Topic 37 – Cardiac rehabilitation, exercise, cardiovascular prevention, patient education

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0215

High intensity exercise training failed to improve NO pathway in SHR rats: implication of eNOS uncoupling

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Aim: Exercise training is a well recognized strategy to improve vascular endothelial function by increasing nitric oxide (NO) signalling pathway. However, in hypertensive subjects, previous studies reported that high intensity aerobic exercise (HT) may no longer improve endothelial function. Consequently, the aim of this work was to investigate, in spontaneously hypertensive rats (SHR), the impact of HT exercise on vascular function and especially on NO pathway.

Method: Rats were divided in 3 groups: WKY, sedentary SHR and SHR-Ex, exercised on a treadmill, 1 hour at 85% of their maximal aerobic velocity, 5 days a week for 6 weeks. Arterial function was evaluated on isolated aortic rings in response to ACh or SNP in presence or not of indomethacin, TRAM 34 and Amapin to avoid the contribution of EDHF and cyclooxygenase on endothelium-dependent vasorelaxation. ENOS expression and activation state (phosphorylation at ser1177) were evaluated by western blot. Total Aortic and eNOS-dependent ROS production were assessed using Electron paramagnetic resonance in presence or not of NAC or tetrahydrobiopterin (BH4).

Results: Although eNOS level and phosphorylation were higher in aorta of SHR exercised rats, no beneficial effects of HT were reported on endothelium and eNOS-dependent vasorelaxation. This result was explained by increased eNOS uncoupling in aorta of SHR-Ex rats. Indeed, HT in SHR rats resulted in increased eNOS-dependent ROS production, which was blunted by the use of the recoupling agent BH4 or by the thiol reducing agent (NAC).

Conclusion: The lack of positive effect of HT on endothelial function in SHR rats was the consequence of altered redox state which contribute to uncouple eNOS, switching it from NO to O2-.- generation.

0233

Response to exercise training is not predicted by exercise oxygen pulse profile

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Introduction: The gain of peak VO2 after exercise training has prognostic value in CHF patients. The predictive factors influencing this response remain debated. As oxygen pulse is correlated with the stroke volume, it could reflect cardiac adaptation during exercise. The aim of this study is to evaluate the cardiac participation in benefits of exercise training (ET).

Method: We included prospectively 53 CHF patients (mean age: 57± 12 years, LVEF 29 ± 6 %) who underwent two cardiopulmonary exercises (CPX) before and after 20 endurance exercise training sessions. We analysed for the two CPX heart rate, workload, VO2, oxygen pulse and calculated stroke volume and cardiac output at rest, anaerobic threshold (AT) and peak exercise. We measured BNP levels before and after the exercise training program. Patients were considered as responders if the gain of peak VO2 was >10%.

Mean change in peak VO2 after exercise training is 17 % for global population, 36 % for responders (n=27) and 4 % for non responders (n=26). At baseline, responder patients have a lower workload at AT and at peak exercise (52.6 ± 19 vs 62.2 ± 27 watts p: 0.035 and 68.9 ± 28 vs 86.6 ± 27 watts p:0.035); a lower oxygen uptake (14.8 ± 4.8 vs 17.5 ± 4.6ml/kg/min p: 0.04), a chronotropic incompetence (max heart rate 99.8 ± 19.8 vs 116 ± 25 b/min p:0.01); a lower maximal cardiac output (6.6 ± 2.5 vs 8.0 ± 2.3/min p:0.019) and a higher BNP serum level (median 506 vs 279 pg/l p:0.019). However oxygen pulse trends or left ventricular function do not influence changes in peak VO2 at any time and regardless of the training type (continuous vs interval training).

Conclusion: Cardiac adaptations in CHF patients do not seem to play major role in the response to exercise. Benefits of exercise training on exercise tolerance in CHF patients are mainly due to peripheral improvements.

0111

Role of endoplasmic reticulum stress in the deleterious cardiovascular consequences of chronic intermittent hypoxia. Beneficial effects of high-intensity interval training

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Background: Chronic intermittent hypoxia (IH) is described as the major detrimental factor leading to cardiovascular morbi-mortality in obstructive sleep apnea (OSA) patients. Previous animal studies demonstrated that IH increases myocardial susceptibility to ischemia-reperfusion (IR). Among mechanisms involved in the pathophysiology of IR, modulation of endoplasmic reticulum (ER) stress seems to play a major role. Exercise is known to exert beneficial effects on the cardiovascular system and a growing body of evidence demonstrates a particular efficiency of high-intensity interval training (HT). The aim of the present study was 1) to evaluate the effects of HT on IH-induced increased susceptibility to IR; 2) to determine whether ER stress was involved.

Method: Wistar male rats were exposed to 21 days of IH (21-5% FiO2, 60s cycle, 8h/day) or normoxia (N). After one week of IH alone, rats were daily submitted to both IH and HIT (2*24min, 15 to 30min/min). Rat hearts were either submitted to an IR protocol ex-vivo (30min-global ischemia followed by 120 min-reperfusion, Langendorff technic) or rapidly frozen to evaluate ER stress by Western Blot.

Results: IH induced a significant increase in infarct size (35.4±3.2% vs 22.7±1.7% of ventricles, in IH and N respectively, p<0.05) that was corrected by HIT (28.8±3.9 vs 21.0±5.1% of ventricles, in IH and N respectively). This was accompanied by a myocardial ER stress IH-dependent, characterized by the increased expression of the ER stress sensor (i.e. GRP78) and the activation of the proapoptotic ER stress pathway (i.e. pPERK, ATF4 and CHOP). HIT conditioning prevented this IH-induced proapoptotic ER stress.

Conclusion: These findings show that HIT prevented the IH-dependent increase in myocardial susceptibility to IR, probably through a down-regulation of proapoptotic ER stress pathway. HIT could represent a good preventive strategy to limit myocardial ischemia reperfusion-related damages in OSA patients.

0108

A new animal model of induced DT2 and its application in evaluating exercise benefits

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Type 2 diabetes (DT2) is a major risk factor of atherosclerosis. As Hypertension or dyslipidemia, DT2 can occur in patients with metabolic syndrome and may result in endothelial dysfunction. Physical activity is a part of the preventive treatment of endothelial dysfunction. The aims of this study were to develop a new animal model of induced DT2 and to investigate the impact of exercise on the DT2 development. Male Wistar rats were supplemented with a fructose enriched...