Association of Physical Activity and Body Composition With Insulin Sensitivity in a Community Sample of Adolescents

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Objective: To examine how body composition and physical activity are related to insulin sensitivity and secretion in adolescents.

Design: Cross-sectional.

Setting: Baltimore, Maryland.

Participants: Fifty-six healthy adolescents (34 boys and 22 girls; mean [SD] age, 13.3 [1.3] years; 95% were African American) who had been recruited at infancy from a health care clinic serving a low-income, urban community.

Main Exposures: Physical activity was measured for 5 to 7 days by a uniaxial accelerometer placed on the right ankle. Proportion of time spent in play-equivalent physical activity (PEPA) was defined as 1800 or more counts per minute. Body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) was converted to an age- and sex-specific z score.

Main Outcome Measures: Insulin sensitivity, insulin secretion, and disposition index calculated from a fasting oral glucose tolerance test.

Results: Thirty-nine percent of the adolescents had a BMI in the 85th percentile or higher; half of those were overweight (BMI ≥ 95th percentile). Play-equivalent physical activity and BMI z score were not correlated. In multivariate analyses, BMI z score and time spent in PEPA together explained 21% of the variance in insulin sensitivity and 18% in insulin secretion. Independent of each other, high BMI z score and low proportion of PEPA were significantly associated with low insulin sensitivity (partial $r^2=0.14$ and 0.10, respectively) and high insulin secretion (partial $r^2=0.10$ and 0.10, respectively), but not with disposition index.

Conclusions: In a cohort of urban, predominantly African American adolescents, both body composition and physical activity were independently associated with insulin sensitivity. At this point, insulin secretion is appropriately regulated.

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serving a low-income, urban community. All youths had been
born at term (>37 weeks) with birth weight appropriate for ges-
tational age and had no documented congenital or disabling con-
ditions. Seventeen percent of the youths had experienced growth
faltering in the first 2 years of life (weight for age or weight for
height <fifth percentile based on age- and sex-adjusted growth
charts), but by 6 years of age, all faltering children had experi-
enced growth recovery, their growth parameters being higher than
the fifth percentile.16 None of the youth had a chronic disease
associated with an increased risk of type 2 diabetes and none had
been referred for services related to overweight. Among ethnic
and racial groups defined by the investigators with a write-in cat-
egory, 93% of the adolescents identified themselves as African
American and 5%, as white. This ethnic/racial information is re-
ported because the prevalence of diabetes differs between eth-
nic and racial groups.17 Those who identified as white are in-
cluded in the report despite their low number, making up a racially
mixed but socioeconomically homogeneous sample.

The protocol was approved by the institutional review board
of the University of Maryland. Signed consent was obtained from
parents and signed assent, from youths. Parents and adoles-
cents were compensated for transportation and participation.

PROCEDURES

Anthropometric and Sociodemographic Measures

The adolescents and parents participated in a baseline evalu-
ation at our clinical laboratory. Body weight was measured to the
nearest 0.1 lb and converted to kilograms; height was measured
with a wall-mounted stadiometer to the nearest 0.1 cm. Body mass
index (BMI) was calculated as weight in kilograms divided by
height in meters squared. The BMI values were converted to z
scores and percentiles based on the 2000 Centers for Disease Con-
trol and Prevention age- and sex-specific tables18 using algo-
rithms obtained from and explained at the Centers for Disease
Control and Prevention Web site.19 In brief, the z score for a given
BMI was calculated from empirical age and sex LMS parameters
where M is the median, S, the generalized coefficient of varia-
tion; and L, the power in the Box-Cox transformation. Subjects
were divided into the following categories based on their age-
adjusted, sex-specific BMI percentiles: normal weight (<85th per-
centile), at risk for overweight (85th percentile and <95th per-
centile), and overweight (≥95th percentile).

Parents completed questionnaires on demographic infor-
mation and identified family members with diabetes. Using the
poverty ratio equation provided by the US Census Bureau,20 the
family’s poverty ratio was calculated and compared with the
Poverty Index.

Physical Activity

At the conclusion of the baseline evaluation, a uniaxial acceler-
ometer (Actiwatch; Mini Mitter Co Inc. Bend, Oregon) was
placed on the right ankle with a nonremovable, reinforced hos-
pital band. The accelerometer was worn next to the skin, un-
der socks. The accelerometer summarized activity as “counts”
per 1-minute epoch. Discarding data from the first and last days
of wear, which were incomplete, data were available for 5 (n=3),
6 (n=27), or 7 consecutive days (n=26), respectively. Al-
though the 5- and 6-day periods disproportionately repre-
sented weekends, during which the adolescents were less ac-
tive—approximately 13% fewer daily counts on Saturdays and
Sundays compared with nonweekend days—the resulting over-
all systematic underestimation in subjects wearing the accel-
rometers for 5 and 6 days was calculated to be a modest 1.6%
and 0.8%, respectively. When the adolescents returned to the
clinic to have the accelerometers removed, data were ex-
tracted from the accelerometer’s memory and processed with
a program written in SPSS (SPSS Inc, Chicago, Illinois) as fol-
lows. Each hour with a mean activity of less than 53 counts/
min was considered “sleep.” The proportion of nonsleep time
spent in play-equivalent physical activity (PEPA), defined as
more than 1800 counts/min (see next paragraph), was calcu-
lated. In addition, we calculated mean daily activity counts as
a measure of total activity.

The Actiwatch accelerometer worn on the knee has been vali-
dated as a measure of energy expenditure against indirect calo-
rimetry in children.21 We placed the accelerometer on the right
ankle, rather than the knee, because our experience indicated
better acceptability. To identify an appropriate threshold for PEPA
and to compare ankle and knee placement, we conducted a sepa-
rate substudy with 25 participants (10 boys and 15 girls; mean
[SD] age, 14.6 [1.7] years) who wore an Actiwatch accelerom-
eter on the right knee and ankle during a 20-minute free-play
session in a gymnasium furnished with age-appropriate exer-
cise equipment and toys. The mean (SD) ankle counts per minute
were 3003 (1338). All individual means were higher than 1800
counts/min (range, 1941-5924 counts/min), except 3 individu-
als who had mean values ranging from 235 to 670 counts/min
and stood out by having spent the entire session riding station-
ary bicycles. Therefore, we chose 1800 counts/min as a thresh-
old for PEPA. The ankle and knee placement counts were highly
correlated (r=0.94; P<.001). knee counts amounting to ap-
proximately two-thirds of ankle counts, including in those who
rode stationary bicycles. In summary, the methodological sub-
study showed that (1) the 1800 counts/min PEPA threshold con-
sistently identified a wide range of free-play activities, with the
exception of stationary bicycling, and (2) ankle counts during
free play were highly correlated with knee counts, shown by oth-
ers20 to be correlated with energy expenditure.

Each accelerometer was used multiple times (median num-
ber of uses, 11). The accelerometers were delivered calibrated
to the manufacturer’s standards. For each accelerometer, we
tested for subsequent calibration drift by (1) visually examin-
ing plots of mean daily activity counts (7-day mean for each
subject) against recording start date and (2) testing, by mul-
tiple linear regression adjusting for age and sex, whether re-
cord start date was a determinant of mean daily activity
counts. We did not identify any drift.

Body Composition

When the youths returned to have the accelerometer re-
moved, they participated in tests at the General Clinical Re-
search Center, following a standardized protocol. First, a
total-body dual energy x-ray absorptiometry (DEXA) scan was
performed on a Hologic QDR 4500 W scanner (Hologic Inc,
Bedford, Massachusetts).

Percentages of body fat and abdominal fat were calculated
using software provided by the scanner manufacturer. Abdomi-
nal fat was defined as the percentage of fat in an abdominal region-
of-interest rectangle. The horizontal sides of the rectangle were
drawn at the upper edge of the body of the second lumbar vert-
tebra and the lower edge of the body of the fourth lumbar ver-
tebra, respectively. The vertical sides connected the lateral infer-
ior borders of the rib cage and the iliac crest. The usefulness of
abdominal region-of-interest analysis of DEXA in predicting intra-
abdominal fat has been independently validated.22,23

Oral Glucose Tolerance Test

Immediately following the DEXA scan, a fasting 2-hour oral
glucose tolerance test (OGTT) was performed according to
American Diabetes Association guidelines observing the pediatric dosing regimen. Determination of plasma glucose concentration was performed by the glucose oxidase method, using automated equipment. Plasma insulin concentration (in microunits per milliliter) was determined by an enzyme-linked immunosorbent assay method using commercial kits (Linco Research Inc, St Charles, Missouri). Impaired glucose tolerance was defined as a fasting plasma glucose level lower than 126 mg/dL and a 2-hour plasma glucose level of 140 mg/dL or higher and lower than 200 mg/dL.

Insulin sensitivity (SI) was calculated as per Matsuda and DeFronzo as 10,000 divided by the square root of (fasting insulin level × fasting glucose level × mean OGTT insulin × mean OGTT glucose) where mean OGTT insulin and glucose are the mean levels at the 30-, 60-, 90-, and 120-minute points of the OGTT. The Matsuda and DeFronzo index has been validated in children against the hyperinsulinemic, euglycemic clamp.

Insulin secretion was quantified as the corrected insulin response (CIR) based on glucose and insulin levels at the 30-minute point of the OGTT (CIR30), calculated as insulin30/(glucose30 × (glucose30–70 mg/dL)). This index has been validated against the acute insulin response to glucose, determined 3 to 5 minutes after the administration of a 25-g intravenous glucose bolus. None of the subjects had glucose30 values lower than 70 mg/dL. SI and CIR30 will be reported without their units in this article.

The DI was calculated as $SI \times CIR_{30}$.

DATA ANALYSIS

Comparisons of variables by BMI category were done using analysis of variance for continuous variables and $\chi^2$ tests for categorical variables. Bivariate relationships among variables were examined using Pearson correlation. Multiple regression analysis was used to find the determinants of insulin sensitivity. Insulin sensitivity index and other normally distributed variables were log transformed to approximate a normal distribution. With a sample size of 56, we had 81% power to detect a (true) effect size of $r = 0.36$, as determined with Power and Precision software (Biostat, Englewood, New Jersey). Fewer than 5% of the data points were missing, primarily because of clerical or administrative error. Imputation by mean substitution within BMI category was used to replace missing values.

RESULTS

Table 1 shows physical characteristics by BMI category. Of all 56 youths, 23 had a family history of diabetes, among either parents (n = 3), grandparents (n = 18), or both (n = 2). Being overweight was associated with having a history of diabetes in the parents (P = .02) or both the parents and the grandparents (P = .02), but not in the grandparents alone. Neither age, sex, time spent in PEPA, fasting glucose level, household income, poverty level, or history of failure to thrive differed by BMI category. Four subjects had impaired glucose tolerance. Three of these had a BMI higher than the 95th percentile. Thus, of the 11 adolescents in the overweight (≥95th percentile) BMI category, 3 (27%) had impaired glucose tolerance. Boys and girls did not differ by BMI z score, but on average, boys had a lower percentage of body fat (mean [SD], 19.1% [10.0%] vs 26.6% [8.2%]) and abdominal fat (mean [SD], 16.4% [11.5%] vs 23.0% [10.1%]) than girls, spent 36% more time in PEPA, and collected 14% more accelerometer counts overall (for all sex comparisons, P < .05). Insulin sensitivity did not differ by sex, but girls had lower fasting plasma glucose levels and higher insulin secretion.

BIVARIATE CORRELATIONS

Table 2 shows bivariate correlations between the variables. When boys and girls were considered separately, PEPA declined with age in girls ($r = −.52; P = .01$) but not in boys ($r = −.24; P = .16$). Figure 1 shows the relation between insulin secretion and insulin sensitivity. This relation is hyperbolic, with values clustering around the curve representing the median DI (4.38). Eight of the 11 overweight teens had values lower than the median DI but the difference in the proportion of overweight youths vs youths with a BMI lower than the 95th percentile who were below the median DI did not reach statistical significance ($P = .20$). Two normal-weight girls stood out as having very high CIR30 insulin secretion values (>14). Mathematically, their high CIR30 insulin secretion values were explained by the fact that they had the lowest glucose30 values of the whole sample (75 mg/dL and 80 mg/dL, respectively) accompanied by typical insulin30 values.
MULTIVARIATE RELATIONSHIPS

Table 3 shows multiple regression models that include the significant determinants of insulin sensitivity and insulin secretion. Neither age nor sex was a significant determinant in any tested model. The models with BMI z score and time spent in PEPA as the sole determinants of insulin sensitivity explained 21% of the variance in insulin sensitivity (r² = 0.21; partial r² = 0.14 and 0.10, respectively) and 18% of the variance in insulin secretion, (r² = 0.18; partial r² = 0.10 and 0.10, respectively). Models in which BMI z score was replaced by other measures of adiposity (BMI, percentage of total body fat, or percentage of abdominal fat) provided an almost identical fit. Models that included more than 1 measure of adiposity were not tested because of collinearity and high variance inflation estimates (eg, for total fat and abdominal fat, r = 0.95; variance inflation estimate = 16.9). When PEPA was replaced by mean daily activity counts to evaluate the importance of cumulative activity rather than intensity, insulin sensitivity was no longer significantly correlated with activity (P = .09), only with BMI z score (P = .009). Insulin secretion, on the other hand, was correlated with mean daily activity counts (P = .03) and BMI z score (P = .03). Neither history of failure to thrive, family income, poverty, or family history of type 2 diabetes nor the adiposity × PEPA interaction was a significant determinant in any model.

In a linear regression model in which the dependent variable was DI, neither PEPA nor BMI z score (or any other measure of activity or body composition) was a significant independent determinant. However, as shown in Figure 2, where the markers are coded to identify subjects higher and lower than the median of PEPA, teens higher than the median for PEPA were preferentially toward the right end of the curve (higher than the median insulin sensitivity) (18 of 28; P < .05 by χ² test; ratio identical after adjustment for body composition).

Based on studies in adults, the disease process leading to type 2 diabetes is classically described in 2 stages.28 The first stage is characterized by a decline in the sensi-

**Table 2. Bivariate Correlations**

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Age</th>
<th>BMI</th>
<th>BMI z score</th>
<th>Total Body Fat, %</th>
<th>Abdominal Fat, %</th>
<th>Mean Daily Activity Counts</th>
<th>PEPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting insulin level</td>
<td>0.06 (0.65)</td>
<td>-0.15 (0.27)</td>
<td>0.87 (&lt;.001)</td>
<td>0.86 (&lt;.001)</td>
<td>-0.86 (&lt;.001)</td>
<td>-0.97 (&lt;.001)</td>
<td>0.91 (&lt;.001)</td>
</tr>
<tr>
<td>Fasting glucose level</td>
<td>0.08 (0.71)</td>
<td>0.05 (0.70)</td>
<td>0.007 (0.96)</td>
<td>-0.19 (0.17)</td>
<td>-0.13 (0.35)</td>
<td>0.91 (0.14)</td>
<td></td>
</tr>
<tr>
<td>2-h glucose</td>
<td>0.02 (0.90)</td>
<td>0.09 (0.52)</td>
<td>0.05 (0.71)</td>
<td>-0.002 (0.99)</td>
<td>0.07 (0.62)</td>
<td>0.05 (0.71)</td>
<td></td>
</tr>
<tr>
<td>Log (insulin sensitivity)</td>
<td>0.07 (0.64)</td>
<td>-0.16 (0.23)</td>
<td>-0.08 (0.58)</td>
<td>-0.23 (0.09)</td>
<td>-0.18 (0.20)</td>
<td>0.24 (0.07)</td>
<td></td>
</tr>
<tr>
<td>Disposition index</td>
<td>-0.12 (0.35)</td>
<td>0.23 (0.09)</td>
<td>0.30 (0.02)</td>
<td>0.30 (0.03)</td>
<td>0.30 (0.02)</td>
<td>-0.30 (0.02)</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Multivariate Regressions

<table>
<thead>
<tr>
<th>Independent Variables</th>
<th>Model 1: Insulin Sensitivity</th>
<th>Model 2: Insulin Secretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI z score</td>
<td>P = .005; −198 ± 68 × 10⁻³</td>
<td>P = .02; 255 ± 104 × 10⁻³</td>
</tr>
<tr>
<td>PEPA</td>
<td>P = .02; 7.40 ± 3.09</td>
<td>P = .02; −11.61 ± 4.73</td>
</tr>
<tr>
<td>r²</td>
<td>0.21</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; PEPA, play-equivalent physical activity. a Each column corresponds to a multivariate model whose dependent variable is log-transformed insulin sensitivity or log-transformed insulin secretion and whose independent variables are BMI z score and proportion of time spent in PEPA. Numbers are P values and regression coefficients ± SE.
tivity of peripheral insulin receptors to insulin. This decline, referred to as insulin resistance, is observable long before the onset of diabetes and is associated with a high percentage of body fat, especially abdominal body fat, and low levels of physical activity. The insulin resistance is initially accompanied by a compensatory increase in insulin secretion by the pancreatic beta cells. In the general nondiabetic population with intact beta-cell function, insulin secretion and sensitivity are therefore related to obesity and physical activity in a converse fashion. The arithmetic product of insulin secretion and insulin sensitivity tends to equal a constant, termed the disposition index. Consequently, in a coordinate system with the absissa representing insulin sensitivity and the ordinate representing insulin secretion, the curve connecting individual values of insulin secretion and sensitivity takes the shape of a hyperbola, as confirmed in multiple populations. Relatively insulin-resistant individuals may be on the hyperbolic curve derived from the general population if their insulin secretion is high enough to compensate for the insulin resistance and maintain glucose homeostasis. With intact beta-cell function, perturbations in insulin sensitivity are accompanied by complementary changes in insulin secretion that fit the hyperbolic model, as observed in studies of pregnancy, lipid infusion, weight gain, or weight loss.

The second stage of the 2-stage model ensues when the beta cells are unable to maintain sufficient insulin secretion to compensate for the declining insulin receptor sensitivity. As demonstrated by Weyer et al in prospective studies of subjects who gained weight, subjects who progress to diabetes do not move leftward along the hyperbolic curve (ie, experience a concomitant decrease in insulin sensitivity and increase in insulin secretion) but in a direction perpendicular to and below the curve (ie, experience a concomitant decrease in insulin sensitivity and insulin secretion) toward a lower DI. Consistent with these observations, the most immediate indicator of impending beta-cell failure and diabetes is a decrease in DI. Independently of insulin sensitivity, defects in insulin secretion (a low first-phase insulin response) predict the development of diabetes.

In our study, both adiposity and level of physical activity were significant, independent determinants of insulin sensitivity and secretion, such that a high degree of adiposity and a small proportion of time spent in PEPA activity are accompanied by complementary changes in insulin secretion that fit the hyperbolic model, as observed in studies of pregnancy, lipid infusion, weight gain, or weight loss.

Prospective studies showing that insulin resistance predicts diabetes suggest that if left unchecked, insulin resistance and consequent increased insulin secretion will often lead to beta-cell failure. In the present study, analysis by BMI category or PEPA level did not identify any group whose DI was diminished in a statistically significant fashion, suggesting that at the group level, beta-cell insulin secretion was appropriate. Inference from Weyer et al suggests that as long as DI has not deterio-

ated, an effective behavioral intervention to increase physical activity and reduce weight might achieve the goal of averting diabetes.

The multivariate models were practically identical regardless of the measure of adiposity (BMI z score, BMI, percentage of total body fat, or percentage of abdominal fat). If anything, relations were stronger with BMI z score than with percentages of total body or abdominal fat, which is surprising because accretion of body fat, especially abdominal fat, is thought to underlie the association between insulin resistance and a high BMI. We speculate that BMI z score has extra leverage in the models compared with the DEXA-derived measures because BMI z scores express individual deviation from the norm as a multiple of the empirical age- and sex-specific standard deviation. The DEXA-derived measures were not transformed to z scores because of a lack of normative data.

Of the 11 adolescents in the overweight (≥95th percentile) BMI category, 3 (27%) had impaired glucose tolerance, a prevalence close to the 21% reported in a multiethnic cohort of 11- to 18-year-olds referred to an obesity treatment clinic and the 27% reported in 8- to 13-year-old Hispanic children with a BMI higher than the 85th percentile.

A history of failure to thrive was not related to physiological precursors of type 2 diabetes. Thus, although there is evidence that reduced prenatal growth is associated with metabolic disturbances, our study does not provide evidence that reduced growth in the immediate postnatal period influences insulin sensitivity later in childhood.

Analogous to other cross-sectional studies in children, we did not demonstrate an association between physical activity levels and body composition. Although one might expect a correlation based on the notion that physical activity leads to weight loss or, as supported by prospective studies in adults, that overweight leads to inactivity, the absence of a correlation between activity level and body composition in this or any other cross-sectional study does not refute cause-and-effect relations between physical activity and body composition. As other investigators, we found that physical activity in girls declined in adolescence.

In addition to the cross-sectional nature of the study, which limits our ability to make inferences about caus-
sality and temporality, several methodological issues should be considered in interpreting these findings. First, a larger sample size would have yielded increased statistical power to uncover associations. Second, we did not use a rigorous selection strategy to achieve a statistically representative sample of a particular defined population. Although we cannot rule out some selection bias, our community sample compares favorably with referred samples in being representative of mostly African American, urban youth. Because the subjects were infrequently in contact with the research team throughout their lives, it is unlikely that having been observed from infancy influenced behavior. Third, the age group studied (11-16 years) coincides with the onset of puberty, which influences insulin sensitivity and fat accretion. Self-reported Tanner staging of pubertal development was part of the protocol but approximately two-thirds of subjects chose to skip the questions. However, the typical time curve and direction of adiposity changes that differ between boys and girls during puberty were accounted for by the age and sex standardization incorporated in BMI z score.

In addition to the use of a community sample as opposed to a referred sample, the strengths of the study include the sophistication of the measurements (i.e., the use of an OGTT as opposed to fasting measurements to explore insulin dynamics and the use of accelerometry to objectively assess activity).

In conclusion, the study shows that in a community sample of African American adolescents, both adiposity and lack of PEPA are independent statistical determinants of low insulin sensitivity and high insulin secretion, both of which have been identified as precursors of type 2 diabetes. Together, adiposity and PEPA, both of which are influenced by the environment, explained 18% to 21% of the variance in insulin sensitivity and secretion. Further analysis involving the DI, a measure of beta-cell secretory capacity, was consistent with these observations.

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