THE RATE OF LOSS OF WEIGHT IN SKELETAL MUSCLE AFTER NERVE SECTION WITH SOME OBSERVATIONS ON THE EFFECT OF STIMULATION AND OTHER TREATMENT.

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OUR observations on the effect of physostigmine on denervated muscle[1] gave us an opportunity of noting the effect of nerve section on the weight of the muscle. In all cases but one the internal popliteal (tibial) nerve was cut, and the gastrocnemius, soleus and plantaris muscles with their tendons up to the level of insertion of the tendo Achillis were weighed after death; these muscles for brevity may be spoken of as the gastrocnemius group. In one case the external popliteal (peroneal) nerve was cut, and the tibialis anticus muscle and extensor digitorum ped. com. weighed.

In Table I the results are given of the observations in which the nerve was cut on one side only and in which there was no massage or stimulation employed. We give also (*a*) the weights of the tibialis anticus muscle and ext. digitorum ped. com. as an indication of the normal variation in weight of the muscles on the two sides; and (*b*) the weights of the rabbits at the time of death in order that some idea may be formed of the loss of weight in the cases in which the nerve supply of both muscles was severed; it will be seen that though in general the weights of the gastrocnemius and of the animal run fairly parallel, there are some not inconsiderable exceptions. It is possible that these exceptions are in part due to differences in the amount of food in the alimentary canal, and it would probably be better in future experiments to weigh the animals after removing the stomach and cæcum. The calculation of the percentage change in weight is made on the supposition that the muscle of the denervated side would have been of the same weight as the muscle of the intact side but for the nerve

[1] This *Journal*, XLIX. p. 410. 1915.

section. The data given in Table I of the weights of the m. tibialis anticus on the two sides indicate that the error involved in this supposition is as a rule small.

TABLE I. *Gastrocnemius group denervated on one side.*

The weight is in grams; the figures for the weight on the denervated side are in italic type.

Exp.	Days after section of nerve	Weight of gastrocnemius, soleus and plantaris		Percentage gain or loss	Tibialis anticus and ext. dig. ped. com.		Weight of rabbit at death
		right	left		left	right	
1	1	*5·08*	5·25	− 3·2	1·95	1·93	1150
2	1¼	5·85	*5·87*	+ 0·3	2·46	2·45	1250
3	2	7·38	*7·28*	− 1·4	2·43	2·49	1250
4	2	*9·68*	9·59	+ 0·09	3·08	3·06	1720
5	3	6·60	*6·25*	− 5·3	2·13	2·12	1080
6	4	*9·77*	10·13	− 3·5	3·14	3·53	1700
7	5	*8·56*	9·11	− 6·0	2·84	3·09	1420
8	7	10·99	*9·69*	− 11·8	3·50	3·52	1650
9	12	10·47	*8·05*	− 23·1	3·76	3·73	1550
10	14	8·44	*6·05*	− 28·3	3·01	2·82	1360
11	30	10·92	*6·07*	− 44·4	3·95	3·78	1650
12	35	9·40	*4·95*	− 47·3	3·36	3·45	1450

The percentage change in weight in the several experiments is shown graphically in Fig. 1 by the solid black dots. The symbol ⊙ represents experiments in which the denervated muscle was stimulated and will be referred to later. Since the rabbits were not fully grown the "loss of weight" represents the actual decrease in muscle weight + the amount which the muscle would have gained but for the nerve section. It will be seen that the loss of weight begins in two to three days, is rapid for about a fortnight, at the end of which time it is nearly 30 %, and then continues at a decreasing rate, the loss being in five weeks nearly 50 %. The curve drawn in Fig. 1 represents what we take to be the general course of the loss of weight in the denervated gastrocnemius, but this no doubt varies somewhat according to the state of nutrition.

In surgical practice for the restoration of nervous control after severance of nerves in man, the muscles are massaged and stimulated electrically in order to delay muscular atrophy. The stimulation is based on the view that the muscle atrophy is due to inactivity. This view has lost some of its force, for, as we have shown elsewhere (*op. cit. supra*), the atrophying muscle of the rabbit—and so probably that of other mammals—is in a state of continuous fibrillation, *i.e.* the muscle fibres have a rapid rhythmic contraction which, though weak, never ceases. It is a matter of guess work whether this activity is less or more than the normal activity, though it is obviously of a different character.

We have made some observations on the effect of massage, extension, and electrical stimulation on the rate of atrophy of denervated muscle. It must be noticed that the gastrocnemius muscle in the rabbit is a very unfavourable muscle for electric stimulation, since the larger upper part of it is covered up by the thigh muscles, and this part does not contract when the electrodes are applied to the skin unless very strong currents are employed, which is undesirable on several grounds.

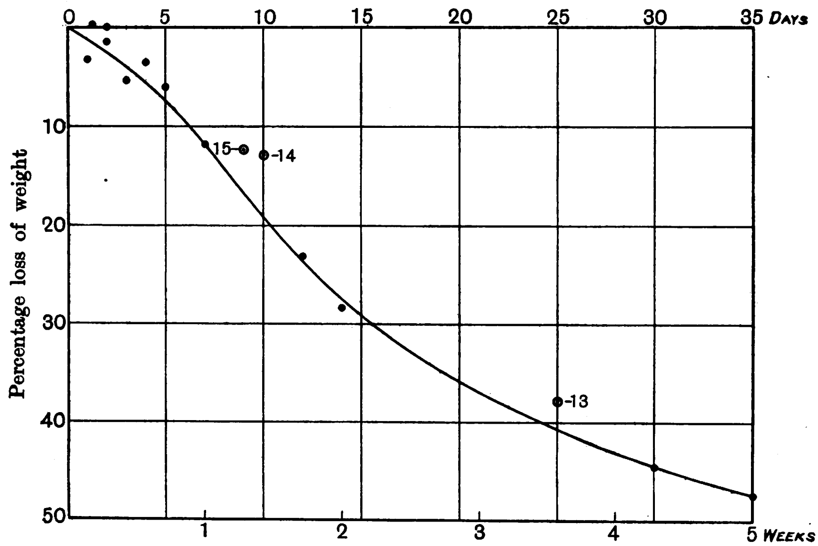

Fig. 1.

The experiments were of two kinds: in one the nerve was cut on one side only and the denervated muscle stimulated; in the other the nerves were cut on both sides and the muscle on one side stimulated. The treatment in the several cases is given in Table II with other data. In the Table, "massage" means gentle kneading of the muscle and squeezing it from below upwards; "extension" means that the leg was alternately flexed and extended at the ankle. The stimulation was by condenser shocks, ·016–·025 microfarad (Lewis Jones' apparatus[1]).

As regards the experiments in which the nerve was cut on one side the effect of stimulation, if any, can only be ascertained by comparing

[1] Lewis Jones. *Proc. Roy. Soc. Med.* VI. p. 49. 1913.

the loss of weight in the denervated muscle with the loss in the cases in which the nerve was cut and not stimulated (see Table I). Taking the curve in Fig. 1 as representing the rate of atrophy in unstimulated denervated muscle, we have the following results. In Exp. 13 there were brief massage and during the last 14 out of the 25 days slight electrical stimulation; the loss of weight was 37·8 % against 41 % of the unstimulated muscle. In this case the treatment had at most little, and may have had no effect. In Exp. 14, the daily massage was of about the same duration, but it was combined with rhythmic extension of the muscle; the loss of weight in nine days was 12·3 % against 16·4 % of unstimulated muscle. The difference is not outside the limits of error, but it tends we think to show that rhythmic extension has some beneficial effect. In Exp. 15 the muscle was effectively stimulated with condenser shocks, the loss of weight in 10 days was 12·9 % against 18·5 % of the unstimulated muscle. The difference here is greater, and though it cannot be said with certainty to be outside the limits of error, it indicates so far as it goes that electrical stimulation is beneficial and more beneficial than rhythmic extension.

The experiments in which the nerves were cut on both sides give a more satisfactory basis for drawing conclusions, although there is a source of error in the normal difference in the weight of the muscles on the two sides of the body. Ordinarily this is slight, but in particular instances it may be considerable. In Exp. 16 brief massage for 17 days with slight electrical stimulation for the last seven days had no appreciable effect on the muscle. In the other three experiments two on the gastrocnemius group and one on the tibialis anticus group, the muscle was distinctly heavier on the stimulated side. This affords some evidence that a certain degree of electrical stimulation delays muscular atrophy. The evidence is not conclusive because the number of experiments is small. Moreover the details of the results present certain difficulties. In the two gastrocnemius experiments the gain in weight is not proportional to the degree of stimulation; the gain was greater in Exp. 17 though the stimulation was less. In the course of the experiments we noticed that the stimulation often caused flexion of the leg of the opposite side, usually without any body movement. Accurate observation of this was not made, since attention was concentrated on observing on the stimulated side the slight movement of the foot showing contraction of the gastrocnemius. But on analysing the figures of the weights of the muscles on the two sides, it was obvious that the weight on the unstimulated side was greater than that which

TABLE II. *Effect of electrical and other treatment on the loss of weight of denervated muscle.*

The weights are given in grams, that of the stimulated muscle is in italic type.

Tibial nerve cut on one side.

Exp.	Days after section of nerve	Weight of gastr., soleus and plantaris		Percentage decrease of weight in denervated muscle	Weight of tib. ant. and ext. dig. p. com.		Weight of rabbit at death	Treatment (in all cases this was twice daily, and was begun the day after the operation)
		left	right		left	right		
13	25	9·25	*5·75*	37·8	3·85	3·17	1510	Massage for five minutes till the 10th day. Condenser shocks for four minutes with subsequent massage for three minutes on the following 14 days. The large positive pole (3 × 2 inches) was placed on the thigh, the small negative pole (·5 cm.) was placed at different points of the calf of the leg. The stimulation caused contraction of the thigh muscles; contraction of the gastrocnemius was only obtained with a minority of the stimuli.
14	10	6·35	*5·53*	12·9	2·49	2·47	1200	On nine days condenser shocks 36 times a minute for eight mins. Two small electrodes were used and both placed on the lower part of the calf of the leg. Contraction of the gastrocnemius was obtained with nearly all the stimuli.
15	9	4·22	*3·70*	12·3	1·61	1·56	1050	On eight days massage for eight minutes and about a dozen extensions and flexions at the ankle joint.

Tibial nerve cut on both sides.

				Percentage gain on stimulated side				
16	18	*6·5*	6·3	—	3·05	3·35	1585	Massage for five minutes till the 10th day. Condenser shocks in manner of Exp. 13, with subsequent massage for three minutes on the following seven days.
17	28	*9·4*	7·65	22·9	3·49	3·25	1670	Massage for five minutes till the 10th day. Condenser shocks in manner of Exp. 13, with subsequent massage for three minutes on the following 17 days.
18	36	*8·40*	7·65	9·8	3·36	3·42	1750	A short steel peg was passed through the gastrocnemius into the plantaris; at death the peg was slightly corroded, but had caused no inflammation. About 200 condenser shocks in manner of Exp. 14. Massage after the first eight days for two minutes before and after stimulation.

Peroneal nerve cut on both sides.

19	71	10·05	10·35	10·3	*2·15*	1·95	1650	As in Exp. 18, but no peg inserted in muscle.

it should be on the basis of the curve of atrophy of Fig. 1. Thus in Exp. 17 the unstimulated muscles after 28 days' denervation weighed 7·65 grams. According to the curve (Fig. 1) the muscles should have lost 43 % of their original weight, so that the original weight should have been 13·4 grams. But the rabbit at death only weighed 1670 grams, and the maximum weight of the gastrocnemius group which we have found in a rabbit of 1670 grams is 10·99 grams. Reckoning in the same way the original weight of the muscles in Exp. 18 should have been 14·8 grams. Either then both of these rabbits formed great exceptions to the ordinary relation of weight of the gastrocnemius group to body weight, or the stimulation on one side had delayed the atrophy on the other side. Now Exp. 15 (Table II) suggested that rhythmic extension of the muscle delays atrophy; if this is so the flexion of the leg, which we have mentioned as often occurring on the opposite side to that stimulated, would delay the atrophy. Thus the difference in the weights of the two muscles would depend not only on the degree of active contraction produced on one side, but also on the relative degree of passive extension produced reflexly on the two sides.

In Exp. 19 in which the peroneal nerve was cut on both sides and the m. tibialis anticus with more or less of the extensor dig. ped. com. on one side was stimulated, the weight of the muscles on the unstimulated side after 71 days was 2·15 grams. If we take 3·5 grams. as the weight the muscle would have had but for the nerve section (in accordance with the general results given in Table I) the loss of weight was 44·3 %. In the experiments on the gastrocnemius group (cf. Table I) in which the tibial nerve was cut on one side and neither side stimulated, there was an equal loss in 30 days. The slower atrophy in the tibialis anticus may have been due to more frequent passive extension of the muscle or to the natural rate of atrophy being slower than in the gastrocnemius.

In these experiments we think it is certain that the stimulation rarely caused contraction of the deeper fibres of the upper end of the gastrocnemius and plantaris. Both with bipolar and with unipolar stimulation of the exposed muscle the contraction was more or less confined to the superficial fibres, especially in the later stages of denervation. If then the greater muscle weight found on the stimulated side in the foregoing experiments was really due to contraction, it follows that the gain would have been appreciably greater if the whole of the fibres had been caused to contract. It was from this point of view that in Exp. 18 we passed a piece of wire through the gastrocnemius into the plantaris. Although in this case the procedure had no obvious effect we cannot but think that if more efficiently applied it would be advantageous in certain cases. It is practically certain that if electrical stimulation has a beneficial effect, the optimal effect will be with that current which is just strong enough to cause contraction. In the ordinary methods of stimulating muscle through the skin—whether by unipolar or bipolar methods, with currents of short or of long duration—the intensity of the current is much greater in the superficial than in the deep fibres, and we think it doubtful whether the latter can be stimulated without using currents injurious to the former.

It is well known that denervation besides causing loss of weight in a muscle causes it to become less excitable to electrical stimuli of short duration, and to contract more slowly. We did not make many observations on these changes, but after 28 and 71 days the muscle on the side which had been daily stimulated gave a very local contraction with condenser shocks, and both contraction and relaxation were markedly slower than in the early stage. And the daily stimulation did not prevent the occurrence of fibrillation. Either then the daily induced contractions were insufficient in number to replace the normal contractions, or the change in the muscle following nerve section is not simply an "inactivity atrophy."

Summary and Remarks.

Observations were made on the change of weight in muscle caused by section of its nerve. They were made on growing rabbits so that the difference in the weight of the denervated and of the normal muscle was, in the cases of longer duration, not wholly due to loss of substance but in part to absence of growth. For convenience however the less weight of the denervated muscle is spoken of as due to atrophy.

In twelve experiments the tibial nerve was cut upon one side, and after a variable time the gastrocnemius, soleus and plantaris muscles on the two sides weighed. The curve formed with the percentage loss of weight as ordinates (the normal weight being taken to be that of the muscle with intact nerve) and duration of denervation as abscissæ, was fairly regular. The group of muscles begin to lose weight in about three days and then lose it rapidly so that by the end of the second week the loss is nearly 30 %, the rate of loss then decreases but at the end of five weeks is nearly 50 %. The rate however no doubt varies in different nutritive conditions and with different degrees of exercise.

The fact that in the rabbit—and so probably in other mammals—denervated muscle is in a state of continuous fibrillation makes it *a priori* an open question whether the further activity caused by electrical stimulation will be beneficial or no. A few experiments were made on the effect of electrical stimulation and other treatment. The experiments were not numerous enough to give decisive results, but they tended to show that electrical stimulation with condenser shocks delays the atrophy, that rhythmic extension of the muscle has a similar but less effect, and that gentle massage for a like time has little if any effect. The stimulation did not prevent the fibrillation, nor the sluggish contraction characteristic of denervated muscle.

It was found that stimulation of a denervated muscle through the skin caused the superficial fibres only to contract, unless strong currents were used. It is probably important to equalise the strength of contraction. This consideration suggests that it may be an advantage in certain cases to pass one or more platinum wires through the muscle in order to facilitate the stimulation of the deeper fibres.

It is of considerable practical importance to determine the best means of delaying muscle atrophy, since the better the condition of the muscle the quicker will be complete restoration of voluntary control after motor nerves have been severed. The observations recorded in this Paper seem to us to emphasise the need of a comprehensive investigation of the subject.