J Pediatr (Rio J). 2016;92(5):521–527

Jornal de Pediatria
www.jped.com.br

ORIGINAL ARTICLE

Lack of association between genetic polymorphism of *FTO*, *AKT1* and *AKTIP* in childhood overweight and obesity☆

Patrícia de Araújo Pereira[a,1], **António Marcos Alvim-Soares Jr.**[a,*,1], **Valéria Cristina Sandrim**[d], **Carla Márcia Moreira Lanna**[c], **Débora Cristine Souza-Costa**[b], **Vanessa de Almeida Belo**[b], **Jonas Jardim de Paula**[a], **José Eduardo Tanus-Santos**[b], **Marco Aurélio Romano-Silva**[a], **Débora Marques de Miranda**[a]

[a] *Universidade Federal de Minas Gerais (UFMG), INCT de Medicina Molecular, Belo Horizonte, MG, Brazil*
[b] *Universidade de São Paulo (USP), Faculdade de Medicina de Ribeirão Preto (FMRP), Departamento de Farmacologia, Ribeirão Preto, SP, Brazil*
[c] *Universidade Federal de Juiz de Fora (UFJF), Instituto de Ciências Biológicas, Departamento de Fisiologia, Juiz de Fora, MG, Brazil*
[d] *Universidade Estadual Paulista (UNESP), São Paulo, SP, Brazil*

Received 15 July 2015; accepted 15 December 2015
Available online 21 June 2016

KEYWORDS
Single-nucleotide polymorphisms;
Childhood obesity;
Fat mass and obesity associated;
Gene;
AKT1;
AKTIP

Abstract
Objective: Obesity is a chronic disease caused by both environmental and genetic factors. Epidemiological studies have documented that increased energy intake and sedentary lifestyle, as well as a genetic contribution, are forces behind the obesity epidemic. Knowledge about the interaction between genetic and environmental components can facilitate the choice of the most effective and specific measures for the prevention of obesity. The aim of this study was to assess the association between the *FTO*, *AKT1*, and *AKTIP* genes and childhood obesity and insulin resistance.
Methods: This was a case–control study in which SNPs in the *FTO* (rs99396096), *AKT1*, and *AKTIP* genes were genotyped in groups of controls and obese/overweight children. The study included 195 obese/overweight children and 153 control subjects.
Results: As expected, the obese/overweight group subjects had higher body mass index, higher fasting glucose, HOMA-IR index, total cholesterol, low-density lipoprotein, and triglycerides. However, no significant differences were observed in genes polymorphisms genotype or allele frequencies.

☆ Please cite this article as: Pereira PA, Alvim-Soares AM, Sandrim VC, Lanna CM, Souza-Costa DC, Belo VA, et al. Lack of association between genetic polymorphism of *FTO*, *AKT1* and *AKTIP* in childhood overweight and obesity. J Pediatr (Rio J). 2016;92:521–7.

* Corresponding author.
E-mail: antonioalvimjr@gmail.com (A.M. Alvim-Soares Jr.).

[1] Both Authors contributed equally to this paper.

http://dx.doi.org/10.1016/j.jped.2015.12.007

Conclusion: The present results suggest that *AKT1*, *FTO*, and *AKTIP* polymorphisms were not associated with obesity/overweight in Brazilians children. Future studies on the genetics of obesity in Brazilian children and their environment interactions are needed.

PALAVRAS-CHAVE
Polimorfismos de nucleotídeo único;
Obesidade infantil;
Massa de gordura obesidade associadas;
Gene;
AKT1;
AKTIP

Falta de associação entre o polimorfismo genético do *FTO*, *AKT1* e *AKTIP* e o sobrepeso e a obesidade infantis

Resumo
Objetivo: A obesidade é uma doença crônica sustentada por fatores ambientais e genéticos. Estudos epidemiológicos documentaram que maior ingestão de energia e um estilo de vida sedentário, bem como a contribuição genética, são forças por trás da epidemia de obesidade. O conhecimento sobre a interação entre os componentes genéticos e ambientais pode facilitar a escolha das medidas mais efetivas e específicas para a prevenção da obesidade. O objetivo deste estudo foi avaliar a relação entre os genes *FTO*, *AKT1* e *AKTIP* e a obesidade infantil e resistência à insulina.
Métodos: Estudo de caso-controle no qual SNPs nos genes *FTO* (rs99396096), *AKT1* e *AKTIP* foram genotipados em grupos de controle e de crianças obesas/acima do peso. Foram recrutadas 195 crianças obesas/acima do peso e 153 indivíduos controle.
Resultados: Como esperado, os indivíduos do grupo obeso/acima do peso apresentaram maior índice de massa corporal, maior glicemia de jejum, índice de HOMA-IR, colesterol total, lipoproteína de baixa densidade e triglicerídeos. Contudo, não encontramos diferenças significativas no genótipo de polimorfismos gênicos ou nas frequências alélicas.
Conclusão: Nossos resultados sugerem que os polimorfismos *AKT1*, *FTO* e *AKTIP* não estavam associados à obesidade/sobrepeso em crianças brasileiras. São necessários estudos futuros sobre a genética da obesidade em crianças brasileiras e suas interações ambientais.

Introduction

Childhood obesity is a public health problem worldwide. Over the past decades, rates of overweight and obesity among children have largely increased both in developed and developing countries.[1] Obesity is a result of environmental factors interacting with a polygenic background; the heritability ranges from 40% to 70%.[2] A recent meta-regression analysis showed that heritability was higher in children than in adults.[3] Long-term studies have shown that childhood obesity leads to clustering of metabolic syndrome (MetS) components,[4] which include abdominal obesity, dyslipidemia, insulin resistance, type II diabetes, and hypertension.[5] It is well known that overweight and obese children have a higher risk to become obese in adulthood.[6]

Genome-wide association studies (GWAS) identified the Fat mass and obesity associated gene (*FTO*) as associated with human adiposity.[7] The *FTO* gene is related to obesity risk, especially the single nucleotide polymorphism (SNP) rs9939609, which has been further confirmed by others independent studies in different human populations.[8–11] Due to the close relationship between diabetes and obesity, another interesting gene is the V-Akt murine thymoma viral oncogene homolog 1 (*AKT1*), which is thought to mediate many metabolic, mitogenic, and anti-apoptotic effects of insulin, IGF-1, and IL-3, and other growth factors and cytokines.[12–14] Moreover, Akt also stimulates glucose uptake and glycogen synthesis,[14] as well as protein synthesis.[15] Several studies correlate insulin resistance to impairments at Akt pathway and, in certain conditions, these alterations can be of genetic origin. *AKT1*-binding protein (*AKTIP* or Ft1), located near to *FTO* at the same GWAS risk locus for obesity at chromosome 16 (16q12.2),[16] appears to be another target for investigation. *AKTIP*, as a direct-ligand of AKT, modulates integration signaling pathways.[17]

Energy balance is influenced by a number of variables such as diet, social structures, metabolic factors, modern sedentary lifestyle, inexpensive energy-dense foods, and genetics. Probably, common obesity is the result of an adverse obesogenic environment and a susceptible genotype.[4] To date, evidence for the possible clinical benefits of genetic studies for common complex diseases has been limited. Furthermore, the search for genetic factors involved in obesity is a challenge, and can provide extra data to answer such a complex question. Through these observations, this study aimed to investigate the statistical association of polymorphisms in the *FTO*, *AKT1*, and *AKTIP* genes with childhood obesity in Brazilian children.