

Racial Differences in Insulin Secretion and Sensitivity in Prepubertal Children: Role of Physical Fitness and Physical Activity

Ching-Yi Ku, Barbara A. Gower, Gary R. Hunter, and Michael I. Goran*

Abstract

KU, CHING-YI, BARBARA A. GOWER, GARY R. HUNTER, AND MICHAEL I. GORAN. Racial differences in insulin secretion and sensitivity in prepubertal children: Role of physical fitness and physical activity. *Obes Res.* 2000;8:506–515.

Objective: To investigate in prepubertal children whether physical fitness and/or physical activity are: 1) associated with insulin secretion and sensitivity and 2) account for racial differences in insulin secretion and sensitivity.

Research Methods and Procedures: Subjects included 34 African American and 34 white nondiabetic children aged 5 to 11 years. Data were divided into two sets according to the availability of VO_{2max} and physical activity data. Body composition was measured by dual-energy X-ray absorptiometry. Subcutaneous abdominal adipose tissue and intra-abdominal adipose tissue were examined by computed tomography. Insulin sensitivity (S_I) and acute insulin response (AIR) were determined by a frequently sampled intravenous glucose tolerance test. An all-out, progressive treadmill exercise test was used for measuring VO_{2max} . Physical activity data were collected by questionnaire.

Results: African American children had lower S_I and higher AIR than white children, after adjusting for total body fat mass. African Americans reported higher levels of physical activity (hours/wk) than whites, but had a lower VO_{2max} . In multiple linear regression analysis, hours/wk of activity and hours/wk of vigorous activity, but not moderate activity, were independently related to S_I and AIR after adjusting for

race, total body fat mass or fat distribution, and total lean tissue mass. VO_{2max} was not related to AIR, and was inversely related to S_I , after adjusting for body composition. Race remained significantly associated with both S_I and AIR, even after adjusting for body composition, fat distribution, and hours/wk of activity or hours/wk of vigorous activity.

Discussion: In summary, overall physical activity and, especially, vigorous activity were associated with insulin secretion and sensitivity. However, neither physical activity nor VO_{2max} explained the racial difference in insulin secretion (higher in African Americans) and sensitivity (lower in African Americans). Thus, racial (African American to white) differences in aspects of insulin action seem to be due to factors other than body composition, fat distribution, cardiovascular fitness, and amount of physical activity.

Key words: race, African American, exercise, insulin

Introduction

Previous studies in adults have shown that African Americans have a higher fasting insulin concentration and a lower insulin sensitivity than whites (1–4). These racial differences have also been noted in children and adolescents (5–9), although not in all studies (10). Thus, the greater prevalence of type 2 diabetes among African Americans vs. whites may be due to racial differences in insulin secretion and action.

Physical activity may be a determinant of type 2 diabetes through its relationships with adiposity, insulin sensitivity, glucose metabolism, and muscle mass and morphology (11,12). In adults, physical activity is inversely associated with insulin concentration and development of type 2 diabetes and positively related to insulin sensitivity and insulin clearance (13–17). In prepubertal children, information regarding the role of physical fitness and physical activity in insulin secretion and sensitivity is limited. However, an inverse relationship between maximal oxygen consumption (VO_{2max}) and fasting insulin concentration has been re-

Submitted for publication February 13, 1999.

Accepted for publication in final form March 29, 2000.

Division of Physiology and Metabolism, Department of Nutrition Sciences, and Clinical Nutrition Research Center, University of Alabama at Birmingham, Birmingham, Alabama.

*Current address: Institute for Prevention Research, Department of Preventive Medicine, 1540 Alcazar St., Rm. 208-D, University of Southern California, Los Angeles, CA 90033. Address correspondence to Barbara A. Gower, Ph.D., Division of Physiology and Metabolism, Department of Nutrition Sciences, University of Alabama at Birmingham, Birmingham, AL 35294-3360. E-mail: bgower@uab.edu

Copyright © 2000 NAASO

ported in children (18), suggesting that the relationship between physical activity and insulin action develops early in life.

Few studies have attempted to examine whether racial differences in aspects of insulin action are associated with differences in physical activity, particularly in children. African American children are reported to have lower VO_{2max} (5,19) and a lower level of physical activity (20) than white children. Therefore, the role of physical fitness and physical activity in racial differences in insulin secretion and action warrants investigation. Arslanian et al. (5) showed that physical fitness, determined by VO_{2max} , might account for the racial difference between African American children and white children in insulin secretion. In their study, the racial difference in first-phase insulin secretion during a hyperglycemic clamp was eliminated after adjusting for VO_{2max} , gender, and insulin-like growth factor I. However, the contribution of VO_{2max} alone to the variance in insulin secretion was not given. Additionally, data on habitual activity were not available to examine activity patterns that might contribute to racial differences in VO_{2max} . In the study by Arslanian et al., insulin sensitivity did not differ with race, and the relationship between VO_{2max} and insulin sensitivity was not reported. Thus, questions remain regarding the importance of physical fitness and physical activity in aspects of insulin action in children and with respect to racial differences in insulin action.

Therefore, the purpose of this study was to investigate in prepubertal children whether physical fitness and/or physical activity were: 1) associated with insulin secretion and sensitivity and 2) accounted for the racial differences in insulin secretion and sensitivity previously observed in this subject population (8,9).

Research Methods and Procedures

Subjects

Subjects in this study were 34 African American ($n = 17$ boys, $n = 17$ girls) and 34 white ($n = 16$ boys, $n = 18$ girls) children. Race was defined by self-report. Children from 5 to 11 years of age were recruited through advertisements in newspapers, radio, bulletin boards, and word of mouth in the Birmingham, Alabama metropolitan area. Tanner stage was assessed by a pediatrician (breast and pubic hair development for girls; testicular enlargement for boys). Children at Tanner stage 2 or higher were excluded from our study. To further evaluate maturation in the resultant cohort, serum levels of dehydroepiandrosterone sulfate (DHEAS), estradiol, and testosterone were measured. All but one subject had undetectable levels of estradiol (<15.42 pM); the single measured value was 41.8 pM (testosterone was not detectable in this subject, a white female). Likewise, most subjects had undetectable levels of testosterone (<0.41 nM); when

detectable (8 cases), levels of testosterone ranged from 0.42 to 1.29 nM, suggesting a minimal degree of maturation (below Stage 2) (21). The children with measurable testosterone were two African American males, two African American females, three white males, and one white female. Children were healthy and free from any major diseases, syndromes, or disabilities. Exclusion criteria were medications known to affect body composition or physical activity, or having previously been diagnosed with syndromes affecting body composition or fat distribution (eg, Cushing's syndrome, Downs' syndrome, type 1 diabetes, or hypothyroidism). The study was approved by the Institutional Review Board at the University of Alabama at Birmingham (UAB), and parents were asked to give informed consent before testing commenced.

Protocol

All required measurements were obtained during one overnight visit to the General Clinical Research Center (GCRC) and one out-patient visit to the Department of Nutrition Sciences at UAB. Children were admitted to the GCRC in the late afternoon. On arrival, anthropometric measurements were obtained. Subcutaneous abdominal adipose tissue (SAAT) and intra-abdominal adipose tissue (IAAT) were examined by computed tomography (CT). Dinner was served at approximately 5:00 PM. An evening snack was allowed, and after 8:00 PM, only water and energy-free, noncaffeinated beverages were permitted until after the morning testing. The following morning, blood samples were collected for the frequently sampled intravenous glucose tolerance test (FSIGT) in the fasted state. Physical activity information was collected by self-report of children's parents or by interviewing the children and parents during the inpatient visit using a structured questionnaire. Two weeks later, the children arrived at the Department of Nutrition Sciences at 7:00 AM in the fasted state. VO_{2max} was determined by an all-out, progressive, continuous treadmill test appropriate for children (25), and body composition was measured by dual-energy X-ray absorptiometry (DXA).

Body Composition and Anthropometry

Body composition (total body fat mass and non-bone lean tissue mass) was measured by DXA using a Lunar DPX-L densitometer (Lunar Radiation Corp., Madison, WI). We have previously validated the use of DXA against carcass analysis in a pig model that encompassed the pediatric weight range (22). Subjects were scanned in light clothing, while lying flat on their backs with arms at their sides. DXA scans were performed and analyzed with pediatric software version 1.5e.

Each child was measured for height without shoes using a stadiometer. Weight was measured while they wore light clothing on an electronic scale.

Body Fat Distribution

SAAT and IAAT were measured by CT scanning with a HiLight/Advantage Scanner (General Electric, Milwaukee,

WI), as previously described (23). A single-slice scan (5 mm) of the abdomen was performed at the level of the umbilicus and analyzed for cross-sectional area of adipose tissue using a density contour program (Hounsfield units for adipose tissue set at -190 to -30). CT data were presented as a cross-sectional area of tissue (cm^2). We have shown the test-retest reliability for IAAT to be 1.7% (24). All scans were analyzed by the same person. The total body radiation dose to each subject was approximately 0.26 rad. This total body radiation dose is less than that received from a standard chest X-ray.

Insulin Sensitivity Testing

Insulin sensitivity (S_I) was determined with the tolbutamide-modified FSIGT (25,26). The FSIGT involved intravenous administration of glucose (11.4 g/m^2) at time (t) = 0 minutes followed in 20 minutes by administration of tolbutamide (125 mg/m^2). Blood samples (2.0 mL) were collected at $t = -20, -15, -5, -1, 2, 3, 4, 5, 6, 8, 10, 14, 19, 22, 25, 30, 40, 50, 70, 100, 140,$ and 180 minutes (relative to glucose administration). Sera were subsequently analyzed for glucose and insulin concentrations. Calculation of S_I was done with a mathematical model that uses serum insulin and glucose values from the FSIGT (25,26) as input. Acute insulin response (AIR), based on the area above baseline insulin concentration, was calculated by trapezoidal method during 0 to 10 minutes (27). Fasting insulin was taken as the average of baseline values. S_I reflects the increase in fractional glucose disappearance per unit of insulin increase, where disappearance can result from either an increase in peripheral glucose uptake or a decrease in hepatic glucose production. AIR reflects first-phase insulin secretion.

Assay of Glucose and Hormones

Glucose was measured in 10 μL sera using an Ektachem DT II system (Johnson and Johnson Clinical Diagnostics). In our laboratory, this analysis has a mean intra-assay coefficient of variation (CV) of 0.61% and a mean interassay CV of 1.45%. Insulin was assayed with Diagnostic Products Corp. (Los Angeles, CA) "Coat-A-Count" kits. According to the supplier, cross-reactivity of this assay with proinsulin is approximately 40% at midcurve; C-peptide was not detected. In our laboratory, this assay has a sensitivity of 11.4 pM, a mean intra-assay CV of 5%, and a mean interassay CV of 6%. Commercial quality control sera of low, medium, and high insulin concentration ("Lyphochek"; Bio-Rad, Anaheim, CA) were included in every assay to monitor variation over time. DHEAS was measured with a coated-tube radioimmunoassay (RIA) (Diagnostic Systems Laboratories, Webster, TX). In our laboratory, this assay can detect 2.3 $\mu\text{g/dL}$ and has a mean intra-assay CV of 11.7% and a mean interassay CV of 7.2%. Estradiol was measured by double-antibody RIA, and testosterone was measured by

coated-tube RIA (both from Diagnostic Products Corp.). In our laboratory, these assays could detect 15.42 pM estradiol and 0.41 nM testosterone. Intra- and interassay CVs for estradiol were 3.6% and 5.2%, respectively, and for testosterone were 2.7% and 8.6%, respectively. Insulin-like growth factor-1 (IGF-1) was measured using an immunoradiometric assay (Diagnostic Systems Laboratories; intra-assay CV was 3.71%, inter-assay CV was 7.34%).

Exercise Testing

Exercise testing was conducted in the fasted state during the outpatient visit, and started at 7:00 AM. Subjects practiced walking on the motorized treadmill to become familiar with the testing equipment, which included mouthpiece and head gear. Thereafter, children performed an all-out, progressive, continuous treadmill test appropriate for children (28). Carbon dioxide, oxygen, and heart rate were recorded continuously during the test. CO_2 and O_2 were measured by open circuit spirometer and analyzed using a metabolic cart (Model 2900; SensorMedics Corp., Yorba Linda, CA), which was calibrated before the testing. Heart rate was monitored by a Polar Vantage XL heart rate monitor (Model 61204).

Subjects walked for 4 minutes at the initial level of 0% grade and speed of 4 km/h. Submaximal oxygen consumption and submaximal heart rate were measured while children were walking at the initial grade (0%). After finishing the first level, the speed remained constant but the grade was increased to 10% for 2 minutes, and then increased by 2.5% increments at subsequent 2-minute intervals. Speed remained constant until 20% grade was reached, at which time it was increased by 0.83 km/h at 2-minute intervals until subjects reached exhaustion.

Three criteria were used to determine whether a successful maximal test had been performed: a leveling or plateauing of oxygen consumption, defined as an increase in $\text{VO}_{2\text{max}}$ of less than 2 mL of O_2/kg of body weight/min; heart rate greater than 195 beats/min; and respiratory exchange ratio (CO_2 produced/ O_2 consumed) greater than 1.0. $\text{VO}_{2\text{max}}$ was defined by attainment of two of the three criteria. Only data from children who successfully attained $\text{VO}_{2\text{max}}$ were used. Data from 21 children were eliminated due to lack of attainment of $\text{VO}_{2\text{max}}$; four children were unable to perform the test due to illness.

Physical Activity by Questionnaire

Information on physical activity in the subjects was collected by a modification of the questionnaire of Kriska et al. (29), which was designed to investigate the relationship between physical activity and type 2 diabetes in Pima Indians. The original questionnaire was modified by deleting those activities that were not appropriate for our sample of children (e.g., hiking through the mountains and rodeo) and adding activities in which our group of children did partic-

ipate (e.g., cheerleading and boxing). For each specific activity listed in the questionnaire, month per year, times per week, and hours or minutes per time were collected. For statistical analysis, physical activity was expressed as hours per week.

The intensity of each physical activity on the questionnaire was obtained from existing tables (30) and expressed as metabolic equivalent values (METs). One MET is equal to 0.0165 kcal/kg/min. All the activities in our questionnaire had MET values above or equal to 3.0. Vigorous activity was defined as the sum of hours/wk of activities greater than or equal to a MET value of 6.0. Moderate activity was defined as the sum of hours/wk of activities below a MET value of 6.0.

Questionnaires that were incomplete or that contained ambiguous data were not used.

Statistical Analysis

All data were analyzed with SAS software version 6.10 (SAS Institute Inc., Cary, NC). Statistical significance was defined as p values of <0.05 . Because not all children completed both the treadmill test and the physical activity questionnaire, data were divided into two data sets on the basis of the availability of VO_{2max} or physical activity data. All statistical analyses were performed separately in the two data sets.

Differences in demographic characteristics, body fat indices, insulin parameters, VO_{2max} , and physical activity were examined by two-way ANOVA with gender by race as the grouping variables. Analysis of covariance (ANCOVA) also was performed to examine gender or racial differences in S_1 and AIR using total body fat as the covariate. Insulin parameters and body composition indices were log-transformed to attain normal distribution. Body weight, SAAT, hours/wk, and VO_{2max} were not normally distributed after log transformation; thus a nonparametric test (Wilcoxon scores [rank sums]) was used to examine between-group differences (gender and race). Multiple linear regression analysis was used to examine the relationships between the dependent variables S_1 and AIR, and various independent variables. The independent variables in the regression models were race, either total body fat mass or central fat (IAAT and SAAT), lean tissue mass, and either VO_{2max} or physical activity. The selection of body fat index or indices for use as adjusting variables in the regression models was based on the model square of multiple correlation coefficient (R^2); the body fat index (or indices) resulting in a model that explained the largest amount of variance in a dependent variable was selected. Because S_1 is a significant determinant of pancreatic responsiveness (31), additional analyses were performed for the dependent variable AIR, including S_1 as an independent variable.

Results

Twenty-seven African Americans ($n = 12$ boys, $n = 15$ girls) and 25 whites ($n = 14$ boys, $n = 11$ girls) were in the

dataset with questionnaire data. In the dataset with VO_{2max} measurements, there were 19 African Americans ($n = 9$ boys, $n = 10$ girls) and 24 whites ($n = 13$ boys, $n = 11$ girls). Data from 27 children, which included 12 African Americans ($n = 4$ boys, $n = 8$ girls) and 15 whites ($n = 11$ boys, $n = 4$ girls), were in both datasets.

Analysis of Physical Activity Data

When analyzed by ANOVA, age, body weight, total fat, lean tissue mass, and serum DHEAS were not different between African Americans and whites; serum IGF-1 was greater in African Americans (Table 1A). AIR was higher in African American children, but S_1 did not differ (Table 1B). After adjusting S_1 and AIR for total body fat mass with ANCOVA, S_1 was lower ($p = 0.01$) and AIR was higher ($p < 0.001$) among African Americans. Boys were more active than girls, and African Americans were more active than whites in our sample.

Multiple linear regression analysis was used to examine the influence of physical activity, race, and body composition on S_1 and AIR. Gender did not emerge as significant in any model, and therefore was removed from the analyses. Physical activity was positively related to S_1 and negatively related to AIR (Table 2). These relationships were independent of race, total body fat mass, and lean tissue mass. Substitution of SAAT or IAAT for total body fat did not explain any additional variance in S_1 or AIR. Race remained significantly related to S_1 (lower in African Americans) and AIR (higher in African Americans) after adjusting for total body fat mass, lean tissue mass, and hours/wk of physical activity.

With regard to the intensity of physical activity, hours/wk of vigorous activity was positively associated with S_1 and negatively associated with AIR (Table 3). These relationships were independent of race, total body fat mass, and lean tissue mass. Replacing total body fat mass with SAAT or IAAT in the regression models did not explain any additional variance in S_1 or AIR. Race independently explained a portion of the variance in S_1 and AIR after adjusting for total body fat mass, lean tissue mass, and hours/wk of vigorous activity. Moderate activity was not independently associated with any insulin variable.

Inclusion of IGF-1 in the models did not alter the results. In all cases, IGF-1 did not make an independent contribution (p values of 0.59 to 0.88), and race remained significant (same p value as original model; data not shown). Inclusion of S_1 in the models for AIR eliminated the independent relationship of AIR with physical activity ($p = 0.319$ for hours/wk, and $p = 0.181$ for hours/wk of vigorous activity; data not shown).

Analysis of VO_{2max} Data

For the subjects included in the VO_{2max} analysis, there were no gender or racial differences in age, body weight, lean tissue mass, or serum DHEAS; serum IGF-1 was

Table 1. Subgroup with questionnaire data

A) Descriptive data, mean ± SD (range)	Whites			
	African Americans		Whites	
	Boys (n = 12)	Girls (n = 15)	Boys (n = 14)	Girls (n = 11)
Age (years)	8.9 ± 1.2 (7.2–10.9)	8.7 ± 1.9 (5.7–11.0)	9.2 ± 1.6 (6.6–11.8)	9.2 ± 1.2 (7.2–11.0)
Body weight (kg)	43.0 ± 16.2 (26.4–72.5)	34.9 ± 13.7 (22.0–65.0)	35.9 ± 9.4 (22.1–54.4)	40.01 ± 15.4 (24.7–77.9)
Total body fat mass (kg)	10.6 ± 8.8 (2.0–28.6)	10.2 ± 8.2 (1.9–28.0)	8.8 ± 6.8 (2.0–23.6)	13.7 ± 8.6 (4.7–33.8)
BMI (kg/m ²)	22 ± 6 (17–35)	19 ± 5 (14–31)	20 ± 4 (14–28)	21 ± 5 (16–31)
SAAT (cm ²)	90.2 ± 87.3 (9.9–270.0)	109.7 ± 120.3 (8.8–436.1)	90.2 ± 93.5 (19.5–287.8)	154.4 ± 114.6 (36.6–414.9)
IAAT (cm ²)	40.8 ± 25.8 (13.9–111.0)	27.0 ± 19.3 (9.4–76.1)	40.8 ± 21.3 (14.3–92.1)	54.0 ± 29.5 (15.2–104.3)
Total lean tissue mass (kg)	27.1 ± 5.1 (19.6–35.3)	23.0 ± 5.6 (15.5–34.3)	24.5 ± 3.4 (17.9–29.4)	24.3 ± 6.9 (17.6–41.3)
Fasting insulin (pM)	89 ± 63 (24–216)	86 ± 51 (24–240)	70 ± 27 (42–120)	98 ± 64 (36–222)
IGF-1 (ng/mL)	261 ± 38 (180–329)	288 ± 101 (131–471)	204 ± 71 (78–367)	177 ± 53 (107–296)
DHEAS (μg/dL)	59 ± 35 (20–133)	45 ± 26 (9–96)	45 ± 32 (8–133)	51 ± 31 (10–111)
Physical activity (hours/wk)	16.0 ± 4.4 (8.5–22.5)	8.0 ± 5.2 (1.0–17.9)	11.2 ± 6.6 (4.9–31.6)	4.4 ± 4.3 (0.6–15.1)
Vigorous activity (hours/wk)	7.7 ± 4.6 (3.1–17.3)	3.3 ± 3.7 (0.03–11.0)	6.9 ± 6.5 (0.9–23.7)	2.1 ± 1.9 (0.04–5.3)
Moderate activity (hours/wk)	8.9 ± 4.6 (2.5–20.3)	5.7 ± 3.5 (0.7–10.7)	5.6 ± 2.7 (2.2–9.7)	2.8 ± 4.4 (0.2–15.1)

B) S ₁ and AIR data; geometric mean ± SEM, and adjusted geometric mean ± SEM	Whites			
	African Americans		Whites	
	Boys (n = 12)	Girls (n = 15)	Boys (n = 13)	Girls (n = 11)
S ₁ (×10 ⁻⁵ /min ⁻¹ /pM)	6.0 ± 1.5	4.7 ± 1.0	9.0 ± 2.1	7.1 ± 1.9
S ₁ (×10 ⁻⁵ /min ⁻¹ /pM)†	5.7 ± 1.0	4.6 ± 0.7	7.9 ± 1.2	9.2 ± 1.7
AIR (pM)	942 ± 174	978 ± 156	354 ± 60	408 ± 78
AIR (pM)†	965 ± 155	994 ± 142	376 ± 56	356 ± 62

* Two-way ANOVA or Wilcoxon test (for body weight, SAAT, and physical activity); significant effects ($p < .05$) of gender, race, and gender × race are indicated.
 † Adjusted for total body fat.
 ‡ NS, no significant main effects (gender, race, or gender × race).

Table 2. Multiple linear regression models with hours/wk of all physical activity

Independent variable	Parameter	
	estimate \pm SEE	<i>p</i>
Dependent variable = Log S_1 ($R^2 = 0.65$)		
Race*	-0.26 ± 0.06	0.0001
Log total body fat mass	-0.50 ± 0.11	0.0001
Log total lean tissue mass	-0.98 ± 0.42	0.0251
Hours/wk	0.02 ± 0.00	0.0018
Dependent variable: Log AIR ($R^2 = 0.60$)		
Race	0.45 ± 0.06	0.0001
Log total body fat mass	0.22 ± 0.11	0.0614
Log total lean tissue mass	0.60 ± 0.42	0.1676
Hours/wk	-0.01 ± 0.00	0.0324

* Whites = 1, African Americans = 2.

greater in girls and tended to be greater in African Americans (Table 4A). Gender differences were found in S_1 and AIR, with girls having higher AIR and lower S_1 than boys (Table 4B). In addition, African American children had higher AIR than white children. After adjusting S_1 and AIR for total body fat mass with ANCOVA, gender differences in S_1 and AIR were eliminated; however, significant racial differences were apparent in S_1 and AIR. Compared with African Americans, whites had a higher mean VO_{2max} .

Multiple linear regression analysis was conducted to examine the influence of VO_{2max} , race, and body composition on S_1 and AIR (Table 5). Because gender differences in insulin variables were eliminated after controlling for total body fat mass, gender was not included in multiple regression models. Lean tissue mass was included in each regression model due to its strong association with VO_{2max} . Because of the constraint of our sample size ($n = 43$), we did not include IAAT and SAAT in the same regression model due to insufficient statistical power. Race remained independently related to S_1 (lower in African Americans) and AIR (higher in African Americans) after controlling for total body fat mass, lean tissue mass, and VO_{2max} . Replacing total body fat mass with either SAAT or IAAT did not explain any additional variance in S_1 or AIR. VO_{2max} was independently and negatively associated with S_1 but was not significantly associated with AIR.

Inclusion of IGF-1 in the models did not alter the results. In both cases, IGF-1 did not make an independent contribution (p values of 0.66 and 0.83 in the models for S_1 and AIR, respectively), and race remained significant (same p value as original model; data not shown).

Table 3. Multiple linear regression models with hours/wk of vigorous activity

Independent variable	Parameter	
	estimate \pm SEE	<i>p</i>
Dependent variable = Log S_1 ($R^2 = 0.62$)		
Race*	-0.21 ± 0.06	0.0011
Log total body fat mass	-0.53 ± 0.12	0.0001
Log total lean tissue mass	-0.72 ± 0.43	0.1012
Hours/wk of vigorous activity	0.02 ± 0.01	0.0169
Dependent variable: Log AIR ($R^2 = 0.60$)		
Race	0.42 ± 0.06	0.0001
Log total body fat mass	0.23 ± 0.11	0.0511
Log total lean tissue mass	0.44 ± 0.41	0.2889
Hours/wk of vigorous activity	-0.01 ± 0.01	0.0288

* Whites = 1, African Americans = 2.

Discussion

The purpose of this study was to examine whether VO_{2max} (an index of physical fitness), physical activity, or both were associated with insulin secretion and sensitivity in prepubertal children, and whether these indices of physical activity could explain differences between African American and white children in insulin secretion and sensitivity. The present study found significant associations between physical activity and both S_1 and AIR, independent of body composition and race. More active children had a lower insulin secretion and a greater insulin sensitivity. With respect to the intensity of physical activity, vigorous, but not moderate, activity was independently related to S_1 and AIR. AIR was greater, and S_1 lower, in African Americans vs. whites, after adjusting for total body fat. Race remained significantly associated with both S_1 (lower in African Americans) and AIR (higher in African Americans) when data were further adjusted for either physical activity or VO_{2max} . Thus, potential differences in physical fitness or physical activity are unlikely to explain observed racial differences in insulin secretion and sensitivity.

Based on the multiple regression analysis, physical activity was independently related to S_1 and AIR in prepubertal children after controlling for race, total (or central) body fat, and lean tissue mass. This finding is consistent with previous results suggesting that physical activity is positively associated with insulin sensitivity and negatively associated with insulin concentration and secretion in adults

Table 4. Subgroup with VO_{2max} data

A) Descriptive data, mean \pm SD (range)	Whites			
	African Americans		Whites	
	Boys (n = 9)	Girls (n = 10)	Boys (n = 13)	Girls (n = 11)
Age (years)	8.8 \pm 1.6 (6.5–10.7)	9.4 \pm 1.4 (6.9–11.0)	9.6 \pm 1.4 (7.3–11.8)	9.5 \pm 1.2 (7.2–11.2)
Body weight (kg)	42.3 \pm 19.5 (22.0–72.5)	41.7 \pm 15.1 (22.1–65.0)	37.3 \pm 12.7 (22.1–63.9)	50.4 \pm 21.1 (27.9–84.4)
Total body fat mass (kg)	10.4 \pm 10.1 (1.7–28.6)	14.3 \pm 10.1 (1.9–28.0)	9.4 \pm 7.7 (2.0–24.0)	19.9 \pm 1.2 (6.1–44.7)
BMI (kg/m ²)	22 \pm 7 (16–35)	22 \pm 7 (14–31)	20 \pm 4 (14–26)	24 \pm 6 (16–32)
SAAT (cm ²)	87.6 \pm 99.7 (9.7–270.0)	166.6 \pm 150.4 (8.8–436.1)	119.4 \pm 103.8 (19.5–297.0)	222.1 \pm 146.6 (39.7–414.9)
IAAT (cm ²)	34.9 \pm 33.9 (10.0–111.0)	32.5 \pm 22.8 (11.6–76.1)	38.5 \pm 20.6 (14.6–76.8)	69.5 \pm 39.1 (21.7–141.5)
Total lean tissue mass (kg)	25.2 \pm 5.8 (17.1–34.3)	25.5 \pm 5.5 (15.9–34.3)	25.4 \pm 4.7 (17.9–35.6)	27.7 \pm 7.9 (17.9–41.0)
Fasting insulin (pM)	88 \pm 70 (36–216)	104 \pm 54 (60–240)	63 \pm 23 (24–108)	137 \pm 76 (42–234)
IGF-1 (ng/mL)	208 \pm 58 (131–300)	314 \pm 91 (169–471)	198 \pm 88 (78–415)	232 \pm 98 (113–418)
DHEAS (μ g/dL)	46 \pm 36 (8–133)	41 \pm 24 (9–86)	54 \pm 48 (13–178)	54 \pm 34 (10–111)
VO_{2max} (liters/min)	1.4 \pm 0.5 (0.9–2.2)	1.3 \pm 0.3 (0.8–1.9)	1.6 \pm 0.4 (1.1–2.3)	1.6 \pm 0.5 (0.9–2.6)

B) S_I and AIR data; geometric mean \pm SEM, and adjusted geometric mean \pm SEM	Whites			
	African Americans		Whites	
	Boys (n = 12)	Girls (n = 15)	Boys (n = 13)	Girls (n = 11)
S_I ($\times 10^{-5}/\text{min}^{-1}/\text{pM}$)	6.1 \pm 2.3	2.8 \pm 1.0	10.0 \pm 3.0	4.7 \pm 1.6
S_I ($\times 10^{-5}/\text{min}^{-1}/\text{pM}$) [†]	4.8 \pm 1.2	3.1 \pm 0.7	7.8 \pm 1.6	7.2 \pm 1.6
AIR (pM)	960 \pm 216	1134 \pm 240	300 \pm 54	630 \pm 126
AIR (pM)	1074 \pm 207	1091 \pm 196	334 \pm 53	518 \pm 93

* Two-way ANOVA or Wilcoxon test (for body weight, SAAT, and VO_{2max}); significant effects ($p < 0.05$) of gender, race, and gender \times race are indicated.

[†] Adjusted for total body fat.

Abbreviations: NS = no significant main effects (gender, race, or gender \times race); SAAT = subcutaneous abdominal adipose tissue; IAAT = intraabdominal adipose tissue; S_I = insulin sensitivity; AIR = acute insulin response; [†] = trend ($0.05 < P < 0.1$).

Table 5. Multiple linear regression models for insulin parameters with VO_{2max}

Independent variable	Parameter	
	estimate \pm SEE	<i>p</i>
Dependent variable = Log S_I ($R^2 = 0.69$)		
Race*	-0.40 ± 0.09	0.0001
Log total body fat mass	-0.56 ± 0.16	0.0009
Log total lean tissue mass	-1.36 ± 0.65	0.0427
VO_{2max}	-0.48 ± 0.23	0.0395
Dependent variable: Log AIR ($R^2 = 0.62$)		
Race	0.43 ± 0.08	0.0001
Log total body fat mass	0.22 ± 0.13	0.1144
Log total lean tissue mass	1.22 ± 0.88	0.1719
VO_{2max}	-0.02 ± 0.19	0.9293

* Whites = 1, African Americans = 2.

and adolescents (13–17). Thus, the beneficial influence of physical activity on insulin secretion and action, and thereby on reduction of disease risk, seems to be operative early in life. Inclusion of S_I in the model for AIR eliminated the independent relationship of AIR with physical activity ($p = 0.319$ for hours/wk, and $p = 0.181$ for hours/wk of vigorous activity; data not shown). These results suggest the influence of physical activity on AIR is indirect, and is mediated through improvement in S_I .

With regard to the intensity of physical activity, vigorous activity was independently related to S_I and AIR after controlling for race, total (or central) body fat, and lean tissue mass. However, moderate activity was not associated with any insulin variable. This may imply that the observed relationship between hours/wk (total) physical activity and insulin secretion and sensitivity in prepubertal children (Table 2), may be due to hours/wk vigorous activity. However, a recent study indicated that both moderate and vigorous activity may increase insulin sensitivity in adults (17). The disagreement between the two studies may be due to the age of the subjects (prepubertal children vs. adults) or to differences in the questionnaire used. The intensity of physical activity may be more important for children than for adults in modifying insulin action, but this hypothesis should be tested with a more thorough questionnaire or by a more rigorous means of assessing physical activity. Because physical activity may play a role in reducing disease risk (13–17), the importance of intensity should be clarified through future studies.

VO_{2max} is frequently used as an index of physical fitness, but is not necessarily indicative of habitual physical activity in

children (32). Previous results indicate that insulin concentration is negatively associated with VO_{2max} in children (18), suggesting that greater physical fitness is related to greater insulin sensitivity in children. However, in the present study, VO_{2max} was not independently associated with AIR in the regression analysis, and was negatively associated with S_I , after controlling for race, total (or central) body fat, and lean tissue mass. Thus, our data suggest that VO_{2max} is either unrelated to insulin parameters, or that greater VO_{2max} is associated with lower insulin sensitivity. Several explanations can be suggested for the absence of the expected associations between VO_{2max} and insulin parameters. First, because our protocol involved eliminating subjects who did not meet at least two of the three criteria for reaching VO_{2max} (potentially subjects with lower fitness levels), the mean fitness of the remaining children ($n = 43$) may not have reflected that of the general population and may have had a limited range of VO_{2max} values. Second, the likelihood that VO_{2max} reflects factors other than physical fitness would add variance to the association between VO_{2max} and insulin parameters, limiting the ability to detect the expected positive relationship between physical fitness and insulin sensitivity. Finally, genetic differences in VO_{2max} (33,34) may confound relationships between VO_{2max} and insulin parameters. However, it is also possible that VO_{2max} is not associated with insulin sensitivity and first-phase insulin secretion in young children.

In the present study, as observed previously (8,9), racial differences in S_I and AIR were detected. AIR was higher, and S_I lower, in African American children than in white children after controlling for total body fat mass. These results were consistent in both data sets. Moreover, these ethnic differences remained significant after further controlling for lean tissue mass and either physical activity or VO_{2max} . These results indicate that African American children had a higher postchallenge insulin secretion and were more insulin-resistant. Our findings are consistent with previous findings in adults and adolescents, indicating that African Americans have higher insulin secretion and lower S_I than whites (1,2,6,35,36). Combining our results with previous findings, it seems that the racial differences in insulin secretion and sensitivity may have their origin in childhood and are unlikely to be explained by a difference in physical fitness or physical activity.

In contrast, results from a previous study have suggested that racial differences in physical fitness explain differences in insulin secretion in children (5). In this earlier study, the racial difference in first-phase insulin secretion measured by the hyperglycemic clamp was eliminated after adjusting for VO_{2max} , IGF-1, and gender. The association between VO_{2max} and S_I was not reported, and S_I did not differ between African American and white children. In the present study, racial differences in S_I and AIR were detected, but inclusion of VO_{2max} in the regression models did not eliminate the independent influence of race. Further

inclusion of IGF-1 in the models likewise did not alter the results (race was still strongly related to S_1 and AIR). The reason for the difference between studies is not clear. It seems reasonable to conclude that the association between VO_{2max} and insulin secretion and sensitivity in prepubertal children, as well as the potential contribution of VO_{2max} to racial differences in insulin parameters, needs further study.

Our study found African American children were more active than white children. This result was in contrast to a recent epidemiological study (20) that found lower levels of activity in African American children than in white children. However, both studies indicated that girls were less active than boys. Disagreement between studies with respect to the influence of race may be due to sample size ($n = 52$ vs. $n = 4063$), populations studied, or methodology. Children in our study were younger (~5 to 12 years old) than children in the earlier study (8 to 16 years), and the instrument for assessing activity differed; whereas our questionnaire required subjects to comment on their participation in specific activities, that of the earlier study (20) asked subjects to estimate the times per week they exercised enough to "sweat or breathe hard."

Because fat distribution influences insulin sensitivity in adults (37), we investigated the possibility that adjusting for central body fat (IAAT and SAAT) affected the relationship of race with S_1 and AIR. This was accomplished by substituting IAAT and SAAT for total fat mass in the multiple linear regression models. The racial differences in S_1 and AIR remained significant when total body fat was replaced with either IAAT or SAAT. This finding indicates that a difference in fat distribution does not contribute to racial differences in insulin secretion and sensitivity.

Limitations of the current study include its small sample size, cross-sectional design, the assumption of no recall bias and general reporting accuracy of the questionnaire, the absence on the questionnaire of activities below three METS, and incomplete VO_{2max} and questionnaire data. However, these factors are assumed to have a limited impact on the conclusions reached. Because the questionnaire we used was based on physical activity performed over the past year, the responses are likely to have reflected typical activity of the subjects. And, because our results indicated that vigorous activity, rather than moderate activity, was independently related to insulin secretion and sensitivity, it is unlikely that we would have detected a relationship between low intensity activities and insulin parameters, had we added low intensity activities to the questionnaire. However, the present findings should be replicated with a more extensive questionnaire to fully test the hypothesis that racial differences in S_1 and AIR are not related to physical activity. Because a complete questionnaire and VO_{2max} test results were not available on all children, bias may have been introduced by using data only from children for whom results were available. This is particularly true with respect

to the VO_{2max} test, because children who successfully completed the test may have been more physically fit and favorably inclined toward the test. In addition, data on hematocrit or hemoglobin were not available; these factors could influence VO_{2max} and perhaps contribute to the observed difference between racial groups. Prospective and/or intervention studies are required to determine if changes in physical activity are reflected in changes in insulin secretion and/or sensitivity in prepubertal children of different races.

To our knowledge, this is the first study to investigate the role of both physical fitness and physical activity in determining insulin secretion and sensitivity, after adjusting for body fat or fat distribution in African American and white prepubertal children. In addition, this is also the first study to examine whether physical fitness or physical activity alone can explain the racial differences in insulin secretion and sensitivity in prepubertal children. The results revealed significant relationships between physical activity and insulin secretion and sensitivity that were independent of body fat and fat distribution. Moreover, neither physical fitness nor physical activity, as assessed with our questionnaire, explained the racial difference in insulin secretion and sensitivity. Investigating the determinants of racial differences in insulin metabolism should be an important consideration in future studies.

Acknowledgments

The assistance of study coordinator Tena Hilario and the staff of the GCRC, and the participation of the children and their families, are gratefully acknowledged. This research was supported by the United States Department of Agriculture, the National Institute of Child Health and Human Development (R29 HD 32668; R01 HD/HL 33064), the National Institute on Aging (K01AG00740), and in part by a GCRC grant (MO1-RR-00032).

References

1. **Haffner SM, D'Agostino RJ, Saad MF, et al.** Increased insulin resistance and insulin secretion in non-diabetic African-Americans and Hispanics compared to non-Hispanic whites: the Insulin Resistance Atherosclerosis Study. *Diabetes*. 1996;45:742-8.
2. **Lovejoy JC, de la Bretonne J, Klemperer M, Tulley R.** Abdominal fat distribution and metabolic risk factors: effects of race. *Metabolism*. 1996;45:1119-24.
3. **Karter AJ, Mayer-Davis EJ, Selby JV, et al.** Insulin sensitivity and abdominal obesity in African-American, Hispanic, and non-Hispanic white men and women. *Diabetes*. 1996;45:1547-55.
4. **Osei K, Shuster DP.** Effects of race and ethnicity on insulin sensitivity, blood pressure, and heart rate in three ethnic populations: comparative studies in African-Americans, African immigrants (Ghanaians), and white Americans using ambulatory blood pressure monitoring. *Am J Hypertens*. 1996;9:1157-64.
5. **Arslanian S, Suprasongsin C, Janosky JE.** Insulin secretion and sensitivity in black vs. white prepubertal healthy children. *J Clin Endocrinol Metab*. 1997;82:1923-27.

6. **Arslanian S, Suprasongsin C.** Differences in the in vivo insulin secretion and sensitivity of healthy black versus white adolescents. *J Pediatr.* 1996;129:440–3.
7. **Gower BA, Nagy TR, Trowbridge CA, Dezenberg C, Goran MI.** Fat distribution and insulin response in African-American and Caucasian children. *Am J Clin Nutr.* 1998;67:821–7.
8. **Gower BA, Nagy TR, Goran MI.** Visceral fat, insulin sensitivity, and lipids in prepubertal children. *Diabetes.* 1999;48:1515–21.
9. **Lindquist CH, Gower BA, Goran MI.** The role of dietary factors in ethnic differences in early risk of cardiovascular disease and type 2 diabetes. *Am J Clin Nutr.* 2000;71:725–32.
10. **Yanovski JA, Yanovski SZ, Filmer KM, et al.** Differences in body composition of black and white girls. *Am J Clin Nutr.* 1996;64:833–9.
11. **Kriska AM, Blair SN, Pereira MA.** The potential role of physical activity in the prevention of non-insulin-dependent diabetes mellitus: the epidemiological evidence. *Exerc Sport Sci Rev.* 1994;22:121–43.
12. **Spelsberg A, Manson JE.** Physical activity in the treatment and prevention of diabetes. *Comprehens Ther.* 1995;21:559–64.
13. **Tuominen JA, Ebeling P, Koivisto V.** Exercise increases insulin clearance in healthy men and insulin-dependent diabetes mellitus patients. *Clin Physiol.* 1997;17:19–30.
14. **Raitakari OT, Porkka KV, Viikari JS.** Relations of life-style with lipids, blood pressure, and insulin in adolescents and young adults: the Cardiovascular Risk in Young Finns Study. *Atherosclerosis.* 1994;111:237–46.
15. **Coleman E, Toth MJ, Katzell LI, Fonong T, Gardner AW, Poehlman ET.** Body fatness and waist circumference are independent predictors of the age-associated increase in fasting insulin levels in healthy men and women. *Int J Obes.* 1995;19:798–803.
16. **Perseghin G, Price TB, Petersen KF, et al.** Increased glucose transport-phosphorylation and muscle glycogen synthesis after exercise training in insulin-resistant subjects. *N Engl J Med.* 1996;335:1357–62.
17. **Mayer-Davis EJ, D'Agostino R Jr, Karter AJ, et al.** Intensity and amount of physical activity in relation to insulin sensitivity: The Insulin Resistance Atherosclerosis Study. *JAMA.* 1998;279:669–74.
18. **Gutin B, Islam S, Manos T, Cucuzzo N, Smith C, Stachura ME.** Relation of percentage of body fat and maximal aerobic capacity to risk factors for atherosclerosis and diabetes in black and white seven- to eleven-year-old children. *J Pediatr.* 1994;125:847–52.
19. **Trowbridge CA, Gower BA, Nagy TR, Hunter GR, Treuth MS, Goran MI.** Maximal aerobic capacity in Caucasian and African-American children. *Am J Physiol.* 1997;273:E809–E14.
20. **Andersen RE, Crespo CJ, Bartlett SJ, Cheskin LJ, Pratt M.** Relationship of physical activity and television watching with body weight and level of fatness among children: results from the third National Health and Nutrition Examination Survey. *JAMA.* 1998;279:938–42.
21. **Klein KO, Martha PMJ, Blizzard RM, Herbst T, Rogol AD.** A longitudinal assessment of hormonal and physical alterations during normal puberty in boys II. Estrogen levels as determined by an ultrasensitive bioassay. *J Clin Endocrinol Metab.* 1996;81:3203–7.
22. **Pintauro SJ, Nagy TR, Duthie CM, Goran MI.** Cross-calibration of fat and lean measurements by dual-energy X-ray absorptiometry to pig carcass analysis in the pediatric body weight range. *Am J Clin Nutr.* 1996;63:293–8.
23. **Treuth MS, Hunter GR, Kekes-Szabo T.** Estimating intra-abdominal adipose tissue in women by dual-energy X-ray absorptiometry. *Am J Clin Nutr.* 1995;62:527–32.
24. **Goran MI, Kaskoun MC, Shuman WP.** Intra-abdominal adipose tissue in young children. *Int J Obes.* 1995;19:279–83.
25. **Bergman RN, Prager R, Volund A, Olefsky JM.** Equivalence of the insulin sensitivity index in man derived by the minimal model method and the euglycemic glucose clamp. *J Clin Invest.* 1987;79:790–800.
26. **Yang YJ, Youn JH, Bergman RN.** Modified protocols improve insulin sensitivity estimation using the minimal model. *Am J Physiol.* 1987;253:E595–E602.
27. **Matthews JNS, Altman DG, Campbell MJ, Royston P.** Analysis of serial measurements in medical research. *Br Med J.* 1990;300:230–5.
28. **Astrand PO.** *Exercise Studies of the Physical Walking Capacity in Relation to Sex and Age.* Copenhagen: Enjar Munksgaard; 1952.
29. **Kriska AM, Knowler WC, Laporte RE, et al.** Development of questionnaire to examine relationship of physical activity and diabetes in Pima Indians. *Diabetes Care.* 1990;13:401–11.
30. **Ainsworth BE, Haskell WL, Leon AS.** Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc.* 1993;25:71–80.
31. **Kahn SE, Prigeon RL, McCulloch DK, et al.** Quantification of the relationship between insulin sensitivity and β -cell function in human subjects: evidence for a hyperbolic function. *Diabetes.* 1993;42:1663–72.
32. **Pate RR, Dowda M, Ross JG.** Associations between physical activity and physical fitness in American children. *Am J Dis Child.* 1990;144:1123–9.
33. **Bouchard C, Daw EW, Rice T, et al.** Familial resemblance for VO_2 max in the sedentary state: the HERITAGE family study. *Med Sci Sports Exerc.* 1998;30:252–8.
34. **Swallow JG, Garland T Jr, Carter PA, Zhan W-Z, Sieck GC.** Effects of voluntary activity and genetic selection on aerobic capacity in house mice (*Mus domesticus*). *J Appl Physiol.* 1998;84:69–76.
35. **Osei K, Schuster DP.** Ethnic differences in secretion, sensitivity, and hepatic extraction of insulin in black and white Americans. *Diabet Med.* 1994;11:755–62.
36. **Jiang X, Srinivasan SR, Radhakrishnamurthy B, Dalferes ERJ, Berenson GS.** Racial (black-white) differences in insulin secretion and clearance in adolescents: the Bogalusa Heart Study. *Pediatrics.* 1996;97:357–60.
37. **Després J-P, Lemieux S, Lamarche B, et al.** The insulin resistance-dyslipidemic syndrome: contribution of visceral obesity and therapeutic implications. *Int J Obes.* 1995;19(Suppl 1):S76–S86.