tolerance is reported when prior exercise has been practiced less than 3 h before, although the physiological consequences of exercise should be the highest. It is therefore crucial to determine the clinical efficiency of exercise, the functional and cellular mechanisms of its effect, and the most appropriate modalities (eg, resistance, endurance or mixed) for improving the implementation of training programme in T2D. Mechanistically, the role of increased muscle glucose uptake due to glycogen depletion and the insulin-mimetic effect of muscle contraction have been well documented, but the contribution of the autonomous nervous system (ANS) is still discussed. We recently conducted a series of studies in non-diabetic subjects about the relations between postprandial glucose, substrate oxidation and ANS assessed by heart rate variability (HRV), when the meal is consumed after a submaximal exercise session (<1 h). Our results confirmed the increased postprandial glucose incremental profile, with relative hyperglycemia, preprandial baselines being lower after exercise than after rest. Since exercise-induced fat oxidation was maintained over the postprandial interval, these glucose and fat profiles were considered as beneficial. Interestingly, exercise was followed by a reduced activity of the parasympathetic component of ANS over the whole postprandial interval. Six weeks of training in fasted or fed conditions did not modify this profile. Thus, kinetics and metabolic parameters should be considered in the relations between exercise and postprandial glucose profile.

ISP15: Functional and morphological changes in the arterial wall in diabetes and aging. Role of AGEs
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Advanced glycation end-products (AGEs) are a group of heterogeneous molecules found at higher level during diabetes, end stage renal failure and aging. AGEs are formed consecutively to the non-enzymatic binding of a reducing sugar to the free amino groups in macromolecules. Vascular alteration is correlated with their accumulation during retinopathy or glomerulosclerosis. AGEs stimulate endothelial cell via the interaction with the receptor for AGEs (RAGE), leading to endothelial dysfunction. RAGE interaction with AGEs triggers reactive oxygen species production and NFXB pathway activation. Aside from the effects of endogenously formed AGEs, food is a part of the glycation burden in diabetic patients but also in healthy subjects. The consequences of dietary AGEs on inflammation and vascular tone have been reported. Agents that inhibit AGE formation, stimulate their degradation or neutralize their binding to RAGE represent new approaches to limit the deleterious activities of AGE.

ISP16: Endothelial dysfunction in type 2 diabetes
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Early after the seminal paper by Furchgott and Zawadzki in 1980 [1] demonstrating that the endothelium is responsible for the vascular relaxation induced by the muscarinic receptor agonist, acetylcholine, endothelial dysfunction was demonstrated in experimental animal models of diabetes [2], and its mechanisms were described by Bucala et al. [3]. McVeigh and co-workers [4] were the first to produce evidence in man of the presence of endothelial dysfunction in type 2 diabetes. More in details, forearm resistance vessels vasodilation in response to both endothelium- or smooth muscle cell-dependent stimuli was impaired, while neither the vascular structure nor unstimulated (basal) endothelium-dependent blood flow was compromised. The authors also showed that this vascular dysfunction is caused by a reduced NO release. These findings have been confirmed by subsequent work. In particular, the impaired vasodilatory response to nitrates, a somewhat neglected aspect of vascular dysfunction in diabetes, was fully confirmed by other investigators, notably in the elegant study by Creager et al. [5]. Similarly, the lack of significant associations between the vascular dysfunction and presence of vascular complications or degree of metabolic control, although quite surprising, has been reported by subsequent studies [6,7].

Endothelial dysfunction has then been detected in several other vascular districts: in epicardial vessels and resistance vessels of the coronary circulation (assessed by measuring lumen diameter or blood flow changes in response to acetylcholine), in leg and arm conductance vessels (evaluated with the use of the flow-mediated dilatation technique) and in skin microcirculation (by laser-Doppler iontophoresis). Notably, endothelial dysfunction of both coronary and forearm arteries has been shown to predict coronary events.

Patients with type 2 diabetes show not only an impaired vasodilatation but also a basal (unstimulated) enhanced release of endothelin-1, a potent vasoconstrictor [8]. The endothelium produces other vasoconstrictors, the prostanoids, but they do not seem to contribute to the vascular dysfunction of diabetes [5].

In a cohort of 95 patients with type 2 diabetes, we observed that the factors responsible for the reduced response to acetylcholine were more related to the triad, inflammation-insulin-resistance-obesity, than to diabetes per se. This interpretation is based not only on other cross-sectional association studies [6,7] but also on prospective randomized clinical trials [9] and clinical investigations showing that the contribution of both chronic [10] and acute [11] hyperglycaemia - at least within the concentration range commonly seen in type 2 diabetes - is marginal.

The mechanisms underlying endothelial dysfunction have been partly clarified: impaired vasodilatation is caused by a reduced NO bioavailability, which in turn results from enhanced oxidative stress. In addition to hyperglycaemia-induced mitochondrial dysfunction probably relevant at extreme glucose concentrations - two enzymes seem to play a key role in superoxide production by endothelial cells in response to inflammation: NAD(P)H-oxidase and xanthine-oxidase [12]. Interestingly, from a therapeutic perspective both enzymes are activated by angiotensin II and xanthine-oxidase is inhibited by allopurinol, the anti-hyperuricaric drug. In addition it is rather well documented that endothelial dysfunction can be reversed; randomized double-blind, placebo-controlled studies have in fact shown that enalapril [13], allopurinol [14], metformin [15] and thiazolidinediones [9] significantly improve endothelial function in patients with type 2 diabetes.

References:

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