TACSM Abstract

Cisplatin Blunts Muscle Hypertrophy in Exercise Trained Mice

JADEN WELLS, JAINIL DAREDIA, MICHAEL WIGGS, & CORY DUNGAN

Dungan Lab; Health, Human Performance, & Recreation; Baylor University; Waco, TX

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Advisor / Mentor: Dungan, Cory (Cory_Dungan@baylor.edu)

ABSTRACT

Cisplatin is a chemotherapeutic agent known to cause skeletal muscle atrophy and cachexia; however, the long-term effect of cisplatin on skeletal muscle adaptations to exercise remains unclear. **PURPOSE**: The purpose of this study was to assess if prior administration of a clinically relevant cycle of cisplatin blunts exercise adaptations in response to 8 weeks of exercise training. **METHODS**: Female CD2F1 mice, n = 7-8/group, were treated with 5 mg/kg of cisplatin, or vehicle, once per week for 4 weeks, then given a 4-week washout. Afterwards, mice were singly housed and subjected to either progressive weighted wheel running (PoWeR) for 8 weeks or remained sedentary in their cages. **RESULTS**: Differences between groups were examined using a two-way ANOVA. Body weight was consistent between group (average range: 27.0 g to 27.5 g), and muscle mass was nearly identical in sedentary vehicle- and cisplatin-treated mice. In vehicle-treated mice, 8 weeks of PoWeR caused whole-muscle hypertrophy in the soleus (+28% normalized wet weight) and plantaris (+18% normalized wet weight) muscle when compared to sedentary mice. This was accompanied by an elevation in muscle fiber cross-sectional area (CSA) by 18% and 14% in the soleus and plantaris, respectively. PoWeR trained mice treated with cisplatin displayed signs of anabolic resistance, which included significantly lower soleus (-22%) and plantaris (-19%) weight when compared to vehicle treated. Muscle fiber CSA was also lower in the soleus (-15%) and plantaris (-13%) muscles compared to vehicle. Interestingly, the exercise-mediated glycolytic-to-oxidative fiber-type transition was the same between the groups. **CONCLUSION**: Collectively, our data indicate that previous exposure to cisplatin leads to anabolic resistance in mice. Additional analysis and follow-up studies are required to elucidate the mechanisms driving this response.