Distinct effects of aerobic exercise training and weight loss on glucose homeostasis in obese sedentary men

DONALD R. DENGEL, RICHARD E. PRATLEY, JAMES M. HAGBERG, ELLEN M. ROGUS, AND ANDREW P. GOLDBERG

Division of Gerontology, Department of Medicine, University of Maryland School of Medicine, and Geriatric Service and Geriatric Research, Education, and Clinical Center, Baltimore Veterans Affairs Medical Center, Baltimore 21201; and Center on Aging, University of Maryland, College Park, Maryland 20742

Dengel, Donald R., Richard E. Pratley, James M. Hagberg, Ellen M. Rogus, and Andrew P. Goldberg. Distinct effects of aerobic exercise training and weight loss on glucose homeostasis in obese sedentary men. J. Appl. Physiol. 81(1): 318–325, 1996.—The decline in glucose homeostasis with aging may be due to the physical deconditioning and obesity that often develop with aging. The independent and combined effects of aerobic exercise training (AEX) and weight loss (WL) on glucose metabolism were studied in 47 nondiabetic sedentary older men. There were 14 men in a weekly behavioral modification/WL program, 10 in a 3 times/wk AEX program, 14 in an AEX + WL program, and 9 in the control (Con) group. The 10-mo intervention increased maximal oxygen consumption ($V_{O_{2max}}$) in both the AEX and AEX + WL groups [0.33 ± 0.05 and 0.37 ± 0.09 (SE) l/min, respectively], but $V_{O_{2max}}$ did not significantly change in the WL (0.01 ± 0.06 l/min) and Con groups (-0.04 ± 0.05 l/min; P > 0.05). The AEX + WL and WL groups had comparable reductions in body weight (-8.5 ± 0.9 and -8.8 ± 1.2 kg, respectively) and percent fat (-5.5 ± 0.7 and -5.9 ± 1.1%, respectively) that were significantly greater than those in the Con and AEX groups. Oral glucose tolerance tests showed significant reductions in insulin responses in the AEX, WL, and AEX + WL groups, but the decrease in insulin response in the AEX + WL group was significantly greater than that in the other three groups. The glucose area decreased significantly in the WL and AEX + WL groups but did not change in the Con or AEX groups. There were significant increases in insulin-mediated glucose disposal rates as measured by the hyperinsulinemic (600 pmol·m -2·min -1) euglycemic clamps in the AEX and AEX + WL groups [1.66 ± 0.50 and 1.76 ± 0.41 mg·kg -1·min -1 (FFM -1·min -1), respectively] that were significantly greater than those in the WL (0.13 ± 0.31 mg·kg FFM -1·min -1) and Con groups (0.05 ± 0.51 mg·kg FFM -1·min -1; n = 5). These data suggest that AEX and WL improve glucose metabolism through different mechanisms and that the combined intervention of AEX + WL is necessary to improve both glucose tolerance and insulin sensitivity in older men.

AEROBIC EXERCISE TRAINING (AEX) and weight reduction are nonpharmacological therapies that can potentially improve glucose metabolism in healthy older obese individuals. Most studies (12, 17, 20, 24) examining the effect of AEX without a concurrent loss in body weight on glucose homeostasis show no significant change in oral glucose tolerance despite reduced plasma insulin responses. Although AEX does not appear to alter oral glucose tolerance, it does increase tissue sensitivity to insulin (8, 16, 20, 30). Weight reduction appears to produce different effects on glucose metabolism than does AEX. Unlike AEX, weight loss (WL) improves glucose tolerance in young (2, 24) and older (4, 5, 31) obese individuals, but it appears that it has little (4, 24) or no effect (2) on tissue sensitivity to insulin. When WL is combined with an AEX program, there are improvements in insulin sensitivity and glucose tolerance in diabetic as well as in glucose-intolerant young and middle-aged adults (2).

Based on these findings, we hypothesized that AEX and WL would improve different aspects of glucose metabolism in older obese men and that the combination of the two would improve both oral glucose tolerance and tissue sensitivity to insulin. This study was designed to compare and contrast the independent effects of WL and AEX on oral glucose tolerance and insulin sensitivity in older sedentary overweight men and to determine whether these effects are complementary.

METHODS

Subjects

Forty-seven sedentary nonsmoking Caucasian men over the age of 45 yr who were between 120 and 160% of ideal body weight (22) were studied. Volunteers were recruited from the Baltimore-Washington metropolitan area through newspaper advertisements. All subjects were community dwelling and in good health. The subjects provided written informed consent according to the guidelines of the Institutional Review Boards at the University of Maryland and the John Hopkins Bayview Medical Center, Baltimore, MD. The subjects were screened for disease with a medical history, physical examination, fasting plasma glucose, and routine blood chemistries. Individuals were excluded from participation if they exceeded 160% of ideal body weight (22) or if they had a fasting plasma glucose > 7.8 mmol/l, blood pressure > 160/90 mmHg, or an underlying illness based on medical history, physical examination, and biochemical blood analyses. Each subject had resting supine and upright 12-lead electrocardiograms and blood pressures measured before undergoing a graded-exercise treadmill test (3) to a minimum of 85% of age-predicted maximal heart rate. Subjects who were limited by symptoms of cardiovascular decompensation during the graded-exercise treadmill test were excluded from the study.

To eliminate the effect of diet on glucose metabolism, all subjects were instructed in the principles of a weight-maintaining American Heart Association (AHA) step I diet (1) over an 8-wk period before baseline testing. This diet consisted of 50–55% of calories as carbohydrate, 30–35% as fat, 15–20% as protein, 300–350 mg/day of cholesterol, and 3 g/day of sodium. The subjects were counseled weekly to maintain their diet composition throughout the length of this
study. Adherence was monitored by registered dietitians who reviewed weekly food records and body weights and calculated dietary composition from biweekly 7-day food records (Nutritionist III, N-Squared Computing, Salem, OR). At baseline and after the intervention, the subjects were weight stable for 4 wk before testing. During this period, the subjects were instructed to maintain their body weight within 1 kg.

**Interventions**

The subjects were randomly assigned to an intervention that lasted for 10 mo. During the last month, weight and physical activity were stabilized for all the interventions.

**AEX intervention.** The subjects took part in an aerobic exercise program that met three times per week. Exercise training consisted of stationary cycling and walking and jogging on a treadmill starting at 50–60% of each individual’s heart rate reserve for three 5- to 10-min periods. Target heart rate was calculated for each individual with the equation of Karvonen et al. (18). Training intensity was gradually increased by 5–10% of the heart rate reserve every month. At 3 mo, the maximal oxygen consumption \( \text{VO}_{2\text{max}} \) test was repeated, and the intensity was adjusted until 40 min of training per session was achieved at an intensity of 75 85% of heart rate reserve. All training sessions were supervised by the research staff. The subjects were instructed by a dietitian to increase their caloric intake to offset the increase in energy expenditure due to the increase in physical activity.

**WL intervention.** The subjects in the WL group participated in a behavioral modification/WL program conducted once a week by a registered dietitian. Food intake was restricted by a weekly recorded and reviewed, and the subjects were counseled individually as necessary to promote WL.

**AEX + WL intervention.** The subjects in the AEX + WL group exercised 3 times/wk using the same program as the AEX group. In addition, they attended the same weekly behavioral modification/WL classes as the WL group.

**Control (Con) group.** Nine men served as the Con group. Subjects in the Con group were seen biweekly by a registered dietitian to review the AHA step I diet (1).

**Measurement of Body Composition**

Body weight was measured \( \pm 50 \text{ g} \) with a Homms beam balance (Western, San Francisco, CA). The waist-to-hip circumference ratio (WHR) was measured as the ratio of the buttocks at the maximal gluteal protuberance. Body density was determined by hydrostatic weighing (19) and corrected for residual lung volume measured with either the helium-dilution (23) or nitrogen-washout method (32). Percent body fat was calculated with the Siri (28) equation, and fat-free mass (FFM) was calculated as body mass minus fat mass.

**Measurement of \( \text{VO}_{2\text{max}} \)**

A treadmill \( \text{VO}_{2\text{max}} \) test was performed on each subject on at least 2 separate days, as previously described (9). A true \( \text{VO}_{2\text{max}} \) was considered to be attained if two of the following three criteria were met: 1) respiratory exchange ratio at maximal exercise > 1.10, 2) maximal heart rate > 90% of age-predicted maximum (220 – age), and 3) a plateau in oxygen consumption (<200 ml/min change in oxygen consumption) during the last stages of exercise. If a true \( \text{VO}_{2\text{max}} \) was not attained on the second test or the \( \text{VO}_{2\text{max}} \) results for the two exercise tests differed by >200 ml/min, additional \( \text{VO}_{2\text{max}} \) tests were performed until these criteria were met.

**Metabolic Testing**

For 3 days before each metabolic test, the subjects were provided with a calculated weight-maintaining diet of comparable composition to their own AHA step I diets prepared in the metabolic kitchen of the General Clinical Research Center. Body weight varied by <0.5 kg during periods of testing. All metabolic tests were performed in the morning after a 12-h overnight fast. During the final metabolic testing phase of this study, those subjects in the two AEX interventions continued to exercise three times per week. Final metabolic testing was performed 24–36 h after the last exercise training session in the two AEX groups.

**Oral glucose tolerance test (OGTT).** Blood samples were drawn before and at 30-min intervals for 2 h after the ingestion of 40 g of glucose/m2 body surface area (5). Plasma glucose was measured by a glucose oxidase method (Beckman Instruments, Fullerton, CA), and plasma insulin was measured by a radioimmunoassay (34). The areas under the curves for the glucose and insulin responses during the 2-h OGTT were calculated above the basal level by using a trapezoidal model.

**Hyperinsulinemic euglycemic-clamp protocol.** The subjects underwent a hyperinsulinemic euglycemic clamp, as previously described by DeFronzo et al. (7). Nineteen of the forty-three subjects underwent a single primed continuous infusion of regular insulin (Humulin-R, Eli Lilly, Indianapolis, IN) at a rate of 600 pmol m-2 min-1 for 180 min. Twenty-four subjects had sequential primed continuous 90-min infusions of insulin at 120 and 600 pmol m-2 min-1, each for 90 min, for a total duration of 180 min. Only five individuals in the Con group underwent the hyperinsulinemic euglycemic-clamp procedure. Plasma insulin levels during the last 90 min of the single and two-step clamps at the 600 pmol m-2 min-1 were comparable at baseline (2,010 ± 100 and 1,802 ± 76 pmol/l, respectively; \( P = \) not significant) and after intervention (1,870 ± 98 and 1,664 ± 69 pmol/l, respectively; \( P = \) not significant). We have previously shown that both clamp protocols result in the same rate of glucose disposal at the 600 pmol m-2 min-1 dose when performed in the same subjects on different days (26). All subjects had the same clamp protocol at baseline and after intervention. Mean glucose disposal rates were calculated during the last 30 min of the glucose clamp and normalized for FFM. Steady-state plasma insulin levels were determined in plasma blood samples drawn every 10 min during the last 30 min of the insulin infusion.

**Reevaluation**

At the completion of the interventions, the diets were reviewed, and the subjects’ weight was stabilized on the AHA step I diet for 4 wk before measurement of body composition, \( \text{VO}_{2\text{max}}, \) oral glucose tolerance, and insulin action (hyperinsulinemic euglycemic clamp). The subjects were again provided with metabolic test diets for 3 days before testing.

**Statistical Analysis**

Data were analyzed with standard statistical software packages (Statview, Abacus Concepts, Calabasas, CA). An alpha level of 0.05 was accepted for statistical significance. To determine whether there were differences in baseline or final values and absolute changes in measurements of body composition, \( \text{VO}_{2\text{max}}, \) and glucose metabolism among the four groups, analyses of variance with differences among groups deter-
Table 1. Characteristics of subjects

<table>
<thead>
<tr>
<th></th>
<th>Control Group (n = 9)</th>
<th>WL Group (n = 14)</th>
<th>AEX Group (n = 10)</th>
<th>AEX + WL Group (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>62.8 ± 2.5</td>
<td>59.6 ± 2.4</td>
<td>60.3 ± 2.4</td>
<td>57.6 ± 1.6</td>
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<tr>
<td>Weight, kg</td>
<td>90.1 ± 4.0</td>
<td>89.1 ± 9.8</td>
<td>94.8 ± 4.8</td>
<td>94.8 ± 3.2</td>
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<tr>
<td><strong>Baseline</strong></td>
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<tr>
<td>Relative fat, %</td>
<td>-0.2 ± 0.9</td>
<td>-8.6 ± 1.1 (%)</td>
<td>-0.5 ± 0.6</td>
<td>-8.8 ± 0.9 (%)</td>
</tr>
<tr>
<td><strong>Final</strong></td>
<td>30.1 ± 15</td>
<td>28.5 ± 1.7 (%)</td>
<td>30.8 ± 1.6</td>
<td>28.7 ± 1.2 (%)</td>
</tr>
<tr>
<td><strong>Difference</strong></td>
<td>-0.3 ± 0.7</td>
<td>-8.6 ± 1.0 (%)</td>
<td>0.2 ± 0.7</td>
<td>-5.8 ± 0.7 (%)</td>
</tr>
<tr>
<td>Fat mass, kg</td>
<td>27.7 ± 2.4</td>
<td>26.5 ± 2.1</td>
<td>29.7 ± 2.2</td>
<td>27.9 ± 1.4</td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td>27.4 ± 2.3</td>
<td>19.4 ± 2.1 (%)</td>
<td>29.2 ± 2.4</td>
<td>20.4 ± 1.3 (%)</td>
</tr>
<tr>
<td><strong>Final</strong></td>
<td>-0.4 ± 0.8</td>
<td>-7.1 ± 1.1 (%)</td>
<td>-0.5 ± 0.8</td>
<td>-7.5 ± 0.8 (%)</td>
</tr>
<tr>
<td><strong>Difference</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>WHR</td>
<td>0.98 ± 0.01</td>
<td>0.95 ± 0.02</td>
<td>0.99 ± 0.02</td>
<td>0.95 ± 0.01</td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td>0.90 ± 0.02</td>
<td>0.93 ± 0.01 (%)</td>
<td>0.98 ± 0.02</td>
<td>0.93 ± 0.01 (%)</td>
</tr>
<tr>
<td><strong>Final</strong></td>
<td>0.00 ± 0.01</td>
<td>-0.01 ± 0.01</td>
<td>-0.01 ± 0.01</td>
<td>-0.02 ± 0.01</td>
</tr>
<tr>
<td><strong>Difference</strong></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of subjects. *Significant change from baseline value, P < 0.05. Significant difference (P < 0.05) from: † control group; § WL group; $ AEX group.

mined by post hoc tests (Fisher’s least significant difference) were used. Changes in variables resulting from the respective interventions were compared within groups with analysis of variance. Pearson correlation coefficients were calculated between changes in glucose metabolism vs. changes in body composition and cardiovascular fitness. All data are reported as means ± SE.

RESULTS

Subject Characteristics at Baseline

The initial age, body weight, percent fat, and VO2max were comparable among the Con, WL, AEX, and AEX + WL groups (Table 1). At baseline, 60% of the OGTTs (28 out of 47) were classified as impaired and 40% were normal according to World Health Organization (WHO) criteria (33). There also were no significant differences in either fasting glucose or insulin levels or their responses during an OGTT among the four groups (Table 2).

Changes After the Interventions

Body composition and VO2max (Table 1). There were significant decreases in body weight, fat mass, and percent fat in the AEX + WL and WL groups that were significantly greater than those in the Con and AEX groups. There was a significant decrease in FFM in the

Table 2. Oral glucose tolerance

<table>
<thead>
<tr>
<th></th>
<th>Control Group (n = 9)</th>
<th>WL Group (n = 14)</th>
<th>AEX Group (n = 10)</th>
<th>AEX + WL Group (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting glucose, mmoV/l</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Baseline</td>
<td>390.4 ± 35.4</td>
<td>394.2 ± 35.9</td>
<td>415.4 ± 47.6</td>
<td>375.5 ± 47.8</td>
</tr>
<tr>
<td>Final</td>
<td>402.0 ± 45.2</td>
<td>321.4 ± 32.2 (%)</td>
<td>412.0 ± 42.1</td>
<td>297.3 ± 27.3 (%)</td>
</tr>
<tr>
<td>Difference</td>
<td>82.1 ± 42.5</td>
<td>-72.8 ± 18.8 (%)</td>
<td>-2.9 ± 26.6</td>
<td>-75.3 ± 28.6 (%)</td>
</tr>
<tr>
<td>Glucose area, mmoV·min⁻¹·l⁻¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>43.12 ± 7.724</td>
<td>48.591 ± 7.077</td>
<td>60.205 ± 10.654</td>
<td>52.752 ± 5.789</td>
</tr>
<tr>
<td>Final</td>
<td>52.992 ± 13.024</td>
<td>36.708 ± 5.576 (%)</td>
<td>48.999 ± 9.014 (%)</td>
<td>30.443 ± 3.195 (%)</td>
</tr>
</tbody>
</table>

Values are means ± SE; n, no. of subjects. * Significant change from baseline value, P < 0.05. Significant difference (P < 0.05) from: † control group; ‡ WL group; § AEX group.
WL and AEX+WL groups; however, this decrease in FFM was not significantly different from in the Con and AEX groups. There was a significant decrease in the WHR in the AEX+WL group (-0.03±0.01), which was significantly greater than that in the Con group but did not differ from the changes in the AEX (-0.01±0.01) or WL group (-0.01±0.01). There were comparable increases in V02max in both the AEX (0.33±0.05 l/min) and AEX+WL groups (0.37±0.09 l/min), which were significantly greater than the changes in V02max in the Con and WL groups (-0.04±0.05 and 0.01±0.06 l/min, respectively).

Glucose and insulin responses to an OGTT (Table 2, Figs. 1 and 2). There were no changes in fasting glucose levels in any of the four groups after their respective interventions. The reductions in glucose area in the AEX+WL and WL groups were significantly greater than the change in either the Con or AEX groups, where changes were minimal and nonsignificant.

There was a significant reduction in fasting insulin levels only in the AEX+WL group, and this decrease was significantly greater than that in the Con or AEX groups. The AEX, WL, and AEX+WL groups all had significant reductions in their insulin areas after intervention. However, the decrease in the insulin area in the AEX+WL group was significantly greater than those in the AEX, WL, and Con groups. The reductions in the insulin areas in both the AEX and WL groups were significantly greater than that in the Con group.

Hyperinsulinemic euglycemic clamp (Fig. 3). The plasma insulin levels during the hyperinsulinemic euglycemic clamp in the Con, AEX, WL, and AEX+WL groups were not significantly different at baseline (1,846±221, 1,954±186, 1,790±101, and 1,786±120 pmol/l, respectively) or after intervention (2,033±137, 1,764±143, 1,687±111, and 1,712±90 pmol/l, respectively) within and among the four groups. After 10 mo of intervention, there was no change in glucose disposal in either the Con or WL groups (-0.05±0.51 and 0.13±0.31 mg·kg·FFM⁻¹·min⁻¹, respectively). However, the glucose disposal rate increased significantly and to the same magnitude in both the AEX (1.66±0.50 mg·kg·FFM⁻¹·min⁻¹) and the AEX+WL groups (1.76±0.41 mg·kg·FFM⁻¹·min⁻¹) after inter-

![Fig. 1. Plasma glucose during oral glucose tolerance tests at baseline (○) and after intervention (□) in aerobic exercise training (AEX; A), weight-loss (WL; B), AEX+WL(C), and control (Con; D) groups. Values are means ± SE.](image-url)
Intervention. This 22% increase in the glucose disposal rate in the two AEX groups was significantly greater than those in the WL and Con groups ($P < 0.05$).

Relationship of changes in $\text{VO}_{2\max}$ and body composition to glucose metabolism (Figs. 4 and 5). Regression analyses were performed to determine whether changes in body composition (weight, percent fat, and WIIR) or cardiovascular fitness ($\text{VO}_{2\max}$) as a result of the interventions were related to changes in glucose metabolism (fasting glucose and insulin, glucose and insulin areas, and glucose disposal) in these obese older men. The change in glucose area was positively correlated with changes in body weight ($r = 0.51; P = 0.0001; n = 47$) and percent fat ($r = 0.53; P = 0.0001; n = 47$; Fig. 4). In addition, there was a trend for the change in glucose area to be positively related to the change in $\text{VO}_{2\max}$; however, this relationship did not reach statistical significance ($r = 0.27; P = 0.07; n = 43$). There was a trend for the change in insulin area to be related to changes in body weight ($r = 0.28; P = 0.06; n = 47$), percent fat ($r = 0.28; P = 0.06; n = 47$), and $\text{VO}_{2\max}$ ($r = 0.25; P = 0.10; n = 47$); none of these relationships reached statistical significance. The improvement in glucose disposal correlated positively with the increase in $\text{VO}_{2\max}$ ($r = 0.40, P = 0.01; n = 43$; Fig. 5) in these subjects; however, there was no significant relationship between the improvement in glucose disposal and

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**Fig. 2.** Plasma insulin during oral glucose tolerance tests at baseline (○) and after intervention (▲) in AEX (A), WL (B), AEX+WL (C), and Con (D) groups. Values are means ± SE. Significantly different after intervention: *$P < 0.05$, **$P < 0.01$.**

**Fig. 3.** Baseline (solid bars) and after intervention (open bars) glucose disposal rates. FFM, fat-free mass. Values are means ± SE; $n$, no. of subjects. *Significantly different from baseline, $P < 0.05$.**
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changes in body composition ($r = 0.00-0.22; P = 0.17-0.99$). None of these variables were significantly related to WHR.

**DISCUSSION**

Abnormalities in glucose homeostasis frequently occur in the elderly. These abnormalities may be due to decreases in physical activity and/or the development of obesity that typically occur with aging (11). The results of this study indicate that the decline in glucose metabolism in older obese sedentary individuals is modifiable by changes in both physical activity and dietary habits. Interventions of AEX alone or combined

with WL increased insulin-mediated glucose utilization and reduced plasma insulin levels in older obese sedentary men by increasing peripheral tissue glucose disposal. However, glucose responses during an OGTT improved only when aerobic exercise was accompanied by WL; aerobic exercise alone did not improve glucose area during the OGTT. In contrast, WL alone was associated with decreases in glucose and insulin responses during the glucose tolerance test but with no change in insulin-mediated glucose disposal. These findings are strengthened by the significant correlations between changes in glucose area during the OGTT and changes in body fat and between glucose disposal rates and $V_{O_2\text{max}}$.

To the best of our knowledge, this is the first study to compare and contrast the effects of WL and AEX alone and combined on body composition, maximal aerobic capacity, glucose tolerance, and insulin sensitivity in a healthy population of obese sedentary older men of comparable age, obesity, and $V_{O_2\text{max}}$. The magnitude of the improvements in glucose homeostasis in these obese sedentary older men suggests that a regular program of AEX combined with a reduction in body weight might prevent the development of non-insulin-dependent diabetes mellitus in older obese individuals.

In the present study, AEX improved insulin action, as evidenced by the increase in insulin-mediated glucose disposal. The lack of change in glucose responses during the OGTT with AEX despite an increase in insulin action could be due to an adaptation in insulin secretion. This adaptation results in a reduction in insulin levels that was apparent after an oral glucose challenge. These findings are similar to other studies where reduced insulin responses to oral glucose (12, 20, 27, 30) and intravenous glucose and arginine (17) and enhanced tissue sensitivity to insulin (17, 30) with AEX were not associated with improvements in glucose responses during an OGTT. This study confirms the hypothesis that a sedentary lifestyle is a determinant of insulin resistance (17). In addition, these results support the research of Kahn et al. (17) that AEX can improve insulin sensitivity but does not improve glucose responses to an oral glucose challenge.

Improvement in insulin-mediated glucose disposal with AEX may be due to a variety of mechanisms, one of which may be an enhanced delivery of insulin and glucose to muscle tissue. Dela et al. (8) observed that improvements in insulin-mediated glucose disposal through 10 wk of one-legged training coincided with enhancement of insulin-mediated muscle blood flow and enhanced glucose extraction. Another possible mechanism, which may coexist with an increase in muscle blood flow and glucose extraction, is an increase in glucose transporters in muscle (i.e., GLUT-4). Previous studies (10, 15, 16) have reported increased amounts of glucose transporters due to aerobic exercise. Thus an increase in glucose transporters would provide the muscle with a mechanism capable of removing the glucose from the blood, thereby increasing glucose disposal.
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AEX increases the capacity for the storage of glucose as muscle glycogen by means of increases in glycogen synthase activity (25). Ebeling et al. (10) observed that during a 4-h insulin infusion muscle glycogen content increased by 39% in young athletes but remained unchanged in sedentary control subjects. Along with this increase in glycogen content, basal glycogen synthase activity was 33% greater in athletes than in sedentary control subjects. Along with this increase in blood flow during the insulin infusion. Dela et al. (8) observed that 10 wk of one-legged training not only increased insulin-mediated glucose disposal but also resulted in significant improvements in glycogen synthase mRNA levels. These data suggest that the increase in insulin-stimulated glucose disposal observed with AEX is likely to be due to an increase in glucose and insulin delivery to the muscle and to greater uptake and storage of glucose by the cell.

Similar to AEX, the WL intervention also reduced insulin responses to an oral glucose challenge. In contrast, the WL group improved the glucose area during the OGTT but did not increase insulin action as measured by the hyperinsulinemic euglycemic clamp. The reduction in both glucose and insulin responses after WL is reported in several studies (5, 29, 31). However, we expected the combination of reduced glucose and insulin responses to an oral glucose challenge to be associated with a concomitant increase in insulin-mediated glucose disposal. It is unclear to us why the WL group did not increase glucose disposal detectable during the glucose-clamp procedure; however, similar results were reported by Bogardus et al. (2). In contrast to our findings, however, WL was accompanied by an increase in tissue sensitivity to insulin when it was accomplished over a shorter period, utilizing very low-calorie high-protein diets in non-insulin-dependent diabetic subjects (13, 14, 21). In those studies, the subjects were still losing weight at the time of reevaluation. A hypocaloric glycogen-depleted state could account for an increased tissue sensitivity to glucose. In the present study, the subjects lost weight over a longer period on a moderate hypocaloric AHA step I diet and were weight stable for 4 wk before reevaluation. These results suggest that unless there is an improvement in skeletal muscle metabolism (the primary site of glucose disposal) (6), there may not be an improvement in insulin sensitivity. Because WL has little effect on skeletal muscle metabolism, it did not increase whole body sensitivity to insulin in these obese older men. An alternative explanation for these findings is that insulin sensitivity did improve and contributed to enhanced glucose disposal during the OGTT but was not detectable at the insulin infusion rate used during hyperinsulinemic euglycemic clamp in the present study. This would be supported by previous research from our group (4) reporting improvements in glucose disposal measured during hyperglycemic clamp at low plasma insulin levels but not at higher plasma insulin levels.

It appears that aerobic exercise and WL reduce insulin responses to an oral glucose challenge by distinct mechanisms because the combined effects of the two interventions were additive and resulted in a greater reduction in the insulin responses than the two single interventions. The reduction of fat tissue that occurred with WL and the improvement in insulin-mediated glucose disposal during AEX may both affect insulin responses to an oral glucose challenge.

In summary, these results suggest that in healthy nondiabetic older obese sedentary men AEX and weight reduction have different effects on glucose metabolism. AEX alone increased insulin-mediated glucose disposal and reduced insulin responses but not glucose responses to an oral glucose challenge. Weight reduction reduced both glucose and insulin responses to an oral glucose challenge without enhancing insulin-mediated glucose disposal during a hyperinsulinemic euglycemic clamp. The combined intervention of AEX and weight reduction improved both insulin and glucose responses to an oral glucose challenge and enhanced insulin-mediated glucose disposal. Therefore, it appears that in older sedentary overweight men the combined intervention of AEX and weight reduction is needed to improve both glucose tolerance and tissue sensitivity to insulin.

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Present address and address for reprint requests: D. Dengel, GRECC (11G), Ann Arbor VA, 2215 Fuller Rd., Ann Arbor, MI 48105.

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