NEUROTROPHIC CONTROL OF MYOSIN SYNTHESIS BY GUINEA PIG SLOW MUSCLE

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The structural and functional characteristics of skeletal muscles are under neurotrophic control [3]. It has been suggested that nervous influences on muscle are realized through trophic factors synthesized in the perikarya of motoneurons and transported to muscle by axon transport system, and may also be determined by the character of the spike discharge of the motoneuron [4, 10]. Division of a motor nerve, i.e., deprivation of the target of both components of neurotrophic control, has different effects on fast and slow muscle fibers (MF). For instance, the relative content of the "fast" light chain (LC 3) in myosin of denervated slow muscle increases, whereas in fast MF, on the other hand, the content of LC 1, characteristic of myosin of the slow type [6], is increased. However, it is not clear how the disturbance of axonal transport affects expression of the different myosins of skeletal muscle. Application of the alkaloid colchicine to the motor nerve is used experimentally to block axonal transport, for it is considered that in this way there is no disturbance of the flow of impulses along the axon.

Virtually all data on changes in the composition of myosins under conditions of disturbance of neutrotrophic control have been obtained by electrophoresis [8, 9], but if isoforms of myosins possessing closely similar electrophoretic parameters are present, the results may be difficult to interpret. The most adequate methods for identification of the myosins in MF must therefore be taken to be immunocytochemical methods, using antibodies (AB) to concrete myosins or their fragments [5].

We have used an immunocytochemical method to study slow muscle myosins when axonal transport is disturbed.

EXPERIMENTAL METHOD

The slow soleus muscle of adult male guinea pigs weighing 350-400 g was studied. Activity of myosin ATPase was detected histochemically in frozen sections 6 μ thick [7], and monoclonal AB to fast myosin heavy chains (from "Sigma") were subjected to indirect immunohistochemical staining (the PAP method) [5, 12]. The sciatic nerve was divided in animals of one group (n = 6), animals of the other group had colchicine solution applied to their sciatic nerve. The animals' muscles were studied three weeks after the beginning of the experiment. The operative techniques and formation of the control were described by the writers previously [1, 2].

EXPERIMENTAL RESULTS

The soleus muscle of intact guinea pigs is homogeneous with respect to its level of ATPase activity: all MF have low activity of the enzyme and belong to the group of type I slow MF (Fig. 1a). Treatment of the muscle with AB demonstrated the absence of fast myosin in MF (Fig. 1b).

The muscle preserved its original histochemical profile after denervation: MF had low ATPase activity and did not react with AB (Fig. 2). Blockade of axonal transport by application of the cytostatic to the nerve did not alter ATPase activity in MF (Fig. 3a), but on staining AB we recorded the appearance of MF interacting with AB to fast myosin, evidence of its appearance in the muscle (Fig. 3b).

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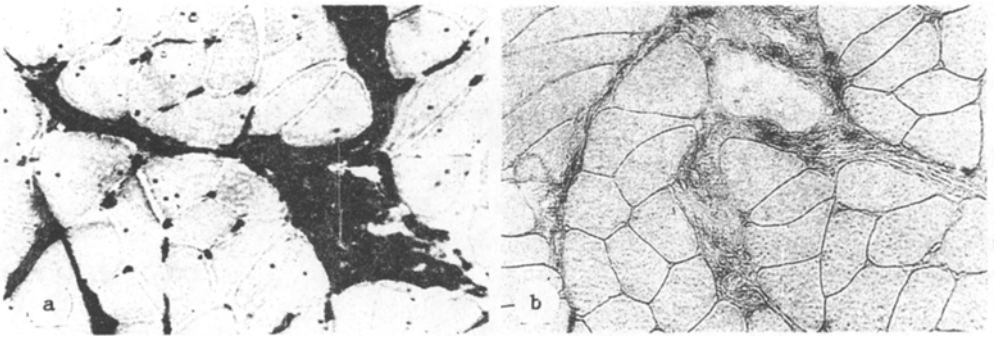

Fig. 1. Soleus muscle of intact guinea pig. Here and in Figs. 2 and 3: a) myosin ATPase activity (pH 9.4); b) immunohistochemical staining (PAP method) by monoclonal AB to fast myosin heavy chains.

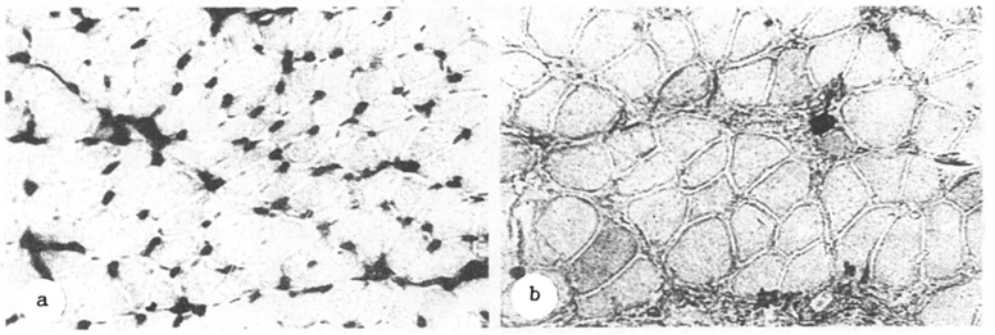

Fig. 2. Denervated soleus muscle of guinea pig.

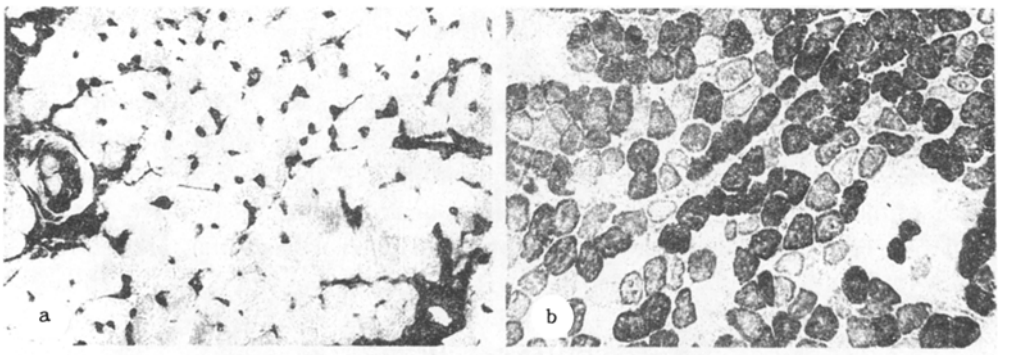

Fig. 3. Soleus muscle of guinea pig after application of colchicine to sciatic nerve. Pale MF are slow, dark MF are fast.

The results of this investigation demonstrate that application of colchicine, unlike denervation, induces reprogramming of myosins in some MF, by triggering synthesis of the fast myosin isoform. The fact that in the series with blockade of axonal transport the muscle was homogeneous for its level of ATPase activity, although in some MF fast myosin was present, is in contradiction with generally held views regarding correlation of activity of this enzyme with the qualitative composition of the myosin [11]. Changes taking place in myosin under these conditions evidently do not affect the active center of the enzyme. Hence it follows that activity of myosin ATPase is not always a reliable marker for typing MF. Denervation of the soleus muscle does not lead to the appearance of fast myosin, which is found only when axonal transport is blocked. Division of the motor nerve, depriving the muscle of mobility, probably prevents the synthesis of fast myosin, the appearance of which requires a functional load. Another possible explanation of this phenomenon could be the influence of spike activity on expression of fast

myosin genes in MF. Thus the action of trophic factors and spike activity of motor neurons evidently regulate synthesis of contractile proteins by independent mechanisms.

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MORPHOMETRIC AND IMMUNOHISTOCHEMICAL FEATURES OF THE GASTRIC AND DUODENAL MUCOSA IN SYSTEMIC LUPUS ERYTHEMATOSUS

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KEY WORDS: systemic lupus erythematosus; gastric and duodenal mucosa; morphometry; immunohistochemistry

The overwhelming number of publications devoted to the state of the gastrointestinal tract in systemic lupus erythematosus (SLE) in adults and children have been based on studies of autopsy material [1-3, 6, 7, 3]. The morphometric and immunohistochemical features of the gastric and duodenal mucosa in SLE have not yet been studied.

With this aim we undertook morphometric and immunohistochemical investigations of 108 biopsy specimens of mucosa from the body and antrum of the stomach, and the bulk and descending portions of the duodenum from 27 children with SLE. The disease in 17 children was categorized as the II degree of activity, whereas in 10 it was in the stage of remission. The comparison group consisted of 36 biopsy specimens of mucosa from the same parts of the stomach and duodenum from 12 children with exacerbation of chronic gastroduodenitis.

EXPERIMENTAL METHOD

The biopsy specimens of the mucosa were fixed in 10% neutral buffered formalin and embedded in paraffin wax. Sections were stained with hematoxylin and eosin. The PAS reaction revealed neutral glycosaminoglycans. Parameters character-

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