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Exercise with weight loss improves adipose tissue and skeletal muscle markers of fatty acid metabolism in postmenopausal women

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Abstract

Objective—The effects of six-months weight loss (WL) versus aerobic exercise training (AEX) +WL on fat and skeletal muscle markers of fatty acid metabolism were determined in normal (NGT) and impaired (IGT) glucose tolerant African-American and Caucasian postmenopausal women with overweight/obesity.

Methods—Fat (gluteal and abdominal) lipoprotein lipase (LPL), and skeletal muscle LPL, acyl-CoA synthase (ACS), β-hydroxacyl-CoA dehydrogenase, carnitine palmitoyltransferase (CPT-1), and citrate synthase (CS) activities were measured at baseline (n=104) and before and after WL (n=34) and AEX+WL (n=37).

Results—After controlling for age and race, muscle LPL and CPT-1 were lower in IGT, and the ratios of fat/muscle LPL activity were higher in IGT compared to NGT. Muscle LPL was related to insulin sensitivity (M), and inversely related to G_{120}, fasting insulin, and HOMA-IR. AEX+WL decreased abdominal fat LPL and increased muscle LPL, ACS, and CS. The ratios of fat/muscle LPL decreased after AEX+WL. The change in VO_2max was related to the changes in LPL, ACS, and CS and inversely related to the changes in fat/muscle LPL activity ratios.

Conclusions—Six-month AEX+WL, and not WL alone, is capable of enhancing skeletal muscle fatty acid metabolism in postmenopausal African-American and Caucasian women with NGT, IGT, and overweight/obesity.

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Keywords

lipoprotein lipase; acyl-CoA synthase; carnitine palmitoyltransferase; β-hydroxacyl-CoA dehydrogenase; citrate synthase

Introduction

A decrease in partitioning of lipid from storage in skeletal muscle and adipose tissue to oxidation in skeletal muscle may contribute to the pathogenesis of obesity and insulin resistance in postmenopausal women (1). Some studies show African-American postmenopausal women with overweight and obesity have lower systemic fat oxidation (2), greater intramuscular fat (IMAT), and lower insulin sensitivity (3) compared to Caucasian women with obesity, although the cellular mechanisms for these racial differences are not fully understood.

Six- to 12-month dietary weight loss and exercise training programs, alone or combined, significantly improve insulin sensitivity in postmenopausal women with overweight and obesity (4, 5). However, aerobic exercise training is necessary to improve skeletal muscle insulin action in postmenopausal women with impaired glucose tolerance (IGT), as determined by insulin activation of glycogen synthase during a hyperinsulinemic euglycemic clamp (5). Similarly, although weight loss alone decreases systemic fat oxidation in postmenopausal women, aerobic exercise training is essential to blunt the decline in fat oxidation during weight loss (6).

Key enzymes involved in lipid partitioning, fatty acid metabolism, and oxidation include adipose tissue and skeletal muscle LPL, and skeletal muscle ACS, CPT-1, β-HAD and CS. The activities of fat and skeletal muscle LPL and skeletal muscle CPT-1 and CS are affected by obesity in men and in premenopausal women (7, 8, 9). There are also differences in the activities of muscle LPL (10) and ACS (11), and in skeletal muscle palmitate oxidation (11) in premenopausal African-American compared to Caucasian women. Exercise training increases the activities of skeletal muscle LPL (12), CPT-1(13), β-HAD, and CS (14) in men and in premenopausal women. Detraining of athletes increases the ratio of fat to muscle LPL activity, favoring the shunting of circulating lipid from oxidation in muscle to storage in adipose tissue (15).

This study examines the activities of enzymes that regulate the uptake, storage, and oxidation of fatty acids in adipose tissue and skeletal muscle in postmenopausal African-American and Caucasian women with normal and impaired glucose tolerance, and the effects of weight loss with and without aerobic exercise training on the activities of these enzymes. We tested the hypothesis that there are racial differences and differences based on glucose tolerance status in fatty acid metabolism in older women with overweight and obesity, and that aerobic exercise training with weight loss will be more effective than weight loss alone to improve activities of enzymes involved in fatty acid metabolism in women at greatest risk of developing type 2 diabetes.

Methods

Subjects

Postmenopausal healthy women with overweight and obesity (BMI >25 kg/m^2; range of 25-47 kg/m^2) and normal (NGT) or IGT (two hour plasma glucose after 75-g OGTT, 7.8-11.0 mmol/L (16)) between the ages of 50-75 years were screened by medical history questionnaire, physical examination, and fasting blood profile. Women were weight stable (<2.0 kg weight change in past year), sedentary (<20min of aerobic exercise 2x/wk), and nonsmokers. Women showed no evidence of cancer, liver, renal or hematological disease, or other medical disorders and underwent a Bruce graded treadmill test to exclude those with asymptomatic coronary artery disease. Individuals with poorly controlled hypertension (>160/90 mmHg (10 women in WL group, 11 women in AEX+WL group) or hyperlipidemia (2 women in WL group, 3 in AEX+WL group) were referred to their doctor for therapy and entered the study after treatment with an antihypertensive or lipid-lowering drug that did not affect glucose metabolism. The treatment regimens were maintained throughout the study.

These subjects were part of a larger study examining the effects of WL and AEX+WL on insulin sensitivity and skeletal muscle glycogen synthase activity (5). The enzyme activities in skeletal muscle and adipose tissue presented here have not been previously reported. One-hundred seventeen women had data from adipose tissue and/or skeletal muscle samples included in the baseline portion of this study (Table 1 and Figure 1). Of these women, seventy-one completed WL (n=34) or AEX+WL (n=37) and have data included before and after intervention (Tables 2-3, and Figure 2). The Institutional Review Board of the University of Maryland and the Baltimore VA Research & Development Committee approved all methods and procedures. Each participant provided written informed consent to participate in the study.

Study Protocol

The WL and AEX components and compliance with the study protocol were described previously (5). Briefly, women in both groups attended weekly weight loss classes led by a registered dietitian and were instructed to reduce their caloric intake by 500 kcal/d. Women in the WL group were encouraged to maintain the same activity habits as when they enrolled and throughout the study, and women in both groups wore biaxial accelerometers to access physical activity (17). Women in the AEX+WL intervention exercised at the VAMHCS exercise facility 3X/week for 6 months using treadmills and elliptical trainers at >85% heart rate reserve for 45 minutes. Adherence was > 85% for WL and AEX+WL.

Whole body insulin sensitivity (M) was measured in WL (n=21) and AEX+WL (n=32) using the hyperinsulinemic-euglycemic clamp technique (18) as previously described (5). The clamp procedure was not performed in 17 women due to scheduling conflicts or difficulties in venous access. Plasma glucose and insulin during each clamp period were similar before and after WL (5±0.1 vs 4.9±0.1 mmol/l and 1119±46 vs. 1156±58 pmol/l) and AEX+WL (5±0.1 vs 5±0.1 mmol/l and 1138±33 and 1136±30 pmol/l).

VO_2max was measured using a continuous treadmill test protocol (19). Height (cm) and weight (kg) were measured to calculate body mass index (BMI) and waist and hip circumference were determined. Fat mass and fat-free mass (lean+bone) were determined by dual-energy X-ray absorptiometry (Prodigy, LUNAR Radiation Corp., Madison, WI). A single computed tomography (Siemens Somatom Sensation 64 Scanner, Fairfield, CT) scan at L_4-L_5 region was used to determine visceral adipose tissue area, subcutaneous adipose tissue area, and analyzed using Medical Image Processing, Analysis and Visualization, v. 7.0.0. A second scan at the mid-thigh was used to quantify muscle area, total fat area, and low density lean tissue area by Hounsfield units (19); values of the right leg were used in the statistical analyses. Low density lean tissue measured by CT has been used to quantify intramuscular adipose tissue in numerous studies (20).

Adipose tissue aspirations of the gluteal and abdominal regions were performed as previously described (21), and frozen at -80°C until assay. Vastus lateralis muscle sampling was performed under local anesthesia, with samples frozen immediately in clamps cooled in liquid nitrogen, and stored @ -80°C until lyophilization. Muscle and fat sampling were performed after an overnight fast, and in the AEX+WL group, 36-48 hours after the last bout of exercise.

Adipose tissue (heparin elutable) LPL activity

Three hundred fifty μL of PBS containing heparin (50 μL/ml) was added to frozen adipose tissue sample (50 mg) and kept at ambient temperature. After 1 hr, 100 μL aliquots were assayed in triplicate with 100 μL of substrate (22) prepared by sonication of 10 μCi of 1-^{14}C-glycerol triolein, 50 mg unlabeled triolein and 6 mg lecithin in 8 ml of 0.233 M Tris buffer, pH 8.2, containing 7% free-fatty acid (FFA)-free BSA and 400 μL fasting serum (source of apolipoprotein CII). The enzyme reaction was stopped after 45 min at 37°C by addition of Belfrage's extraction mixture (23) to separate the product, labeled FFA, from unreacted substrate. The labeled FFAs were quantitated by LSC and after correction for recovery during extraction. Adipose tissue LPL activity was normalized for fat cell size and expressed as nmol FFA produced/min•10^6 cells.

Skeletal muscle (total extractable) LPL activity

Lyophilized, microdissected muscle samples were homogenized (1:15 w/v) in ice cold buffer (pH 8.2) containing 25 mmol/l NH3, 5 mmol/l EDTA, 1% triton X-100, 0.1% SDS, 25 IU heparin/ml, protease inhibitors (Complete, Mini, EDTA-free, Roche) and centrifuged @ 10,000 x g for 10 min @ 4°C (24). Triplicate 5 μl of supernatant and 95 μL of PBS were incubated with substrate as above.

For both adipose tissue and skeletal muscle LPL assays, post heparin plasma control serum was run with each assay to determine substrate quality and for internal control, and pre and post intervention samples were run in the same assay. The ratio of fat to muscle LPL activity provides a measure of the propensity for storage of FFA derived from TG in adipose tissue versus oxidation in skeletal muscle (15, 25).

Skeletal muscle ACS, CPT-1, β-HAD and CS activities

Ten milligrams of lyophilized microdissected skeletal muscle were homogenized in 300 μL ice cold buffer (1:30) containing (in mmol/l) 250 sucrose, 10 Tris•HCl, 1 EDTA, pH 7.4 and protease inhibitors (Roche 11836170001). Thirty μL of the 1:30 homogenate were diluted to 1:150 in homogenization buffer, frozen in liquid nitrogen, and stored at -80°C until assay for CS, β-HAD, ACS and total protein. ACS, CPT-1, β-HAD and CS activities were measured as previously described (26).

All skeletal muscle enzyme activities were corrected for total protein content (Coomassie Plus, Pierce). The homogenates prepared from skeletal muscle samples from WL and AEX +WL individuals were run together and each sample was run in triplicate.

Statistics

At baseline, the effects of race (African-American vs. Caucasian) adjusted for glucose tolerance status (NGT vs. IGT) on subject characteristics and enzyme activity (variable) were compared using ANOVA with interactions. As age was different by race and glucose tolerance status, we analyzed the effects of race and glucose tolerance status adjusting for age. After adjusting for age, there were no race * glucose tolerance status interactions at baseline; the term was dropped from the model and the analysis rerun to determine effects by race and glucose tolerance status, again adjusting for age. The effect of the intervention (WL vs. AEX+WL) adjusted for race and glucose tolerance was compared using ANOVA: change in variable = baseline value + intervention + race + glucose tolerance status + intervention × race + intervention × glucose tolerance status. After adjusting for age, there were no intervention × race or intervention × glucose tolerance status interactions. Therefore, the interactions were dropped from the model and the analysis rerun to determine the effects of intervention, race, and/or glucose tolerance status, again adjusted for age. Pearson correlations were used to assess relationships between key variables, reporting two-tailed probability. All data are presented as mean ± SE, with statistical significance set at $p \leq 0.05$.

Results

Baseline Subject Characteristics (Table 1)

At baseline there were no significant race x glucose tolerance status interactions. The interaction terms were therefore dropped from the models. Women with IGT were older than women with NGT ($p<0.0005$), and Caucasian women were older than African-American women ($p=0.05$). Therefore, all further effects tested by race and glucose tolerance status were adjusted for age. African-American women had higher subcutaneous abdominal fat than Caucasian women ($p<0.005$), and lower VO_2max ($p<0.01$), regardless of glucose tolerance status. Percent body fat was similar between groups. Women with IGT were heavier ($p<0.05$), and had higher VAT ($p<0.05$), fasting glucose ($p=0.01$) and G_{120} ($p<0.0001$), fasting insulin levels ($p<0.01$), HOMA-IR ($p=0.003$), insulin sensitivity (M) ($p<0.001$) than women with NGT. African-American women had higher IMAT compared to Caucasian women ($p<0.01$, Figure 1) and IMAT was inversely related to VO_2max ($r=-0.26$, $p<0.01$, $n=98$).

Baseline enzyme activities by race and glucose tolerance status (Figure 1)

There were no significant race x glucose tolerance interactions. Skeletal muscle LPL ($p<0.05$) and CPT-1 ($p<0.01$) activities were lower in women with IGT than NGT. Gluteal and abdominal adipose tissue LPL activity and CS activity did not differ among women by race or glucose tolerance status. The ratio of adipose tissue to skeletal muscle LPL activity was determined as it is a marker for partitioning/storage of circulating lipids between the two tissues. The ratios of both gluteal ($p<0.05$) and abdominal ($p<0.0001$) fat/muscle LPL activity were higher in women with IGT than NGT. ACS and β-HAD activities were 20% and 15% lower in African-American compared to Caucasian women, respectively, but were not significantly different between races.

Relationships between subject characteristics and enzyme activities at baseline

Skeletal muscle LPL activity was inversely related to body weight ($r=-0.33$, $p<0.005$), VAT ($r=-0.32$, $p<0.01$), G_{120} ($r=-0.28$, $p=0.01$), insulin ($r=-0.28$, $p=0.01$), and HOMA-IR ($r=-0.25$, $p<0.05$); muscle LPL activity was directly related to M ($r=0.38$, $p<0.005$). The ratio of abdominal fat/muscle LPL activity was directly related to body weight ($r=0.28$, $p<0.05$), VAT ($r=0.33$, $p<0.01$), G_{120} ($r=0.30$, $p=0.01$), insulin ($r=0.28$, $p<0.05$), and HOMA-IR ($r=0.30$, $p=0.01$); the ratio of abdominal fat/muscle LPL activity was inversely related to M ($r=-0.29$, $p<0.05$).

Effects of Interventions: Subject Characteristics (Table 2)

There were no intervention (WL vs. AEX+WL) by race or glucose tolerance status interactions for any of the variables presented in Table 2. The interaction terms were therefore dropped from the models. All effects tested by race and glucose tolerance status were adjusted for age.

Overall, the women had decreases in body weight, percent body fat, visceral adipose tissue, fasting glucose, fasting insulin (all $P<0.0005$) and IMAT ($P<0.01$), and comparable increases in M ($p<0.05$) regardless of intervention, race, or glucose tolerance status. There were intervention effects for the change in SAT (greater decrease following AEX+WL, $p<0.01$) and VO_2max (L/min) (increase only following AEX+WL, $p<0.0001$). Women with IGT had greater reductions in G_{120} level (NGT vs. IGT: 0.32±0.22 vs. -1.28±0.26 mmol/l, $P<0.0007$) and HOMA-IR (-0.60±0.14 vs. -1.4±0.36, $p=0.05$) than women with NGT.

Effects of Interventions: Enzyme Activities (Table 3 and Figure 2)

There were no intervention (WL vs. AEX+WL) by race or glucose tolerance status interactions for any adipose or skeletal muscle enzyme activities. The interaction terms were therefore dropped from the models.

Both interventions reduced gluteal fat activity (overall effect for % decrease $p=0.0004$). WL did not significantly affect abdominal fat LPL activity whereas AEX+WL decreased abdominal fat LPL activity (overall effect for % decrease $p<0.0001$). There was an intervention effect for % change in skeletal muscle LPL activity ($p=0.009$); muscle LPL activity did not change with WL but increased with AEX+WL.

There was an intervention effect for the % change in the ratios of both gluteal fat/muscle LPL activity (p=0.02) and abdominal fat/muscle LPL activity (p=0.01). The ratios were not affected following WL alone whereas both ratios decreased following AEX+WL (both p<0.05).

There were overall effects on % changes in ACS and CPT-1 activities (both p<0.05). AEX +WL increased ACS activity (p=0.05) and the % change tended to be different between AEX+WL and WL (p<0.06). There was no change in CS following WL in contrast to an increase following AEX+WL (p=0.05). The percent increase in ACS activity was correlated with the increase in CS activity in the AEX+WL group (r=0.74, p<0.0001).

Relationships between changes in VO_2max and enzyme activities—The % increase in VO_2max was associated with the % increases in muscle LPL (r=0.26, p=0.05), ACS (r=0.53, p<0.001) and CS activities (r=0.43, p<0.001), and the % decreases of both fat/ muscle LPL ratios (both r=-0.32, p<0.05).

Discussion

African-American women with IGT and obesity are at greatest risk for the development of type 2 diabetes. The results of our study indicate that although postmenopausal African-American women have higher IMAT and SAT, and lower VO_2max compared to older Caucasian women, there are no significant differences in the activity of key enzymes involved in fatty acid metabolism between African-American and Caucasian women, after adjusting for age. On the other hand, women with IGT, who have higher VAT, fasting insulin, and HOMA-IR, and lower M compared to women with NGT, have lower skeletal muscle LPL and CPT-1 activity, and higher fat (gluteal and abdominal)/muscle LPL activity ratios, after adjusting for age. In addition, we show that AEX+WL, and not WL alone, reduces the activity of abdominal fat LPL, and increases the activities of skeletal muscle LPL, ACS, and CS, and reduces the ratio of fat (gluteal and abdominal)/muscle LPL activity. The change in VO_2max is related to changes in all three enzyme activities, and inversely related to changes in both fat/muscle LPL activity ratios. The significant differences in the changes of muscle LPL activity and ratio of fat/muscle LPL activities between the two interventions are independent of race and glucose tolerance status, suggesting that African-American and Caucasian women with either NGT or IGT comparably improve fatty acid metabolism, specifically partitioning, after participation in a well-controlled lifestyle intervention of AEX+WL.

We previously reported that postmenopausal African-American women were more insulin resistant and had higher IMAT than their age-matched Caucasian counterparts (3). Although neither insulin sensitivity (M) nor HOMA-IR were different between races in the current study, the African-American women had higher IMAT compared to the Caucasian women. This difference was driven by the Caucasian women with NGT, who had 25% lower IMAT compared to the other three groups. Furthermore, within the Caucasian group, the women with NGT had 60% higher muscle LPL and CPT-1 activities, both likely contributing to increased fatty acid oxidation and lower IMAT in these women. The ratio of fat (abdominal and gluteal adipose tissue)/muscle LPL activity, an index of the preferential storage of

circulating lipids in adipose tissue (15), was 80% lower in the women with NGT, indicative of greater oxidation of circulating lipids in skeletal muscle vs. storage in fat.

Our study is the first to report lower muscle LPL activity in postmenopausal women with overweight and obesity and IGT compared to women with NGT. African American women with NGT had 64% lower muscle LPL activity than Caucasian women with NGT. Contrary to our findings, Berk et al showed 3-fold higher skeletal muscle LPL activity in premenopausal African-American compared to Caucasian women, although the data were not stratified by glucose tolerance status (10). The difference between results could be explained by the difference in subject characteristics (e.g. premenopausal versus postmenopausal) and methodologies. We measured total extractable LPL activity in lyophilized microdissected muscle, which removes visable fat. Berk et al measured heparin elutable LPL in frozen, non-microdissected muscle. Thus, it is possible that contaminating fat in the muscle sample contributed to the LPL results in the Berk study. Another reason for the discrepancy could be the majority of muscle LPL is found in the extractable fraction, unlike adipose tissue LPL, which is found mostly in the heparin elutable fraction (27). In agreement with Berk's study, we did not find differences in fat LPL activity between African-American and Caucasian women.

Although skeletal muscle LPL activity and the ratios of fat (abdominal and gluteal)/muscle LPL were different between NGT and IGT at baseline, the increase in muscle LPL activity and decreases in fat/muscle LPL activity ratios following AEX+WL were similar between women with NGT and IGT. Detraining of healthy athletes reduces skeletal muscle LPL activity by 45% and increases abdominal fat LPL by 86% (15), corresponding to a greater than eight-fold increase in the ratio of adipose/muscle LPL. In our study, the increase in skeletal muscle LPL activity and decrease in abdominal fat LPL activity would favor an increase in skeletal muscle fatty acid uptake and oxidation in the postmenopausal women following AEX+WL.

We are not aware of any reports on the effects of weight loss or exercise training on ACS activity, but a two-month aerobic exercise training program in lean men increased acyl-CoA synthase long chain family member 1 (ACSL1), CPT1, and LPL gene expression, and the changes in ACSL1 and CPT1 gene expression following training and detraining were related to the change in palmitate oxidation (28). Similarly, in our study, the activities of skeletal muscle LPL and ACS were increased following AEX+WL.

Several studies in middle-aged men and women (premenopausal) reported an increase in CPT-1 activity following exercise training (13, 29). In older men, six-week endurance training tended to increase skeletal muscle CPT-1 activity (35%, $p<0.08$) and significantly increased CS activity 46% (30). In the current study, CS activity increased 32%, and there was an overall effect of the interventions to increase CPT-1 activity. Although we did not see an increase in β-HAD activity following AEX+WL in the postmenopausal women, some studies have reported an increase in β-HAD activity following high-intensity interval training in premenopausal women (31, 32).

There are several strengths of this research study, including a large sample size of well-characterized women, several enzyme activity measurements in skeletal muscle, and cross sectional and longitudinal data. A major limitation of this study is that we were unable to determine mitochondrial respiration and ATP generation (both requiring fresh tissue), the results of which may have verified alterations in fatty acid oxidation in postmenopausal women with IGT, and improvements following AEX+WL regardless of glucose tolerance status.

Postmenopausal women with overweight/obesity and impaired glucose tolerance have lower activities of skeletal muscle LPL and CPT-1, and greater fat/muscle LPL activity ratios, which could all contribute to reduced skeletal muscle fatty acid oxidation and increased adipose tissue storage compared to women with normal glucose tolerance. Following AEX +WL, postmenopausal women with overweight and obesity, regardless of race or glucose tolerance status, have improvements in the activities of skeletal muscle LPL, ACS, and CS, and in the ratios of fat/muscle LPL, which could all contribute to enhanced fatty acid metabolism.

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Study importance

What is already known about this subject?

- Exercise training plus weight loss has been shown to improve insulin activation of glycogen synthase in postmenopausal women with obesity and impaired glucose tolerance, whereas weight loss alone does not affect insulin activation of glycogen synthase in this population.
- Exercise training has been shown to increase the activities of skeletal muscle lipoprotein lipase, carnitine palmitoyltransferase-1, β-hydroxyacyl-CoA dehydrogenase, and citrate synthase in men and in *premenopausal women*.
- There are differences in skeletal muscle lipoprotein lipase activity and axcyl-CoA synthase activity between African-American and Caucasian *premenopausal* women with obesity.

What does our study add?

- We show that postmenopausal women with obesity and impaired glucose tolerance have lower activities of skeletal muscle LPL and CPT-1 activity, and higher fat/muscle LPL activity ratios compared to women with normal glucose tolerance, independent of race.
- We show that aerobic exercise training plus weight loss, and not weight loss alone, improves skeletal muscle LPL, ACS, and CS activities, and reduces the ratio of adipose tissue to skeletal muscle LPL activity, independent of race of glucose tolerance status, in postmenopausal women with obesity.

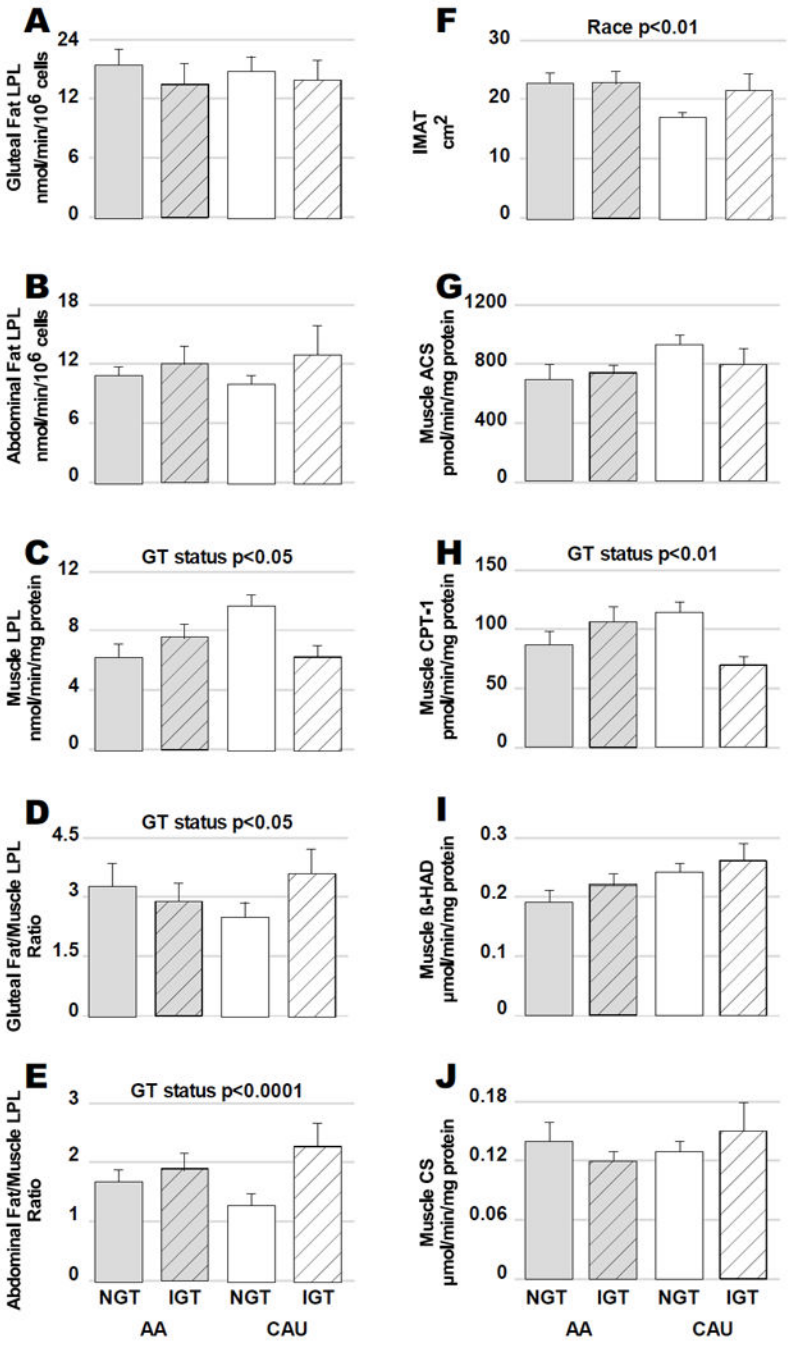

Figure 1.

Baseline intramuscular adipose tissue and enzyme activities in African-American (AA) (gray bars) and Caucasian (Cau) women (white bars) with normal glucose tolerance (NGT) (clear bars) or impaired glucose tolerance (IGT) (striped bars). Data presented after controlling for age. **Panel A**: Gluteal fat lipoprotein lipase (LPL) activity is not different between groups. n= 15 (AA NGT), 11 (AA IGT), 33 (Cau NGT), 14 (Cau IGT). **Panel B**: Abdominal fat lipoprotein lipase (LPL) activity is not different between groups. n= 15 (AA NGT), 11 (AA IGT), 33 (Cau NGT), 14 (Cau IGT). **Panel C**: Muscle LPL activity is higher

in NGT than IGT. n= 15 (AA NGT), 9 (AA IGT), 41 (Cau NGT), 14 (Cau IGT). **Panel D**: The ratio of gluteal fat/muscle LPL activity is higher in IGT than in NGT women. n= 13 (AA NGT), 9 (AA IGT), 32 (Cau NGT), 12 (Cau IGT). **Panel E**: The ratio of abdominal fat/muscle LPL activity is higher in IGT than in NGT women. n= 13 (AA NGT), 9 (AA IGT), 32 (Cau NGT), 12 (Cau IGT). **Panel F**: Intramuscular adipose tissue (IMAT) is higher in AA than in Cau women. n= 21 (AA NGT), 19 (AA IGT), 54 (Cau NGT), 16 (Cau IGT). **Panel G**: Muscle acyl-CoA synthase (ACS) activity is not different between groups. n= 21 (AA NGT), 17 (AA IGT), 52 (Cau NGT), 14 (Cau IGT). **Panel H**: Muscle carnitine palmitoyltransferase-1 (CPT-1) activity is higher in NGT than IGT. n= 13 (AA NGT), 11 (AA IGT), 31 (Cau NGT), 13 (Cau IGT). **Panel I**: Muscle β-hydroxylacyl-CoA dehydrogenase (β-HAD) activity is not different between groups. n= 20 (AA NGT), 18 (AA IGT), 50 (Cau NGT), 15 (Cau IGT). **Panel J**: Muscle citrate synthase (CS) activity is not different between groups. n= 21 (AA NGT), 18 (AA IGT), 50 (Cau NGT), 15 (Cau IGT).

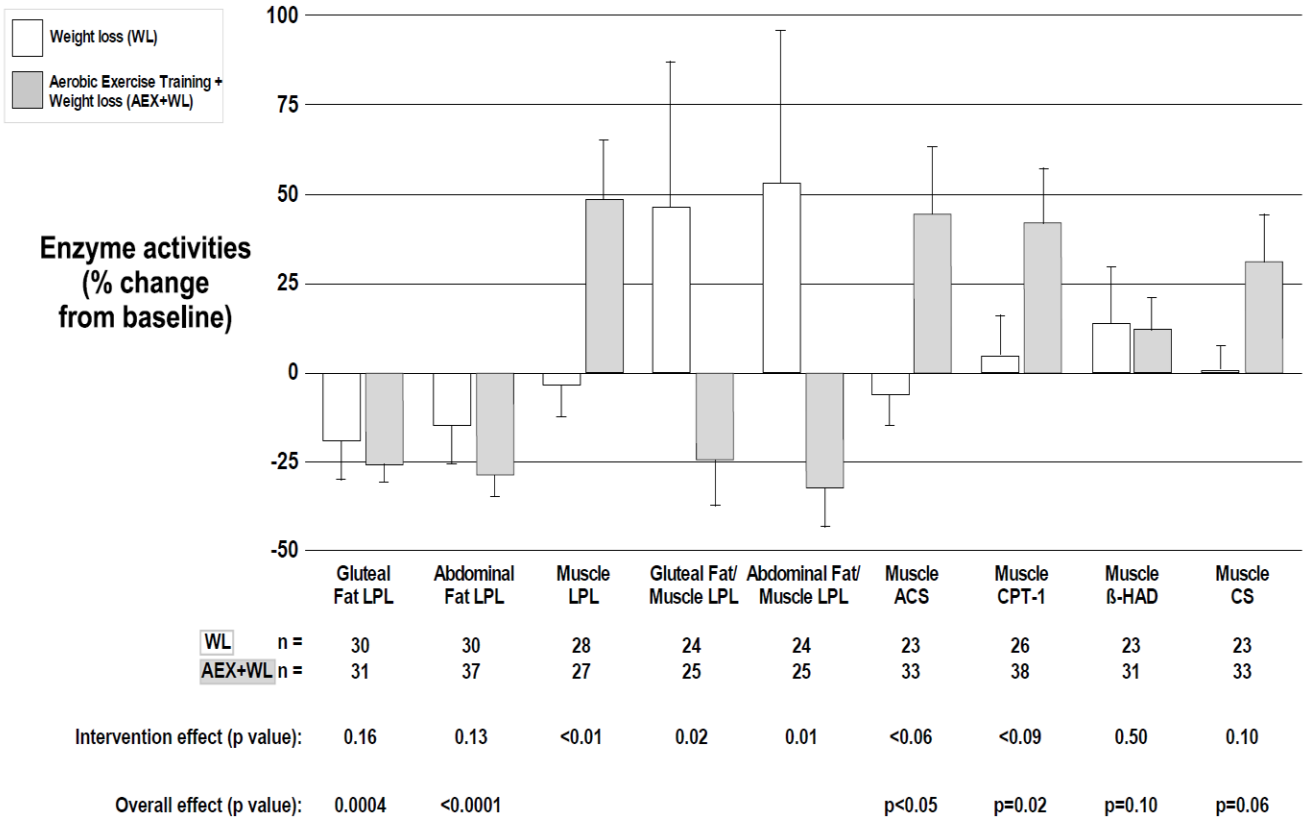

Figure 2.

Effects of interventions, Weight Loss (white bars) vs. Aerobic Exercise Training + Weight Loss (gray bars), on enzyme activities (percent change from baseline). The percent change data were calculated as the average of the individual differences between pre and post value, divided by the pre value, multiplied by 100. The data shown are the average and SE of the individual data points. Data presented after controlling for race, glucose tolerance status, and age. There were significant effects of intervention on muscle LPL activity, the ratio of gluteal fat/muscle LPL activity, and the ratio of abdominal fat/muscle LPL activity. There were overall effects for gluteal and abdominal fat LPL, muscle ACS, and muscle CPT-1 activities.

Table 1

Subject Characteristics of African American and Caucasian Women

	AA NGT	AA IGT	CAU NGT	CAU IGT	Race	GT
	mean ± SE	**mean ± SE**	**mean ± SE**	**mean ± SE**	**p value**	**p value**
Age (years)	55±1 (n=23)	62.5±1.5 (n=20)	59.1±0.9 (n=57)	62.8±2.2 (n=17)	**0.05**	**0.0002**
The following analyses were adjusted for age						
Weight (kg)	91.6±3.3 (n=23)	93.0±3.0 (n=20)	83.1±1.5 (n=57)	90.0±5.0 (n=17)	0.07	**<0.05**
Body Fat (%)	47.3±1.1 (n=23)	48.6±0.8 (n=20)	46.6±0.6 (n=57)	48.0±1.3 (n=17)	0.24	0.83
VAT (cm^2)	136±16 (n=21)	157±11 (n=19)	140±7 (n=53)	177.0±22 (n=16)	0.22	**0.02**
SAT (cm^2)	491±34.3 (n=20)	488±32 (n=17)	414±14 (n=48)	390±31 (n=13)	**0.004**	0.52
VO_2max (ml/kg/min)	19.5±1.2 (n=19)	15.3±1.0 (n=18)	20.3±0.6 (n=50)	18.5±1 (n=17)	**0.007**	0.08
Fasting Glucose (mmol/l)	5.1 ± 0.1 (n=23)	5.6 ± 0.1 (n=20)	5.2 ± 0.1 (n=57)	5.4 ± 0.1 (n=17)	0.40	**0.01**
Glucose 120 (mmol/l)	6.0 ± 0.2 (n=23)	9.2 ± 0.2 (n=20)	5.7 ± 0.1 (n=57)	8.7 ± 0.2 (n=17)	0.33	**<0.0001**
Fasting Insulin (pmol/l)	91 ± 8 (n=22)	122 ± 13 (n=20)	75 ± 7 (n=53)	99 ± 13 (n=17)	0.12	**0.009**
HOMA-IR	3.4 ± 0.3 (n=22)	5.1 ± 0.6 (n=20)	2.9 ± 0.3 (n=53)	4.1 ± 0.7 (n=17)	0.18	**0.003**
M (μmol/kg FFM/min)	70.8±3.8 (n=20)	48.6±3.9 (n=15)	69.1±2.4 (n=49)	56±4.9 (n=15)	0.44	**0.0002**

VAT, visceral adipose tissue
SAT, subcutaneous adipose tissue
Glucose 120 measured during an OGTT
M, insulin sensitivity

Table 2

Change in Subject Characteristics of Women following WL and AEX+WL, adjusted for age

	WL	AEX+WL	Intervention	Race	GT	Overall
	mean ± SE	**mean ± SE**	**p value**	**p value**	**p value**	**p value**
Δ Weight (kg)	-7.0 ± 0.6 (n=34)	-6.9 ± 0.6 (n=37)	0.24	0.95	0.62	**<0.0001**
Δ % Body Fat	-3.0 ± 0.4 (n=34)	-3.6 ± 0.5 (n=37)	0.30	0.60	0.06	**<0.0001**
Δ VAT (cm^2)	-18.8 ± 6.8 (n=31)	-25.7 ± 9.3 (n=36)	0.16	0.40	0.93	**<0.0001**
Δ Intramuscular fat	-0.75 ± 0.7 (n=32)	-1.78 ± 0.7 (n=33)	0.49	0.31	0.15	**0.01**
Δ SAT (cm^2)	-48.5 ± 16.9 (n=23)	-58.6 ± 17.1 (n=26)	**0.01**	0.11	0.08	
Δ VO_2max (L/min)	-0.05 ± 0.03 (n=34)	0.23 ± 0.04 (n=37)	**<0.0001**	0.68	0.39	
Δ Fasting Glucose (mmol/l)	-0.32 ± 0.1 (n=34)	-0.20 ± 0.1 (n=37)	0.61	0.78	0.46	**0.0002**
Δ Glucose 120 (mmol/l)	-0.33 ± 0.3 (n=34)	-0.29 ± 0.2 (n=37)	0.57	0.93	**0.0007**	
Δ Fasting Insulin (pmol/l)	-20 ± 5 (n=33)	-18 ± 5 (n=37)	0.93	0.21	0.12	**<0.0001**
Δ HOMA-IR	-0.98 ± 0.2 (n=33)	-0.87 ± 0.3 (n=37)	0.93	0.51	**0.05**	
Δ M (μmol/kg FFM/min)	3.6 ± 2.7 (n=21)	5.5 ± 2.7 (n=32)	0.82	0.38	0.56	**<0.05**

VAT, visceral adipose tissue
SAT, subcutaneous adipose tissue
M, insulin sensitivity

Table 3

Enzyme Activities Before and After WL and AEX+WL

	WL (mean ± SE)		p value	AEX+WL (mean ± SE)		p value
	Pre	**Post**	**Pre vs. Post**	**Pre**	**Post**	**Pre vs. Post**
Gluteal LPL (nmol/min/10^6 cells)	20.6 ± 2.4	14.8 ± 2.1	0.01	20.1 ± 1.7	14.1 ± 1.4	0.0002
Abdominal LPL (nmol/min/10^6 cells)	11.3 ± 1.2	8.9 ± 1.6		11.8 ± 1.1	7.4 ± 0.6	<0.0001
Skeletal muscle LPL (nmol/min/mg protein)	8.8 ± 0.8	8.6 ± 1.3		8.1 ± 0.8	10.9 ± 1.4	<0.05
Gluteal/muscle LPL	2.9 ± 0.4	3.6 ± 1		3.2 ± 0.4	2.1 ± 0.5	<0.05
Abdominal fat/muscle LPL	1.5 ± 0.2	2.2 ± 0.8		2.0 ± 0.3	1.2 ± 0.8	0.005
ACS (pmol/min/mg protein)	891 ± 94	813 ± 95		624 ± 63	781 ± 91	0.05
CPT-1 (pmol/min/g)	10.8 ± 1.1	10.5 ± 1.2		10.6 ± 1.6	11.0 ± 1.4	
β-HAD (μmol/min/mg protein)	0.28 ± 0.02	0.28 ± 0.03		0.25 ± 0.02	0.28 ± 0.03	
CS (μmol/min/mg protein)	0.16 ± 0.02	0.15 ± 0.01		0.13 ± 0.01	0.16 ± 0.02	0.05