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Aerobic exercise training improves insulin sensitivity without changes in body weight, body fat, adiponectin, and inflammatory markers in overweight and obese girls

George P. Nassis[a,b], Katerina Papantakou[a], Katerina Skenderi[a], Maria Triandafillopoulou[d], Stavros A. Kavouras[a], Mary Yannakoulia[a], George P. Chrousos[c], Labros S. Sidossis[a,*]

[a]*Laboratory of Nutrition and Clinical Dietetics, Department of Nutrition and Dietetics, Harokopio University, 17671 Athens, Greece*
[b]*Department of Sport Medicine and Biology of Physical Activity, Faculty of Physical Education and Sport Science, University of Athens, 17237 Athens, Greece*
[c]*First Department of Pediatrics, Athens University Medical School, 11527 Athens, Greece*
[d]*Department of Endocrinology, Alexandra's Hospital, 11528 Athens, Greece*

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Abstract

The aim of this study was to examine the effect of aerobic exercise training on insulin sensitivity in overweight and obese girls. Nineteen overweight and obese girls (mean ± SD: age, 13.1 ± 1.8 years; body mass index, 26.8 ± 3.9 kg/m^2) volunteered for this study. Body composition (dual-energy x-ray absorptiometry), insulin sensitivity (oral glucose tolerance test and homeostasis model assessment estimate of insulin resistance; n = 15), adiponectin, C-reactive protein (CRP), interleukin (IL) 6, insulin-like growth factor-1, soluble intercellular adhesion molecule-1 and soluble vascular cell adhesion molecule-1 serum levels, and blood lipids and lipoproteins were assessed before and after 12 weeks of aerobic training. Cardiorespiratory fitness increased by 18.8% ($P < .05$) as a result of training. The area under the insulin concentration curve (insulin area under the curve) decreased by 23.3% (12 781.7 ± 7454.2 vs 9799.0 ± 4918.6 μU · min/mL before and after intervention, respectively; $P = .03$). Insulin sensitivity was improved without changes in body weight (preintervention, 67.9 ± 14.5 kg; postintervention, 68.3 ± 14.0 kg) or percent body fat (preintervention, 41.4% ± 4.8%; postintervention, 40.7% ± 5.2%). The lower limb fat-free mass increased by 6.2% ($P < .01$) as a result of training, and changes in lower limb fat-free mass were correlated with changes in the insulin area under the curve ($r = -.68$; $P < .01$). Serum adiponectin, IL-6, and CRP concentrations did not change (preintervention vs postintervention: adiponectin, 9.57 ± 3.01 vs 9.08 ± 2.32 μg/mL; IL-6, 1.67 ± 1.29 vs 1.65 ± 1.25 pg/mL, CRP, 3.21 ± 2.48 vs 2.73 ± 1.88 mg/L) whereas insulin-like growth factor-1 was lower after training (preintervention, 453.8 ± 159.3 ng/mL; postintervention, 403.2 ± 155.1 ng/mL; $P < .05$). In conclusion, 12 weeks of aerobic training improved insulin sensitivity in overweight and obese girls without change in body weight, percent body fat, and circulating concentrations of adiponectin, IL-6, CRP, and other inflammatory markers. These findings suggest that increased physical activity may ameliorate the metabolic abnormalities associated with obesity in children with a mechanism other than the parameters cited earlier.

1. Introduction

Pediatric obesity is an increasing problem worldwide. Insulin resistance, which is associated with the development of cardiovascular disease, is high among obese children [1]. Although fatal episodes occur later in life, the early pathological manifestations of cardiovascular disease appear in childhood. Accordingly, effective early interventions for the treatment of obesity and its metabolic abnormalities are urgently needed.

Because insulin resistance is related to excess body fat, particularly in the visceral area, and to low levels of physical activity [2,3], it is assumed that reduction in body fat and increase in physical activity will improve insulin sensitivity. Intervention studies in adults have shown that weight loss and exercise training may improve insulin action on target tissues [4,5]. It is of interest that aerobic exercise training may improve insulin sensitivity even without body weight loss [2,6,7]. Limited information exists on the influence of regular exercise training on insulin sensitivity in children [8,9].

The link between adiposity and insulin sensitivity may be through the presence of certain adipokines and inflammatory markers in the blood. Insulin resistance is associated

* Corresponding author.
E-mail address: lsidossis@hua.gr (L.S. Sidossis).

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with high blood levels of tumor necrosis factor-α, interleukin (IL) 6, and C-reactive protein (CRP) and low levels of adiponectin [10-13]. Regular exercise and/or weight loss may result in tumor necrosis factor-α and IL-6 decrease and adiponectin increase in adults according to some studies and these changes have been associated with improved insulin sensitivity [5,10]. Data on aerobic exercise training–induced changes in IL-6 levels in children are limited [14] whereas no data exist at all on adiponectin changes as a result of physical training. C-Reactive protein and other inflammatory molecules have also been associated with total body adiposity, visceral adipose tissue, and low fitness in children [15,16] and adults [13]. C-Reactive protein may play a role in the pathogenesis of atherosclerosis because high blood CRP levels have been associated with lower brachial artery flow–mediated dilatation and greater carotid artery intima-media thickness in 10-year-old children [17]. Very limited information exists in the literature on exercise training–induced alterations in CRP levels in children [15].

The aim of this study was to examine the effect of 12-week aerobic exercise training on insulin sensitivity in overweight and obese girls aged between 9 and 15 years. The secondary aim was to examine the effect of aerobic training on adiponectin and certain inflammatory markers in these children.

2. Methods

2.1. Participants

Twenty-one girls aged between 9 and 15 years volunteered for this study. Participants were recruited by word of mouth and were all living in the area of Athens, Greece. All volunteers were overweight and obese as defined by the cutoff values for body mass index [18] and the triceps skinfold thickness [19], did not participate in a weight loss program at least over the past 6 months, had a sedentary lifestyle, were not taking any medication, and were nonsmokers. Informed consent was obtained from the children and their parents before the start of the study. Approval to conduct the study was given by the Bioethics Committee of the Harokopio University (Athens, Greece). Of the 21 subjects recruited, 2 did not complete the final week of training because of their unwillingness to follow the posttraining data collection. Four girls did not want to have an oral glucose tolerance test (OGTT; 2 before training and the other 2 after training). Thus, 15 girls had an OGTT performed both before and after exercise training. Fasting blood samples were collected from the 19 girls who completed the study.

2.2. Overall design of the study

Volunteers reported to the Harokopio University Laboratory of Nutrition and Clinical Dietetics between 7:30 and 8:00 AM after a 10- to 12-hour fast. A short questionnaire was given to them and to their parents to verify that volunteers followed the guidelines regarding their lifestyle for the 3 days before the visit. Participants were asked to follow a prescribed weight-maintaining high-carbohydrate diet (~250 g/d) and to refrain from hard exercise for 3 days before the tests. Diet was prescribed on an individual basis by a dietician.

After emptying their bladder, body weight and height were recorded. A 2-hour OGTT was then performed followed by a standard, light breakfast (sandwich with ham and cheese, orange juice). One and a half hour after breakfast, anthropometric data were collected, dual-energy x-ray absorptiometry was performed, and Tanner stage was determined. Finally, the physical work capacity at 170 beats per minute (PWC170) test was performed to assess cardiorespiratory fitness. The exact, same procedure was followed after completion of the 12-week training period in all volunteers. Posttraining OGTT was conducted 58 to 60 hours after the last exercise session in 9 of 15 subjects and ~37 hours after the last exercise session in the rest of girls (mean time elapsed, 50 hours). This time elapsed seems to be adequate to exclude any effect of last exercise bout on insulin resistance [20].

2.3. Anthropometry, dual-energy x-ray absorptiometry, and puberty status determination

Body weight was determined with an accuracy of 100 g on a SECA scale (SECA, Hamburg, Germany)and height was determined with an accuracy of 0.100 cm with a SECA stadiometer; from these values, body mass index was calculated. Skinfold thickness at certain sites (biceps, triceps, subscapular, suprailiac, abdomen, thigh, and medial calf) was measured with a skinfold caliper according to standard procedures. Waist circumference was determined at the level of the natural waist between the ribs and the iliac crest at the end of a normal expiration. Visceral adipose tissue was estimated from a sagittal abdominal diameter and waist-to-hip circumference according to the equation of Owens et al [21] for 12-year-old obese children. The estimated error for visceral adipose tissue with this equation is 23.9% [21]. All anthropometric measures were performed by the same experimenter. Dual-energy x-ray absorptiometry was used to assess total body composition (DPX-MD, Lunar Corporation, Madison, Wis) while subjects maintained a relaxed supine position. Lower limb fat mass and fat-free mass as well as trunk fat mass were determined with the same system with the use of specific anatomical landmarks [22]. Total body bone mineral content (BMC) was also estimated using the appropriate software. Puberty maturation status was determined with breast and pubic hair development as assessed by a physician. Six girls reported no menstrual cycle, 7 girls reported 1 to 2 years since the beginning of their menstrual cycle, and 6 girls reported 3 to 4 years since the beginning of their menstrual cycle at the pretraining examination.

2.4. Cardiorespiratory fitness assessment

Cardiorespiratory fitness was assessed before and after intervention with the PWC170 test. Briefly, each subject

performed 9 minutes of exercise on a Monark cycle ergometer (Ergo Medic 839E; Monark Sports and Medical, Sweden) at an intensity lower than 170 beats per minute at the end of the test. Exercise load progressively increased every 3 minutes based on heart rate at the final minute of the previous stage. From these data, the power output at 170 beats per minute was calculated. Values were corrected for body mass. The PWC170 test is a valid tool for maximal oxygen consumption assessment in children [23]. The correlation coefficient for repeated measures in 8 children was .90 in our laboratory. During the 9-minute test, O_2 uptake and CO_2 production were determined with a previously calibrated metabolic cart (V̇max 2130, Sensor-Medics, Palm Springs, Calif) and from these values the respiratory exchange ratio was calculated.

2.5. Oral glucose tolerance test

Volunteers consumed a weight-maintaining diet containing ~250 g of carbohydrates per day for 3 days before OGTT and refrained from vigorous physical activity at the same period. An antecubital vein of the arm was cannulated for blood sampling. Baseline or fasting blood samples were obtained after approximately 10 minutes of rest following the placement of the cannula. An OGTT was then performed with the administration of 1.75 g of glucose per kilogram of body weight (maximal dose, 75 g) [1]. Because the lowest body weight was 51.5 kg, all subjects consumed 300 mL of water solution with 75 g of dextrose in 5 minutes both before and after training. Blood samples were drawn for glucose and insulin determination every 30 minutes for 2 hours. The total area under the curve (AUC) for glucose and insulin responses during the 2-hour OGTT was calculated by using a trapezoidal model. The homeostasis model assessment estimate of insulin resistance (HOMA-IR) was calculated from fasting insulin (I_F) and fasting glucose (G_F) as follows: HOMA-IR = ($I_F \times G_F$)/22.5 (I_F in μU/mL and G_F in mmol/L) [24]. The HOMA-IR has been previously validated against the euglycemic clamp in obese children and adolescents [24]. First-phase insulin secretion was estimated with the following indices: (*a*) incremental 30-minute [insulin] = 30-minute [insulin] − fasting [insulin] (insulin in pmol/L) [25] and (*b*) insulin release index = 30-minute [insulin] − fasting [insulin]/30-minute [glucose] − fasting [glucose] (insulin in μU/mL and glucose in mg/dL) [26]. Both indices have been previously used in children [25,26]. Incremental 30-minute insulin secretion has been validated in adults [27].

2.6. Aerobic training

Aerobic training, which was supervised by the same experienced physical education instructor, was performed 3 d/wk (Thursday, Saturday, and Sunday) for 12 weeks. Each session lasted for 40 minutes and included the following: 10 minutes of warm up, 25 minutes of physical training games, and 5 minutes of cool down. Training content was based on a program developed for obese children [28]. In particular, during the first 10 minutes, children performed running, step benching, stair climbing, and jump rope. For the next 30 minutes, children participated in group activities such as basketball, volleyball, and handball [28]. All games were modified to minimize breaks or the time spent waiting for one's turn. Children were encouraged to maintain a heart rate higher than 150 beats per minute most of the time. Heart rate was continuously recorded telemetrically (Sport Tester PE3000, Polar Electro, Oy, Kempele, Finland). After each training session, the minute-by-minute heart rate was downloaded and displayed to the youth. To encourage children to attend the sessions and maintain or exceed the target heart rate of 150 beats per minute, we used a system wherein the children would earn points toward small prizes such as T-shirts and CDs.

2.7. Dietary assessment

Three-day dietary food records were collected by all children at the beginning as well as during the final week of the intervention period. Dietary records were analyzed for

Table 1
Correlation coefficients at baseline between I_F, insulin AUC, adiponectin, inflammatory markers, and adiposity and cardiorespiratory fitness in overweight and obese girls

	Body mass index (kg/m^2)	Body fat (%)	Trunk fat (%)	VAT (cm^2)	WaistC (mm)	PWC170 (W/kg)	Insulin AUC ($\mu U \cdot min/mL$)
I_F (μU/mL)	.33	.43	.41	.23	.27	−.47*	.76**
Insulin AUC ($\mu U \cdot min/mL$)	.65**	.44	.55***	.72**	.67**	−.58***	–
Adiponectin (μg/mL)	−.78***	−.60*	−.61*	−.43	.54	.34	−.80***
CRP (mg/L)	−.07	−.01	.09	.20	−.03	−.35	.20
IL-6 (pg/mL)	.52***	.49***	.47*	.52***	.59***	−.32	.11
IGF-1 (ng/mL)	.04	.16	−.01	−.23	.15	.17	−.27
sICAM-1 (ng/mL)	.06	.11	.17	.29	−.02	−.23	−.00
SVCAM-1 (ng/mL)	−.05	.37	.37	.12	−.17	−.30	−.19

n = 15 for insulin AUC; n = 11 for adiponectin; n = 19 for CRP; n = 12 for IGF-1; and n = 17 for IL-6, sICAM-1, and sVCAM-1. VAT indicates visceral adipose tissue (estimated); WaistC, waist circumference; sICAM-1, soluble intercellular adhesion molecule-1; sVCAM-1, soluble vascular cell adhesion molecule.

* $P < .07$.

** $P < .01$.

*** $P < .05$.

Table 2
Correlation coefficients between the time since the start of menstrual cycle and certain variables of the present study (N = 19)

Variable	R	P
I_F (μU/mL)	−.50	.10
G_F (mmol/L)	−.16	.54
Insulin AUC (μU · min/mL)	−.28	.31
HOMA-IR (U)	−.43	.12
LLFFM (kg)	.58	<.01
Body fat (%)	−.20	.46

total caloric intake and macronutrient intake with the Nutritionist V program (version 1.0, First DataBank, San Bruno, Calif) adapted for Greek food.

2.8. Blood sample analysis

After collection, blood samples were centrifuged at 4°C and plasma- and serum-containing tubes were stored at −70°C until analysis. Serum insulin was determined by radioimmunoassay (DiaSorin, Italy). The assay sensitivity is lower than 4 μU/mL, whereas the within-assay and between-assay coefficients of variation are 6.6%, 10.6%, and 5.5% and 6.2%, 10.8%, and 9.7%, respectively, for insulin concentrations of 24.1, 73.6, and 130.8 μU/mL, respectively. Serum insulin-like growth factor (IGF) 1 was determined with chemiluminescence immunoassay (Nichols Institute Diagnostics, San Clemente, Calif). The sensitivity of the assay is 6 ng/mL, whereas the intra–assay and inter-assay coefficients are 4.8%, 5.2% and 4.4% and 7.1%, 5.7%, and 7.4%, respectively, for mean IGF-1 values of 63, 208, and 766 ng/mL, respectively. Adiponectin was measured with radioimmunoassay (Linco, St Charles, Mo). The assay sensitivity is 1 ng/mL. The intra-assay and inter-assay coefficients of variation are 3.6%, 6.2%, and 1.8% and 9.3%, 6.9%, and 9.3%, respectively, for sample concentrations of 1.5, 3, and 7.5 μg/mL, respectively. Plasma glucose, serum cholesterol, triglyceride, and high-density lipoprotein cholesterol (HDL-C) analyses were performed with the BAYER-ADVIA 1650 Clinical Chemistry System (Bayer Corp, Tarrytown, NY), whereas CRP, apolipoprotein (Apo) A1, and ApoB were measured by means of particle-enhanced immunonephelometry using a Dade-Behring ProSpec nephelometer (Dade-Behring Marburg GmBH, Marburg, Germany). Low-density lipoprotein cholesterol (LDL-C) values were calculated, with the Friedewald formula, from the total cholesterol, HDL-C, and triglyceride values. IL-6, Soluble intercellular adhesion molecule, and soluble vascular cell adhesion molecule levels were assayed using a validated commercial enzyme-linked immunosorbent assay (Quantikine, R&D Systems, Minneapolis, Minn). All analyses were performed in duplicate.

Table 3
Effect of 12-week aerobic training on cardiovascular and metabolic responses to submaximal exercise in overweight and obese girls (N = 19)

Variable	Pretraining	Posttraining
PWC170 (W/kg)	1.30 ± 0.47	1.60 ± 0.42*
Exercise heart rate (beats per minute)		
First stage	134.0 ± 9.4	129.6 ± 9.4*
Second stage	146.1 ± 11.2	140.0 ± 9.9*
Third stage	157.3 ± 10.3	149.6 ± 9.3*
RER		
First stage	0.99 ± 0.07	0.96 ± 0.07*
Second stage	1.04 ± 0.07	0.99 ± 0.06*
Third stage	1.04 ± 0.06	1.01 ± 0.06*

Values are expressed as mean ± SD. RER indicates respiratory exchange ratio.
* $P < .05$.

Table 4
Anthropometric data before and after 12-week aerobic training in overweight and obese girls (N = 19)

Variable	Pretraining	Posttraining
Age (y)	13.05 ± 1.75	–
Body mass (kg)	67.9 ± 14.5	68.3 ± 14.0
Height (m)	1.58 ± 0.10	1.59 ± 0.09*
Body mass index (kg/m^2)	26.8 ± 3.9	26.7 ± 3.8
Body fat (%)	41.4 ± 4.8	40.7 ± 5.2
LLFFM (kg)	12.2 ± 2.0	13.0 ± 2.1*
Total body FFM (kg)	36.7 ± 6.6	37.1 ± 6.1
BMC (g)	2348.2 ± 548.1	2461.0 ± 568.6*
WaistC (mm)	78.6 ± 8.5	79.7 ± 7.6**
Sum of 7 skinfolds (mm)	168.7 ± 30.8	165.7 ± 27.1
Estimated VAT (cm^2)	60.5 ± 14.7	62.5 ± 14.5
Maturity		
Breast (Tanner stage)	3.6 ± 1.3	3.9 ± 1.2
Pubic hair (Tanner stage)	3.5 ± 1.7	3.8 ± 1.3
Time from the beginning of menstrual cycle (y)	1.6 ± 1.4	–

Values are expressed as mean ± SD. FFM indicates fat-free mass.
* $P < .01$ from preintervention values.
** $P < .05$ from preintervention values.

2.9. Statistical analyses

Table 5
Metabolic parameters before and after 12-week aerobic training in overweight and obese girls (N = 19 unless otherwise stated)

Variable	Pretraining	Posttraining
I_F (μU/mL)[a]	20.8 ± 6.5	24.0 ± 8.9
G_F (mmol/L)[a]	5.1 ± 0.5	5.2 ± 0.3
Insulin AUC (μU · min /mL)[a]	12 781.7 ± 7454.2	9799.0 ± 4918.6*
Glucose AUC (mmol · min/L)[a]	865.8 ± 158.6	806.6 ± 98.2
HOMA-IR	4.34 ± 1.10	4.39 ± 0.82
Incremental 30-min insulin (pmol/L)	714.3 ± 488.3	571.8 ± 346.2
Insulin release index	2.6 ± 2.8	2.1 ± 1.7
Adiponectin (μg/mL)[b]	9.57 ± 3.01	9.08 ± 2.32
IL-6 (pg/mL)[c]	1.67 ± 1.29	1.65 ± 1.25
CRP (mg/L)[d]	3.21 ± 2.48	2.73 ± 1.88
IGF-1 (ng/mL)[b]	453.8 ± 159.3	403.2 ± 155.1*
sICAM-1 (ng/mL)[c]	280.8 ± 61.4	276.9 ± 73.8
sVCAM-1 (ng/mL)[c]	290.3 ± 82.3	296.9 ± 100.9

Values are expressed as mean ± SD.
[a] n = 15.
[b] n = 11.
[c] n = 16.
[d] n = 18.
* $P < .05$.

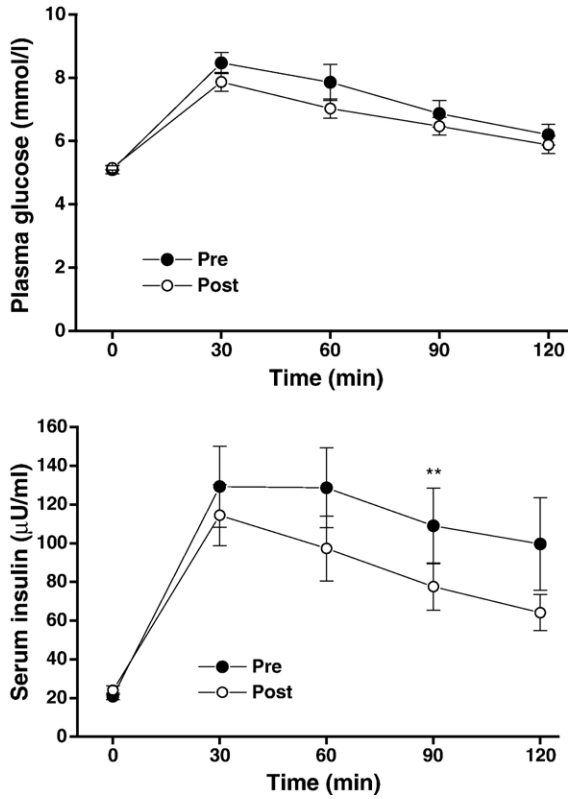

Fig. 1. Plasma glucose (top panel) and serum insulin (bottom panel) responses during the 2-hour OGTT before and after 12 weeks of aerobic training in overweight and obese girls (n = 15). Values are means ± SE; double asterisk in the bottom panel indicates $P < .01$ vs postintervention.

The normality of distribution was checked for all variables with the Kolmogorov-Smirnov test. All variables were normally distributed. Pretraining and posttraining differences were assessed with the Student t test for dependent samples. The relations between variables were tested with Pearson's correlation coefficient. A P level of less than .05 was used as criterion of statistical significance. Statistical analysis was completed with Statistica (version 5.0; StatSoft Inc, Tulsa, Okla). Values are presented as mean ± SD in the text and mean ± SE in the figures.

3. Results

Baseline correlations are presented in Table 1. Total body adiposity was related to insulin AUC, adiponectin, and IL-6 levels whereas central adiposity, assessed with waist circumference and estimated visceral fat, was positively correlated with insulin AUC and IL-6. Cardiorespiratory fitness was negatively associated with insulin AUC ($P < .05$) and presented a strong tendency for negative correlation with I_F ($r = -.47$; $P = .06$; Table 1). Time since the beginning of the menstrual cycle was correlated with lower limb fat-free mass (LLFFM) (Table 2).

The mean duration of each training session was 38.2 ± 1.7 minutes. Mean heart rate was 161.2 ± 2.3 beats per minute, whereas time with heart rate higher than 150 beats per minute was 28.4 ± 1.8 minutes. Exercise training caused certain cardiovascular and metabolic adaptations as shown by the 18.8% increase in PWC170 and the lower heart rates (Table 3). The respiratory exchange ratio was also lower after training (Table 3). However, it must be noted that the absolute difference between the pretraining and posttraining values represents only a small difference in substrate oxidation. Body weight and body fat remained unchanged whereas LLFFM increased by 6.2% after training (Table 4). The BMC was higher after the intervention period ($P < .001$). Energy intake did not differ at the start and the end of the intervention (8008 ± 1935 vs 7285 ± 1921 kJ/, respectively) whereas fat intake was lower at the end of intervention (90.2 ± 20.7 vs 79.1 ± 26.0 g/d, respectively; $P < .05$). As a result of training, insulin AUC declined ($P < .05$) whereas glucose AUC did not change (Table 5 and Fig. 1). Individual glucose and insulin responses are shown in Fig. 2. Of 15 subjects, 11 presented lower insulin AUCs after aerobic training. Changes in

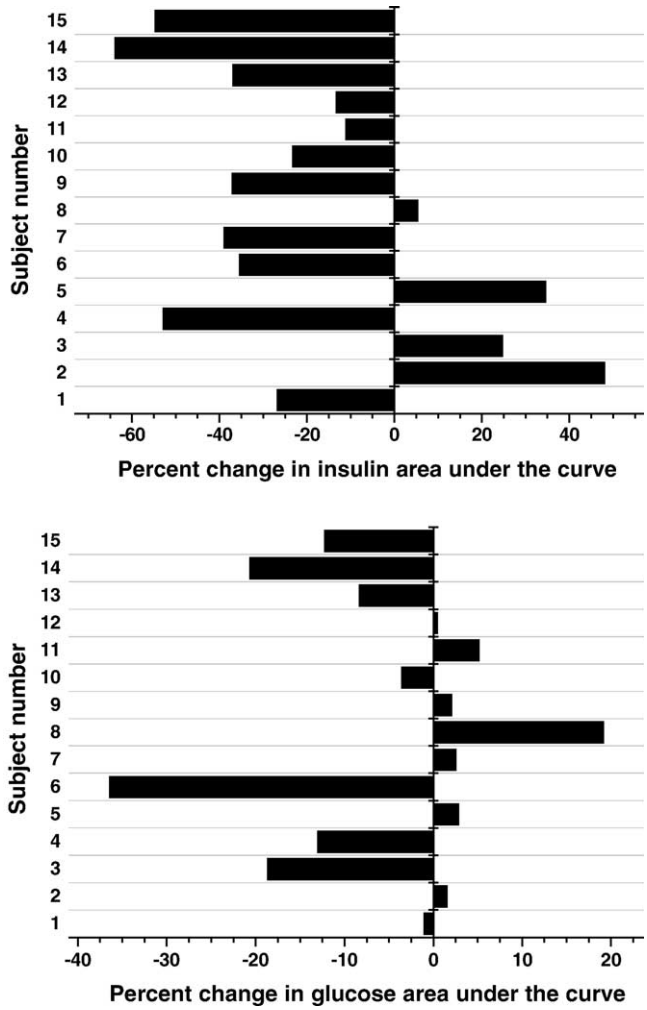

Fig. 2. Individual percent change in insulin AUC (top panel) and glucose AUC (bottom panel) after 12 weeks of aerobic training in overweight and obese girls (n = 15).

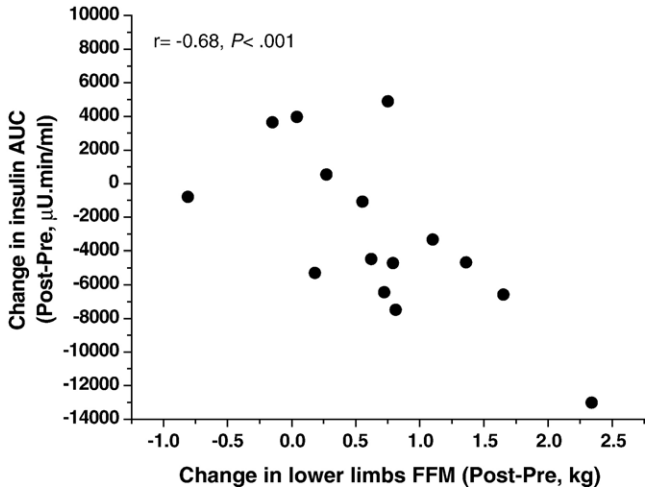

Fig. 3. Relationship between changes in LLFFM and changes in insulin AUC after 12 weeks of aerobic training in overweight and obese girls (n = 15).

insulin AUC were strongly correlated with changes in LLFFM ($r = -.68$; $P < .01$; Fig. 3).

Insulin-like growth factor-1 declined ($P < .05$) whereas adiponectin, IL-6, CRP, soluble intercellular adhesion molecule-1, and soluble vascular cell adhesion molecule-1 concentrations did not change after 12 weeks of aerobic training (Table 5). Triglyceride, HDL-C, and ApoA1 concentrations did not change (preintervention vs postintervention: triglycerides, 0.81 ± 0.25 vs 0.88 ± 0.36 mmol/L; HDL-C, 1.30 ± 0.24 vs 1.35 ± 0.17 mmol/L; ApoA1, 130.9 ± 19.5 vs 136.5 ± 13.4 mg/dL). Finally, total cholesterol, LDL-C, and ApoB were elevated ($P < .05$) after training (preintervention vs postintervention: total cholesterol, 4.53 ± 0.76 vs 4.89 ± 0.84 mmol/L; LDL-C, 2.86 ± 0.69 vs 3.13 ± 0.75 mmol/L; ApoB, 71.0 ± 16.2 vs 77.9 ± 17.5 mg/dL).

4. Discussion

The main finding of this study was that 12 weeks of aerobic training improved insulin sensitivity in overweight and obese girls. The beneficial effect of increased physical activity on glucose metabolism was observed without changes in body weight, body fat, and circulating levels of adiponectin and several inflammatory substances and markers. To our knowledge, this is the first study to show that aerobic exercise training may enhance insulin sensitivity in children independently of changes in body mass.

The insulin AUC during the OGTT improved by 23.3% after the 12-week intervention period in the present study, and this is in agreement with previous investigations in adults [6,29]. The effect of training on insulin sensitivity in young people has been examined in 2 studies [8,9]. In the study by Landt et al [8], a 23% improvement in insulin sensitivity, evaluated with the euglycemic clamp technique, was reported after 12 weeks of aerobic training in 16-year-old children with type I diabetes. Unfortunately, body weight and fat mass values were not reported. In the study by Kelly et al [9] on the other hand, no change in 2-hour glucose concentration after a glucose tolerance test was reported in 11-year-old overweight boys and girls who trained aerobically for 8 weeks.

An interesting finding of the present study is that insulin sensitivity was improved without changes in body weight and percent fat mass. Similar findings were also observed in adults [2,6,29-32], suggesting that regular physical activity may improve insulin sensitivity independently of changes in body mass and fat mass. It is also of interest that waist circumference, an index of abdominal fat, was increased and estimated visceral fat did not change as a result of training yet insulin sensitivity improved. These findings are also in agreement with those of previous studies on adults that suggest that exercise training–induced improvements in insulin sensitivity with no change in total body and visceral fat may be caused by changes in the ability of muscles to metabolize glucose [30]. The increase in the LLFFM is in accordance with this concept.

Adiponectin concentration did not change after 12 weeks of training in the present study. However, insulin sensitivity improved in these children. Similar results have been reported in adults [33-35]. In a recent study [35], 3-week aerobic training resulted in 26% improvement in insulin sensitivity without change in adiponectin levels. Based on our results, it seems that adiponectin did not contribute to the exercise-induced improvement in insulin sensitivity observed in our subjects.

It has been suggested that IL-6 and CRP are associated with insulin resistance [12,13]. Insulin sensitivity improved in the present study however, without alterations in IL-6 and CRP levels. In adults, a reduction in these plasma cytokine levels with approximately 4% loss of body fat with diet and exercise has been associated with improvements in insulin sensitivity [5]. In children, a similar reduction in body fat with aerobic training did not result in CRP changes [15]. It may be that more substantial change in adiposity is needed before a significant improvement in CRP and IL-6 levels can be observed in children. Nevertheless, our findings suggest that improved insulin sensitivity in children was not related to IL-6 and CRP levels in the blood, at least under the present conditions.

An enhanced activity of the IGF-1/growth hormone axis has also been suggested to contribute to insulin resistance of normal puberty [36]. In the present study, IGF-1 declined after a 12-week intervention despite absence of a negative energy balance. However, insulin sensitivity was improved in these children. In previous training studies on children, IGF-1 also declined [14,37] or remained unchanged [38] as a result of aerobic training. It should be noted that the IGF-1 concentrations measured in our study represent the total rather than the free active fraction of this hormone.

An interesting finding of this study was that LLFFM increased by 6.2% after training (Table 4) and that this change

was strongly associated with enhanced insulin sensitivity (Fig. 3). Although body height and BMC were also higher after the 12-week intervention period, it seems unlikely that the observed increase in LLFFM was caused by growth alone. Actually, the ratio of total body fat-free mass to body height did not differ before and after training (pretraining, 23.2 kg; posttraining, 23.3 kg), and this indicates a minor or no effect of growth on fat-free mass in these girls within the 12-week intervention period. Because the skeletal muscle is the primary target tissue for insulin action, it is tempting to suggest that the observed exercise training–induced increase in muscle mass may, at least in part, explain the enhanced insulin sensitivity in these children. Exercise training may also improve insulin action through an increase in GLUT-4 concentration in skeletal muscle, and this adaptation may be independent of body mass loss [39].

Aerobic training was associated with increases in muscle capillarization and enhancement of muscle blood flow in a previous investigation [40]. Physical training also resulted in an increase of the amount of highly oxidative and insulin-sensitive type I fibers [41] and in elevations of muscle glycogen synthase activity [42]. These aerobic training–induced adaptations are known to be associated with improvements in insulin sensitivity [41]. Other studies also suggested that a decreased amount of muscle lipid content [41] and/or lipid droplet size [43] as well as enhanced fat oxidation [41], as a result of exercise training, were associated with exercise-induced improvements in insulin sensitivity. Finally, changes in insulin signaling within the working skeletal muscle [41] were yet another mechanism accounting for improved insulin sensitivity following aerobic exercise.

Total cholesterol, LDL-C, and ApoB increased after aerobic training in the present study. Other studies on children have shown a decline, an elevation, or no change in cholesterol and LDL-C after 8 weeks of training [9,44-46]. Because dietary fat intake was lower after intervention in the present study, these findings could be attributed to daily biologic variations in blood lipid levels [47] and/or to variability presented during the course of the menstrual cycle [48]. The timing of blood collection over the menstrual cycle was not controlled in the present study, which could have affected the blood lipid and lipoprotein responses [48]. Based on previous research on healthy women [49], it seems that insulin sensitivity was not influenced by the menstrual cycle phase of the girls in the present study.

In conclusion, the findings of this study suggest that 12 weeks of increased physical activity improve insulin sensitivity in overweight and obese girls despite no change in body weight and fat mass. Serum levels of adiponectin, IL-6, and CRP remained unchanged, suggesting that enhanced insulin sensitivity was independent of changes in these parameters. Our results suggest that overweight and obese children should be encouraged to increase their physical activity levels, which may result in significant improvements in insulin sensitivity independently of changes in body composition. These findings support the idea that increased physical activity may ameliorate the hazards of obesity in the pediatric population [50].

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