Topic 5 – Diabetes, Lipids, metabolism – A

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0396

Prebiotics supplementation improves the endothelial dysfunction induced by a nutritional deficiency in n-3 polyunsaturated fatty acids (PUFA)

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Nutritional disorders are associated with a high risk of developing cardiovascular diseases, endothelial dysfunction being an early key marker. We have demonstrated that metabolic alterations induced by a nutritional depletion in n-3 PUFA are improved by a supplementation in prebiotics (non-digestible fructans). The present work focusses on the impact of prebiotics on the endothelial dysfunction induced by the n-3 PUFA depletion in ApoE⁻/⁻ mice model.

C57Bl/6j (WT) and ApoE⁻/⁻ (KO) mice were fed a n-3 PUFA depleted-diet (DEF) for 12 weeks. For the last fifteen days, mice were or not supplemented with prebiotics (PRE). The vascular morphology and function were evaluated in first, second and third order mesenteric arteries by histology and wire myograph. Micro-arteries from KO DEF PRE mice develop an increased basal tone and present a larger vessel diameter, compared to vessels from non-supplemented mice. The PRE supplementation in KO DEF mice leads to an increased media thickness in first order mesenteric arteries, this is even higher in the second order branch, in comparison to non-supplemented mice. KO DEF PRE micro-arteries contract significantly more in response to a KCl challenge than vessels from non-supplemented mice. As expected micro-arteries from KO DEF mice present an endothelial dysfunction after 12 weeks of n-3 PUFA depletion with a significant decrease of endothelium-dependent relaxation in comparison to WT DEF arteries. The PRE supplementation is able to improve the endothelial function by restoring the endothelial-dependent relaxation in arteries from KO DEF mice.

We point out fructan-type prebiotics as a potential therapeutic tool in endothelial dysfunction. Our results argue in favor of an outward muscular remodeling in mesenteric arteries, leading to an increased blood flow and a better vascular reactivity. The results on endothelial function evoke an important implication of the nitric oxide pathway in this phenomenon.

0061

Exercise training impaired energy metabolism and function of the type 2 diabetic Goto-Kakizaki ( GK) rat heart during ischaemia-reperfusion injury

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Background: Information about the effects of exercise training on diabetes-induced myocardial dysfunctions are lacking. Consequently, we investigated the effect of exercise training on the sensitivity of the type 2 diabetic Goto-Kakizaki (GK) rat heart to ischaemia-reperfusion injury by using a multiparametric approach combining 31P magnetic resonance spectroscopy (MRS) with simultaneous measurement of contractile function. Total adenine nucleotides (TAN) and energy charge (EC) were determined in freeze-clamped tissues by HPLC.

Results: Heart to body weight ratios were significantly higher in both untrained and trained diabetic groups (p<0.02) versus Control. During reperfusion, rate pressure product and recoveries of PCr and ATP were significantly lower (p<0.05) in trained GK versus untrained GK and Control rat hearts. TAN and EC were significantly decreased in trained GK compared with Control (p<0.0052 and p<0.0156) and untrained GK (p<0.0024 and p<0.0005) rat hearts.

Conclusion: The intensity of exercise training exacerbated the sensitivity of the type 2 diabetic 8-month-old Goto-Kakizaki rat to myocardial ischaemia-reperfusion by impairing energy metabolism and myocardial performance. Other exercise protocols and/or therapeutic approaches need to be explored to limit myocardial ischaemia-reperfusion injury in type 2 diabetes.

0205

Exercise training prevents microvascular dysfunction in a rat model of diet-induced metabolic syndrome

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Introduction: Metabolic syndrome (MetS) is associated with increased risk of cardiovascular disease (CVD). One important key feature underlying the pathophysiology of CVD is microvascular dysfunction. Although, exercise training is a well recognized strategy to reduce cardiovascular and metabolic disorders, the impact on MetS induced microvascular dysfunction is poorly described and the underlying mechanisms remain unknown. Thus this work was to evaluate the effect of physical activity on microvascular reactivity in a rat model of MetS.

Methods: Rats were fed with standard (Ctrl group) or high-fat and sucrose diet (HFS group) for 14 weeks. After 6 weeks, HFS rats were randomly assigned into 2 groups: sedentary (HFS) and trained group (HFS-Ex). In vivo endothelial function was evaluated by skin Laser Doppler technique associated to transcutaneous iontophoresis at 06 and 14 weeks. Body weight, metabolic parameters and blood pressure were also measured.

Results: High-fat and sucrose diet induced a significant body weight increase accompanied by the increase of serum level of glucose, triglycerides, HDL and LDL-cholesterol. All of these parameters were restored after 4 weeks of exercise training in HFS-Ex group. In addition, skin endothelium-dependent dilation, which was decreased in HFS compared to Ctrl, was prevented by exercise training. This result could be explained by increased level of eNOS expression and phosphorylation on its activation site (ser1177).

Conclusion: These results mainly suggest that an exercise training strategy, which is able to partially correct metabolic disorders in a model of MetS in rats, also prevents in vivo microvascular dysfunction.

0158

Effect of polyphenols of olive oil, hydroxytyrosol and its glucuronides on the vascular reactivity in a type 2 diabetes context

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Hydroxytyrosol (HT) and Resveratrol (RES) are recognized as strong antioxidant polyphenolic compound. While RES antioxidative mechanisms are well known, those of HT are controversial because of its low intestinal absorb-
Catabolism of leucine in the heart inhibits glucose transport

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Effects of piceatannol on cardiac remodelling in obese Zucker rats

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Background/Objective: Despite piceatannol is a polyphenol belonging the stilbene family as resveratrol, only very scarce studies have assessed its effects in obesity. Thus, our objective was to analyze the potential effects of piceatannol on cardiac tissue remodelling associated with the development of diabetes and obesity in Zucker rats (fa/fa) rats. This study was part of the POLYFrÉSNOL study granted by the REFIBIO network.

Methods: Zucker rats aged 6 weeks purchased from Charles River (France) were placed in an air-conditioned room (22°C ± 2°C with a 12 h light – dark cycle. They were fed with a normal diet and received 15 mg/kg (P15, n=10) or 45 mg/kg (P45, n=10) of piceatannol or vehicle (Ctl, n=10) during 42 days. After euthanasia, hearts were removed for histomorphological analysis including measurement of cardiomyocyte size (membranes were stained using WGA) and quantification of fibrosis (trichrome of Masson) as well as measurement of the cardiac expression of ephrin-B1 (western-blot). Data are presented as mean ± SD and were analyzed using one-way ANOVA.

Results: Piceatanol, whatever its dosage, failed to prevent the weight increase induced by HFD (Ctl: 170±32 g, P15: 168±23 g, P45: 169±26 g). No differences in heart weight/body weight ratio (mg/g) was noticed (Ctl: 2.74±0.20, P15: 2.55±0.20, P45: 2.58±0.22, NS). Piceatannol (15 and 45 mg/kg) failed to reduce cardiomyocyte hypertrophy or heart fibrosis deposition. A significant increase in ephrin-B1 expression (p<0.01 vs Ctl) was noticed in the P45 group but not in the P15 group (Fig 1).

Conclusion: Piceatannol does not prevent cardiac tissue remodeling associated with obesity and diabetes in this model. However, the increase in ephrin-B1 expression suggests that it could have some protective properties against cardiomyocyte lateral membrane remodeling. This finding would justify new studies investigating its effect on lateral membrane structure using electron microscopy.