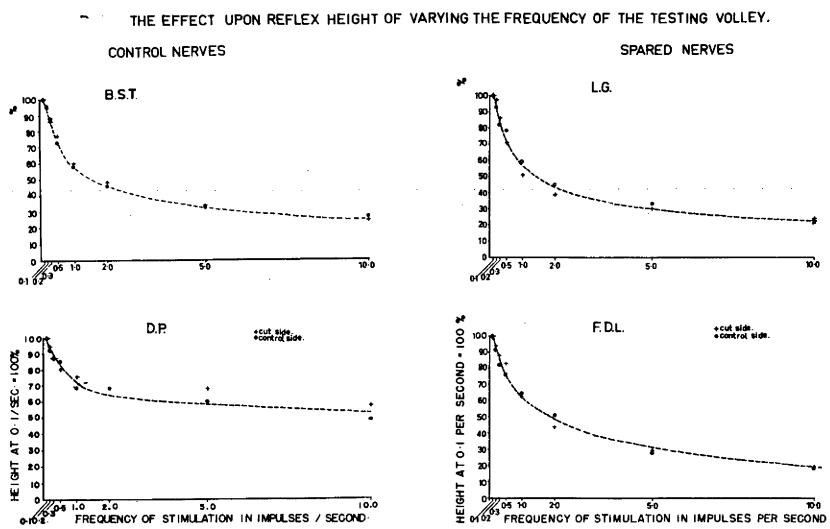

Figure 39.

In this figure is shown the effect upon reflex height of varying the frequency of the testing volley.

The arrangement of the figure, its description and abbreviations are identical to those used in Figure 13. Each point is the mean of results from four different animals.

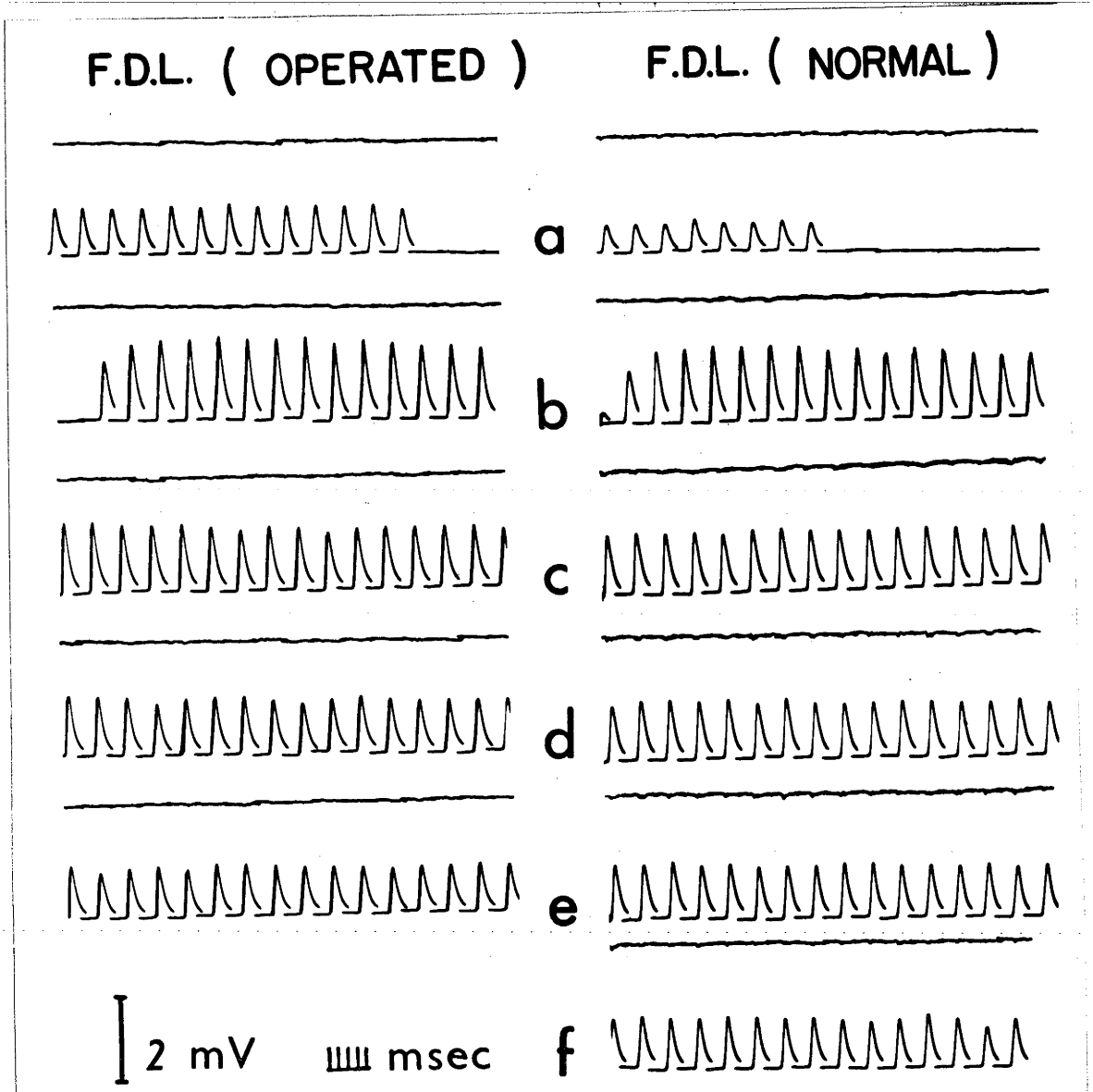

Figure 40. These records from the nerves to Flexor digitorum longus in one typical experiment illustrate the time course of post-tetanic potentiation. Records were obtained in the same manner as those in Figure 14, with the same frequency (0.3/sec) of testing volleys.

Note the absence of any reflex in S1 ventral root (upper beam) and the enhanced reflexes into L7 ventral root from the operated side. This enhancement is much more evident before (a) than after (b - f) tetanic conditioning with the standard tetanus.

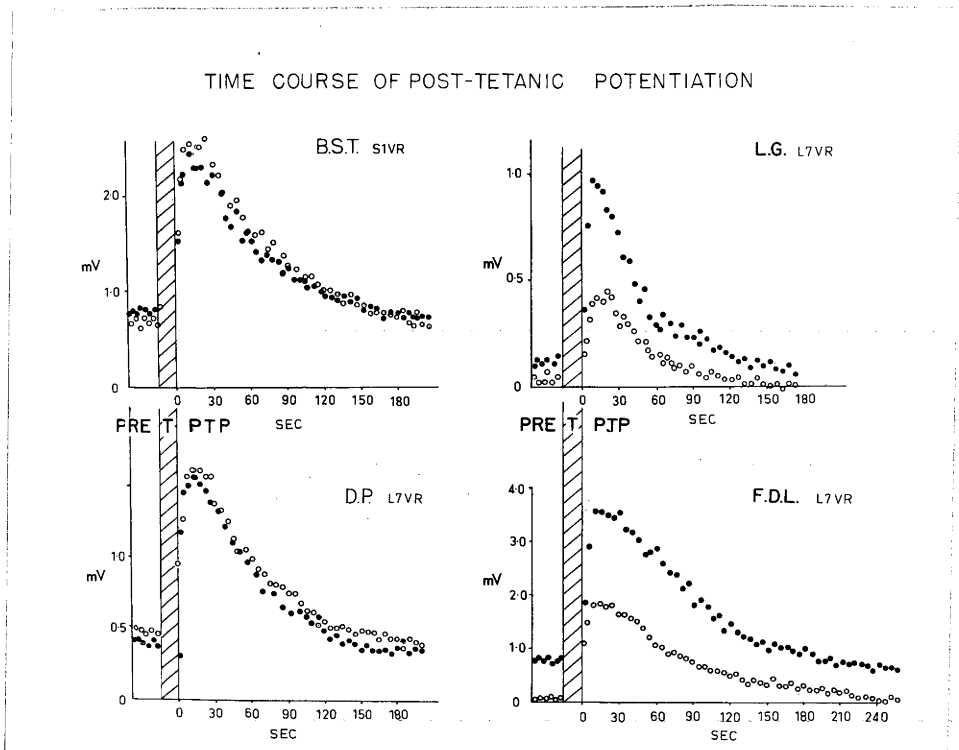

Figure 41. Nerve Sections.

This shows the time course of post-tetanic potentiation for nerves to control and spared muscles, for a single typical experiment.

The arrangement of this figure, its description and abbreviations are identical to those of Figure 15.

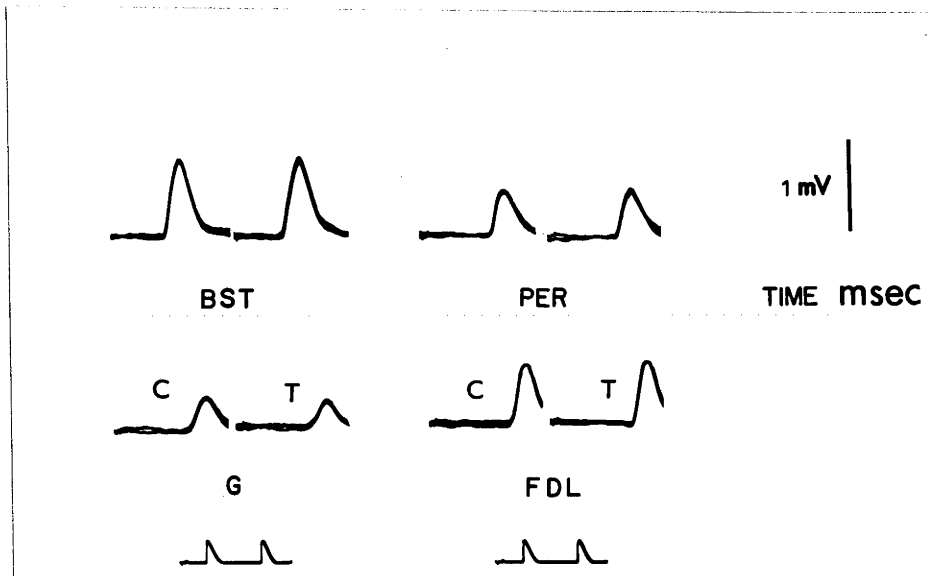

Figure 42. Nerve Section Procedure.

These records show afferent ingoing volleys recorded monophasically from various corresponding pairs of ventral roots. The description and abbreviations for this figure are the same as that for Figure 18.

Note the good symmetry of volleys from corresponding nerves.

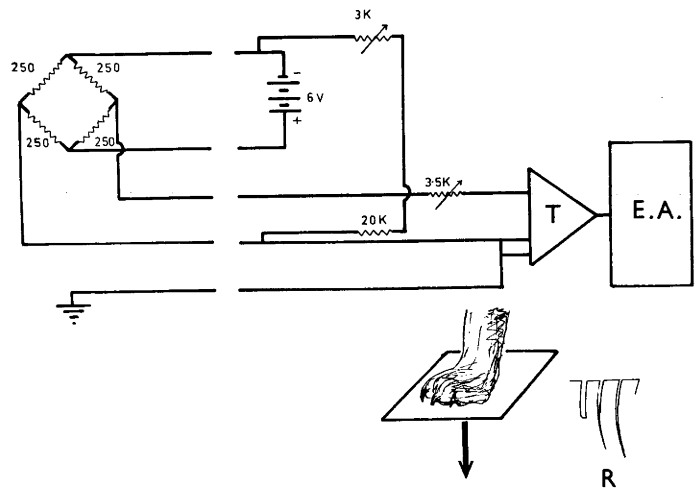

Figure 43.

This diagram illustrates the block circuit of the apparatus used for measuring pressures exerted by cats' limbs during walking.

A Grass force-displacement transducer 0 - 1 Kg was used, being incorporated in the bridge circuit shown. Signals were amplified (T) by a Texas Instrument model 301 D C Amplifier, and fed into an Esterline Angus 0-1 m A pen recorder. Typical records obtained are shown in Figure 44, but are also shown as an inset (R) in this diagram.

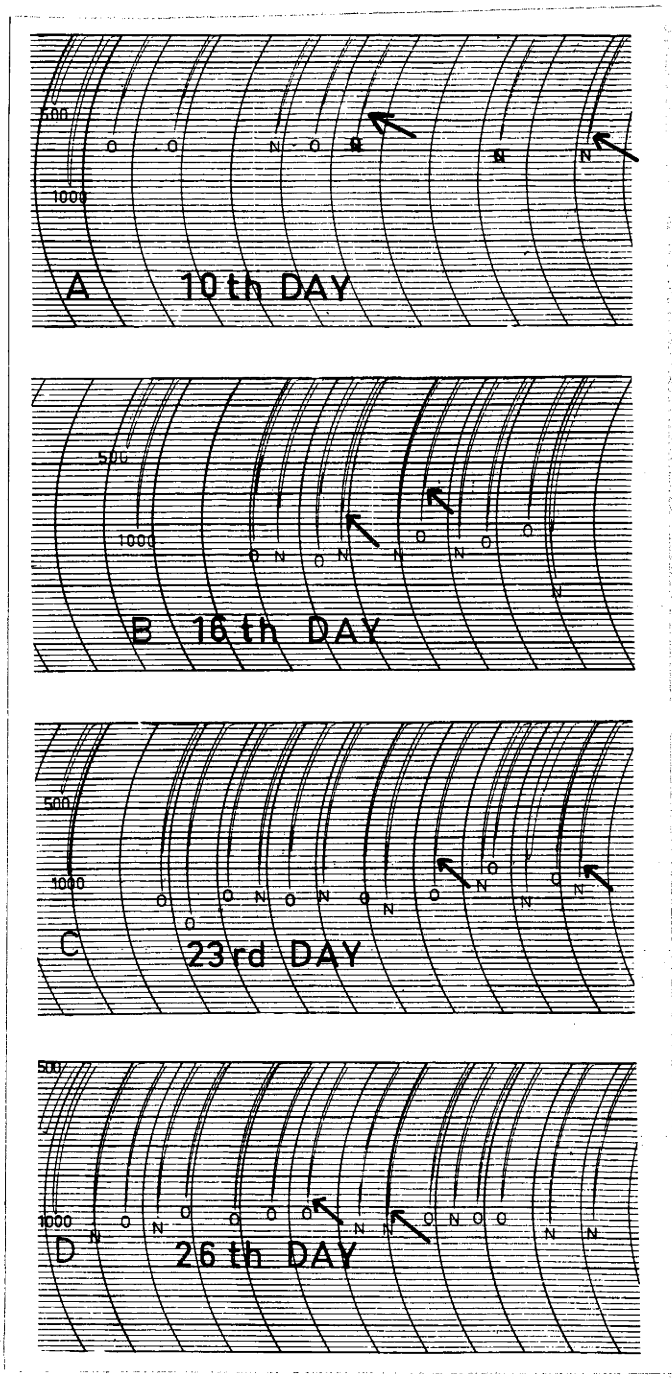

Figure 44.

These are actual records taken from one animal (W104) Calibrations of 500 and 1000 grams are seen at the start of each record. On most occasions during each passage along the corridor, one forepaw pressed on the strain guage platform, the ipsilateral hindpaw also followed, being placed in contiguity behind the

P.T.O

Figure 44. Legend Continued.

forepaw in the instant after the latter was raised for the next step. This characteristic pattern of movement is seen in the records as a large deflection caused by the forepaw, with an inflection on the recovery phase due to the hindlimb pressure. The force exerted by the hindlimbs during walking were almost always smaller than the forelimb pressures. Typical summits of both operated and normal hindlimb pressures are marked by arrows.

Deflections N represent pressures of fore or hind paws of the normal side of the animal while those marked O are caused by limbs of the operated side.

In A, note that while forelimb pressures show approximate symmetry, the pressures of the operated hindlimb are much below those of the normal hindlimb. This difference is reduced with increasing time postoperatively, until in D there is approximate symmetry of the hindlimb pressures.

Note also in D that the hindlimb pressures are now only slightly less than forelimb pressures of A where all hindlimb pressures fall short of the forelimb pressures.

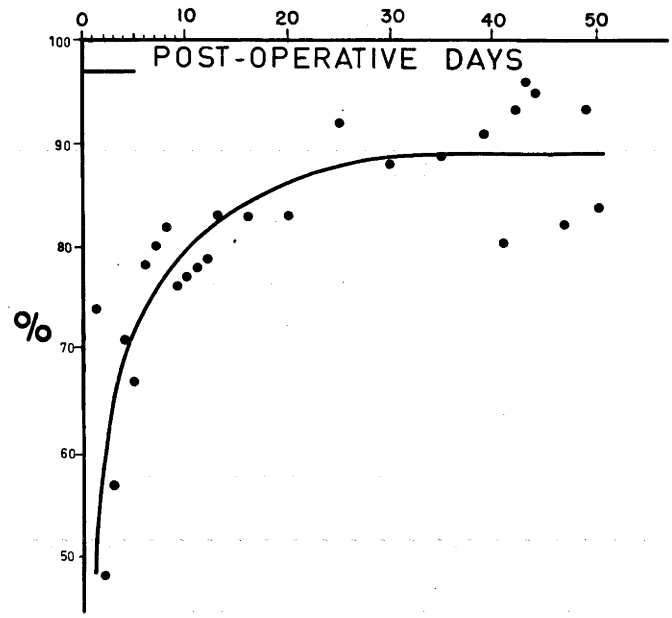

Figure 45.

Points are the mean results from 6 cats.

The ordinate represents the sum of the hindleg pressures as a % of the sum of foreleg pressures. The abscissa depicts postoperative days.

This figure shows a general shift of the body support towards the forelimbs during the first week after operation, with recovery to a more normally balanced position in the subsequent three weeks.

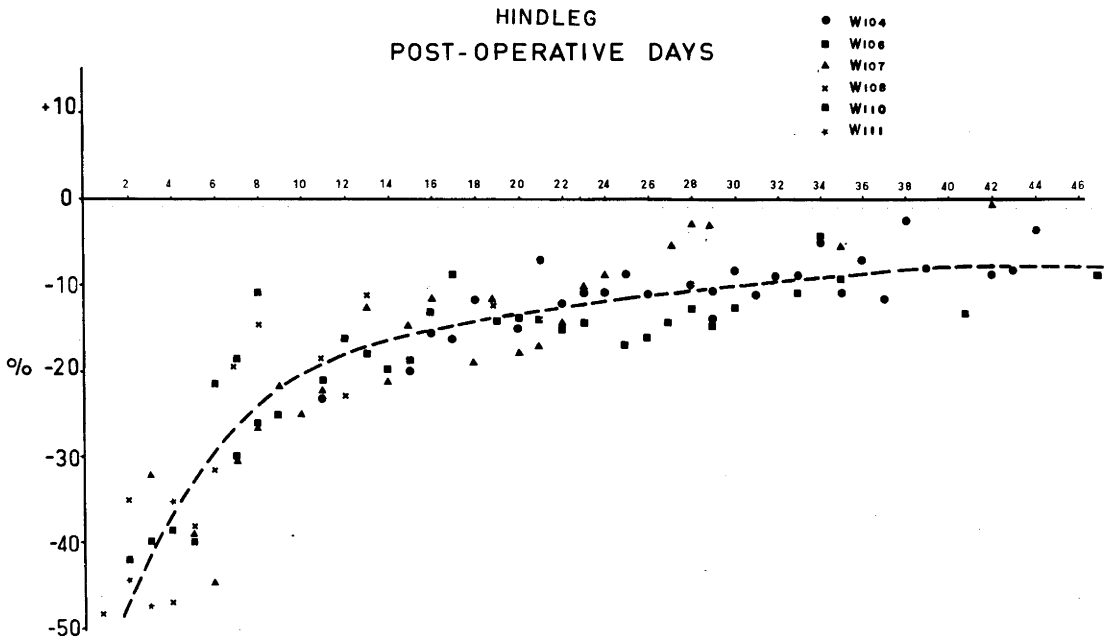

Figure 46.

Each point depicts results from at least 20 pressures of each limb. Symbols for individual animals as shown.

The ordinate represents the percentage difference of the force exerted by the hindleg in which there were nerve sections, compared to the contralateral control hindlimb pressures.

The abscissa shows postoperative interval in days.

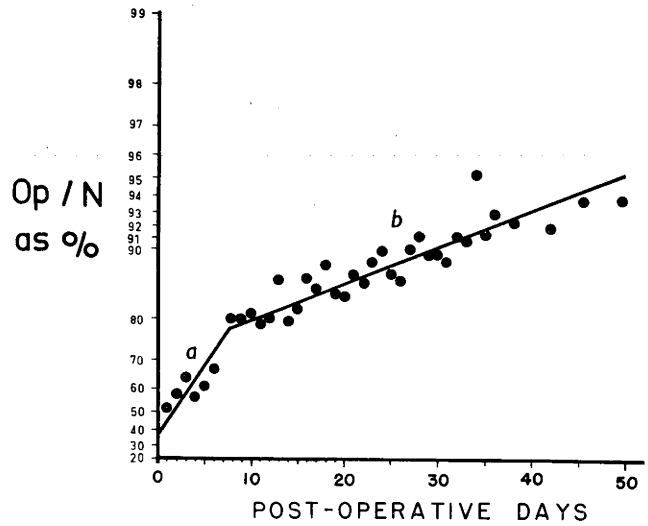

Figure 47.

This graph, in which ordinate and abscissa are representing the same as the previous graph, depicts the results from the previous graph plotted with a logarithmic scale on the ordinate. Each point represents averaged results of all cats, unlike the preceding graph.

The graph shows an increase, with postoperative time, of the operated hindlimb thrust compared to the control hindlimb, and the points are most conveniently described by the straight line b, with initial deviation a as a separate line.

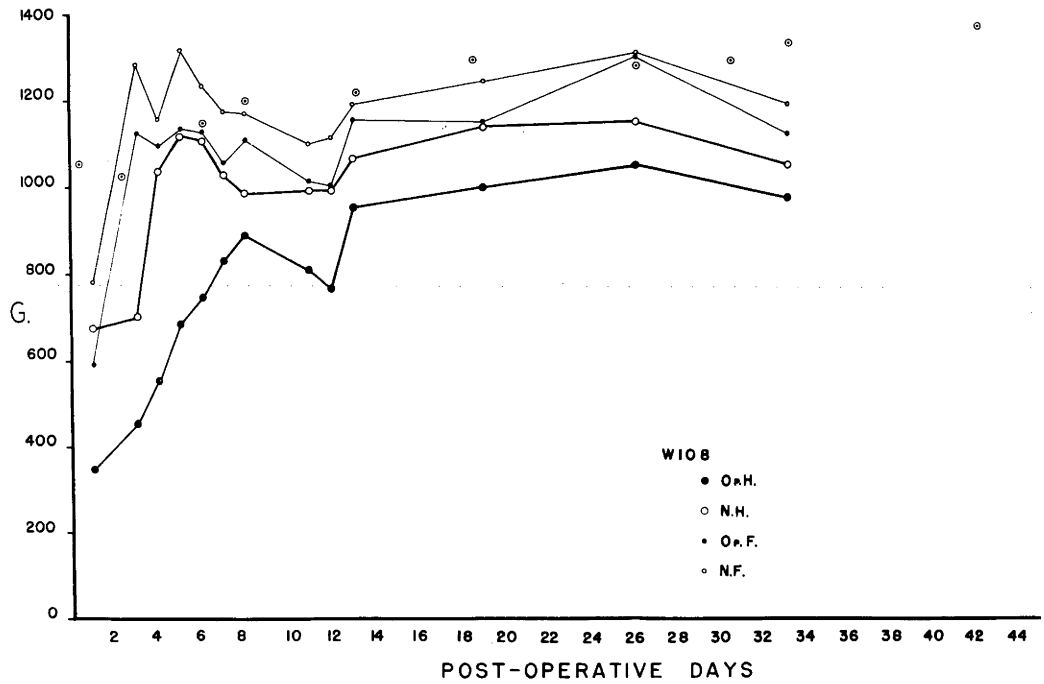

Figure 48.

This graph shows for one cat W108, force in grams along the ordinate, the abscissa representing postoperative days. The symbols for the various legs are:

N.F. = Normal side forelimb.
N.H. = Normal side hindlimb.
Op.F = Operated side forelimb.
Op.H = Operated side hindlimb.

The circled points show the values of half the cat's body weight on given postoperative days.

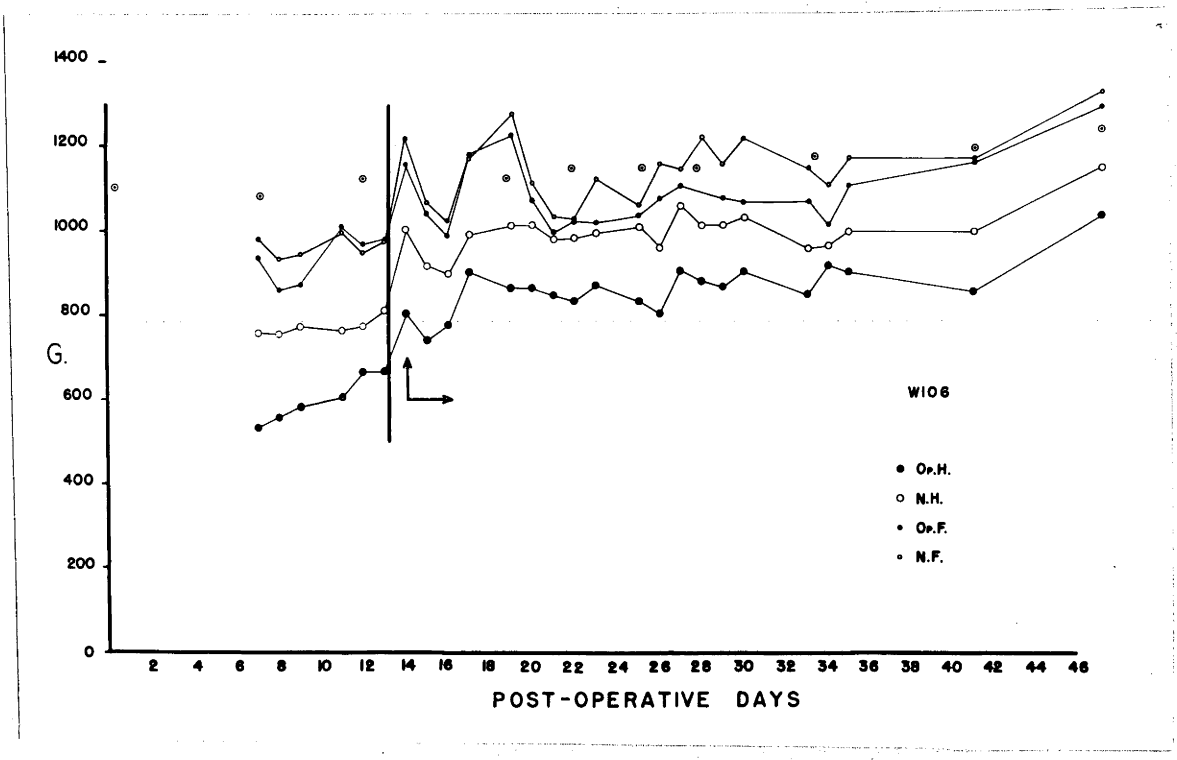

Figure 49.

This graph depicts the results from a single animal, W106, using the same ordinate, abscissa and symbols as those in the previous figure.

All the points after the vertical line, as shown by the arrows, indicate results obtained using Estafoam.

Note the sudden increase in the absolute pressures exerted on the first and fourth days of using Estafoam, but the absence thereafter of any permanent deviation from the steady trend of the graph.

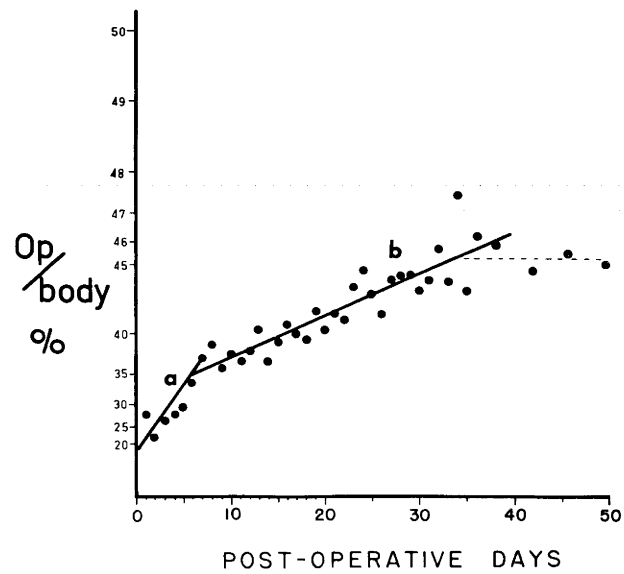

Figure 50.

The ordinate represents the mean pressures exerted by the operated hindlimb, expressed as a percentage of the body weight, on a logarithmic scale. The abscissa is postoperative days.

The graph shows an increasing percentage of the body weight borne by the operated hindlimb up to 40 days but from 40-50 days little increase occurs.

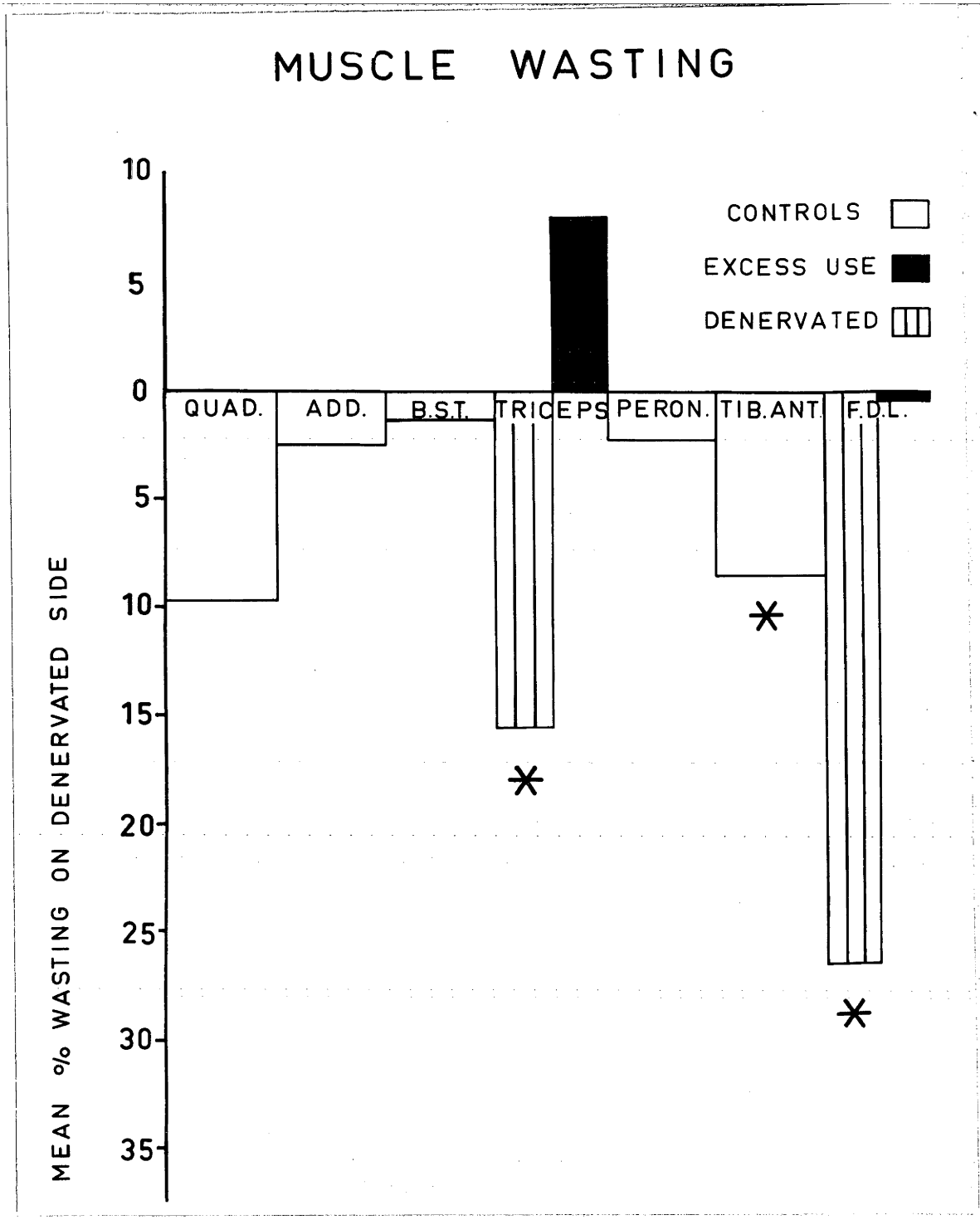

Figure 51.

Muscle wasting with nerve sections and spinal transection.

The ordinate represents the mean % wasting of the muscle groups on the side of the nerve sections.

The abscissa shows the various muscle groups whose symbols are identical to those in Figure 7.

The results asterisked * are significant at the 1% level.

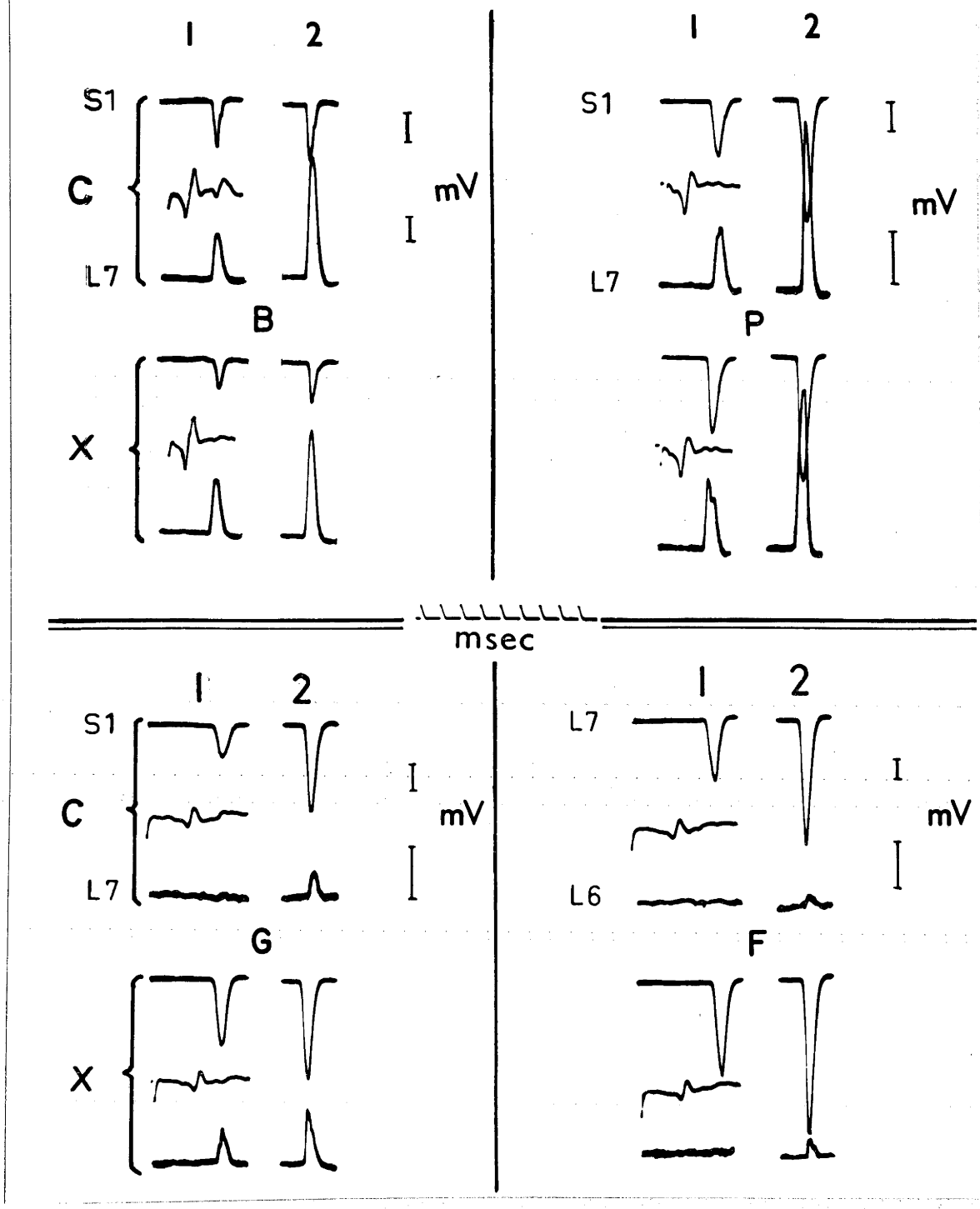

Figure 52. These are actual records of monosynaptic reflex responses from one typical experiment from the series of animals with nerve sections together with spinal transection.

P.T.O

Figure 52. Legend Continued.

The arrangement of the figure, and the abbreviations used are identical to those used in Figures 8, 11, and 25, except that horizontal rows X represent the responses from the various nerves from the operated hindlimb, and rows C denote those from the normal side. The results are very similar to those in Figure 37. Note symmetry of bilateral control reflexes and the marked enhancement of reflexes from nerves to spared muscles both before, 1, and after, 2, tetanic stimulation.

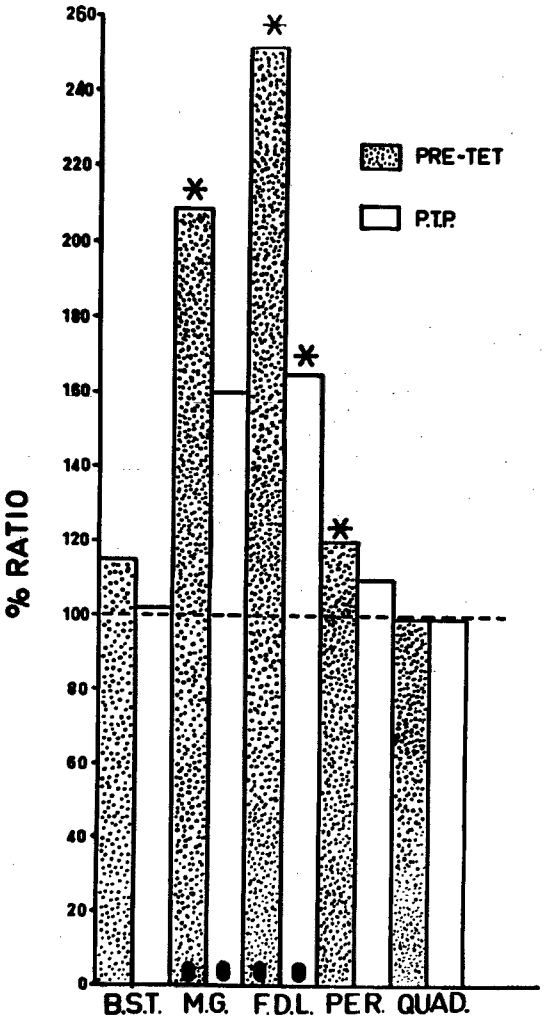

Figure 53. Monosynaptic reflexes - nerve section procedure.

This histogram displays the results given in Table 14 for the series nerve sections plus spinal transection. For the description and symbols refer to the legend of Figure 9. Note how closely the results shown in this figure parallel those in Figure 38.

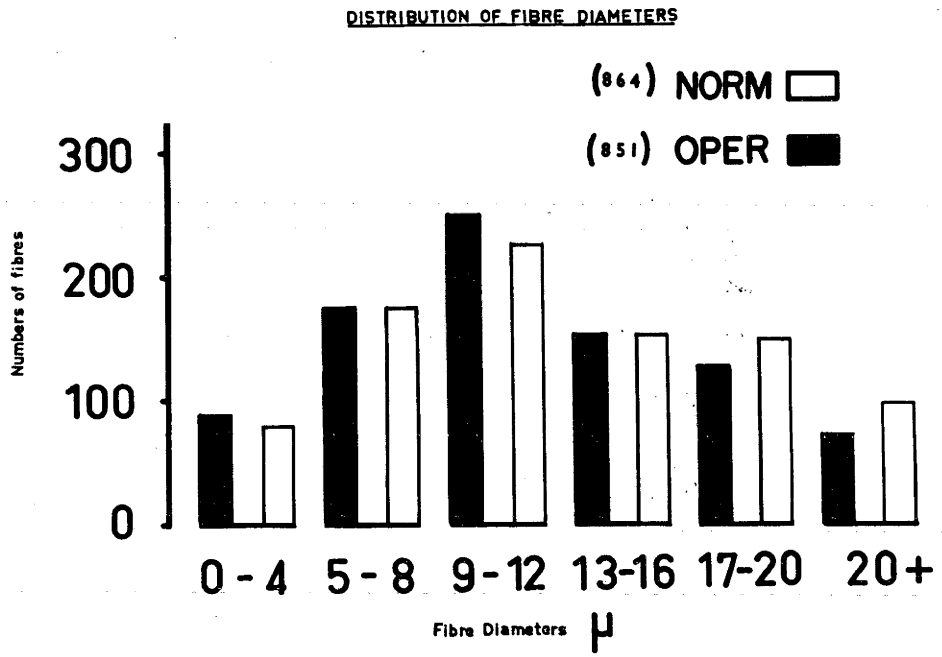

Figure 54. This histogram illustrates the spectrum of fibre diameters determined from the S1 ventral roots of one animal 26 days after the nerve section procedure A. The ordinate displays the number of fibres, and the abscissa depicts the various ranges of diameter in microns.

The operated side (filled columns), by comparison with the normal side (open columns), shows fewer fibres of larger diameter, and slightly more fibres of smaller diameter. That is, there is a small but definite shift of the spectrum to the left.

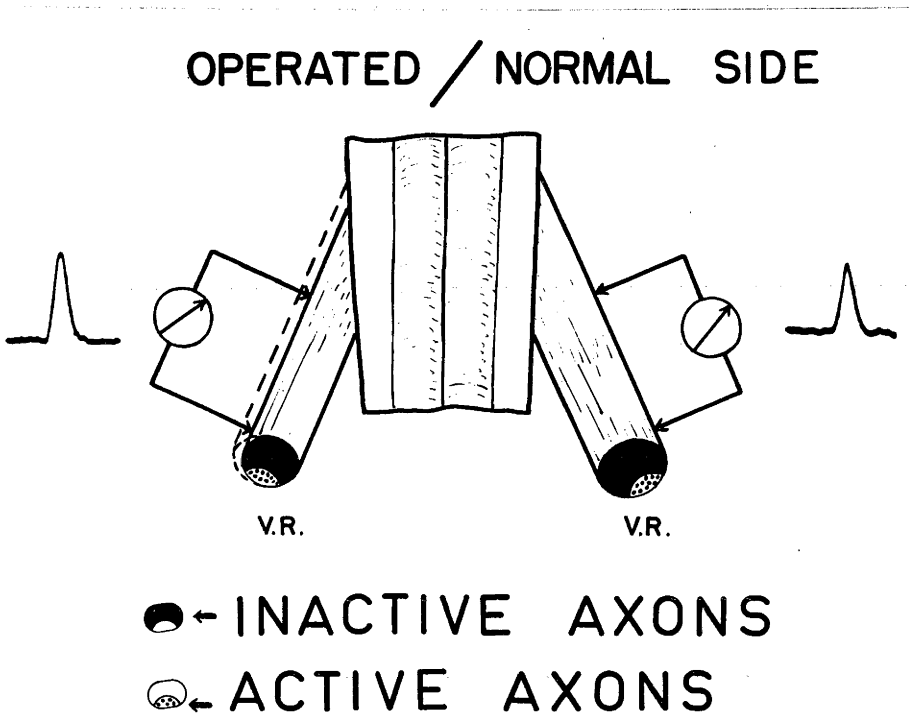

Figure 55. Nerve Section Series.

This diagram represents one segment of spinal cord with ventral root attached. The degree of shrinkage of the ventral root resulting from the nerve sections on the operated side has been exaggerated.

The reflexes inset represent responses from corresponding control nerves on both sides, and show the 15% enhancement of reflexes from control nerves on the operated side.

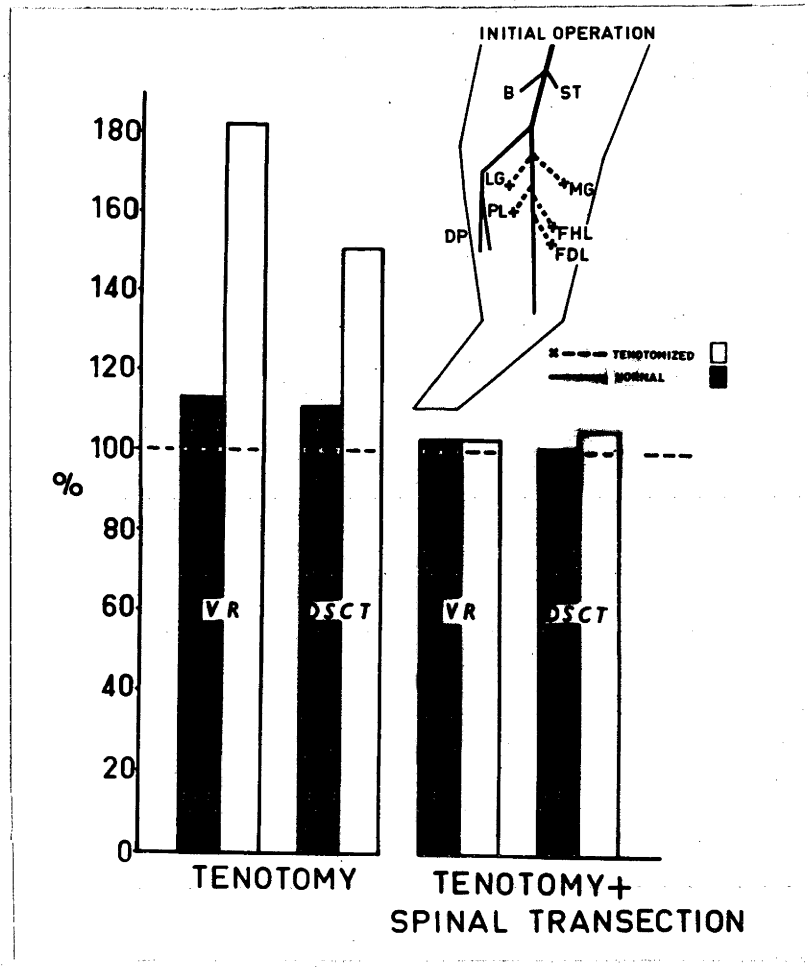

Figure 56. This histogram summarises the results obtained in Section A. Inset is a diagram depicting which of the nerves tested supply tenotomized muscles. The symbols used are the same as those in Figure 35.

The ordinate, as for reflex comparisons in previous figures, gives as a % the ratio tenotomized side response / normal side response, 100% thus indicating bilateral symmetry. Results in the two groups along the abscissa are obtained by averaging all reflexes in the catagories shown, for all animals.

Filled columns indicate average ratios of reflexes from control nerves. Open columns display results for nerves to tenotomized muscles.

V.R = monosynaptic reflexes recorded from the ventral roots. (The values of reflexes after tetanic conditioning are not shown in this figure).

DSCT = Responses from Dorsal Spinocerebellar tract.

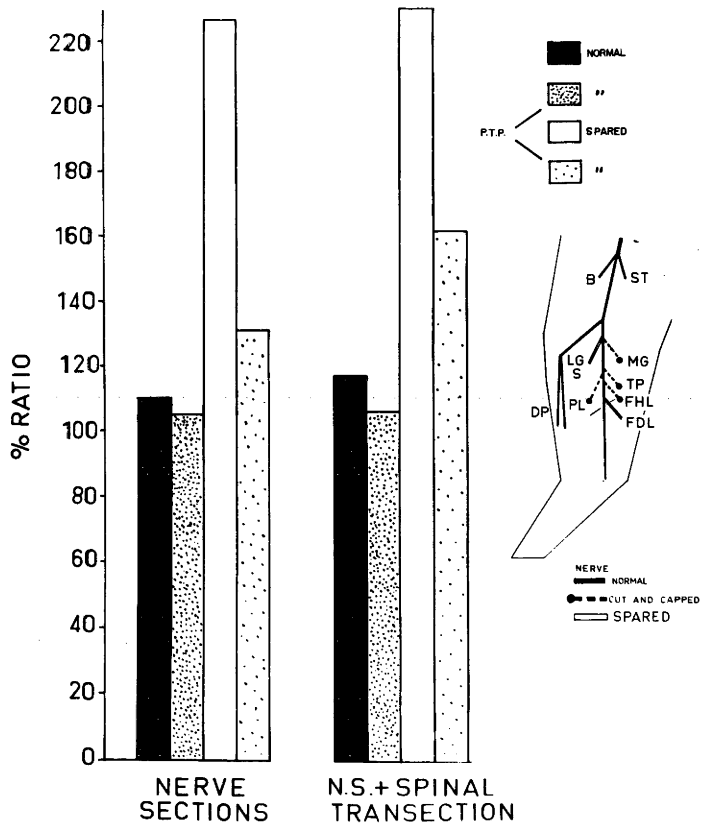

Figure 57.

This histogram summarises the results from Section C. Inset is a diagram showing one of the two alternative operative procedures described in detail in Figure 35. The symbols used are the same as those in Figure 35.

The ordinate, as in the previous figure, gives as a % the ratio cut side responses / normal side responses. Bilateral symmetry is thus represented as 100%. Results in the two groups along the abscissa are obtained by averaging all reflexes in the catagories shown, for all animals. All figures are obtained from monosynaptic reflexes recorded in Ventral roots, both before (solid and open columns) and after (heavy and light stippling) tetanic conditioning.

The term spared designates the nerve to the remaining innervated muscle from a group of denervated synergic muscles.