Glucose and Insulin Responses Following 16 Months of Exercise Training in Overweight Adults: The Midwest Exercise Trial

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The current study examined the insulin and glucose response during an oral glucose tolerance test (OGTT) in overweight young adults prior to and following exercise training in the Midwest Exercise Trial (MET). Subjects (N = 66) were randomly assigned to non-exercise control (CON; 16 females, 13 males) or exercise (EX; 22 females, 15 males) groups. EX performed supervised and verified exercise on 3 to 5 days per week in 20- to 45-minute sessions at 60% to 75% of heart rate reserve. OGTTs and assessments for body mass, body composition, and maximal oxygen consumption ($\dot{V}O_2$ max) were performed at baseline, and after 9 and 16 months of training. Blood was collected during a 75-g OGTT and analyzed for glucose and insulin concentrations with the total area under the glucose and insulin curves used in the analysis. The EX males had significant decreases from baseline to 9 months in body mass (94.8 ± 12.5 to 89.2 ± 9.8 kg) and percent fat (28.3 ± 4.8 to 24.2 ± 3.9) with no further changes at 16 months. CON females had significant increases in body mass (78.2 ± 6.4 to 81.1 ± 8.1 kg) and percent fat (36.6 ± 4.2 to 37.8 ± 4.7) from baseline to 16 months. $\dot{V}O_2$ max increased significantly from baseline to 9 months in the EX males (3.67 ± 0.62 to 4.36 ± 0.55 L/min) and EX females (2.53 ± 0.32 to 2.99 ± 0.42 L/min). For glucose area under the curve, there were no significant differences between EX or CON across the 16 months of the study. For insulin area under the curve, there was a significant decrease for male EX from baseline to 9 months (12,535 ± 6,114 to 8,390 ± 4,231 μU/L/180 min). We conclude that regular exercise in healthy, previously sedentary overweight adult males leads to improvements in $\dot{V}O_2$ max and weight loss and a reduction in the insulin concentration required to dispose of a set glucose load. In females, improvement in $\dot{V}O_2$ max without weight loss does not lead to improvement in insulin sensitivity.

THE REGULATION of blood glucose concentrations is critical to ensuring normal physiological function in humans. Non–insulin-dependent diabetes mellitus (NIDDM) is a commonly occurring disease in individuals living in Western industrialized countries and is associated with high-fat diets and a lack of physical activity.[1,2] There is a general belief that increased levels of physical activity will result in an improvement in both insulin sensitivity and glucose metabolism. Davidson et al[3] and Bjorntorp et al[4,5] were among the first to demonstrate that physical training improves insulin sensitivity. A blunted insulin response to a set glucose load has been demonstrated in a variety of individuals who regularly exercise at moderately high intensities.[5-10]

Research in this area has been somewhat focused on special populations that have an increased risk for abnormal glucose metabolism, including those with impaired glucose tolerance,[11,12] NIDDM,[11,12] hyperinsulinemia with normal glucose tolerance,[12] older individuals, 13-15 or obese persons.[14,16-18] There is relatively less information available on subjects who are younger and relatively healthy. Much of the available literature on insulin sensitivity and glucose tolerance is cross-sectional in nature.[7-10,13] and the limited longitudinal information has focused more on older and obese populations at risk for abnormal glucose metabolism.[12,19-23] To our knowledge there are no published long-term randomized controlled trials in younger subjects who have participated in supervised exercise training. The purpose of this investigation was to examine the effects of 16 months of verified, supervised exercise training on insulin and glucose concentrations during an oral glucose tolerance test (OGTT) in young overweight, previously sedentary male and female subjects with normal glucose metabolism. Additionally, we wanted to examine any relationships that might occur between insulin sensitivity and glucose metabolism and changes in body mass, body composition, waist and hip circumferences, and maximal oxygen consumption ($\dot{V}O_2$ max) subsequent to the exercise training program.

MATERIALS AND METHODS

Subjects

The subjects in this experiment were part of the Midwest Exercise Trial (MET), a large multiyear trial examining body weight and body composition changes in response to 16 months of exercise.[24] One hundred thirty-one overweight or moderately obese individuals were randomized to either an exercise intervention or control condition for 16 months. Sixty-six subjects completed the control (CON; 16 females, 13 males) or exercise (EX; 22 females, 15 males) conditions and all laboratory testing as described herein. All subjects completed a health history questionnaire and provided written informed consent in accordance with university guidelines for human experimentation. The subjects were between the ages of 17 and 35 years and were overweight or moderately obese with a body mass index (BMI) between 25.0 and 34.9. Prior to beginning the study, the subjects were sedentary and did not exceed 500 calories of physical activity per week as measured by a physical activity recall questionnaire.[25] Exclusionary criteria included a history of chronic disease (eg, diabetes, heart disease, etc), elevated blood pressure (>140/90), elevated lipids (cholesterol > 6.72 mmol/L; triglycerides >5.65 mmol/L), or elevated fasting glucose (>7.8 mmol/L). Additionally, subjects were excluded if they were smokers, took medications that would affect physical performance or metabolism (eg,

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beta blockers), or if they lacked the ability to perform the laboratory tests or participate in moderate intensity exercise.

Research Design

Subjects reported for testing at baseline, 9 months, and 16 months during which the subjects were measured for body mass, body composition, waist and hip circumferences, and VO_2 max, and participated in an OGTT. After baseline testing, the subjects were randomized at approximately a 2:1 ratio (~65% to the EX group and ~35% to the CON group) under the supervision of a project investigator. This assignment ratio was in anticipation of greater attrition in the EX group compared to the CON group. Throughout the study period subjects consumed an ad libitum diet that was 30% to 35% fat, 45% to 55% carbohydrate, and 10% to 25% protein.

Body Mass, Composition, and Circumferences

Body mass was determined between the hours of 7 AM and 9 AM using a digital scale accurate to ±0.1 kg. The subjects were weighed prior to breakfast and after attempting to void. The subjects removed all jewelry and wore a standardized hospital gown for body mass assessment. Body composition was determined via hydrostatic weighing at residual volume. Residual volume was determined in duplicate immediately prior to the underwater weighing using the nitrogen dilution method as described by Wilmore et al.[26] Body density was calculated using the equations of Goldman and Buskirk,[27] and percent body fat was calculated with the equations of Brozek et al.[28] Circumference measurements were taken at the smallest girth around the trunk and at the widest protrusion of the buttocks. Three circumference measurements were taken per site with a Gullick II circumference measurement tape.[29] Additional measures were taken if the measurements varied by more than 2 cm. The average of the 3 measurements were used in the statistical analysis.

Maximal Oxygen Consumption

Subjects participated in a maximal graded exercise test (GXT) on a treadmill to determine cardiorespiratory fitness. VO_2max was considered as the highest observed value during the GXT. Heart rate was recorded at 1-minute intervals with an electrocardiograph and blood pressures were recorded during the last 30 seconds of each 3-minute stage. Expired air was measured for oxygen and carbon dioxide at 1-minute intervals using a Sensormedics 2900 metabolic measurement cart. The system was calibrated before each test according to the specifications of the manufacturer (SensorMedics Corp, Yorba Linda, CA). A test was considered maximal if any 3 of the 4 following criteria were achieved: a plateau in oxygen consumption with an increase in exercise intensity, a respiratory exchange ratio (RER) $\geq$ 1.10, a maximal heart rate within ±10 beats per minute of age-predicted maximum, and the subject reached exhaustion.[30]

Oral Glucose Tolerance Testing

The subjects reported to the laboratory at 6 AM for an OGTT having refrained from food or any liquids except water for 12 hours and from any exercise for 36 hours prior to testing. After a 15-minute rest an indwelling catheter was inserted into a prominent forearm vein and kept patent with isotonic saline. Blood samples were collected at −15, −7.5, 0, 15, 30, 45, 60, 90, 120, and 180 minutes. Seventy-five grams of glucose mixed in 225 mL of water was consumed at the 0 time point. Serum blood samples were analyzed for glucose and insulin using standard biochemical procedures at the General Clinical Research Center at the University of Colorado at Denver Health Sciences Center. Glucose concentration was measured using an autoanalyzer (Beckman, Fullerton, CA) and insulin was measured using a doubly labeled antibody technique.[31] After the data were collected the total areas under the curve were calculated for glucose and insulin using the trapezoidal method.[32] Fasting and 2-hour values for glucose and insulin were also identified and used in the statistical analysis.

Energy Intake

Dietary intake was ad libitum and was measured for energy and macronutrient composition at baseline, 9 months, and 16 months by weigh and measure techniques.[33] Each measurement consisted of a 2-week period where the participants ate ad libitum in the university cafeteria. Food consumption outside the cafeteria (ie, snacks) was measured by multiple pass 24-hour recall procedures that used food models and standardized, neutral probing questions.[34] Results from the weigh and measure approach and from diet recalls were entered into a computerized nutrition data base for analysis (ESHA, Research, Version 7.1, Salem, OR). This technique has been shown to be accurate for total energy intake when compared to doubly labeled water.[35]

Intervention Program

Each subject's initial exercise prescription was calculated from the GXT at baseline. Exercise duration progressed from 20 minutes at baseline to 45 minutes at 6 months, while exercise intensity progressed from 60% of the heart rate reserve at baseline to 75% at 6 months. This exercise duration and intensity was maintained for the remainder of the study. This level of exercise corresponded to 55% to 70% of VO_2max. The targeted, minimum energy expenditure of exercise was approximately 400 calories per session (~2,000 cal/wk). This was gradually achieved during the first 6 months of training and then maintained for the duration of the study. This level of energy expenditure of exercise is in agreement with the recommendations of the American College of Sports Medicine for exercise programs designed for weight reduction, as well as the recent position statement regarding appropriate strategies for weight loss and prevention of weight regain for adults.[36-38]

Exercise consisted primarily of walking on motor-driven treadmills; however, alternate activities such as stationary biking and walking on stationary elliptical trainers were allowed for 20% of the total exercise sessions (1 out of 5 days). All exercise was performed under direct supervision of research personnel. The participants reported to a research assistant prior to the initiation of any exercise and remained under the supervision of the research assistant throughout the exercise session. Verification of exercise intensity was achieved during each exercise session by use of a Polar Heart Rate Monitor (Accurex Plus, Woodbury, NY). To document the level of energy expenditure achieved during the exercise sessions, energy expenditure was measured during at least 2 exercise sessions by indirect calorimetry at approximately 4-month intervals. In addition to measuring the energy expenditure of exercise, a maximal GXT was completed at baseline and 4, 9, and 12 months to allow for adjustments of the exercise prescription as changes in VO_2 max occurred.

Subjects in the CON group participated in the identical testing as the EX group with the exception of the additional GXTs performed at 4 and 12 months. The subjects were instructed to maintain their normal physical activity and dietary intake patterns throughout the study.

Statistical Analysis

Primary analyses were performed for those 66 subjects that completed the entire 16-month study and all associated laboratory testing. Descriptive statistics were calculated at each assessment period for all dependent measures. All analyses were conducted separately for men and women because of body weight differences between the genders at baseline. Group, time, and group × time effects were determined using a mixed modeling procedure with baseline measures used as the covariates. When appropriate, least square means was used as a post-hoc test. Relationships between changes in glucose and insulin and changes in body mass, body composition, circumference measures, and $\dot{V}O_2$max subsequent to the exercise training program were examined using a Pearson product moment correlation. Type I error rate was set at $P \leq .05$. All analyses were performed using PC-SAS Version 8.2 (Cary, NC).

RESULTS

There were no significant differences between groups within gender for any of the measured dependent variables at baseline, indicating that randomization of the subjects was effective. The results are provided for between-groups within-gender analyses as there were significant gender differences for most dependent variables at baseline and it was not the intent of the study to make a gender comparison.

Exercise Adherence

Adherence to the exercise protocol was excellent, with 90.3% and 89.6% of the total sessions completed for men and women, respectively. The average exercise heart rates across the 16-month study were 154 ± 11 bpm for men and 156 ± 9 bpm for women. Men achieved a significantly greater level of energy expenditure (668 ± 116 kcal/session) compared to the women exercisers (439 ± 88 kcal/session) due to their greater body mass even though the exercise was completed at the same relative intensity and duration as women.

Body Mass, Composition, and Circumferences

Table 1 lists the values for body mass, body composition, and waist and hip circumferences. Body mass significantly decreased in the male EX group from baseline to 9 months and then remained unchanged at 16 months. In the male CON group, body mass did not significantly change over the course of the 16 months. For the female EX subjects, there were no significant changes in body mass. The CON females significantly gained body mass over the 16-month study. Percent body fat significantly decreased in the male EX subjects from baseline to 9 months and then remained unchanged at 16 months. In the male CON subjects, body mass did not significantly change over the course of the 16 months. There were no significant changes in body composition in the female EX and CON subjects. Abdominal and hip circumference was significantly reduced in both the male and female EX subjects compared to the CON subjects.

Maximal Aerobic Power

Table 2 shows the changes in $\dot{V}O_2$max during the course of the 16-month study. Both male and female EX subjects significantly improved $\dot{V}O_2$max (in L/min and mL/kg/min) from baseline to 9 months, with no further increase at 16 months. The male and female CON subjects had no significant changes in $\dot{V}O_2$max during the course of the study.

Oral Glucose Tolerance Testing

The total areas under the curve for glucose and insulin are listed in Table 3. For glucose, there were no significant differences between the EX or CON groups in total area under the curve for the male or female subjects. Furthermore, there were no significant differences across time for male or female EX or CON subjects. For insulin total area under the curve, there was a significant decrease from baseline to 9 months for the male EX subjects, with no further change at 16 months. There were no other significant differences across time or between EX and CON subjects.

Table 4 illustrates the fasting and 2-hour glucose and insulin concentrations obtained during the OGTT. The female EX subjects had significantly lower fasting glucose at 9 and 16 months compared to CON subjects. There were no significant differences between the male EX or CON subjects for either fasting glucose or fasting insulin. The male EX subjects had a significant decrease in the 2-hour insulin concentration from baseline to 9 months. The female EX subjects' 2-hour glucose concentration was significantly lower than the CON subjects at 9 months.

Table 1. Body Mass and Body Composition Values at Baseline and After 9 Months and 16 Months of Verified Supervised Exercise in Previously Sedentary Young Adults (means ± SD)

	Baseline	9 Months	16 Months
Body mass (kg)			
Males			
EX (n = 15)	94.8 ± 12.5	89.2 ± 9.8*	89.4 ± 9.4*
CON (n = 13)	93.9 ± 11.5	92.9 ± 11.3	93.9 ± 12.3
Females			
EX (n = 22)	78.2 ± 11.6	78.2 ± 12.8	78.8 ± 13.1
CON (n = 16)	78.2 ± 6.4	80.1 ± 7.3*	81.1 ± 8.1*
Body composition (%fat)			
Males			
EX	28.3 ± 4.8	24.2 ± 3.9	24.4 ± 5.3
CON	26.9 ± 4.5	26.7 ± 5.4	26.2 ± 6.4
Females			
EX	35.3 ± 4.7	35.4 ± 5.1	34.6 ± 4.8
CON	36.6 ± 4.2	38.0 ± 4.6	37.8 ± 4.7
Abdominal circumference (cm)			
Males			
EX	94.9 ± 7.2	90.0 ± 5.5†	90.1 ± 6.5†
CON	94.5 ± 5.7	93.3 ± 7.2	93.9 ± 7.4
Females			
EX	82.3 ± 7.2	81.6 ± 8.0†	82.4 ± 8.6†
CON	84.8 ± 4.9	86.2 ± 4.6	86.8 ± 6.2
Hip circumference (cm)			
Males			
EX	110.5 ± 6.9	106.4 ± 6.0*	106.5 ± 6.0*
CON	107.4 ± 6.7	106.4 ± 5.6	106.9 ± 5.6
Females			
EX	110.1 ± 8.1	108.5 ± 8.0	109.0 ± 8.6
CON	107.5 ± 5.9	109.8 ± 6.2	109.8 ± 6.2
Waist/hip ratio			
Males			
EX	.859 ± .053	.847 ± .049	.846 ± .053
CON	.880 ± .037	.876 ± .050	.878 ± .043
Females			
EX	.749 ± .055	.752 ± .056	.755 ± .055
CON	.789 ± .032	.785 ± .033	.791 ± .037

*Significant difference from baseline.
†Significant difference from control.

Table 2. Maximal Oxygen Consumption at Baseline and After 9 Months and 16 Months of Verified Supervised Exercise in Previously Sedentary Young Adults (means ± SD)

	Baseline	9 Months	16 Months
VO_2max (L/min)			
Males			
EX (n = 15)	3.67 ± 0.62	4.36 ± 0.55*	4.34 ± 0.58*
CON (n = 13)	3.67 ± 0.50	4.00 ± 0.69	4.03 ± 0.55
Females			
EX (n = 22)	2.53 ± 0.32	2.99 ± 0.42*	3.03 ± 0.42*
CON (n = 16)	2.52 ± 0.32	2.67 ± 0.33	2.71 ± 0.24
VO_2max (mL/kg/min)			
Males			
EX	38.8 ± 5.2	49.0 ± 4.4*	48.5 ± 4.2*
CON	39.4 ± 6.0	43.5 ± 8.7	43.3 ± 6.2
Females			
EX	32.7 ± 4.4	38.8 ± 5.2*	39.0 ± 5.5*
CON	32.3 ± 3.1	33.5 ± 5.0	33.7 ± 4.1

*Significant difference from baseline.

Energy Intake

Table 5 illustrates the total energy intake and macronutrient content for each measurement time. Dietary intake was consistent across the 16 months of study. There were no significant differences within or between groups for either males or females.

Correlations

For the EX subjects (men and women together) there was a significant correlation between the change in glucose total area under the curve and the change in body mass (r = .36, P = .03). There were no other significant correlations between glucose area under the curve and change in body composition or VO_2max. There were significant correlations between insulin total area under the curve and change in body mass (r = .56, $P < 0.003$), change in body fat (r = .335, P = .04), change in waist circumference (r = .40, P = .01), and change in hip circumference (r = .43, P = .008). For the CON subjects, there were significant correlations between change glucose area under the curve and change in body mass (r = .45, P = .01), change in body fat (r = .46, P = .01), change in waist circumference (r = .53, P = .003), and change in waist/hip ratio (r = .53, P = .003). There were significant correlations between change in insulin area under the curve and VO_2 max (r = −.41, P = .03), change in waist circumference (r = .45, P = .01), and change in waist/hip ratio (r = .39, P = .03).

DISCUSSION

Changes in fitness level, body mass reduction, and alterations in body composition are considered key components in reducing the risk of developing abnormal glucose metabolism including impaired glucose tolerance and NIDDM. The main findings of this investigation were that in healthy, previously sedentary overweight young adult males improvements in VO_2max and decreases in body mass and body fat leads to an improvement in insulin sensitivity, while in previously sedentary overweight females, improvements in VO_2max without concurrent changes in body mass or body fat do not lead to an improvement in insulin sensitivity.

There are relatively few long-term (≥6 months) randomized clinical trials that have examined the effect of regular aerobic exercise on glucose tolerance and insulin sensitivity in overweight/obese[19,23] subjects. Dengel et al[19] found that improvements in both glucose tolerance and insulin sensitivity occurred in response to improvements in VO_2max and weight loss in older men. Glucose area under the curve was reduced only when there was weight loss, while the area under the curve for insulin was decreased when changes in both VO_2max and weight loss were observed.[19] Katzel et al[23] demonstrated that weight loss resulted in significant reductions in fasting glucose and insulin, and areas under the curve for glucose and insulin during an OGTT. In contrast, in those subjects who increased VO_2 max but had no change in body weight, there were no alterations in fasting glucose and insulin or area under the curve for glucose. However, there was a reduction in the area under the curve for insulin. The results of the current long-term clinical trial support these previous data. We observed significant reductions in fasting insulin and insulin area under the

Table 3. Glucose and Insulin Areas Under the Curve Values During an Oral Glucose Tolerance Test at Baseline and After 9 Months and 16 Months of Verified Supervised Exercise in Previously Sedentary Young Adults (means ± SD)

	Baseline	9 Months	16 Months
Glucose (mmol/L/180 min)			
Males			
EX (n =15)	27,109 ± 3,522	25,516 ± 2,690	23,868 ± 2,850
CON (n = 13)	24,565 ± 3,859	25,272 ± 2,424	23,774 ± 2,903
Females			
EX (n = 22)	24,111 ± 3,008	23,148 ± 4,468	22,036 ± 3,566
CON (n = 16)	24,791 ± 4,411	25,920 ± 5,006	23,938 ± 5,122
Insulin (μU/L/180 min)			
Males			
EX	11,639 ± 4,433	8,266 ± 3,996	7,672 ± 3,610*
CON	9,460 ± 5,864	8,828 ± 3,542	9,351 ± 5,164
Females			
EX	9,723 ± 4,721	9,425 ± 6,838	9,042 ± 6,712
CON	14,036 ± 9,056	13,461 ± 8,613	13,041 ± 8,144

*Significant difference from baseline.

Table 4. Fasting and 2-Hour Glucose and Insulin Values During an Oral Glucose Tolerance Test at Baseline and After 9 Months and 16 Months of Verified Supervised Exercise in Previously Sedentary Young Adults (means ± SD)

	Baseline	9 Months	16 Months
Fasting glucose (mmol/L)			
Males			
EX (n = 15)	5.52 ± 0.37	5.42 ± 0.39	5.08 ± 0.44
CON (n = 13)	5.61 ± 0.48	5.12 ± 0.42	5.23 ± 0.51
Females			
EX (n = 22)	5.43 ± 0.39	5.37 ± 0.38†	5.06 ± 0.52†
CON (n = 16)	5.50 ± 0.39	5.66 ± 0.82	5.35 ± 0.79
Fasting insulin (μU/mL)			
Males			
EX	12.33 ± 3.53	9.82 ± 2.71*	10.20 ± 4.94*
CON	12.41 ± 4.63	10.18 ± 4.23	10.92 ± 4.63
Females			
EX	12.19 ± 4.24	11.32 ± 3.94	11.26 ± 7.06
CON	15.31 ± 5.27	17.25 ± 10.55	18.44 ± 13.93
2-hour glucose (mmol/L)			
Males			
EX	8.42 ± 2.12	7.40 ± 1.9*	7.35 ± 1.44*
CON	6.79 ± 1.63	7.12 ± 1.01	6.40 ± 1.72
Females			
EX	7.27 ± 1.07	6.96 ± 1.42†	6.37 ± 1.43
CON	7.15 ± 1.36	7.77 ± 1.87	6.65 ± 1.74
2-hour insulin (mmol/L)			
Males			
EX	85.4 ± 54.1	52.3 ± 35.0*	45.5 ± 34.1*
CON	52.8 ± 45.5	49.7 ± 21.2	42.3 ± 36.9
Females			
EX	58.2 ± 32.7	50.4 ± 33.1	49.8 ± 45.0
CON	77.5 ± 43.6	87.0 ± 92.0	71.1 ± 51.2

*Significant difference from baseline.
†Significant difference from control.

curve during an OGTT only in the male subjects who had both improvements in $\dot{V}O_2$max and weight loss. In the female exercise subjects, long-term exercise prevented a deterioration in many of the variables that are associated with a decline in insulin sensitivity, such as body weight and waist circumference.

In shorter duration (3 to 5 months) nonrandomized trials improvements in insulin action have been observed without concurrent changes in body composition.[12,21] It is important to note that in many of these previous investigations the subject population was middle-aged or older.[12,20-22] In our group of younger subjects, improvement in insulin sensitivity occurred only in the male EX subjects who had significant increases in $\dot{V}O_2$ max and decreases in body mass and body fat. While the female EX subjects improved $\dot{V}O_2$max, there was no significant improvement in insulin action. These results could indicate that the mechanisms for changing insulin sensitivity following exercise and weight loss may change as one ages and becomes at greater risk for insulin resistance or NIDDM. The data from our female subjects support the short-term results of Segal et al,[39] who found no change in glucose or insulin area under the curve or body composition subsequent to 3 months of aerobic exercise training.

While glucose area under the curve was not altered by regular exercise and weight loss, there appeared to some modification to the process of glucose removal, because insulin concentrations were decreased in the male EX group after 9 months of training. Insulin-mediated glucose disposal may be enhanced following aerobic exercise as a result of a variety of mechanisms, including an enhanced delivery of insulin and glucose to muscle tissue. Dela et al[40] observed that improvements in insulin-mediated glucose disposal following 10 weeks of 1-legged training corresponded with enhancement of insulin-mediated muscle blood flow and enhanced glucose extraction. Improvements in insulin sensitivity[41-43] or an increase in glucose 4 transport proteins[14,17,44] may be also be responsible for the lower insulin concentration required to dispose of set glucose load.

Abdominal obesity is an independent risk factor for development of NIDDM.[45,46] Furthermore, weight loss and loss of central fat in older men has been shown to improve glucose metabolism.[23,47-49] The significant correlations observed in the current investigation support previous data and suggest that changes in the levels of body fat can play a role in the alteration

Table 5. Total Energy Intake and Macronutrient Content at Baseline and After 9 Months and 16 Months of Verified Supervised Exercise in Previously Sedentary Young Adults (means ± SD)

	Baseline	9 Months	16 Months
Energy intake (kcal)			
Males			
EX (n = 15)	3,172 ± 455	3,135 ± 572	3,259 ± 693
CON (n = 13)	3,536 ± 818	3,529 ± 1,088	3,465 ± 788
Females			
EX (n = 22)	2,574 ± 504	2,373 ± 484	2,427 ± 538
CON (n = 16)	2,294 ± 489	2,402 ± 827	2,382 ± 578
Carbohydrate content (g)			
Males			
EX	411.6 ± 68.8	400.4 ± 76.9	418.4 ± 118.9
CON	452.4 ± 104.2	472.3 ± 145.7	459.0 ± 108.0
Females			
EX	362.8 ± 65.2	335.6 ± 77.0	336.1 ± 81.5
CON	332.1 ± 82.2	329.1 ± 108.8	322.0 ± 90.7
Fat content (g)			
Males			
EX	122.1 ± 25.1	121.6 ± 30.8	124.7 ± 29.2
CON	136.1 ± 44.4	134.0 ± 49.6	125.5 ± 35.8
Females			
EX	92.2 ± 30.4	84.6 ± 25.7	88.4 ± 26.7
CON	80.7 ± 20.2	92.0 ± 38.9	90.6 ± 23.8
Protein content (g)			
Males			
EX	104.3 ± 21.7	107.1 ± 25.0	108.9 ± 25.5
CON	121.2 ± 26.9	121.8 ± 52.9	120.8 ± 29.3
Females			
EX	80.7 ± 16.8	74.8 ± 13.7	76.8 ± 17.0
CON	68.8 ± 18.6	75.5 ± 31.7	74.9 ± 26.0

*Significant difference from baseline.
†Significant difference from control.

of glucose metabolism and thereby decrease the risk for cardiovascular disease[15] and NIDDM.[50]

Fasting levels of insulin are considered to be very good markers of impaired glucose tolerance and insulin resistance.[51,52] As with several of the other measures in this investigation, the fasting insulin concentration decreased in the exercising males, who had improvements in both $V\text{O}_2$ max and weight loss and not in the females who only had improvements in $V\text{O}_2$ max. These data would tend to support the importance of both improvements in cardiovascular fitness and changes in body weight and body fat for improving insulin sensitivity.

It is of interest to determine the mechanism(s) that influenced the results of the current investigation. Previous studies have observed increases in energy intake in response to moderate intensity exercise in female rats, but not male rats.[53,54] The possibility exists that the female subjects in the current study compensated with an increase in energy intake, but this is not supported by the energy intake data (Table 5). It is possible that the females under-reported their energy intake, but they probably under-reported just as much at baseline as they did at 9 months and 16 months. Another possible explanation is that the female exercisers decreased their physical activity at other times during the day and, thus, decreased their 24-hour energy expenditure. The volume of exercise for the female subjects may not have been large enough and they were able to compensate more easily with a decrease in 24-hour energy expenditure. In contrast, the men expended more energy during exercise and their energy intake did not change; consequently, they lost weight because their 24-hour energy expenditure was increased.

The strengths and limitations of this investigation warrant some consideration. A major strength is the randomized controlled trial design that minimized the potential for selection bias. To avoid the potentially confounding effects of disease and medications on metabolic function, we only accepted individuals who were healthy with no overt disease and we excluded subjects who were receiving medications. Additionally, all subjects consumed diets of similar composition, which eliminated the confounding effect of dietary heterogeneity on the metabolic response to the intervention. The direct supervision of the subjects allowed us to monitor exercise accurately and ensured the completion of the exercise prescription. Finally, because we included only healthy young subjects, generalizability of our results and the conclusions based on the subject's responses to the intervention may not applicable to older men and women or individuals who have impaired glucose metabolism or other comorbid diseases.

In conclusion, the effects of 16 months of verified, supervised exercise in healthy overweight young adults resulted in improvements in insulin sensitivity when there was an increase in cardiorespiratory fitness and decreases in body mass and body fat. This has important implications for exercise prescription and the prevention of conditions such as impaired glucose tolerance or insulin resistance. These data suggest that in young overweight or mildly obese subjects, improvements in insulin sensitivity can be expected to occur with changes in body weight or body composition, but insulin sensitivity may not change in younger adults who experience only changes in cardiorespiratory fitness.

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