Exercise Training Improves Cardiac and Skeletal Muscle Metabolism in Rats with Pulmonary Arterial Hypertension

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In patients with pulmonary arterial hypertension (PAH), a shift from oxidative to glycolytic metabolism promotes right ventricular (RV) and skeletal muscle dysfunction that contributes to reduced exercise tolerance. As seen for other cardiopulmonary diseases, exercise training (ExT) may ameliorate this glycolytic switch in PAH and improve exercise capacity. The purpose of this research is to investigate ExT in a rat model of PAH on markers of glycolytic and oxidative metabolism in RV and skeletal muscle. Male Sprague-Dawley rats received monocrotaline (MCT, 40 mg/kg, s.q.) to induce PAH (n= 13), or saline, for healthy controls (n=5). After 2 wks, with MCT-induced PAH established, 6 wks of treadmill (TM) ExT was initiated for a subset of PAH animals (PAH-ExT, n= 6) and healthy controls (CON-ExT, n=3). ExT runs progressed up to 60 min at mild relative intensity, 50% of maximal aerobic capacity (VO_2max). VO_2max was assessed at baseline, in pre-training and post-training TM testing via analysis of expired gases. Abundance of Glut-1, a marker of glycolytic metabolism, was evaluated in cryosections of RV and soleus with immunofluorescent (IF) staining and quantification. Data are presented as mean±SE. MCT-ExT rats maintained aerobic capacity over 6 wks better than sedentary counterparts (MCT-SED)(ΔVO_2max= -134±109 vs. -521±129 ml/kg/hr, p=0.04) and was not different than CON-ExT (-201±31 ml/kg/hr, p=0.82). A lower abundance of Glut-1 was observed in both RV and soleus myocytes of PAH-ExT rats (MPI= 10.9 ±0.9 for RV; 13.7±0.8 for soleus) compared to PAH-SED rats (15.7±2.4, p=0.05, for RV; 17.4±1.4, p=0.04, for soleus) and was similar to CON-ExT rats (13.0±2.2, p=0.33, for RV; 9.0±2.3, p=0.26, for soleus), indicative of a shift toward greater dependency on oxidative metabolism. Exercise training attenuates functional decline following MCT administration in rats. Preservation of aerobic capacity may be explained by promotion of more efficient RV and skeletal muscle mitochondrial substrate utilization.

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