THE GRADATION OF REGENERATIVE CAPACITIES OF A NEURON AFTER TRAUMATIC INJURY OF ITS AXON AND THE EFFECT OF REPEATED SECTION OF A NERVE ON ITS SPEED OF REGENERATION

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Manyfold investigations [3, 4, 6, 7,11 and others] of the processes of degeneration and regeneration of the peripheral nerves have proved that the intensity of the phenomena of regeneration is in direct ratio to the degree of injury to the nerve trunk. The regenerative processes are less evident when the degree of neural trauma is high than when it is low.

The greater the injury to the axon, the more evident are retrograde changes in the neuron.

The study of the problem of the effect of repeated trauma on the regeneration processes of a nerve represents a certain interest since operative interference with an injured nerve in the form of "freshening" the central culture is a repeated trauma of the peripheral nerve. M. A. Usievich [9] in 1929 discovered by physiological methods that the process of nerve fiber regeneration proceeds almost twice as fast if the nerve trunk under investigation is cut again. In 1940, T. T. Alekseev, L. S. Gracheva, M. A. Usievich [2], on the basis of physiological data, again confirmed that repeated trauma speeds the process of regeneration of a nerve.

In 1952, O. V. Aleksandrovskaya [1] indicated, on the basis of morphological investigations but without physiological verification, that repeated injury in the vicinity of the central segment is regenerated very quickly by the nerve fibers. "Activation" of the neurons, caused by the first injury, is supposed to facilitate this.

We carried out experimental histological investigations with the purpose of establishing the effect of the degree of trauma to the peripheral nerve and of repeated trauma on the rate of regeneration of the nerve.

EXPERIMENTAL METHODS

The experiments were carried out on 40 experimental animals (15 cats and 25 rabbits).

Of this number of animals, experiments with repeated neural trauma were carried out on 8 rabbits, whose right sciatic nerve was injured twice in the same place.

The right sciatic nerve of the cats was injured at two levels: at a distance of 1.5-2 cm and of 5 cm from the foramen ischiadicus along the path of the sciatic nerve on the hip. The traumatic neural injury consisted of neurotomy with subsequent neurorrhaphy of the nerve segments. The success of the regeneration of the sensory nerve fibers was checked by the method of Yu. M. Konorsky and L. Ya. Lyubinskaya [5] on the 7th day after the operation (3 animals), on the 20th day (2 animals), on the 35th day (2 animals), on the 50th day (2 animals), on the 65th day (2 animals), on the 87th day (2 animals), on the 107th day (2 animals).

At each time a check was made of animals with peripheral nerve injuries at different levels.

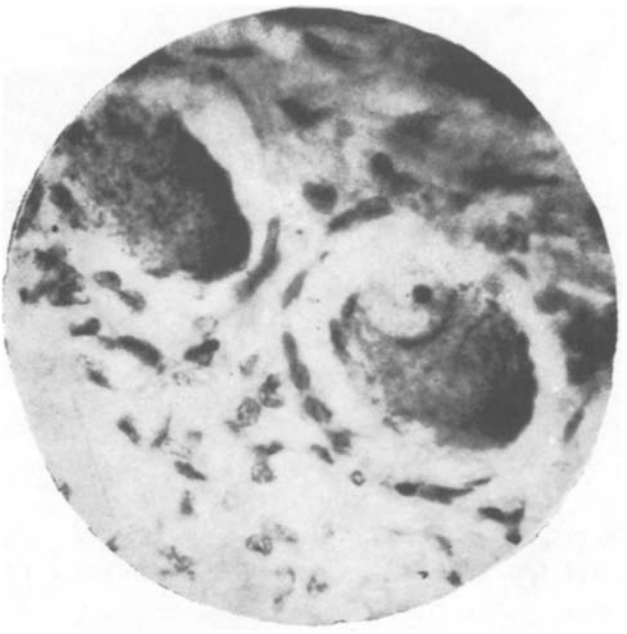

Fig. 1. Degeneration of the neurons in the L_7 spinal ganglion 7 days after cutting the sciatic nerve.

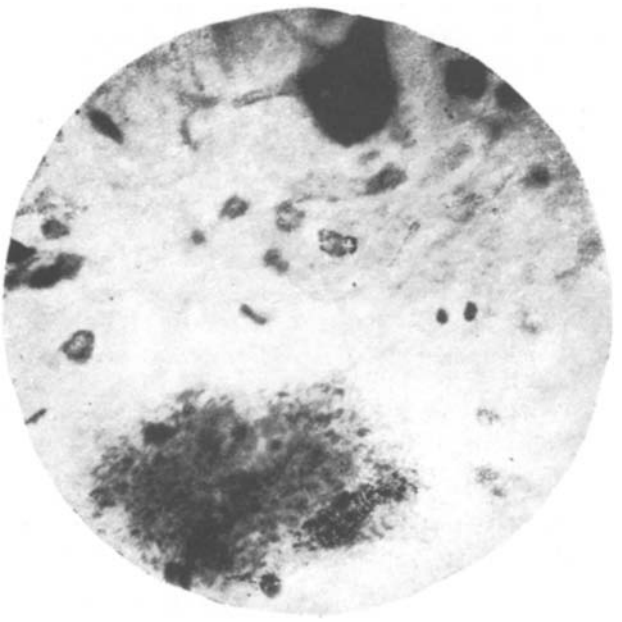

Fig. 2. Degeneration of the neurons in the cut horns of the L_7 spinal segment on the 20th day after cutting the sciatic nerve.

Since the purely physiological methods of Yu. M. Konorsky and L. Ya. Lyubinskaya are only applicable to the verification of the regeneration of the sensory nerve fibers, we checked the speed of regeneration of nerve fibers by histological methods on the rabbits. In addition, we judged the speed of regeneration of motor fibers by the "fan" symptom in the rabbits: if the rabbit is lifted by the dorsal skin, the digital phalanges of its hind legs diverge in all directions like a fan. The reflex disappeared immediately after the operation on the side of the injured sciatic nerve and reappeared only after the motor nerve fibers grew into the plantar interossei muscles.

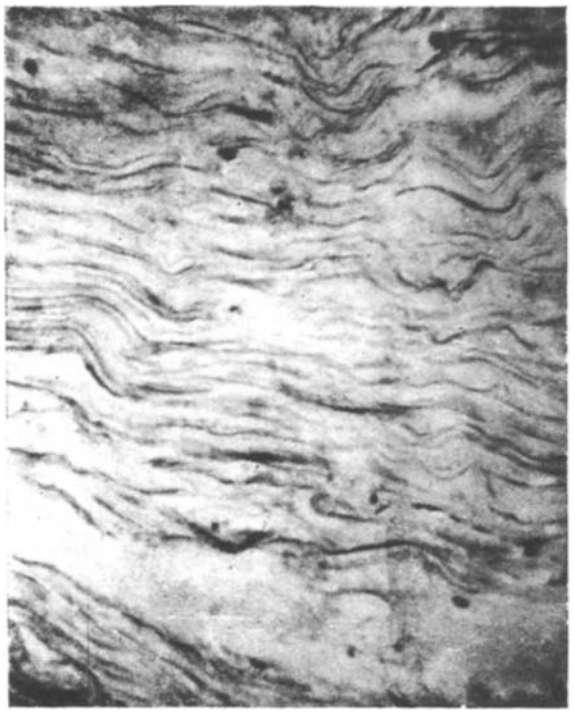

Fig. 3. Regeneration of the nerve fibers after a repetition of the cutting of the sciatic nerve.

Single trauma of the right sciatic nerve of the rabbits also represented neurotomy with subsequent neurorrhaphy of the nerve segments. The observations were carried out on 17 rabbits. We traumatized three different levels of the nerve: at a distance of 1.5 cm from the foramen ischiadicus in 6 rabbits; at a distance of 5 cm in 6 rabbits and at a distance of 10 cm in 5 rabbits. The animals were killed 1, 7, 20, 44, 46, 64, 91, 148 and 160 days from the time of the operation. Various sections of the right peripheral nerve, segments of the spinal column and spinal ganglions corresponding to them, sections of the right plantar interossei muscle were examined histologically.

EXPERIMENTAL RESULTS

It has been found that the speed of regeneration of the sensory nerve fibers differs with different levels of nerve trauma and different lengths of time after trauma. The results are presented in the Table.

Analyzing the data obtained, it can be noted that the speed of the regeneration of the nerve fibers progressively slowed at the time of regeneration and the length of the outgrowth of the peripheral nerve increased. In other words, the longer the axon grows, the slower is its rate of regeneration. The fact that during the first 20 days, with various levels of nerve trauma the rate of regeneration of the axons is almost equal draws attention. Later, the rate of regeneration at a low level of trauma becomes greater than the rate of regeneration of the axons at a higher traumatic level.

In the process of observing the nature of the regenerative and destructive changes in the sciatic nerves and in the centers, we noted that the morphological phenomena in the cellular structures differed little from the morphological descriptions of B. S. Doinikov, L. I. Smirnov, B. A. Favorsky and others [3, 8, 10]. The phenomena of retrograde changes in the neurons of the spinal ganglions and spinal column, which correspond to the centers of the sciatic nerve, were considerably more evident at a higher level of trauma than at low traumatic levels, while the reverse development of these retrograde changes was less evident. The number of degenerated neurons, in the ganglions as well as in the spinal column at the corresponding segments, was rather considerable on the injured side at a high level of trauma, while at lower traumatic levels the degeneration of the neurons was insignificant.

As regards the regenerating axons, a more rapid advancement of the "growth bulbs" could be noted at a low traumatic level and a slowing of their advancement at a higher level of injury. The thickness of the regenerating axons in the distal segments of the nerve at a high traumatic level of the nerve was less in all cases than the thickness of the regenerating axons at low traumatic levels.

According to our observations, there is a gradation of the regenerative abilities of the neuron which is evidenced in the fact that when trauma of a neuron's axon occurs, the regeneration of the lost section occurs more easily the further the trauma occurred from the body of the neuron. As the traumatic level approaches the body of the neuron, the regeneration of the lost section of the axon slows. Finally, at a certain close distance from the body of the neuron, trauma of the axon leads to the degeneration of the neuron.

Time of observation	Speed of regeneration, mm/day			
	at a high level of trauma (1.5-2 cm from f. ischiadici)		at a low level of trauma (5 cm from f. ischiadici)	
	n. tibialis	n. peroneus communis	n. tibialis	n. peroneus communis
7 days later	Axons were found partly grown through the scar, partly at the place of healing or at the beginning of the scar (found histologically)			
20 th day	2.7	2.7	2.7	2.7
35 th day	2.3	2.3	2.6	2.5
50 th day	1.7	1.7	2.3	2.2
65 th day	1.5	1.4	2.0	1.8
87 th day	1.2	1.2	1.7	1.6
107 th day	1.1	1.0	1.5	1.4

We measured the distance from the place of trauma to the segmental centers of the nerve and the distance from the place of transsection to the end apparatuses, located at various distances.

Let us use an example from Experiment No. 7. The level of the trauma to the sciatic nerve was 1.5 cm from its exit through the foramen ischiadicus. At autopsy, the distance from the place of transection to L_7 was 5 cm, to S_1 was 4.3 cm, to S_2 was 3.7 cm. The length of the regenerating peripheral segment of the axon, which previously innervated the proximal sections of the musc. biceps femoris, was 1 cm; the length of the regenerating peripheral segment of the axon, which previously innervated the plantar interossei muscle was equal to 20 cm. If both axons extended from the L_7 segment, then the total length of the shorter axon was 6 cm, while the length of the segment which goes to the plantar interossei muscles was 25 cm. Although the place of trauma of both axons was the same, the percentage of loss (by the peripheral segment due to the trauma with respect to the total length of the axon was equal to. 16.6% for the short axon, 80% for the long axon. Any combination of relations of the losses of the axons, if it is calculated from the distances of the centers, makes the loss greater for the longer axon. We consider that the level of a single location of trauma to a nerve is not proportional for each individual nerve fiber.

We did not observe the "fan" symptom in rabbits with trauma of the sciatic nerve at a distance of 1.5 cm from the f. ischiadicus on account of the widespread trophic disturbances of the sole of the foot and the loss of phalanges. The average calculation of the greatest speed of regeneration of the motor fibers according to the "fan" symptom for the middle and lower levels of nerve trauma gave the following rates: 2.4 to 2.7 mm/day at the middle level; 2.9 to 3 mm/day at the lower level

There were two levels of injury among the 8 rabbits whose right sciatic nerve was injured twice. In 4 rabbits, it was at a distance of 10 cm and, in 4, at a distance of 1.5 cm from the f. ischiadicus.

The repeated trauma (neurotomy with subsequent neurorrhaphy) of the right sciatic nerve was carried out 61 to 90 days after the first trauma.

Study of microscopical preparations of various sections of the right sciatic nerve, L_7-S_1-$_2$ segments of the spinal cord and spinal ganglions [Fig. 1,2, 3] showed the following. Regenerative phenomena of the nerve fibers of animals which suffered repeated trauma were considerably less evident than among the animals which had suffered a single injury to the nerve. The number of regenerating nerve fibers was less, the advancement of the "growth bulbs" toward the periphery slower, the thickness of the axons less. Varicose thickenings along the axons were more evident. But the phenomena of retrograde changes in the central axons and in the bodies of the neurons were more profound than among the animals with single trauma. In the segmental centers and in the spinal ganglions, which corresponded to the centers of the sciatic nerve, a great number of degenerating neurons could be observed, phenomena of proliferation of the glial cells and phagocytosis of the neurons could be observed. It should be noted that all the above phenomena were considerably more evident among the animals which had a high level of trauma (at a distance of 1.5 cm from f. ischiadicus) than among animals with a low level of trauma (at a distance of 10 cm from the f. ischiadicus).

The speed of regeneration according to the "fan" symptom, calculated from the time of secondary trauma, showed that the speed of regeneration was 1 mm/day on the average.

SUMMARY

Histological study of 40 animals after cutting the n. ischiadicus allowed us to draw following conclusions. On any level of nerve injury, the place of trauma eventually creates different injury levels of every single nerve fiber included in the nerve trunk. This phenomenon is due to the anatomic structure of peripheral nerves, consisting of the axial cylinders. There is a gradation of the regenerative ability of the traumatized neurons, which finds its expression in the fact that the further from the nerve cell body is located the trauma, the more readily and rapidly proceeds the reduction of the lost part. With the approach of the trauma level to the neuron, regeneration of the lost part is inhibited, slackened and may bring about the destruction of the nerve. Repeated trauma of the peripheral nerve decreases the regneration ability of the injured neurons, and brings about more intensive and irreversible phenomena in nerve cells. Regeneration of peripheral nerves is less complete and proceeds less rapidly.

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