Insulin Sensitivity, Cardiorespiratory Fitness, and Physical Activity in Overweight Hispanic Youth

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Abstract

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Objective: To determine whether cardiorespiratory fitness and/or physical activity (PA) were related to measures of insulin sensitivity and secretion independent of body composition in overweight Hispanic children.

Research Methods and Procedures: Ninety-five Hispanic children ($n = 55$ boys; $n = 40$ girls; 8 to 13 years old) participated in this investigation. The frequently sampled intravenous glucose tolerance test was used to determine the insulin sensitivity index (SI), the acute insulin response, and the disposition index. Cardiorespiratory fitness [maximal oxygen uptake ($V\mathrm{O}_{2\mathrm{max}}$)] was evaluated using a treadmill protocol, and PA was determined by an interviewer-administered questionnaire. Body composition was measured using DXA.

Results: Unadjusted correlations indicated that $V\mathrm{O}_{2\mathrm{max}}$ (milliliters of O_2 per minute) was negatively related to SI ($r = -0.46$, $p < 0.05$) and disposition index ($r = -0.31$, $p < 0.05$) and positively associated with fasting insulin ($r = 0.29$, $p < 0.05$), but these relationships were no longer significant once gender, Tanner stage, fat mass, and soft lean tissue mass were included as covariates (all $p > 0.05$). Multivariate linear regression analysis showed that body fat mass explained 53% of the variance in SI and that $V\mathrm{O}_{2\mathrm{max}}$ (milliliters of O_2 per minute) was not independently related to SI. Cardiorespiratory fitness was positively related to both fat mass ($r = 0.43$, $p < 0.001$) and soft lean tissue mass ($r = 0.89$, $p < 0.001$). PA was not related to any measure of insulin sensitivity and secretion.

Discussion: Cardiorespiratory fitness, as determined by $V\mathrm{O}_{2\mathrm{max}}$ (milliliters of O_2 per minute), was not independently related to insulin sensitivity or secretion, suggesting that $V\mathrm{O}_{2\mathrm{max}}$ influences insulin dynamics indirectly through fat mass.

Key words: Hispanic, children, physical fitness, body composition

Introduction

The prevalence of overweight in youth has increased dramatically in recent years and has disproportionately affected many ethnic groups including Hispanics. The most recent data from the 1999 to 2000 National Health and Nutrition Examination Survey indicate that ~40% of 6- to 11-year-old Hispanic youth possess an age- and gender-specific BMI ≥ 85th percentile, a level that is approximately double that found in whites (1). It is clear that the health risks, such as fat hyperinsulinemia (2), impaired glucose tolerance (IGT)[1] (3), and type 2 diabetes (4), that accompany a high degree of body fat manifest early in life. Although a host of hereditary and environmental variables are linked to these health risks, the relationships between metabolic risk factors for type 2 diabetes and lifestyle-related variables, including cardiorespiratory fitness and

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[1] Nonstandard abbreviations: IGT, impaired glucose tolerance; PA, physical activity; $V\mathrm{O}_{2\mathrm{max}}$, maximal oxygen uptake; FSIVGTT, frequently sampled intravenous glucose tolerance test; OGTT, oral glucose tolerance test; GCRC, General Clinical Research Center; RER, respiratory exchange ratio; SI, insulin sensitivity index; AIR, acute insulin response; DI, disposition index; NGT, normal glucose tolerance.

physical activity (PA), have not been investigated previously in overweight Hispanic youth with a family history of type 2 diabetes, a subgroup of children that is at increased health risk.

Current reviews (5–7) suggest that a physically active lifestyle has beneficial effects on glucose homeostasis and insulin sensitivity through a number of mechanisms including increased expression of glucose transporters (e.g., glucose transporter-4) (8), enhanced expression and/or activity of proteins involved in insulin signaling transduction in skeletal muscle (9), and increased glycogenolysis during exercise that may stimulate glucose uptake (5). Maximal oxygen uptake ($V\text{O}_{2\text{max}}$), a measure of cardiorespiratory fitness that may also reflect chronic PA behaviors, is positively related to glucose transporter-4 concentration and insulin-dependent glucose disposal in muscle (10). To date, most of the data supporting a positive relationship between fitness/activity and insulin sensitivity are derived from adults, but extending findings from adults to younger populations would be inappropriate given the physiological changes that occur during periods of growth and maturation. The few studies that have explored such associations have been equivocal. Some have suggested a positive relationship between an active lifestyle and insulin sensitivity (11,12), whereas others have shown that cardiorespiratory fitness and PA are not independently related to insulin concentrations (13,14). These discrepant findings may be the result of several factors including the various methodologies used to estimate body composition, insulin sensitivity, cardiorespiratory fitness, and PA and/or the different age groups, levels of maturation, and ethnicities of the study populations. Several (13–16), but not all (12), previous studies have used fasting insulin as a measure of insulin sensitivity, but more specific and direct testing procedures should provide a better estimate of insulin dynamics.

In the current study, we evaluated the relationships between insulin sensitivity/secretion and fitness/activity using sensitive methodologies including the frequently sampled intravenous glucose tolerance test (FSIVGTT) and an all-out, progressive, continuous treadmill protocol, respectively. The direct relationships between insulin sensitivity/secretion and fitness/activity variables were explored after controlling for body fat and lean tissue mass because body composition is known to influence both insulin and fitness measures. To date, very little research has evaluated the potential relations between lifestyle-related behaviors and risk factors for type 2 diabetes in youth, and we are unaware of any analyses carried out with young Hispanics. We have observed previously that Hispanic children have ~13% lower cardiorespiratory fitness levels compared with white boys and girls (G.Q. Shaibi, G.D.C. Ball, and M.I. Goran, unpublished data). Because overweight Hispanic youth are at increased risk of developing type 2 diabetes early in life, we postulated that low cardiorespiratory fitness and/or PA may result in decreased insulin sensitivity and/or secretion. Thus, the goals of the present investigation were to determine whether cardiorespiratory fitness and/or PA were associated with measures of insulin sensitivity and/or secretion and if these associations were independent of body composition in a sample of overweight Hispanic youth with a family history of type 2 diabetes.

Research Methods and Procedures

Subjects

Boys and girls were recruited for this investigation from in and around the greater Los Angeles County area through medical referrals, advertisements, and word of mouth. The current analyses included 95 children ($n = 55$ boys and $n = 40$ girls) who are part of the University of Southern California Study of Latino Adolescents at Risk for Diabetes, an ongoing longitudinal study exploring behavioral and metabolic risk factors for type 2 diabetes. Study participants had to satisfy the following criteria for inclusion: age- and gender-specific BMI ≥ 85th percentile (17), Hispanic background (all four grandparents of Hispanic descent), 8 to 13 years of age, positive family history for type 2 diabetes (sibling, parent, or grandparent), and absence of diabetes evaluated through an oral glucose tolerance test (OGTT) and established diagnostic criteria (18). The children in this study, selected from a larger population, represent a subgroup of boys and girls for whom complete data for all variables were available. Participants were not currently taking any medications or carrying a previous clinical diagnosis known to influence body composition, insulin sensitivity, physical activity, or dietary intake. Before the onset of testing, informed consent and assent were obtained from parents and children, respectively. This investigation was approved by the Institutional Review Board of the University of Southern California, Health Sciences Campus.

Protocol

Outpatient Screening Visit. Children arrived at the University of Southern California General Clinical Research Center (GCRC) at ~8 AM after an overnight fast. Physical maturation was assessed by a pediatrician according to the criteria of Marshall and Tanner (19,20); Tanner staging was based on breast stage in girls and pubic hair stage in boys. The clinical nursing staff measured height to the nearest 0.1 cm using a wall-mounted stadiometer and weight to the nearest 0.1 kg using a medical balance beam scale; BMI was subsequently calculated. A topical anesthetic (EMLA cream, Aztrozeneca LP, Wilmington, DE) was applied to one arm, and at ~9 AM, a flexible intravenous catheter was placed in an antecubital vein. For the OGTT, subjects ingested 1.75 grams of oral glucose solution per kilogram body weight (to maximum 75 grams) at time 0. Blood was sampled and assayed for glucose at −5 minutes (fasting)

and 2 hours after the glucose load. There were no diagnoses of type 2 diabetes in this sample, although 28% were identified as having IGT.

Inpatient Visit. At least 7 days after the OGTT outpatient visit, children were admitted to the GCRC at the Los Angeles County Hospital in the afternoon for an in-patient visit. Boys and girls underwent a brief physical exam and completed body composition, cardiorespiratory fitness, PA, and FSIVGTT measurements.

Body Composition. A DXA scan was used to measure total body composition (fat mass, soft lean tissue mass, total bone mineral content, and percentage body fat) using a Hologic QDR 4500W (Bedford, MA).

Cardiorespiratory Fitness. Participants completed an all-out, progressive, continuous treadmill protocol (21). After being familiarized with the exercise equipment, the children practiced walking on the motorized treadmill until they were able to walk without holding the railings. The children walked for 4 minutes at 0% grade and 4 km/h, after which the treadmill grade was raised to 10%. Each ensuing work level lasted 2 min, during which the grade was increased by 2.5%. The speed remained constant until a 22.5% grade was reached, at which time the speed was increased by 0.6 km/h until the subject reached exhaustion. Respiratory gases were collected and measured using open circuit spirometry and analyzed on a MedGraphics CardiO_2/CP Combined Exercise System (St. Paul, MN). Heart rate was measured continuously using a Polar Vantage XL heart rate monitor (Port Washington, NY). Absolute $V_{O_{2max}}$ (milliliters of O_2 per minute) was used as a measure of cardiorespiratory fitness. $V_{O_{2max}}$ was achieved if individuals satisfied two of the following three criteria: respiratory exchange ratio (RER) $>$ 1.0, heart rate $\geq$ 195, and a leveling or plateauing of V_{O_2} defined as an increase of oxygen uptake $<$ 2 mL/kg per minute with a concomitant increasing workload.

Physical Activity. Qualitative and quantitative information regarding recreational PA was estimated using the structured activity questionnaire of Kriska et al. (22). Interviewers read a comprehensive list of sports and activities and had subjects and their parents indicate how much time was spent on each extracurricular activity outside of school during the previous 12-month period. The average number of hours per week of recreational PA was subsequently calculated to represent the activity level of each child over the past year.

FSIVGTT. After anthropometric, body composition, cardiorespiratory fitness, and physical activity measurements, boys and girls were served dinner and an evening snack; all food was consumed before 8 P.M. Only water was permitted between 8 P.M. and testing the following morning. At 6:30 AM the following morning, a topical anesthetic was applied to the antecubital area of both arms, and intravenous catheters were inserted into both arms at ~7:30 AM. Two fasting blood samples were drawn at -15 and -5 minutes for determining basal insulin and glucose. At time 0, the FSIVGTT was initiated with glucose (25% dextrose, 0.3 g/kg body weight) being administered intravenously. Subsequently, blood samples were collected at the following time points: 2, 4, 8, 19, 22, 30, 40, 50, 70, 100, and 180 minutes. Insulin (0.02 units/kg body weight) (Humulin R; Eli Lilly, Indianapolis, IN) was injected intravenously at 20 minutes. Plasma was analyzed for glucose and insulin concentrations, and these values were subsequently entered into the MINMOD MILLENIUM 2003 computer program (5.16, Richard N. Bergman, Los Angeles, CA) for determining the insulin sensitivity index (SI), the acute insulin response (AIR), and the disposition index (DI) (23–25). SI reflects the increase in fractional glucose disappearance per unit of insulin increase with disappearance resulting from either increased peripheral glucose uptake or decreased hepatic glucose production. AIR reflects the first phase endogenous insulin secretion (within the first 10 minutes) in response to the glucose infusion, whereas DI is the product of SI $\times$ AIR and assesses pancreatic function (26). Glucose was measured in duplicate using a 2700 Analyzer (Yellow Springs Instrument, Yellow Springs, OH) and a glucose oxidase kit. Insulin was assayed in duplicate using a specific human insulin enzyme-linked immunosorbent assay kit (Linco, St. Charles, MO). Because the $V_{O_{2max}}$ test was performed the day before the FSIVGTT, potential existed for this physical activity to have had an acute effect on insulin sensitivity. Although intense, this short bout of exercise (10 to 15 minutes) did not seem to impact SI the following day. Based on data from our laboratory, we have found similar SI levels between those children who did perform a $V_{O_{2max}}$ the previous day ($n = 126$; SI $= 2.1 \pm 1.3 \times 10^{-4}$/min[$\mu$IU/mL]) vs. those children who did not perform a $V_{O_{2max}}$ test the previous day ($n = 38$; SI $= 2.0 \pm 1.3 \times 10^{-4}$/min[$\mu$IU/mL]) (M.I. Goran, unpublished data).

Statistical Analyses

Gender differences in demography, anthropometry, body composition, cardiorespiratory fitness, PA, and biochemical variables were explored using multivariate ANOVA with Bonferroni adjustments for making multiple comparisons. Qualitative (i.e., histograms) and quantitative (i.e., Kolmogorov-Smirnov test of normality) procedures were used to assess data normality. Because of nonnormal distributions, the following variables underwent log transformations: fat mass, soft lean tissue mass, $V_{O_{2max}}$, PA, SI, AIR, DI, fasting insulin, and fasting glucose. Unadjusted Pearson correlations were used to assess the relationships between the dependent (log SI, log AIR, log DI, log fasting insulin, and log fasting glucose) and independent (log $V_{O_{2max}}$ and log PA) parameters. After adjusting for gender, Tanner stage, fat mass, and soft lean tissue mass, partial correlations were calculated for the aforementioned dependent and independent variables. Log SI, log AIR, log DI, log fasting insulin,

Table 1. Anthropometric, body composition, and maturational characteristics (mean ± SD)

	(n = 55)	Girls (n = 40)	Total (n = 95)
Age (years)	11.1 ± 1.7	11.0 ± 1.8	11.1 ± 1.7
Tanner stage	1.9 ± 1.2*	2.9 ± 1.4	2.3 ± 1.4
Height (cm)	150.5 ± 11.4	148.9 ± 12.3	149.8 ± 11.8
Weight (kg)	63.4 ± 18.0	66.4 ± 24.1	64.7 ± 20.7
BMI (kg/m^2)	27.5 ± 4.8	29.2 ± 7.8	28.2 ± 6.4
BMI percentile	97.1 ± 3.0	97.0 ± 3.1	97.0 ± 3.0
Fat mass (kg)	22.9 ± 8.9	26.0 ± 11.7	24.2 ± 10.2
Soft lean tissue mass (kg)	38.1 ± 10.2	36.5 ± 11.4	37.4 ± 10.7

* $p < 0.05$ (boys < girls).

and log fasting glucose were also entered individually into multivariate linear regression models to determine whether the independent variables (log $V\text{O}_{2\text{max}}$ and log PA) contributed significantly to variance in these measures of insulin sensitivity and secretion. Gender, Tanner stage, fat mass, and soft lean tissue mass were entered as covariates in these regression models. SI was also included as a covariate when log AIR was entered as the dependent variable. All statistical tests were performed using SPSS/PC statistical program (version 11.0 for Windows; SPSS, Inc., Chicago, IL) with an a priori significance level set at $p < 0.05$.

Results

The boys and girls in this sample did not differ in any of the anthropometric and body composition variables we measured, although girls were more physically mature than boys (Table 1). Children represented a range of maturational stages [for genders combined: Tanner stage I, 37.9% (n = 36); Tanner stage II, 28.4% (n = 27); Tanner stage III, 10.5% (n = 10); Tanner stage IV, 12.6% (n = 12); and Tanner stage V, 10.5% (n = 10)). Regardless of how cardiorespiratory fitness ($V\text{O}_{2\text{max}}$) was expressed, in absolute terms, relative to body weight, or relative to lean tissue mass, boys possessed greater fitness levels than girls (Table 2). However, no gender differences were observed regarding maximum heart rate, maximum RER, or PA. Boys had higher fasting glucose levels than girls, but both group means were within the normally accepted range. There were no other significant gender differences with respect to measures of insulin sensitivity. Data from boys and girls were combined for all other analyses.

Pearson Correlation Analyses

Log $V\text{O}_{2\text{max}}$ (milliliters of O_2 per minute) was negatively related to log SI and log DI and positively related to log fasting insulin in the unadjusted correlations (Table 3). However, these associations were no longer significant once demographic and body composition variables were controlled for in the partial correlation analyses (Table 3). The adjusted correlation between log SI and log $V\text{O}_{2\text{max}}$ (Figure 1) highlights the fact that once covariates were included in the analysis, there was no significant and independent relationship between SI and cardiorespiratory fitness. In addition, log $V\text{O}_{2\text{max}}$ was positively related to both log fat mass (r = 0.43, $p < 0.001$) and log soft lean tissue mass (r = 0.89, $p < 0.001$). Log PA was associated with log DI (positively) and log fasting glucose (inversely) in both the unadjusted and adjusted correlations (Table 3). However, on further analysis, we observed that one subject had the highest fasting glucose concentration (119 mg/dL), the lowest DI score (326×10^{-4}/min), and the lowest activity level (0.06 h/wk) within the sample. When the extreme values for this individual were excluded from the analysis, the correlations between log PA and log fasting glucose (unadjusted $r = -0.13$, $p = 0.21$; adjusted $r = -0.12$, $p = 0.26$) and log physical activity and log DI (unadjusted $r = 0.05$, $p = 0.62$; adjusted $r = 0.12$; $p = 0.27$) were no longer significant. Because we found no valid reason to exclude this child from our analyses, we present correlations with and without this child included so that our findings can be interpreted accordingly. All of the correlations between measures of insulin sensitivity/secretion and fitness/activity were also calculated separately for gender (boys and girls) and glucose tolerance [IGT and normal glucose tolerance (NGT)], but these relationships did not differ from those with both genders and glucose tolerance categories combined (data not shown). Because results did not differ when children with IGT were excluded, all analyses included children across the spectrum of glucose tolerance. In addition, children were grouped based on Tanner stage (I to V), but this

Table 2. Sample characteristics of cardiorespiratory fitness, physical activity, and measures of insulin sensitivity (mean ± SD)

	Boys (n = 55)	Girls (n = 40)	Total (n = 95)
$V\text{O}_{2\text{max}}$ (mL/min)	2333.9 ± 633.9*	2021.1 ± 527.1	2202.2 ± 608.5
$V\text{O}_{2\text{max}}$ (mL O_2/kg body weight/min)	37.7 ± 7.3*	32.0 ± 6.6	35.3 ± 7.5
$V\text{O}_{2\text{max}}$ (mL O_2/kg lean tissue mass/min)	61.7 ± 7.0*	56.4 ± 6.6	59.5 ± 7.3
Maximum RER	1.12 ± 0.08	1.12 ± 0.08	1.12 ± 0.08
Maximum heart rate (beats/min)	201 ± 8	201 ± 8	201 ± 8
Physical activity (hours/week)	15.9 ± 20.2	14.9 ± 17.0	15.5 ± 18.8
SI [($\times 10^{-4}$/min^{-1}/(μIU/mL)]	2.00 ± 1.02	2.30 ± 1.58	2.12 ± 1.29
AIR (μIU/mL)	1647 ± 1054	1440 ± 1045	1560 ± 1049
DI ($\times 10^{-4}$/min^{-1})	2636 ± 1219	2357 ± 1223	2518 ± 1222
Fasting insulin (μIU/mL)	17.9 ± 8.5	19.5 ± 10.7	18.6 ± 9.5
Fasting glucose (mg/dL)	93.8 ± 6.3*	90.8 ± 8.5	92.5 ± 7.5

* $p < 0.05$ (boys > girls).

classification system did not yield significant associations between insulin sensitivity/secretion and fitness/activity either (data not shown).

Multivariate Regression Analyses

Log SI, log AIR, log DI, log fasting insulin, and log fasting glucose were all entered systematically as dependent variables into multivariate linear regression models with $V\text{O}_{2\text{max}}$ (milliliters of O_2 per minute) and PA included individually as independent variables. Gender, Tanner stage, fat mass, and soft lean tissue mass were included in all of the regression models as covariates. When log SI was entered as the dependent variable, total body fat mass explained 53% of the variance in the model, and $V\text{O}_{2\text{max}}$ (milliliters of O_2 per minute) was not independently related to SI (Table 4). Similarly, in all of the remaining models, neither $V\text{O}_{2\text{max}}$ (milliliters of O_2 per minute) nor PA had independent effects on variance in any of the measures of insulin dynamics (data not shown).

Discussion

The purpose of this investigation was to determine whether cardiorespiratory fitness and/or PA were related to measures of insulin sensitivity and secretion in a sample of overweight Hispanic youth with a family history of type 2 diabetes and if these associations were independent of body composition. Although the unadjusted correlations revealed several significant relationships between insulin dynamics and fitness/activity, our analyses showed that once demography, maturation, and body composition were appropriately controlled for, these associations disappeared. Ultimately, log $V\text{O}_{2\text{max}}$ (milliliters of O_2 per minute) was not independently related to any measure of insulin sensitivity or secretion after controlling for gender, Tanner stage, fat mass, and soft lean tissue mass, suggesting that the effect of fitness on insulin is indirect and likely is a function of body composition. After careful examination, we revealed that PA (hours of recreational activity per week) was not independently related to measures of insulin sensitivity and secretion.

Complicating the true relationship between cardiorespiratory fitness and insulin sensitivity is the strong correlation that these variables share with body composition. Indeed, we found that log fat mass was related to log SI ($r = -0.69$, $p < 0.001$) and log $V\text{O}_{2\text{max}}$ ($r = 0.43$, $p < 0.001$), whereas log soft lean tissue mass was associated with log SI ($r = -0.62$, $p < 0.001$) and log $V\text{O}_{2\text{max}}$ ($r = 0.89$, $p < 0.001$). These interrelationships underscore the fact that discordant conclusions may be reached depending on how fitness data are presented and related to health outcomes. For example, in our data set, when we expressed cardiorespiratory fitness in relative terms (as a ratio) with weight as the denominator ($V\text{O}_{2\text{max}}$ per kilogram of body weight), fitness was positively related to SI ($r = 0.42$; $p < 0.05$), suggesting that fitter individuals have a higher degree of insulin sensitivity. Although methodologies differ slightly, similar relationships have been reported previously (13,27). $V\text{O}_{2\text{max}}$ is often expressed relative to body weight as a means of adjusting for individual differences in body size, but this method of expressing cardiorespiratory fitness may be confounding the actual relationship between fitness and insulin sensitivity. Alternatively, when we correlated absolute $V\text{O}_{2\text{max}}$ (milliliters of O_2 per minute) with SI and adjusted for the independent effects of fat mass and soft lean tissue mass (along

Table 3. Unadjusted Pearson correlations and adjusted Pearson partial correlations (adjusting for gender, Tanner stage, fat mass, and soft lean tissue mass)

	Log	
	VO_{2max}	Physical activity
Unadjusted Pearson correlations		
Log SI	−0.46*	−0.03
Log AIR	0.16	0.17
Log DI	−0.31*	0.20†‡
Log fasting insulin	0.29*	0.03
Log fasting glucose	0.06	−0.25*‡
Adjusted Pearson partial correlations		
Log SI	−0.01	0.03
Log AIR	−0.09	0.17
Log DI	−0.13	0.25*§
Log fasting insulin	−0.07	0.01
Log fasting glucose	0.10	−0.27*§

* $p < 0.05$

† $p = 0.05$

‡ One subject had the highest fasting glucose concentration and the lowest DI and physical activity levels. When these extreme values were excluded, the correlations between both log PA and log DI (unadjusted $r = 0.05$; $p = 0.62$) and log PA and log fasting glucose (unadjusted $r = -0.13$; $p = 0.21$) became nonsignificant.

§ One subject had the highest fasting glucose concentration as well as the lowest DI and PA levels. When these extreme values were excluded, the correlations between both log PA and log DI (adjusted $r = 0.12$; $p = 0.27$) and log PA and log fasting glucose (adjusted $r = -0.12$; $p = 0.26$) became nonsignificant.

with gender and Tanner stage) in covariate analysis, this relationship was no longer significant ($r = -0.01$, $p > 0.05$), suggesting that VO_{2max} (milliliters of O_2 per minute) does not have an independent effect on SI in our sample of overweight Hispanic children. Consistent with previous research (11,28) and given that fat mass and lean tissue mass are known to have unique associations with both fitness and insulin sensitivity (28–30), we believe that expressing fitness in absolute terms and covarying for body composition is a more appropriate means of statistically evaluating the connection between the body's maximal ability to use oxygen (physiological fitness) and insulin sensitivity independent of body composition.

We initially observed that PA was positively related to DI and inversely related to fasting glucose, suggesting that an active lifestyle may be beneficial with respect to diabetes risk. However, after reviewing these relationships critically, we cannot state with confidence that PA is associated with

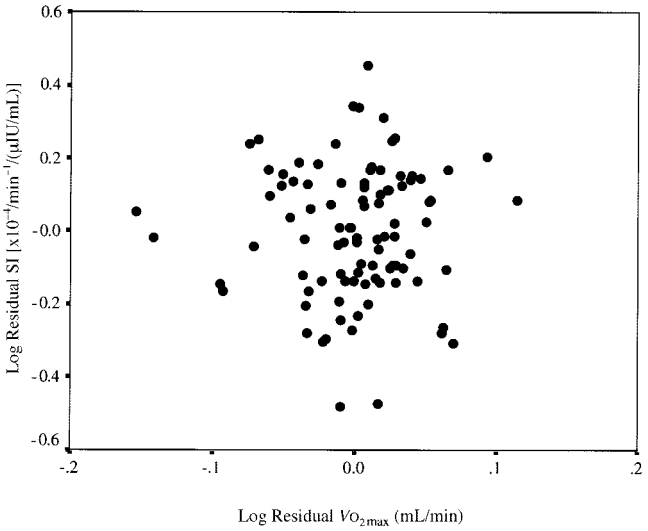

Figure 1: Partial correlation between log SI and log VO_{2max} ($r = -0.01$, p = not significant) after adjusting for the effects of gender, Tanner stage, fat mass, and soft lean tissue mass. This relationship highlights the observation that once body composition is controlled for appropriately, there is no independent influence of cardiorespiratory fitness on insulin sensitivity, suggesting that the association between VO_{2max} and SI is a function of body composition.

DI and fasting glucose in our sample because one individual appeared to exert a disproportionate amount of influence on these correlations. To further explore the associations, we conducted several follow-up analyses using our complete data set. Compared with the variability observed in fasting glucose, we noted greater inter-subject variability in 2-hour glucose concentrations derived from the OGTT. Therefore, we evaluated the relationships among 2-hour glucose, log VO_{2max} (milliliters of O_2 per minute), and log PA to deter-

Table 4. Multivariate linear regression analysis of the contribution of VO_{2max} on log SI after adjusting for covariates

Dependent variable	Independent variables	$\beta \pm$ SEE	p
Model 1 $R^2 = 0.53$			
Log SI	Gender	0.10 ± 0.06	0.07
	Tanner stage	−0.03 ± 0.03	0.24
	Fat mass	−0.016 ± 0.004	<0.001
	Soft lean tissue mass	−0.001 ± 0.008	0.88
	VO_{2max}	0.02 ± 0.09	0.87

mine whether fitness and/or activity were related to glucose tolerance. We then assessed independently the relationships among 2-hour glucose concentrations from the OGTT and fitness/activity in those children who were classified as having IGT ($n = 29$) or NGT ($n = 66$). In each of these situations, we did not observe any significant relationships between outcome variables [IGT, 2-hour glucose vs. log $V\text{O}_{2\text{max}}$ ($r = 0.08$, $p = 0.67$) and log PA ($r = -0.08$, $p = 0.68$); NGT, 2-hour glucose vs. log $V\text{O}_{2\text{max}}$ ($r = -0.24$, $p = 0.06$) and log PA ($r = 0.12$, $p = 0.33$)]. When we included log DI and log fasting glucose as dependent variables in separate multivariate regression models with gender, Tanner stage, fat mass, and soft lean tissue mass included as covariates, log PA did not explain any variance in either measure. Although partial correlations and multivariate regression analyses evaluate relationships between independent and dependent variables using slightly different statistical procedures, collectively, these analyses lend support to our belief that PA (hours of recreational activity per week) was not independently related to DI and glucose concentrations in the present sample of overweight Hispanic youth.

Previous cross-sectional research has revealed that cardiorespiratory fitness and/or activity are related to risk factors for type 2 diabetes in youth, suggesting that regular exercise may play a positive role in insulin resistance. In a sample of prepubertal white and African-American children, Ku et al. (11), using similar methodologies as the current study, revealed that recreational PA and moderate to vigorous activity were both independently and positively related to insulin sensitivity within the group as a whole. However, $V\text{O}_{2\text{max}}$ (milliliters of O_2 per minute), after adjusting for race, fat mass, and lean tissue mass, was inversely related to log SI, suggesting, paradoxically, that a higher degree of cardiorespiratory fitness was associated with lower insulin sensitivity. In another sample of white and African-American children (13), cardiorespiratory fitness (peak $V\text{O}_2$ per kilogram body weight) was inversely related to fasting insulin, whereas percentage body fat (measured by DXA) proved to be the only independent predictor of insulin concentrations in multiple regression analyses. It is not known whether similar conclusions would have been reached if absolute $V\text{O}_2$ and a more precise measure of insulin sensitivity had been included in the analyses. Schmitz and colleagues (12) found that leisure-time PA was positively related to insulin sensitivity assessed using the euglycemic-hyperinsulinemic clamp ($r = 0.13$, $p = 0.001$) and to fasting insulin ($r = -0.12$, $p = 0.03$) independently of age, gender, Tanner stage, and race in a sample of 10- to 16-year-old youth. Although these correlations were significant, the strength of these relationships was modest and may be a reflection of the relatively large sample size ($n = 357$). Although few studies have explored the potential impact of fitness/activity on insulin sensitivity in youth, the available data suggest that recreational PA and moderate to vigorous activity behaviors are more proximal correlates of insulin sensitivity, whereas cardiorespiratory fitness is either inversely related or unrelated to measures of insulin sensitivity. More definitive evidence is still required to help clarify whether these relationships are universally observed across genders, maturational stages, and ethnic groups, especially in high-risk subgroups.

Given that previous research has supported a relationship between PA and insulin dynamics (11,12), we were surprised when we did not find our estimate of activity to be related to SI, AIR, DI, or fasting insulin concentrations. However, several explanations can be suggested for the lack of an association among these variables. First, our questionnaire measured recreational PA only and did not take into consideration specific aspects of activity (i.e., moderate or vigorous PA) that others have shown may be more closely related to insulin sensitivity (11,31). This issue may be particularly relevant in our study population because Hispanic youth have lower levels of vigorous activity compared with white boys and girls (32) and because the odds of becoming overweight decline in Hispanic boys and girls as moderate to vigorous activity increases (33). Second, previous research in a sample of nonoverweight and overweight white and African-American children in Alabama linked recreational PA (using a similar questionnaire) and insulin sensitivity/secretion (11), so it is plausible that this instrument lacks sensitivity to capture all relevant activity behaviors in young, overweight Hispanics living in Los Angeles. Third, it is possible that recreational PA is simply not related to insulin sensitivity/secretion in overweight Hispanic children. We know that total body fat mass and body fat distribution are intimately associated with insulin dynamics in children (34), so the independent contribution of activity to insulin sensitivity and secretion within this sample of overweight boys and girls may be diminished by the overriding effect of adiposity. Because all of the subjects in this analysis possessed an age- and gender-specific BMI $\geq$ 85th percentile, we cannot conclude that PA is unrelated to insulin sensitivity in Hispanic children who are not overweight. Moreover, given the cross-sectional nature of the study design, we cannot conclude cause-and-effect associations between measurement outcomes. Measuring PA using more objective procedures (e.g., accelerometry), determining time spent in activity outside of recreational hours (e.g., school games and sports participation), and assessing different aspects of activity behaviors (e.g., time spent viewing television) may provide a broader perspective of the role of PA behaviors on diabetes risk.

Although we did not find $V\text{O}_{2\text{max}}$ (milliliters of O_2 per minute) to be independently related to measures of insulin sensitivity or secretion, we cannot conclude that other aspects of fitness aside from cardiorespiratory fitness are not uniquely related to insulin dynamics. For example, it may be useful for future investigations to include both body

weight-dependent (e.g., time to $V_{O_{2max}}$ using a treadmill protocol) and body weight-independent (e.g., muscular strength) measurements to more comprehensively assess the relationships among the different components of fitness and insulin measures. Evaluating a host of fitness variables and how they relate to metabolic risk may be particularly relevant for overweight populations. For example, if activities such as strength training lead to improvements in muscular strength, and, in turn, muscular strength is inversely related to SI, such findings would promote the utility of strength training for overweight populations at increased health risk (35). Strength training may have a number of other beneficial metabolic effects for overweight individuals, including improved body composition (increased muscle mass and decreased fat mass) and fat distribution (reduced visceral fat) (36–38). Because strength training may be easier for overweight youth to perform than aerobic training (perhaps due to exercise intolerance), we believe that this mode of activity is appropriate for a number of reasons and may be better tailored to the specific capabilities of this population (39).

In summary, our data demonstrated that cardiorespiratory fitness was not independently related to insulin sensitivity and secretion in overweight Hispanic children with a family history of type 2 diabetes once the influences of gender, Tanner stage, and body composition were appropriately controlled for in the analyses. Our findings also highlight the fact that conclusions may vary depending on how fitness data are expressed, which fitness indicators are included in the analyses, and how differences in body composition are considered in the analyses. Recreational PA was not related to insulin dynamics in our sample of overweight Hispanic youth. Because several of the significant relationships we observed between insulin sensitivity/secretion and cardiorespiratory fitness were diminished once fat mass and lean tissue were controlled for, we speculate that the association between insulin dynamics and $V_{O_{2max}}$ is indirect and operational through body composition. For diabetes risk to improve, it appears that improvements in body composition may be required, and this may be facilitated by increasing time spent performing vigorous physical activities. Ultimately, achieving a greater understanding of whether cardiorespiratory fitness, PA, and/or specific aspects of fitness and PA are related to insulin dynamics is necessary to help guide treatment and prevention initiatives for populations such as overweight Hispanic children who are at elevated risk for developing chronic diseases such as type 2 diabetes early in life.

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