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The effect of four weeks hypoxic resistance training on myostatin and follistatin expression in skeletal muscle of rats

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Objective Loss of skeletal muscle weight is a common phenomenon in hypoxic environment. It has been recognized that resistance training can reduce hypoxia-induced skeletal muscle atrophy, but its molecular mechanism is still unclear. Myostatin is a major factor that inhibits muscle growth and differentiation, and Follistatin can inhibit Myostatin. Therefore, this study is to clarify the effect of 4-week hypoxic resistance exercise on Myostatin and Follistatin gene expression in skeletal muscle of rats.

Methods Twenty four 8-week-old male SD rats were randomly divided into normoxic control group (group C: 6 rats), normoxic exercise group (group R: 6 rats), hypoxic control group (group H: 6 rats) and hypoxic exercise group (group HR: 6 rats). Rats in each hypoxic group were fed in a hypoxic chamber (atmospheric hypoxia) with oxygen concentration of 12.7% (simulated 4000m altitude). Rats in each exercise group were trained according to the rat's resistance training program developed in our laboratory. After all the intervention, DEXA was used to analyze the body composition. The soleus, extensor digitorum longus and biceps brachii muscles of rats were taken and the wet weight of individual muscles was measured. The data were processed by SPSS17.0 statistical software. The expression level of skeletal muscle mRNA was expressed as "median (25-75%)" and the data of body composition and muscle wet weight were expressed as "mean±standard deviation". The differences between the groups were evaluated using a one-way analysis of variance (ANOVA) test. The significance level for the study was less than 0.05.

Results Body composition analysis after 4 weeks of hypoxic intervention showed that the body weight of rats in group H decreased significantly (p=0.012), and the muscle mass decreased more significantly (p<0.001). But resistance exercises obviously reduced the muscle atrophy (p<0.01) caused by hypoxia. After analyzing the changes of the wet weight of individual muscles, it was found that the wet weight of biceps brachii in HR group was significantly higher than that in H group (p=0.048). After 4 weeks of hypoxic intervention and hypoxic resistance exercise, the expression of Myostatin mRNA in individual muscles of each group changed differently. The expression of Myostatin mRNA in soleus muscle of H group was significantly higher than that of C group (371.2%) after 4 weeks of hypoxia intervention. Myostatin mRNA expression in soleus and biceps brachii of HR group was significantly lower than that of H group (591.1% and 478.4% respectively). However, there was no significant difference in the expression level of Myostatin mRNA in the extensor digitorum longus between each group (p=0.259). The change of Follistatin mRNA expression in different groups also showed a different trend. The expression of Follistatin mRNA in soleus muscle and biceps brachii muscle was significantly different among groups (p=0.003, p=0.004, respectively). However, there was no significant difference in the expression level of Follistatin mRNA in the extensor digitorum longus between each group (p=0.734). Myostatin mRNA/Follistatin mRNA ratio (M/F) showed a more significant difference. The M/F ratio of soleus muscle in group H was significantly lower than that in group C (p<0.001), but the M/F ratio in group HR was significantly higher than that in group H (p<0.001). The M/F ratio of biceps brachii in group H was significantly lower than that in group C (p<0.001), but the M/F ratio in group HR showed a higher trend than that in group H (p=0.051).

Conclusions Hypoxic exposure results in an increase in Myostatin mRNA expression in skeletal muscle, but hypoxic resistance exercise reduces such an increase. On the contrary, the level of Follistatin mRNA expression in skeletal muscle decreased after hypoxic exposure, and hypoxic resistance exercise could slow down the decline. As a result, rat resistance exercise significantly slowed down hypoxia-induced muscle atrophy. In conclusion, the mutual restriction between Myostatin and Follistatin is one of the main links of resistance exercise to reduce hypoxia-induced skeletal muscle atrophy. However, the process of resistance training to reduce the hypoxia-induced skeletal muscle atrophy is very complex. There are many molecular signaling pathways involved, which need further study.