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Trans-fatty acids aggravate anabolic steroid-induced metabolic disturbances and differential gene expression in muscle, pancreas and adipose tissue

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ABSTRACT

Aims: Although anabolic steroids (AS) and trans-fatty acids overload exerts systemic toxicity and are independent risk factors for metabolic and cardiovascular disorders, their interaction remains poorly understood. Thus, we investigated the impact of a diet rich in trans-fatty acids (HFD) combined with AS on glycemic control, lipid profile, adipose tissue, skeletal muscle and pancreas microstructure and expression of genes involved in energy metabolism.

Main methods: Forty-eight C57BL/6 mice were randomized into 6 groups treated for 12 weeks with a standard diet (SD) or a diet rich in C18:1 trans-fatty isomers (HFD), alone or combined with 10 or 20 mg/kg testosterone cypionate (AS).

Key findings: Our results indicated that AS improved glycemic control, upregulated gene expression of *Glut-4* and *CPT-1* in skeletal muscle, *FAS*, *ACC* and *UCP-1* in adipose tissue. AS also reduced total and LDL cholesterol in mice fed a SD. When combined with the HFD, AS was unable to induce microstructural adaptations in adipose tissue, pancreatic islets and β-cells, but potentiated *GCK* and *Glut-2* (pancreas) and *Glut-4* and *CPT-1* (skeletal muscle) upregulation. HFD plus AS also downregulated *FAS* and *ACC* gene expression in adipose tissue. Combined with HFD, AS increased triacylglycerol circulating levels, improved insulin sensitivity and glycemic control in mice.

Significance: Our findings indicated that HFD and AS can interact to modulates glycemic control and lipid profile by a mechanism potentially related with a reprogramming of genes expression in organs such as the pancreas, adipose tissue and skeletal muscle.

1. Introduction

Dyslipidemias are metabolic disturbances with increasing incidence and prevalence worldwide [1,2]. These conditions have been closely correlated with several metabolic (*i.e.*, obesity, diabetes mellitus, and non-alcoholic fatty liver disease) and cardiovascular (*i.e.*, atherosclerosis, systemic arterial hypertension, myocardial infarction, and cardiac insufficiency) diseases, which are potentially preventable causes of death in general population [3,4]. Dyslipidemias exhibit a complex and multifactorial etiology, in which genetic determinants are central mediators of the lipid metabolism that orchestrate the pathophysiology of these diseases [5,6]. However, by acting as genetic modulators, environmental factors such as dietary habits and exposition to hormonal drugs are also implicated in dyslipidemias development [2,3].

Inadequate eating habits, with excessive ingestion of highly processed foods rich in carbohydrates and fats have been strongly implicated with the establishment of a low-grade and chronic pro-oxidant and pro-inflammatory status and the increased occurrence of a broad spectrum of metabolic diseases [7,8]. While dietary polyunsaturated

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