Acute Exercise Activates Pulmonary eNOS and Lowers Pulmonary Pressure in Rats with Pulmonary Arterial Hypertension

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NO-dependent arterial relaxation is impaired in pulmonary arterial hypertension (PAH). Exercise may be beneficial in PAH, just as it is for systemic vascular disease, via upregulation of endothelial nitric oxide synthase (eNOS) expression and activity. However, exercise-induced cardiac stress in PAH could also promote detrimental RV inflammation. We investigated pulmonary pressure and eNOS, as well inflammatory indicators in the RV, following a single 45 min run bout at moderate intensity in a rat model of PAH. Male Sprague-Dawley rats received either monocrotaline to induce PAH, or saline, for healthy controls. A subset of PAH and healthy controls performed 4 wks of progressive TM familiarization (15-30min, 8-20 m/min) in preparation for their final 45 min run @ 75% of VO_2max. Immediately following the run, RV systolic pressure was measured and RV and lung tissues were harvested and cryofixed. eNOS and phosphorylated (at Ser1177) eNOS (p-eNOS) was measured via immunoblotting in lung homogenates and expressed normalized to vinculin. Immunofluorescence for inflammatory markers CD45/68 in cryofixed RV sections evaluated the acute inflammatory response to exercise. MCT reduced VO_2max and caused RV hypertrophy (expressed as RV/LV+septum) as consistent with this model. RVSP (normalized by systemic BP) was lower in PAH-Ex vs. unexercised PAH with no difference between exercised and unexercised controls. Greater p-eNOS was measured in PAH-Ex lung compared to unexercised PAH, with no difference between exercised and unexercised controls. PAH-Ex also tended to have greater pulmonary eNOS than their unexercised counterparts. No greater exercise-induced CD45/68 infiltration was observed in RV of PAH compared to that of controls. In rats with moderate MCT-induced PAH, a single exercise bout does not increase acute RV inflammation but lowers pulmonary pressure, possibly mediated in part via pulmonary eNOS activation.

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