



Original article

Effect of exercise training intensity on adipose tissue hormone sensitive lipase gene expression in obese women under weight loss

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Abstract

Background: Hormone sensitive lipase (HSL) is an enzyme that regulates adipose tissue lipolysis and plays an important role in chronic exercise-induced changes in adipose tissue metabolism. The purpose of this study was to determine whether aerobic exercise intensity influences abdominal adipose tissue *HSL* gene expression in obese women under weight loss.

Methods: Thirty women (body mass index (BMI) = 33.0 ± 0.7 kg/m², age = 58 ± 1 years) completed one of three 20-week interventions: caloric restriction alone (CR only, $n = 8$), CR plus moderate-intensity exercise (CR + moderate-intensity, 45%–50% heart rate reserve (HRR), 3 day/week, $n = 9$), or CR plus vigorous-intensity exercise (CR + vigorous-intensity, 70%–75% HRR, 3 day/week, $n = 13$). Each group had a similar prescribed energy deficit comprised of underfeeding alone (2800 kcal/week for CR only) or underfeeding (2400 kcal/week) plus exercise (400 kcal/week). Body composition and maximal aerobic capacity (VO₂max) were measured, and subcutaneous abdominal adipose tissue samples were collected before and after the interventions. Adipose tissue *HSL* gene expression was measured by real time reverse-transcriptase polymerase chain reaction.

Results: All three interventions reduced body weight, fat mass, percent fat, and waist to a similar degree (all $p < 0.01$). In addition, all interventions did not change absolute VO₂max, but increased relative VO₂max ($p < 0.05$ to $p < 0.01$). Compared to pre-intervention, neither CR only nor CR + moderate-intensity changed adipose tissue *HSL* gene expression, but CR + vigorous-intensity significantly increased adipose tissue *HSL* gene expression ($p < 0.01$). The changes of *HSL* gene expression levels in the CR + vigorous-intensity group were significantly different from those in the CR only ($p < 0.05$) and CR + moderate-intensity ($p < 0.01$) groups. In the whole cohort, changes in adipose tissue *HSL* gene expression correlated positively to changes in absolute ($r = 0.55$, $p < 0.01$) and relative ($r = 0.32$, $p = 0.09$) VO₂max.

Conclusion: These results support a potential effect of aerobic exercise training intensity on hormone sensitive lipase pathway in adipose tissue metabolism in obese women under weight loss.

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Keywords: Abdominal obesity; Adipose tissue; Diet; Exercise intensity; Hormone sensitive lipase; Weight loss

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1. Introduction

Obesity is a risk factor for several chronic diseases, including type 2 diabetes and cardiovascular disease.^{1,2} Lifestyle interventions, such as dietary weight loss and increasing physical activity (PA), are advocated for the treatment of



obesity and prevention of future chronic diseases.^{3,4} The mechanisms through which dietary weight loss and exercise training alter adipose tissue lipid metabolism and lower adiposity need to be investigated.

Lipolysis is the process by which triglycerides stored in adipocytes are broken down and free fatty acids and glycerol are released. One of the important enzymes to regulate adipocyte lipolysis is hormone sensitive lipase (HSL).⁵ HSL and adipose triglyceride lipase (ATGL) work hierarchically to regulate complete lipolysis.⁶ Currently, HSL and ATGL have been considered to be the major regulators of lipolysis under catecholamine-stimulated and basal lipolysis, respectively.⁷ In the absence of adipose tissue HSL or ATGL, energy metabolism was altered and exercise performance was impaired in mice.^{8,9} However, fasting, but not exercise, up-regulated ATGL expression in human adipose tissue,¹⁰ suggesting that exercise may be more effective in regulating HSL, but not ATGL in adipose tissue.

The role of exercise training intensity on adipose tissue metabolism has been reported by several studies. In exercise-only studies, vigorous-intensity, but not moderate-intensity exercise, tended to increase adipose lipolysis.^{11,12} However, it is unclear if this is due to an exercise training effect on adipose tissue HSL expression. In an animal study, exercise training increased adipose tissue HSL amount and activity.¹³ It is well known that an acute exercise session increases catecholamine levels and the release of catecholamines is directly related to exercise intensity.¹⁴ It is highly possible that acute and chronic exercise intensity also influences HSL, which is the key enzyme to regulate catecholamine-stimulate lipolysis. However, the effect of exercise training intensity on adipose tissue HSL has not been studied, especially in obese individuals during dietary weight loss.

Identification of effective lifestyle interventions is needed for the treatment of obesity. Changes in adipose tissue metabolism by lifestyle interventions may be reflected in current or future changes in adiposity. It is important to understand as the effects of exercise training intensity on specific metabolic parameters, including its effects on HSL in adipose tissue. A potentially beneficial effect of higher intensity exercise on adipose tissue metabolism, such as *HSL* gene expression, would provide evidence for creating new guidelines of designing exercise programs in obese individuals. Thus, we tested the hypothesis that caloric restriction plus vigorous-intensity aerobic exercise training would increase adipose tissue *HSL* gene expression to a greater extent than caloric restriction plus moderate-intensity aerobic exercise training or caloric restriction alone in obese older women.

2. Methods

2.1. Subjects

All women were recruited from the north central area of North Carolina according to the following inclusion/exclusion criteria: (1) overweight or obese (BMI = 25–40 kg/m² and waist girth > 88 cm), (2) older (age = 50–70 years, and at

least one year without menses), (3) non-smoking, (4) not on hormone replacement therapy, (5) sedentary (<15 min of exercise, 2 times/week) in the past 6 months, and (6) weight-stable (<5% weight change) for at least 6 months prior to enrollment. The study was approved by the Wake Forest University Institutional Review Board for Human Research. All women signed informed consent to participate in the study.

Women with evidence of untreated hypertension (blood pressure > 160/90 mmHg), hypertriglyceridemia (triglycerides > 400 mg/dL), insulin-dependent diabetes, active cancer, liver, renal or hematological disease were excluded after an initial screening included a medical history review, physical examination, fasting blood profile (lipoprotein lipids, glucose, and insulin) and 12-lead resting electrocardiogram. In addition, all subjects underwent a graded treadmill exercise test to exclude those with an abnormal cardiovascular response to exercise. Fifty women were randomly assigned to either a caloric restriction alone (CR only, $n = 16$), CR plus moderate-intensity exercise (CR + moderate-intensity, $n = 15$), or CR plus vigorous-intensity exercise (CR + vigorous-intensity, $n = 19$) intervention for a period of 20 weeks.

2.2. Study design

This sub-study used data from the Diet, Exercise, and Metabolism for Older Women Study, a randomized completed from 2003 to 2007.^{15–18} Baseline measurements of body composition, metabolic variables, maximal aerobic capacity (VO₂max), and adipose tissue biopsies were performed after at least 2 weeks of weight stability before the interventions. Body composition and VO₂max were measured on the same day. Blood draw (for the repeated determination of metabolic variables) and fat biopsies were performed in a morning after an over-night fast, and at least 5 days after the VO₂max test. The women were retested in the same manner after the 20-week interventions. The post-intervention blood draw and adipose tissue biopsies occurred at least 2 days after the last exercise session.

2.3. Study interventions

During the 20-week interventions, all women were provided food for their lunch and supper, which was prepared by the Wake Forest University General Clinical Research Center (GCRC) metabolic kitchen staff. These meals were prepared individually after the women chose from a hypocaloric menu designed by a registered dietitian (RD). Women purchased and prepared their breakfast meal, in consultation with the RD. They were allowed 2 free days per month, during which they were given guidelines for diet intake and asked to report all intake. The composition of the diet was 25%–30% fat, 15%–20% protein, and 50%–60% carbohydrate. They were also allowed to consume as many non-caloric, non-caffeinated beverages as they liked. In addition, all women were provided with a daily calcium supplement (1000 mg/day). All women were asked to keep a log of all foods consumed, and the records were monitored weekly by the RD to verify compliance.

The diet only group was asked not to alter their (PA) habits during the study. Both diet plus exercise groups walked on a treadmill 3 days/week at a target heart rate calculated from the Karvonen equation ($\text{HRR} \times (\text{intensity}) + \text{resting heart rate}$),¹⁹ where heart rate reserve (HRR) is maximal heart rate minus resting heart rate obtained from each subject's VO_2max test. The duration and intensity of the exercise progressed from 15 to 20 min at 45%–50% of HRR during the first week to 55 min at 45%–50% HRR for the moderate-intensity group, and 30 min at 70%–75% HRR for the vigorous-intensity group by the second month. The calorie deficits of all women were adjusted to ~ 2800 kcal/week. The deficits for the diet only group resulted totally from reduction in dietary intake, whereas deficits for the diet plus exerciser groups resulted from both reductions in dietary intake (~ 2400 kcal/week) and in exercise expenditure (~ 400 kcal/week). The average daily calorie intake recorded by all women was $100.0\% \pm 0.3\%$ of the provided calorie level. The exercise compliance (attendance at scheduled sessions) was $91.4\% \pm 1.9\%$ for the moderate-intensity exercise group, and $90.0\% \pm 1.5\%$ for the vigorous-intensity exercise group.

2.4. PA energy expenditure

PA energy expenditure was monitored for approximately one week per month using an RT3 activity monitor (Stay-healthy, Monrovia, CA, USA). Age, height, weight, and gender were entered to start the monitor. The three-dimension movement of each woman was recorded and energy expenditure calculated *via* proprietary software.

2.5. Body composition

Height and weight of each woman were measured to calculate BMI (kg/m^2). Waist (minimal circumference) was measured by a tape measure. Fat mass, lean mass and percent body fat were measured by dual energy X-ray absorptiometry (Hologic Delphi QDR, Bedford, MA, USA).

2.6. Metabolic variables

Plasma glucose was measured with the glucose hexokinase method (Bayer Diagnostics, Tarrytown, NY, USA). Plasma insulin was determined by a chemiluminescent immunoassay, using an IMMULITE analyzer (Diagnostics Products, Los Angeles, CA, USA). The estimate of insulin sensitivity by homeostasis model assessment (HOMA) score was calculated with the following formula: $\text{fasting plasma insulin } (\mu\text{IU}/\text{mL}) \times \text{glucose } (\text{mg}/\text{dL})/405$.

2.7. Maximal aerobic capacity

VO_2max was measured on a motor-driven treadmill (Medical Graphics Corporation, Minneapolis, MN, USA) during a graded exercise test. A ramp treadmill protocol was used. Each test was set for a duration of 12 min with a goal of 12 metabolic equivalents, and the treadmill self-adjusted the incline to reach that

goal. A valid VO_2max was obtained when a respiratory exchange ratio (RER) of 1.10 had been reached. If the participant did not reach this criterion, the test was repeated.

2.8. Adipose tissue HSL gene expression

Subcutaneous abdominal adipose tissue was taken by aspiration with a 16-gauge needle under local anesthesia (2% xylocaine) after an overnight fast. The samples were put in warm saline and transported immediately to the laboratory where they were washed twice with saline to eliminate blood and other connective tissue. Immediately after the washing, approximately 0.5 g of tissue was snap frozen in liquid nitrogen and then stored at -80°C for later isolation of total RNA for HSL gene expression.

Total RNA was isolated from frozen adipose tissue samples with the RNeasy lipid tissue kit (Qiagen, Valencia, CA, USA). The isolated total RNA was quantified by measurement of absorbency at 260 and 280 nm, and its integrity was verified using agarose gels (1%) stained with ethidium bromide. Total RNA samples were stored at -80°C until measurement of gene expression.

HSL mRNA expression was measured by real-time RT-PCR. First, 1 μg of total RNA was used for the reverse transcription reaction to synthesize the first-strand cDNA, using the random hexamer primers and following the instructions of the Advantage RT-for-PCR Kit (Clontech, Palo Alto, CA, USA). Real-time quantification of HSL to β -actin mRNA was performed, using ABI Taqman PCR kits on an ABI PRISM 7900 Sequence Detection System (Applied Biosystems, Foster City, CA, USA). HSL mRNA and β -actin mRNA were amplified in different wells and in duplicates, and the increase in fluorescence was measured in real time. Data were obtained as threshold cycle (C_T) values. Relative gene expression was calculated using the formula $(1/2)^{C_T \cdot \text{HSL} - C_T \cdot \beta\text{-actin}}$.

2.9. Statistics

Statistical analyses were performed using IBM SPSS Statistics 19 (Armonk, NY, USA). First, within-group differences between pre- and post-intervention measures of all variables were determined using a paired *t*-test. Differences among the intervention groups at baseline and over-time changes in response to the interventions were determined using one-way analysis of variance (ANOVA). The LSD *post-hoc* test was used to determine any group differences if an overall group effect was ascertained. Spearman's correlation coefficients were calculated for relationships between HSL gene expression levels and maximal aerobic capacity. All data are presented as mean \pm SE, and the level of significance was set at $p < 0.05$ for all analyses.

3. Results

3.1. Subject characteristics

Of the 50 women who were randomized into the three interventions, six women dropped out of the study due to life changes

Table 1
General characteristics of the study participants.

	CR only (n = 8)	CR + moderate- intensity (n = 9)	CR + vigorous- intensity (n = 13)
Age (years)	59 ± 3	57 ± 2	59 ± 1
Post-menopause (years)	15 ± 4	12 ± 4	12 ± 2
Percent African American (%)	37.5	44.4	23.1

Abbreviation: CR = caloric restriction.

unrelated to the study interventions, including unanticipated illness, work schedule changes, or family reasons. Forty-four women (CR only, $n = 14$; CR + moderate-intensity, $n = 14$; CR + vigorous-intensity, $n = 16$) completed the interventions, and 30 women (CR only, $n = 8$; CR + moderate-intensity, $n = 9$; CR + vigorous-intensity, $n = 13$) had sufficient adipose tissue sample amounts for analysis of gene expression at both time points. General characteristics of these 30 women are shown in Table 1 by intervention group. There were no group differences in age, years post-menopause, or percent of African Americans. Average daily PA energy expenditure levels during the 20-week interventions were calculated in all three groups (CR only: 449 ± 23 kcal/day; CR + moderate-intensity: 635 ± 53 kcal/day; CR + vigorous-intensity: 633 ± 48 kcal/day). By design, both CR + moderate-intensity and CR + vigorous-intensity groups had significantly higher PA energy expenditure than the CR only group (both $p < 0.01$). There was no group difference between CR + moderate-intensity and CR + vigorous-intensity in PA energy expenditure during the 20-week interventions.

3.2. Effects of caloric restriction alone, caloric restriction plus moderate-intensity exercise, and caloric restriction plus vigorous-intensity exercise on body composition and metabolic variables

Body composition and metabolic variables before and after the interventions in all three groups are shown in Table 2. At

baseline, there were no group differences in any of these variables. All three interventions reduced body weight, fat mass, lean mass, percent body fat, waist and hip circumferences ($p < 0.05$ to $p < 0.01$). All three groups lost a similar amount of body weight (CR only: $-10.5\% \pm 1.0\%$; CR + moderate-intensity: $-13.4\% \pm 1.9\%$; CR + vigorous-intensity: $-11.4\% \pm 1.0\%$), consisting of approximately 70%–80% adipose tissue. Likewise, there were similar reductions in percent body fat and waist circumference in all three groups. In addition, there were similar reductions in insulin levels and HOMA scores in all three groups (all $p < 0.05$). However, glucose levels only decreased in the CR group ($p < 0.05$).

3.3. Effects of caloric restriction alone, caloric restriction plus moderate-intensity exercise, and caloric restriction plus vigorous-intensity exercise on maximal aerobic capacity

Maximal aerobic capacity values before and after the interventions in all three groups are also shown in Table 2. At baseline, there were no group differences in absolute or relative VO_2max . All three interventions did not change absolute VO_2max , but increased relative VO_2max (CR only: $p < 0.05$; CR + moderate-intensity: $p < 0.01$; CR + vigorous-intensity: $p < 0.01$). As shown in Fig. 1, there were no significant group differences among changes in absolute or relative VO_2max ; however, there was a clear trend for a direct relationship between changes in maximal aerobic capacity and exercise intensity across the three groups.

3.4. Effects of caloric restriction alone, caloric restriction plus moderate-intensity exercise, and caloric restriction plus vigorous-intensity exercise on adipose tissue HSL gene expression

Adipose tissue HSL gene expression levels before and after the interventions in all three groups are shown in Table 2. At

Table 2
Body composition, metabolic variables, maximal aerobic capacity and adipose tissue HSL gene expression before and after interventions.

	CR only (n = 8)		CR + moderate-intensity (n = 9)		CR + vigorous-intensity (n = 13)	
	Pre	Post	Pre	Post	Pre	Post
Weight (kg)	91.4 ± 3.4	81.9 ± 3.6 [†]	87.7 ± 3.5	75.9 ± 4.1 [†]	87.5 ± 4.1	77.6 ± 3.7 [†]
Fat mass (kg)	40.0 ± 2.7	33.5 ± 2.8 [†]	37.5 ± 1.9	29.3 ± 2.4 [†]	39.1 ± 2.5	31.5 ± 2.2 [†]
Lean mass (kg)	53.9 ± 1.1	49.5 ± 1.5 [†]	52.7 ± 2.9	48.8 ± 2.5 [†]	51.3 ± 1.8	48.2 ± 1.7 [†]
Percent fat (%)	42.3 ± 1.6	40.0 ± 1.9 [†]	41.6 ± 1.0	37.3 ± 1.6 [†]	42.9 ± 0.9	39.0 ± 1.2 [†]
Waist (cm)	103 ± 3	94 ± 3 [†]	100 ± 3	90 ± 4 [†]	97 ± 3	87 ± 3 [†]
Hip (cm)	118 ± 4	114 ± 4*	116 ± 3	106 ± 3 [†]	117 ± 3	109 ± 3 [†]
Insulin (μIU/mL)	10.7 ± 2.3	5.6 ± 0.9*	10.7 ± 1.7	7.4 ± 1.9*	7.5 ± 0.8	5.6 ± 0.6*
Glucose (mg/dL)	102.9 ± 3.7	93.6 ± 4.2*	97.6 ± 4.1	91.5 ± 2.9	90.9 ± 4.2	90.7 ± 2.2
HOMA score	2.82 ± 0.69	1.34 ± 0.27*	2.58 ± 0.40	1.71 ± 0.47*	1.73 ± 0.25	1.26 ± 0.13*
Absolute VO_2max (L/min)	1.78 ± 0.09	1.69 ± 0.09	1.89 ± 0.08	1.84 ± 0.07	1.66 ± 0.11	1.69 ± 0.09
Relative VO_2max (mL/min/kg)	19.8 ± 1.1	21.2 ± 1.1*	21.1 ± 1.0	23.8 ± 0.9 [†]	19.2 ± 1.2	23.0 ± 0.7 [†]
HSL mRNA (HSL/β-actin ratio)	0.0039 ± 0.0010	0.0033 ± 0.0007	0.0020 ± 0.0005	0.0021 ± 0.0004	0.0025 ± 0.0005	0.0044 ± 0.0008 [†]

Note: All data are means ± SE.

Abbreviations: CR = caloric restriction; HOMA = homeostasis model assessment; VO_2max = maximal aerobic capacity.

* $p < 0.05$, [†] $p < 0.01$ compared with baseline.

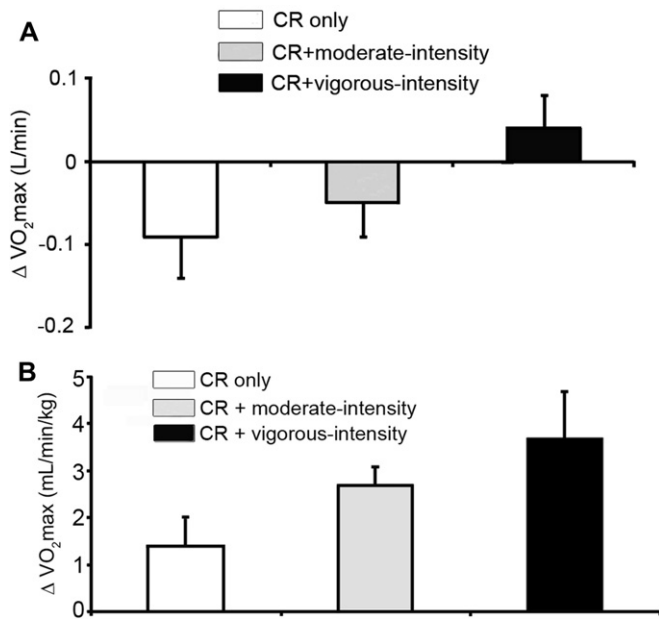


Fig. 1. Changes in maximal aerobic capacity in the three intervention groups: (A) absolute $VO_2\text{max}$; (B) relative $VO_2\text{max}$. CR = caloric restriction.

baseline, there were no group differences in adipose tissue *HSL* mRNA levels. Compared to pre-intervention, neither CR only nor CR + moderate-intensity changed adipose tissue *HSL* gene expression, but CR + vigorous-intensity significantly increased adipose tissue *HSL* gene expression ($p < 0.01$). Changes in adipose tissue *HSL* gene expression levels after the 20-week interventions in the three groups are shown in Fig. 2. The changes of *HSL* gene expression levels in the CR + vigorous-intensity group were significantly different from those in the CR only ($p < 0.01$) and CR + moderate-intensity ($p < 0.05$) groups.

3.5. Relationship of changes in adipose tissue *HSL* gene expression to changes in maximal aerobic capacity

The relationship of changes in adipose tissue *HSL* gene expression to changes in maximal aerobic capacity is shown in Fig. 3. In the whole cohort, changes in adipose tissue *HSL* gene expression were positively related to changes in absolute

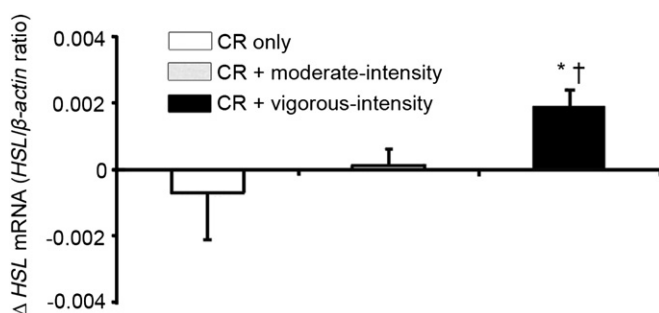


Fig. 2. Adipose tissue *HSL* gene expression changes in the three intervention groups. * $p < 0.05$ compared to CR + moderate-intensity, † $p < 0.01$ compared to CR only. CR = caloric restriction.

$VO_2\text{max}$ ($r = 0.55$, $p < 0.01$), and tended to be positively related to changes in relative $VO_2\text{max}$ ($r = 0.32$, $p = 0.09$).

4. Discussion

This study investigated whether caloric restriction alone, caloric restriction plus moderate-intensity aerobic exercise and caloric restriction plus vigorous-intensity aerobic exercise differentially influenced adipose tissue *HSL* gene expression in obese older women. The findings showed that caloric restriction plus vigorous-intensity exercise, but not caloric restriction plus moderate-intensity exercise or caloric restriction alone, increased adipose tissue *HSL* gene expression. There were significant group differences in changes in adipose tissue *HSL* gene expression after the interventions. The effect of vigorous-intensity exercise on *HSL* gene expression indicates that higher intensity exercise could be more beneficial in altering adipose tissue metabolism in obese individuals.

Adipose tissue *HSL* is regulated by several hormones in the circulation. Catecholamines are a key factor to up-regulate *HSL* expression/activity; moreover, glucagon up-regulates, while insulin down-regulates, adipose tissue *HSL*.²⁰ Insulin activates a protein phosphatase that dephosphorylates both the regulatory and basal phosphorylation sites of hormone-sensitive lipase.²¹ In obese individuals, insulin resistance and hyperinsulinemia are strongly associated with lower *HSL* mRNA and protein expression, independent of fat mass.²² Therefore, the declines in *HSL* expression may be due to the endocrine dysfunctions associated with obesity.

Our previous study showed that in obese women undergoing dietary weight loss, stimulated adipocyte lipolysis

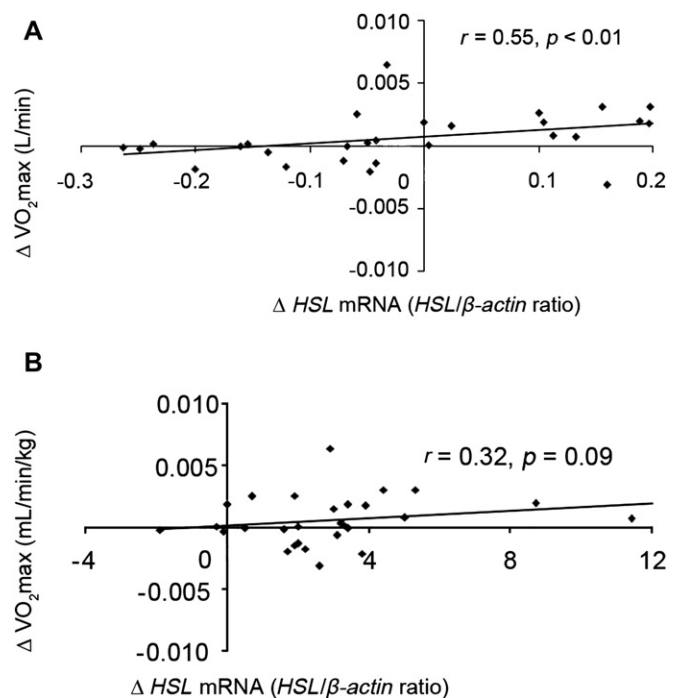


Fig. 3. Relationship of changes in adipose tissue *HSL* gene expression to changes in maximal aerobic capacity in the whole cohort: (A) absolute $VO_2\text{max}$; (B) relative $VO_2\text{max}$.

decreased, possibly due to the metabolic adaptation of adipose tissue to negative energy balance caused by reduced caloric intake.²³ Addition of aerobic exercise to the hypocaloric diet maintained the stimulated lipolytic rate.²³ In the current study, although lipolysis data are not available, adipose tissue *HSL* gene expression levels slightly (but not statistically significantly) decreased with caloric restriction, consistent with our previous findings that lipolytic rate is decreased under these conditions.

Previous findings also indicated that addition of aerobic exercise training can prevent declines in adipocyte basal and adrenergic receptor- and postreceptor-stimulated lipolysis in obese women undergoing dietary weight loss.²³ However, the effects of aerobic exercise training intensity on adipose tissue *HSL* expression and lipolysis during weight loss were not previously known. Yet, the effect of exercise training intensity, in the absence of weight loss, on adipose tissue lipolysis was previously investigated in two studies. In obese men, 70% VO_2max exercise training, but not 40% VO_2max or no exercise training, increased adrenergic-mediated lipolysis.¹² In normal-weight and overweight older women, 80% VO_2max exercise training, but not 65% or 50% VO_2max exercise training, improved insulin-stimulated suppression of adipose tissue lipolysis.¹¹ Both studies support an effect of higher-intensity aerobic exercise training on adipose tissue lipolysis. However, neither of these studies measured adipose tissue *HSL* gene or protein expression. The current study, for the first time, indicates that exercise training intensity affects adipose tissue *HSL* gene expression, which may contribute to the mechanism through which exercise intensity influences catecholamine-stimulated adipocyte lipolysis.

Exercise training increases basal and/or stimulated adipocyte lipolysis in both lean and obese individuals.^{24–29} Evidence from animal studies indicates that the exercise-induced increase in adipocyte lipolysis is a true metabolic adaptation, not secondary to reduced adipocyte size.³⁰ Exercise training increases adipocyte responsiveness to catecholamines at a metabolic step distal to stimulus recognition by adrenoreceptors, possibly at the level of lipases.³¹ *HSL*-null animals have reduced capacity to perform aerobic exercise and maintain adequate lipolysis to protect liver glycogen stores.⁸ Indeed, animal studies indicate that exercise training increased intra-abdominal adipose tissue *HSL* amount and *HSL* sensitivity to adrenaline stimulation,¹³ which suggests that *HSL* is a key step responsible for the increased lipolysis by exercise training. Surprisingly, a recent study reported that 12-week exercise training reduced subcutaneous adipose tissue *HSL* gene expression and there was no difference between low and high intensity exercise training on *HSL* gene expression in middle-aged women.³² These findings could be due to the differences in subject characteristics and interventions between their study and our current study.

Our findings that aerobic exercise training intensity affects adipose tissue *HSL* gene expression are interesting, especially considering the role of exercise training in preventing decline in lipolysis during a hypocaloric diet. Our findings, combined with findings from further studies, could potentially provide

evidence for advocating higher-intensity exercise as a component of a weight loss program for obese individuals. It is notable that stimulated adipocyte lipolysis data are not available in the current study; however, stimulated lipolysis levels are related to adipose tissue *HSL* gene expression considering *HSL* is an important enzyme for this process.^{7,8} Since *ATGL* and *HSL* work hierarchically to regulate the complete lipolysis, and exercise training increases *ATGL* expression in human skeletal muscle,³³ it would be interesting to know if exercise also affects adipose tissue *ATGL* expression or activity. However, recent findings that fasting, but not exercise, up-regulated *ATGL* expression in human adipose tissue¹⁰ may suggest that exercise training is more effective in up-regulating *HSL*, but not *ATGL* in adipose tissue. A potentially beneficial effect of higher intensity exercise on adipose tissue metabolism would provide evidence for creating new guidelines of designing exercise programs in obese individuals. Future studies are still needed to confirm the differences between *HSL* and *ATGL* in their responses to exercise training.

5. Conclusion

Caloric restriction plus vigorous-intensity exercise, but not caloric restriction plus moderate-intensity exercise or caloric restriction alone, increased adipose tissue *HSL* gene expression in obese older women. Also, changes in adipose tissue *HSL* were directly related to improvements in maximal aerobic capacity. These findings are consistent with other research showing that exercise training intensity influences adipocyte lipolysis. Moreover, our results support a potential exercise training intensity effect on hormone sensitive lipase pathway in adipose tissue metabolism in obese individuals undergoing a weight loss intervention.

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