

Obesity, Regional Fat Distribution, and Syndrome X in Obese Black Versus White Adolescents: Race Differential in Diabetogenic and Atherogenic Risk Factors

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The incidence of type 2 diabetes mellitus in children is increasing with the increasing prevalence of obesity, particularly in African-American children. We hypothesized that African-American obese adolescents are more insulin resistant than their white peers, but have lower insulin secretion, thus increasing their risk of type 2 diabetes mellitus. The present study investigated insulin sensitivity and secretion, visceral adiposity (VAT), and cardiovascular disease (CVD) risk profile in black obese adolescents (BOA) vs. white obese adolescents (WOA).

Twenty-four BOA and 26 WOA underwent a hyperinsulinemic-euglycemic clamp to assess insulin sensitivity, a hyperglycemic clamp to determine insulin secretion, dual energy x-ray absorptiometry for body composition and computed tomography scan at L4–L5 to measure VAT and sc abdominal adipose tissue. Fasting lipid and automated blood pressure measurements were obtained. The WOA and BOA groups were divided into low VAT and high VAT groups.

BOA compared with WOA of similar body mass index and percent body fat had less visceral adiposity, lower hepatic

glucose production, and lower lipid levels. Visceral adiposity was associated with lower insulin sensitivity in both groups [low vs. high VAT; BOA, 2.9 ± 0.4 vs. 1.7 ± 0.2 $\mu\text{mol/kg}\cdot\text{min}$ per pmol/liter ($P = 0.016$); WOA, 2.6 ± 0.5 vs. 1.5 ± 0.1 ($P = 0.032$)]. However, this was compensated by higher insulin secretion in whites (low VAT, 934.8 ± 121.8 ; high VAT, 1590.6 ± 232.8 pmol/liter ; $P = 0.037$), but not in blacks (low VAT, 1398.9 ± 214.0 ; high VAT, 1423.7 ± 108.7 pmol/liter). Glucose disposition index (insulin sensitivity \times first phase insulin) was lower in high VAT vs. low VAT BOA, but not in WOA. In each racial group, high VAT groups had elevation of systolic and diastolic blood pressure, but dyslipidemia was worse in WOA with high VAT.

In conclusion, a given level of body mass index confers different metabolic risks for WOA vs. BOA. Although differences in fat patterning may help explain the more atherogenic risk profile in whites, the cause of the more diabetogenic insulin sensitivity/secretion profile in blacks remains unknown and needs to be investigated further. (*J Clin Endocrinol Metab* 88: 2534–2540, 2003)

THE INCIDENCE OF youth type 2 diabetes mellitus (T2DM) is increasing dramatically (1–3). It typically occurs in youth who are obese, at midpuberty, from minority ethnic groups (1–6). Similarly, the prevalence and severity of obesity is increasing in children more dramatically in blacks than in whites. Obesity prevalence [body mass index (BMI) above the 95th percentile for age and sex] has increased to 21.5% in African-American (AA) children vs. 12.3% in white children (7). Obesity, particularly visceral adiposity (VAT), is associated with insulin resistance, hyperinsulinemia, dyslipidemia, and hypertension, the cluster of syndrome X or the metabolic syndrome (8–11). We and others have demonstrated that healthy black youth are insulin resistant and hyperinsulinemic compared with their white peers (12–15). A recent study of ours showed that despite similar BMI, percent body fat, and VAT, insulin sensitivity is 20% lower, and insulin secretion is higher in black vs. white prepubertal children (15). This hyperinsulinemia is over and above the compensatory response to the lower insulin sensitivity (15).

Abbreviations: AA, African-American; BMI, body mass index; BOA, black obese adolescents; CT, computed tomography; CVD, cardiovascular disease; FFA, free fatty acids; HDL, high density lipoprotein; LDL, low density lipoprotein; SAT, sc abdominal adipose tissue; TAT, total abdominal adipose tissue; T2DM, type 2 diabetes mellitus; VAT, visceral adiposity; WOA, white obese adolescents.

On the other hand, we have shown that in blacks, although insulin sensitivity is lower in adolescents compared with prepubertal children, insulin secretion is not higher (16). The hypothesis tested in the present study is that black obese adolescents (BOA) are more insulin resistant than white obese adolescents (WOA), but have lower insulin secretion, thus explaining their increased risk of type 2 diabetes.

We specifically aimed at investigating 1) insulin sensitivity and secretion in BOA vs. WOA, 2) CVD risk profile in the two groups, and 3) the relationship between VAT and the components of syndrome X in each racial group.

Subjects and Methods

Study population

Fifty adolescents were studied. These included 24 BOA and 26 WOA. All studies were approved by the human rights committee of Children's Hospital of Pittsburgh. Study participants were recruited through newspaper advertisements in the community. Parental informed consent and child assent were obtained from all participants. Clinical characteristics of the study subjects are summarized in Table 1. Besides obesity, subjects were documented to be in good health by history, physical examination, and routine hematological and biochemical tests. None were receiving any medical treatment. Pubertal development was assessed by physical examination according to Tanner criteria and was confirmed by measurement of plasma testosterone in males, estradiol in females, and dehydroepiandrosterone sulfate in all (Table 1). All participants were instructed to follow a weight-maintaining diet containing 55% carbo-

TABLE 1. Study subjects

	BOA (12M + 12F)	WOA (14M + 12F)	<i>P</i>
Age (years)	13.4 ± 0.3	13.3 ± 0.4	NS
Tanner stage			
II–III	13	16	
IV–V	11	10	
BMI (kg/m ²)	35.6 ± 1.1	35.2 ± 1.0	NS
Fat mass (kg)	38.1 ± 1.6	37.1 ± 1.7	NS
% Body fat	43.6 ± 0.8	43.4 ± 1.2	NS
TAT (cm ²)	597.0 ± 35.2	630.3 ± 32.4	NS
SAT (cm ²)	536.8 ± 32.2	542.1 ± 29.0	NS
VAT (cm ²)	60.2 ± 5.8	88.3 ± 7.9	0.006
DHEAS (μmol/liter)	3.3 ± 0.4	4.3 ± 0.5	NS
Estradiol ^a (pmol/liter)	296.2 ± 77.1	275.3 ± 84.1	NS
Testosterone ^b (nmol/liter)	6.5 ± 1.9	6.4 ± 1.2	NS

Data are mean ± SEM. M, Males; F, females; NS, not significant.

^a Estradiol in females only.

^b Testosterone in males only.

hydrate, 30% fat, and 15% protein for 1 wk before the testing. All investigations were performed in the General Clinical Research Center after 10–12 h of overnight fasting.

Clamp studies

Each participant had a hyperglycemic clamp and a hyperinsulinemic-euglycemic clamp study that were performed in random order at 1- to 2-wk intervals. All studies were performed after 10–12 h of overnight fasting. For the clamp studies, two iv catheters were inserted. One was placed in a vein on the forearm for administration of glucose and insulin infusions, and the second was placed on the dorsum of the contralateral heated hand for sampling of arterialized venous blood. Fasting hepatic glucose production was measured with a primed (2.2 μmol/kg) constant rate infusion of [6,6-²H₂]glucose (Isotech, Miamisburg, OH) at 0.22 μmol/kg from 0730–0930 h (16). Calculations for fasting hepatic glucose production were made over the last 30 min of the 2-h isotope infusion. Blood samples were obtained every 10 min over the last 30 min for determination of fasting glucose, insulin, and plasma isotopic enrichment. Insulin-mediated glucose metabolism and insulin sensitivity were evaluated during a 3-h hyperinsulinemic-euglycemic clamp from 0930–1230 h (16, 17). Intravenous crystalline insulin (Humulin, Eli Lilly & Co., Indianapolis, IN) was infused at a constant rate of 80 mU/m²·min as described by us previously (18). Plasma glucose was clamped at 5.6 mmol/liter with a variable rate infusion of 20% dextrose. The rate of the glucose infusion was adjusted based on 5-min arterialized plasma glucose determinations. A 2-h hyperglycemic clamp was performed from 0900–1100 h to evaluate first and second phase insulin secretion as reported previously (16, 18, 19). Briefly, glucose was acutely elevated to 12.5 mmol/liter and clamped at that level with a variable rate infusion of 20% dextrose in water. Blood samples for insulin were obtained every 2.5 min for the first 15 min and then every 15 min until the end of the clamp. Before the start of the clamp, a fasting blood sample was obtained for determination of cholesterol; low (LDL), high (HDL), and very low density lipoproteins; and triglycerides.

Body composition

Body composition was determined by dual energy x-ray absorptiometry. Subcutaneous abdominal adipose tissue (SAT) and visceral adipose tissue (VAT) were examined by a single slice computed tomography (CT) scan at intervertebral space L4–L5. Both dual energy x-ray absorptiometry and CT methods were described by us previously (17). Blood pressure was measured when the subjects were resting in the supine position in bed. As described previously, measurements were performed with an automated sphygmomanometer every 10 min for 1 h between 2200–2300 h before the subjects fell asleep and between 0600–0700 h before awakening (20). The mean of seven measurements during each hour was the outcome for statistical analysis.

Biochemical measurements

Plasma glucose was measured by the glucose oxidase method with a glucose analyzer (YSI, Inc., Yellow Springs, OH), and the insulin concentration was determined by RIA (15). Plasma lipid levels were measured using the standards of the Centers for Disease Control and Prevention as described previously (21). Plasma free fatty acids (FFA) were quantitated by an enzymatic colorimetric method with the use of the nonesterified fatty acid C test kit (Wako Pure Chemical Industries Ltd., Osaka, Japan). Deuterium enrichment of glucose in the plasma was determined on a Hewlett-Packard Co. 5971 mass spectrometer (Palo Alto, CA) coupled to a 5890 series II gas chromatograph as we previously reported (15–17). Plasma samples were deproteinized with methanol. The aldolnitrile pentaacetate derivative of glucose was analyzed for ²H enrichment in the electron impact mode. Selective ion monitoring software was used to monitor the mass to charge ratio for m/z 200 and 202, reflecting unlabeled and labeled glucose. Standard curves of known enrichments were performed with each assay.

Fasting hepatic glucose production was calculated during the last 30 min of the fasting 2-h isotope infusion period according to steady state tracer dilution equations reported by us previously (16, 17). The insulin-stimulated glucose disposal rate was calculated during the last 30 min of the euglycemic clamp to be equal to the rate of exogenous glucose infusion. Insulin sensitivity was calculated by dividing the glucose disposal rate by the steady state clamp insulin level as reported previously (20, 22). Insulin clearance was calculated as reported by us previously (15).

During the hyperglycemic clamp, the first phase insulin concentration was calculated as the mean of five insulin determinations at 2.5, 5.0, 7.5, 10.0, and 12.5 min of the clamp, and the second phase as the mean of eight determinations from 15–120 min of the clamp. The glucose disposition index was calculated as the product of insulin sensitivity × first phase insulin level (15).

Statistics

Statistical analyses were performed using the *t* test for two group comparisons. A two-way ANOVA was performed to examine the main effect of ethnicity (black *vs.* white), the main effect of VAT (low *vs.* high), and the interaction of ethnicity and VAT for each of the variables of interest. Each variable of interest was analyzed separately. Pearson or Spearman correlation analysis was used when applicable to examine bivariate relationships. To evaluate multivariate relationships, multiple regression analysis was applied. All statistical assumptions were met. Data are presented as the mean ± SEM. *P* ≤ 0.05 was considered statistically significant.

Results

Study subjects

The BOA and WOA groups had similar age, BMI, fat mass, percent body fat, and Tanner stage distribution (Table 1). They had similar total abdominal adipose tissue (TAT) and SAT. However, the BOA had significantly lower VAT (60.2 ± 5.8 *vs.* 88.3 ± 7.9 cm²; *P* = 0.006). Among BOA, males and females did not differ significantly in SAT (531.1 ± 39.1 and 543.0 ± 54.2 cm²), VAT (66.6 ± 8.6 and 53.2 ± 7.4 cm²), and TAT (597.7 ± 43.7 and 596.3 ± 58.3 cm²). However, among WOA, males had significantly higher VAT compared with females (104.9 ± 11.5 *vs.* 68.6 ± 7.5 cm²; *P* = 0.016), with no significant differences in SAT (562.2 ± 44.5 *vs.* 518.3 ± 35.8 cm²) or TAT (667.1 ± 52.1 *vs.* 586.9 ± 32.9 cm²). BOA males had significantly lower VAT than WOA males (66.6 ± 8.6 *vs.* 104.9 ± 11.5 cm²; *P* = 0.01). There were no significant differences in VAT between black and white females.

Fasting metabolic data and blood pressure

Table 2 depicts fasting metabolic profile of BOA and WOA. BOA and WOA had similar fasting plasma glucose and in-

sulin. Hepatic glucose production was significantly higher in WOA than BOA (13.9 ± 0.5 *vs.* 12.2 ± 0.4 $\mu\text{mol}/\text{kg}\cdot\text{min}$; $P = 0.045$). Fasting cholesterol, triglycerides, LDL and the ratio of total cholesterol/HDL were significantly higher in WOA than in BOA (Table 2). Fasting FFA levels were not different

between BOA and WOA (0.35 ± 0.03 *vs.* 0.33 ± 0.02 mmol/liter). Systolic and diastolic blood pressure levels were similar in WOA and BOA.

Insulin sensitivity and secretion

Steady state concentrations of plasma glucose, insulin, and FFA over the last 30 min of the hyperinsulinemic-euglycemic clamp were not different between BOA and WOA (glucose, 5.6 ± 0.03 *vs.* 5.6 ± 0.03 mmol/liter ; insulin, 1772.3 ± 83.6 *vs.* 1744.7 ± 93.9 pmol/liter ; FFA, 0.07 ± 0.01 *vs.* 0.05 ± 0.01 mmol/liter). Similarly, insulin sensitivity, insulin clearance, and first phase insulin were not different between BOA and WOA groups (Table 2). However, second phase insulin secretion was higher in WOA *vs.* BOA (2015.4 ± 180.6 *vs.* 1468.7 ± 102.8 pmol/liter ; $P = 0.01$). The glucose disposition index was not significantly different between BOA and WOA (3.0 ± 0.4 *vs.* 2.4 ± 0.2 $\text{mmol}/\text{kg}\cdot\text{min}$).

Visceral adiposity in BOA and WOA

Because BOA had significantly lower VAT than WOA despite similar BMI and percent body fat, and to assess the impact of visceral fat within each race, the BOA and WOA were divided into low VAT and high VAT groups (Table 3). The low VAT group had VAT within 2 SD above the mean, and the high VAT group had VAT greater than 2 SD above the mean VAT of nonobese pubertal adolescents of the same race. The mean VAT + 2 SD of normal weight white adolescents was 65.1 cm^2 [$n = 12$ males and 11 females; age, 12.5 ± 1.2 ($\pm\text{SD}$) yr], and the mean VAT + 2 SD of normal weight AA adolescents was 47.9 cm^2 ($n = 15$ males and 10

TABLE 2. Metabolic profile of BOA and WOA

	BOA	WOA	<i>P</i>
Fasting glucose (mmol/liter)	5.5 ± 0.1	5.4 ± 0.1	NS
Fasting insulin (pmol/liter)	230.7 ± 24.0	250.2 ± 18.0	NS
Hepatic glucose production ($\mu\text{mol}/\text{kg}\cdot\text{min}$)	12.2 ± 0.4	13.9 ± 0.5	0.045
Insulin sensitivity ($\mu\text{mol}/\text{kg}\cdot\text{min}$ per pmol/liter)	2.2 ± 0.2	2.1 ± 0.2	NS
Insulin clearance (ml/kg·min)	7.2 ± 0.4	7.7 ± 0.5	NS
1st Phase insulin (pmol/liter)	1424.8 ± 96.1	1310.4 ± 146.4	NS
Cholesterol (mmol/liter)	3.94 ± 0.18	4.68 ± 0.15	0.003
Triglycerides (mmol/liter)	1.01 ± 0.08	1.63 ± 0.16	0.002
LDL (mmol/liter)	2.44 ± 0.14	2.87 ± 0.13	0.031
HDL (mmol/liter)	1.06 ± 0.04	1.08 ± 0.04	NS
Cholesterol/HDL	3.8 ± 0.2	4.5 ± 0.2	0.027
Evening systolic BP (mm Hg)	118.1 ± 2.2	118.9 ± 2.6	NS
Evening diastolic BP (mm Hg)	66.9 ± 1.8	64.5 ± 1.9	NS

NS, Not significant; BP, blood pressure.

TABLE 3. Body composition and metabolic profile of high-VAT *vs.* low-VAT groups

	WOA		BOA		Significant main effects in two-way ANOVA
	Low-VAT (8F + 2M)	High-VAT (3F + 11M)	Low-VAT (4F + 4M)	High-VAT (7F + 8M)	
BMI (kg/m^2)	34.0 ± 1.3	36.5 ± 1.5	33.6 ± 2.1	37.1 ± 1.3	None
Fat mass (kg)	37.9 ± 3.2	37.7 ± 2.1	34.3 ± 2.8	40.8 ± 1.8	None
SAT (cm^2)	519.2 ± 39.2	558.4 ± 41.6	476.0 ± 55.0	569.2 ± 38.5	None
VAT (cm^2)	55.4 ± 2.1	111.8 ± 9.3^a	28.0 ± 3.5	77.4 ± 4.0^a	Race, $P < 0.001$
Insulin sensitivity ($\mu\text{mol}/\text{kg}\cdot\text{min}$ per pmol/liter)	2.6 ± 0.5	1.5 ± 0.1^b	2.9 ± 0.4	1.7 ± 0.2^b	VAT, $P = 0.001$
1st Phase insulin (pmol/liter)	934.8 ± 121.8	1590.6 ± 232.8^b	1398.9 ± 214.0	1423.7 ± 108.7	VAT, $P = 0.07$
2nd Phase insulin (pmol/liter)	1657.8 ± 235.2	2308.8 ± 272.4^b	1338.8 ± 226.5	1540.8 ± 114.4	Race, $P = 0.02$
Glucose disposition index (mmol/kg·min)	2.3 ± 0.4	2.2 ± 0.2	3.8 ± 0.6	2.5 ± 0.4^b	Race, $P = 0.038$
Cholesterol (mmol/liter)	4.2 ± 0.1	4.9 ± 0.2^b	4.1 ± 0.4	3.9 ± 0.1	Race, $P = 0.027$
Triglycerides (mmol/liter)	1.2 ± 0.1	1.7 ± 0.2^b	1.0 ± 0.1	1.0 ± 0.1	Race, $P = 0.005$
HDL (mmol/liter)	1.2 ± 0.1	1.0 ± 0.0^b	1.1 ± 0.1	1.0 ± 0.1	None
LDL (mmol/liter)	2.5 ± 0.1	3.1 ± 0.2^b	2.6 ± 0.4	2.4 ± 0.1	None
Cholesterol/HDL	3.8 ± 0.3	5.0 ± 0.3^b	3.8 ± 0.4	3.9 ± 0.2	VAT, $P = 0.027$
Evening systolic BP (mm Hg)	111.6 ± 3.2	125.4 ± 3.4^b	114.7 ± 4.8	120.5 ± 2.2	VAT, $P = 0.006$
Evening diastolic BP (mm Hg)	59.3 ± 2.6	69.1 ± 2.4^b	63.4 ± 2.8	68.9 ± 2.4	VAT, $P = 0.006$

Two WOA, a male and a female, and a female BOA did not have VAT data. F, Females; M, males; BP, blood pressure.

^a $P < 0.001$ and ^b $P \leq 0.05$, high-VAT *vs.* low-VAT within the same race by *t* test. Significant main effects of two-way ANOVA are shown. No interaction effect of race and VAT was seen for any of the outcome measures.

females; age, 12.4 ± 1.3 yr). The obese low VAT and high VAT groups had similar BMI, percent body fat, and SAT (Table 3). The high VAT BOA group included 9 subjects at Tanner stage II to III and 6 subjects at Tanner stage IV to V. The low VAT group included 4 subjects at Tanner stage II to III and 4 subjects at Tanner stage IV to V. In the high VAT WOA group, 11 adolescents were at Tanner stage II to III and 3 were at Tanner stage IV to V. In the low VAT WOA group, 4 subjects were at Tanner stage II to III and 6 were at Tanner stage IV to V. Data for VAT was missing in 1 BOA and 2 WOA.

Table 3 depicts metabolic and CVD risk parameters in BOA and WOA subgrouped according to low and high VAT. Two-way ANOVA revealed a main effect of VAT on insulin sensitivity ($P = 0.001$), systolic and diastolic blood pressure, and cholesterol/HDL ratio. For first and second phase insulin secretion, a main effect of VAT approached statistical significance ($P = 0.07$ for each). A main effect of race was observed on glucose disposition index, second phase insulin, cholesterol, and triglycerides. No interaction effects of race and VAT were observed for any of the outcome measures.

Figure 1 depicts insulin sensitivity, first phase insulin, and glucose disposition index in low vs. high VAT groups for

each race. Insulin sensitivity was significantly lower in the high vs. low VAT groups in both races. The first phase insulin level was significantly higher in WOA with high vs. low VAT ($P = 0.037$). However, in BOA the first phase insulin level was not higher in high vs. low VAT despite significantly lower insulin sensitivity. Consequently, the glucose disposition index was significantly lower in high vs. low VAT BOA, whereas it was comparable in the WOA with high vs. low VAT. Steady state clamp FFA levels were higher in WOA with high vs. low VAT (0.07 ± 0.01 vs. 0.04 ± 0.01 mmol/liter; $P = 0.041$). During hyperinsulinemia, the percent suppression of FFA levels from baseline was lower in high vs. low VAT WOA ($77.2 \pm 2.0\%$ vs. $87.6 \pm 2.1\%$; $P = 0.002$). This was not the case in BOA with high vs. low VAT ($81.7 \pm 1.7\%$ vs. $78.7 \pm 2.7\%$).

Correlations

Figure 2 shows the relationship between first phase insulin secretion and insulin sensitivity in WOA ($r = -0.41$; $P = 0.04$) and BOA. In WOA, VAT correlated with first phase insulin ($r = 0.51$; $P = 0.01$), LDL ($r = 0.42$; $P = 0.04$), systolic blood pressure ($r = 0.57$; $P = 0.004$), and diastolic blood pressure

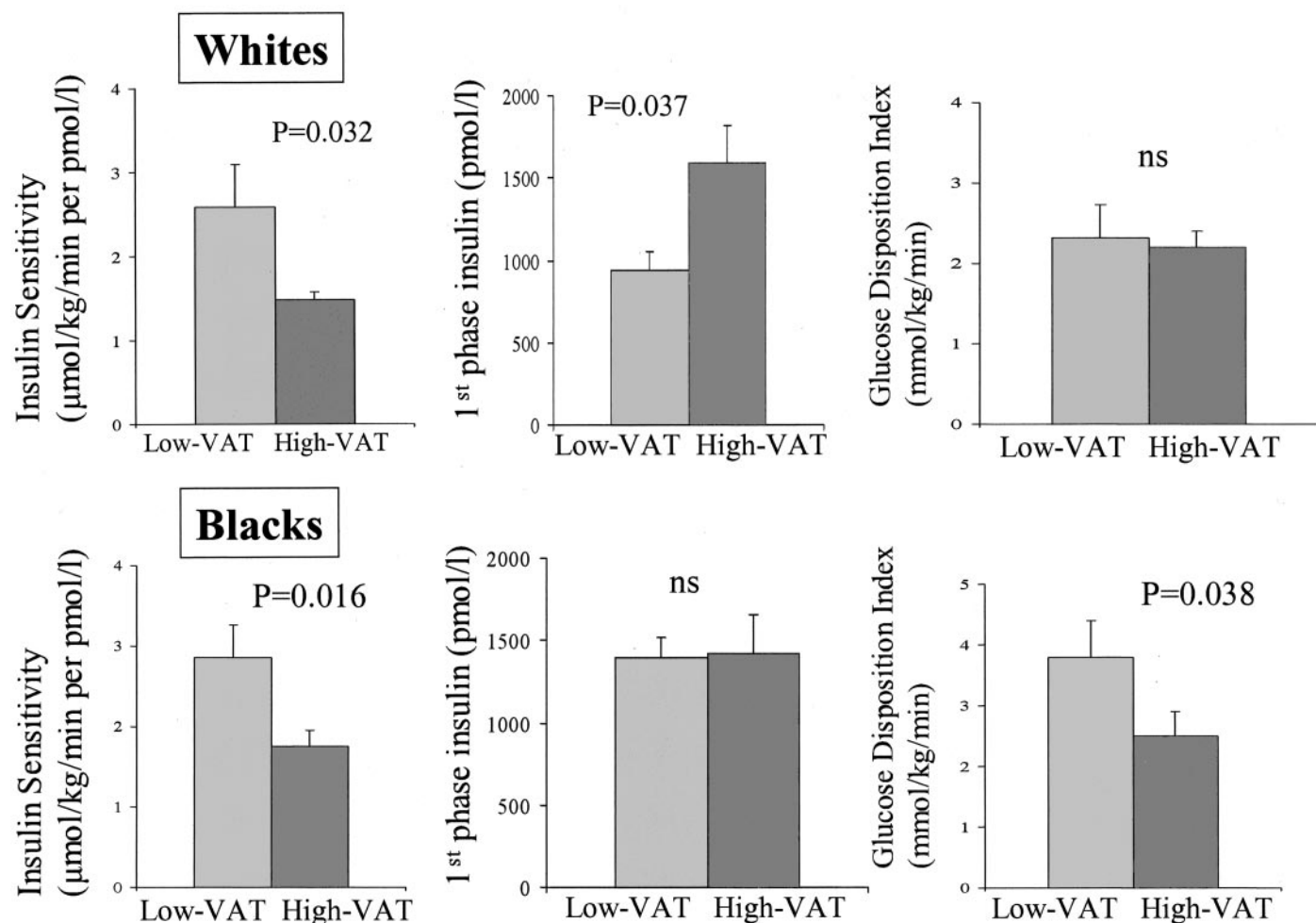


FIG. 1. Insulin sensitivity (IS), insulin secretion, and glucose disposition index in the low vs. high VAT groups in whites (upper panel) and blacks (lower panel).

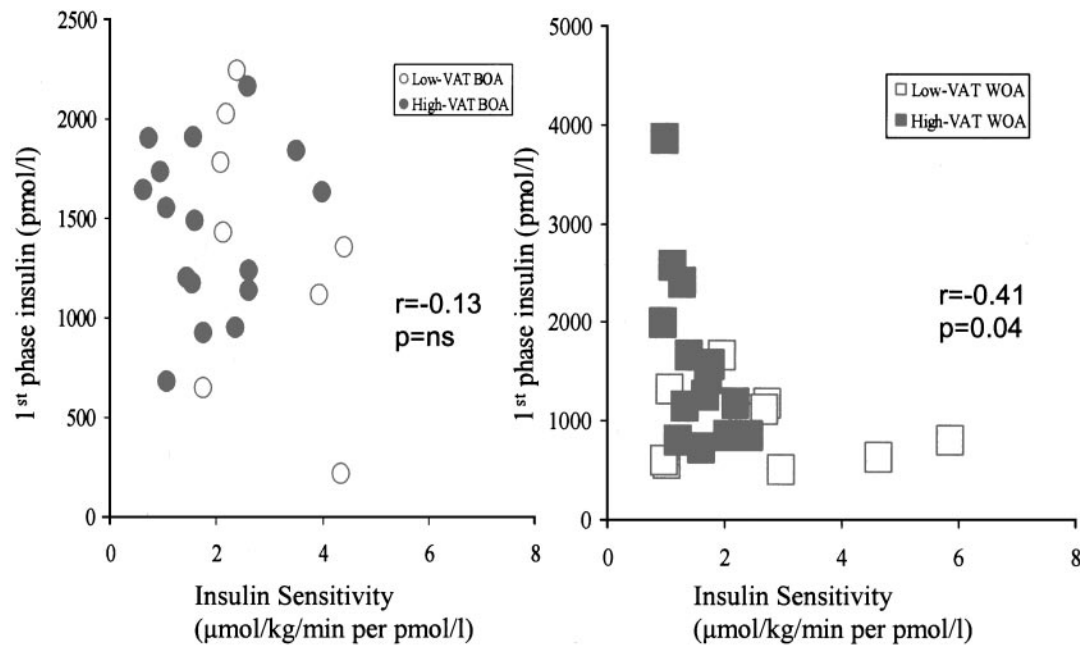


FIG. 2. Relationship of first phase insulin secretion to insulin sensitivity in BOA (left panel) and WOA (right panel).

($r = 0.54$; $P = 0.006$). There were no other significant correlations in WOA between body composition parameters and syndrome X cluster. On the other hand, in BOA VAT correlated only with systolic blood pressure ($r = 0.52$; $P = 0.012$) with no other correlations. In BOA, total body, and not regional adiposity, showed significant correlations. In BOA, total cholesterol and LDL correlated with BMI ($r = 0.44$; $P = 0.03$ and $r = 0.48$; $P = 0.02$, respectively), and LDL correlated with fat mass ($r = 0.44$; $P = 0.046$). Multiple regression analysis revealed a significant effect of VAT ($P < 0.01$) on systolic and diastolic BPs independent of total fat or percent body fat in both racial groups.

Discussion

At first glance, the present study would suggest that African-American adolescents, with similar degrees of obesity (BMI, fat mass, and percent body fat) as their white peers, are better off with respect to the metabolic consequences of obesity. As shown in Table 2, hepatic glucose production, cholesterol, triglycerides, and LDL levels are significantly lower in BOA. Contrary to our hypothesis, insulin sensitivity and secretion are not different in BOA *vs.* WOA. However, a more in-depth evaluation of body fat distribution with assessment of VAT reveals important racial differences. Not only do African-American adolescents have lower visceral fat, but the relationship between VAT and its comorbid conditions of syndrome X differ significantly between the races. Despite similar BMI, total body fat, and percent body fat, BOA had approximately 30% less VAT than WOA. The lower VAT could explain the better lipid profile and lower hepatic glucose production observed in blacks. This could be mediated through decreased delivery of FFA to the liver (10, 11). On the other hand, despite lower visceral fat in blacks, peripheral insulin sensitivity is not higher than that in whites. This could be related to the observations that blacks in general

have lower insulin sensitivity than whites (12–15, 47). When the data are analyzed according to VAT, important racial differences emerge. In WOA, visceral fat accumulation appears to increase the atherogenic risk, whereas in BOA, it increases the diabetogenic risk.

Race differences in body fat distribution are clearly evident in that lower VAT is found in black adults compared with whites (23–29). Similar differences are also described in children (30–33). Among normal weight girls, aged 7–10 yr, blacks at similar body weights had less VAT, SAT, and TAT than whites measured by magnetic resonance imaging (30). Prepubertal black girls and boys compared with whites, with a wide range of BMI (13.1–35.0 kg/m²), had lower VAT (13, 31). Moreover, over a 3- to 5-yr period of growth in children, VAT growth was significantly higher in white compared with black children (32). The present study complements as well as adds to the existing literature by showing that despite similar BMI, total body fat, and percent body fat, black obese adolescents have lower VAT than their white peers.

Visceral obesity independent of overall obesity is considered a risk factor for insulin resistance, diabetes mellitus, atherogenic lipid profile, and hypertension in both Caucasians and African-Americans (10, 11, 29, 34–37). In agreement with this, our data demonstrate that WOA have a more atherogenic lipid profile than their black counterparts due to having more VAT. This is consistent with findings in adults, with black men and women having a more cardioprotective lipid profile than whites (27, 29, 38). Studies in children, however, are inconsistent. In one study despite lower VAT in black girls, there were no significant differences between black and white girls in serum cholesterol, triglycerides, HDL, and LDL cholesterol (30). In the pediatric literature most studies have used crude anthropometric indexes of circumferences and skin-fold thickness to demonstrate either a weak correlation of fat distribution to CVD risk factors or

no correlation (39, 40). Studies that have directly measured intraabdominal and sc abdominal adipose tissues using magnetic resonance imaging have shown that in obese, mostly white, adolescent girls, intraabdominal fat correlated positively with triacylglycerol and negatively with HDL, and in obese black and white youth, it correlated directly with triacylglycerol and total and LDL cholesterol (33, 41, 42). In other studies of prepubertal black and white children, visceral fat, measured by CT scan, independently correlated with triglycerides (13, 43). In prepubertal children, contrary to our findings in adolescents, fat distribution did not explain the lower triglycerides in blacks (44). This could be attributed to the observation that significant race-related differences in fat patterning emerge after puberty.

We and others have demonstrated that black children have lower insulin sensitivity and clearance and are hyperinsulinemic compared with their white peers (13–15, 45). Because of this, we hypothesized that BOA will be more insulin resistant than WOA. Contrary to our theory, peripheral insulin sensitivity was not different between BOA and WOA. This could potentially be due to the overriding effect of obesity-related insulin resistance masking race-related differences in insulin sensitivity. Another way of interpreting this, however, would be that despite 30% lower VAT in BOA, insulin sensitivity is not higher than that in WOA, *i.e.* blacks are relatively more insulin resistant.

A question frequently raised is whether generalized and/or regional obesity are associated with different health risk factors in blacks *vs.* whites. In the present investigation visceral obesity played a major role in modulating insulin sensitivity in both BOA and WOA. In contrast, a previous study showed that insulin sensitivity was significantly influenced by total body fat, but not VAT, in white and black children (46). However, the study population included children with a wide age range (7.2–12.2 yr), who were prepubertal and pubertal and had a wide spectrum of percent body fat (6.8–53%). Our study only included adolescents who were obese (percent body fat, 32.1–51.1%). Differences in study population and methodology (minimal model *vs.* clamp technique) may be responsible for the different results (46). Also, in contrast to our results, BOA were reported to have greater insulin responses during oral and iv glucose tolerance tests compared with WOA (47). However, blacks were significantly younger than whites, and there was no sensitive assessment of total or abdominal adiposity. In the present study when we subdivided each of the WOA and BOA groups into those with low and high visceral fat, interesting racial differences surfaced. In both racial groups, high VAT was associated with significant and equal reductions in peripheral insulin sensitivity (~38% in whites and blacks). However, the compensatory insulin response to this reduction in insulin sensitivity was significantly different between the two races. In WOA there was a robust, approximately 1.7-fold compensatory increase in first phase insulin secretion, whereas in BOA, there was no change in insulin secretion. Consequently, BOA with high VAT had lower glucose disposition index than those with low VAT, suggestive of a higher diabetogenic risk. It is, however, possible that the observed lack of a difference in first phase insulin in BOA and in glucose disposition index in WOA (low *vs.* high VAT)

is due to inadequate statistical power. Also, as depicted in Fig. 2, in BOA the normal hyperbolic relationship between insulin sensitivity and secretion is disrupted, unlike that in WOA. This is suggestive of a limited capacity of the β -cell to increase insulin secretion to compensate for the insulin resistance associated with high VAT in blacks. This impaired ability of the β -cell to compensate for decreasing insulin sensitivity is believed to be an early abnormality leading to IGT and progressing to type 2 diabetes (48). Therefore, it is possible that the increased rates of type 2 diabetes in black obese adolescents are a consequence of a limited capacity of the β -cell to compensate for insulin resistance. We did not perform OGTTs in these obese adolescents, all of whom had normal hemoglobin A_{1c} levels. It is however possible that some of the subjects had impaired glucose tolerance, which we have demonstrated to be associated with low first phase insulin secretion, at least in obese PCOS girls (20).

The race-related differential impact of VAT is also evident with respect to CVD risk factors, but in favor of BOA. Fasting lipid levels were not different in BOA with high *vs.* low VAT. On the contrary, in WOA, total and LD cholesterol and triglycerides were significantly higher, and HDL cholesterol was significantly lower in the high VAT *vs.* low VAT group. Conducive to this lipid profile and consistent with the adult data, WOA with high VAT had a significantly lesser ability to suppress FFA levels during hyperinsulinemia, suggestive of insulin resistance in suppressing lipolysis (28). This phenotype of lipid metabolism consistent with increased visceral obesity was not present in BOA. However, this could be related to the fact that BOA in either the low or high VAT group had lower VAT overall than their respective groups among WOA.

Another health risk factor of obesity and syndrome X is hypertension. Large school-based studies have shown that among overweight children, greater central adiposity is associated with increased clustering of CVD risk factors, including blood pressure (49–51). In agreement with these epidemiological data, our study demonstrates that VAT has a main effect on blood pressure and shows that total body fat correlates independently with systolic and diastolic blood pressure in both whites and blacks. Our results are also in agreement with other studies in black and white children showing that fat distribution is a more important independent correlate of systolic blood pressure than percent body fat (33, 52).

In summary, the present study demonstrates the importance of measuring the VAT depot to better identify obesity and race-related health risks. Even though a similar level of BMI appears to affect metabolism or the cluster of syndrome X differently between blacks and whites, differences in fat distribution partially explain some of these. WOA have higher visceral fat and a more atherogenic risk profile. On the other hand, despite lower visceral fat in blacks, peripheral insulin sensitivity is not better, and insulin secretion appears to be impaired, *i.e.* blacks have a more diabetogenic metabolic profile. We conclude that although increases in VAT adversely affect the cluster of syndrome X in both black and white adolescents, its impact on the delicate balance between insulin sensitivity and secretion and glucose homeostasis is differentially modulated by race.

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