

**THE EFFECTS OF CONGESTIVE HEART FAILURE AND FUNCTIONAL  
OVERLOAD ON RAT SKELETAL MUSCLE**

by

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THE EFFECTS OF CONGESTIVE HEART FAILURE AND FUNCTIONAL

## OVERLOAD ON RAT SKELETAL MUSCLE

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Abstract

Numerous references have suggested that alterations in exercise capacity during congestive heart failure (CHF) are not simply due to changes in myocardial function. Recent evidence has indicated that reductions in skeletal muscle strength and endurance during CHF significantly impact exercise capacity of the CHF patient. Currently, it is believed that alterations in skeletal muscle phenotype, or more specifically a slow to fast transformation in protein isoforms contribute to the reductions in muscle function. However, currently there are few data which directly document this slow to fast transformation of the skeletal muscle.

Interestingly, it is established that exercise training can cause changes in skeletal muscle phenotype, more specifically in the fast to slow direction. This is in direct contrast to what is known to occur during CHF. However, it is unclear if similar adaptations will result from training in a CHF patient. Also, it is not clear if the adaptations are due to alterations in the myocardium or changes directly imposed upon the muscle by the exercise training.

Therefore, the purpose of this study was two-fold: 1) to clarify the changes in skeletal muscle myosin heavy chain (MHC) during CHF and 2) to determine if skeletal muscle can adapt to increased activity levels, utilizing functional overload (FO).

In the first study the mixed plantaris muscles from rats afflicted with severe CHF demonstrated a significant ( $p < 0.05$ ) increase in fast MHC (*e.g.* IIb expression at the expense of IIx expression) compared to the control animal (SHAM). The mixed red gastrocnemius, regardless of the severity of CHF, exhibited significant ( $p < 0.05$ ) changes in all of the MHC isoforms. The soleus and white gastrocnemius did not display any

significant changes in MHC expression. The changes in MHC isoform significantly correlated with indicators of disease severity, suggesting there may be an existing relationship between skeletal muscle MHC expression and alterations in myocardial function.

In the second study, no differences were detected between CHF and SHAM absolute or specific plantaris mass. There was a significant ( $p < 0.05$ ) 30% increase in both absolute and specific mass of the plantaris in the CHF-FO and SHAM-FO groups compared to the CHF and SHAM groups. There was a significant ( $p < 0.05$ ) 3.5% increase in slow MHC I expression and a significant ( $p < 0.05$ ) 6.5% decrease in fast MHC IIb expression in the CHF-FO group compared to the CHF group. In the SHAM-FO group, there was a significant ( $p < 0.05$ ) 4% increase in MHC I expression and a subsequent 8% decrease in fast MHC IIx+IIb in the SHAM-FO compared to the SHAM groups. No differences were detected in the rates of  $\text{Ca}^{2+}$  uptake between the CHF-FO, SHAM, and SHAM-FO. However,  $\text{Ca}^{2+}$  uptake rates were significantly ( $p < 0.05$ ) elevated by 44% in the CHF group when compared to the other three groups. There were few changes in plantaris SERCA 1 or 2 protein expression between the four groups.

These data suggest that during CHF there are alterations in skeletal muscle isoform expression. However, at least some of the data suggest that changes in function are not always associated with changes in phenotype. Instead, it seems that the changes in  $\text{Ca}^{2+}$  handling may be due to an alteration in a regulatory mechanism. Also, the data indicate that skeletal muscle is adaptable to increases in activity levels without significantly altering myocardial morphology.