Effects of Resistance Training on Insulin Sensitivity in Overweight Latino Adolescent Males

GABRIEL Q. SHAIBI[1], MARTHA L. CRUZ[2], GEOFF D. C. BALL[3], MARC J. WEIGENSBERG[4], GEORGE J. SALEM[1], NOE C. CRESPO[5], and MICHAEL I. GORAN[5,6]

[1]*Department of Biokinesiology and Physical Therapy, University of Southern California, Los Angeles, CA;* [2]*Department of Health Promotion, College of Health Sciences, University of Texas El Paso, El Paso, TX;* [3]*Department of Pediatrics and Child Health, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, CANADA; and* [4]*Departments of Pediatrics,* [5]*Preventive Medicine, and* [6]*Physiology and Biophysics, University of Southern California, Keck School of Medicine, Los Angeles, CA*

ABSTRACT

SHAIBI, G. Q., M. L. CRUZ, G. D. C. BALL, M. J. WEIGENSBERG, G. J. SALEM, N. C. CRESPO, and M. I. GORAN. Effects of Resistance Training on Insulin Sensitivity in Overweight Latino Adolescent Males. *Med. Sci. Sports Exerc*., Vol. 38, No. 7, pp. 1208–1215, 2006. **Purpose:** Insulin resistance is thought to be a core defect in the pathophysiology of obesity-related comorbidities in children, such as type 2 diabetes. Exercise training is known to improve insulin resistance and reduce the risk of type 2 diabetes in adults. However, very little is known regarding the effects of exercise on insulin resistance in youth. Therefore, we examined the effects of a 16-wk resistance training exercise intervention on insulin sensitivity in youth at high risk for developing type 2 diabetes. **Methods:** Twenty-two overweight Latino adolescent males were randomly assigned to either a twice-per-week resistance training group (RT = 11) or a nonexercising control group (C = 11) for 16 wk. Strength was assessed by one-repetition maximum, body composition was quantified by dual-energy x-ray absorptiometry, and insulin sensitivity was determined by the frequently sampled intravenous glucose tolerance test with minimal modeling. **Results:** Significant increases in upper- and lower-body strength were observed in the RT compared with the C group. The RT group significantly increased insulin sensitivity compared with the C group ($P < 0.05$), and this increase remained significant after adjustment for changes in total fat mass and total lean tissue mass ($P < 0.05$). Compared with baseline values, insulin sensitivity increased 45.1 ± 7.3% in the RT group versus −0.9 ± 12.9% in controls ($P < 0.01$). **Conclusion:** A twice-per-week 16-wk resistance training program can significantly increase insulin sensitivity in overweight Latino adolescent males independent of changes in body composition. **Key Words:** CHILDREN, INSULIN RESISTANCE, TYPE 2 DIABETES, EXERCISE

Insulin resistance is a hallmark feature of obesity in adults (21) and children (3). Moreover, insulin resistance is hypothesized to be a key central component in the etiology of obesity-related disorders in youth, including type 2 diabetes (13). The metabolic comorbidities appear to be amplified in minority youth such as Latinos. For example, Latino youth are more insulin resistant compared with their Caucasian counterparts (14), and it has been projected that approximately 50% of Latino children born in 2000 will develop type 2 diabetes in their lifetime (29). Thus, lifestyle interventions to improve insulin resistance and reduce risk for type 2 diabetes in overweight minority youth are important public health priorities.

Investigations in adults provide preliminary evidence that exercise can prevent or delay type 2 diabetes in high-risk populations (23). The exercise-induced reductions in diabetes risk are thought to be due, in part, to improvements in insulin sensitivity (5). It is well established that endurance exercise training increases insulin sensitivity in normal and insulin-resistant individuals (17). Several recent investigations have extended these findings to other modes of exercise such as resistance training (19,31). Resistance-training–related improvements in insulin sensitivity are similar in magnitude to those observed following endurance exercise training (20). In addition to improvements in insulin sensitivity, resistance training can favorably enhance several other physiologic parameters related to metabolic

Address for correspondence: Michael I. Goran, Ph.D., Professor of Preventive Medicine and Physiology & Biophysics Keck School of Medicine, University of Southern California, 1540 Alcazar Street, Room 208-D, Los Angeles, CA, 90033; E-mail: goran@usc.edu.
Submitted for publication August 2005.
Accepted for publication March 2006.

0195-9131/06/3807-1208/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1249/01.mss.000227304.88406.0f

health including total and regional body composition, blood pressure, and HDL cholesterol (38). Furthermore, incorporating resistance training into a multidisciplinary weight management program for overweight children may improve program retention (36). Despite these interesting observations, no randomized controlled studies have investigated the effects of exercise on direct measures of insulin sensitivity in overweight youth. Given the relatively poor compliance of traditional exercise interventions in overweight individuals (25), resistance training may be a more acceptable form of physical activity for this population because it is less aerobically taxing and because success, in terms of strength gains, are readily observed.

Therefore, the purpose of the present investigation was to conduct a randomized clinical study to examine the effects of a 16-wk progressive resistance training program on directly measured insulin sensitivity while considering the confounding effects of body composition in overweight Latino adolescent males. We hypothesized that adolescents in the resistance training group would exhibit significantly greater increases in insulin sensitivity compared with controls.

RESEARCH DESIGN AND METHODS

Subjects

Participants were recruited from greater Los Angeles County through medical clinics, advertisements, and local schools. Study participants satisfied the following criteria for inclusion: male gender, age- and gender-specific BMI ≥ 85th percentile (CDC, 2000), Latino ethnicity (i.e., parents and grandparents of Latino descent by self-report), and pubic hair Tanner stage ≥ 3. Participants were excluded if they were using a medication or diagnosed with a condition known to influence body composition or insulin/glucose metabolism, had an orthopedic condition that would limit their ability to perform exercise, or had performed structured resistance training exercise within 6 months prior to enrollment. Of the 28 youth randomized to resistance training (RT) or control (C) groups, six individuals did not return for postintervention testing (RT = 3, C = 3). Of the six who did not return, two relocated, one was dissatisfied with control group assignment, and three withdrew for personal reasons. Baseline demographic and metabolic data from the six individuals who did not return was not significantly different from baseline measures of the 22 participants who completed all aspects of the intervention (data not shown). We excluded insulin sensitivity data from one control participant deemed an outlier, as his change in insulin sensitivity was deemed not physiologic and likely an indication of a problem with the measurement (insulin sensitivity increased by 345%, which was > 8 SD from the mean change in other control participants.) Prior to any testing procedure, informed written consent from parents and assent from the children were obtained. This investigation was approved by the institutional review board of the University of Southern California, Health Sciences campus.

Study Protocol

Outpatient visit. Participants arrived at the USC General Clinical Research Center (GCRC) at approximately 0800 h after an overnight fast. A comprehensive medical history and physical examination was performed including anthropometry as well as Tanner staging by a licensed pediatrician. Following the exam, an oral glucose tolerance test (OGTT) was performed. This test included the application of a topical anesthetic (EMLA cream, Aztrozeneca LP, Wilmington, DE) applied to the antecubital fossa of one arm, and approximately 45 min later a flexible intravenous (i.v.) catheter was placed in an antecubital vein. Subjects then ingested 1.75 g of oral glucose solution per kilogram of body weight (to a maximum of 75 g). Blood was sampled and assayed for glucose and insulin at −5 min (fasting) and 120 min (2 h). Impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and type 2 diabetes were defined according to the American Diabetes Association (2). Participants with IFG ($N = 4$) and IGT ($N = 6$) were included in the study. One prospective participant had undiagnosed type 2 diabetes and was excluded from the study and referred to his primary care physician.

Anthropometry. Height and body weight were recorded to the nearest 0.1 cm, and 0.1 kg, respectively. BMI and BMI percentiles for age were determined using CDC computer software EpiInfo Version 3.3, 2004.

Inpatient visit. Approximately 7–14 d after the outpatient visit, participants were admitted to the USC GCRC at approximately 1300 h. Total body composition (fat mass and soft lean tissue mass) was determined by a whole-body dual-energy x-ray absorptiometry (DEXA) scan using a Hologic QDR 4500W (Bedford, MA). Upper- and lower-body strength were assessed by one-repetition maximum (1RM) in the bench press and leg press, respectively, using procedures similar to Faigenbaum et al. (10). Briefly, participants were introduced to the exercise equipment and given instructions by the research team on proper lifting form and technique for both the bench press and leg press. They then practiced the exercises without resistance before performing one set of 6–8 repetitions with a light load. This was followed by 3–4 repetitions with a moderate load. Thereafter, single repetitions were subsequently attempted with increasing loads (1.0–4.0 kg) until the participant was unable to lift the weight through a full range of motion using proper form. Cardiovascular fitness ($\dot{V}O_{2peak}$) was assessed during a progressive exercise test to volitional fatigue on an electronically braked cycle ergometer (Ergoline 900, Bitz, Germany). The protocol consisted of a 3-min warm-up period of unloaded pedaling at 60 rpm followed by a ramped increase in work rate (20–30 $W \cdot min^{-1}$). The test was terminated when the participant was unable to maintain pedaling at 60 rpm despite verbal encouragement from research staff. Breath-by-breath respiratory gasses were collected and measured via open circuit spirometry and analyzed on a MedGraphics $CardiO_2$ combined exercise system (St. Paul, MN). Heart rate was measured continuously throughout the test using an integrated four-lead

electrocardiogram. $\dot{V}O_{2peak}$ was determined from the highest 20-s average achieved with the respiratory exchange ratio > 1.0.

After strength and fitness testing, participants were served a standardized dinner and an evening snack, with only water permitted after 2000 h. At approximately 0730 h the following day, a frequently sampled i.v. glucose tolerance test (FSIVGTT) was performed (EMLA cream was applied 45 min prior to insertion of flexible i.v. catheters placed in both arms). Fasting blood samples were collected to determine basal glucose and insulin concentrations At time zero, glucose (25% dextrose, 0.3 $g \cdot kg^{-1}$ body weight) was administered intravenously. Blood samples were then collected at the following time points: 2, 3, 4, 5, 6, 8, 10, 14, 19, 22, 25, 30, 40, 50, 70, 100, 140, 180, and 210 min. Insulin (0.02 $U \cdot kg^{-1}$ body weight; Humulin R (regular insulin for human injection; Eli Lilly, Indianapolis, IN)) was injected intravenously at 20 min. Plasma was analyzed for glucose and insulin, and values were entered into the Minmod Millenium 2003 computer program (version 5.16, Richard N. Bergman, USC) for determination of insulin sensitivity, the acute insulin response to glucose, and the disposition index (a measure of pancreatic β-cell function). The FSIVGTT is an accurate and valid technique for the measurement of insulin sensitivity in overweight youth (7).

Assays. Blood samples taken during the OGTT were separated for plasma and immediately transported on ice to the Los Angeles County–USC Medical Center Core Laboratory, where glucose was analyzed on a Dimension clinical chemistry system using an *in vitro* hexokinase method (Dade Behring, Deerfield, IL). Blood samples taken during the FSIVGTT were centrifuged immediately to obtain plasma, and aliquots were frozen at −70°C until assayed at the USC GCRC Core Laboratory. Glucose was assayed using a Yellow Springs Instruments analyzer, which uses a membrane-bound glucose oxidase technique (YSI Inc., Yellow Sprigs, OH; intraassay CV was 1.0%, interassay CV was 2.9%). Insulin was assayed using an automated random-access enzyme immunoassay system Tosoh AIA 600 II analyzer (Gibbco Scientific, Inc. Coon Rapids, MN; intraassay CV was 2.9%, interassay CV was 5.6%) using an immunoenzymemetric assay method.

Resistance training program. After completion of the outpatient and inpatient visits, subjects were randomized to either a resistance training group or a wait-list control group. Participants randomized to the resistance training group subsequently underwent a comprehensive orientation at the Los Angeles Boys and Girls Club where the 16-wk exercise intervention was conducted. Participants were familiarized with the facilities, equipment, and the exercise training staff, which consisted of undergraduate and graduate students in the exercise science discipline, certified in personal training. As part of the comprehensive orientation, the initial amount of resistance to be lifted for each exercise was determined. Training sessions took place on two nonconsecutive days per week (e.g., Monday and Wednesday or Tuesday and Thursday) and did not exceed 1 h in duration. For the two nonconsecutive training days, day 1 consisted of compound lower-body exercises and isolated upper-body exercises, and day 2 included compound upper-body exercises and isolated lower-body exercises. Each session consisted of single- and multiple-joint resistance exercises including leg press, bench press, dead lift, lat pull-down, biceps curl, triceps push-down, leg curl, leg extension, and shoulder press, using both free weights and machine weights, as well as 5-min warm-up and cool-down periods including stretches and abdominal exercises (Table 1). The exercise program was periodized and progressive in nature, with the number of sets, repetitions, and resistance used increased as the participant's technique and strength improved. In adults, progressive periodized resistance training is thought to optimize skeletal muscle adaptation in response to resistance training (1). Although the optimal resistance training program to increase insulin sensitivity is unknown, investigations in adults have suggested that changes in the amount and quality of skeletal muscle proteins are the primary mechanisms responsible for improvements in glucose regulation (18,31). Thus, the current intervention program was designed to stimulate protein adaptation by incorporating moderate-intensity higher-volume training while incorporating multiple sets with continued increases in load as tolerated (1).

The intervention as a whole was 16 wk; however, during the first 4 wk of the program, emphasis was placed on proper lifting technique rather than maximal strength gains. As such, this period consisted of one set of 10–15 repetitions to promote the development of appropriate motor patters. During weeks 5–10, the subjects performed two sets of 13–15 repetitions. The final 6 wk of the program consisted of three sets of 8–12 repetitions. As strength and appropriate motor patterns developed throughout the training program, loads were adjusted weekly to maintain adequate resistance within the repetition ranges. Trainers were instructed to increase the resistance if participants were able to perform greater than the preassigned number of repetitions for a given phase while maintaining proper lifting technique. Additionally, a modified rate of perceived exertion scale was used to subjectively gauge whether the participant considered the set to be easy, medium, or hard. All sessions were monitored closely by training staff (no more than three participants to one trainer), and participants were called and

TABLE 1. Resistance training program overview.

Weeks 1–4	Weeks 5–10	Weeks 11–16
One set of 10–15 repetitions	Two sets of 3–15 repetitions	Three sets of 8–12 repetitions
~62–71% of baseline 1 RM	~74–88% of baseline 1 RM	~92–97% of baseline 1 RM
1–2 min of rest between exercises	1–2 min of rest between sets/exercises	1–2 min of rest between sets/exercises
Day 1 exercises		**Day 2 exercises**
Leg press		Bench press
Dead lift		Lat pull-down
Biceps curl		Leg extensions
Triceps extension		Leg curls
Shoulder press		Calf raises

TABLE 2. Changes in physical characteristics of participants.

	Resistance Training (N = 11)				Control (N = 11)			
	Pre	Post	Change	% Change	Pre	Post	Change	% Change
Age (yr)	15.1 ± 0.5	–	–	–	15.6 ± 0.5	–	–	–
Tanner stage	4.1 ± 0.2	–	–	–	4.6 ± 0.3	–	–	–
Height (cm)	166.3 ± 3.1	167.0 ± 2.8	0.7 ± 0.4	0.5 ± 0.3	168.0 ± 1.6	169.0 ± 1.5*	1.0 ± 0.4	0.6 ± 0.2
Weight (kg)	90.0 ± 5.7	91.9 ± 5.6	1.9 ± 1.1	2.3 ± 1.3	98.3 ± 6.9	100.0 ± 6.5*	2.1 ± 0.9	2.6 ± 1.1
BMI ($kg \cdot m^{-2}$)	32.5 ± 1.6	32.8 ± 1.6	0.4 ± 0.4	1.3 ± 1.1	34.6 ± 2.0	35.0 ± 2.0	0.4 ± 0.3	1.4 ± 1.0
BMI percentile	97.3 ± 1.1	97.5 ± 1.0	0.2 ± 0.6	0.3 ± 0.6	98.2 ± 0.5	98.6 ± 0.4	0.4 ± 0.3	0.4 ± 0.3
Total fat mass (kg)	31.4 ± 3.4	30.1 ± 3.2	−1.3 ± 0.9	−3.7 ± 3.1	30.8 ± 3.5	30.7 ± 3.2	−0.2 ± 0.7	1.0 ± 3.3
Total lean mass (kg)	54.4 ± 3.2	58.1 ± 3.1*	3.7 ± 0.9	7.4 ± 1.6†	62.3 ± 3.2	64.3 ± 3.0*	2.0 ± 0.6	3.4 ± 0.9
Percent body fat (%)	35.3 ± 2.4	32.8 ± 2.1*	−2.5 ± 0.8	−6.7 ± 2.3	31.4 ± 1.6	30.7 ± 1.4	−0.6 ± 0.6	−1.5 ± 2.2
1RM bench press (kg)	43.4 ± 3.0†	53.9 ± 3.0*	10.5 ± 1.5†	26.1 ± 4.5†	55.8 ± 4.2	59.9 ± 3.9*	4.1 ± 1.6	8.5 ± 2.9
1RM leg press (kg)	183.9 ± 12.1	234.8 ± 15.8*	50.9 ± 7.3†	28.0 ± 3.7†	212.2 ± 12.5	221.9 ± 14.4	9.7 ± 9.9	5.3 ± 4.5
$\dot{V}O_{2peak}$ ($L \cdot min^{-1}$)	3.1 ± 0.2	2.9 ± 0.2	−0.02 ± 0.1	−4.5 ± 11.1	3.1 ± 0.2	3.1 ± 0.2	0.01 ± 0.1	1.1 ± 14.4

Data are means ± SEM. * $P < 0.05$ vs corresponding pre value; † $P < 0.05$ vs control group.
BMI, body mass index; 1RM, one-repetition maximum.

rescheduled if a session was missed. Additionally, control participants were called periodically throughout the program by research staff and were offered the training program following the acquisition of posttesting data.

Posttesting procedures. At the conclusion of the 16-wk exercise/control period, participants returned to the USC GCRC for follow-up testing. The procedures were identical to those described previously in the inpatient visit. This visit, which included a physical exam by a pediatrician and measurement of insulin sensitivity via the FSIVGTT, took place 48–72 h after the final training session to minimize the acute effects of the last training bout on insulin action and glucose homeostasis. A final outpatient visit and oral glucose tolerance test were performed approximately 1 wk after the final FSIVGTT. To minimize detraining effects, participants repeated the previous week's training program between these two procedures.

Statistics. Group differences at baseline were evaluated using independent sample *t*-tests. Intervention effects were examined by paired sample *t*-tests to determine within-group changes as well as by independent sample*t*-tests on change scores (post minus baseline) to determine between-group differences for the variables of interest including height, weight, BMI, BMI percentile, total fat mass, total soft lean tissue mass, percent body fat, 1RM in the bench press, 1RM in the leg press, fasting insulin, fasting and 2-h glucose, insulin sensitivity, acute insulin response, and disposition index. Change scores for insulin sensitivity were also entered into a general linear model with group assignment entered as a fixed factor and change in total fat mass and total soft lean tissue mass entered as covariates to adjust for changes in body composition. All data analyses, including baseline characteristics, were performed only in those participants who completed the entire protocol (pre- and posttesting). Adolescents in the RT group were required to attend a minimum of 80% (26 of 32) training sessions in addition to the pre- and posttesting visits. Participants in RT group attended approximately 96% of the 32 sessions, and no participant was excluded for failing to attend the minimum number of sessions. Furthermore, time between initial baseline testing and follow-up testing was not significantly different between groups (RT = 129.3 ± 2.6 d vs C = 128.3 ± 2.6 d). Although the resistance training loads were not determined from the individuals baseline 1RM scores, training logs were reviewed to provide intensity ranges the participants lifted as a function of their baseline strength (Table 1). All analyses were performed using SPSS version 11.0 (SPSS Inc., Chicago, IL) with a type I error set at $P < 0.05$. Data presented are means ± standard error.

RESULTS

Comparison of baseline characteristics between resistance training and control groups. The RT and C groups did not differ significantly at baseline in any physical characteristic with the exception of upper-body strength, where the C group was significantly stronger in the bench press 1RM compared with the RT group (Table 2). Likewise, there were no differences between groups at baseline with respect to measures of insulin dynamics (Table 3).

Changes in strength, fitness, and body composition. Significant increases from baseline in bench press and leg press 1RM were observed in the RT group, whereas the C group increased only in bench press 1RM (Table 2). Change scores in the bench press and leg press were significantly greater in the RT group than the C group (Table 2). Both the RT and C group significantly increased lean tissue mass over the 16 wk, but there was no change in

TABLE 3. Changes in measures of insulin dynamics from the FSIVGTT.

	Resistance Training (N = 11)			Control (N = 10)		
	Pre	Post	Change	Pre	Post	Change
Fasting insulin ($\mu U \cdot mL^{-1}$)	12.8 ± 2.1	11.5 ± 2.5	−1.3 ± 1.2	17.4 ± 2.1	19.1 ± 2.7	1.7 ± 1.9
Fasting glucose ($mg \cdot dL^{-1}$)	91.3 ± 1.8	93.8 ± 1.9	2.5 ± 1.8	90.6 ± 1.9	91.7 ± 2.0	1.1 ± 2.6
Insulin sensitivity ($\times 10^{-4}$ $min^{-1} \cdot \mu U^{-1} \cdot mL^{-1}$)	2.3 ± 0.3	3.2 ± 0.3*	0.9 ± 0.1†	1.7 ± 0.4	1.8 ± 0.6	0.1 ± 0.3
AIR ($\mu U \cdot mL^{-1} \times 10$ min)	936.2 ± 213.9	762.1 ± 127.8	−174.1 ± 132.0	1153.8 ± 213.1	1339.1 ± 196.1	185.4 ± 184.6
Disposition index	1881.4 ± 287.4	2246.3 ± 338.5	365.0 ± 283.7	1542.8 ± 205.3	1741.0 ± 313.6	198.2 ± 393.0

Data are means ± SEM. * $P < 0.05$ vs corresponding pre value; † $P < 0.05$ vs control group change. AIR, acute insulin response.

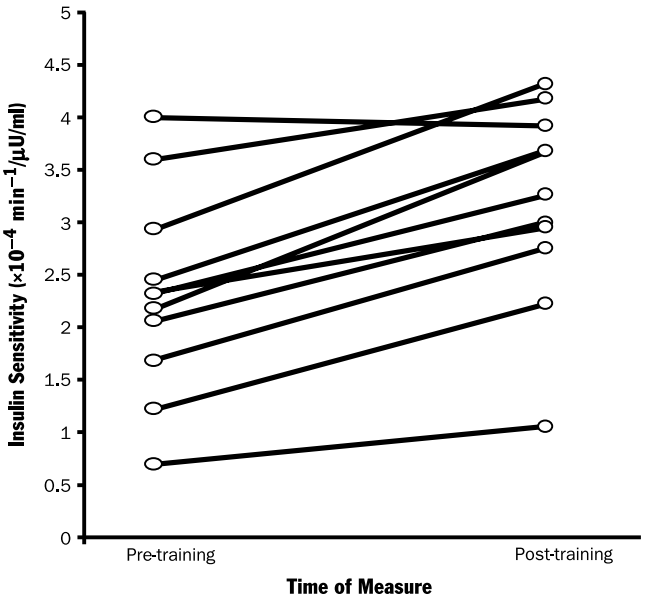

FIGURE 1—Individual changes in insulin sensitivity in the resistance training group.

total body fat mass, whereas percent body fat significantly decreased only in the RT group (Table 2). There were no differences in change scores in either total fat mass or total lean tissue mass. However, the reduction in percent body fat tended to be greater in the RT group compared with controls ($P = 0.08$, Table 2). No significant change in $\dot{V}O_{2peak}$ was noted in either group.

Changes in insulin sensitivity/dynamics. Variables related to insulin sensitivity and dynamics are presented in Table 3. The RT group significantly increased mean insulin sensitivity compared with baseline. No other changes from baseline were noted in either group. Mean change scores for insulin sensitivity were significantly higher in the RT group compared with controls (Table 3). Furthermore, in univariate analysis controlling for change in total fat mass and total lean tissue mass, the change in insulin sensitivity in the RT group remained significantly greater than controls (change in RT group = $0.9 \pm 0.2 \times 10^{-4}$ $min^{-1} \cdot \mu U^{-1} \cdot mL^{-1}$ vs $0.1 \pm 0.1 \times 10^{-4}$ $min^{-1} \cdot \mu U^{-1} \cdot mL^{-1}$ in the C; $P < 0.05$). Individual changes in insulin sensitivity for the RT group are illustrated in Figure 1. Ninety-one percent (10/11) of the participants in the RT group exhibited an improvement in insulin sensitivity, whereas 60% (6/10) of C participants experienced a deterioration in insulin sensitivity. When the magnitude of change in insulin sensitivity (i.e., percent increase or decrease from baseline) was compared across groups, there was a highly significant between group effect ($45.1 \pm 7.3\%$ change in the RT group versus a $-0.9 \pm 12.9\%$ change in controls; $P = 0.005$). No significant between-group differences were noted for changes in the acute insulin response or the disposition index (Table 3).

DISCUSSION

Insulin resistance is thought to be a critical factor in the pathogenesis of type 2 diabetes in adults (33,37) as well as children (6,34). Therefore, identifying interventions that can improve insulin sensitivity are critical for defining effective approaches for preventing metabolic diseases associated with obesity, especially in at-risk individuals, such as overweight Latino youth. Thus, we tested the hypothesis that 16 wk of progressive resistance training would lead to improvements in insulin sensitivity in overweight adolescent Latino males. We found that youth who participated in the resistance training intervention significantly increased insulin sensitivity ($45.1 \pm 7.3\%$) compared with nonexercising controls ($-0.9 \pm 12.9\%$). Furthermore, the increase in insulin sensitivity was independent of changes in body composition, suggesting that mechanisms other than alterations in body composition were operative for the enhanced insulin sensitivity.

It is well established that endurance exercise (both acute and chronic bouts) improves insulin sensitivity (17). Because muscle contractions transiently increase glucose uptake, and skeletal muscle mass provides a metabolic "sink" for glucose disposal, earlier studies suggested that resistance training, similar to endurance training, could lead to improvements in insulin resistance as well. Several investigations subsequently extended the glycemic benefits of chronic endurance training to resistance training but only used surrogate measures of insulin sensitivity (e.g., plasma insulin concentrations during an OGTT) (28,35). Whereas indirect measures of insulin sensitivity may provide reasonable clinical estimates of risk, they are not as sensitive as dynamic measures of whole-body insulin sensitivity (26). Recently, several studies have suggested that resistance training may be a useful intervention to enhance directly measured insulin sensitivity in normal (27, 31) and insulin-resistant adults (19). To our knowledge, our study is the first to demonstrate that resistance training improves insulin sensitivity in an overweight pediatric population. In fact, the approximately 45% improvement in insulin sensitivity we observed is similar to the magnitude of improvement noted in adult studies (9,19). Whereas earlier investigations suggested that resistance-training–induced improvements in insulin-stimulated glucose metabolism could be attributed mainly to increases in lean tissue mass (27,31), recent data in animals (23) and humans (18) provide mechanistic evidence that resistance training produces qualitative changes in skeletal muscle that contribute to enhanced insulin action.

Recently, Krisan and colleagues (24) established that 12 wk of resistance training effectively reversed diet-induced insulin resistance by increasing insulin-mediated glucose uptake in rodents. The improvements in glucose metabolism were associated with increases in GLUT4 protein concentrations as well as several key proteins involved in the insulin-signaling cascade. These findings were extended to humans by Holten and colleagues (18), who investigated the effects of a 6-wk resistance training program in adults with type 2 diabetes. The training program consisted of 3–4 sets of single-leg lower-body exercises three times per week. The authors reported that leg glucose clearance in the trained leg was significantly increased compared with glucose clearance in nonexercising leg (euglycemic–hyperinsulinemic clamp with arteriofemoral venous catheterization). Further, the increased glucose

clearance was not likely attributable solely to skeletal muscle hypertrophy, as changes in leg volume and muscle fiber size via biopsy were minimal. Thus, the investigators concluded that the mechanisms responsible for the improvements in insulin action included both upregulation of components in the insulin-signaling cascade, such as protein concentrations of the insulin receptor, protein kinase B, and glycogen synthase, as well as the glucose transporter GLUT4. Collectively, these investigations support our finding that resistance training improves insulin action in insulin-resistant youth even in the absence of changes in body composition.

Although the increase in insulin sensitivity was independent of changes in total fat mass and soft lean tissue mass, it is plausible that reductions in specific fat depots associated with insulin resistance such as intrahepatic lipid or intramyocellular lipid (IMCL) may have contributed to the improvements in insulin sensitivity. Given that exercise training has been shown to either increase (32) or have no effect (16) on IMCL, and that little is known regarding the effects of exercise on intrahepatic lipid, we are hesitant to speculate reductions in these depots as potential mechanisms for the observed increases in insulin sensitivity.

Despite the robust increases noted in insulin sensitivity, we did not observe significant changes in fasting insulin, insulin secretion (AIR), or pancreatic β-cell function (as measured by the disposition index). This is not altogether surprising because the youth in this study were all nondiabetic and presumably had, for the most part, healthy β-cells. As such, changes in insulin sensitivity may not necessarily correspond to changes in an already normally functioning β-cell. Boule and colleagues (4) found that in the absence of dietary modification, exercise training increases insulin secretion in individuals with poorly functioning β-cells, whereas secretion is actually decreased in those with apparently healthy β-cells. Furthermore, the authors reported that approximately 44% of the 596 participants from the HERITAGE family study exhibited either no change or a decrease in β-cell function in response to 20 wk of training. It is possible that longer training periods coupled with dietary modification are required for robust improvements in β-cell function.

In addition to the improvements in insulin sensitivity, the participants in the resistance training group significantly increased upper- and lower-body strength compared with the controls. It is well established that youth can improve muscular strength beyond that observed as a result of growth and maturation (30). Interestingly, baseline adiposity has been shown to significantly impact strength gains observed following a resistance training program in youth (12). However, the overall aim of our investigation was to examine the effects of resistance training on directly measured insulin sensitivity in high-risk youth. Therefore, we did not design our intervention program to optimally increase strength gains nor did we incorporate repeated measures of strength assessment at baseline or throughout the program. Although participants in the resistance training group did increase strength by approximately 25% over baseline, the mechanisms by which these strength gains occurred cannot be determined. It is plausible that had the intervention been designed to specifically target strength gains by incorporating higher intensity and a lower volume of exercises, greater strength increases may have been observed. A longer intervention period (i.e., greater than 16 wk) may have further enhanced the observed strength and metabolic gains. Further, the periodized model of progressive overload used in this investigation makes it difficult to isolate which independent acute program parameter (i.e., sets, repetitions, and intensity) contributed to the overall physiologic outcomes observed. Future studies are warranted to better understand the interrelations of volume, intensity, frequency, and duration on changes in muscular strength and metabolic properties in various pediatric populations.

The strengths of our study include a randomized controlled investigation with a homogenous population of at-risk youth, accurate estimates of body composition by DEXA, a direct and precise measure of insulin sensitivity via FSIVGTT, and a high attendance rate. The 96% attendance rate may be one of the most impressive findings of our investigation. We feel that delivering the intervention within a community center (rather than a hospital or university setting) and employing personal trainers with whom the participants could relate to provide a more comfortable environment for the youth. In addition, resistance training may be an attractive form of activity for this population, which may have contributed to the high attendance rates. Overweight youth experience increased criticism during physical activities and sports (11), which may be related in part to decreased performance during weight-bearing physical activities compared with nonoverweight counterparts (8). However, overweight youth achieve greater scores during activities requiring muscular strength (8) and thus may be more enthusiastic and compliant in resistance training programs. We acknowledge several limitations worthy of mention. First, neither physical activity (outside of the intervention) nor nutrition was formally controlled for. It is possible that this information may have influenced our ability to detect changes in some of our outcome measures. However, the participants were instructed to maintain their normal activity and dietary habits during the course of the study, and no nutrition education/information was provided to the participants. Furthermore, the lack of a significant change in fitness suggests that activity patterns outside of the resistance training program were not responsible for the observed improvements in insulin sensitivity. Second, given the limitations of research in the pediatric population, we were unable to employ invasive measures of skeletal muscle adaptation such as muscle biopsies to determine the physiologic mechanisms responsible for the observed increases in insulin sensitivity.

In summary, we have demonstrated that a 16-wk resistance training program can significantly improve insulin sensitivity in overweight Latino adolescent males. Moreover, this improvement appears to be independent of changes in body composition. Given the relatively limited success in terms of fat loss and health improvements following even the most intensive endurance exercise interventions in overweight children (15,22), the increases in insulin sensitivity, coupled

with our high attendance and compliance rates, suggest that resistance training may be a viable and efficacious exercise modality to improve metabolic health in overweight youth. In the beginning stages of a comprehensive disease prevention program for overweight youth, resistance training could be considered an integral exercise component, as early successes in terms of strength gains may correspond to long-term adherence to the overall program (36). As the program progresses, other modes of exercise, including aerobic training, could be included to optimize the associated health benefits of regular exercise. The results of our study must be taken in the context of the 4-month time frame in which the intervention took place. Therefore, our observations reflect early adaptations to a novel exercise stimulus where the potential for improvement may be optimal. Longitudinal investigations, which follow high-risk youth into adulthood, are necessary to determine whether improvements in insulin sensitivity during adolescence correspond to prevention of type 2 diabetes over their lifetime.

We are grateful to the staff at the Los Angeles Boys and Girls Club and to the staff at Advantage Fitness Products for their support in designing the exercise facility. Additionally, we thank the participants and their families for their involvement in the study. This work was supported by the Thrasher Research Fund (02817-1), the USC Center for Interdisciplinary Research, and USC GCRC (M01 RR 00043).

REFERENCES

1. American College of Sports Medicine. Position stand: progression models in resistance training for healthy adults. *Med. Sci. Sports Exerc.* 34:364–380, 2002.
2. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 28:S37–S42, 2005.
3. Arslanian, S., and C. Suprasongsin. Insulin sensitivity, lipids, and body composition in childhood: is "syndrome X" present? *J. Clin. Endocrinol. Metab.* 81:1058–1062, 1996.
4. Boulé, N., S. Weisnagel, T. A. Laaka, et al. Effects of exercise training on glucose homeostasis: the HERITAGE family study. *Diabetes Care* 1:108–114, 2005.
5. Carroll, S., and M. Dudfield. What is the relationship between exercise and metabolic abnormalities? A review of the metabolic syndrome. *Sports Med.* 34:371–418, 2004.
6. Cruz, M. L., M. J. Weigensberg, T. T. Huang, G. Ball, G. Q. Shaibi, and M. I. Goran. The metabolic syndrome in overweight Hispanic youth and the role of insulin sensitivity. *J. Clin. Endocrinol. Metab.* 89:108–113, 2004.
7. Cutfield, W. S., R. N. Bergman, R. K. Menon, and M. A. Sperling. The modified minimal model: application to measurement of insulin sensitivity in children. *J. Clin. Endocrinol. Metab.* 70: 1644–1650, 1990.
8. Deforche, B., J. Lefevre, I. D. Bourdeaudhuij, A. P. Hills, W. Duquet, and J. Bouckaert. Physical fitness and physical activity in obese and nonobese flemish youth. *Obes. Res.* 11: 434–441, 2003.
9. Eriksson, J., J. Tuominen, T. Valle, et al. Aerobic endurance exercise or circuit-type resistance training for individuals with impaired glucose tolerance? *Horm. Metab. Res.* 30:37–41, 1998.
10. Faigenbaum, A. D., L. A. Milliken, and W. L. Westcott. Maximal strength testing in healthy children. *J. Strength Cond. Res.* 17: 162–166, 2003.
11. Faith, M. S., M. A. Leone, T. S. Ayers, M. Heo, and A. Pietrobelli. Weight criticism during physical activity, coping skills, and reported physical activity in children. *Pediatrics* 110:e23, 2002.
12. Falk, B., E. Sadres, N. Constantini, L. Zigel, R. Lidor, and A. Eliakim. The association between adiposity and the response to resistance training among pre- and early-pubertal boys. *J. Pediatr. Endocrinol. Metab.* 15:597–606, 2002.
13. Goran, M. I., G. D. Ball, and M. L. Cruz. Obesity and risk of type 2 diabetes and cardiovascular disease in children and adolescents. *J. Clin. Endocrinol. Metab.* 88:1417–1427, 2003.
14. Goran, M. I., R. N. Bergman, M. L. Cruz, and R. Watanabe. Insulin resistance and associated compensatory responses in african-american and Hispanic children. *Diabetes Care* 25:2184–2190, 2002.
15. Gutin, B., P. Barbeau, S. Owens, et al. Effects of exercise intensity on cardiovascular fitness, total body composition, and visceral adiposity of obese adolescents. *Am. J. Clin. Nutr.* 75: 818–826, 2002.
16. Helge, J. W., and F. Dela. Effect of training on muscle triacylglycerol and structural lipids: a relation to insulin sensitivity? *Diabetes* 52: 1881–1887, 2003.
17. Henriksen, E. J. Invited review: effects of acute exercise and exercise training on insulin resistance. *J. Appl. Physiol.* 93:788–796, 2002.
18. Holten, M. K., M. Zacho, M. Gaster, C. Juel, J. F. Wojtaszewski, and F. Dela. Strength training increases insulin-mediated glucose uptake, GLUT4 content, and insulin signaling in skeletal muscle in patients with type 2 diabetes. *Diabetes* 53:294–305, 2004.
19. Ishii, T., T. Yamakita, T. Sato, S. Tanaka, and S. Fujii. Resistance training improves insulin sensitivity in NIDDM subjects without altering maximal oxygen uptake. *Diabetes Care* 21: 1353–1355, 1998.
20. Ivy, J. L. Role of exercise training in the prevention and treatment of insulin resistance and non-insulin-dependent diabetes mellitus. *Sports Med.* 24:321–336, 1997.
21. Kahn, B. B., and J. S. Flier. Obesity and insulin resistance. *J. Clin. Invest.* 106:473–481, 2000.
22. Kang, H. S., B. Gutin, P. Barbeau, et al. Physical training improves insulin resistance syndrome markers in obese adolescents. *Med. Sci. Sports Exerc.* 34:1920–1927, 2002.
23. Knowler, W. C., E. Barrett-Connor, S. E. Fowler, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N. Engl. J. Med.* 346:393–403, 2002.
24. Krisan, A. D., D. E. Collins, A. M. Crain, et al. Resistance training enhances components of the insulin signaling cascade in normal and high-fat-fed rodent skeletal muscle. *J. Appl. Physiol.* 96:1691–1700, 2004.
25. Martin, J. E., P. M. Dubbert, A. D. Katell, et al. Behavioral control of exercise in sedentary adults: studies 1 through 6. *J. Consult. Clin. Psychol.* 52:795–811, 1984.
26. Matsuda, M., and R. A. DeFronzo. Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. *Diabetes Care* 22:1462–1470, 1999.
27. Miller, J. P., R. E. Pratley, A. P. Goldberg, et al. Strength training increases insulin action in healthy 50- to 65-yr-old men. *J. Appl. Physiol.* 77:1122–1127, 1994.
28. Miller, W. J., W. M. Sherman, and J. L. Ivy. Effect of strength training on glucose tolerance and post-glucose insulin response. *Med. Sci. Sports Exerc.* 16:539–543, 1984.
29. Narayan, K. M., J. P. Boyle, T. J. Thompson, S. W. Sorensen, and D. F. Williamson. Lifetime risk for diabetes mellitus in the United States. *JAMA* 290:1884–1890, 2003.
30. Payne, V. G., J. R. Morrow, L. Johnson, and S. N. Dalton. Resistance training in children and youth: a meta-analysis. *Res. Q. Exerc. Sport* 68:80–88, 1997.
31. Poehlman, E. T., R. V. Dvorak, W. F. DeNino, M. Brochu, and P. A. Ades. Effects of resistance training and endurance training

on insulin sensitivity in nonobese, young women: a controlled randomized trial. *J. Clin. Endocrinol. Metab.* 85:2463–2468, 2000.
32. Pruchnic, R., A. Katsiaras, J. He, D. E. Kelley, C. Winters, and B. H. Goodpaster. Exercise training increases intramyocellular lipid and oxidative capacity in older adults. *Am. J. Physiol. Endocrinol. Metab.* 287:E857–E862, 2004.
33. Reaven, G. M. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes* 37:1595–1607, 1988.
34. Scott, C. R., J. M. Smith, M. M. Cradock, and C. Pihoker. Characteristics of youth-onset noninsulin-dependent diabetes mellitus and insulin-dependent diabetes mellitus at diagnosis. *Pediatrics* 100:84–91, 1997.
35. Smutok, M. A., C. Reece, P. F. Kokkinos, et al. Effects of exercise training modality on glucose tolerance in men with abnormal glucose regulation. *Int. J. Sports Med.* 15:283–289, 1994.
36. Sothern, M. S., J. M. Loftin, J. N. Udall, et al. Safety, feasibility, and efficacy of a resistance training program in preadolescent obese children. *Am. J. Med. Sci.* 319:370–375, 2000.
37. Weyer, C., C. Bogardus, D. M. Mott, and R. E. Pratley. The natural history of insulin secretory dysfunction and insulin resistance in the pathogenesis of type 2 diabetes mellitus. *J. Clin. Invest.* 104:787–794, 1999.
38. Winett, R. A., and R. N. Carpinelli. Potential health-related benefits of resistance training. *Prev. Med.* 33:503–513, 2001.