

Effects of aerobic exercise training on diaphragm muscle metabolism in a rat model of Pulmonary Arterial Hypertension.

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Pulmonary arterial hypertension (PAH) is characterized by a progressive increase in pulmonary vascular resistance that leads to right ventricular (RV) overload and eventually RV failure and death. PAH is associated with diaphragm muscle dysfunction and increased work of breathing which contributes to the exercise intolerance that is hallmark in this patient population. Our lab and others have described a shift in substrate utilization toward non-oxidative (glycolytic) metabolism in the RV and skeletal muscle of PAH rodent models as well as in patients. This project will determine if 'glycolytic shift' also occurs in the diaphragm muscle which may contribute to exercise intolerance and dyspnea. Since regular aerobic exercise is well-known to promote adaptations enhancing oxidative metabolism in cardiac muscle and skeletal muscle of the extremities, this project will also investigate the impact of exercise training on diaphragm muscle metabolism. Diaphragm muscles were harvested upon completion of a 6 week, 4x/wk. treadmill training program that consisted of 60 min runs at a relative intensity of 50% of aerobic capacity (VO<sub>2</sub>max). Abundance of glucose transporter Glut-1, a marker of glycolytic metabolism, is being evaluated by Immunofluorescent (IF) staining at the cell membrane of diaphragm myocytes. We expect to find that PAH rats have greater abundance of diaphragm Glut-1 and that exercise training at least partially ameliorates this PAH-induced 'glycolytic shift'.

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