Hyperinsulinemia in African-American Children

Decreased Insulin Clearance and Increased Insulin Secretion and Its Relationship to Insulin Sensitivity

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African-American (AA) children are hyperinsulinemic and insulin resistant compared with American White (AW) children. This study investigated *1*) whether AA/AW differences in insulinemia are associated with differences in insulin clearance; *2*) whether dietary patterns, mainly carbohydrate and fat intake, play a role; and *3*) whether the quantitative relationship between insulin sensitivity and secretion is similar between AA and AW children. Forty-four prepubertal children (22 AA and 22 AW) with comparable body composition and visceral adiposity were studied. All underwent a 3-h hyperinsulinemic (40 mU · m^{-2} · min^{-1})-euglycemic clamp to calculate insulin sensitivity and insulin clearance and a 2-h hyperglycemic clamp (12.5 mmol/l) to assess first- and second-phase insulin responses. Twenty-four–hour food recalls were analyzed for macronutrient intake. Insulin clearance (19.5 ± 0.7 vs. 22.9 ± 1.1 ml · min^{-1} · kg^{-1} fat-free mass [FFM]; *P* = 0.011) and insulin sensitivity were lower in AA versus AW children (14.8 ± 1.0 vs. 18.9 ± 1.4 μmol · min^{-1} · kg^{-1} FFM; *P* = 0.021). Both insulin clearance and insulin sensitivity correlated inversely with dietary fat/carbohydrate ratio, which was higher in AA than in white children. Fasting C-peptide and insulin were higher in AA children with no difference in proinsulin levels. First- and second-phase insulin concentrations and glucose disposition index (insulin sensitivity × first-phase insulin) were higher in AA than in white children (12.8 ± 2.1 vs. 7.2 ± 0.6 μmol · min^{-1} · kg^{-1} FFM; *P* = 0.019). In conclusion, the hyperinsulinemia observed in AA children is due to both lower insulin clearance and higher insulin secretion compared with their white peers. The quantitative relationship between insulin secretion and sensitivity is upregulated in AA children. This suggests that increased insulin secretion in AA children is not merely a compensatory response to lower insulin sensitivity. Dietary factors may have a role. Additional studies are needed to determine whether metabolic/nutritional factors, possibly mediated through free fatty acids, may play a role in the hyperinsulinism observed in AA children. *Diabetes* 51:3014–3019, 2002

W e and others have demonstrated that African-American (AA) children are hyperinsulinemic compared with their American white (AW) peers (1–4). This hyperinsulinemia has typically been explained as a compensatory adaptation to low insulin sensitivity in AAs (2–4). However, another explanation is decreased insulin clearance based on the observation of lower C-peptide to insulin ratios in AA adolescents and adults compared with AWs (5,6). Therefore, one aim of this study was to assess whether AA/AW differences in insulinemia are associated with differences in insulin clearance measured during a hyperinsulinemic-euglycemic clamp. Alternatively, the hyperinsulinemia in AA children could at least in part be the result of primary hypersecretion of insulin. Therefore, we measured first- and second-phase insulin responses during a hyperglycemic clamp. The third aim in our effort to explain racial differences in insulinemia/insulin resistance was to assess whether dietary patterns, particularly carbohydrate and fat intake, play a role. In adults, high fat intake is associated with reduced insulin sensitivity, whereas high carbohydrate intake is associated with enhanced insulin sensitivity (7–10).

AAs are at increased risk for type 2 diabetes. Compared with AWs, rates of diabetes are 70–100% higher in AA men and women (11,12). Parallel with the adult epidemic of type 2 diabetes, there is an "emerging epidemic" of type 2 diabetes in children with overrepresentation of AA children (13,14). The increased risk of type 2 diabetes in AAs has been attributed to insulin resistance. However, insulin resistance alone does not cause diabetes. Glucose homeostasis depends on the balance between insulin sensitivity and insulin secretion. This balance is a hyperbolic relationship between insulin sensitivity and insulin secretion (sensitivity × secretion = disposition index [DI]) (15,16). The DI seems to be a heritable characteristic (16). Those at risk for diabetes have a lower DI, reflecting the inability of the β-cells to compensate for insulin resistance. Thus, the final aim of the present investigation was to evaluate the relationship between insulin sensitivity and β-cell function in AA children in comparison with their AW peers.

RESEARCH DESIGN AND METHODS

All evaluations were performed in the General Clinical Research Center at Children's Hospital of Pittsburgh. Each subject was studied twice, 1–2 weeks

TABLE 1
Study subjects' characteristics

	Black	White	P
n	22	22	
Age (years)	9.9 ± 0.2	9.8 ± 0.2	NS
BMI (kg/m^2)	18.5 ± 0.8	17.8 ± 0.4	NS
Fat mass (kg)	8.0 ± 1.2	7.4 ± 0.7	NS
% Body fat	20.7 ± 2.1	21.3 ± 1.4	NS
FFM (kg)	26.0 ± 0.7	25.4 ± 0.9	NS
VAT (cm^2)	17.6 ± 3.1	16.3 ± 2.6	NS
Testosterone (nmol/l)	20.1 ± 3.8	23.6 ± 3.1	NS
Estradiol (pmol/l)	20.9 ± 1.8	18.3 ± 0.1	NS
DHEAS (μmol/l)	1.2 ± 0.1	1.5 ± 0.2	NS

Data are means $\pm$ SE. Testosterone in boys only and estradiol in girls only. DHEAS, dehydroepiandrosterone sulfate; VAT, visceral adipose tissue.

apart, once during a 3-h hyperinsulinemic-euglycemic clamp to assess insulin sensitivity and clearance and once during a 2-h hyperglycemic clamp to assess insulin secretion, in random order. Clamp experiments were performed after a 10- to 12-h overnight fast. For each study, two intravenous catheters were inserted after the skin and subcutaneous tissues were anesthetized with EMLA cream (Astra Pharmaceutical Products, West Borough, MA). One catheter was placed in a forearm vein for administration of stable isotopes, insulin, and glucose. The second catheter was placed in the dorsal contralateral hand vein, which was heated for sampling of arterialized blood.

Subjects. Twenty-two AA (10 boys and 12 girls; 8.6–11.9 years of age) and 22 AW (10 boys and 12 girls; 8.0–11.7 years of age) prepubertal children participated in this study. Some of these subjects were reported previously (17). All studies were approved by the Human Rights Committee of the Children's Hospital of Pittsburgh. All subjects were in good health assessed by history, physical examination, and routine hematological and biochemical tests. Pubertal development was assessed by careful physical examination according to the criteria of Tanner (18) and confirmed to be Tanner stage 1 by measurements of plasma testosterone in boys, estradiol in girls, and dehydroepiandrosterone-sulfate in both. Table 1 depicts the clinical characteristics of the study participants.

In vivo insulin sensitivity and clearance. Hepatic glucose production was measured with a primed (2.2 μmol/kg)-constant infusion of [6,6-^{2}H$_2$]glucose (Isotech, Miamisburg, OH) at $0.22 \text{ μmol} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ for a total of 2 h as described by us previously (19). Blood was sampled at the start of the stable isotope infusion (-120 min) and every 10 min from -30 to 0 time (basal period) for determination of plasma glucose, insulin, and isotopic enrichment of glucose. Blood was sampled for fasting C-peptide and proinsulin at -60, -20, and -10 min. Fasting turnover calculations were made during the last 30 min (-30 to 0) of the basal 2-h infusion period.

After the 2-h baseline isotopic infusion period, in vivo insulin sensitivity and clearance were evaluated during a 3-h hyperinsulinemic-euglycemic clamp. The insulin infusion rate was $40 \text{ mU} \cdot \text{m}^{-2} \cdot \text{min}^{-1}$. Plasma glucose was clamped at ~5.6 mmol/l with a variable rate infusion of 20% dextrose in water. The rate of glucose infusion was adjusted on the basis of arterialized plasma glucose measurements every 5 min. During the hyperinsulinemic-euglycemic clamp, blood was sampled every 10–15 min for determination of insulin concentrations.

In vivo insulin secretion. First- and second-phase insulin secretions were assessed during a 2-h hyperglycemic clamp as described by us before (2,3). Plasma glucose was increased rapidly to 12.5 mmol/l by a bolus infusion of 25% dextrose and maintained at that level by a variable rate infusion of 20% dextrose for 2 h.

Body composition and abdominal fat. Body composition was assessed at the Obesity/Nutrition Research Center of the University of Pittsburgh with dual-energy X-ray absorptiometry (19). Intra-abdominal fat was assessed by a 10-mm single axial computed tomography scan of the abdomen at the level of L$_{4-5}$ vertebrae as described by us previously (19).

Dietary intake. A 24-h weekday food recall was administered by a trained nutritionist using food models and containers to assess quantity. Children themselves were the primary reporters of their own dietary information, with parents as backup resources to supply more detail as needed. This approach has been used successfully in the Dietary Intervention Study in Children (20). Three 24-h recalls were obtained within a 3-week period, and the mean of the three was analyzed, using the Nutrition Data System of the University of Minnesota (21), to determine total kilocalorie intake, carbohydrate, fat, and

protein. This service was provided through the National Institutes of Health–funded Obesity/Nutrition Research Center of the University of Pittsburgh.

Biochemical measurements. Plasma glucose was measured by the glucose oxidase method with a YSI glucose analyzer (Yellow Springs Instruments, Yellow Springs, OH). Plasma insulin was analyzed by radioimmunoassay using guinea pig anti-human insulin antibodies (Linco Cat #1011, Lot H15-30P [2T]). This insulin assay was among those tested in the task force organized by the American Diabetes Association to assess comparability of blood insulin measurements among various laboratories (22). Cross-reactivity of this assay with C-peptide is <0.1% and with split-proinsulin and proinsulin is 50–60%. However, in the task force, this assay did not read higher for insulin compared with other assays that had narrow specificity to insulin. Neither did the addition of proinsulin result in higher readings of insulin levels (22). Plasma proinsulin and C-peptide determinations were performed at Esoterix, Inc., Endocrinology (previously called Endocrine Sciences, Calabasas Hills, CA) by immunochemiluminescent assays. Deuterium enrichment of glucose in the plasma was determined on a Hewlett-Packard 5971 mass spectrometer coupled to a 5890 series II gas chromatograph as reported by us before (19). Selective ion-monitoring software was used to monitor mass-to-charge ratio (m/z) 200 and 202, reflecting unlabeled and labeled glucose. Standard curves of known enrichments were performed with each assay.

Calculations. The basal rate of appearance of glucose or hepatic glucose production was calculated during the last 30 min of the basal fasting period according to steady-state tracer dilution equations as reported previously (19). Insulin-stimulated glucose disposal was calculated during the last 30 min of the $40 \text{ mU} \cdot \text{m}^{-2} \cdot \text{min}^{-1}$ hyperinsulinemic clamp as described by us before (19). Insulin sensitivity was calculated by dividing insulin-stimulated glucose disposal by steady-state plasma insulin concentration during the $40 \text{ mU} \cdot \text{m}^{-2} \cdot \text{min}^{-1}$ hyperinsulinemic clamp as reported before (23,24). Metabolic clearance rate of insulin was calculated by dividing insulin infusion rate by the Δ increase in circulating insulin concentrations during the $40 \text{ mU} \cdot \text{m}^{-2} \cdot \text{min}^{-1}$ hyperinsulinemic steady state as described by DeFronzo et al. (23) and reported by us before (24). Data are expressed per metabolically active fat-free mass (FFM).

During the hyperglycemic clamp, the first-phase insulin concentration was calculated as the mean of five determinations every 2.5 min during the first 10 min after the bolus dextrose injection. The second phase was calculated as the mean of eight determinations from 15 to 120 min (2,3). Stored plasma samples from the hyperglycemic clamp for C-peptide analyses were destroyed because of thawing after a freezer malfunctioned.

Statistical analysis. Comparison between AA and AW children was made using two-tailed Student's t test for continuous variables. Least-squares regression analysis was used for univariate relationships, and multiple regression analysis was used to assess multivariate relationships. Data are presented as mean $\pm$ SE. Statistical significance was set at $P \leq 0.05$. For examining the hyperbolic relationship between insulin sensitivity and first-phase insulin, statistical modeling was done. The data from the two groups of children were modeled separately. Both linear and nonlinear models were tested. The criteria of statistical significance, a priori set at $P \leq 0.05$, followed by parsimony were used to assess the models. After the model that fit these criteria for the AA and AW children separately was identified, the parameters from the two models were tested for statistical significance and compared. All statistical assumptions were met.

RESULTS

Physical characteristics. The two groups were not different in regard to age, BMI, total body and abdominal adiposity, and pubertal hormonal profile (Table 1).

Basal metabolic data. Fasting glucose concentration was not different between AA (5.2 ± 0.07 mmol/l) and AW children (5.2 ± 0.06 mmol/l). Similarly, hepatic glucose production was not different (17.6 ± 1.4 vs. 16.6 ± 0.7 $\mu\text{mol} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$). However, both fasting insulin and C-peptide levels were higher in AA children compared with AW children (101.0 ± 9.6 vs. 80.2 ± 5.4 pmol/l [$P = 0.03$]; and 0.44 ± 0.03 vs. 0.35 ± 0.02 nmol/l [$P = 0.03$]). Fasting proinsulin levels were not different between AA and AW children (7.1 ± 0.8 and 7.5 ± 0.8 pmol/l). Fasting free fatty acids (FFAs) were not different between the two groups (272 ± 33 vs. 244 ± 22 μmol/l).

Insulin sensitivity and clearance. Steady-state plasma glucose concentration during the hyperinsulinemic-eugly-
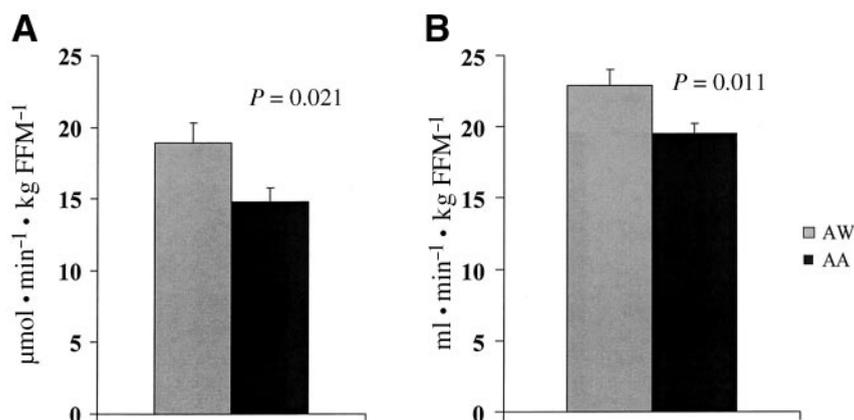
FIG. 1. In vivo insulin sensitivity (*A*) and insulin clearance (*B*) measured during a 40 mU · m^{-2} · min^{-1} hyperinsulinemic-euglycemic clamp in AA and AW children.

cemic clamp was not different between AA (5.6 ± 0.03 mmol/l) and AW (5.7 ± 0.02 mmol/l) children. Steady-state plasma insulin concentration was higher in AA children compared with AW children (668.5 ± 23.2 vs. 580.6 ± 24.6 pmol/l; $P = 0.013$). Insulin-stimulated glucose disposal was similar between the two groups (95.0 ± 5.2 vs. 103.9 ± 4.6 μmol · min^{-1} · kg FFM^{-1}). However, insulin sensitivity was lower in AA versus AW children (14.8 ± 1.0 vs. 18.9 ± 1.4 μmol · min^{-1} · kg FFM^{-1} per pmol/l; $P = 0.021$; Fig. 1). Metabolic clearance rate of insulin was lower in AA compared with AW children (19.5 ± 0.7 vs. 22.9 ± 1.1 ml · min^{-1} · kg FFM^{-1}; $P = 0.011$; Fig. 1). Results were similar when data were expressed in ml/min (505 ± 20 vs. 573 ± 24; $P = 0.033$) or in ml · m^{-2} · min^{-1} (14.5 ± 0.7 vs. 16.8 ± 0.9; $P = 0.037$).

Insulin secretion. First-phase and second-phase glucose concentrations were not different between the two groups (12.3 ± 0.1 vs. 12.6 ± 0.1 and 12.3 ± 0.1 vs. 12.4 ± 0.1 mmol/l, respectively). However, insulin levels were higher in AA children compared with AW children (first phase 993.5 ± 177.1 vs. 391.8 ± 17.7 pmol/l, $P = 0.003$; second phase 905.8 ± 133.7 vs. 554.0 ± 30.6 pmol/l, $P = 0.017$; Fig. 2). In AA but not AW children, first- and second-phase insulin concentrations correlated positively with FFA levels ($r = 0.38$, $P < 0.05$ and $r = 0.41$, $P < 0.05$, respectively).

Glucose DI. The product of insulin sensitivity × first-phase insulin concentration was higher in AA compared with AW children (12.8 ± 2.1 vs. 7.2 ± 0.6 mmol · kg^{-1} · min^{-1} FFM; $P = 0.019$; Fig. 2). Statistical modeling to examine the relationship between insulin sensitivity and first-phase insulin revealed significant racial differences (Fig. 3). In the AA group, the best fit model was [first-phase insulin = a + b/insulin sensitivity], where a = −44.0 and b = 13393.6 ($R^2 = 0.37$, $P = 0.0026$). In AW children, the best fit relationship was [first-phase insulin = a + b/insulin sensitivity], where a = 279.8 and b = 1,862.3 ($R^2 = 0.32$, $P = 0.0057$). The slopes (b value) of the relationship between insulin sensitivity and first-phase insulin were statistically different between the AA and AW groups ($P < 0.05$). Similar relationships were observed between insulin sensitivity versus fasting insulin and fasting C-peptide (Fig. 4).

Dietary intake. AA children reported lower carbohydrate intake (235 ± 15 vs. 322 ± 17 g/day; $P < 0.001$), lower percentage of calories from carbohydrate (50 ± 2 vs. 56 ±

2%; $P = 0.025$), and higher fat/carbohydrate ratio in their diet (0.38 ± 0.03 vs. 0.28 ± 0.02; $P = 0.012$). There were no significant racial differences in daily protein (66 ± 5 vs. 72 ± 5 g/day) and fat intake (86 ± 6 vs. 88 ± 7 g/day). Differences in reported energy intake approached significance (56.7 ± 3.9 vs. 66.5 ± 3.9 kcal · kg^{-1} · d^{-1}; $P = 0.084$). Table 2 depicts the relationship between dietary factors and metabolic parameters. Increased fat/carbohydrate ratio in the diet correlated negatively with insulin sensitivity and insulin clearance and positively with fasting FFA and first-phase insulin. Within each racial group, the correlations were consistent with the total group.
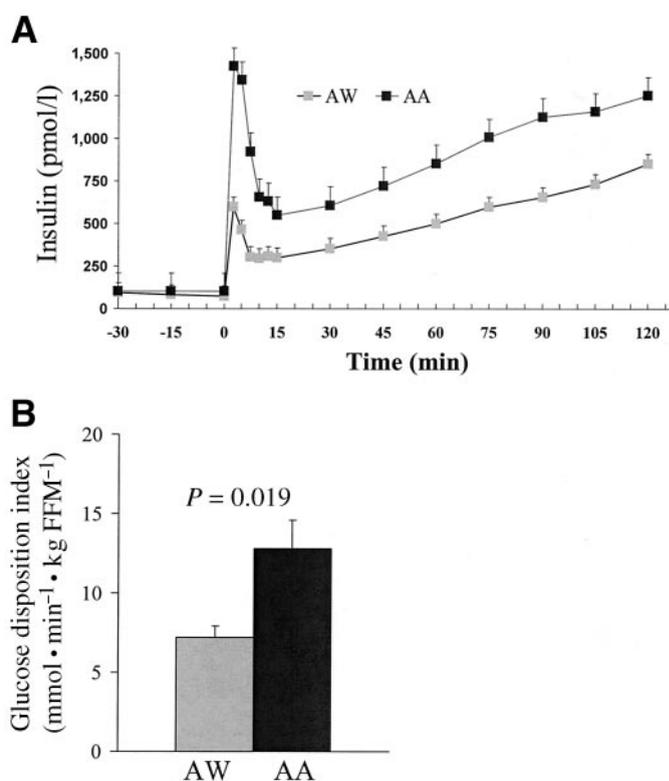

FIG. 2. *A*: Insulin concentrations during a 2-h hyperglycemic clamp (12.5 mmol/l) in AA and AW children. *B*: Glucose DI, the product of insulin sensitivity and first-phase insulin in AA and AW children.
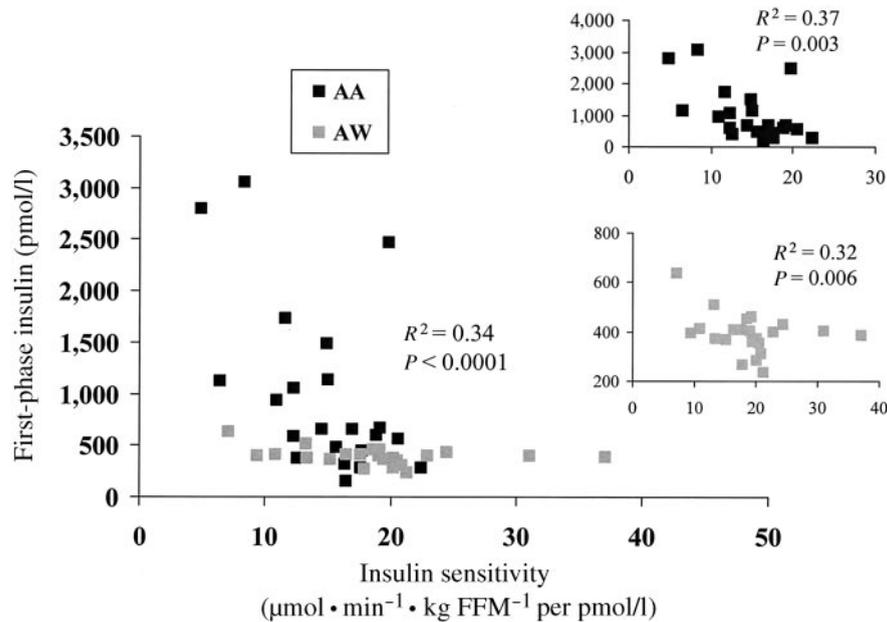
FIG. 3. The relationship between insulin sensitivity and first-phase insulin secretion in AA and AW children. The minimized inserts depict this relationship in each race separately. Please notice the difference in scales for both X and Y.

DISCUSSION

Several studies have demonstrated that AA children have higher fasting and stimulated insulin levels compared with AW children (1–5,25,26). Similar observations have been made in adults (27,28). In general, this hyperinsulinemia is attributed to an adaptive mechanism to compensate for the lower insulin sensitivity by increased insulin secretion
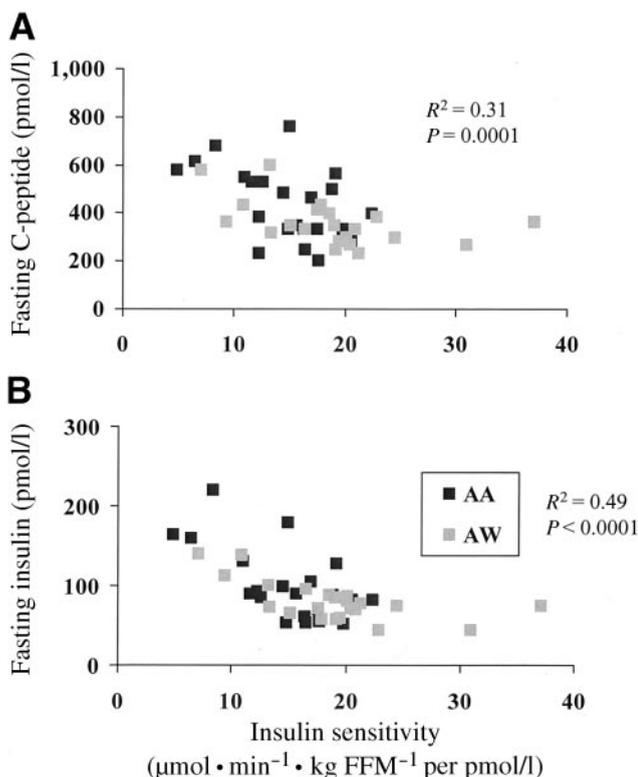

FIG. 4. *A*: Relationship between insulin sensitivity and fasting C-peptide in AA and AW children. *B*: Relationship between insulin sensitivity and fasting insulin in AA and AW children.

in AAs (2–4,26,27). However, it has been demonstrated that diminished insulin clearance is an important underlying mechanism for the hyperinsulinemia found in various insulin-resistant conditions, notably obesity (29,30). In one study, AA adolescents had lower C-peptide to insulin ratio, suggestive of decreased insulin clearance in AAs (5). Similarly, in AA adults, fasting and after oral glucose tolerance test, C-peptide–to–insulin ratios were significantly lower compared with AWs (6). Our results from the present study reveal that insulin clearance is ~15% lower in AA compared with AW children. The lower insulin clearance in AA children is unlikely to be due to body composition differences because AA and AW children had comparable total body and abdominal adiposity. The inverse relationship between dietary fat/carbohydrate ratio and insulin clearance would lead us to postulate that racial differences in dietary intake might be responsible. In animal experiments, after only one week of a diet enriched with a moderate amount of fat, there is a decline in insulin clearance (31). This has been proposed to be a compensation for fat-induced insulin resistance preceding the increase in insulin secretion (31).

Previously, using the hyperglycemic clamp, we reported lower insulin sensitivity in AA adolescents but not in prepubertal AA children compared with AWs (2,3). The present study demonstrates that during a 40 mU · m^{-2} ·

TABLE 2
Correlation of dietary intake with metabolic parameters in both black and white children

	Fat/CHO ratio		% CHO	
	r	P	r	P
Insulin sensitivity	−0.55	<0.001	0.56	<0.001
Insulin clearance	−0.42	0.005	0.44	0.003
First-phase insulin	0.27	0.08	NC	
Fasting FFA	0.55	<0.001	−0.53	<0.001

CHO, carbohydrate; NC, no correlation.

min^{-1} hyperinsulinemic-euglycemic clamp, insulin sensitivity is ~20% lower in AA prepubertal children matched with their AW peers for body composition and abdominal adiposity. The absence of body composition and abdominal fat assessments, the difference in methodologic approach (hyperglycemic versus hyperinsulinemic), and the fewer number of study subjects in the past are most likely responsible for the different results. Other investigators using frequently sampled intravenous glucose tolerance test and oral glucose tolerance test have demonstrated similar findings of lower insulin sensitivity in AA children (4,26). The question is whether this is an inherent race-related reduction in insulin sensitivity or environmentally modulated. Lifestyle differences in dietary intake and physical activity could potentially be responsible. High-fat diets have been implicated in the cause of insulin resistance in adults (10,11,32). In the current study, the higher fat/carbohydrate ratio in the diet of AA children and the inverse relationship with insulin sensitivity suggest that dietary habits may play a role. AA children have been reported to have high fat intake in some (33,34) but not all studies (35). In the study by Lindquist et al. (35), carbohydrate consumption was positively correlated with insulin sensitivity similar to our findings. In a study of adult AA and AW women, consumption of a high-fat diet for only 3 weeks reduced insulin sensitivity in both races (36). However, the magnitude of increase in insulin sensitivity on a low-fat diet was greater in AW women (36). Conversely, low levels of physical activity and physical fitness, which have been described in AA children, may also play a role (37–39). However, in one study, neither physical activity nor maximum oxygen consumption could explain the racial difference in insulin secretion and sensitivity (39).

Consistent with several previous publications, glucose-stimulated insulin response is significantly higher in AA children (1–4). Considering that insulin clearance is decreased in AA children, the higher insulin levels could be partly attributed to lower clearance. In the present study, first-phase insulin was ~150% higher in AA children. In the absence of simultaneous C-peptide levels during the hyperglycemic clamp, it cannot be determined what proportion is due to increased insulin secretion versus decreased insulin clearance. Future studies should include C-peptide measurements simultaneous with insulin to get a better picture. However, in our study, fasting C-peptide levels were ~25% higher in AAs, suggesting that there is significant hypersecretion of insulin in AAs even under fasting euglycemic conditions.

In the current investigation, we detected significant correlations between FFA levels and first- and second-phase insulin concentrations in AAs with no such relationship in AWs. The acute stimulating effect of FFAs on glucose-stimulated insulin secretion has been well described in vitro and in vivo in animals and humans (40–43). In vitro, short-term exposure of islets to fatty acids enhances glucose-stimulated insulin secretion, whereas long-term exposure decreases insulin secretion, hence the term "β-cell lipotoxicity" (40,42). Is it possible that insulin secretion in AA versus AW children may be modulated differentially with metabolic signals? It is our theory that in AA children, FFAs may have a more prominent role in insulin secretion. The positive correlation between FFA levels and dietary fat/carbohydrate ratio suggests that dietary habits may have an impact on FFA levels and consequently insulin secretion. Basal FFA levels support ~30% of basal insulin secretion in adults (44). However, enhancement of glucose-stimulated insulin secretion by FFAs could differ among individuals as has been shown to be the case for obese versus nonobese adults (45). It remains to be determined whether FFAs have an impact on insulin secretion differently in AAs and AWs.

The relationship between insulin sensitivity and secretion is best described by a hyperbolic function (15,16). This indicates that insulin sensitivity $\times$ β-cell function is a constant for a given glucose tolerance. This hyperbolic relationship suggests that differences in insulin sensitivity must be balanced by reciprocal changes in β-cell function to maintain glucose tolerance (16). On the basis of this concept, β-cell function should be assessed relative to insulin sensitivity. The present investigation reveals that glucose DI is significantly higher in AA children. Even though insulin sensitivity is ~22% lower in AAs, glucose DI is ~75% higher. This suggests that for the same degree of insulin sensitivity, insulin secretion is higher in AA children as is evident in Fig. 3. The hyperinsulinism observed in AA children does not seem to be only a compensatory adaptation to lower insulin sensitivity. There seems to be an additional element of insulin hypersecretion that may potentially be modulated through FFAs. The positive correlation between first-phase insulin and dietary fat/carbohydrate ratio approached significance. Additional large-scale studies are needed to determine whether dietary lifestyle differences play a role. Collectively, these findings are of considerable pathophysiologic interest.

In conclusion, the present study demonstrates that AA children have *1*) lower insulin clearance, *2*) lower insulin sensitivity, *3*) higher insulin secretion, and *4*) what seems to be an upregulated β-cell function relative to insulin sensitivity. The observed correlations between dietary habits and metabolic parameters suggest that lifestyle factors may contribute to the observed insulin hypersecretion in AAs. Additional studies are needed to investigate whether intrinsic metabolic factors or extrinsic dietary lifestyle factors are responsible for the racial difference in insulinemia/insulin action. A comprehensive evaluation and understanding of the mechanisms underlying racial differences in insulin resistance in childhood are essential for reducing future morbidity and mortality.

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