MORPHOLOGY AND PATHOMORPHOLOGY

Effect of Unilateral Damage to Sciatic Nerve on Phenotype of Lumbrical Muscles in Experimental and Contralateral Legs in Rats

R. R. Islamov and V. V. Valiullin

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Expression of slow myosin in fast lumbrical muscle during unilateral damage to the sciatic nerve was studied in rats. Four weeks after unilateral excision of sciatic nerve segment or its crushing, the content of slow fiber in the lumbrical muscle of the contralateral leg tended to increase (detected using monoclonal antibodies against slow myosin). The extrapyramidal system seems to modulate the phenotype of muscle fibers via motoneurons of the spinal cord, while the compensatory activation of this system manifests in pronounced "deceleration" of both the fast and slow muscles in the hind legs.

Key Words: *skeletal muscle; denervation; myosin isoforms; contralateral leg*

Informational cell-cell interactions in the motoneurons-skeletal muscle system regulate activity of various genes, which determine the phenotypic signs of both cell partners. Impulse activity of motoneurons and the neurogenic molecules secreted from nerve terminals regulate gene expression in skeletal muscle fibers (MF) [8,9]. In its turn, the muscle synthesizes myogenic neurotrophic factors, which are transported to the perikaryon and stimulate expression of specific genes in nerve cells [10]. Trauma of the peripheral nerve interrupting the regulatory relationships between motoneurons and skeletal muscles not only induces posttraumatic alterations in motoneurons, but also disturbs vital processes in MF. In addition to motoneurons directly connected to MF via synapses, an important role in neural regulation of skeletal muscle is played by pyramidal and extrapyramidal systems, which regulate activity of these neurons [2].

Using histochemical methods we showed that unilateral damage to rat sciatic nerve innervating the slow soleus muscle induces pronounced decrease in the relative content of fast MF in the contralateral leg in comparison with the same muscle in intact rats [4]. Phylogenetically, the extrapyramidal system is known to be related to the regulation of structure and function of slow muscles. It suggests that increased relative content of slow MF in soleus muscle of the contralateral leg is related to the reflex influence of extrapyramidal system on the phenotype of slow muscle. Bearing in mind the hypothesis that the extrapyramidal system after activation by unilateral damage to peripheral nerve modulates the phenotype of postural slow muscles, we used similar experimental paradigm to study the phenotype of fast lumbrical muscle responsible for precise voluntary movements controlled by the pyramidal system.

MATERIALS AND METHODS

Experiments were carried out on random-bred mature male albino rats (n=15). Surgery was performed under intraperitoneal ketamine narcosis (1.5 mg/100 g). In group 1 rats (n=6) denervation of the right hindleg was

Department of Histology, Kazan State Medical University. ***Address for correspondente:*** islamru@yahoo.com. R. R. Islamov

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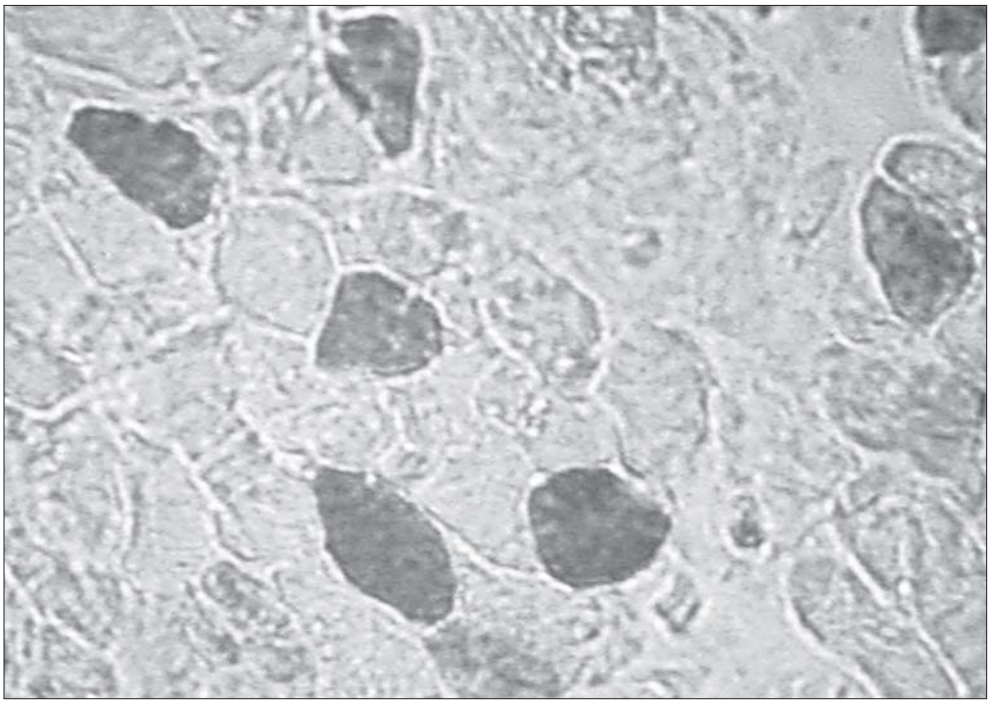

Fig. 1. Lumbrical rat muscle. Immunohistochemical staining with monoclonal antibodies against slow myosin. Light muscle fibers are fast, and the dark ones are slow, ×250.

performed by excision of a 5-mm segment of the sciatic nerve, while in group 2 rats (n=6) denervation was made by 30-sec crushing of the sciatic nerve with a thin hemostatic mosquito clip. The control data (n=3) were obtained on muscles of intact rats. After 4 weeks, the rats were sacrificed under deep ether narcosis, and lumbrical muscles were isolated from both legs.

Paraffin transversal muscle sections were prepared routinely. Immunohistochemical staining of paraffin sections was performed with monoclonal antibodies against slow myosin (1:200 dilution, Novocastra). The immune reaction with primary antibodies was revealed with streptavidin-biotin system (Dako). The immune complexes were visualized with ethyl carbazole. The sections were photographed with a digital camera under a Jenawal microscope (Zeus). No less than 200 MF were counted in the preparations, after which the relative content of slow MF was calculated [4]. The results were analyzed statistically using Student's t test at $p<0.05$.

RESULTS

The rat lumbrical muscle belongs to fast skeletal muscles with pronounced prevalence of fast MF. In intact rats histochemical analysis showed that the share of slow MF is 11.15±4.70% (Fig. 1).

After excision of sciatic nerve segment, the relative content of slow MF in lumbrical muscle did not change in the experimental leg, although the contralateral leg demonstrated pronounced increase of slow MF content (Fig. 2). By contrast, crushing of the nerve with a thin clamp increased the content of slow MF in both legs, the relative content of these fibers in the experimental and contralateral muscles was similar.

Comparison of our previous data [4] with these findings proved similar alterations in slow soleus and fast lumbrical muscles of the contralateral leg caused by unilateral damage to the sciatic nerve. Such changes in cell architectonics in fast and slow muscles of the contralateral leg corroborate our hypothesis about the effect of extrapyramidal system on morphological and functional parameters of leg muscles.

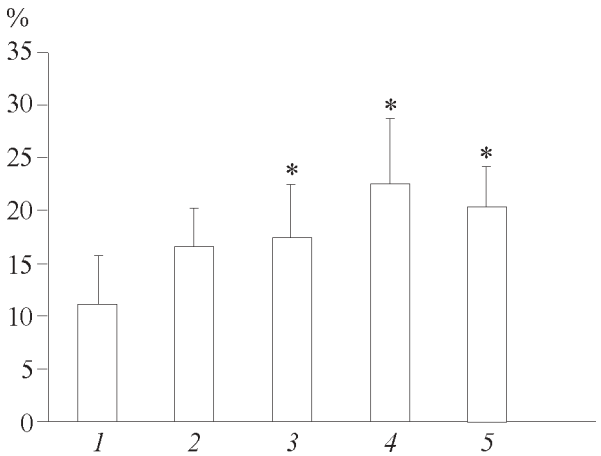

Fig. 2. Effect of denervation on relative content (%) of slow muscle fibers in rat lumbrical muscle in experimental and contralateral limbs. *1*) intact rats; *2*) denervation by segment excision in experimental limb; *3*) denervation by segment excision in contralateral limb; *4*) denervated by nerve crushing in experimental limb; *5*) denervated by nerve crushing in contralateral limb. *$p<0.05$ compared to intact muscle.

The composition of skeletal muscles is highly heterogeneous. They are plastic and specifically change their morphological and functional parameters in response to disturbances of neurotrophic regulation. The determinant sign of any muscle or individual fiber is qualitative composition of contractile proteins (most of all, skeletal muscle myosin isoforms), which makes it possible to identify fast and slow MF. Several isoforms of myosin can be simultaneously synthesized in the definitive MF [7]. This expression of different myosin isoforms in individual MF underlies plasticity of skeletal muscle [6].

Numerous factors, such as trophic influence of the corresponding peripheral nerve, various modes of muscle work, and the regulation by humoral system of the organism can maintain genetically determined and unique for each muscle set of different MF, which forms muscle architectonics. At the same time, different MF are phenotypes of the same myogenic cell type with possibility to transform of MF into other fiber types after, for example, cross-reinnervation [5] or under the action of thyroid hormones [1].

The revealed phenomenon of deceleration of muscles in the contralateral leg induced by unilateral damage to the supplying nerve can be explained by the compensatory bilateral activation of spinal motor centers under these conditions [3,11]. At the same time, it can be hypothesized that the impulses originated from damaged afferent fibers travel via the ascending pathways, cerebellum, and reticular formation coming finally to γ-motoneurons, which trigger the intrafusal MF in the contralateral leg. This excitation is reverberated via the ascending pathways, cerebellum, and the red nucleus to α-motoneurons of the same (contralateral) leg, where it enhances the tone of extrafusal MF and elevates the content of slow fibers.

Therefore, extrapyramidal system seems to modulate the phenotype of MF via spinal motoneurons. The compensatory activation of this system is reflected by pronounced deceleration of fast and slow skeletal muscle in the extremities.

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REFERENCES

1. V. V. Valiullin and N. P. Rezvyakov, *Byull. Eksp. Biol. Med.*, **96**, No. 9, 38-40 (1983).
2. P. Duus, *Topic Diagnosis in Neurology* [in Russian], Moscow (1996).
3. A. M. Eremeev, I. N. Pleshchinskii, and T. V. Babynina, *Ros. Fiziol. Zh.*, **86**, 1673-1679 (2001).
4. R. R. Islamov, D. S. Guseva, Yu. A. Chelyshev, and V. V. Valiullin, *Byull. Eksp. Biol. Med.*, **131**, No. 4, 477-480 (2001).
5. N. P. Rezvyakov and E. E. Nikol'skii, *Fiziol. Zh. SSSR*, **64**, 1117-1123 (1978).
6. E. G. Ulumbekov, in: *Problems of Myogenesis* [in Russian], Leningrad (1981), pp. 175-187.
7. G. W. Amphlett, S. V. Perry, H. Syska, *et al.*, *Nature*, **257**, 602-604 (1975).
8. D. L. Bishop and R. L. Milton, *Exp. Neurol.*, **154**, 366-370 (1998).
9. D. Meyer, T. Yamaai, A. Garratt, *et al.*, *Development*, **124**, 3575-3586 (1997).
10. K. Sakuma, K. Watanabe, M. Sano, *et al.*, *Brain Res.*, **907**, 1-19 (2001).
11. P. S. Stein, J. C. Victor, E. C. Field, and S. N. Currie, *J. Neurosci.*, **15**, 4343-4355 (1995).