THE EFFECT OF IRRADIATION OF THE RECIPIENT WITH X-RAYS ON HOMOPLASTIC TRANSPLANTATION OF A PERIPHERAL NERVE

Yu. M. Gudzovskaya

Department of Histology (Head – Prof. A. A. Braun) of the Kirghiz Medical Institute, Frunze

(Presented by Active Member AMN SSSR V. N. Chernigovskii)

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The peripheral nerves possess well-known powers of regeneration, but their integrity is restored only if their central and peripheral cut ends are brought sufficiently closely to each other. The regenerating axons grow along a path within the sheath of Schwann of the degenerating peripheral segment, and subsequently form here mature, functioning nerve fibers. Axons which fail to enter the sheath of Schwann very quickly undergo degeneration [5, 6]. The sheath of Schwann is an essential medium for the axons, which is concerned in the metabolism of the nerve fiber and forms the myelin sheath. When there is a gap or defect in the nerve trunk, the process of regeneration is made more difficult, the regenerating axons are lost in the surrounding tissues and they fail to reach the peripheral segment. Numerous attempts to provide a suitable path for the newly formed axons have not given the desired results. This problem requires further experimental investigation.

We considered that a segment of nerve, transplanted into a defect, would not simply be a path along which the axons could grow, but would also take part in the formation of mature nerve fibers, would undergo Wallerian degeneration, and would create the necessary conditions for the perfect regeneration of a nerve at the site of the defect. Such conditions, of course, could only be obtained by the use of fresh nerves as material for the graft.

Segments of nerve trunks, when transplated in animals, are known to undergo Wallerian degeneration [2, 7]. Autotransplantation of the nerve gives the highest percentage of lasting preservation; homotransplantation of nerves ends in failure in the overwhelming majority of cases, for homografts last for only 18 days in a state of Wallerian degeneration [7], after which their Schwann cells die and are absorbed. This phenomenon of death of the homograft is explained by the incompatibility of the graft and the host; the body reacts to the homograft as to an antigen. When using homografts it is therefore necessary to find effective ways of overcoming these manifestations of incompatibility.

This biological incompatibility of the tissues of the donor and the recipient has been overcome by decreasing the antigenic properties of the graft, and also by weakening the reactivity of the host. Research in recent years has shown that the immune reactions of the body depend on the state of the central nervous system. By producing inhibition in the central nervous system as the result of induction of sleep by drugs, M. I. Efimov and Sh. V. Musina [5] successfully obtained the survival of a skin homograft, and Yu. M. Gudzovskaya [3] – survival of a nerve homograft.

Irradiation of an animal with x-rays has also been shown to lead to inhibition of tissue processes.

A. A. Braun and K. M. Akylbekov [1] obtained true survival of skin homografts in rats in 40% of cases, by preliminary irradiation of the animals with a certain dose of x-rays.

In this way we decided to attempt to overcome the intolerance of the recipient towards a nerve graft, by irradiation of the host with x-rays.

METHODS

Experiments were carried out on rabbits. For 14 days before operation, the rabbits were given whole-body irradiation from the ventral aspect, under the following conditions: 180 kv, 20 ma, filter – Cu 0.5 mm, skin-focus distance 60 cm, dose rate 19 r/min, total dose 500 r. Two weeks after irradiation, under general anesthesia, a segment of the sciatic nerve, 1-1.5 cm long, was excised from the rabbits on the right side. The defect thus produced was closed by means of a homograft of suitable size. The rabbits of a control group underwent the operation without preliminary irradiation.

Rabbits were sacrificed at three times: 14-20 days, 30-35 days, and 2 months after operation. The nerves of the limb on which the operation had been performed were excised, fixed in 90% alcohol, impregnated with silver by Cajal's method, and embedded in paraffin wax; serial sections were then studied.

RESULTS

In the control group of animals (4 rabbits) one month after operation, in general no growth of axons

through the graft could be observed. All the grafts consisted of empty sheaths of Schwann; solitary nerve fibers were encountered mainly in the peripheral parts of the graft.

In the peripheral segment of the nerve, nerve fibers were completely absent; this also consisted of empty sheaths of Schwann.

In the experimental group of animals, sacrificed 14-20 days after operation (3 rabbits) we observed the following. In one rabbit the histological picture showed no difference from that described in the control animals i.e., the whole graft appeared empty; solitary nerve fibers were encountered only in the peripheral areas of the graft. The peripheral segment was completely without nerve fibers. In the second rabbit, very fine nerve fibers were found throughout the thickness of the graft, few in number, and in places pursuing a highly irregular course. A larger number of fibers was observed in the peripheral parts of the graft. The bulk of the sheath of Schwann, however, contained no nerve fibers. Nerve fibers were also absent from the peripheral segment. In the third animal of this group, at this time, the whole graft appeared to be filled with nerve fibers, which were quite thickly packed and followed a parallel course. In this case axons had grown through the sheath of Schwann, and in places, nuclei of the Schwann cells could be seen. No axons were found in the peripheral segment of the nerve in all three rabbits.

In the irradiated animals that were sacrificed 30-35 days after operation (5 rabbits) the following microscopic changes were observed. In all the animals of this group nerve fibers were growing through most of the graft; in 2 rabbits, however, there were only a few nerve fibers, quite a long way apart from each other, in the whole thickness of the graft. In the 3 remaining rabbits nerve fibers were fairly closely packed together in the graft, and they were parallel to each other.

Nuclei of Schwann cells could be clearly seen among the nerve fibers in 2 animals. In one animal the nerve fibers attained a great thickness and had a very irregular course, so that they appeared interrupted in the section. In one case it could be seen that small trunks of nerve fibers left the graft and went in the direction of the muscles alongside it. No regenerating axons could yet be seen in the peripheral segment of the nerve in all 5 rabbits.

At a later period – 2 months after operation (6 rabbits) – in one rabbits there was no general regeneration of nerve fibers, but only solitary nerve fibers were encountered in the peripheral areas of the graft. In another animal a considerable number of nerve fibers was seen in the peripheral parts of the graft, and in the central part of the graft only few fibers were seen, having a very irregular course. In the remaining 4 animals of this group, large numbers of nerve fibers had grown through the graft (Fig. 1). In transverse sections it could be seen that axons were embedded

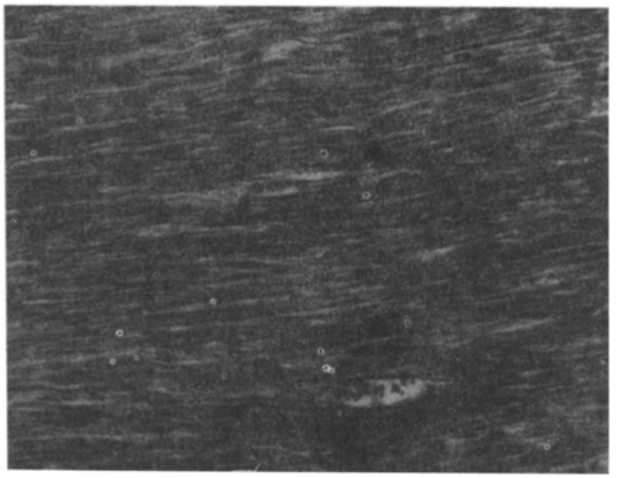

Fig. 1. Longitudinal section in the region of a nerve homograft 2 months after transplantation in a rabbit exposed to preliminary irradiation. Nerve fibers, nuclei of Schwann cells, and blood vessels are clearly visible in the graft. Microphotograph. Magnification: ocular 7 ×, objective 40 ×. Cajal's silver impregnation.

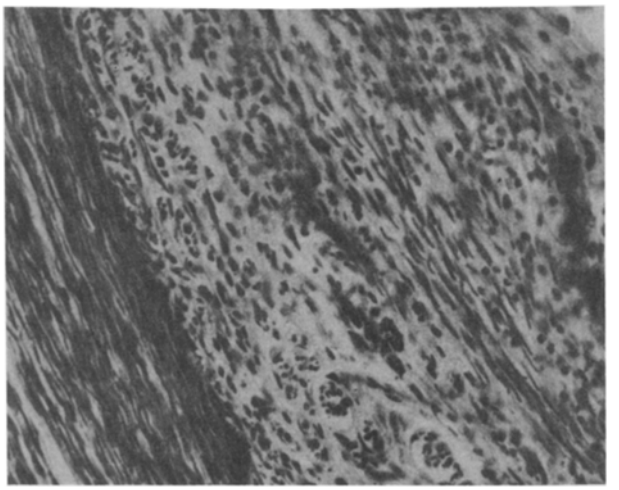

Fig. 2. Transverse section in the region of a nerve homograft 2 months after transplantation in a rabbit exposed to preliminary irradiation. Axons are seen, singly and a few at a time, embedded in the sheath of Schwann. Microphotograph. Magnification: ocular 7 ×, objective 40 ×. Cajal's silver impregnation.

singly or, more often, a few at a time in the sheath of Schwann (Fig. 2). Blood vessels with blood cells and nuclei of Schwann cells were clearly visible in places in the grafts. It was readily seen that nerve fibers, after passing through the region of the scar, grew from the graft into the peripheral segment. Here, in the peripheral segment of the nerve axons were now present, but the nerve fibers were fewer and further apart than in the graft, although they had the usual appearance and were parallel to each other (Fig. 3).

It follows from these findings that preliminary whole-body irradiation of a rabbit with a dose of 500 r

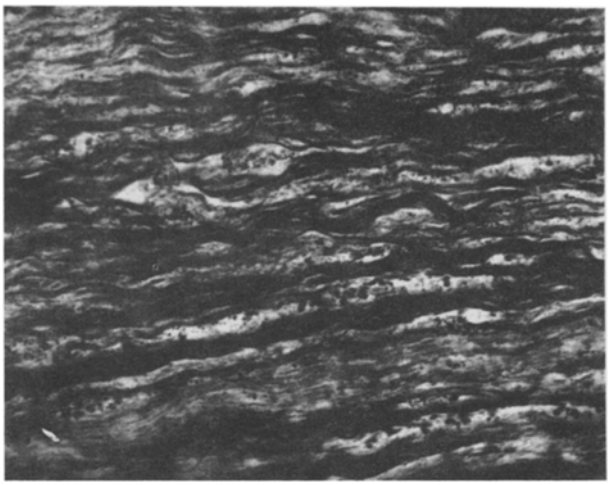

Fig. 3. Longitudinal section through the peripheral segment of a nerve 2 months after operation. The nerve fibers have the usual appearance and are arranged parallel to each other, but a considerable distance apart. Microphotograph. Magnification: ocular 7×, objective 40×. Cajal's silver impregnation.

of x-rays lowers the reactive properties of the animal and thereby protects the homograft, i.e., its Schwann cells, from death; this thus creates favorable conditions for nerve fibers to grow out from the central segment of the nerve, through the graft, into the peripheral end. With a defect of 1-1.5 cm and a nerve homograft of suitable length, regeneration of nerve fibers in the peripheral segment is observed 2 months after operation.

SUMMARY

The author studied the regeneration of the nerves at defects. A nerve homotransplant was used to replace the defect, the necrosis of the graft being prevented by preliminary X-ray irradiation of the host animal in a dose of 500 r. As a result, a few axons could be seen in the transplant 20 days after implantation; in a month's time this number had greatly increased, while in 2 months there were even more axons present, and they were present within the Sheath of Schwann. During this period, a small number of axons appeared in the peripheral section of the nerve.

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