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ORIGINAL ARTICLE

Trp64Arg polymorphism of the *ADRB3* gene associated with maximal fat oxidation and LDL-C levels in non-obese adolescents☆,☆☆

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Abstract
Objective: To analyze the association between the *Trp64Arg* polymorphism of the *ADRB3* gene, maximal fat oxidation rates (FATMAX) and the lipid profile levels in non-obese adolescents.
Methods: 72 schoolchildren, of both genders, aged between 11 and 17 years, participated in the study. The anthropometric and body composition variables, in addition to total cholesterol (TC), high density lipoprotein (HDL-c), low density lipoprotein (LDL-c), triglycerides (TG), insulin (INS), and basal glycemia (GLIC), were evaluated. The sample was divided into two groups according to the presence or absence of the polymorphism: non-carriers of the *Arg64* allele, *i.e.*, homozygous (*Trp64Trp*: $n = 54$), and carriers of the *Arg64* allele (Trp64Arg + Arg64Arg: $n = 18$), in which the frequency of the *Arg64* allele was 15.2%. The maximal oxygen uptake and peak of oxygen uptake during exercise were obtained through the symptom-limited, submaximal treadmill test. Maximal fat oxidation (FATMAX) was determined according to the ventilatory ratio proposed in Lusk's table.
Results: Adolescents carrying the less frequent allele (*Trp64Arg* and *Arg64Arg*) had higher LDL-c levels ($p = 0.031$) and lower FATMAX rates ($p = 0.038$) when compared with non-carriers (*Trp64Trp*).

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Conclusions: Although the physiological processes related to lipolysis and lipid metabolism are complex, the presence of the *Arg 64* allele was associated with lower rates of FATMAX during aerobic exercise, as well as with higher levels of LDL-c in adolescents.

PALAVRAS-CHAVE
Polimorfismo genético;
Exercício;
Metabolismo de lipídeos;
Lipólise;
Adolescentes

Polimorfismo *Trp64Arg* do Gene *ADRB3* associado à oxidação máxima de gorduras e à concentração de LDL-c em adolescentes não obesos

Resumo

Objetivo: Analisar a associação entre o polimorfismo *Trp64Arg* do gene *ADRB3*, as taxas de oxidação máxima de gorduras (FATMAX) e as concentrações do perfil lipídico em adolescentes não obesos.
Métodos: Participaram do estudo 72 escolares, de ambos os sexos, com idade entre 11 e 17 anos. Foram avaliadas as variáveis antropométricas e de composição corporal, além do colesterol total (CT), lipoproteína de alta densidade (HDL-c), lipoproteína de baixa densidade (LDL-c), triglicerídeos (TG); insulina (INS) e glicemia basal (GLIC). A amostra foi dividida em dois grupos, segundo a presença ou não do polimorfismo: não portadores do alelo *Arg64*, ou seja, homozigotos (*Trp64Trp*: *n* = 54) e portadores do alelo *Arg64* (*Trp64Arg* + *Arg64Arg: n* = 18), em que a frequência do alelo *Arg64* foi de 15,2%. O consumo máximo de oxigênio e pico de consumo máximo de oxigênio durante o exercício foram obtidos por meio do teste aeróbio submáximo de sintoma limitado em esteira. A oxidação máxima de gorduras (FATMAX) foi determinada de acordo com a razão de trocas ventilatórias propostas na Tabela de *Lusk*.
Resultados: Os adolescentes portadores do alelo menos frequente (*Trp64Arg e Arg64Arg*) apresentaram maiores concentrações de LDL-c (p = 0,031) e menores taxas de FATMAX (p = 0,038) quando comparados aos não portadores (*Trp64Trp*).
Conclusões: Embora os processos fisiológicos relacionados à lipólise e ao metabolismo de lipídeos sejam complexos, a presença do alelo *Arg64* associou-se a menores taxas de FATMAX durante exercício aeróbio, bem como maiores níveis de LDL-c em adolescentes.

Introduction

Aerobic exercise is one of the main strategies in body weight regulation, prevention, and treatment of complex obesity and type 2 diabetes mellitus (DM2), because in addition to potentiating the energy expenditure, it increases glucose absorption of muscle cells and promotes a decrease in insulin resistance.[1] However, the general population does not benefit from the practice of physical exercise, as, in addition to the exercise itself, these effects depend on other environmental factors, such as diet and individual genetic background.[2] The significant role that specific genes play in weight regulation through the action of their products on energy expenditure, substrate oxidation, appetite modulation, lipid metabolism, thermogenesis, and cell differentiation has been well described.[2,3]

In this context, the adrenergic is one of the most important system, acting on the energy balance regulation through brown adipose tissue thermogenesis and white adipose tissue lipolysis, both in humans and in other species.[4,5] Part of this system is found in the β3 receptor, located on chromosome 8p 11.23, expressed mainly in visceral and subcutaneous adipose tissue, acting as lipolysis mediator and, in brown adipose tissue, as thermogenesis regulator, with both functions performed in response to catecholamine stimulation.[6,7]

Changes in the functionality and amount of the expressed β3 receptors may permeate individual differences in energy expenditure in response to physical activities. Some of its variants associated with metabolic dysfunctions include the single nucleotide polymorphism (SNP) *Trp64Arg* (rs4994), which consists in the substitution of a thymine by a cytosine (T > C), resulting in the exchange of a tryptophan for an arginine at position 64 of the mature protein and corresponding to the first intracellular loop of the β3[8] receptor. *Arg64* allele carriers have shown to be more resistant to weight loss and decreased visceral fat,[9] in addition to being more likely to have lipid alterations, obesity, DM2,[7] and reduced rates of fat oxidation.[10]

Both the normal metabolic processes that culminate in fat oxidation and the metabolic changes related to the lipid profile are complex systems involving multiple pathways and interactions of exogenous (environmental) and endogenous factors.[11] Despite the underlying complexity of these processes, studies have sought to identify the small portion that can be attributed to allelic variants of genes whose products may influence the abovementioned physiological processes. Therefore, the present study aimed to verify