Effect of work-load exercise on the compensatory muscle hypertrophy in the albumin-deficient rat

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Summary

To study the role of albumin in the work-induced hypertrophy in skeletal muscle, effect of work-load exercise on skeletal muscles of the albumin-deficient rat (Nagase Analbuminemia Rat; NAR) was compared with those of normal rats. The work-induced muscle hypertrophy, which is constantly observed with normal rats, failed to take place in NAR.

Key Words: Albumin, Skeletal muscle, Compensatory hypertrophy, Albumin-deficient rat

Introduction

Much interest has been focused in recent years on the mechanisms leading to compensatory hypertrophy in skeletal muscle (1, 2, 3, 4, 5). In the previous paper (5), we reported that the tenotomy-induced hypertrophy in the rat skeletal muscle accompanies a significant increase in the level of a specific protein with a molecular weight of approximately 64,000 Daltons. This protein, designated "64KDa protein", has been identified as rat albumin based on biochemical and immunological criteria (5). Moreover, the result of isotope incorporation experiments suggested that albumin in rat skeletal muscle is most likely to be synthesized in muscle cells and the rate of its synthesis is significantly elevated in the hypertrophied muscle (5). These observations imply a possible correlation between albumin and the compensatory muscle hypertrophy. Thus, the present experiments have been designed to elucidate the role of albumin in the work-induced enlargement of skeletal muscle. For the purpose of these experiments, we took advantage of using a mutant rat strain which has a defect in albumin synthesis. The albumin deficient rat, termed "Nagase analbuminemia Rat" (abbreviated as NAR), is a mutant of the Sprague Dawley rat which lacks albumin in serum (6). The molecular processes which bring about the absence of serum albumin in this mutant rat have been recently established. The NAR has a defect in the nuclear splicing of the primary transcript from the albumin gene, producing a non-functional albumin mRNA (7). If albumin in skeletal muscle is coded for by the gene which also cordes for serum albumin and if albumin participates in muscle enlargement, then the processes leading to the compensatory muscle hypertrophy should be impaired in NAR. In the present study, changes in muscle weight and protein components in the work-loaded skeletal muscles of NAR were compared with those of normal rats.

Materials and Methods

Animals

Nagase analbuminemia rats (NAR) derived from JCL-Sprague Dawley rats were kindly supplied by Dr. Sumi Nagase, Sasaki institute, Tokyo. Normal Sprague-Dawley rats were obtained from the stock of CLEA Japan, Kanagawa.

Tenotomy

Rats of the same developmental stage were divided into control and experimental groups by weight-matching. Tenotomy and sham-operation of the hind legs were performed in the same manner as described previously (5). The plantaris and the soleus muscles in both operated and contralateral limbs were removed for examination 7 days after operation.

Polyacrylamide gel electrophoresis

Polyacrylamide gel electrophoresis was performed as described by Laemmli (8) on 10% acrylamide slab gels. Total muscle proteins were dissolved in a sample buffer, containing 25 mM Tris-HCl, 2% SDS, pH 6.5 and heated in boiling water for 2 min. Electrophoresis was performed at 25 mA constant current until the bromophenol blue tracking dye moved to the end of the gel. After electrophoresis, proteins were stained with Coomassie blue (5).

Results

Effect of tenotomy and exercise on muscle hypertrophy in the analbumineia rat

To study the effect of work-load exercise on the muscle hypertrophy in NAR, the soleus and the plantaris muscles of one limb were work-loaded by tenotomy of the synergistic gastrocnemius muscle. The contralateral limb which received only sham-operation served as control. During one week following tenotomy, the work-loaded muscles of the tenotomized limb of NAR failed to exhibit statistically significant changes in wet weight as compared to those of control muscles (Table 1). By contrast, we routinely observed 30-50% weight gain in the work-loaded muscles of normal rats when the synergistic muscle was tenotomized (5).

Effect of tenotomy on muscle protein components

To ascertain whether the work-load exercise brings about qualitative or quantitative change in the protein components of the skeletal muscles of NAR, total protein from the work-loaded and control muscle were analyzed by means of SDS polyacrylamide gel electrophoresis. Densitometric tracings of the staining patterns clearly demonstrate that the amount of albumin in the muscle preparations of NAR, either work-load or control, is negligible, while marked increase in albumin content is noticed in the work-loaded muscle of normal rat (Fig. 1). These results not only reaffirms that 64 KDa protein is rat albumin, but also strongly suggest a correlation between albumin and exercise-induced muscle hypertrophy.

Table 1. Effect of tenotomy and exercise on weight of skeletal muscles of normal and analbuminemia rats

Rat Strain	Muscle	Control	Work-loaded
NAR (n=5)	Plantaris	95.0 ± 13.1	109.4 ± 19.7
	Soleus	59.6 ± 4.5	84.4 ± 26.9
Normal (n=5)	Plantaris	103.5 ± 7.4	140.8 ± 8.9*
	Soleus	60.3 ± 10.8	83.7 ± 10.3*

Values are means ± SD for 5 muscles. * $P<0.01$

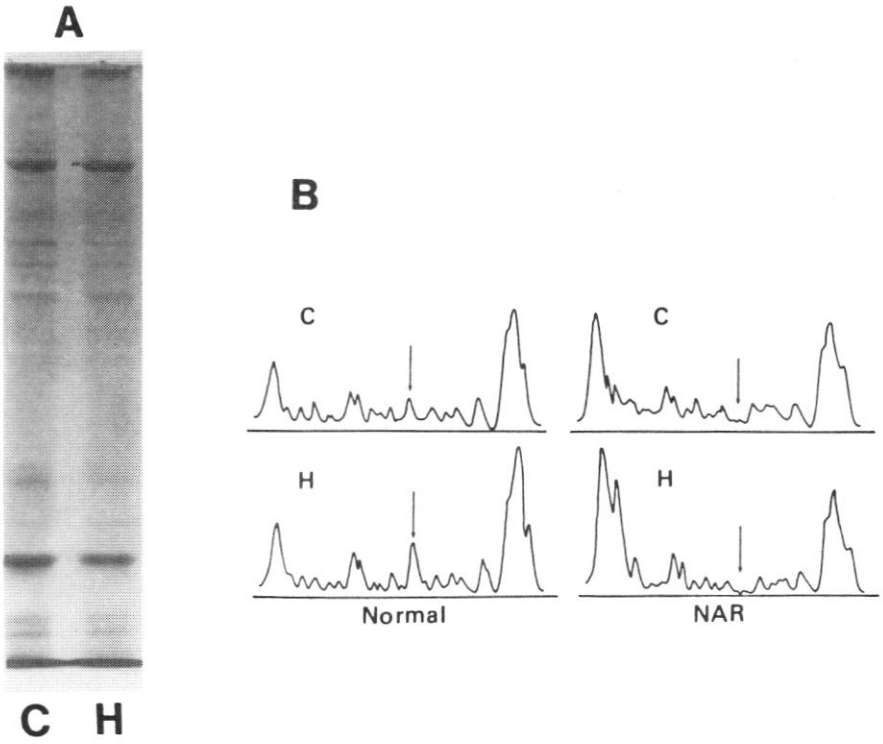

Fig. 1. SDS-polyacrylamide gel electrophoresis of muscle proteins. The plantaris muscles from the tenotomized (H) and sham-operated (C) limbs of NAR were removed 7 days after operation and each muscle was solubilized with 4 ml of SDS sample buffer (3). Each 15 μl of solution (20 μ g protein) was subjected to SDS-polyacrylamide gel electrophoresis and stained for protein with Coomassie blue (A). Electrophoreograms of muscle proteins were traced by a densitometer (B). Arrows indicate the position of muscle albumin. Direction of electrophoresis was from left to right.

Discussion

In the previous paper, compensatory hypertrophy in the rat skeletal muscle accompanies an increase in muscle concentration of albumin (5). Studies on the physiological role of albumin in compensatory muscle hypertrophy would be greatly facilitated by the availability of a rat strain defective in albumin biosynthesis (6, 7). In the present experiments, tenotomy was performed on the skeletal muscle of albumin deficient rats (NAR) and changes in weight and protein composition of the work-loaded synergistic muscles were compared with those of normal rats. In contrast to the case with normal rats, we found that NAR fails to develop significant muscle hypertrophy in response to the work-load training. The result strongly suggests the positive involvement of albumin in the work-induced enlargement of skeletal muscle, though mechanisms by which albumin participates in the muscle hypertrophy remain to be elucidated.

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