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Ultrastructural changes of injured sciatic nerve after neurosurgical reconstruction and long-term electrostimulation in rabbits



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ABSTRACT

Peripheral nerve injury is an extremely important problem during the war in Ukraine. In the overall pattern of injury, 5 % of patients have peripheral nerve injuries and 1 % have brachial plexus injuries. Under conditions of hostilities, this indicator increases to 70 % or more. The victims are mainly young people of working age, which indicates the great medical and socio-economic significance of the problem.

MATERIALS AND METHODS. The study was conducted on 28 rabbits: suture of the sciatic nerve and implantation of the non-working antenna of the electrical stimulation device (group 1); sciatic nerve suture + implantation of an electric stimulator antenna in the same route as in group 1 and the beginning of stimulation on the 2nd day (group 2); sciatic nerve suture + implantation of an electric stimulator antenna in the same route as in group 1 and the beginning of stimulation 3 weeks after operation, when the first signs of regeneration occurred (group 3); autograft of the sciatic nerve + implantation of an electric stimulator antenna and the beginning of stimulation at a time point that will coincide with the beginning of signs of reinnervation of the effector muscle (group 4). The control of regeneration was carried out in 12 weeks. Electronic microscopy of nerve trunks was performed, measuring axial cylinder (AC) diameter, myelin thickness (MS) and MS/AC ratio.

RESULTS. A statistically significant increase of AC and MS indicators in the study group 2 relatively to comparison group 1 was shown, by 1.8 and 1.75 times, respectively. The increase of AC and MS in group 2, relatively to the comparison group and a visual decrease at the ultrastructural level of the number of destructively changed myelin sheaths (strengthening of reparative and regenerative processes) were detected.

CONCLUSION. Therefore, long-term invasive electrostimulation of the damaged peripheral nerve has a positive effect on the regeneration of the neuromuscular complex.

KEY WORDS: peripheral nerve injury; nerve regeneration; electrostimulation; electronic microscopy

The frequency of combat injuries of peripheral nerves (PN) in modern wars reaches 70-75 %, of which more than 75 % are mine-explosive injuries. Basically, there are not only isolated nerve injuries, and the injuries themselves are often complicated by massive bleeding and shock. The degree of a patient's injury severity is determined by the caliber and type of projectile that injures, the presence of combined damage to vessels, nerves, bones of the limbs and soft tissues, which makes up to 80 % and is often complicated by bleeding and shock [1, 2].

The time during which the sprouting of nerve fibers takes place is of critical importance, since the denervation of the muscle, even after immediate restoration of the integrity of the nerve, leads to the loss of

65 % of the muscle functional potential. In the case of chronic muscle denervation, the loss of functional potential decreases to 10 %. Another factor is the number of Schwann cells and their ability to migrate from the proximal end of the damaged nerve to the distal end and participate in the reinnervation of the muscle [3]. In addition, the deficiency of motor units may arise because of insufficient number of axons due to the peculiarities of reconstructive surgery on the nerve trunk (e.g. during nerve transfer, nerve gap restoration, size discrepancy and histoarchitectonics of the nerve endings) [4].

The regeneration of axons through the nerve suture line is slow and axons sprout through it within 3-4 weeks. One of the methods of influen-

cing the speed and efficiency of nerve regeneration is the electromagnetic field [5]. There are data that regeneration is accelerated by electrical stimulation with a frequency of 20 Hz within 1 hour after performing a nerve suture, and stimulation of regeneration occurs mainly due to an increase in the speed of axon sprouting, not their number [6]. The positive effect of electrical stimulation on the regeneration of PN was proven *in vitro* on the cell culture of spinal ganglia that were exposed to a sinusoidal electromagnetic field for 10 minutes. The result of this experiment was an increase in enzyme activity and protein synthesis [7, 8]. An *in vitro* experiment with cultured neurons of the spinal cord demonstrated that the expression of BDNF and its high-affinity receptor, tyrosine kinase B receptor, increases under the influence of an electromagnetic field.

Also, the stimulating effect of an electromagnetic field on the growth of axons at the molecular level was proven by an experiment on transgenic mice in which neurotrophin receptors were knocked out. In such animals, PN regeneration did not occur after injury under the influence of an electromagnetic field [9]. The issue of the impact of long-term invasive electrical stimulation of the damaged peripheral nerve on the regeneration of the neuromuscular complex, namely the ultrastructural changes that occur in its components, remains open.

PURPOSE. To investigate ultrastructural changes of peripheral nerve after long-term electrical stimulation in experiment.

MATERIALS AND METHODS

This study was conducted in strict accordance with the recommendations of the National Institutes of Health's Guide for the Care and Use of Laboratory Animals. The research protocol with animal experimentation was approved by the Scientific Ethics Committee of State Institution "Romodanov Neurosurgery Institute of NAMS of Ukraine" (Protocol Number: 17/2022). All surgeries were performed under general anesthesia, asepsis and antisepsis conditions and every effort was made to minimize suffering of experimental animals.

The study was carried out on 28 rabbits, 2 months-old, mean weight 2-2.5 kilograms kept in the vivarium of the State Institution "Romodanov Institute of Neurosurgery NAMS of Ukraine". Under general anesthesia with 10 % solutions of ketamine hydrochloride 50 mg/kg (*Farmak, Ukraine*), 2 % xylazine hydrochloride Sedazin 5 mg/kg (*Biowet Puławy Sp. z o.o., Poland*) and atropine sulfate 0.05 mg/kg (*Darnitsa, Ukraine*), the surgical approach to the sciatic nerve in a rabbit was performed (**Fig 1. A**).

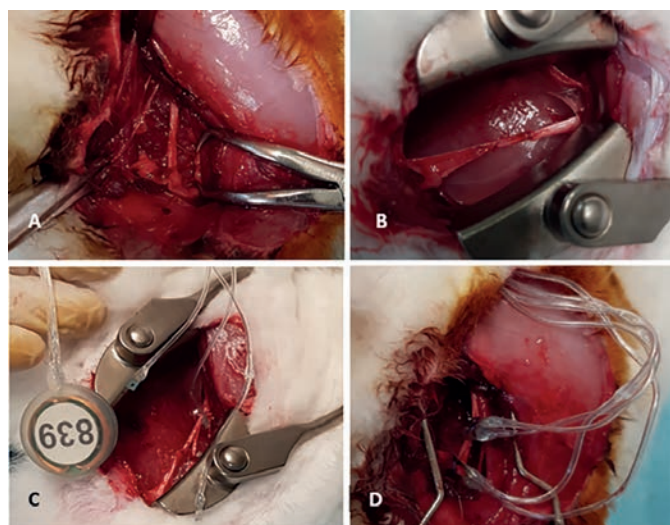


Fig. 1. A – sciatic nerve exposure. B – sciatic nerve autograft. C – the beginning of electrostimulator antenna implantation. D – electrodes are fixed to epineurium.

Distribution of groups depending on the method of surgical intervention:

Group 1 (n = 7): sciatic nerve suture and implantation of the non-working antenna of the electrical stimulation device. This group of animals was not stimulated. In group 1, we performed the approach to sciatic nerve, at a distance of 30 ± 1.5 mm from the point of its exit from the pelvic cavity, cut the nerve with a blade and performed epineural suture using monofilament Polyamide 9/0 (*Olymp, Ukraine*). The antenna of electrostimulation device (NeySi-3M) was implanted subcutaneously (at high level) and electrodes were sutured to epineurium by atraumatic sutures, layer-by-layer suturing of the wound (**Fig. 1 C, D**).

Group 2 (n = 7): sciatic nerve suture + implantation of an electric stimulator antenna in the same way as in group 1 and the beginning of stimulation on the 2nd day.

Group 3 (n = 7): sciatic nerve suture + implantation of an electric stimulator antenna in the same way as in group 1 and the beginning of stimulation 3 weeks after the surgery, when the first signs of regeneration occurred.

Group 4 (n = 7): autograft of the sciatic nerve + implantation of an electric stimulator antenna and the beginning of stimulation at a time point that coincides with the beginning of the signs of effector muscle re-innervation (**Fig. 1 B**). A nerve gap with a length of up to 10 ± 2 mm was cut out using a blade (at a distance of 30 ± 1.5 mm from the point of its exit from the pelvic cavity). After turning the fragment by 180° , 3-6 epineural sutures were applied using an atraumatic needle with a monofilament Polyamide 9/0 using an operating microscope ($\times 12$ magnification). This method simulates the nerve autografting surgery in the clinic.

The NeSy-3M (*VEL, Ukraine*) electrostimulation device, state registration certificate No. 7439/2008, is included in the State Register of Medical Equipment and Medical Products of Ukraine and is approved for the use in medical practice.

The electrostimulation mode was used with a variable frequency of pulses per cycle: half of the T period – pulse generation, half of the T period – pulse in function, T – from 0.5 s to 15 s, minimum frequency (F_{\min}) – 2 Hz, maximum frequency (F_{\max}) – 120 Hz, and with a fixed frequency of 20 Hz and 80 Hz. The amplitude of the pulses in all modes with a load resistance of 10 k Ω was from 8 V to 20 V. Electrical stimulation sessions lasting 5 minutes per day were conducted every day.

The control of regeneration was carried out after 12 weeks. After the animal was anesthetized, an access to the sciatic nerve was performed, and it was removed together with the calf muscles. After the collection of materials, animals were euthanized by injection of a lethal dose of Ketamin 100 mg/kg (*Farmak, Ukraine*).

Electron microscopy technique. The tissue fragments of injured nerve trunk of the innervation zone on the side of the sciatic nerve injury, measuring 1-2 mm³, were taken immediately after the animals were euthanized, fixed in the mixture of 4 % formaldehyde (*Aldrich, Germany*), 2.5 % glutaraldehyde (*Raaraal, Hungary*) and 0.1 M cacodylate buffer pH 7.4 (*Agar scientific, Germany*) with subsequent fixation in a 1 % solution of osmium tetroxide (*Agar scientific, Germany*) [10], were dehydrated in the increasing concentrations of ethanol and oxypropylene and embedded in the mixture of epoxy resins Epon-araldite (*Fluka, Switzerland*) according to standard generally accepted methods of electron microscopy. Ultrathin sections with a thickness of 70 nm were made on an LKB ultratome (*Bromma, Sweden*). To increase the contrast, they were counterstained with uranyl acetate and lead citrate according to the classic Reynolds method and viewed in an electron microscope PEM 100-1 (*SELMi, Ukraine*) at an accelerating voltage of 75 kV. Semi-thin sections with a thickness of 100-150 nm were made from epoxy blocks for targeted ultratomo-graphy and in-depth evaluation, stained with methylene blue-pyronine, and examined under an optical microscope Axiophot (*OPTON, Germany*). The criteria for recovery were the diameter of the axial cylinder (μm), the thickness of the myelin sheath (μm), [11] and the coefficient of the ratio of the myelin sheath (MS) thickness to the diameter of the axial cylinder (AC) [12].

Morphometric studies were carried out on semi-thin sections on an image analyzer SAI-01AVN (*SELMi*, Ukraine) using the software (*Kappa opto-electronics GmbH*, Germany) at the same magnification (objective $\times 40$, adapter $\times 2$, eyepiece $\times 10$) examining of 30 randomly taken myelinated axons per 1 case.

Variational statistics methods were used for the analysis of the obtained data. The normality of data distribution was checked by the Shapiro-Wilk W-test. Since the test did not confirm that the distribution was normal, the nonparametric Kruskal-Wallis H-test was used for multiple between-group comparisons of the means of independent groups, followed by pairwise group comparisons in the Kruskal-Wallis test dialog in STATISTICA 7, which is equivalent to multiple comparisons using the Mann-Whitney U-test. The average values were presented as a median with interquartile ranges: M (25 %; 75 %). P value ≤ 0.01 was statistically significant. The electronic database was created using the spreadsheet program MS Excel 2013 (*Microsoft*, USA). Statistical analysis and graphical presentation of the results were performed using the STATISTICA 7 (*StatSoft Inc.m* USA) and Prizm v. 8.0 software (*GraphPad*, USA, free trial license).

RESULTS AND DISCUSSION

The results of control group I (nerve injury with stimulator implantation without stimulation). Electron-microscopic examination of the regeneration neuroma area of the injured sciatic nerve trunk proved that cellular elements and nerve fibers during this period of study were characterized by the predominance of reactive changes over destructive ones. Schwann cells were characterized by a large nucleus filled with euchromatin, often with the presence of one eccentrically located dense nucleolus, nuclear membranes sometimes had slight invaginations, the cytoplasm was characterized by moderate reactive changes manifested by the expansion of mitochondrial cristae and tubules and cisternae of the endoplasmic reticulum (**Fig. 2**).

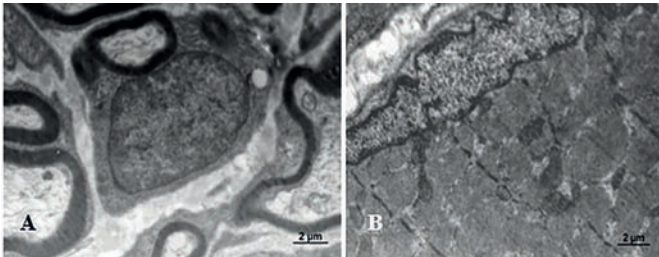


Fig. 2. Electron micrographs of ultrastructural changes in group I. A – Schwann cells with the signs of increased functional activity and myelin fibers with a restored original structure. B – peripherally located nucleus, moderate cytoarchitectonic disturbance of myofibrils with the presence of foci of swelling. Mitochondria with focal swelling of cristae or unchanged structure. Scale – 2 μm .

In myelinated nerve fibers, the myelin sheath was focally defibrinated, while the axial cylinders appear intact and contain a moderate amount of axonal cytoskeletal ultrastructures – microtubules and neurofilaments, as well as intraaxonal mitochondria with dense cristae. In the area of regeneration neuroma of the animals of this study group, the diameter of the AC was 3.22 (2.08; 4.48) μm (**Fig. 6**), the thickness of the MS is 0.73 (0.59; 0.91) μm (**Fig. 6**), and the ratio of MS/AC is 0.24 (0.16; 0.36) (**Fig. 8**).

The results of group II (nerve injury with the implantation of a stimulator and start of stimulation on the 2nd day after the surgery, 12 weeks after the injury, stimulation during 12 weeks after the injury). Electron mi-

croscopic examination of this group tissue demonstrated the absence of pronounced destructive changes in the myelin sheath of axons, although axons with local partial defibrillation of the lamellae were found. Axial cylinders are characterized by the restoration of the axoskeleton with the presence of numerous microtubules and neurofilaments and newly formed mitochondria with dense cristae. The degenerating myelinated axons are rare. Numerous newly formed unmyelinated nerve fibers appear intact (**Fig. 3**). Schwann cells are in a state of reactive change activation with increased activity of the protein-synthesizing apparatus (nucleus, nucleolus, endoplasmic reticulum, ribosomes).

For the statistical analysis of the effects of long-term electrical stimulation according to different schemes (research groups), the Kruskal-Wallis test was applied to the morphofunctional state of the myelin sheaths of nerve fibers, according to which the indicator of the diameter of the AC at the end of the experiment – H (4, N = 150) = 41.87 μm ; $p < 0.0001$.

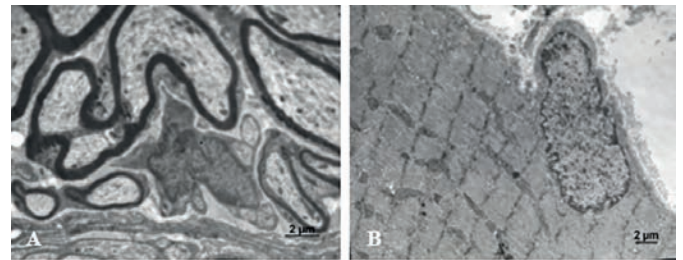


Fig. 3. Electron micrographs of ultrastructural changes in group II. A – Myelinated nerve fibers. A Schwann cells wraps several unmyelinated fibers. B – Peripherally located nuclei, moderate cytoarchitectonic disturbance of myofibrils with the presence of foci of swelling. Mitochondria with focal swelling of cristae or unchanged structure. Scale – 2 μm .

For the MS thickness index H (4, N = 150) = 58.38 μm ; $p < 0.0001$, that is, there was a highly significant difference between the groups that were compared. Thus, in the region of the regeneration neuroma of the animals of this study group, the diameter of the AC was 5.72 (4.64; 6.59) μm , and it increased statistically significantly compared to the comparison group (Group I) by 1.8 times (U-Mann-Whitney test; $p_{1-2} < 0.0001$) (**Fig. 6**). The index of MS thickness in this group was 1.28 (1.14; 1.43) μm and was also statistically significantly increased relative to the comparison group by 1.75 times (U-Mann-Whitney test; $p_{1-2} < 0.0001$). The ratio of MS/AC was 0.23 (0.19; 0.31).

The MS/AC coefficient according to the Kruskal-Wallis test was H (4, N = 150) = 1.24, $p = 0.872$ and there were no statistically significant differences between the study groups according to this indicator. In this research group, the relation between the increase in MS and AC indicators relative to the comparison group and the visual decrease at the ultrastructural level of the number of pathologically changed myelin sheaths and the decrease of interlamellar edema in myelinated axons was noted.

The results of group III (nerve injury with stimulator implantation, and the beginning of stimulation after the appearance of signs of recovery of the effector muscles, 12 weeks after the injury, stimulation for 8 weeks, the beginning of stimulation 3 weeks after the injury). During the electron microscopic examination of the regeneration neuroma area, Schwann cells were represented both by cells at the stage of activation of reparative processes, and by a fraction of cells with structural differences in destructive and degenerative changes. The cytoplasm of the latter was characterized by the presence of mitochondria with varying degrees of cristae destruction: from their partial fragmentation to complete vacuolization. A significant number of newly formed unmyelinated fibers were observed and an increase in their number relative to myelinated axial cylinders were visualized (**Fig. 4 A**).

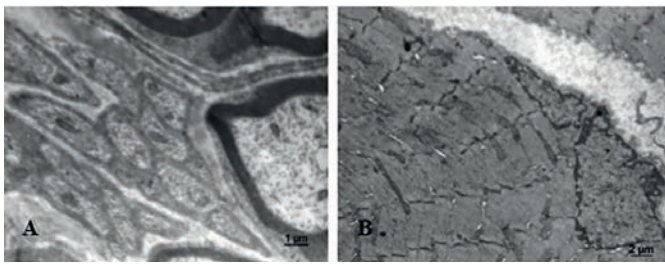


Fig. 4. Electron micrographs of ultrastructural changes in group III. A – Against the background of dystrophically changed myelinated axons, the appearance of a large number of newly formed unmyelinated fibers. B – peripherally located nucleus, preservation of myofibril cytoarchitectonics of with the presence of swelling foci. Mitochondria with focal swelling of cristae or unchanged structure. Scale – 2 μm .

In the area of neuroma regeneration in animals of this group, the diameter of the AC 4.31 (3.14; 5.90) μm was statistically insignificant (probably due to the increase in the degree of dispersion of the interquartile range), relative to both the comparison group and all other study groups except for group IV (distal neuroma), which showed a moderately statistically significant increase – 1.4 times (U-Mann-Whitney test; $p_{3,5} = 0.023$) (Fig. 6). The thickness of the MS in this group 0.92 (0.78; 1.06) μm was statistically significantly reduced compared to group II by 1.4 times (U-Mann-Whitney test; $p_{2,3} = 0.0013$), while no statistically significant difference was detected in our samples with any other group, in particular, with the comparison group (Fig. 7). The MS/AC ratio in this group was 0.21 (0.17; 0.28) and had no statistically significant differences with any other study group.

The results of group IV (nerve autoplasty with stimulator implantation and the start of stimulation after the appearance of signs of effector muscle recovery, 12 weeks after the injury, stimulation for 8 weeks, and the start of stimulation 12 weeks after the injury). According to the results of the histological examination of the injured nerve trunk, the formation of regenerative neuromas on both sides (proximal and distal) was established. Electron microscopic examination of these areas revealed both reactive (swelling of a part of intracellular organelles) and significant destructive-degenerative changes in Schwann cells (up to vacuolar dystrophy), which were of the same type in both studied areas (proximal and distal regeneration neuroma).

In myelinated nerve fibers, the orderliness and compactness of the fibrous structure was disturbed, the myelin sheath with local degenerative-destructive changes was focally defibrinated, or represented by a homogeneous unstructured substance, which is a sign of irreversible destruction. Single degenerating myelinated axons were also found. Numerous newly formed unmyelinated fibers attracted attention. Areas of

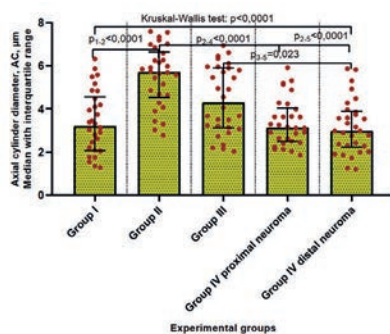


Fig. 6. Comparative characteristics of the indicators of the axial cylinders diameter in the regeneration neuroma area of the injured nerve trunk of different experimental group animals. Explanation in the text.

growth of dense connective tissue containing collagen fibers, strands of fibrin and a small amount of cellular elements were revealed. Some fibroblasts showed signs of increased phagocytic activity and/or have signs of lipid and vacuole dystrophy (Fig. 5 A, B).

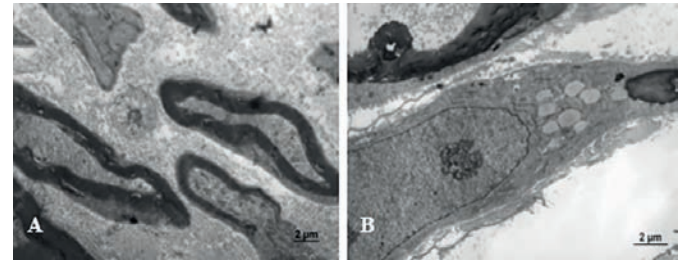


Fig. 5. Electron micrographs of ultrastructural changes in group IV. A – proximal neuroma. Partial demyelination of myelinated axons with fragmentary defibrillation of the lamellae of the myelin sheath. Partial exposure of the axial cylinder of the myelinated axon. B – distal neuroma. A degenerating nerve fiber and a destructively changed fibroblast with signs of vacuolar dystrophy and phenomena of active phagocytosis. Scale – 2 μm .

In the area of the proximal regenerative neuroma of animals of group IV, the diameter of the AC was 3.14 (2.52; 3.98) μm , and in the area of the distal regenerative neuroma – 2.98 (2.29; 3.86) μm , these indicators were statistically insignificant compared to all study groups, except for group II, where a statistically significant decrease by 1.8 and 1.9 times was found, respectively (U-Mann-Whitney test; $p_{2,4} < 0.0001$, $p_{2,5} < 0.0001$) (Fig. 6).

The MS thickness index in the area of the proximal regenerative neuroma was 0.77 (0.64; 0.98) μm and 0.70 (0.61; 0.86) μm in the area of the distal regenerative neuroma, did not show statistically significant differences in all study groups, except for the group II, in which it decreased statistically significantly by 1.7 and 1.8 times, respectively (U-Mann-Whitney test; $p_{2,4} < 0.0001$, $p_{2,5} < 0.0001$) (Fig. 7). At the same time, the MS/AC ratio was 0.25 (0.17; 0.34) in the proximal area and 0.23 (0.18; 0.32) in the distal regenerative neuroma area and also had no statistically significant differences either among themselves or with any other study group (Fig. 8).

It was showed that axial cylinder diameter and myelin thickness indicators in the study group, where electrostimulation begins on the second day after surgery, relative to the comparison group I increased by 1.8 and 1.75 times, respectively. In this group, there was a connection between the increase in the axial cylinder diameter and myelin thickness indicators relative to the comparison group and a visual decrease at the ultrastructural level of the number of destructively changed myelin sheaths (strengthening of reparative and regenerative processes).

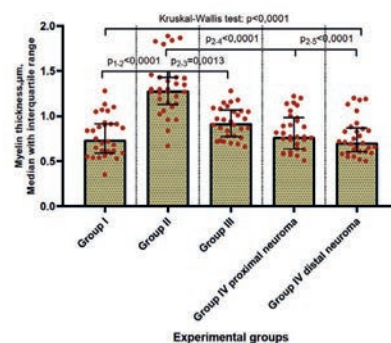


Fig. 7. Comparative characteristics of indicators of the myelin sheath thickness in the regeneration neuroma area of the injured nerve trunk of different experimental group animals. Explanation in the text.

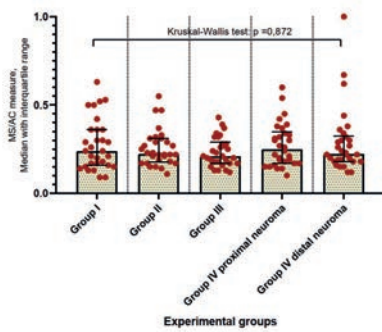


Fig. 8. Comparative characteristics of the indicators of the MS/AC ratio in the regeneration neuroma area of the damaged nerve trunk of different experimental group animals. Explanation in the text.

The positive effect of electrical stimulation on the regeneration of peripheral nerve is also demonstrated in the experiments of other authors. Electrostimulation methods are especially relevant under conditions of impossibility of microsurgical intervention in the acute period. Huang et al. showed that electrical stimulation with a frequency of 20 Hz and a duration of 20 min. improves peripheral nerve regeneration, even under con-

ditions of chronic denervation, lasting 24 weeks. The ability of Schwann cells to support regeneration has been proven *in vitro* [13]. After the peripheral nerve injury, due to Wallerian degeneration, a microenvironment favorable for nerve regeneration is created in the distal stump. Short-term low-frequency electrical stimulation is an effective treatment for peripheral nerve injury, but the mechanism underlying its effect on Wallerian degeneration remains unclear. In their work, Li et al. [14] suggested that electrical stimulation can improve nerve regeneration by accelerating the processes of Wallerian degeneration. The authors modeled the transection of the sciatic nerve in rats and then stimulated its distal stump. The injured nerve was then evaluated 1, 4, 7, 14, and 21 days after injury. The results showed that ES significantly promoted the degeneration and clearance of axons and myelin, as well as the dedifferentiation of Schwann cells. There is evidence that electrical stimulation of peripheral nerves stimulates the restoration of the leading pathways of the nervous system as a whole. Low-frequency (4 Hz) electrical stimulation m. soleus in rabbits accelerated the recovery of muscle function after axotomy and nerve suture of the motor nerve of the same muscle. Similar data were also obtained in an experiment on rats: low-frequency electrical stimulation within 1 hour after a complete transection and suture of the sciatic nerve accelerated the regeneration of axons and contributed to the restoration of motor and sensory function, which was confirmed by electrophysiological methods and determination of temperature sensitivity [15].

CONCLUSION

The electron microscopic examination of the tissue in the area of the regeneration neuroma of the injured sciatic nerve trunk testified to the presence and coexistence of both reactive and destructive changes on the part of nerve fibers and cellular elements of the peripheral nerve stroma of varying degrees of severity, while in group of autoplasty, relative to research groups II, were nerve stimulation were performed on the second day after operation and group III, were nerve stimulation began when the signs of regeneration occurred (the 3rd week) the degree of severity of destructive changes increases.

Therefore, long-term invasive electrostimulation of the injured peripheral nerve has a positive effect on the regeneration of the neuromuscular complex.

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Ультраструктурні зміни травмованого сідничного нерва кроля після хірургічної реконструкції та довготривалої електростимуляції



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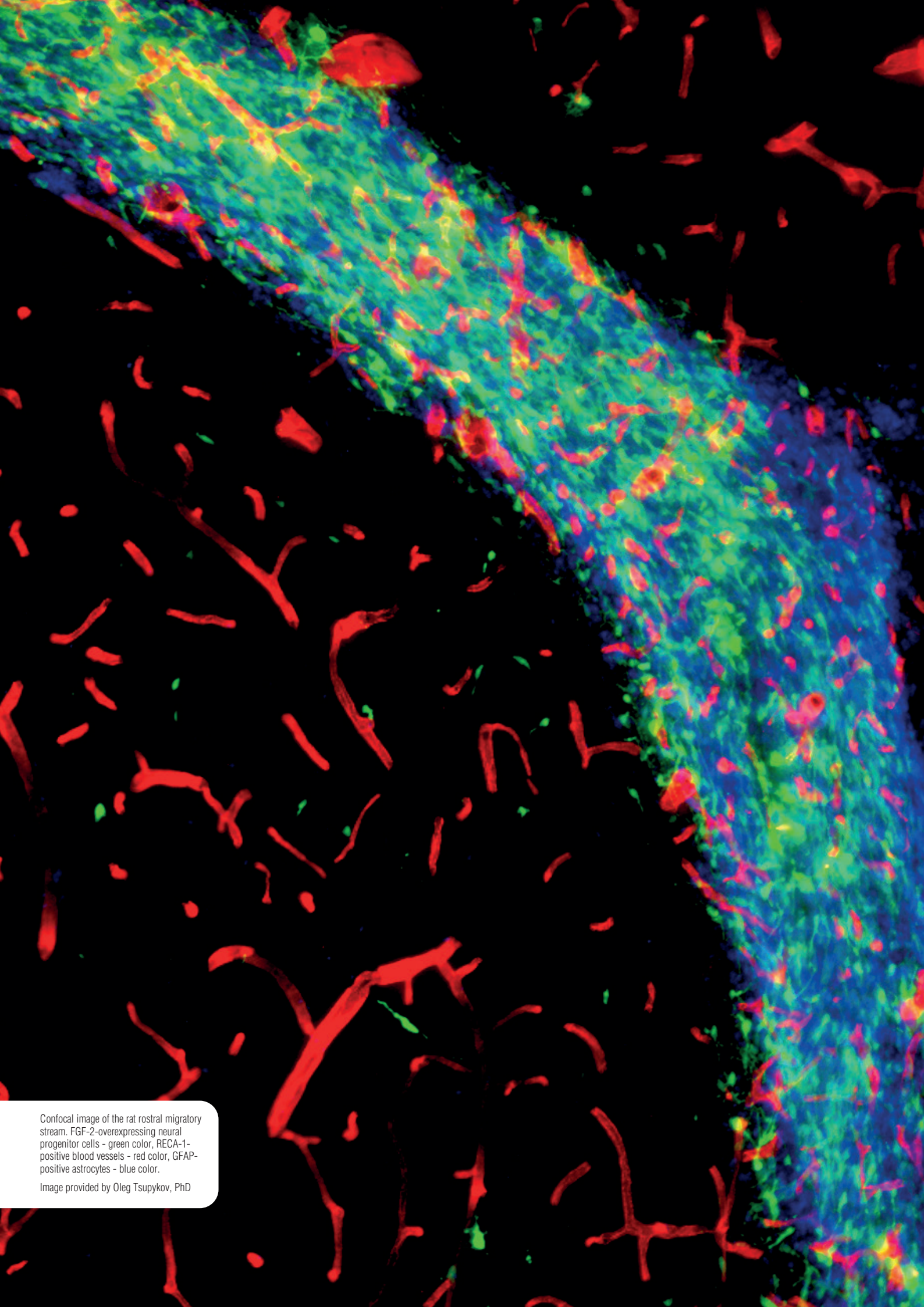
РЕЗЮМЕ

Травма периферичних нервів є надзвичайно актуальною проблемою сьогодення, особливо під час війни в Україні. У структурі загального травматизму, 5 % усіх пацієнтів мають травму периферичних нервів, і 1 % є потерпілими з травмою плечового сплетення. Під час бойових дій цей показник зростає майже до 70 % та більше. Потерпілими є молоді працездатні люди, що вказує на велику медичну та соціально-економічну значущість проблеми.

МАТЕРІАЛИ ТА МЕТОДИ. Дослідження проведене на 28 кролях, які були розподілені на 4 групи. Група 1: шов сідничного нерва та імплантація неробочої антени електростимулюючого пристрою. Група 2: шов сідничного нерва, аналогічно як у групі 1 + імплантація електростимулятора і початок стимуляції на 2-гу добу. Група 3: шов сідничного нерва + імплантація електростимулятора і початок електростимуляції у часовій точці, яка співпадала з початком ознак реіннервації м'язів-ефекторів. Група 4: аутонейропластика сідничного нерва + імплантація електростимулятора і початок стимуляції у часовій точці, яка співпадала з початком ознак реіннервації м'язів-ефекторів. Контроль регенерації проводився через 12 тижнів після операції. Проводилася електронна мікроскопія сідничних нервів із визначенням діаметру осьового циліндра, товщини мієлінової оболонки та їх співвідношення.

РЕЗУЛЬТАТИ. Виявлено статистично значуще збільшення показників діаметру осьового циліндра і товщини мієлінової оболонки у групі 2, в порівнянні з групою 1 у 1,8 та 1,75 разів, відповідно. Відзначалося також ультраструктурне зменшення руйнування мієлінової оболонки (посилення репаративних та регенеративних змін) у групі 2 відносно групи порівняння.

КЛЮЧОВІ СЛОВА: травма периферичного нерва; регенерація нерва; електростимуляція; електронна мікроскопія



Confocal image of the rat rostral migratory stream. FGF-2-overexpressing neural progenitor cells - green color, RECA-1-positive blood vessels - red color, GFAP-positive astrocytes - blue color.

Image provided by Oleg Tsupykov, PhD