

bacteria to potentiate the enzymic transformation of arachidonic acid into PG *in vitro*. The positive effect of indomethacin on the state of hemostasis and the microstructure of the kidneys is evidence that the genesis of these changes is linked with an increase (under the influence of ET) in PG synthesis.

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#### CONTRACTILE PROPERTIES OF REINNERVATED SKELETAL MUSCLE AND THEIR DEPENDENCE ON THE LEVEL OF NERVE INJURY

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The absence of selectivity of reinnervation of skeletal muscle in mammals leads to changes in the ratio between the types of muscle fibers in it, their spatial grouping, and the functional characteristics of the muscle [1, 6-8, 12]. Differences in the functional profile of motor units (MU) of the muscle with completion of the reinnervation process lasts for several years after nerve injury [9]. Several factors determining the development of a certain characteristic histochemical composition, or a distinctive kind of contractile properties in a reinnervated muscle have recently been established [6, 14].

The object of this investigation was to study the contractile properties of muscle, and changes in the mean size and number of its MU depending on the time after denervation and the level of nerve injury.

#### EXPERIMENTAL METHOD

Experiments were carried out under ether anesthesia and under sterile conditions on 22 mature rats weighing 150-220 g. The sciatic nerve (SN) was isolated on one side at the level of its division in the popliteal fossa and above. The peroneal nerve (PN) was crushed at the level of the lateral condyle of the femur or SN at the level of the ischial tuberosity by the method in [2], after which the wound was sutured. Depending on the time after the operation and the level of crushing the animals were divided into three groups: 1) rats taken in the experiments 2 weeks after crushing of PN (eight muscles were tested on the side of injury to PN, n = 8), 2) 4 weeks after crushing of PN (n = 5), 3) 6-7 weeks after crushing of SN (n = 6). Control experiments were carried out in some cases on the tibialis anterior muscle (TAM) on the side opposite to the operation, and also on TAM of three intact animals (n = 17).

In the animals of group 1 reinnervation of the anterior group of leg muscles after crushing of SN was found to begin on the 8th day [2] and to be largely completed after 2 weeks [15]. Consequently, in the animals of group 1 the test TAM was in the stage of incomplete reinnervation, whereas in the animals of groups 2 and 3 it was in a stage of complete reinnervation.

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TABLE 1. Contractile Properties of Reinnervated TAM of a Rat, with Mean Magnitude and Number of Its MU ( $M \pm m$ )

Group of animals	Weight, kg	$P_t$ , g	$P_t/mw$ , g/mg	$T$ , sec	$1/2$ RT, sec	CT, sec	mMU, mV	nMU	$P_t/n$ , MU
Control	$418 \pm 16,5$ (16)	$16,4 \pm 1,6$ (17)	$0,041 \pm 0,005$	$0,167 \pm 0,015$ (17)	$0,027 \pm 0,002$ (17)	$0,036 \pm 0,002$ (17)	$0,47 \pm 0,08$ (14)	$11,6 \pm 1,4$ (14)	$1,60 \pm 0,23$ (14)
1	$299 \pm 18,0^{***}$ (8)	$14,5 \pm 2,9$ (8)	$0,050 \pm 0,01$ (8)	$0,190 \pm 0,02$ (8)	$0,050 \pm 0,003^{***}$ (8)	$0,040 \pm 0,002$ (8)	$0,20 \pm 0,04^{**}$ (6)	$9,2 \pm 2,6$ (6)	$2,85 \pm 1,01$ (6)
2	$361 \pm 23,0^*$ (5)	$30,0 \pm 7,1^*$ (5)	$0,08 \pm 0,02^*$ (5)	$0,140 \pm 0,01$ (5)	$0,030 \pm 0,004$ (5)	$0,090 \pm 0,006$ (5)	$0,24 \pm 0,08^*$ (3)	$11,0 \pm 0,6$ (3)	$2,66 \pm 0,6$ (3)
$P_{2-1}$	$<0,05$	$<0,05$		$<0,05$	$<0,0001$				
3	$370 \pm 20,0^*$ (6)	$13,8 \pm 4,5$ (6)	$0,036 \pm 0,008$ (5)	$0,24 \pm 0,04$ (6)	$0,041 \pm 0,003^{***}$ (6)	$0,050 \pm 0,008^{**}$ (6)	$0,43 \pm 0,06$ (6)	$10,5 \pm 1,1$ (6)	$1,64 \pm 0,28$ (6)
$P_{2-3}$		$<0,05$	$<0,05$	$<0,05$	$<0,02$				

Legend. Number of muscles tested given in parentheses. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$  relative to control.

At the times established above, under urethane anesthesia (4 ml/kg, 20% solution) atraumatic buried electrodes were inserted into the isolated SN above the site of crushing. SN above the electrodes and all its branches except PN were divided and the wound was closed. The contractile characteristics of TAM under isometric conditions were tested *in vivo* by the method in [5]. The tension developed by the muscle in response to single supramaximal pulses 0.2 msec in duration was transmitted to a strain gauge. Signals from the strain gauge resistors were amplified by the Topaz-3-01 amplifier and then recorded on the Mingograf mg-34 (Siemens-Elema, Sweden). Before the experiments began, the test muscle was assigned its optimal length. Traces of contractions were analyzed by the method in [5, 13]. The following parameters were determined:  $P_t$ ) the force developed by the muscle in response to a single supramaximal pulse;  $P_{t/mw}$ ) the force developed by the muscle per unit mass; CT) the contraction time;  $\frac{1}{2}RT$ ) the semirelaxation time; T) the time of the complete phase of contraction and relaxation.

The method of calculating the mean value of MU (mMU) and the number of MU (nMU), introduced by McComas and subsequently meeting with certain objections in clinical studies, has however been successfully used in experiments involving vivisection [4, 10]. A detailed account of the method is given in [4, 5, 10, 11]. Having determined nMU it is possible to calculate the force developed by a single MU, namely  $P_t/nMU$  [4, 5]. Action potentials for calculating the mean value and number of motor units in the muscle were recorded by the M-42 electromyograph (Medicor, Hungary) and the set of electrodes included with it.

#### EXPERIMENTAL RESULTS

Two weeks after crushing of PN the muscle lost weight compared with the control, its semirelaxation period was increased, and mMU was reduced. Four weeks after this same manipulation the weight of the muscle was reduced relative to the control,  $P_t$  was increased, and the value of mMU remained low. Comparison of the animals of groups 1 and 2 revealed an increase in weight of the muscle in the later stages after crushing of the nerve, together with an increase in the rate of semirelaxation (Table 1). These results can be explained by an increase in the degree of reinnervation of the muscle fibers. Axons from "slow" motoneurons have a high rate of regeneration after injury [7], and for that reason at the state of incomplete reinnervation (group 1) contractile properties characteristic of a slower muscle were observed in TAM. However, with the completion of reinnervation (group 2), besides a tendency for nMU to increase, contractile characteristics indicating transformation into a "faster" type, approximating to its initial state, appeared. A decrease in the weight of the muscle relative to the control and an increase in the contraction and semirelaxation times were observed 5-6 weeks after crushing of SN (group 3; Table 1). Comparison of the properties of muscles of these two groups (2 and 3) in the stage of completed reinnervation, differing in the level of crushing of the nerve, showed that after injury to the nerve at a level more distant from the muscle (group 3) it develops a smaller force, has a longer semirelaxation time, and a longer duration of the whole contraction cycle (Table 1).

Histochemical investigations [14] have shown that the soleus muscle, which normally contains only 10.5% of fast (type II) fibers, during reinnervation after injury to the tibial nerve, contained 34.0%, and after injury to SN, 73.0% of fibers of this type. The reinnervated slow muscle thus acquires a larger number of fast fibers, the further away the nerve is injured. In the present experiments, investigation of the contractile characteristics showed that the muscle, on the contrary, acquires properties characteristic of a slower muscle, and this is accompanied by a tendency for the mean value of MU to increase. The rat TAM has been shown to consist chiefly of type II fibers [3]. Consequently, the results now obtained, indicating "slowing" of the reinnervated muscle after injury to the nerve at a greater distance from it, can be explained by the participation of axons from "slow" motoneurons in its reinnervation. The probability that they reach the fast TAM after crushing of SN is increased (for SN contains more axons running to slow muscles than PN), whereas selectivity has been found [1, 12] not to exist in the reinnervation of different muscles and different types of fibers.

The differences discovered in the contractile characteristics depending on the level of nerve injury can be used to develop methods of clinical tensometric diagnosis of the level of a peripheral nerve injury.

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## EFFECT OF DISTURBANCE OF MOTOR FUNCTION ON PROPERTIES OF THE SKELETAL MUSCLE FIBER MEMBRANE

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Denervation of frog muscle depresses the resting membrane potential (RMP), modifies the passive electrical properties of the membrane, and leads to the appearance of extrasynaptic sensitivity to acetylcholine (ACh) [2, 3]. It is suggested that the neurotrophic control of the above-mentioned parameters of the muscle membrane is effected with the participation of substances carried to the muscle by axoplasmic transport [2, 3]. Denervation-like changes arising in the membrane after blocking of axoplasmic transport by colchicine differ quantitatively to some extent from those arising after denervation of the muscle. It has been postulated that these differences are due to the fact that after division of a nerve or blockade of axoplasmic transport the muscle finds itself in different situations: in the first case it is immobile, whereas in the second its motor activity is preserved [1].

Immobilization of frog muscle by botulinus toxin is also known to cause a denervation-like increase in postsynaptic sensitivity to ACh [5], although to a lesser degree than denervation. In this connection the view is held that nervous impulses and motor activity of the muscle connected with them, are essential for maintaining the differentiated state of the muscle membrane. However, experiments with immobilization of a muscle by acting on its nervous apparatus do not solve the problem of what is more important: motor activity of the muscle as such or the presence of a certain type of nervous impulsation [2]. To solve this problem, it is therefore interesting to conduct experiments with immobilization of a muscle without any direct action on neuromuscular transmission. Experiments of this kind are of practical importance for various forms of immobilization of the limbs are used in clinical practice as a method of treatment after trauma to them.

The aim of the present investigation was to study the effect of tenotomy and immobilization of the limb on the properties of the frog muscle fiber membrane.

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