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AEROBIC METABOLISM AND OXIDATIVE STRESS ARE REGULATED BY EXERCISE AND MYOSTATIN/ACTIVIN BLOCKING IN DYSTROPHIC MICE

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Objectives.

Exercise and blocking myostatin/activin may independently counteract progressive muscle wasting in Duchenne Muscular Dystrophy (DMD). Thus, the combined and independent effects of these treatments are investigated in the muscles of model for DMD, young mdx mice. Methods. The effects of soluble activin receptor-Fc (sActRIIB-Fc) administration and voluntary running were tested alone or in combination for seven weeks. Gastrocnemius muscle was analyzed by expression microarray and western blotting.

Results.

Decreased pathways of aerobic (FDR<0.005) and antioxidant glutathione (FDR=0.07) metabolism were observed in mdx mice compared to healthy mice. Aerobic metabolism was further downregulated upon sActRIIB-Fc treatment in hypertrophied muscles (FDR<0.05). However, exercise activated aerobic metabolism and counteracted the effect of sActRIIB-Fc. sActRIIB-Fc increased thioredoxin-interacting protein (TXNip), an endogenous inhibitor of antioxidant thioredoxin, but this response was attenuated by exercise. The combination of exercise and sActRIIB-Fc increased glutathione metabolism coinciding with increased protein carbonylation and the phosphorylation of Sirtuin1 (P<0.05).

Conclusion.

Exercise enhances aerobic metabolism and prevents the decrease induced by myostatin/activin blocking in dystrophic mice. However, the combination of these treatments shows signs of increased protein oxidation and altered antioxidant metabolism.