Effects of Aerobic or Resistance Exercise and/or Diet on Glucose Tolerance and Plasma Insulin Levels in Obese Men

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OBJECTIVE — This study had two objectives. First, we examined whether the influence of diet combined with either aerobic (DA) ($n = 10$) or resistance (DR) ($n = 10$) exercise has effects on insulin and glucose levels that are different in obese men. Second, we tried to determine whether the combination of diet and exercise is associated with improvements in insulin and glucose levels that are greater than those associated with diet alone (DO) ($n = 9$).

RESEARCH DESIGN AND METHODS — Insulin and glucose levels were measured after an overnight fast and a 75-g oral glucose challenge (OGTT). Visceral adipose tissue (AT), subcutaneous AT, and skeletal muscle were measured by magnetic resonance imaging (MRI) before and after treatment (16 weeks).

RESULTS — Reductions in weight (12.4 ± 3.8 kg) and in visceral (37 ± 15.1%) and subcutaneous AT (24.3 ± 8.6%) were not different between treatments ($P > 0.05$). Skeletal muscle was maintained in the DA and DR groups but was reduced (7.3 ± 2.8%) in the DO group ($P < 0.05$). Independent of treatment, fasting glucose and OGTT glucose did not change ($P > 0.05$). However, fasting insulin and OGTT insulin decreased within all treatments ($P < 0.05$). Reductions in the OGTT insulin area under the curve were greater ($P < 0.05$) within the DA (52 ± 12%) and DR (42 ± 17%) treatments than in the DO (20 ± 15%) treatment. Collapsed across group, reductions in visceral AT were related to reductions in fasting and OGTT glucose ($P < 0.05$), whereas reductions in abdominal subcutaneous AT correlated with reductions in fasting insulin ($P < 0.05$).

CONCLUSIONS — Weight loss induced by diet and aerobic or resistance exercise has similar positive effects on lowering fasting and OGTT insulin values that are greater than those with diet alone. Because changes in glucose and insulin were related to reductions in visceral and abdominal subcutaneous AT, we conclude that reduction in abdominal obesity consequent to diet and exercise-induced weight loss is important for attaining improvements in plasma insulin levels, observations that strengthen the concept that abdominal obesity has an important role in mediating insulin resistance.

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Diet-induced weight loss is associated with improvements in insulin sensitivity and glucose tolerance in men and women (1–4). Exercise is also associated with improvements in insulin sensitivity independent of weight loss (5–9). These observations suggest that the combination of diet and exercise should have effects on insulin and glucose metabolism that are greater than those of diet alone. Indeed, Dengel et al. (6) reported that diet and exercise–induced weight loss is associated with greater reductions in insulin values than is diet alone in obese older men. However, in that study and others (4,6–9,12), insulin values were obtained within 36 h of the last exercise session; thus, it is unclear whether the fall in insulin is a consequence of chronic training or the residual effect of the last exercise session (10). Consistent with this observation, Segal et al. (11) reported that aerobic exercise is not associated with improved insulin sensitivity after controlling for the effects of the last exercise bout.

Although the majority of evidence evaluating whether exercise enhances insulin action has been determined using aerobic exercise, Smotuk and colleagues (7,8) have twice reported that resistance exercise reduced insulin values in response to a glucose challenge in populations with abnormal glucose tolerance. It is also reported that resistance exercise is associated with concomitant improvements in insulin sensitivity in postmenopausal women (9) and elderly men (12). Comparison of aerobic and resistance exercise effects on carbohydrate metabolism is restricted to two studies wherein the corresponding improvements in glucose tolerance and insulin sensitivity were not different in men at risk for coronary heart disease (7,8). Absent from the literature are studies that simultaneously examine whether the combination of diet and aerobic or resistance exercise has effects on glucose tolerance and insulin action that are different from each other, or from diet alone, in obese populations.

Improvements in insulin sensitivity with weight loss may be partially mediated by associated reductions in adipose tissue

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Abbreviations: AT, adipose tissue; AUC, area under the curve; DA, diet and aerobic exercise; DO, diet only; DR, diet and resistance exercise; MRI, magnetic resonance imaging; OGTT, oral glucose tolerance test.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Descriptive characteristic of subjects*

Variable	DO	DA	DR
n	9	10	10
Anthropometry			
Age (years)	44.4 ± 6.1	47.4 ± 6.7	39.8 ± 13.2
Weight (kg)	99.1 ± 11.2	100.9 ± 12.7	109.9 ± 9.2
BMI (kg/m^2)	31.9 ± 2.8	32.3 ± 3.7	33.8 ± 4.2
Waist-to-hip ratio	0.96 ± 0.04	1.01 ± 0.06	1.02 ± 0.04
Waist circumference (cm)	106.9 ± 7.3	113.4 ± 7.7	118.5 ± 10.7
MRI variables (liters)			
Total AT	34.2 ± 7.9	34.5 ± 7.1	39.6 ± 10.9
Subcutaneous AT	27.1 ± 7.0	26.4 ± 6.5	33.0 ± 9.1
Abdominal	6.6 ± 2.1	7.0 ± 2.2	8.6 ± 2.8
Lower body	11.8 ± 2.9	10.6 ± 2.7	14.3 ± 3.5
Visceral AT	4.6 ± 1.6	4.6 ± 1.5	4.1 ± 2.4
Intraperitoneal	3.6 ± 1.4	3.4 ± 1.2	3.1 ± 1.9
Extraperitoneal	0.9 ± 0.3	1.0 ± 0.3	0.8 ± 0.4
Skeletal muscle	34.8 ± 3.7	33.2 ± 4.6	35.2 ± 5.1
Metabolic			
Fasting glucose (mmol/l)	5.8 ± 0.6	5.6 ± 0.4	5.9 ± 1.4
Fasting insulin (pmol/l)	97.4 ± 18.3	134.2 ± 89.1	145.0 ± 52.0
Glucose AUC (mmol · l^{-1} · 2 h)	15.5 ± 3.0	14.2 ± 3.7	16.1 ± 7.2
Insulin AUC (pmol · l^{-1} · 2 h)	1,093 ± 380	1,145 ± 503	1,321 ± 448

Data are means ± SD.

(AT), in particular visceral and abdominal subcutaneous AT, as both are established correlates of plasma insulin and glucose levels (13–19). Although it follows that reductions in these tissues should be related to corresponding improvements in carbohydrate metabolism, few studies have investigated this issue and those that have report equivocal findings. Whereas some suggest that reductions in visceral adiposity is related to corresponding improvements in insulin sensitivity (16,20,21), evidence to the contrary is also reported (22,23). To our knowledge, no study has examined whether changes in abdominal subcutaneous AT are related to changes in glucose tolerance or plasma insulin levels.

The aim of this study was twofold: first, to examine in obese men whether diet (caloric restriction) combined with aerobic or resistance exercise has effects on glucose tolerance and insulin action that are different from each other; second, to determine whether the combination of diet and exercise would be associated with greater improvements in plasma insulin and glucose levels than those associated with diet alone. We employed a whole-body magnetic resonance imaging (MRI) protocol to clarify whether changes in visceral, subcutaneous, and skeletal muscle tissues are related to concurrent changes in glucose and insulin responses to an oral glucose challenge.

RESEARCH DESIGN AND METHODS

Subjects

Forty obese but otherwise healthy men were recruited from the general public and gave their informed consent to participate in this study. Entry criteria required that the men be nonsmokers, upper-body obese (BMI [kg/m^2] >27, waist-to-hip ratio >0.95), weight stable (±2 kg) for 6 months before enrollment, taking no medication known to affect the study variables, and consume on average fewer than two alcoholic beverages per day. Pre-participation screening included a medical examination and a 5-h oral glucose tolerance test (OGTT).

The subjects were randomly assigned to one of three treatment groups: diet only (DO), diet and aerobic exercise (DA), or diet and resistance exercise (DR). Seven men did not complete the study. Most of them cited time commitments as the primary reasons, and one was transferred out of the region because of job requirements. Of the 33 who complied with the study requirements, 11 in each group—2 subjects from the DO group and 1 each from the DA and DR groups—were removed from the analysis to better match the groups for all metabolic variables before treatment. The descriptive characteristics for all groups are given in Table 1. The three groups were not different with respect to any anthropometric, MRI, or metabolic variable ($P > 0.05$). This study was conducted in accordance with the ethical guidelines of Queen's University.

Anthropometric measurements

Body weight was measured on a balance scale calibrated to 0.1 kg. Barefoot standing height was measured to the nearest 0.1 cm using a wall-mounted stadiometer. Circumference measurements at the hip and waist were acquired by the same investigator before and after treatment according to the procedures described in the Anthropometric Standardization Reference Manual (24). Body fat distribution by anthropometry was estimated using the waist-to-hip circumference ratio.

Tissue measurement by MRI

Magnetic resonance images were obtained with a General Electric Signa Advantage 1.5 T whole-body scanner (Milwaukee, WI). A T1-weighted, spin-echo sequence with a 210-ms repetition time and a 17-ms echo time was used to acquire all the MRI data. The total time required to obtain all magnetic resonance images for each subject was ~25 min. The protocol followed for MRI image acquisition is described in detail elsewhere (25). Briefly, six data sets (seven images per set) were obtained while the subject lay in the magnet in a prone position, arms straight above the head. Transverse images (10-mm thickness) were obtained every 40 mm over the whole body. For each subject, a total of 41 images was acquired. All image data were transferred to a standalone Indigo2 computer (Silicon Graphics, Mountain View, CA) and analyzed using software developed within our laboratory (TomoVision, Montreal, Canada). Whole-body skeletal muscle and subcutaneous AT were calculated using all 41 images; visceral AT and abdominal subcutaneous AT were derived using 5 abdominal images extending from 1 below to 4 above the L4-L5 intervertebral space; lower-body subcutaneous AT was determined using 18 images extending from the femoral head to the foot. Because it has been hypothesized that the complications associated with the accumulation of visceral AT are related to the portally drained depots (omental and mesenteric) located in the peritoneal cavity, we subdivided visceral AT into intraperitoneal and extraperitoneal compartments using a method previously described (26).

Measurement of plasma glucose and plasma insulin levels

A 5-h 75-g OGTT was administered the morning after an overnight fast. Blood samples were collected from the antecubital vein at 0, 60, 120, 180, 240, and 300 min. The glucose oxidase method (Beckman Glucose Analyser; Beckman Instruments, Fullerton, CA) was used for plasma glucose measurement. Plasma insulin was measured by radioimmunoassay (27). Glucose and insulin areas under the curve (AUCs) were determined using a trapezoid model (28) and were calculated for 2 h and 5 h. For both glucose and insulin AUC, the observations using either 2-h or 5-h values were not different, and thus only the 2-h values are presented. Posttreatment OGTT measurements were obtained 5–10 days after the last exercise session.

Dietary protocol

The Harris-Benedict equation (29) multiplied by a factor of 1.5 was used to estimate each subject's energy requirements (30). This energy intake was followed for a 2-week baseline period. For the 16 weeks after the baseline period, energy intake was reduced by 4.18 MJ/day (1,000 kcal/day). All subjects were required to limit dietary fat intake to <30% of total energy intake. All foods were self-selected, and no supplements were prescribed. Daily diet records were kept and submitted weekly for analysis to ensure adherence to the dietary protocol. After the 16-week treatment, the energy intake for weight maintenance was recalculated by deriving the average daily energy intake obtained from the diet records and adding to that number the energy value associated with the weight loss (assuming 32.2 MJ/kg, 3,500 kcal/lb). The derived energy intake value was prescribed for 2 weeks.

Aerobic exercise protocol

In addition to energy restriction, 10 men performed aerobic exercise 5 days/week. Initial duration of each exercise period was ~19 min and gradually progressed to a maximum duration of 60 min based on individual capabilities. The exercise intensity was followed with automated heart-rate monitors (Polar USA, Stanford, CT). Intensity of exercise progressed from 50 to 85% of maximum heart rate, which was determined during a peak oxygen uptake ($V_{O_{2peak}}$) test. The subject determined the mode of exercise, which varied between walking on a motorized treadmill, stationary cycling, or stair stepping using the StairMaster 4000 (Tri-Tech, Tulsa, OK). All exercise sessions were by appointment and monitored by a physical educator.

Resistance exercise protocol

In addition to the energy restriction, 10 men performed resistance exercise 3 days/week. Training sessions began with a 5- to 10-min warm-up of low-intensity stationary cycling and 5 min of static stretching. Resistance training was executed on seven Nautilus (Nautilus, Deland, FL) weight training stations. The resistance training program consisted of one set of the following seven exercises: leg extension, leg flexion, superpullover (latissimus), bench press, shoulder press, triceps extension, and biceps curl. Subjects performed between 8 and 12 repetitions to failure for each exercise. Once subjects could successfully perform 12 repetitions, the load was increased. Sit-ups for the abdominal muscles were also performed each session. Verbal encouragement by the exercise supervisor was given to ensure that the subjects performed to volitional fatigue. Each resistance exercise session lasted ~30 min.

Determination of strength gains was derived using the following equation: $[(a - b)/a] \times 100$, where a equals the number of weight plates lifted (between 8 and 12 repetitions) at the beginning of week 4 and b equals the number of weight plates lifted at the completion of the program (i.e., 16 weeks). Week 4 was chosen as the initial week in an attempt to represent changes in muscle strength that were due to adaptations in skeletal muscle per se, thereby omitting initial increases attributed to neuromuscular factors.

Energy cost of exercise

Aerobic exercise. The oxygen costs of treadmill walking and stationary cycling were determined using the equations given by the American College of Sports Medicine (31). Energy expenditure was subsequently determined by multiplying the oxygen cost by 21.1 kJ/liter (5.04 kcal/liter).

Resistance exercise. Based on data reported by Ballor et al. (32), the energy expenditure of the resistance exercise program was estimated to be 28 kJ (120 kcal) per session.

Peak V_{O_2} determination. Maximal oxygen consumption was determined during a ramp treadmill test before and after the treatment. Standard open-spirometry techniques were employed with a Beckman metabolic cart (Sensormedics, Fullerton, CA).

Statistical analysis

Data are presented as mean ± SD. A two-way analysis of variance, group (DO, DA, DR) by time (pre, post), was used to evaluate main treatment effects and interactions on all dependent variables. Significant differences were analyzed using a Scheffé post hoc comparison technique. Paired *t* tests were used to assess within-group changes for all dependent variables. Unpaired *t* tests were used to determine changes between variables. Bonferroni adjustments ($P < 0.017$) were used for all *t* tests. Pearson regression analysis was used to determine the relationship between MRI and metabolic variables.

Although not significantly different ($P > 0.05$), the groups were not well matched for pretreatment fasting and OGTT insulin values (Table 1). Thus, an analysis of covariance with the pretreatment value acting as the covariate was used to evaluate main treatment effects and interactions for these variables. Data were analyzed using SYSTAT (33).

RESULTS

Adherence to the diet and exercise program

For the DA group, attendance at the exercise sessions averaged 92% (range 74–99%). The mean duration of each session was 37.0 ± 7.0 min, and the exercise intensity was 77.0 ± 4.0% of maximum predicted heart rate (220 − age). The DR group attended 96% of the exercise sessions (range 85–100%). The mean energy expenditure for the DA group (6.4 ± 2.9 MJ; 26,649 ± 12,148 kcal) was significantly greater than that of the DR group (1.3 ± 0.1 MJ; 5,388 ± 302 kcal). Analysis of the diet records indicated that the mean dietary-induced energy deficits for the DO, DA, and DR groups were 255 ± 30 kJ/day (1,065 ± 127 kcal/day), 232 ± 53 kJ/day (968 ± 222 kcal/day), and 271 ± 62 kJ/day (1,132 ± 261 kcal/day), respectively. The corresponding fat intakes were 20.2 ± 4.7%, 21.6 ± 7.1%, and 23.2 ± 3.7%. There were no treatment differences for the energy deficit or fat intake ($P > 0.1$).

Change in cardiovascular and strength performance

The improvement (16.1 ± 14.7%) in peak V_{O_2} was significant ($P < 0.05$) only for the DA group. Muscular strength increased significantly ($P < 0.05$) in both the upper (11.8 ± 5.1%) and lower (17.6 ± 15.2%) body in the DR group.

Table 2—*Changes in selected anthropometric, MRI, and metabolic variables*

Variable	DO		DA		DR	
	Absolute difference	Percent difference	Absolute difference	Percent difference	Absolute difference	Percent difference
Anthropometry						
Weight (kg)	−12.1 ± 3.4*	12 ± 3	−11.5 ± 3.9*	11 ± 4	−13.6 ± 4.1*	13 ± 4
BMI (kg/m²)	−3.9 ± 1.1*	12 ± 3	−3.7 ± 1.1*	11 ± 4	−4.3 ± 1.4*	13 ± 4
Waist-to-hip ratio	−0.02 ± 0.03	2 ± 3	−0.05 ± 0.05*	5 ± 4	−0.05 ± 0.02*	5 ± 2
Waist circumference (cm)	−8.8 ± 3.9*	8 ± 3	−12.9 ± 4.0*	11 ± 3	−11.9 ± 3.9*	11 ± 3
MRI variables (liters)						
Total AT	−8.5 ± 2.9*	25 ± 6	−9.7 ± 4.6*	28 ± 10	−10.8 ± 3.5*	29 ± 11
Subcutaneous AT	−6.5 ± 2.2*	24 ± 6	−6.1 ± 3.0*	23 ± 10	−8.1 ± 2.9*	26 ± 10
Abdominal	−1.6 ± 0.6*	25 ± 8	−2.1 ± 0.8*	30 ± 10	−2.8 ± 0.9*	34 ± 13
Lower body	−2.6 ± 0.7*	22 ± 5	−2.3 ± 1.5*	21 ± 13	−2.6 ± 1.6*	21 ± 11
Visceral AT	−1.5 ± 0.9*	32 ± 9	−1.8 ± 1.0*	40 ± 14	−1.5 ± 0.7*	40 ± 20
Intraperitoneal	−1.3 ± 0.8*	35 ± 9	−1.5 ± 0.9*	44 ± 15	−1.2 ± 0.6*	44 ± 23
Extraperitoneal	−0.2 ± 0.1*	18 ± 11	−0.3 ± 0.2*	29 ± 14	−0.2 ± 0.1*	28 ± 17
Skeletal muscle	−2.5 ± 1.0*†	7 ± 3	+0.3 ± 1.0	+1 ± 3	+0.2 ± 2.2	+1 ± 6
Metabolic						
Fasting glucose (mmol/l)	+0.0 ± 0.4	0 ± 7	−0.2 ± 0.3	3 ± 5	−0.1 ± 0.7	+1 ± 10
Fasting insulin (pmol/l)	−19.0 ± 18.9*	19 ± 18	−58.6 ± 46.6*	41 ± 12	−53.6 ± 49.3*	33 ± 23
Glucose AUC (mmol · l^{-1} · 2 h)	−0.4 ± 2.6	1 ± 14	−2.4 ± 3.1	12 ± 25	−1.7 ± 1.7	9 ± 10
Insulin AUC (pmol · l^{-1} · 2 h)	−208 ± 161*	20 ± 15	−582 ± 244*†	52 ± 12	−594 ± 370*†	42 ± 17

Data are means ± SD. *Significant within-group difference ($P < 0.05$); †significantly different from DO ($P < 0.05$).

Change in anthropometric variables

The changes in selected anthropometric variables are given in Table 2. Within each group, significant ($P < 0.001$) reductions were observed for BMI (12.0 ± 3.4%) and waist circumference (10.3 ± 3.5%). Waist-to-hip circumference ratio decreased (4.6 ± 4.4%) in the DA and DR groups alone ($P < 0.01$). Without exception, the changes in anthropometric variables were not different ($P > 0.05$) between groups.

Change in AT and skeletal muscle

The changes observed in AT and skeletal muscle variables are given in Table 2. Independent of treatment, the relative reductions in visceral AT (38 ± 15.1%) were significantly greater than those in whole-body subcutaneous AT (24.3 ± 8.6%). Within the visceral AT depot, both intraperitoneal and extraperitoneal AT were significantly ($P < 0.001$) reduced. However, independent of treatment, the relative decrease in intraperitoneal AT (42.0 ± 17.2%) was greater ($P < 0.01$) than the decrease in extraperitoneal AT (25.9 ± 14.9%). For the DA and DR groups alone, the relative decrease observed for abdominal subcutaneous AT (32.2 ± 11.5%) was greater ($P < 0.01$) than that observed for femoral subcutaneous AT (21.1 ± 11.7%). Whereas skeletal muscle was preserved in the DA and DR groups ($P > 0.05$), a 7.3 ± 2.8% reduction ($P < 0.001$) in skeletal muscle was observed in the DO group.

Metabolic variables

Fasting insulin and glucose. Independent of treatment, no significant ($P > 0.05$) reductions were observed for plasma glucose levels (Table 2). For plasma insulin, significant decreases ($P < 0.05$) were observed within all groups (Table 2). Although the treatment effect for reductions in fasting insulin did not reach statistical significance, a strong trend was observed ($P = 0.09$).

OGTT. Reductions in OGTT glucose AUC did not reach significance at the 0.02 level within any group, but the 12.7 ± 25.0% reduction observed within the DA group approached significance ($P = 0.03$). Insulin AUC decreased in all groups ($P < 0.01$). Post hoc analysis revealed that compared with the DO group (20.2 ± 15.4%), the reduction in insulin AUC was significantly ($P < 0.05$) greater in the DA (51.8 ± 12.2%) and DR (42.3 ± 17.5%) groups (Fig. 1). This observation remained true when an analysis of covariance was employed to control for initially lower OGTT insulin values within the DO group.

Relationship between anthropometric, MRI, and metabolic variables. The correlation coefficients derived between anthropometric, MRI, and metabolic variables are given in Table 3. Collapsed across group ($n = 29$), pretreatment visceral AT was significantly related to both fasting glucose and OGTT glucose AUC. This remained true after controlling for subcutaneous AT ($P < 0.01$, data not shown). Subdivision of visceral AT into intraperitoneal and extraperitoneal compartments did not substantially change these observations (Table 3).

Whole-body subcutaneous AT was related to fasting insulin values ($P < 0.05$), but not after controlling for visceral AT ($P > 0.05$). On the other hand, abdominal subcutaneous AT was significantly related to pretreatment values for fasting insulin and remained so after controlling for visceral AT ($r = 0.41$, $P < 0.05$).

Because reductions in visceral and subcutaneous AT were not different between groups, the groups were combined to evaluate relationships between reductions in AT and metabolic variables. Correlation coefficients obtained between absolute change score values (pre- minus posttreatment scores) revealed that reductions in visceral AT were significantly ($P < 0.05$) related to reductions in both fasting ($r = 0.47$) and OGTT glucose AUC ($r = 0.38$). Reductions in abdominal subcutaneous AT, but not in lower-body (gluteal/femoral) subcutaneous AT, were significantly related

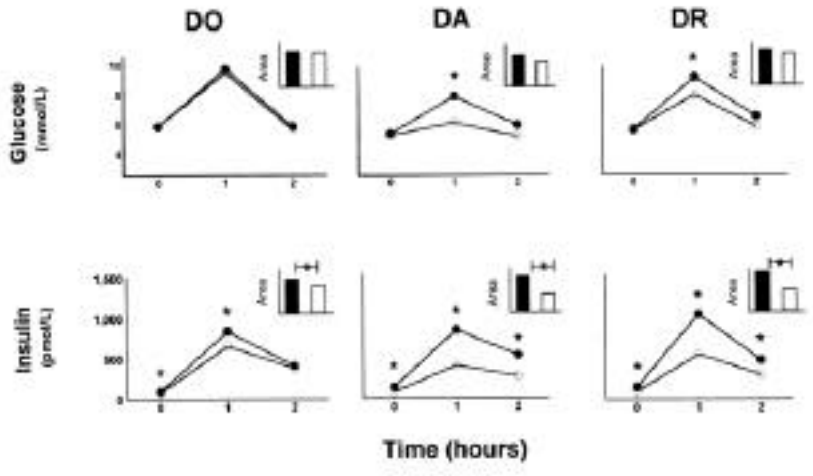

Figure 1—*Plasma glucose and insulin concentrations in the fasting state (0 h) and during a 2-h OGTT before (●) and after (○) weight loss induced by diet alone (DO), diet and aerobic exercise (DA), or diet and resistance exercise (DR) in obese men. Data are presented as group means. *Significant within-group difference (*$P < 0.02$*).*

to corresponding reductions in fasting insulin values ($r = 0.46$, $P < 0.01$).

CONCLUSIONS — The principal finding of this study is that a 1,000 kilocalorie daily energy restriction combined with either aerobic or resistance exercise potentiates the influence of diet alone on fasting and OGTT insulin levels in obese men. This observation provides strong support for the recommendation that either form of exercise be included in therapeutic strategies designed to prevent or manage glucose tolerance and insulin action in obese men. Moreover, the finding that reductions in visceral and abdominal subcutaneous AT were related to corresponding reductions in plasma glucose and insulin levels, independent of total adiposity, strengthens the concept that abdominal obesity has an important role in mediating insulin resistance.

We are aware of two other studies that have examined whether exercise modality influences plasma glucose and insulin values (7,8). In those studies, 20 weeks of aerobic or resistance exercise without weight loss had similar effects on glucose tolerance and insulin sensitivity in middle-aged men with impaired glucose tolerance (7) and at risk for coronary heart disease (8). In both studies, the magnitude of the decrease in OGTT insulin values approximated 22%. This represents about half the reduction in OGTT insulin AUC observed in the exercise and weight-loss groups in this study (~40%). This is reasonable given our finding that insulin AUC decreased by ~18% in the DO group. Taken together, these findings suggest that chronically performed aerobic or resistance exercise, with or without weight loss, has similar effects on OGTT insulin values in men. Moreover, it appears that the combination of diet and exercise induces a twofold greater decrease in OGTT insulin AUC than does diet alone. This notion is compatible with the report that in older men, diet and aerobic exercise reduces OGTT insulin AUC by ~45%, compared with a 20% decrease in response to diet alone (6).

It is known that the euglycemic clamp technique is the gold standard for measurement of insulin resistance. Although fasting or OGTT insulin levels are strong correlates of insulin resistance measured by the clamp method, the variance explained approximates 50% (34). Thus, our knowledge of how a given perturbation influences fasting or OGTT insulin values provides only an estimate of how insulin acts. Nevertheless, our observation of a substantial decrease in fasting insulin has important clinical implications. It has recently been reported that elevated plasma insulin levels, independent of plasma triglyceride, HDL cholesterol, and LDL cholesterol levels, are associated with increased risk of ischemic heart disease (35,36). Our finding that fasting and OGTT insulin levels were reduced in response to diet-induced weight loss confirms a well-established observation (37). However, that either aerobic or resistance exercise potentiate the effect of diet alone on insulin levels to a similar degree extends current knowledge and suggests that both forms of exercise, when combined with a calorie-reduced diet, may play a strong role in reducing the risk of coronary artery disease and type 2 diabetes.

It is known that a single exercise bout is associated with significant improvements in insulin sensitivity (38) and that exercise training enhances this acute effect, because insulin responsiveness is higher in trained compared to untrained individuals 24 h after exercise (39). It is also known that 5 days of detraining (no exercise) can signifi-

Table 3—*Correlation coefficients obtained between MRI and metabolic variables for all 29 subjects using pretreatment and change scores (pre- minus posttreatment)*

MRI variable	Fasting glucose	Fasting insulin	Glucose AUC	Insulin AUC
Pretreatment				
Total AT	‡	0.42 (0.06–0.68)*	‡	‡
Subcutaneous AT	‡	0.38 (0.02–0.65)*	‡	‡
Abdominal	‡	0.41 (0.05–0.67)*	‡	‡
Lower body	‡	‡	‡	‡
Visceral AT	0.54 (0.22–0.76)†	‡	0.63 (0.33–0.80)†	‡
Intraperitoneal	0.53 (0.20–0.75)†	‡	0.63 (0.33–0.80)†	‡
Extraperitoneal	0.46 (0.11–0.71)†	0.37 (0.01–0.65)*	0.54 (0.22–0.76)†	‡
Changes				
Total AT	‡	‡	‡	‡
Subcutaneous AT	‡	‡	‡	‡
Abdominal	‡	0.46 (0.11–0.71)†	‡	‡
Lower body	‡	‡	‡	‡
Visceral AT	0.47 (0.12–0.71)†	‡	0.38 (0.02–0.65)*	‡
Intraperitoneal	0.42 (0.06–0.68)*	‡	‡	‡
Extraperitoneal	0.47 (0.12–0.71)†	‡	‡	‡

Data are Pearson correlation coefficients (95% CI). *$P < 0.05$, †$P < 0.01$, ‡$P > 0.05$.

cantly reduce training-induced improvements in insulin sensitivity (38). Thus, although it is important to control for the acute effects of exercise when trying to determine the influence of exercise training on insulin action, from a clinical perspective it is equally important to appreciate that delays in the measurement of insulin response after treatment (exercise) likely underestimate the impact of daily exercise on insulin sensitivity. In other words, had we measured fasting and OGTT insulin response within 24 h of the last exercise session, it is very likely that the enhanced insulin action observed in response to diet and exercise would have been even more impressive. This observation reinforces the notion that aerobic or resistance exercise performed on a regular basis has a significant therapeutic value and should be included in a regimen designed to prevent or reduce type 2 diabetes or coronary heart disease.

At present, consensus is lacking as to the independent contribution of visceral and abdominal subcutaneous AT to insulin resistance in vivo. Whereas numerous investigators have demonstrated that visceral AT is an independent correlate of insulin resistance (13,14,16), others suggest that abdominal subcutaneous AT is the stronger correlate of insulin sensitivity in men and women (17–19). The findings reported here confirm that visceral and abdominal subcutaneous AT are independent correlates of plasma glucose and insulin levels. That abdominal subcutaneous but not lower-body (gluteal/femoral) subcutaneous AT is related to fasting insulin levels extends the observation that abdominal subcutaneous AT is an independent predictor of insulin levels.

In this study, we sought to examine the extent to which weight loss influenced the relationships between these fat depots and carbohydrate metabolism. That reductions in visceral adiposity are related to corresponding reductions in fasting and OGTT glucose values is consistent with others who report similar findings in obese individuals (16,20,21). To our knowledge, this is the first study to show that changes in abdominal subcutaneous AT are independently related to changes in plasma insulin values with weight loss. This finding buoys the observation that abdominal subcutaneous adiposity is an important determinant of insulin sensitivity. Although the independent contributions of visceral and abdominal subcutaneous AT to insulin resistance in vivo remain to be determined, the observations here suggest that improvements in insulin action with weight loss are in large measure dependent on corresponding reductions in both of the depots that comprise abdominal obesity.

Adaptations in skeletal muscle common to the aerobic and resistance exercise programs prescribed here may partially explain the enhanced improvement in insulin response. The 14% increase in peak V_{O_2} within the endurance-trained group is typically associated with increases in GLUT4 levels (40) and skeletal muscle capillarization. Increases in hexokinase activity (40), muscle blood flow (41,42), and glycogen synthase activity (43) are also common adaptations to aerobic exercise and are known to be associated with improvements in insulin sensitivity.

Because skeletal muscle is a primary target tissue for insulin, it has been argued that improvements in insulin action consequent to resistance training may be explained by corresponding increases in skeletal muscle mass (44). The findings here suggest otherwise because, despite improvements in insulin action, MRI-measured skeletal muscle mass did not change within either exercise group. Thus, changes in muscle mass per se do not appear related to changes in glucose tolerance or insulin action. On the other hand, Miller et al. (12) reported that in older men, resistance exercise performed for 16 weeks is not associated with a change in glucose oxidation, but rather, with a 40% improvement in nonoxidative glucose disposal. Thus, similar to aerobic exercise (5), improvements in the pathways responsible for glycogen storage represent a principal mechanism by which resistance exercise enhances insulin action.

The findings of this study do not argue against the merits of diet alone as a means of reducing adiposity and improving insulin sensitivity. On the contrary, within the DO group, both fasting and OGTT insulin levels decreased by ~19%. This is consistent with others who report similar reductions in response to a 10-kg weight loss in moderately obese men (5,45). That we observed a decrease in MRI-skeletal muscle (~7%) combined with an absence of change in peak V_{O_2} suggests that improvements in OGTT insulin response are unlikely to be explained by changes in muscle mass. The enhanced insulin response is thought to result from improvements in peripheral insulin sensitivity in muscle (46) and/or from less free fatty acid modulation of pancreatic insulin secretion (47).

Regardless of treatment, no reduction in fasting or OGTT glucose levels were observed. This is consistent with the findings of some (5,9,12,44) but not others (7,8). Similar to the present study, investigations that do not observe improvements in glucose tolerance report relatively normal glucose tolerance before treatment (5,9,12,44). However, the finding that glucose tolerance remained unchanged despite significant reductions in OGTT insulin values provides indirect evidence to support the observation that insulin action improved posttreatment.

Summary

In this study, body weight was reduced by ~12% independent of treatment. Whether the improvements observed in insulin action would be further enhanced with increased weight loss is unclear. Furthermore, whether chronic exercise performed at intensities lower than those performed here would accrue the same advantage is also unknown. However, our findings do suggest that weight loss induced by diet and exercise approximating 1–2 lbs per week provides an advantage with respect to improvements in insulin action by comparison with diet alone. Combined with the knowledge that routinely performed exercise improves the long-term maintenance of weight loss (48), our findings support the notion that diet and exercise is a preferred therapeutic strategy for the prevention and management of glucose intolerance and insulin resistance in obese men. Finally, the observation that changes in glucose and insulin were positively related to changes in visceral and abdominal subcutaneous AT reinforces the concept that abdominal obesity has an important role in mediating insulin resistance.

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