GÖSTA HÄGGQVIST, STOCKHOLM:

THE NERVOUS SUBSTRATUM OF MUSCLE TONE[1])

The spasticity which, under certain conditions, makes its appearance in individual muscles, or in the musculature in general of man, is brought about by a disturbance of the regulation of the peculiar muscle-function which is termed *tone*. This tone, like contraction, is dependent on the central nervous system. If the motor nerve serving the muscle be cut, the muscle-tone disappears at the same time that the power of contraction ceases. The tonic function of the muscle, consequently, like the contractile power, is dependent on impulses originating in the nervous system.

There are various theories respecting the path taken by the tonic impulses, from the central nervous system to the muscle, Mosso was the first (1907) to put forward the hypothesis that it was sympathetic fibres which conveyed the tonic excitation, and after Boeke (1910) had described a sympathetic innervation of the skeletal muscles, de Boer (1915, 1921) endeavoured, by means of experimental section of nerves of frogs and cats, to demonstrate that the tonicizing impulses were carried to the muscle by rami communicantes grisei, via the sympathetic system. The demonstrative value of de Boer's experiments is denied, however, by a number of investigators who endeavoured to repeat his experiments, (Dusser de Barenne, 1916; Cobb, 1918; Takahasi 1922, and others).

In 1919, Frank brought forward the theory of a parasym-

[1]) *A lecture given at the Meeting in Stockholm of the Northern Orthopedic Association, 8. September, 1938.*

pathetic tonic innervation, but this was refuted as early as 1920 by Meyer and again, in 1921, by Spiegel.

Finally, the Japanese clinician, Ken Kuré, and his disciples have endeavoured, in a large number of publications (1931—1933), to demonstrate that the skeletal muscles receive four kinds of efferent nervous fibres, viz, motor, sympathetic, parasympathetic and extra-pyramidal. Of these, the last three, say these authors, are tonicizing. As regards the sympathetic and parasympathetic muscle innervation, Kuré cannot be said to have come farther than de Boer and Frank, and so one is compelled still to acknowledge the strength of the evidence brought forward by the objections to the theory of the influence of the autonomous nervous system on the muscles. In this connection, there is still another objection which seems to me worthy of a certain attention, even if it is supported by no more than a theoretic argument. As far as we know, the preganglionar sympathetic nerve-fibres in mammals leave the spinal cord only via the anterior roots C_8—L_3, and the parasympathetic nerves serving the pelvic viscera in man only through S_2—S_4, which, in the higher mammals, probably corresponds to L_7—S_2. The anterior spinal roots serving the muscles of the neck and those of the upper and lower limbs should, consequently, possess neither sympathetic nor parasympathetic nervefibres. In spite of this, a flaccid paralysis makes its appearance in the corresponding muscles if these nerves be cut through, i.e., not only the contraction impulses but also the tonicizing impulses are prevented from being transplanted to the muscles. Consequently, we are compelled to look for the tonicizing nerve-fibres in the anterior roots, whether they are the same fibres which convey the contraction impulses or another fibre system.

With respect to the Kuré-school's theory of an "extrapyramidal" system of peripheral nerve fibres, this system seems to have interested the school in a far less degree than the sympathetic and parasympathetic muscle-innervation, if we are to judge from the number and the volume of their publications on the subject. Kuré and his collaborators assume that in the anterior roots, thin, myelinated fibres run direct from the spinal cord to the muscles together with the thick motor fibres. These thin fibres are supposed to constitute a continuation of the path of Monakow which, according to Kuré, is thinfibred too. In support of his opinion, Kuré, Okinaka, Kawaguzi and Shiba (1931), state that, in 4 cases of amyotrophic lateral sclerosis with spastic paralysis, they have found a destruction not only of coarse fibres in the area of the pyramidal path, but also of the large anterior root-cells and of the coarse fibres in a number of anterior spinal roots which were examined. In these latter, however, the fine fibres were intact. According to Kuré, Shiba, Kawaguzi and Okinaka (1931) the fine resembling the sympathetic terminations in the muscles, but somewhat larger than these latter. In this connection it may be recalled that Eccles and Sherrington (1930) have definitely demonstrated that, in cat, fine fibres in the anterior roots can extend to certain muscles of the hindlegs, as is mentioned below. The authors consider these to be motor-fibres. As, in Kuré's and his collaborators' cases, the pyramidal path is injured, then, from what we already know respecting spasticity in injuries of the pyramidal path, we have only to expect that a spastic paralysis would arise in the muscles which are served by these fine fibres even if those fibres are motor-paths. Consequently, I cannot find that the proof brought forward by Kuré and his collaborators, to show the existence of a peripheric "extra pyramidal" system of nerve-fibres, is conclusive, even if I admit that, in this respect, their theory is in close correspondence with the conception I shall form in this lecture.

When I myself began to study the question of tonic innervation of the skeletal muscles, it was in connection with investigations for quite another purpose, which, however, compelled me to examine the tone problem. A fibre-analysis of the pyramidal-path area in a person who had his pyramidal path destroyed by an embolus in the brain, showed, on comparison with a person in normal health, a disappearance of the fibres in the spinal cord in the 3:rd thoracic segment, as shown by diagram 1. The fibres which were destroyed appeared to vary in thickness between 5 and 17 μ, with an average maximum thickness of 10—11 μ.

Researches which were thereupon undertaken with Rhesus monkeys from which various parts of the cortical motor area

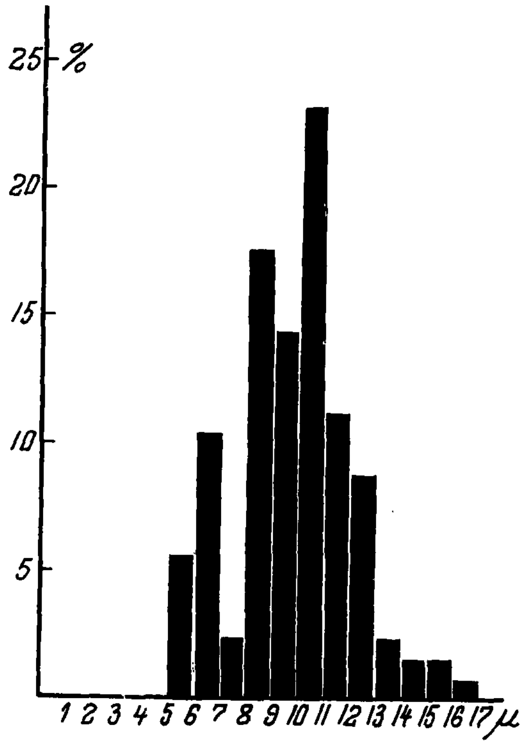


Fig. 1.

of the brain had been excised and fibre-analysis carried out within the pyramidal area in medulla oblongata seemed to show that the fibres which convey the impulses from the cortex to the anterior motor celles in the lumbar and the sacral spinal cord, have a coarser calibre than the fibres which pass from the cortex to the cervical medulla.

In this connection, it seemed to me desirable to learn the composition of the motor roots of the spinal cord. On investigation, I found that the fibres in all the anterior spinal roots in Rhesus were grouped around two maxima. In the upper cervical roots these maxima lie at 3—4 μ and 8—9 μ, respectively, both groups containing approximately the same number (Fig. 2). In

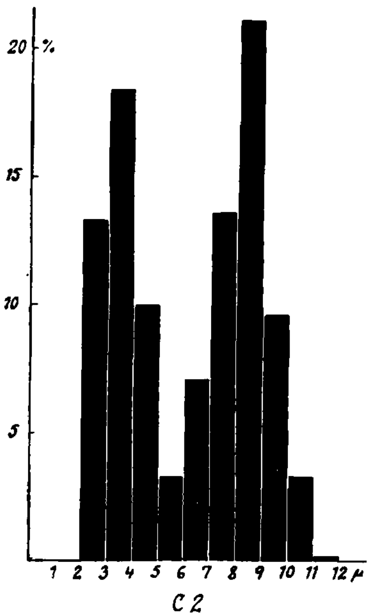


Fig. 2.

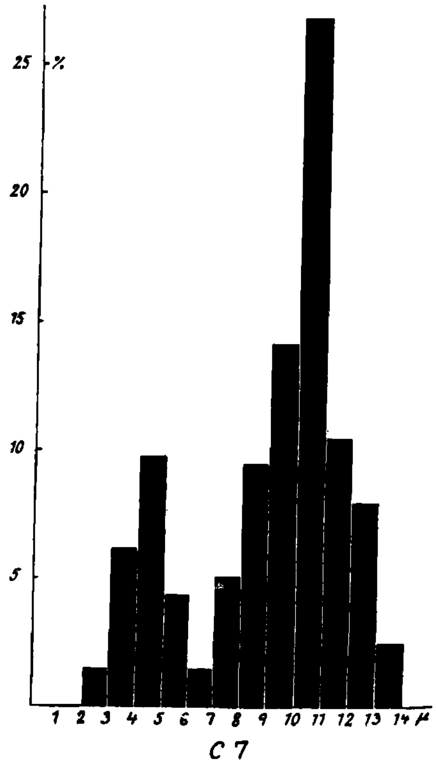


Fig. 3.

the lower cervical roots which serve the muscles of the upper limbs, the number of coarse fibres increases, so that they embrace about 75 % of the whole (Fig. 3). The fibres, both of the coarse and the thin-fibred group become, at the same time, thicker, so that the two maxima are displaced to 4—5 μ and 10—11 μ, respectively. At the transition to the thoracic roots, a sudden change takes place. The fine fibres increase greatly in numbers, while the coarse ones grow fewer and at the same time all the

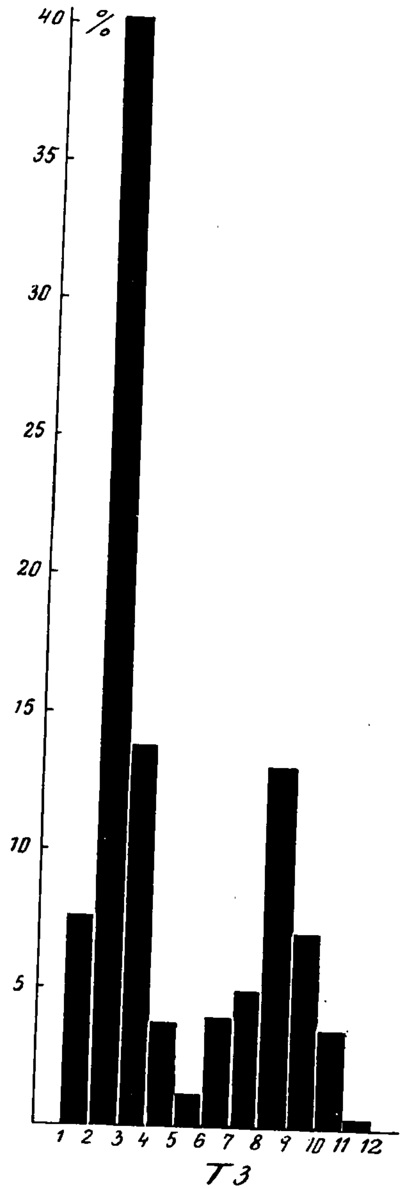


Fig 4

fibres become finer, so that the maxima lie between 2—3 μ and 8—9 μ respectively (Fif. 4). At this point the thin fibres constitute about 75 % of the whole. The fibre aggregate remains thus all the way down to L_1, after which the coarse fibres once more increase in numbers and in thickness, being, at this point, as in the lower cervical marrow, about 75 % of the total (Fig. 5), the maxima in the distribution-curve lying at 4—5 μ and 10—11 μ, respectively. In the sacral roots, the thin-fibred group predominates in S_1 a state of things which is evidently connected with the sacral autonomic system. Otherwise, the groups of coarse fibres are predominant.

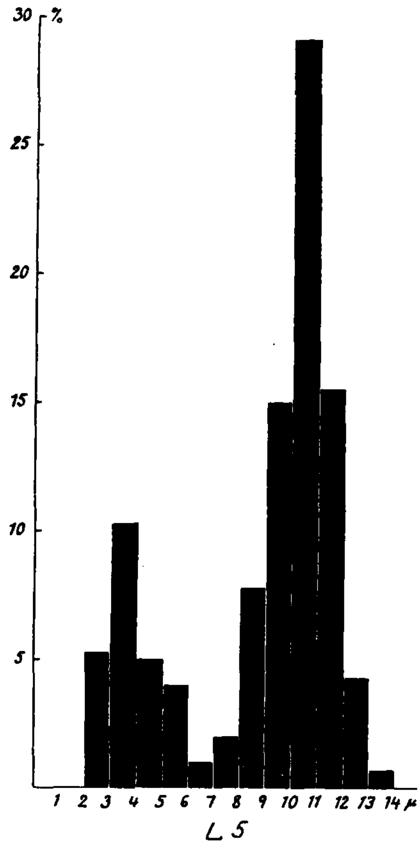


Fig. 5.

In man, Swensson (1938), has lately made a detailed analysis of the fibre aggregate in the anterior spinal-roots and, on the whole, it may be said that it resembles that in Rhesus, even if some few differences are found. In this connection, it is interesting to note the resemblance existing between the groups of coarse fibres in the motor lumbar roots and the fibre-aggregate of the pyramidal tract such as is shown in diagram fig. 1. In the nerve-roots of the limbs, the coarse fibres, in man, are distributed, according to Swensson, around a maximum lying at 10—11 μ, the group extending between approximately 6 and 16 μ. In the pyramidal tract, there are seen to be present at T_3 fibres of a thickness varying between 5 and 17 μ, distributed about a maximum at 10—11 μ. At an earlier date, the studies carried out by numerous investigators showed us that in the roots T_1—L_3 and S_2—S_4, there occur two kinds of fibres, viz, a coarse-fibred motor system and a fine-fibred autonomous one. Fine fibres have been observed in the other roots, too, but most authors have stated them to be few in number, and they have, in general, been assumed to be motoric. For instance, Eccles and Sherrington (1930) communicate observations of some few motor roots in cat, and of certain deafferented muscle-nerves. In the diagrams there could be observed the presence of two categories of fibres. Eccles and Sherrington, however, consider both kinds to be motoric. The difference in the calibre of the fibres, they think, results from the coarser fibres innervating a greater number of muscle fibres than do the finer ones, and, in this connection, they speak of »motor-units« of different sizes.

To me, it seems improbable that both the finer and the coarser calibred fibre-groups in the anterior spinal-roots should possess similar motor functions, since the rate of conductivity in the main mass of the coarse fibres must be assumed to be about 10 times greater than that in the finer ones (Y. Zotterman). The question then arose whether the constant presence of the fine-fibred group could signify that the autonomous system is of greater extension than has been previously supposed, or if we have to assume the existence of a third system of efferent fibres. To judge by Eccles and Sherrington's observations, both fine and coarse fibres can run to the skeletal muscles, and this seemed to me to point to the direction in which the answer was to be sought.

When it was found necessary to go deeper into the problem, I thought it might be possible to obtain conclusive evidence with

Fig. 6.

regard to the functioning of the fine-fibred nerves through an investigation of the motor cerebral nerves.

An analysis of the fibre aggregate in the occulomotor nerve, which, as we know before, is both motoric and autonomous, showed that there existed, as was to be expected, both a coarse- and a fine-calibre group of nerve-fibres. But the trochlear nerve, too, displayed, as Björkman and Wohlfart in my department, were the first to demonstrate, two groups of myelinated fibres. My own investigations showed that, in Rhesus, the thin fibres of this nerve constitute about 25 % of the entire fibre aggregate grouped around a maximum at 2—3 μ. Fig. 6. The maximum of the coarse fibres lay at 8—9 μ. I dissected out the obliques superior muscle of the eye with the nerve appertaining to it all the

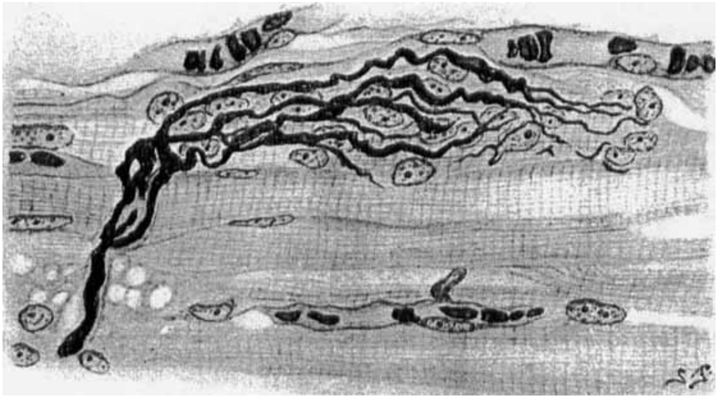


Fig. 7.

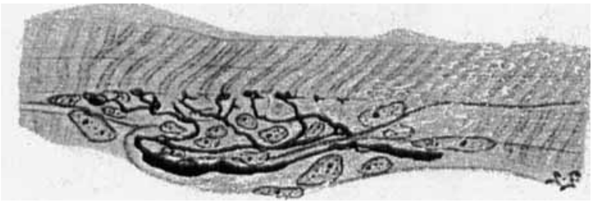


Fig. 8.

way up to where the nerve issued from the brain-stem. I then fixed the nerve-muscle preparation in a stretched position and cross-sectioned the whole of it in serie. I could observe in these sections that both fine and coarse fibres enter into the muscle (Fig. 6), and, in the case of certain fine fibres, I was able to demonstrate that they united themselves to muscle fibres. By means of silver-impregnation according to Bielschowsky-Agduhr, I was able to show that there existed in these muscles two kinds of endplates, viz, »terminaisons en plaque« (Fig. 7) and »terminaisons en grappe« (Fig. 8). Of the two, the former was decidedly in the majority.

In the abducent nerve I could determine the presence of only one kind of nerve-fibres, grouped around a maximum of 7—8 μ (Fig. 9). A peak at 4—5 μ is not statistically certain and as it occurs only in some cases, it is probably of an accidental nature. The fibres in the abducent nerve, consequently, seem

Fig. 9.

to be exclusively of coarse calibre. On silver-impregnation according to Bielschowsky-Agduhr, I could demonstrate in the lateral rectus muscle of the eye nothing but »terminaisons en plaque«.

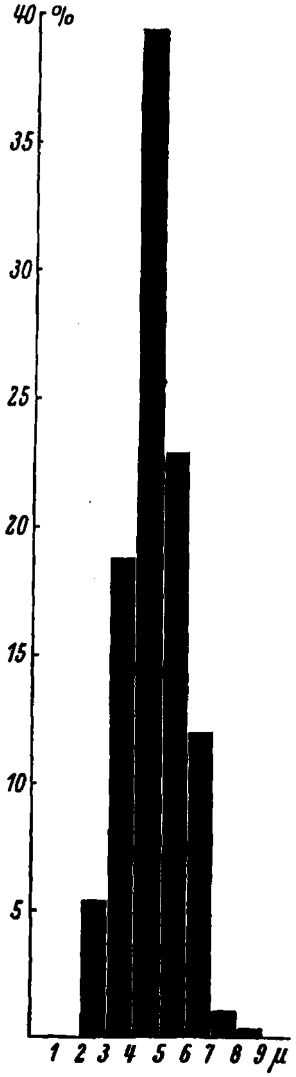


Fig. 10.

In the facial nerve, the fibre aggregate is distributed about a maximum of 4—5 μ (Fig. 10). This nerve, therefore, as far as regards the calibre of the fibres, appears to correspond to the group of fine fibres in the anterior spinal roots. In the facial

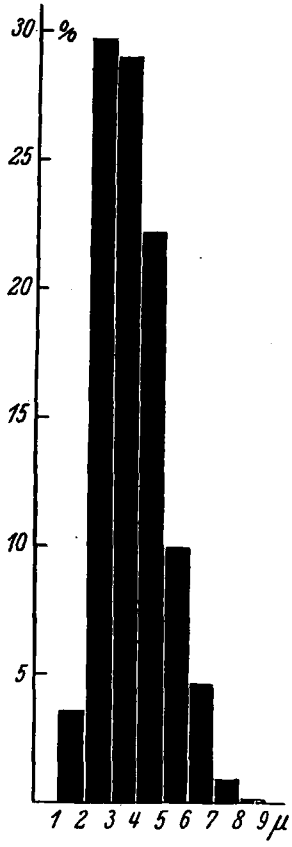


Fig. 11.

muscles in Rhesus and cat, I could find, on silver-impregnation end-plates only of the type "en grappe" (Fig. 8).

The facial muscles being in their kind of working distinctively tonic, I considered that an investigation of musculus sphincter ani externus—which also works tonically—would be of value. The nerve appertaining to it was found to be thin-fibred. On an analysis of the fibre-content, the distribution-curve was found to bear a great resemblance to that of the facial nerve (Fig. 11). On silver-impregnation of the muscle, i saw in it nothing but "terminaisons en grappe".

These observations seemed to me to point to the deduction that there exist two myo-rhabdotic systems of nerves, viz, one

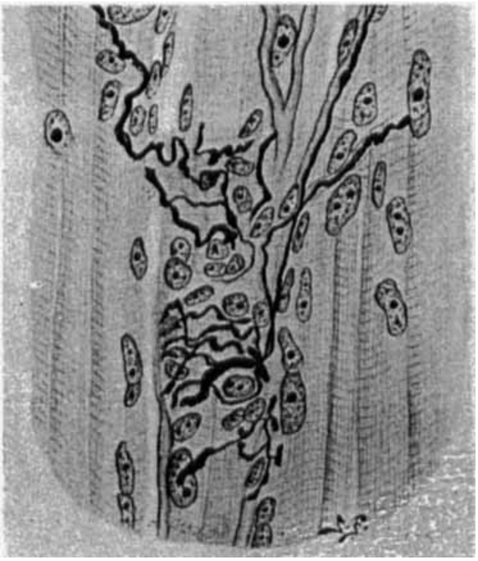


Fig. 12.

coarse-fibred, which serves contraction and which, in the muscle-fibres, terminates hypolemmally in "terminaisons en plaque", while the other is a thin-fibred, myelinated, tonicizing system which, in the muscles, terminates typolemmally, with "terminaisons en grappe".

In the minor portion of the trigeminal nerve and in the hypoglossal nerve, there is present—to judge by the curve of the fibre-aggregate obtained by the fibre-analysis—only one kind of fibres. These fibres are distributed around a maximum at 6—7 μ and, as far as calibre is concerned, occupy a median position between the two groups: the tonicizing and the contraction-exciting fibres. Boeke has described in the tongue terminations which he considers to constitute an intermediate form between "en plaque" and "en grappe" types. I myself have found, in the masticatory muscles of Rhesus, end-plates which appear to me to be of "en plaque" type, although smaller than the ordinary one (Fig. 12).

In the spinal roots, the coarse and the fine fibres lie intermingled. I considered it desirable to endeavour to isolate there one of the systems, for in that way it ought to be possible to gain a more reliable conception of the relative importance of the two kinds of fibres.

A possibility of attaining this end seemed to be offered by Niels Stenson's ("Stenos") experiment, which consists in temporarily cutting off, by compression, the aorta in the rabbit, in a line with the first lumbar vertebra. Doing this brings about a flaccid paraplegia in the hind legs together with paresis of the bladder and of the rectum. If the aorta be compressed for a period of 45 minutes or an hour, the paraplegia becomes permanent, Ehrlich and Brieger being the first to show this. These two authors and other writers have demonstrated that a long-continued ischemia causes a destruction of the nerve cells, especially in the anterior horn and also a destruction of the nerve-fibres in the anterior roots of the lower lumbar and sacral cord.

To me it seemed probable that the large motor cells would be specially sensitive to the arrest of the blood supply, and so it would be possible, by means of a shortened compression, to obtain a relatively isolated destruction of these cells with their appertaining nerve-fibres, while retaining the small cells which, I assumed, are the sources of origin of the fine fibres.

The compression of the aorta has earlier been carried out after exposure of the vessel by means of dorsal section, or else by a bent needle with a ligature being carried from behind around the aorta and the spinal column. In accordance with a suggestion made by Dr. Y. Zotterman I endeavoured to carry out the compression from the outside. The abdominal wall in the rabbit is so flaccid that there is no difficulty in compressing it inwards laterally over the aorta. A clamp was made, of the appearance shown in Fig. 13. Efter displacing the intestines, the disc (A) was carried from the left against the first lumbar vertebra, in such a way that the saddle-shaped clamp (C) rested above the spinous processes. Then, by turning the screw (B), the

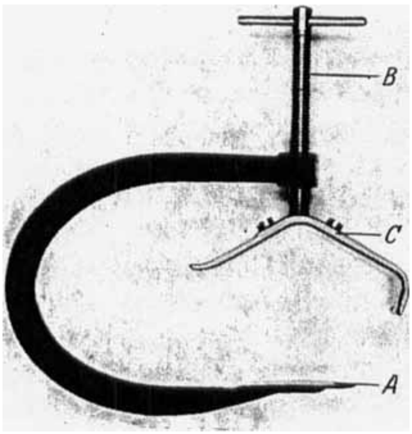


Fig. 13.

disc was pressed still more firmly against the aorta, until the pulsations in the arteries of the hind legs ceased. The control of this operation is of extreme importance, and is attended by a certain difficulty. The pulse in the rabbit is normally very small. After the pulse has ceased for some time it can—probably as a result of an increase in the blood-pressure—return again. If it does, the experiment will be unsuccessful. The duration of the compression varies, with the animals, from 15 to 25 minutes. When it has lasted longer, I have always obtained a flaccid paralysis of the hind legs, together with paresis of the bladder and the rectum.

The compression of the aorta has been carried out under pernoctonnarcosis. After the close of the experiment, the animals always present a flaccid paralysis of the hind legs. If the compression has lasted 15—25 minutes, this paralysis is transformed into rigidity a short time after the animal has regained consciousness. The rigidity is usually attended by contracture in the extensor muscles. If the paralysis is remaining in certain cases, there is a tendency, after some days, to the contractions being transformed into a contracture of the flexor muscles (Fig.

Fig. 14.

14). In certain cases, the rigidity may be transitory, and either disappear altogether, or leave behind it a condition of clonic contractions, which become specially apparent if the animal is lifted so that the hind legs hang down. If the legs are supported, the contractions disappear. If the rigidity or the spastic paralysis, respectively, becomes permanent in both the hind legs, this is usually accompanied by paresis of the bladder and the rectum. This result is absent, however, in those cases where the spastic paralysis is one-sided, or when clonic contractions make their appearance. In the latter state of things, the animal is able to use its hind legs when moving about. In spastic paresis, the rigidity is frequently so severe, that the animal can rest on the tops of its toes, with the whole of its weight, without the legs bending.

The tendon reflexes are increased in the spastic condition.

The electric excitability in the spastic rabbits has been investigated by Rexed, at my Institute. He communicates, in summary, the following observations respecting an animal affected by spastic paresis. At first, there were observed powerful fibrillar twitchings in the extensor muscles, pointing to a degeneration of the anterior horn cells. In addition, there existed an incomplete reaction of degeneration with diminished response to the direct and indirect excitation by the faradic current. In some muscles there were observed slow wormlike twitchings and displacement of the motor point to the tendon. The galvanic irritability was, at first, lowered and, later on, heightened, with displacements. The incomplete of degeneration shows the presence of an injury to the peripheral motor neurone, or in muscular inactionatrophy

A normal rabbit displayed the following values:

Peroneal nerve:	Kathodal closing contractions		0.4	milliamp.
	Anodal ,,	,,	1.2	,,
	Anodal opening	,,	1.2	,,
	Kathodal ,,	,,	> 5	,,
M. biceps femoris	K.C.C.		0.4	,,
	A.C.C.		1.0	,,
	A.O.C.		2.0	,,
	K.O.C.		> 5	,,
M. quadriceps femoris	K.C.C.		0.5	,,
	A.C.C.		1.5	,,
	A.O.C.		2.8	,,
	K.O.C.		> 5	,,

A rabbit with spastic paresis of the hind legs after the abdominal aorta had been compressed 20 minutes, displayed 11 and 16 days later on the following respective values:

		11th day	16th day
N. peronaeus dext.	K.C.C.	0.5 milliamp.	0.4 milliamp.
	A.C.C.	1.5 „	1.8 „
	A.O.C.	1.5 „	1.7 „
	K.O.C.	> 5 „	—[1])
M. biceps dext.	K.C.C.	0.8 „	0.6 „
	A.C.C.	1.8 „	1.6 „
	A.O.C.	> 5.5 „	> 4.0 „
	K.O.C.	—[1])	—[1])
M. quadriceps dext.	K.C.C.	0.6 „	0.9 „
	A.C.C.	1.5 „	1.1 „
	A.O.C.	> 7 „	> 5 „
	K.O.C.	—[1])	—[1])

If we cut the posterior roots of a spastic rabbit, the spasticity disappears, in agreement with Brondgeest's observations when —the first to demonstrate it—he proved the presence of a tonic innervation.

The histological study of a rabbit which, for 22 days, had had a spastic paralysis of the hind legs after a compression of the aorta, demonstrated the following alterations. The compression was made on a level with the 1st lumbar vertebra. In the upper lumbar segments, the alterations in the gray substance are only slightly pronounced but they increase more and more in the lower segments. In the sacral medulla they are clearly pronounced. Here they consist of a complete destruction of the large motor anterior horn cells which latter, too, have been for the most part observed (Fig. 15), the glia tissue appears to be somewhat increased. The anterior horns, consequently, present a peculiar vacuolized structure. In the intermediate zone, too, there occur alterations while it is uncertain if the posterior horns are altered at all. Between the vacuoles after the large motor anterior horn cells there are present small cells which appear to be uninjured. These cells I have assumed to be the

[1]) It was impossible to obtain the contractions in consequence of violent painreactions arising from the necessary strenght of the current.

sources of origin of the fine nerve-fibres of the anterior roots. These cells appear to be somewhat more numerous in the medial part of the anterior horn. In the white substance, Flechsig's path, on staining with Marchi, displays great degeneration. The

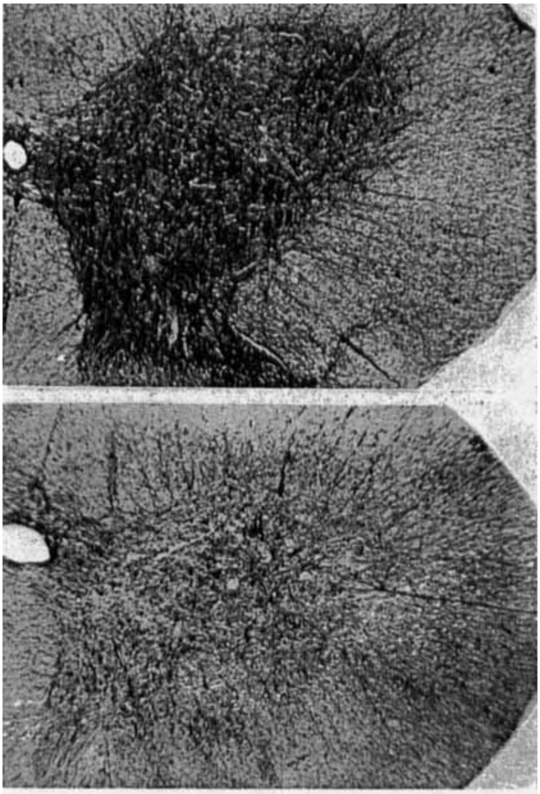
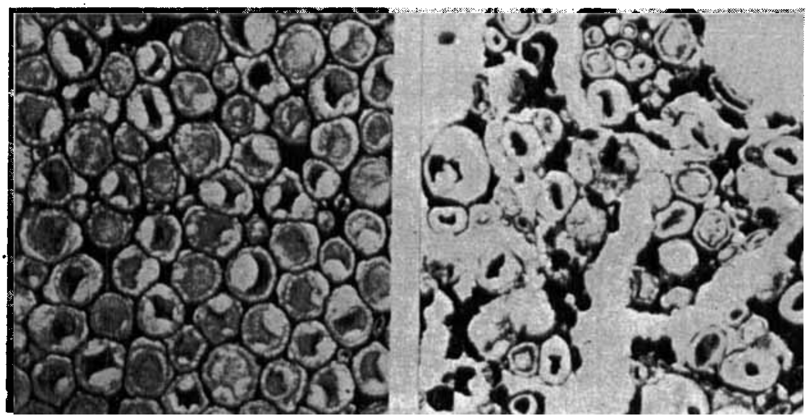


Fig. 15.

pyramidal tract appears to be uninjured; but some few fine fibres, evidently belonging to ascending association paths in the pyramidal area, show, however, signs of degeneration. In the anterior parts of the lateral funiculi, and in the anterior funiculi there is present an evident Marchi reaction. In the posterior funiculi, degeneration is but slightly pronounced.

In the anterior roots from the lower lumbar- and sacral segments, the coarse fibres are almost completely destroyed. Only some few of the finer fibres show signs of degeneration, the others, apparently not being injured (Fig. 16). The fibre-aggregate in the roots L_7—S_3 of spastic rabbit, in comparison with a normal animal is best seen from the diagram (Fig. 17). The



A. normal B. spastic.

Fig. 16.

continuous lines show the fibre-aggregate, arranged according to calibre in μ, in the normal rabbit. The two groups of fibres are clearly visible, arranging themselves around maxima at 3—4 μ and 12—13 μ, respectively. On constructing the diagram I have begun from the maximum value of the fine fibres which I put as 100, after which the other values were calculated in proportion to this figure.

The fibre-aggregate in the spastic rabbit I have marked with a spaced line. Here too I have begun from the top value of the fine fibres which have been given as 100, the remaining values being calculated in proportion to this figure. As is seen by the curves, the coarse fibres are almost entirely absent.

When it becomes a question of analyzing the importance of the observations of which an account has been given above, I consider that the following facts are worthy of special attention.

Through the anterior roots, there are conveyed to the muscles both contractile and tonicizing impulses. If the anterior roots be cut through, the muscle-tone and the power of spontaneous

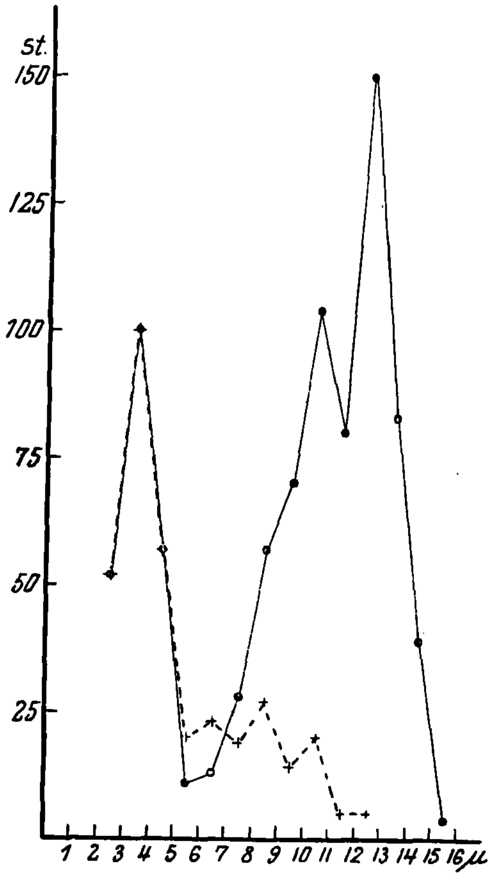


Fig. 17.

contraction both disappear. This has led many investigators, Spiegel, for instance, to consider that the large, motor anterior horn cells also conveyed the tonicizing excitations. That author, after discussing the facts then known respecting the tonic innervation of the skeletal muscles, comes (1928) to the following decision: "When sowohl der Grenzstrang als auch die hinteren

Wurzeln nicht den Weg der statischen Innervation bilden können, kommt nur das Axon der Vorderhornzelle hierfür in Betracht. An der Vorderhornzellen müssen sowohl jene zentralen Mechanismen angreifen, welche der Fortbewegung dienen, als auch jene, welche die Haltung der Skelettmuskulatur aufrechterhalten." In the rabbits which have become spastic in consequence of the compression of the aorta, the large motor anterior horn cells are destroyed, together with the coarse fibres in the motor roots. With this destruction, the contractility of the muscles disappears. The contractile excitations—i.e., those which Spiegel considers are serving motility—must, consequently, be conveyed by means of these cells and the coarse fibres. In those cases the muscle-tone not only remains, but is even strengthened or, more correctly speaking, unchecked, just as the tone in the muscles of the limbs remains unchecked if the pyramidal path be destroyed.

These circumstances make it probable that tone is a condition of the muscles itself which is maintained by excitations passing through the fine anterior fibres. The pyramidal path and the coarse anterior root fibres exercise a regulating effect on this condition. If either of these be destroyed, then the regulation of the tone will be affected and a condition of spasticity will arise.

Spasticity has formerly been considered as evidence of the existence of an injury within the central nervous system, but the above communication shows that this need not necessarily be the case.