

## Abstract

**Background:** The 2-adrenergic receptor (ADRB2) plays a major role in regulating energy expenditure by stimulating lipid metabolism in human adipose tissue. Polymorphisms in the ADRB2 gene have been associated with obesity and various weight-related traits in cross-sectional studies of adults, but little is known about the effects of the ADRB2 gene on childhood obesity or the propensity to gain weight over time.

**Objective:** To assess the effects of a polymorphism in codon 16 (Arg16Gly) of the ADRB2 gene, which has been associated with a decrease in 2-receptor density and efficiency, on longitudinal changes in obesity from childhood to young adulthood in a biracial cohort.

**Design:** Seven cross-sectional screenings of children and five cross-sectional screenings of young adults who were previously examined as children produced longitudinal data from childhood to young adulthood.

**Methods:** Height, weight and subscapular and triceps skinfolds were measured by trained examiners following identical protocols over the course of the study. Gender- and age-stratified analyses using random coefficients models were used to examine longitudinal genetic effects on obesity in 1151 African-American and Caucasian males and females who attended an average of six examinations over a 24 y period from childhood to young adulthood.

**Results:** Age-stratified analyses showed no clear genetic relationships with changes in obesity measures over time in females, but an age-dependent association was observed in males, where the relationship between the Arg16Gly polymorphism and obesity became stronger with age. In males who were 4-9 y of age at the beginning of the study in 1973, body mass index (BMI) was 4% higher in Gly/Gly and Arg/Gly males compared to those with Arg/Arg by 26 y of age. Subscapular skinfold measurements in Gly/Gly males became significantly different from Arg/Arg males (20% higher) by age 20. In the oldest male cohort (10-14 y of age in 1973), BMI increased at a significantly greater rate (0.4%/y) in males carrying the Gly16 form of the receptor relative to Arg/Arg males. BMI was significantly different between homozygous genotypes by approximately 26 y of age, and reached 8% higher in Gly/Gly males by age 32. Subscapular skinfolds also increased at a significantly greater rate (2%/y) in Gly/Gly males compared to Arg/Arg males, becoming significantly different (27%) by approximately 22 y of age and reaching a maximum difference of 50% by age 32.

**Conclusions:** Our data suggest that the 2-adrenergic receptor is associated with the propensity to gain weight from childhood to young adulthood in males. An increased understanding of genetic influences on the development of obesity may improve the effectiveness of interventions designed to reduce excess body weight and help define the role of genetic factors in diabetes and cardiovascular disease.

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