Regulation of fat metabolism during resistance exercise in sedentary lean and obese men

Michael J. Ormsbee,1 Myung Dong Choi,1 Justin K. Medlin,1 Gabriel H. Geyer,1 Lauren H. Trantham,1 Gabriel S. Dubis,1 and Robert C. Hickner1,2

1Human Performance Laboratory, Department of Exercise and Sport Science, College of Health and Human Performance; and 2Department of Physiology, Brody School of Medicine, East Carolina University, Greenville, North Carolina

Submitted 13 November 2008; accepted in final form 3 March 2009

Ormsbee MJ, Choi MD, Medlin JK, Geyer GH, Trantham LH, Dubis GS, Hickner RC. Regulation of fat metabolism during resistance exercise in sedentary lean and obese men. J Appl Physiol 106: 1529–1537, 2009. First published March 5, 2009; doi:10.1152/japplphysiol.91485.2008.—The effect of acute resistance exercise (RE) on whole body energy expenditure (EE) and $\alpha_2$-adrenergic receptor ($\alpha_2$-AR) regulation of lipolysis in subcutaneous abdominal adipose tissue (SCAAT) was determined in sedentary lean (LN) and obese (OB) men. Lipolysis was monitored using microdialysis in 10 LN [body mass index (BMI) 20.9 ± 0.6] and 10 OB (BMI 36.2 ± 2.7) men before, during, and for 24 h after RE. EE was measured before and immediately after RE for 40 min. Changes in interstitial glycerol were measured in SCAAT with three microdialysis probes perfused with a control solution, phentolamine ($\alpha_2$-AR antagonist), or propranolol ($\beta$-AR antagonist). EE and fat oxidation (FOX) were significantly ($P < 0.001$) elevated immediately post-RE compared with pre-RE in LN and OB subjects, with no differences between groups. RE-induced increases in SCAAT glycerol concentrations from rest to peak exercise were greater in LN than in OB men in the control (LN 142.1 ± 30.8 vs. OB 65.4 ± 14.2%, $P = 0.03$) and phentolamine probes (LN 187.2 ± 29.6 vs. OB 66.7 ± 11.0%, $P = 0.002$). Perfusion of propranolol had no effect on interstitial glycerol concentrations over the time course of the experiment in either group. Plasma insulin concentrations were significantly lower ($P = 0.002$) and plasma growth hormone (GH) was significantly higher ($P = 0.03$) in LN compared with OB men. The mechanism behind RE contributing to improved body composition may in part be due to enhanced SCAAT lipolysis and improved EE and FOX in response to RE in LN and OB men. The blunted SCAAT lipolytic response to RE in OB compared with LN men is unrelated to RE-induced catecholamine activation of the antilipolytic $\alpha_2$-ARs and may be due to depressed GH in OB subjects.

microdialysis; lipolysis; fat oxidation

Obesity and diabetes are at the forefront of health concerns in the world today, and their prevalence continues to grow at an alarming rate. However, evidence that resistance exercise (RE) can improve body composition is mounting (8, 57), and it is now recommended as a necessary component to any exercise program (46).

RE has been shown to decrease resting respiratory exchange ratio (RER) after exercise (6, 38, 44), indicating elevated postexercise fat oxidation. Moreover, RE has been shown to have a similar effect on 24-h EE and fat oxidation as a bout of aerobic exercise (AE) with a comparable energy expenditure (37). Recently, Chatzinikolaou et al. (8), using gluteal fat biopsies, reported that 30 min of circuit-style RE increased gluteal triacylglycerol lipase activity in lean (LN) and obese (OB) men. Moreover, we recently demonstrated, using the microdialysis technique, that an acute bout of RE results in elevated subcutaneous abdominal adipose tissue (SCAAT) lipolysis in healthy, young trained males (44). Whether RE has the same lipolytic effect in sedentary LN or OB individuals remains unknown.

The lipolytic response in fat cells is a function of the interplay between the opposing effects of the stimulatory $\beta$-ARs and the inhibitory $\alpha$-ARs that are expressed in human adipocytes (16, 29, 33, 34, 54). In vitro studies using isolated human adipocytes show that $\beta$-adrenergic stimulation of lipolysis is attenuated by activation of $\alpha_2$-ARs by epinephrine and norepinephrine (2, 33, 34, 53). Catecholamines regulate lipolysis in adipose tissue by interacting with both the $\alpha$-ARs and $\beta$-ARs (2, 4, 10, 16, 47). Interestingly, it appears that the antilipolytic $\alpha$-ARs predominates in SCAAT, as opposed to femoral and gluteal adipocytes, and that epinephrine has a higher affinity for $\alpha$-ARs than $\beta$-ARs (5). AE elevates catecholamine release and activates $\alpha$-ARs, resulting in inhibition of stimulated lipolysis (53) in nonobese untrained subjects (9, 53, 55) and particularly in untrained obese subjects (52). This result has been confirmed using isolated human fat cells (36).

The microdialysis technique allows for a relatively noninvasive method to directly monitor lipolysis in SCAAT, and for local perfusion of pharmacological agents such as $\alpha$-AR inhibitors, to investigate the mechanistic properties of adipose tissue lipolysis. In fact, pharmacologically blocking $\alpha$-ARs with phentolamine has been reported to elevate AE-induced lipolysis, especially in OB subjects (52). Due to the paucity of data regarding the effects of RE on lipolysis and fat oxidation and the importance of the antilipolytic $\alpha_2$-AR pathway seen during AE, further study investigating fat metabolism and the role of the $\alpha_2$-AR pathway during and after RE is warranted.

Adipose tissue was studied because it is a major source of endogenous fatty acids that are oxidized by skeletal muscle over prolonged periods of inactivity and activity. In addition, SCAAT appears to be more responsive to catecholamine-stimulation than femoral and gluteal subcutaneous fat depots (2, 5, 35, 58). Wahrenberg et al. (58) concluded that the lipolytic effect of catecholamines was four- to fivefold more marked in abdominal adipocytes than in other depots. Furthermore, android obesity is common among men and is linked to many chronic diseases; therefore it is the critical fat depot to investigate.

Therefore, the purpose of the present investigation was to determine the effect of acute RE on lipolysis in SCAAT and the role of $\alpha$- and $\beta$-ARs in the regulation of lipolysis in sedentary LN and OB men. In addition, the effect of RE on
whole body EE and fat oxidation was explored. We hypothesized that 1) strenuous whole body RE would increase lipolysis, as measured with microdialysis, and whole body fat oxidation immediately following RE, but to a greater extent in LN than OB men in both cases; and 2) pharmacologically blocking the $\alpha_2$-ARs in SCAAT with phentolamine would increase lipolysis to a greater extent in OB than LN men in response to RE.

**MATERIALS AND METHODS**

*Participants.* Ten lean [LN; body mass index (BMI) 20.9 ± 0.6 kg/m$^2$; body fat%, 13.6 ± 1.5] and 10 obese (OB; BMI 36.2 ± 2.7 kg/m$^2$; body fat%, 37.8 ± 2.2) sedentary (exercise <2 days/wk, <30 min/day) men (18–40 yr old) were recruited for this study. All subjects were free of existing acute or chronic illness, known cardiovascular or metabolic disease, did not take any medications or dietary supplements, and were nonsmokers. A preparticipation health history and physical activity questionnaire were used to screen all volunteers for inclusion in this study. All participants were informed both orally and in writing of the purpose, risks, and benefits of the research and gave their written informed consent to participate before beginning the investigation. This study was approved by the East Carolina University Medical Center Institutional Review Board. Subject characteristics are presented in Table 1.

*Study design.* Participants reported to the Human Performance Laboratory at East Carolina University on two separate occasions. The first visit was used to gather baseline information including height, weight, body composition, waist and hip circumferences, and 10-repetition maximum (10RM) lifts. Informed consent was obtained from all participants before any data collection.

Before the second laboratory visit, all participants abstained from vigorous activity, alcohol, and caffeine intake for 24 h. The experimental timeline for day 2 is shown in Fig. 1. All participants remained sedentary in a semirecumbent position in the Human Performance Laboratory for minutes 0–200, with the exception of during the RE session. Dialysate samples were collected every 20 min for 200 min (the in-laboratory portion of the experiment) and, thereafter, were taken every 60 min for the remainder of the day (away from the laboratory in ambulatory subjects). In addition, a single overnight dialysate collection was made for each participant for each probe to determine interstitial glycerol concentration using the extrapolation-to-zero flow method (described below; Refs. 4, 52). Plasma samples were taken every 20 min between dialysate collection times for 180 min (10 collections). The prolonged period of study was performed to monitor the 24-h effects of RE on lipolysis.

*Body composition.* Participants were weighed on an electronic scale with weight recorded to the nearest 0.1 kg, and height was measured with a standard stadiometer. Fat-free mass, fat mass, and percent body fat were determined using dual-energy x-ray absorptiometry (DXA; GE Lunar Prodigy Advance, Madison, WI).

**10RM strength testing and RE protocol.** The participant’s 10RM lifts for the exercises used during the strength testing period were determined using previously described procedures (28, 56) and were performed using the resistance training equipment (Cybex, Medway, MA) that the subjects were familiarized to during preliminary testing. The RE protocol consisted of the following exercises performed in the listed order: chest press, lat pull down, leg press, shoulder press, leg extension, and leg curl. Each exercise was performed for three total sets: two sets of 10 repetitions and a third set to muscular exhaustion with a load equaling 85% of the individual’s previously established 10RM. Rest periods were kept to 90 s between all sets and exercises, and the RE session lasted for a total of 40 min. The workout was designed to be similar to those from other studies in which plasma catecholamines, anabolic hormones, insulin, and lactate concentrations were significantly affected (27, 28, 56). Water intake was allowed ad libitum during the experimental period. All 10RM testing and RE sessions were supervised by a certified strength and conditioning specialist.

**Experimental protocol.** Participants entered the laboratory at 0700 after an overnight fast. Each participant had their body weight measured and then rested in a semirecumbent position for insertion of the microdialysis probes. Three previously sterilized microdialysis probes (CMA 20 Elite, 10-mm membrane, 14/10 PAES, 20-kDa cutoff, CMA Microdialysis; Stockholm, Sweden) were inserted percutaneously into the participant’s SCAAT, at a distance of 5–10 cm from the umbilicus, with techniques previously described (21). Before probe insertion, the skin was cleaned with iodine and the insertion site numbed with ethyl chloride (a topical cold spray) to reduce discomfort. All three probes were attached to portable microdialysis pumps (CMA 107, CMA Microdialysis) that were continuously perfused at 2.0 μl/min with 0.9% sodium chloride (Braun Medical, Irvine, CA) containing ~10 mM ethanol. Ethanol was added to the perfusion medium to estimate local adipose tissue blood flow as previously described (21, 23, 24). After a 60-min equilibration period, one control probe was perfused with 0.9% sodium chloride and ethanol. A second probe was perfused with the control solution plus 0.1 mmol/l of the nonspecific α-AR inhibitor phentolamine (Sigma-Aldrich, St. Louis, MO). The third probe was perfused with the control solution plus 0.1 mmol/l of the nonspecific β-AR inhibitor propranolol (Sigma-Aldrich). The perfusate was collected at the exit end of the probe (dialysate) and stored at 4°C for analysis of ethanol within 24 h and subsequently stored at −20°C until analyzed in batch for dialysate glycerol (an indicator of lipolysis) according to the manufacturers’ instructions using an automated microdialysis analyzer (CMA 600 analyzer, CMA Microdialysis, Solna, Sweden).

An indwelling polyethylene catheter was inserted into the antecubital vein for blood sampling. Blood samples (10 ml) were collected every 20 min, in the middle of each microdialysis sample collection period for the duration of the laboratory portion of the experiment (180 min), and immediately stored at −80°C for later analysis of insulin, epinephrine, norepinephrine, nonesterified fatty acids (NEFA), glucose, glycerol, and GH concentrations. Blood from a heated hand was obtained via a fingertip and immediately analyzed for blood glucose (Accuchek One Touch, Lifescan Inc, Milpitas, CA) to verify compliance with our pretest fasting protocol and to ensure that each participant was not hyperglycemic or diabetic.

EE was determined for 40 min via indirect calorimetry (Parvomedics, True Max 2400, Sandy, UT) before RE. Participants were required to remain awake, quiet, and as motionless as possible while the room was darkened and noise kept to a minimum. Substrate oxidation was calculated using CO$_2$ produced/O$_2$ consumed and calculations developed by Frayn (14). During the pre-RE EE, two 20-min baseline dialysate and blood collections were taken.

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### Table 1. Subject characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lean</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Age, yr</td>
<td>23.2±1.6</td>
<td>27.3±2.4</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>69.6±2.9</td>
<td>120.5±8.4*</td>
</tr>
<tr>
<td>Height, cm</td>
<td>182.1±2.6</td>
<td>183.0±2.4</td>
</tr>
<tr>
<td>BMI, kg/m$^2$</td>
<td>20.9±0.6</td>
<td>36.2±3.7*</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>13.6±1.5</td>
<td>37.8±2.2*</td>
</tr>
<tr>
<td>Fat mass, kg</td>
<td>9.7±1.2</td>
<td>46.8±5.7*</td>
</tr>
<tr>
<td>Fat-free mass, kg</td>
<td>59.9±1.9</td>
<td>73.7±3.3*</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.81±0.01</td>
<td>0.95±0.03*</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>0.8±0.1</td>
<td>3.1±0.6*</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = no. of subjects. BMI, body mass index; HOMA-IR, homeostatic model assessment of insulin resistance. *Significantly different from lean subjets, P < 0.005.
Participants then engaged in the high-intensity RE session. Immediately following RE, each participant laid in a semirecumbent position while the dialysate collection vial was changed and measurement of post-RE EE began for 40 min as described above. Dialysate samples were collected throughout the day. Before going to bed the perfusion pumps were changed from 2.0 to 0.3 μl/min for all three probes. After a 5-min equilibration period an overnight collection vial was placed on each probe while each participant slept overnight to calculate glycerol recovery in each probe.

A perfusion rate of 0.3 μl/min in adipose tissue, in the present study, represents 96% glycerol recovery as assessed by the methods of Stich et al. (52). The estimated interstitial glycerol concentrations were calculated by plotting (after log transformation) the concentration of glycerol in the dialysate measured at 0.3 and 2.0 μl/min against the perfusion rates (52). Linear regression analysis was used to extrapolate dialysate concentration at zero perfusion flow rate, corresponding to the true interstitial glycerol concentration. The in vivo recovery rate for each probe was determined as the ratio between the dialysate glycerol concentration at a perfusion rate 2.0 μl/min and calculated interstitial glycerol concentrations (4, 52). When each probe was analyzed, there was no difference between individual probe recovery rates, and therefore the average recovery rate (33%) was used to calculate interstitial glycerol concentrations.

The following morning, subjects returned to the laboratory for removal of microdialysis probes and collection of all microdialysis samples. While away from the laboratory, participants collected and stored all microdialysis samples in a refrigerator or on ice.

Dietary and activity control. Participants recorded their dietary intake and physical activity for 3 days before the day of the experiment. Diets were analyzed with Nutritionist Pro software (Axxya Systems, Stafford, TX). In addition, each participant completed an activity questionnaire and an in-person interview before participation. Diets were analyzed with Nutritionist Pro software (Axxya Systems, Stafford, TX). In addition, each participant completed an activity questionnaire and an in-person interview before participation. Diets were analyzed with Nutritionist Pro software (Axxya Systems, Stafford, TX). In addition, each participant completed an activity questionnaire and an in-person interview before participation.

Fig. 1. Study timeline. Dialysate and blood samples were collected before, during, and after acute resistance exercise in 10 lean and 10 obese sedentary men. Dialysate samples 1–10 were collected in the laboratory, and the remaining samples were collected at home. Subjects returned to the laboratory the following morning for removal of the microdialysis probes.

For the remainder of the day, the participants were free to leave the laboratory and go through their normal daily activities; however, each participant was assigned an isocaloric diet of Ensure to control for differences in lipolysis due to dietary intake. Compliance was determined by telephone and/or personal contact throughout the day, written documentation of liquid meal ingestion, collection of empty drink containers, and specific questioning of the participants by the research staff.

Blood flow. Ethanol (~10 mM) was included with the perfusion medium to monitor adipose tissue blood flow in the area of the microdialysis probe (21, 23, 24). During perfusion, ethanol diffuses over the dialysis membrane and away from the local area by the microcirculatory blood flow in the immediate vicinity of the probe membrane because ethanol is not metabolized in adipose tissue to any significant extent (24). Ethanol concentrations were subsequently measured in both the dialysate and the perfusion solutions using a multilabel plate reader (Wallac Victor3, Perkin-Elmer, Waltham, MA) and previously described enzymatic fluorometric methods (24). Blood flow is expressed as the ratio of the ethanol concentration in the dialysate (outflow) to the ethanol concentration in the perfusate (inflow):

\[ \text{ethanol outflow/inflow ratio} = \frac{[\text{ethanol dialysate}]}{[\text{ethanol perfusate}]} \]

Therefore, the ethanol outflow/inflow ratio is related to the blood flow in the adipose tissue in an inverse manner (24).

Blood analysis. Blood was analyzed for insulin, glucose, glycerol, NEFA, catecholamines, and growth hormone. All blood was centrifuged, and aliquots of serum and plasma were immediately stored at −80°C for later batch analysis to limit day-to-day assay variability. Plasma glucose and insulin were measured with a YSI model 2300 Stat Plus (Yellow Springs Instrument, Yellow Springs, OH) and Access Immunoassay System (Beckman Coulter, Fullerton, CA), respectively, according to the manufacturer’s instructions. Intra-assay coefficients of variation (CV) for glucose and insulin were 1.9% and 2.1%, respectively. Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated using the following equation (26):

\[ \text{fasting glucose (mmol/l)} \times \text{fasting insulin (μU/ml)} \times 22.5 \]

Plasma glycerol was analyzed with a two-part fluorometric assay adapted from Wieland et al. (59). Briefly, 70 μl of heparinized plasma was added to each well containing 140 μl of buffer solution (0.2 M glycine, 1 M hydrazine, 2 mM magnesium chloride; Sigma-Aldrich), 5 μl of 20 mM NAD (Sigma-Aldrich), and 5 μl of 50 mM ATP (Sigma-Aldrich). After measuring the fluorescence using a multilabel plate reader (Wallac Victor3, Perkin-Elmer), 10 μl of an enzyme solution containing 2 μl of glycerophosphate dehydrogenase (GDH; Sigma-Aldrich), 2 μl of glycerokinase (GK; Sigma-Aldrich), and 6 μl of sterile water was added to each well. After shaking the plate and a 40-min incubation period in the dark (at room temperature), fluorescence was measured using a 355-nm excitation filter and a 430-nm
emission filter. The concentration of plasma glycerol was determined following the calculation of a standard curve using a known amount of glycerol. Intra-assay CV was 4.8%.

Plasma NEFAs were analyzed with a colorimetric reagent kit [NEFA-HR(R), Wako Chemicals, Richmond, VA] according to the manufacturer’s instructions. Intra-assay CV was 4.2%.

Plasma catecholamine concentrations were determined by HPLC utilizing Dionex ICS-3000 instrumentation (Sunnyvale, CA). Intra-assay and interassay CVs were 5.2% and 5.4%, respectively, for norepinephrine and 4.1% and 4.5%, respectively, for epinephrine.

Serum GH was analyzed using the Access Immunossay System (Beckman Coulter, Fullerton, CA) according to the manufacturer’s instructions. Intra-assay CV was 7.6%.

Statistical analysis. Two-way (group × time) repeated-measures ANOVA tests were used to determine differences in EE, RER, fat oxidation, plasma measurements (insulin, glucose, glycerol, NEFAs, catecholamines, and GH), and group-specific SCAAT lipolysis changes (treatment × time). Three-way [group (LN or OB) × treatment (control vs. phentolamine vs. propranolol)] ANOVA tests were used to determine differences in SCAAT lipolysis. Significance was located with Newman-Keuls post hoc analysis. SigmaStat statistical software (Systat, San Jose, CA) was used for all analyses. The level of significance was set at $P < 0.05$, and all values are reported as means ± SE unless otherwise noted.

RESULTS

Subject characteristics. Subject characteristics are presented in Table 1. With the exception of the leg press exercise (OB significantly higher than LN, $P = 0.003$), there were no differences in 10RM for any of the exercises performed (chest press: LN 39.3 ± 2.9 vs. OB 45.7 ± 4.3 kg; lat pull down: LN 35.2 ± 1.7 vs. OB 39.3 ± 1.9 kg; leg press: LN 98.4 ± 4.9 vs. OB 123.4 ± 6.6 kg; shoulder press: LN 27.5 ± 2.1 vs. OB 29.3 ± 2.2 kg; leg extension: LN 38.6 ± 2.9 vs. OB 45.2 ± 3.7 kg; leg curl: LN 39.5 ± 1.9 vs. OB 44.8 ± 5.5 kg). Total volume lifted (weight lifted in kg × no. of repetitions) was significantly greater in OB compared with LN ($P = 0.01$); however, this result was driven primarily by the leg press exercise (Table 2). In addition, no differences were reported in nutritional intake between LN and OB men for total kilocalories, protein, carbohydrate, fat, or alcohol intake (data not shown).

Whole body EE and fat oxidation. EE was significantly greater at baseline in OB patients compared with LN individuals when expressed in kcal/h (LN 76.1 ± 3.6 vs. OB 95.6 ± 4.0 kcal/h, $P < 0.05$). However, this result was completely abolished when expressing EE per kilogram of fat-free mass (Fig. 2). EE was 13 ± 4.4 and 22 ± 4.6% greater after RE in LN and OB groups ($P < 0.001$), respectively, but there were no differences between groups.

RER was significantly reduced immediately following RE in both LN and OB groups ($P < 0.001$; Fig. 3A). Fat oxidation was not different at baseline between LN and OB groups. There was a significant increase in fat oxidation for LN and OB groups immediately following RE (LN 49 ± 31.3%; OB 75 ± 31.1%; $P < 0.001$; Fig. 3B). However, there was no group difference or group-by-time interaction for fat oxidation.

Infractional glycerol concentrations in SCAAT. Infractional glycerol concentrations in SCAAT were not different between LN and OB subjects in the control probes at rest (Fig. 4A). Glycerol concentrations in SCAAT were two- to threefold higher than glycerol concentrations in plasma at rest in both groups. Basal infractional glycerol concentrations were not different between any of the probes or between LN and OB men. At rest, only the propranolol probe yielded infractional glycerol concentrations that were different between groups (LN 104.0 ± 11.9 vs. OB 157.5 ± 19.6 μmol/l, $P = 0.03$; Fig. 4C).

Throughout the entire study period (minutes 0 – 800; Fig. 4), interstitial glycerol concentrations were significantly greater in the LN group compared the OB group in the control and phentolamine probes ($P < 0.05$), but not the propranolol probe ($P = 1.0$).

During the RE period (minutes 40 – 80), the peak interstitial glycerol concentration in the control probe was significantly greater in the LN group than the OB group ($P = 0.03$; Fig. 4A). Phentolamine induced significantly greater interstitial glycerol concentrations compared with the control probe ($P < 0.05$) and resulted in significantly higher interstitial glycerol concentrations over the entire study period in the LN group only (control 159 ± 10.4 vs. phentolamine 202.4 ± 15.3 μmol/l, $P = 0.03$). In OB subjects, interstitial glycerol concentrations were enhanced in response to RE but were not different from the control probe at any time point over the study period.

In the propranolol probe, RE resulted in a significant increase in interstitial glycerol concentrations compared with baseline concentrations in both groups ($P < 0.001$). However,

Table 2. Average total volume of weight lifted (weight lifted in kg × number of repetitions) in sedentary lean and obese men during the resistance exercise lifting protocol

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Lean</th>
<th>Obese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest press</td>
<td>1,115.9±98.9</td>
<td>1,347.3±148.0</td>
</tr>
<tr>
<td>Lat pull down</td>
<td>1,040.8±56.4</td>
<td>1,118.2±88.1</td>
</tr>
<tr>
<td>Leg press</td>
<td>3,124.5±179.8</td>
<td>5,011.4±545.4*</td>
</tr>
<tr>
<td>Shoulder press</td>
<td>681.1±64.8</td>
<td>740.2±99.3</td>
</tr>
<tr>
<td>Leg extension</td>
<td>1,056.5±54.9</td>
<td>1,304.3±88.7</td>
</tr>
<tr>
<td>Leg curl</td>
<td>1,182.5±411.8</td>
<td>1,515.6±887.9*</td>
</tr>
</tbody>
</table>

Values are means ± SE. *Significantly different from lean subjects, $P < 0.05$.
no difference was detected between the propranolol and control probes in either the LN (P = 0.5) or OB (P = 0.2) groups over time (Fig. 4C).

**Plasma catecholamines and serum GH.** Plasma norepinephrine and epinephrine concentrations were not different at rest between LN and OB subjects (Fig. 5). RE induced a significant increase in both plasma catecholamines (P < 0.001) that lasted beyond the completion of RE. There was no group difference or group-by-time interaction for either of the catecholamines.

GH concentrations were not different between the groups at rest. In response to RE, LN subjects had significantly (P = 0.001) elevated GH concentrations compared with resting values and compared with the OB group at 70, 90, 110, and 130 min. Group differences were measured in the GH response between LN and OB men (LN 3.3 ± 0.7 vs. OB 1.0 ± 0.9 ng/ml, P = 0.037; Fig. 6).

**Plasma glucose and insulin.** Plasma insulin concentrations (Table 3) were significantly higher in the OB group than the LN group for the entirety of the study period (LN 13.1 ± 2.8 vs. OB 37.3 ± 6.9 μU/ml; P < 0.002).

Plasma glucose concentrations (Table 3) were significantly higher in the OB group compared with the LN group over the experimental time period (LN 94.0 ± 2.6 vs. OB 102.0 ± 2.6 mg/dl; P < 0.05).
Plasma glycerol and NEFA levels. Plasma glycerol and NEFA concentrations are depicted in Table 3. Plasma glycerol concentrations were significantly elevated \( (P < 0.001) \) at the onset of RE and remained significantly elevated for the entirety of the experiment in both groups.

Plasma NEFA concentrations were similar at rest between LN and OB men and significantly changed over-time \( (P < 0.001) \). With the onset of RE, plasma NEFA concentrations tended to decrease in both groups; however, there were no differences in these measures between LN and OB groups. This result confirms recent reports of a significant increase in EE in LN and OB men with 30 min of circuit-type RE \( (8) \). It is known that EE is elevated for up to 38 h after an acute bout of heavy RE. A reduction in RER has also been reported by others both immediately \( (8, 13, 44) \) as well as hours \( (17, 38, 50) \) after a single bout of RE. The subjects in the present study may therefore have had elevated EE and whole body fat oxidation for a period of time greater than 40 min after RE. A limitation of the present study is not only the lack of 24-h EE data but also the fact that whole body, rather than pool-specific, fat oxidation was measured, as it has been shown that a reduced oxidation of plasma fatty acids is compensated for by an increased oxidation of intramuscular fatty acids in obese individuals during endurance exercise \( (40) \).

We observed a significant increase in plasma glycerol during and following RE in both groups but no difference between LN and OB at any time point (Table 3). Our results verify those of Borsheim et al. \( (7) \) who found an increase in plasma glycerol with aerobic exercise, but no difference between LN and OB.

Ethanol outflow-to-inflow ratio in SCAAT. Blood flow was unchanged in any probe before, during, or after acute RE. The OB group had a higher \( (P < 0.001) \) ethanol outflow-to-inflow ratio \( (LN 0.74 \pm 0.0004 \text{ vs. } OB 0.78 \pm 0.0004, P < 0.001) \) than the LN group in all probes, indicating lower SCAAT blood flow throughout the experimental day. In addition, there was a treatment effect in that both the phentolamine and propranolol probes significantly elevated the ethanol outflow-to-inflow ratio (reduced blood flow) compared with the control probe \( (control 0.73 \pm 0.0005, \text{ phentolamine } 0.77 \pm 0.001, \text{ propranolol: } 0.78 \pm 0.001; P < 0.001) \). There was no main effect of time or group-by-time or group-by-treatment interactions (data not shown).

DISCUSSION

Microdialysis of SCAAT was used to assess lipolysis in situ during physiological and pharmacological stimulation of adipose tissue lipolysis in LN and OB men. To our knowledge, no group has investigated whole body and SCAAT lipolysis in sedentary LN and OB men in response to an acute bout of RE. The major findings of the this investigation suggest that despite a significant increase in whole body energy expenditure and fat oxidation observed in both sedentary LN and OB men following acute RE, SCAAT lipolysis is blunted during RE in OB men, and this impairment is unrelated to RE-induced catecholamine activation of antilipolytic \( \alpha_2 \)-ARs (Fig. 4).

In agreement with our previous work and that of others \( (38, 44, 50) \), EE (Fig. 2) and whole body fat oxidation (Fig. 3) were significantly elevated following RE for a period of at least 40 min; however, there were no differences in these measures between LN and OB groups. This result confirms recent reports of a significant increase in EE in LN and OB men with 30 min of circuit-type RE \( (8) \). It is known that EE is elevated for up to 38 h after an acute bout of heavy RE. A reduction in RER has also been reported by others both immediately \( (8, 13, 44) \) as well as hours \( (17, 38, 50) \) after a single bout of RE. The subjects in the present study may therefore have had elevated EE and whole body fat oxidation for a period of time greater than 40 min after RE. A limitation of the present study is not only the lack of 24-h EE data but also the fact that whole body, rather than pool-specific, fat oxidation was measured, as it has been shown that a reduced oxidation of plasma fatty acids is compensated for by an increased oxidation of intramuscular fatty acids in obese individuals during endurance exercise \( (40) \).

We observed a significant increase in plasma glycerol during and following RE in both groups but no difference between LN and OB at any time point (Table 3). Our results verify those of Borsheim et al. \( (7) \) who found an increase in plasma glycerol with aerobic exercise, but no difference between LN and OB.
throughout the study period, which should have resulted in elevated dialysate glycerol concentrations. Therefore, OB subjects most likely had lower SCAAT glycerol release at rest than LN subjects.

RE-induced increases in interstitial glycerol were significantly greater in LN (+142.1 ± 30.8%) than in OB (+65.4 ± 14.2%) men in the control probe, a result that was not rectified by the α-AR antagonist phentolamine in OB men (Fig. 4B). In fact, phentolamine perfusion enhanced the RE-induced increase in interstitial glycerol in LN rather than OB men, demonstrating that catecholamine stimulation of the antilipolytic α-ARs is not responsible for decreased lipolysis in OB men during RE. This is in contrast to the α-AR-mediated suppression of lipolysis in obese men during endurance exercise (52).

An increase in SCAAT glycerol could be achieved by either elevated local lipolysis or a reduced blood flow in SCAAT (39). Indeed, OB subjects in the present study had a significantly greater ethanol outflow-to-inflow ratio (reduced blood flow) over the course of the experiment compared with LN subjects, which agrees with others (7, 52). One would expect interstitial glycerol concentrations to be artificially elevated in OB men due to reduced blood flow. Despite this lower blood flow in OB men, interstitial glycerol concentrations were markedly lower in OB men compared with LN men. Therefore, the lipolytic response to RE was lower in OB than LN men, and it is possible that the magnitude of this difference was underestimated.

The mechanisms of local SCAAT lipolytic regulation were further elucidated by adding the nonselective β-AR blocker propranolol to the microdialysis perfusate. In the present study, neither LN nor OB subjects had any lipolytic alterations in response to propranolol compared with the control probe at rest or during RE (Fig. 4C). Our results substantiate those of Hellstrom et al. (20) that resting dialysate glycerol levels were not influenced by α- or β-adrenergic blockers. However, during endurance exercise, perfusion of propranolol has previously been shown to reduce endurance exercise-induced increases in interstitial glycerol concentrations (3, 20, 41). The discrepancy between these results and our data could be the use of different types of exercise modalities. The paradoxical increase in SCAAT interstitial glycerol concentrations during RE despite inhibition of adipocyte β-ARs is likely associated

<table>
<thead>
<tr>
<th>Glucose, mg/dl</th>
<th>LN</th>
<th>OB</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>85.9 ± 3.0</td>
<td>94.9 ± 2.0</td>
</tr>
<tr>
<td>30</td>
<td>87.5 ± 2.4</td>
<td>95.4 ± 2.1</td>
</tr>
<tr>
<td>50</td>
<td>93.2 ± 1.5</td>
<td>96.1 ± 1.9</td>
</tr>
<tr>
<td>70</td>
<td>100.7 ± 3.9</td>
<td>94.6 ± 6.6</td>
</tr>
<tr>
<td>90</td>
<td>99.4 ± 4.5*</td>
<td>106.4 ± 4.8*</td>
</tr>
<tr>
<td>110</td>
<td>93.3 ± 3.7</td>
<td>105.5 ± 4.7</td>
</tr>
<tr>
<td>130</td>
<td>84.8 ± 3.1</td>
<td>98.1 ± 4.3*</td>
</tr>
<tr>
<td>150</td>
<td>82.0 ± 2.5</td>
<td>94.8 ± 3.5</td>
</tr>
<tr>
<td>170</td>
<td>94.8 ± 3.0</td>
<td>104.4 ± 3.6</td>
</tr>
<tr>
<td>190</td>
<td>122.6 ± 7.0*</td>
<td>130.1 ± 5.7*</td>
</tr>
</tbody>
</table>

Values are means ± SE. LN, lean; OB, obese; NEFA, nonesterified fatty acids. Resistance exercise took place during minutes 40–80 of the experiment.

*Significantly greater than baseline values, P < 0.001. †Significantly different from LN group, P < 0.05.
with alternative lipolytic regulators. One such regulator is atrial natriuretic peptides (ANP), which has been shown to regulate endurance exercise-induced lipolysis and works via an insulin-independent mechanism (30, 31, 41, 42, 51). Our results suggest that at rest and during RE, the β-AR stimulatory effects on lipolysis may not be as involved in modulating lipolysis as previously shown during aerobic exercise in LN and OB men.

GH, another important regulator of lipolysis, is widely recognized as a stimulator of regional and systemic lipolysis (11, 32, 49). In the present study, GH increased markedly from resting values in response to RE in LN but not OB subjects and remained elevated for 50 min after the RE session (Fig. 6). An increase in GH during and following an acute bout of high-intensity RE, similar to that used in this study has been shown elsewhere in healthy subjects (18, 28). Interestingly, Enevoldsen et al. (12) reported that GH induced lipolysis following, but not during, exercise at 50% maximal oxygen uptake (VO_2max) on a semirecumbent cycle ergometer in healthy, normal-weight young men. In light of this finding, it is apparent that further research regarding the role of GH during RE is warranted. Moreover, it is well established that spontaneous and stimulated serum GH concentrations are suppressed in human obesity (15, 48) and return to normal with normalization of body weight (48). It is possible that the blunted lipolytic response observed in OB compared with LN subjects in SCAAT may, in part, be related to the significantly diminished GH response to RE in the OB.

Several methodological limitations exist in the present study. Participants were ambulatory, and therefore without supervision, following the in-laboratory portion of the experiment. However, the participants were provided all of their daily calories in liquid form to control for any influence of dietary intake on the lipolytic response to RE. In addition, using stable isotopic tracers to monitor lipolysis and fat oxidation would add valuable information and should be included in future investigations.

In conclusion, high-intensity RE improves whole body EE and fat oxidation in LN and OB subjects. However, we demonstrate for the first time that, in SCAAT, OB men have suppressed RE-induced lipolysis compared with LN men and the mechanism for this is unrelated to overstimulation of the antilipolytic α2-AR system by catecholamines. In addition, we determined that β-ARs are not involved in the regulation of lipolysis during RE in sedentary LN or OB men. The blunted lipolytic response to RE in OB subjects could be due to the significantly lower serum GH response to RE compared with LN subjects. It is also a possibility that an alternative lipolytic pathway, such as that induced by ANP, is playing an important role in lipolysis; however, ANP was not measured in the present study. It is important to recognize that the results of the present study are specific to the SCAAT of sedentary LN and OB men during RE.

Nevertheless, the favorable metabolic effects resulting from acute RE are relevant, as alternative or multiple modes of exercise may be necessary to strategically combat the deleterious effects of obesity. Indeed, RE training has been shown to improve catecholamine-mediated lipolysis in OB subjects (45). Furthermore, because RE may be a mode of exercise more suitable for OB individuals than cardiovascular endurance exercise, and RE is gaining popularity as a primary mode of exercise, future studies are warranted to better understand the regulation of lipolysis with acute and chronic RE training.

ACKNOWLEDGMENTS

We acknowledge the technical assistance of Pamela Allen and the University of Colorado Health Sciences Center for the analysis of plasma catecholamine concentrations, and Raymond Kraus, PhD, for insightful assessment of this manuscript.

GRANTS

Grant support for M. D. Choi was provided by Experimental and Applied Sciences, and M. J. Ormsbee was provided grant support by the Gatorade Sports Science Institute and Phi Kappa Phi National Honors Society.

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