J Clin Endocrin Metab. First published ahead of print May 5, 2010 as doi:10.1210/jc.2010-0018

Ethnic Differences in Insulin Action in Obese African-American and Latino Adolescents

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Introduction: African-American children have a greater acute insulin response to iv glucose (AIR) compared with Latino children despite a similar degree of insulin resistance and body composition. It is unclear whether African-Americans demonstrate an exaggerated insulin response to an oral glucose challenge and whether any differences are seen in more obese children in advanced pubertal development.

Purpose: Our objective was to compare glucose and insulin indices derived from an oral glucose tolerance test (OGTT) and iv glucose tolerance test (IVGTT) in sedentary, obese African-American ($n = 59$) and Latino ($n = 83$) adolescents.

Methods: Glucose and insulin incremental area under the curve was measured during an OGTT, and AIR, insulin sensitivity, disposition index, and glucose effectiveness were assessed during an IVGTT. Body composition was assessed via dual-energy x-ray absorptiometry and magnetic resonance imaging.

Results: From the OGTT, glucose and insulin IAUC were 29.1 and 22.5% lower ($P = 0.01$) in African-Americans compared with Latino adolescents. From the IVGTT, insulin sensitivity and glucose effectiveness were 41.7% ($P < 0.01$) and 50.0% ($P = 0.02$) lower in African-Americans compared to Latinos. AIR ($P = 0.001$) and disposition index ($P = 0.02$) were 63.0 and 48.8% higher in African-Americans, respectively, compared with Latinos. These findings persisted after controlling for body composition and fat distribution.

Conclusions: There were marked differences in glucose and insulin indices derived from the OGTT and IVGTT. African-Americans were more insulin resistant as measured by the IVGTT compared with the Latino adolescents. However, the well-described hyperinsulinemia in response to iv glucose was not observed after oral glucose in African-American adolescents. ***(J Clin Endocrinol Metab* 95: 0000–0000, 2010)**

Our laboratory has previously demonstrated that at the same degree of insulin resistance, the metabolic compensation is markedly different between African-American and Latino children, with African-Americans having profound hyperinsulinemia in response to an iv glucose challenge, partly explained by lower insulin clearance in the liver (1). Latinos on the other hand have a more subdued increase in insulin concentrations due to an increase in second-phase insulin secretion (1). Despite our previous findings based on iv glucose administration, it is unclear whether African-Americans demonstrate an exaggerated insulin response during an oral glucose challenge, a condition that resembles real-world physiological conditions. In addition, we were also interested in exam-

ISSN Print 0021-972X ISSN Online 1945-7197
Printed in U.S.A.

doi: 10.1210/jc.2010-0018 Received January 5, 2010. Accepted April 12, 2010.

Abbreviations: AIR, Acute insulin response; BMI, body mass index; CTU, Clinical Trials Unit; DI, disposition index; HOMA, homeostasis model assessment; IAUC, incremental area under the curve; IVGTT, iv glucose tolerance test; OGTT, oral glucose tolerance test; Sg, glucose effectiveness; SI, insulin sensitivity.

ining whether our previous findings (1) for insulin sensitivity (SI), acute insulin response (AIR), and disposition index (DI) in younger, normal-weight African-American and Latino children (Tanner stages I–III) are similar in a more severely obese adolescent population. Therefore, the primary aim of this study was to compare glucose and insulin indices measured during an oral glucose tolerance test (OGTT) and insulin-modified iv glucose tolerance test (IVGTT) in obese African-American and Latino adolescents at the latter stages of pubertal development (Tanner stages IV and V). We hypothesized that the degree of insulin resistance would be similar between ethnic groups; however, AIR would be significantly higher in African-Americans.

Participants and Methods

Participants

All participants met the following inclusion criteria: age- and gender-specific body mass index (BMI) 85th percentile or above but otherwise healthy, African-American or Latino ethnicity (self-report and based on all four grandparents being of the same ethnic group as the child in the study), and attending grades 9–12 (approximately 14–18 yr of age).

During the outpatient visit, participants arrived at the Clinical Trials Unit (CTU) at approximately 0730 h after an overnight fast. A detailed medical history was obtained, and a physical examination was performed by a licensed pediatric healthcare provider. Total body composition was assessed by dual-energy x-ray absorptiometry and magnetic resonance imaging. Glucose and insulin incremental area under the curve (IAUC) were measured during a 3-h OGTT. Approximately 7–14 d after the outpatient visit, participants were admitted to the CTU in the evening hours and completed an IVGTT (2) the following morning.

A detailed description of the methods and protocol used in this study have been previously reported (3).

Statistical analyses

Before analysis, data were evaluated for normality, and natural log transformations were made to the following variables: weight, BMI, sc adiposity, visceral adiposity, fasting glucose, fasting insulin, insulin IAUC, homeostasis model assessment (HOMA), SI, AIR, DI, and glucose effectiveness (Sg). Ethnic differences in physical characteristics were tested using independent-sample *t* tests. Ethnic differences in glucose and insulin indices as well as body composition were tested using analysis of covariance after controlling for preplanned covariates: age, Tanner stage, total fat mass, and total lean tissue mass. For AIR, SI was also included as a covariate. Linear regression was used to assess ethnic differences in the relationship between fat depots (total fat mass, visceral fat, and sc fat) and insulin sensitivity. All analyses were performed using SPSS version 16.0 (Chicago, IL) and PRISM version 5.0a (La Jolla, CA), with significance level set at $\alpha < 0.05$.

Results

There were no significant differences in age between ethnic groups (15.4 ± 0.2 *vs.* 15.4 ± 0.1 yr, $P = 0.99$); however, the African-American cohort had a larger percentage of participants in Tanner stage V compared with the Latino cohort (87 *vs.* 65%, respectively). There was also a higher percentage of females in the African-American compared with Latino cohort (77 *vs.* 66%, respectively). Body composition and body fat distribution also varied by ethnicity with African-Americans having significantly higher body weight (101.5 ± 3.6 *vs.* 90.1 ± 2.4 kg, $P < 0.01$) and fat-free mass (56.0 ± 1.2 *vs.* 50.8 ± 1.3 kg, $P < 0.01$) compared with Latinos. BMI, BMI percentile, and BMI Z-score also tended to be higher in African-Americans compared with Latinos. For body fat distribution, African-American adolescents had significantly higher volumes of sc adipose tissue (15.4 ± 0.9 *vs.* 9.2 ± 0.5 liters, $P < 0.01$) and tended to have lower visceral adipose tissue (1.3 ± 0.1 *vs.* 1.6 ± 0.1 l, $P = 0.08$) compared with Latino adolescents. However, there were no significant differences in fat mass or percentage body fat between ethnic groups.

The adjusted means for glucose and insulin indices from the OGTT are presented in Table 1. Fasting glucose concentrations were similar between African-American and Latino adolescents ($P = 0.26$). However, fasting in-

TABLE 1. Glucose and insulin parameters for African-American and Latino adolescents

	African-Americans	Latinos	*P* value
OGTT			
Fasting glucose (mg/dl)	89.2 ± 1.2	92.1 ± 0.9	0.26
Fasting insulin (μIU/ml)	21.3 ± 1.8	27.9 ± 1.4	<0.01
HOMA	4.8 ± 0.4	6.3 ± 0.4	<0.01
Glucose IAUC (nmol/liter · min)	77.7 ± 6.9	100.3 ± 5.4	0.01
Insulin IAUC (nmol/liter · min)	328.2 ± 35.6	401.9 ± 29.5	0.07
IVGTT			
Insulin sensitivity ($\times 10^4$ $min^{-1}/\mu U \cdot ml$)	1.2 ± 0.1	1.7 ± 0.1	<0.01
AIR (μU/ml × 10 min)	2263 ± 141.9	1380 ± 109.0	<0.01
DI from AIR ($\times min^{-1}$)	2493 ± 160.7	1675 ± 124.6	0.02
Glucose effectiveness (%/min)	0.02 ± 0.003	0.03 ± 0.003	0.02

Data are mean ± SE. Significant was set at $P < 0.05$. *P* values were calculated using ANOVA. Although adjusted means are reported here for all variables, analyses were based on log scores for fasting glucose, fasting insulin, insulin IAUC, HOMA, insulin sensitivity, AIR, DI, and Sg. Conversions are calculated as follows: 1 mM = 18 mg/dl, and 1 μU/ml = 6 pM.

sulin and HOMA values were 30.0% lower in African-American compared with Latino adolescents ($P < 0.01$). In addition, glucose IAUC was 29.1% lower ($P = 0.01$) and insulin IAUC was 22.5% lower ($P = 0.08$) in African-American compared with Latino adolescents.

The values for the key variables associated with insulin action from the IVGTT are shown in Table 1. After controlling for ethnic differences in total fat mass, lean mass, pubertal stage, and sex, SI was 41.7% lower in African-American adolescents compared with Latino adolescents ($P < 0.01$; see Fig. 1). Figure 1A shows the relationship between SI and fat mass in the two ethnic groups, which shows similar slopes ($P = 0.75$) but a significantly lower intercept in the obese African-American adolescents ($P = 0.02$). Additionally, there were no significant differences in the slopes for the relationship between SI and visceral adiposity ($P = 0.85$; Fig. 1B), but again, the intercept was significantly lower in African-American adolescents ($P < 0.01$; Fig. 1B). For the relationship between SI and sc adiposity, the slope was significantly different ($P = 0.03$; Fig. 1C), with Latinos demonstrating a larger decline in SI with similar increases in sc fat compared with African-American adolescents.

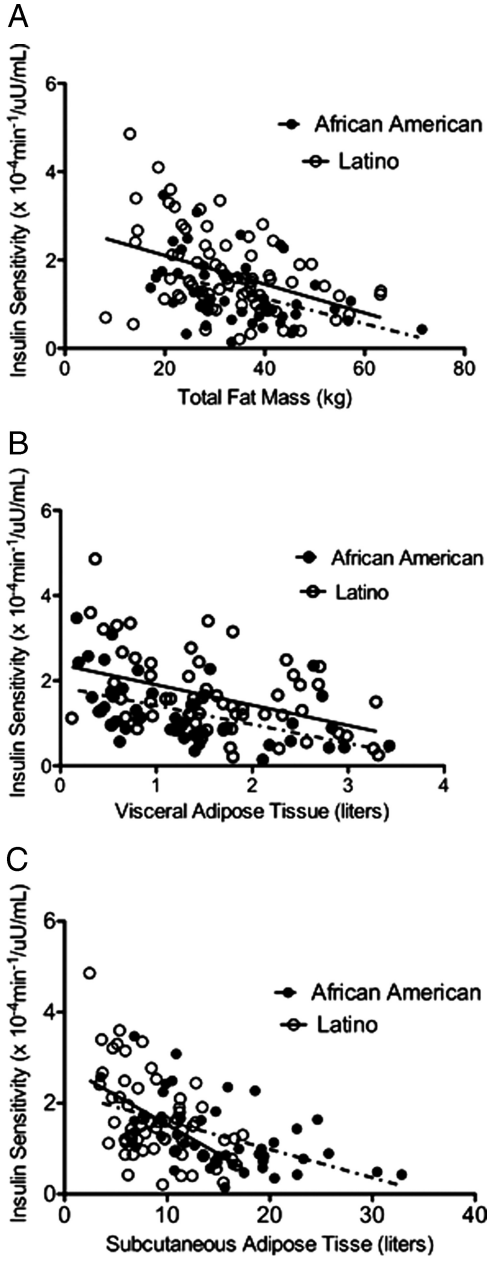

FIG. 1. Relationship between SI and total fat mass (A), visceral fat mass (B), and sc fat mass (C). *Dotted* and *solid lines* represent trendlines for African-Americans and Latinos, respectively. Sample size for African-American (n = 47) and Latino (n = 66).

After controlling for ethnic differences in SI, AIR was 63% higher in the African-American compared with Latino adolescents, even after controlling for ethnic differences in SI ($P = 0.001$). As a result, DI was 48.8% greater in the African-American compared with Latino adolescents ($P = 0.02$). Specifically the trendline slopes for the relationship between SI and AIR was significantly different between African-American and Latino adolescents ($P = 0.003$). Furthermore, Sg was 50.0% lower in African-American adolescents compared with Latino adolescents ($P = 0.02$; Table 1).

Discussion

Previous research from our laboratory and others (1, 4) has reported a distinctly elevated AIR in African-Americans compared with Latino and non-Latino whites. Based on these findings, we had concluded that this higher AIR from iv glucose is a mechanism by which chronic hyperinsulinemia or increased daily cellular exposure to insulin contributes to the increased risk for obesity-related disease outcomes in African-Americans. However, now that we see the tendency for lower insulin concentrations after oral glucose (a condition that more likely resembles real-world physiological conditions during feeding), it is necessary that we revisit the question of underlying mechanisms that contribute to metabolic diseases in African-Americans.

In the present study, the African-American participants were significantly more insulin resistant compared with their Latino counterparts as measured by IVGTT, even after controlling for differences in fat mass and visceral adipose tissue. Hence, the lower SI in African-Americans was not explained by ethnic differences in total fat mass or visceral adiposity. However, the relationship between sc fat and SI was significantly different between African-American and Latino adolescents. Specifically, there was a significant difference in the trendline slopes, with African-Americans demonstrating a smaller decline in SI with similar increases in sc fat compared with Latino adolescents. Hence, the greater insulin resistance in African-

Americans compared with Latinos appears to be related to the greater amount of sc fat in this ethnic group.

Pancreatic β-cells have the ability to increase insulin secretion in response to insulin resistance. This nonlinear hyperbolic relationship between sensitivity and secretion is best described as DI (2). In the present study, insulin secretion (derived from AIR) was significantly higher in African-American compared with Latino adolescents. In essence, the rise in AIR per unit decrease in SI was significantly higher in African-Americans compared with Latinos. Hence, the compensatory increase in AIR in the African-American cohort in the presence of decreased SI likely exacerbated the already increased hyperinsulinemia in the African-American cohort during the IVGTT. Therefore, the African-American adolescents demonstrated greater β-cell function compared with Latino adolescents that likely contributed to the increased glucose tolerance in African-Americans as measured by the OGTT.

To our knowledge, this is the first study to report ethnic differences in Sg between African-American and Latino adolescents. Sg is described as the ability of glucose to enhance its own uptake into skeletal muscle independent of plasma insulin concentrations (5). Hence, if African-American adolescents have lower Sg, this may put an extra burden on the pancreas to increase insulin production to maintain normal glucose levels in the blood. In contrast, the higher Sg values reported in Latino adolescents may represent a compensatory response for the insulin resistance and greater visceral fat reported in this ethnic group. The mechanisms that contribute to changes in Sg in African-Americans and Latinos are unknown; however, it is clear that changes in this parameter are evident early in life and play a role in the progression toward type 2 diabetes.

In summary, our IVGTT data suggest that African-American adolescents are more insulin resistant compared with Latino adolescents, and this difference is independent of total fat mass as well as visceral fat. As a result of this decreased SI, African-American adolescents had a compensatory higher AIR, which further exacerbated their inherently higher AIR responses to glucose. Additionally, β-cell function (as reflected by a greater DI) was enhanced in African-American compared with Latino adolescents. In fact, the decreased glucose IAUC reported in this group may represent an overcompensation of the pancreas to maintain glucose tolerance and slow the progression toward type 2 diabetes. However, the well-described acute hyperinsulinemia in response to iv glucose was not observed after oral glucose ingestion in African-American adolescents. Further research should continue to explore the underlying mechanisms of hyperinsulinemia reported in African-Americans.

Acknowledgments

We thank the Strength and Nutrition Outcomes for Latino Adolescents and Strength Training and Nutrition Development in African-American Youth team as well as the nursing staff at the CTU. In addition, we are grateful for our study participants and their families for their involvement.

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This work was supported by the University of Southern California Transdisciplinary Research on Energetics and Cancer (U54 CA 116848), the National Institute of Child Health and Human Development (RO1 HD/HL 33064), the Dr. Robert C. and Veronica Atkins Foundation, and the National Cancer Institute (T32 CA 09492). C.K.R. was supported during this project by a National Institute on Aging Training Award (5 T32 AG000093-24).

Disclosure Summary: The authors have nothing to disclose.

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