TACSM Abstract

Disuse Atrophy Occurs Without a Change in Mitochondrial Respiratory Control Ratio During Hindlimb Unloading in Mice

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ABSTRACT

Skeletal muscle atrophy commonly occurs during prolonged periods of inactivity, however the precise mechanisms that cause muscle atrophy have yet to be determined. Specifically, a controversy exists on whether mitochondrial dysfunction is a cause or consequence of disuse muscle atrophy. **PURPOSE**: The purpose of this study was to determine if a change in the respiratory control ratio, which is a ratio of maximal O_2 respiration to leak respiration, could be detected prior to muscle atrophy in a time-course study in mice. **METHODS**: Disuse atrophy was induced using hindlimb unloading (HU) in adult, C57BL/6J male mice for 0 (control), 1, 2, 3, or 7 days (n=~6-8/group). Following completion, gastrocnemius and soleus muscles were weighed and assessed for mitochondrial function in permeabilized muscle fibers. Here, we define mitochondrial function as the respiratory control ratio (RCR) determined by maximal ADP stimulated respiration (State 3) divided by leak or ATP synthase inhibited (state 4) respiration. A one-way ANOVA was used to determine differences between means. When significant F ratios were found, a Tukey post-hoc was used to compare differences between means. Values presented are mean ± standard error **RESULTS**: In both the gastrocnemius and soleus, muscle mass was not significantly different from control at day 1, but was significantly lower at 2, 3, and 7-day timepoints. In contrast, there was no significant difference in RCR in gastrocnemius (control 3.11±0.20, 1 day 2.96±0.60, 2 day 3.07±0.31, 3 day 3.08±0.25, 7 day 3.41± .29) or soleus (control 2.33±0.33, 1 day 2.77±0.33, 2 day 3.03±0.51, 3 day 2.93±0.30, 7 day 2.78±0.48). **CONCLUSION**: It is well established that HU causes rapid muscle atrophy. These data support mitochondrial RCR does decrease before muscle atrophy in either gastrocnemius or soleus muscle, and therefore may not be a primary cause of HU-induced muscle atrophy in mice.