# Effect of Dexamethasone on the Development of Denervation Changes in Fast and Slow Skeletal Muscles

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Immunohistochemical study with monoclonal antibodies to fast myosin heavy chains shows that physiological doses of dexamethasone do not affect the immunohistochemical profile of fast *musculus plantaris* and slow *musculus soleus* in guinea pig. Dexamethasone induces *de novo* formation of fast muscle fibers in denervated slow muscle and does not prevent expression of fast myosin after blockade of axonal transport.

**Key Words:** *skeletal muscle; neurotrophic control; dexamethasone; myosins; immunohistochemistry*

The problem of informational intercellular interactions remains one of the most important and poorly understood in the medicine and biology. In this context, neurohumoral regulation of skeletal muscles is of particular interest, because, on the one hand, the pathogenesis of many muscular diseases directly related to disturbances in neural and humoral control of muscular activity remains unclear and, on the other hand, elucidation of the neural and hormonal control of muscular function will make it possible to directly affect the muscle phenotype, which is of primary importance for sports medicine.

Both myofibrils (MF) and skeletal muscle are heterogeneous in respect to a number of structural and functional characteristics. The most important parameters are the rate and force of contraction, and correspondingly all muscles and MF can be divided into slow and fast. The type of muscles and MF can be determined histochemically by activity of myosin ATPase. However, there are recent data that activity of this enzyme does not obligatorily correlate with the qualitative composition of myosin [3]. Therefore, more adequate histochemical methods of identification of fast and slow MF are based on antibodies to various types of myosins, because the qualitative composition of these proteins determines the rate and force of MF contraction.

The morphofunctional characteristics of skeletal muscles are controlled by the nervous and humoral systems. The most important components of this regulation are neurotrophic control effected via motor nerve fibers, and the influence of the endocrine system. The phenotype of skeletal muscles is regulated by trophic protein factors synthesized in the perikaryons of motor neurons and transferred to MF by axon transport. It is also determined by impulse activity in the motor neurons [5,8]. Disturbances in the neurotrophic control affect various parameters of skeletal muscles, in particular, modulate the qualitative composition of myosins [9]. Previously we showed that in contrast to denervation, colchicine blockade of axon transport induces synthesis of fast myosin in guinea pig slow muscles [3]. We proposed that impulse activity of motor neurons is a factor of neurotrophic control regulating the qualitative composition of myosins in skeletal muscles [2].

Less is known on the role of hormonal system in the regulation of morphofunctional properties of skeletal muscles. Most works in this field are devoted to the effects of thyroid hormones [4], androgens, and anabolic steroids on various skeletal muscles [10,11]; however, the possible role of glucocorticoids (GC) in

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the regulation of various parameters of muscles received little attention. Practically nothing is known on the effect of GC on myosin composition in fast and slow muscles, although there were efforts to study their effects on protein composition of muscles [7]. At the same time, clinical practice shows that massive injections of GC can provoke so called GC-myopathy, which is accompanied by destructive processes in muscles caused probably by activation of proteolytic enzymes in MF [6]. While the effects of neurotrophic control and some hormones are partially known, the interaction between these two important systems in the regulation of skeletal muscle phenotype was not studied. It is unknown how various hormones affect the development of denervation-induced disturbances in skeletal muscles. Of particular clinical importance are the effects of GC on denervated skeletal muscles.

Our aim was to examine whether physiological doses of GC dexamethasone (DM) could prevent synthesis of fast myosin in muscle induced by blockade of axon transport. We also studied the effect of DM on intact and denervated fast and slow muscles in guinea pig.

## MATERIALS AND METHODS

Slow *musculus soleus* and fast *musculus plantaris* of male guinea pigs weighing 300-400 g were examined. Cryostate sections (8 μ) were stained by the indirect PAP method with monoclonal antibodies to fast myosin heavy chains (Sigma). Disturbances of the neurotrophic control were modeled as follows: the skin and subcutaneous fat in the dorsal lower one-third of the thigh were cut under ether narcosis, the muscles were displaced, the sciatic nerve was ligated, and a 2-3-mm fragment was dissected. In the experiments with colchicine the nerve was exposed in the same way, ligated, a silicon rubber strip was inserted under the nerve, and a cotton soaked in 10 mM colchicine was applied. The animals treated with physiological saline under the same conditions served as controls [1]. Starting from the next day postoperation, DM was injected intramuscularly during 3 weeks (0.6 mg/kg/day). The muscle was examined 3 weeks postoperation.

## RESULTS

Immunohistochemical staining of fast *m. plantaris* with monoclonal antibodies to fast myosin revealed slow and fast MF, with predominance of fast MF (Fig. 1, *a*). In intact animals *m. soleus* is homogeneous and contains only slow MF, which do not interact with antibodies (Fig. 1, *b*). Denervation does not modify the immunohistochemical profile of the fast and slow muscles. Blockade of axon transport does not affect the

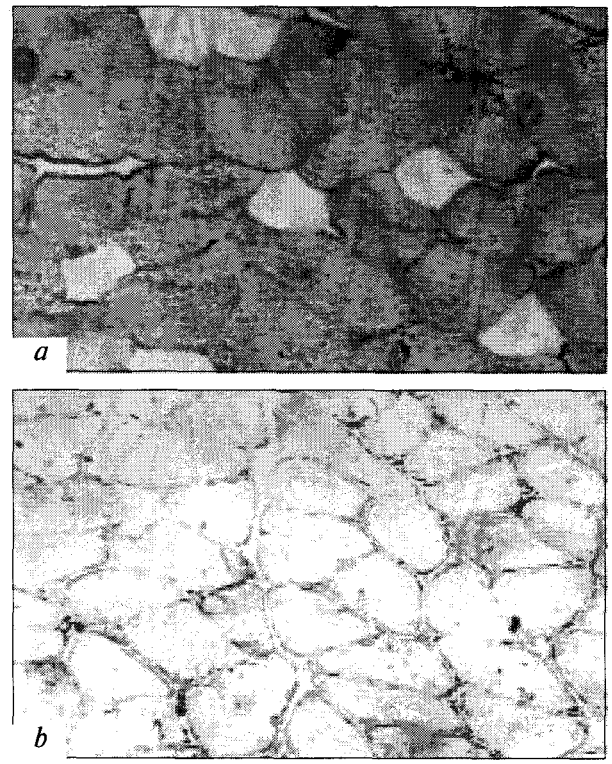


**Fig. 1.** *M. plantaris* (*a*) and *m. soleus* (*b*) from intact guinea pig. Here and on Fig. 2: immunohistochemical staining (PAP-reaction) with monoclonal antibodies to fast myosin heavy chain.

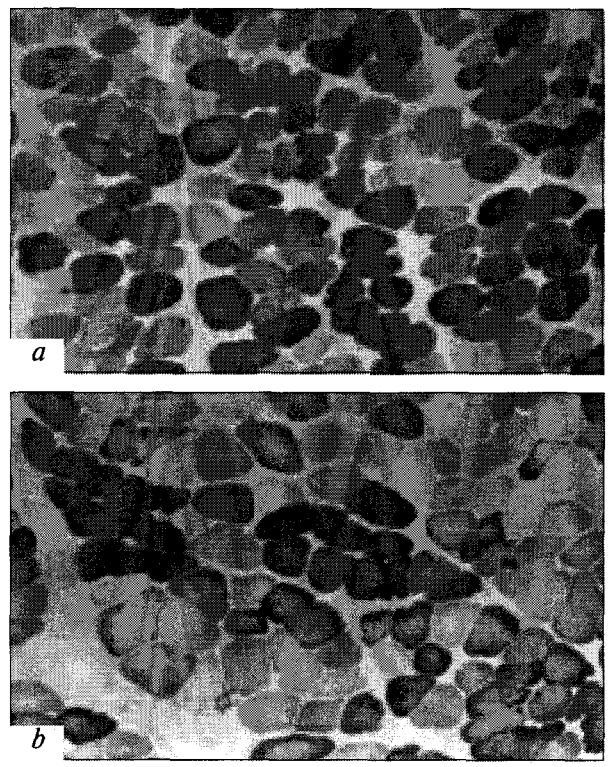


**Fig. 2.** *M. soleus* from guinea pig after application of colchicine to sciatic nerve (*a*) and after denervation and injection of dexamethasone (*b*).

content of fast and slow MF in fast muscle, while in the slow muscle MF containing fast myosin appeared under these conditions (Fig. 2, *a*). DM did not affect the relative proportion between fast and slow MF in both examined muscles with intact innervation. It did not prevent the appearance of fast MF in slow muscle after blockade of axon transport: both types of MF were present in this muscle under these conditions. DM did not change the immunohistochemical profile of fast denervated muscle, but fast MF appeared in denervated slow muscle treated with DM (Fig. 2, *b*).

Our findings provide evidence that DM does not affect the qualitative composition of myosins in fast and slow skeletal muscles of guinea pig. DM did not prevent the appearance of fast MF in slow muscle induced by blockade of axon transport. In denervated slow muscle DM induced synthesis of fast myosin.

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