A. Olah[1], B. Bodi[2], J. Tamas[2], M. Torok[1], C. Matyas[1], A.A. Sayour[1], E. Urban[1], D. Kellermayer[1], M. Ruppert[1], B. Barta[1], K. Stark[1], B. Merkely[1], Z. Papp[2], T. Radovits[1], [1]**Semmelweis University, Heart and Vascular Center - Budapest - Hungary**, [2]University of Debrecen, Department of Cardiology, Division of Clinical Physiology - Debrecen – Hungary:

Characterization of myocardial sarcomerdynamics and myocardial sarcomeric protein alterations in a rodent model of athlete's heart

Abstract: P3988

Characterization of myocardial sarcomerdynamics and myocardial sarcomeric protein alterations in a rodent model of athlete's heart

Authors:
A. Olah[1], B. Bodi[2], J. Tamas[2], M. Torok[1], C. Matyas[1], A.A. Sayour[1], E. Urban[1], D. Kellermayer[1], M. Ruppert[1], B. Barta[1], K. Stark[1], B. Merkely[1], Z. Papp[2], T. Radovits[1], [1]Semmelweis University, Heart and Vascular Center - Budapest - Hungary, [2]University of Debrecen, Department of Cardiology, Division of Clinical Physiology - Debrecen - Hungary,

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Background: In contrast with pathological myocardial hypertrophy, long term exercise-induced cardiac enlargement is associated with functional amelioration. Thus understanding the cellular and molecular processes leading to physiological hypertrophy induced by exercise training might provide a novel therapeutic approach to prevent or treat heart failure. In vivo hemodynamic characterization of athlete's heart in small animal model was previously provided by our research group. Although numerous experimental studies have been designed to deeply understand the underlying mechanisms in exercise-induced myocardial hypertrophy, our knowledge still appears to be insufficient.

Purpose: We aimed at determining left and right ventricular (LV and RV) cardiac sarcomeric modifications at cellular and molecular levels in a rat model of athlete's heart and additionally, examining the reversibility of the observed alterations.

Methods: Young rats were divided into control (Co) and exercised (Ex) groups. Trained rats swam 200 min/day for 12 weeks. To investigate reversibility, detrained rats remained sedentary for 8 weeks after completion of the training protocol. LV morphology was examined by echocardiography, while in vivo hemodynamic porperties were provided by LV pressure-volume analysis. Force assessments on isolated permeabilized cardiomyocytes and molecular biological measurements (qRT-PCR, Western blot) were applied to reveal underlying mechanisms.

Results: Echocardiographic and post mortem measured heart weight data confirmed training-induced cardiac hypertrophy, while pressure-volume analysis revealed increased LV contractility in the hearts of exercised rats. The Ca2+-activated force production of isolated LV and RV cardiomyocytes was improved (Factive: LV 28.0±1.4 kN/m^2 Ex vs. 15.8±0.8 kN/m^2 Co, $P<0.05$; RV 16.8±1.1 kN/m^2 Ex vs. 12.1±1.0 kN/m^2 Co, $P<0.05$) along with increased Ca2+ sensitivity and rate constant of force redevelopment in trained rats. Ca2+-independent passive tension did not differ between the groups. Exercise training did not affect myocardial gene expression of α- and β-myosin heavy chain (MHC) and cardiac troponin I. Cardiac troponin I phosphorylation was decreased (cTnI relative phosphorylation level: LV 0.66±0.06 Ex vs. 1.00±0.02 Co, $P<0.05$; RV 0.65±0.05 Ex vs. 1.00±0.03 Co, $P<0.05$), whereas the phosphorylation of titin and cardiac myosin binding protein-C was not altered in physiological hypertrophy. Complete reversibility of the observed alterations was detected in detrained rats.

Conclusions: Exercise-induced hypertrophy is associated with increased Ca2+-activated force and Ca2+ sensitivity of force production of LV and RV cardiomyocytes, which might be associated with hypophosphorilation of cardiac troponin I. Cellular and molecular alterations regressed completely after 8 weeks of detraining.