修士論文要旨

Muscle Atrophy-induced Changes of Cathepsin and Dipeptide Levels in Rats

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Introduction

It is generally accepted that the magnitude of muscle mass depends on the rates of the protein synthesis and degradation, and muscle atrophy is induced by hypokinesia (reduction in hindlimb movement) and/or hypodynamia (reduction in muscle mechanical loading). Muscle atrophy is characteristic outcomes of prolonged hypokinesia /hypodynamia resulting from bed-rest, gypsum fixation, tenotomy, joint immobili- zation, cage restraint, suspensions and space-flight.

On the other hand, skeletal muscle contains multiple proteolytic systems, which could play an important role in muscle atrophy. Cathepsin B is one of the lysosomal proteases, and is known as a proteolytic enzyme of cellular proteins. Further, skeletal muscle atrophy is known to cause protein degradation and to release muscle dipeptide (carnosine and anserine). However, the relationship between muscle cathepsin B activeties and dipeptide levels in skeletal muscles is still unknown. Therefore, it is important for the elucidation of the processes to study the intracellular changes in atrophic muscles. In the present study, the effects of whole body suspension (WBS) on the muscle weight, muscle protein levels, cathepsin B activities, and muscle dipeptide levels in rats were investigated.

Methods and Materials

1. Experimental procedures and animals : The WBS was carried out for 10 days. 7 wks old male SD rats were divided into the cage control (CON) group and WBS group. After the WBS, skeletal muscles (SOL : *soleus,* PLA : *plantaris,* GAS : gastrocnemius, EDL : *extensor digitorum longus* and TIB : *tibialis anterior*), and visceral organs were isolated, and weighed. Further, protein and dipeptide concentrations, and cathepsin B activities in muscles were assayed.

2. Methods : Muscle protein assays were performed by the phenol methods. Muscle cathepsin B activities were assayed with the fluorescence spectroscopy. Muscle carnosine (CAR) and anserine (ANS) assays were carried out with a high-performance liquid chromatograph.

Results and Discussion

1. Body weights : The body weights (BW) of the final experiments were 21% lower in the WBS than in the CON.

2. Muscle weights : The relative weights of SOL, PLA and GAS ankle joint flexor muscles per BW were 0.62, 0.84 and 0.80 times significantly lower in the WBS than those in the CON, respectively. The relative weights of EDL and TIB ankle joint extensor muscles per BW, however, did not change by the WBS.

3. Muscle protein contents : Both of SOL and GAS muscle protein contents in the WBS were 0.53 times clearly lower than those in the CON.

4. Muscle cathepsin B activities : SOL muscle cathepsin B activities per BW were 1.71 times higher in the WBS than in the CON. GAS muscle cathepsin B activities were 0.90 times lower in the WBS than in the CON.

5. Muscle CAR and ANS concentrations : The WBS decreased muscle CAR concentrations to 0.52 and 0.91 times in SOL and GAS, compared with the CON. The WBS also decreased muscle ANS concentrations to 0.72 times in SOL, compared with the CON. However, muscle ANS concent- rations in GAS did not change by the WBS.

6. Visceral organ weights : The weights of spleen, thymus, and adipose perirenal and periepididymal tissues per BW were 0.74, 0.64, 0.40 and 0.62 times significantly lower in the WBS than in the CON, respectively.

Conclusion

The WBS decreased markedly SOL and GAS muscle protein contents. The muscle atrophy occurring in WBS may be causally related to the increased cathepsin B activities and decreased CAR and ANS concentrations in SOL muscles. Similar phenomena were not observed in GAS muscles, despite the decreased CAR concentration and muscle weight loss. These results suggest that WBS-induced SOL muscle atrophy may be induced at least partly by increased breakdown of muscle proteins and decreased muscle buffering capacities.