

Topic 34 – Cardiac rehabilitation, exercise, cardiovascular prevention, patient education

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0420

Acute exercise preconditioning induced mitochondrial protection against skeletal muscle ischemia-reperfusion injury

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Ischemia-reperfusion (I-R) induces mitochondrial function impairments and oxidative stress in skeletal muscle. In cardiac muscle, one-to-several days of exercise attenuate I-R injury. The objective of the present study was to show that a single exercise (EXO) prior to the I-R period protects the hind limb mitochondrial function. Twenty mice were randomly divided into 2 groups: The control group (CTL I-R, n=10) underwent I-R without exercise and the exercise group (EXO I-R, n=10) ran before I-R. Mice underwent 2 hours of ischemia induced by a rubber band tourniquet applied on the right root of the hind limb (the left leg was used as control leg), followed by a reperfusion period of 2 h. The EXO was performed on a treadmill with 10% incline 1h before I-R. The mice ran at a speed of 30cm until 40cm/sec during 30min. Blood lactate obtained from the tip of the tail at the end of EXO was above 9 mmol/L. In skinned gastrocnemius fibers, I-R significantly decreased the maximal mitochondrial respiration (Vmax) of the ischemic leg in comparison to the control leg in the CTL group (23.6 vs 28.6 pmol/(sec*mg wet weight); p<0.05). EXO I-R mice increased Vmax in comparison to CTL I-R mice (39.5 vs 31.8 pmol/(sec*dw) in the ischemic leg and the control leg respectively; p<0.05). After EXO, the impairment between ischemic leg and control leg was partially restored (p=0.22). Without preconditioning, I-R increased H2O2 production of the ischemic leg in comparison to the control leg (42.6 vs 37.8 umol/mg dw; p=0.23). EXO I-R mice significantly decreased the H2O2 production in comparison to CTL I-R mice (26.6 vs 42.6 umol/mg dw; p<0.01) in the ischemic leg. After EXO, the impairment between ischemic leg and control leg was completely abolished (p=0.8). These results show that a preconditioning exercise protect the maximal mitochondrial respiration in mice and reduce the mitochondrial production of ROS following a period of I-R.

0012

Cardiac effects of a treatment with prolyl-hydroxylase inhibitors (PHI), used to improve exercise performance, in sedentary and trained rats

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Stabilization of the Hypoxia Inducible Factor (HIF) using prolyl-hydroxylase inhibitors (PHI) leads to an EPO synthesis which is suspected to be used as a doping practice. Such a treatment is suspected to improve endurance performance by increasing oxygen transport. However the effects of a PHI treatment on heart morphology and function has never been investigated. Therefore the aim of this study was to evaluate whether potential effects of PHI on cardiac function could contribute to explain its beneficial effect on aerobic performance.

We tested the effects of a 1 week treatment with a PHI (DMOG, 150 mg.kg⁻¹, I.P.) or a placebo (NaCl) on both sedentary (Sed) and trained rats (Ex; trained during 5 weeks before treatment started; 40min at 25 m.min⁻¹ per day; 5days/week). Our first result was that PHI increased running performance (+12%, p<0,05) in both Sed and Ex groups. This increased performance was

associated with a major increase in total hemoglobin in PHI-treated animals (+13% p<0,05). However, regarding cardiac function and cardiac remodeling no beneficial effect of PHI was observed. Indeed, in hearts of sedentary as well as exercised rats no significant change in any morphological parameters (LVEDs, LVEDd, AWTd, PWTd and RWT) was found. Moreover, no change in systolic function likely to explain enhanced exercise performance was observed in PHI-treated hearts, when evaluated by intraventricular pressure probe (Millar®). Finally it is interesting to note that in sedentary rat hearts an impairment of diastolic function characterized by an altered E/A and dp/dt_{min} ratios was found when they were challenged with isoproterenol (0,5 mg.kg⁻¹). These last results obtained in sedentary hearts could suggest that a more prolonged treatment with such PHI could have deleterious consequences on heart health and point out the danger of such a doping strategy; however, this point remains to be more precisely investigated.

0108

Specific alterations in cardiac function induced by a 300 km mountain ultra-marathon

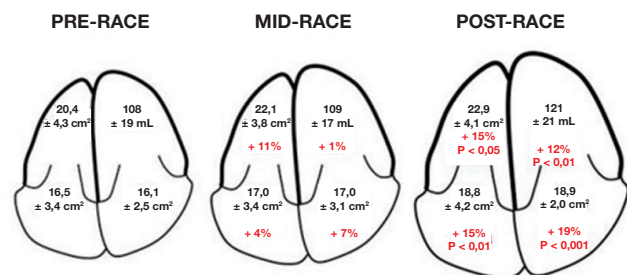
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Purpose: Although popularity of ultra-long endurance races is growing, data on their consequences on cardiac function are still lacking. Thus, we aimed to assess the progressive cardiac consequences of the World's most challenging mountain ultra-marathon (Tor des Geants; Italy; 300km; 24000 m D+).

Methods: Resting cardiac evaluations were conducted prior (pre-), during (mid-; km 150) and after (post-) the race on fifteen participants. Left and right ventricle (LV and RV) morphologies, functions and mechanics were assessed using standard tissue Doppler imaging and Speckle tracking echocardiography.

Results: Runners completed the race in 126±15 h. From pre- to post-, the increase in stroke volume (SV) (103±19 vs. 110±23 vs. 116±21 mL; p<0.001 from pre- to post-race) was concomitant with the increase in LV early filling (i.e. peak E; 72.9±15.7 vs. 74.6±13.1 vs. 82.1±11.5 cm.s⁻¹; p<0.05). Heart cavity sizes were 12-19% higher at post-. Significant correlations were found between percent changes in peak E and LV end-diastolic volume (r=0.56, p<0.05) or left atrial and right ventricle diastolic areas (r=0.66, p<0.05; r=0.80, p<0.001; respectively). Resting heart rate and LV systolic strain rates demonstrated a biphasic adaptation since they were increased at mid- (55±8 vs. 72±11 bpm, p<0.001) but returned to baseline pre- values at post- (55±8 vs. 59±8 bpm, respectively).

Conclusion: Whereas it is well-described that long duration exercise of several hours induces a transient LV dysfunction, we observed specific cardiac adaptations characterized by a progressive increase in SV and diastolic function during much longer exercise; e.g. 4-7 days of mountain running. Our data strongly support the key role of a cardiac volume overload in these alterations. The underlying mechanisms of such specific alterations after an extreme mountain ultra-marathon and their clinical implications remain challenging for the future.



Abstract 0108 – Figure : LV end-diastolic volumes and LA, RA and RV end-diastolic areas at pre-, mid- and post-race. Percentage changes from baseline are presented for each size or volume cavity