The influence of sex and obesity phenotype on meal fatty acid metabolism before and after weight loss

Sylvia Santosa, Donald D Hensrud, Susanne B Votruba, and Michael D Jensen

ABSTRACT

Background: Regional differences in meal fat storage may explain the preservation of fat accumulation in obese persons.

Objective: The objective was to determine whether meal fatty acid (FA) metabolism differs by sex and obesity phenotypes before and after weight loss.

Design: A [3H]triolein-containing meal was given to trace meal FA oxidation (3H2O generation) and adipose tissue uptake (abdominal subcutaneous and gluteal biopsy samples) in 13 upper-body obese (UOb) men, 9 UOb women, and 8 lower-body obese (LOB) women (study 1). Dual-energy X-ray absorptiometry and abdominal computed tomography were used to measure fat distribution. The subjects participated in a diet and exercise weight-loss program, after which 23 subjects returned for an identical study (study 2).

Results: In study 1, the storage of meal FA (mg meal fat/g adipose lipid) was greater in gluteal than in abdominal fat (P = 0.022) in LOB women, but not in UOB women or UOB men. UOB men stored a lesser percentage of meal FAs in both upper- and lower-body subcutaneous fat than did the LOB and UOB women (P = 0.001 and P = 0.044, respectively). The participants who returned for study 2 had lost 14.1 ± 1.1 kg. Changes in the uptake of meal FAs followed a pattern indicative of obesity phenotype maintenance by group. The uptake of meal FAs increased in upper-body subcutaneous fat (P = 0.028) in weight-reduced UOB women and UOB men (P = 0.046) and decreased in lower-body fat (P = 0.025) in UOB men.

Conclusion: The differences in meal FA trafficking by obesity phenotype suggest that meal FA storage may play a role in regulating body fat distribution in obese persons. Am J Clin Nutr 2008;88:1134–41.

INTRODUCTION

An android or upper-body fat distribution is an important factor in predicting the increased health risks of obesity (1–3). A wide range of fat distribution can be seen in both adult men and women, although men typically store fat in the upper body and women store fat in the lower body. The reason for the variation in fat accumulation in different body regions is largely unknown. In order for some fat depots to expand to a greater extent than others, there must be regional differences in adipocyte metabolism, either in lipolysis or fatty acid (FA) uptake. The available evidence suggests that regional variations in lipolysis (eg, defective lipolysis in the larger depots) do not explain fat distribution (4–7), implying that differences in FA uptake could be important in determining body fat patterning. Initial studies in normal-weight men and women have not shown that storage of meal-derived FAs explains differences in body fat accumulation and in the maintenance of distribution in men and women (8–11). These studies, however, do not rule out the possibility that meal fat storage may play a role in preserving fat distribution in obese individuals with certain obesity phenotypes. If meal fat metabolism helps to maintain regional body fat distribution, it may differ between men and women. Whether regional differences in meal fat storage explain the preservation of preferential fat accumulation in obese individuals has yet to be investigated.

The single greatest source of fat for adipose storage is dietary triglyceride. We (8, 10, 12–14) and others (9, 15, 16) have examined whether regional differences in dietary fat storage relate to body fat distribution in a manner that suggests a cause and effect relation. This is done by measuring meal FA uptake with the use of the meal FA tracer/adipose biopsy technique pioneered by Mårin et al (9, 17). Herein we present the results of studies that use this approach to examine how meal triglyceride FA storage into adipose tissue lipid varies by sex and obesity phenotype.

Weight loss improves the comorbidities of obesity, such as hypertension, dyslipidemia, insulin resistance, and type 2 diabetes (18–20). However, weight loss has also been reported to alter substrate oxidation in a manner that favors lipid storage (21, 22), perhaps via changes in lipoprotein lipase (LPL) activity (23). Whether these weight-loss effects are related to how dietary fat is trafficked into storage or oxidative pathways, and whether the effects vary by obesity phenotype, is unknown. To the extent that altered fat oxidation is related to the tendency to regain weight, an understanding of how dietary FA metabolism changes with weight loss might help in the development of more effective ways of treating obesity.

The primary objective of this study was to determine whether meal FA oxidation and uptake into subcutaneous adipose tissue (SAT) vary by sex and body fat distribution. We also examined how weight loss through diet and exercise affect meal FA trafficking in these same groups.

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2 Supported by grants DK45343, DK40484, DK50456, and R00585 from the US Public Health Service and by the Mayo Foundation.
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Received January 9, 2008.
Accepted for publication June 10, 2008.
SUBJECTS AND METHODS

Subjects

Thirty volunteers provided written informed consent to participate in the study. All participants were obese (body mass index [BMI; in kg/m²] ≥30) and weight stable, defined as weight ± 1.0 kg for ≥2 mo before the trial. All participants were sedentary or lightly active previous to participating in the study, as defined by the American College of Sports Medicine (24). Women with a waist-to-hip ratio (WHR) ≥ 0.85 or ≤0.79 were recruited to create 2 groups identified as upper-body obese (UOb) and lower-body obese (LOb), respectively. All men recruited were UOb (WHR ≥ 0.95). A normal complete blood count, serum creatinine concentration, liver function tests, and electrolyte concentrations were required. All female subjects had to be nonpregnant before and during the study periods. No medications that affect FA metabolism were permitted during the studies, and none of the women were taking oral contraceptives.

Materials and assays

Dual-energy X-ray absorptiometry (DXA) (DPX-IQ; Lunar Radiation, Madison, WI) was used to measure fat-free mass (FFM), total body mass, and leg fat mass (FM) (25). Abdominal subcutaneous and visceral adipose tissue areas were determined with the use of a single-slice abdominal computed tomography (CT) scan at the L2–L3 level. The CT data, combined with the DXA-measured total abdominal fat content, were used to calculate visceral fat mass (26).

Resting metabolic rate (RMR) and substrate oxidation were measured via indirect calorimetry by using a DeltaTrac Metabolic Cart (Yorba Linda, CA) after the subjects fasted overnight for 12 h and were in a steady state (27). After the experimental meal (see below) was consumed, measurements were taken every 30 min over the following 5 h. Steady state was achieved with the initial indirect calorimetry measurement that was 30 min in duration with a 5-min acclimatization period. Each indirect calorimetry measurement thereafter was 10 min in duration, which included 5 min to establish steady state. Total body water was measured by using H₂¹⁸O (28).

Protocol

The meal FA metabolism studies were conducted in the Mayo Clinical Studies Unit (CSU) before (study 1) and after (study 2) the weight-loss intervention. Body composition and total body water were measured before the inpatient studies. To isolate the effects of weight loss on fat oxidation and meal fat deposition, the participants were required to remain weight stable for ≥1 mo and consume meals provided by the CSU for 7 d before the meal-tracer studies. The provision of meals ensured that the participants in each group were in an isocaloric state before being studied. The diet provided energy in the form of 35% fat, 50% carbohydrate, and 15% protein. The energy intake required for weight maintenance was estimated on the basis of measured resting energy expenditure by indirect calorimetry multiplied by an activity factor of 1.5; subsequent adjustments were made to maintain weight stability. The participants were required to refrain from vigorous exercise for 2 d before admission, which was the evening before the meal-tracer study.

Weight loss between the study phases of the trial was achieved through a diet and exercise regimen in which subjects were instructed to decrease caloric intake and increase energy expenditure in an amount that would create a deficit of 500 kcal/d. The weight-loss diet consisted of 20–25% fat, 20% protein, and 55–60% carbohydrate. All food was provided by the CSU for the first 4 wk. During the initial 4-wk period, participants were taught dietary principles and weight management and behavioral training techniques. After this 4-wk period, subjects selected, prepared, and consumed food at home. The exercise program started with 15 min of aerobic exercise 3 times/wk at 50% of the heart rate reserve (HRR), defined as the difference between resting and maximal heart rate. After the initial 4-wk period, participants were asked to gradually increase their activity to 45 min of aerobic exercise 4 times/wk at 60–70% of the HRR. The exercise program was not supervised, and adherence was self reported. Volunteers were weighed weekly at the CSU.

Plasma FFA and insulin

Baseline FFAs and postabsorptive insulin were measured in 4 samples collected before the test meal. Postprandial insulin was calculated from the average of 4 and 5 blood samples collected after the test meal. HPLC was used to measure plasma FFAs, and a radioimmunoassay was used to measure insulin.

Meal uptake and oxidation

At 0800 on the morning of the study, the participants consumed a liquid meal (Ensure Plus, Ross Laboratories, Abbott, Columbus, OH). The test meal provided one-third of the resting energy expenditure in UOb men and one-third of the total energy expenditure in LOb and UOb women. The test meals were selected in this manner to avoid huge differences in the energy and fat contents of the meals between men and women. The meal provided 835 ± 15 kcal, 856 ± 24 kcal, and 750 ± 29 kcal for LOb women, UOb women, and UOb men, respectively. The macronutrient distribution and energy content of the experimental meal was assessed according to the volume consumed (to the nearest 5 mL) and the manufacturers’ listed contents. The energy content of the meals for participants who completed both studies was 793 ± 21 kcal before weight loss and 688 ± 21 kcal after weight loss. The energy content of the test meal after weight loss was modified from the initial meal for each participant on the basis of any changes in resting metabolic rate between the first and second studies. The experimental meal contained 57% carbohydrate, 27% fat, and 15% protein. Forty μCi [³H]triolein was sonicated into the meal just before consumption. Quadruplicate 50-μL samples of the test meal were counted on a liquid scintillation counter to determine the exact amount of [³H]triolein consumed. Lunch and supper were provided at 1300 and 1800 and consisted of solid foods with the same macronutrient composition as those provided during the week before admission. During the first 8 h after the test meal, the participants were required to remain in bed except as needed to void. Urine was collected for 24 h after the test meal to assess [³H]H₂O losses. After the subjects voided completely on the morning after the test meal, a second sample of fresh urine was collected and analyzed for [³H]H₂O concentration.

Biopsy samples of SAT from the abdominal and gluteal regions were obtained at 0800 the next day with the use of sterile techniques under local anesthesia. Lipids were extracted from
was then calculated with the following equation:

\[
\% \text{MF}_{\text{regional tissue}} = \frac{\text{SA} \cdot \text{dpm/mg regional tissue}}{\text{total regional tissue mass (mg)}} \cdot \frac{1}{A_{\text{test meal}} \cdot \text{dpm}}
\]

The following equation was used to calculate the percentage of meal fat oxidized:

\[
\% \text{MF}_{\text{oxidized}} = \frac{A_{\text{urine (dpm)}} + A_{\text{total body water (dpm)}}}{A_{\text{test meal}}}
\]

The activity of total body water was determined by plasma SA (dpm/mL) and total body water (mL).

Typically, the sum of the meal FA oxidized and stored does not account for all meal FA consumed. Calculation of percent unaccounted for meal fat is as follows:

\[
\text{Unaccounted for meal fat(\%)} = 100 - \% \text{MF}_{\text{abdominal}} - \% \text{MF}_{\text{gluteal}} - \% \text{MF}_{\text{oxidized}}
\]

**Substrate oxidation**

The amount of energy expended on the morning of the study was determined by indirect calorimetry (27). Before and after the test meal was consumed, maximal oxygen uptake (VO₂) and maximal carbon dioxide uptake (VCO₂) were measured for 15 min at 0, 30, 60, 90, 120, 180, 240, and 300 min. Because participants were weight stable before and during the study, all subjects were assumed to be in nitrogen balance (nitrogen intake = nitrogen losses); therefore, urine nitrogen losses for the purposes of calculating substrate oxidation were considered to be equal to nitrogen intake. Carbohydrate and fat oxidation values at each time point were calculated, and the total oxidation of each substrate was determined from the area under the curve (g) from 0 to 300 min.

**Statistics**

All data were tested for normal distribution with the Shapiro-Wilk test for normality. One-way analysis of variance with a post hoc Tukey test was used to evaluate statistically significant differences in study 1 baseline characteristics, body composition, meal FA uptake, and oxidation between groups. Analysis of covariance was used to examine whether obesity phenotypes or sex differences predicted meal FA oxidation with the use of FFM as a covariate. Analysis of covariance with a post hoc Tukey honestly significant difference was used to compare whether changes in FFA, insulin, meal FA uptake, and oxidation were different between groups after weight loss when baseline values were used as a covariate. Paired t tests were used to determine whether statistically significant within-group differences existed in meal uptake and oxidation between depots and in body composition after weight loss. Pearson’s correlations were used to evaluate how body composition relates to measured meal FA variables and after weight loss. Because the number of hypotheses that were not a priori was limited, no statistical adjustments were made for multiple comparisons. SPSS for Windows (version 12.0.0; SPSS Inc, Chicago, IL) and JMP (version 7.0.1; SAS Institute, Cary, NC) were used for the statistical analysis. Data are presented as means ± SEMs. Differences were defined as statistically significant at a P value < 0.05.

**RESULTS**

**Study 1**

**Subject characteristics**

The characteristics of the volunteers participating in study 1 are provided in Table 1. Of the 30 participants, 9 were UOb women, 13 were UOb men, and 8 were LOb women. The groups were well matched for age and BMI. Resting energy expenditure was greater (P < 0.001) in men than in women. The expected patterns of differences in total and regional fat mass (visceral, leg, and upper-body SAT) were observed.

**Substrate and meal FA oxidation**

For the 5 h after the experimental meal, there were no differences in carbohydrate (P = 0.47) or fat oxidation (P = 0.73) between groups (Table 1). There were no significant between-group differences in 24-h meal FA oxidation (P = 0.32). No variations were found in postabsorptive insulin concentrations (P = 0.14), postprandial insulin concentrations (P = 0.15), or postabsorptive FFA concentrations (P = 0.18).

**Meal FA storage in adipose tissue**

In LOb women, more meal FA was stored in gluteal adipose tissue (P = 0.022) than in abdominal adipose tissue (in mg meal FA/g adipose lipid). No such site differences were detected in UOb women or men (Table 1).

UOb men stored a lesser percentage of meal FAs in both upper- and lower-body subcutaneous fat than did LOb and UOb women (P = 0.001 and P = 0.044, respectively). The percentage of meal fat stored in upper-body and lower-body subcutaneous depots within the same group was not significantly different (P = 0.23 for UOb men, P = 0.45 for LOb women, and P = 0.55 for UOb women). There were no significant differences between groups in meal fat that was unaccounted for: P = 0.44 for UOb men compared with LOb women, P = 0.93 for LOb women compared with UOb women, and P = 0.22 for UOb men compared with UOb women.

**Relations between regional fat distribution and meal FA metabolism**

We observed a trend (P = 0.051) for a positive association (r = 0.37) between abdominal meal FA storage and upper-body subcutaneous fat mass. For the combined group, meal FA storage in gluteal fat (mg meal fat/g adipose lipid) increased in relation to lower-body fat mass (Figure 1). In contrast, the amount of lower-body fat was inversely associated with the storage of meal fat (mg meal fat/g of gluteal adipose lipid; r = −0.74, P = 0.037) in LOb women; however, this was not a prespecified hypothesis to be tested in the LOb women alone.
Subject characteristics and meal study data for participants completing study 1

<table>
<thead>
<tr>
<th></th>
<th>Lower-body obese women (n = 8)</th>
<th>Upper-body obese women (n = 9)</th>
<th>Upper-body obese men (n = 13)</th>
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<tr>
<td>Age (y)</td>
<td>39 ± 2</td>
<td>40 ± 2</td>
<td>42 ± 1</td>
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<tr>
<td>Basal metabolic rate (kcal/d)</td>
<td>1628 ± 68^a</td>
<td>1781 ± 65^a</td>
<td>2057 ± 51^b</td>
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<tr>
<td>BMI (kg/m^2)</td>
<td>33.6 ± 0.6</td>
<td>33.8 ± 0.9</td>
<td>33.0 ± 0.8</td>
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<tr>
<td>Weight (kg)</td>
<td>91.5 ± 3.0^a</td>
<td>93.8 ± 3.0^a</td>
<td>104.1 ± 2.8^a</td>
</tr>
<tr>
<td>Fat (%)</td>
<td>52.1 ± 0.9^a</td>
<td>46.1 ± 1.4^a</td>
<td>32.1 ± 1.6^b</td>
</tr>
<tr>
<td>VAT (kg)</td>
<td>5.3 ± 0.6^a</td>
<td>6.6 ± 0.5^ab</td>
<td>8.1 ± 0.6^b</td>
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<tr>
<td>Lower-body SAT (kg)</td>
<td>17.4 ± 1.6^a</td>
<td>14.3 ± 1.2^ab</td>
<td>10.6 ± 0.8^b</td>
</tr>
<tr>
<td>Upper-body SAT (kg)</td>
<td>25.1 ± 1.1^a</td>
<td>22.5 ± 1.8^a</td>
<td>14.7 ± 1.1^b</td>
</tr>
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</tr>
<tr>
<td>Upper-body SAT (kg)</td>
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<td>22.5 ± 1.8^a</td>
<td>14.7 ± 1.1^b</td>
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</table>

Plasma FFAs and insulin

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<tr>
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<th>Postabsorptive FFA (μmol/L)</th>
<th>Postprandial insulin (pmol/L)</th>
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<tr>
<td>Lower-body SAT</td>
<td>617 ± 33</td>
<td>44 ± 5</td>
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<tr>
<td>Upper-body SAT</td>
<td>730 ± 40</td>
<td>91 ± 9</td>
</tr>
<tr>
<td>Unaccounted for</td>
<td>245 ± 70</td>
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Whole-body 5-h substrate utilization (g)

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<th>Fat</th>
<th>Lower-body SAT</th>
<th>Upper-body SAT</th>
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<tbody>
<tr>
<td>Postprandial insulin (pmol/L)</td>
<td>0.38 ± 0.04^2</td>
<td>0.24 ± 0.04</td>
<td>0.17 ± 0.02</td>
<td>0.20 ± 0.03</td>
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Meal FA storage/utilization (%)

<table>
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<th></th>
<th>Upper-body SAT</th>
<th>Lower-body SAT</th>
<th>Oxidation</th>
<th>Unaccounted for</th>
</tr>
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<tbody>
<tr>
<td>Postprandial insulin (pmol/L)</td>
<td>20.3 ± 1.0^a</td>
<td>22.8 ± 7.8^a</td>
<td>18.5 ± 4.3</td>
<td>38.3 ± 4.0</td>
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</table>

Study 2

Subject characteristics

Twenty-three participants returned for the post–weight loss study (study 2). The characteristics of the participants in study 2 are provided in Table 2, by obesity sub-group. The average age of those returning for study 2 was 42 ± 1 y, and there were no significant differences between the ages (P = 0.20) or initial BMI (P = 0.77) of UOb men, LOb women, or UOb women in study 2. Seven participants did not return to participate in study 2 because they were unable to comply with the study protocol and had difficulty attending scheduled study visits. There were no differences in baseline characteristics between participants who completed study 2 and those who did not.

Meal FA oxidation after weight loss

Overall, the amount of carbohydrate oxidized during the 5-h postmeal interval did not change in participants after weight loss (34.2 ± 3.3 g compared with 40.6 ± 3.3 g; P = 0.15); however, postprandial fat oxidation decreased (20.0 ± 1.8 g compared with 15.2 ± 1.6 g; P = 0.016) after weight loss. There was no difference (P = 0.15) in the change in the amount of meal fat oxidized 24 h after weight loss (7.69 ± 0.79 g compared with 9.33 ± 0.65 g). The percentage of meal FA oxidized in the 24 h after the experimental meal increased (P = 0.014) after the diet and exercise program, which resulted in weight loss (29.2 ± 3.0% compared with 40.7 ± 2.8%).

Plasma FFA and insulin concentrations

For the group as a whole, postabsorptive plasma FFA concentrations decreased (P < 0.001) after weight loss (701 ± 30 μmol/L compared with 478 ± 25 μmol/L; Table 3). There were no significant changes (P = 0.15 and P = 0.34, respectively) in postabsorptive or postprandial plasma insulin concentrations after weight loss (70 ± 13 pmol/L compared with 57 ± 11 pmol/L and 302 ± 49 pmol/L compared with 375 ± 78 pmol/L, respectively).
When examined as subgroups, decreases in postabsorptive FFA concentrations were found in LOB women (P = 0.007) and UOB men (P < 0.001; Table 3). Postprandial insulin concentrations decreased (P = 0.02) after weight loss in LOB women. No differences were found in the changes in substrate and meal FA oxidation or postabsorptive plasma insulin concentrations from study 1 to study 2 in LOB women, UOB women, or UOB men. There was a difference in changes in postabsorptive FFAs (P = 0.049), with a greater decrease in UOB men (−278 ± 31 μmol/L) than in UOB women (−145 ± 44 μmol/L). No between-group differences were found in any of the other abovementioned variables (Table 3).

Meal FA storage after weight loss

Neither upper-body nor lower-body subcutaneous meal FA storage changed after the diet and exercise program, which resulted in weight loss [0.23 ± 0.14 compared with 0.31 ± 0.27 mg meal fat/g lipid (P = 0.32) and 0.34 ± 0.27 compared with 0.40 ± 0.39 mg meal fat/g lipid (P = 0.28), respectively] for the combined group of men and women. Within the obesity subgroups, however, meal FA storage increased in LOB women after weight loss, significantly so (P = 0.028) in abdominal fat (Table 3). Because both groups of obese women also lost substantial amounts of subcutaneous fat, the percentage of meal FA storage in upper- and lower-body subcutaneous fat did not change significantly from study 1 to study 2 (Table 3). In LOB men, we observed a significant increase (P < 0.05) in the percentage of meal FA storage in abdominal SAT from study 1 to study 2 and a small, but significant (P < 0.05), decrease in meal FA storage in lower-body fat (Table 3). A difference (P = 0.004) was found between changes in the percentage of meal fat stored in lower-body SAT between groups after weight loss, where changes in the percentage of meal fat stored in lower-body SAT in LOB women (7.2 ± 4.3%) was different from the change in UOB men (−0.2 ± 2.6%).

After weight loss, the proportion of meal FA that was unaccounted for decreased for the group as a whole (48.5 ± 3.5% compared with 31.4 ± 4.4%; P = 0.006), but there were no significant changes within the subgroups. A difference (P = 0.01) in the change in unaccounted-for meal fat was seen after weight loss, where the change in LOB women (−25.8 ± 8.2%) was larger than that in UOB men (−9.9 ± 5.2%).

Relations between changes in regional fat distribution and meal FA metabolism after weight loss

No statistically significant relations were detected between changes in regional fat distribution and meal FA metabolism after weight loss in the group as a whole. The change in the storage of meal FA (mg/g adipose lipid) tended (r = −0.40, P = 0.059) to increase as a function of the loss of body fat (change in percentage body fat), which would not be surprising in that the same relative amount of dietary fat might be stored in less body fat.

In UOB men, decreases in fat mass were associated (P = 0.008 for both lower- and upper-body fat) with more meal FA storage in abdominal and gluteal SAT (r = −0.72 for both). In addition, meal FA storage per gram of abdominal adipose lipid after the diet and exercise program resulting in weight loss was negatively correlated (r = −0.65; P = 0.022) with changes in upper-body subcutaneous fat mass in UOB men. In UOB men, the changes in lower-body fat after weight loss were also negatively associated (r = −0.77, P = 0.003) with meal storage per gram of gluteal adipose lipid.

DISCUSSION

This study was designed to test whether obese men and women with different body fat distributions would have patterns of meal FA trafficking consistent with their fat patterning. If so, this might suggest that meal fat storage contributes to differences in body fat distribution in obesity. We also sought to understand how meal FA metabolism is affected by a diet and exercise program resulting in weight loss. We found that gluteal fat concentrated meal FA to a greater extent than did abdominal subcutaneous fat in LOB women, but this was not the case in UOB women or UOB men. We also observed that, although UOB men stored the same portion of dietary FA in upper- and lower-body subcutaneous depots under weight-stable conditions, they stored a significantly greater portion of dietary fat in upper-body SAT than in lower-body SAT after weight loss. Thus, in obese adults, storage of dietary fat in different adipose depots may contribute to variations in body fat distribution.

We found it interesting that LOB women stored more meal FA in lower-body fat than in upper-body fat. The finding of preferential storage of meal FA in lower-body fat contrasts with previous reports that meal FA storage (mg meal fat/g adipose lipid)
TABLE 3
Study 2: Meal fat storage and oxidation, plasma free fatty acids (FFAs), and insulin before and after weight loss by group

<table>
<thead>
<tr>
<th></th>
<th>Lower-body obese women</th>
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<th>Upper-body obese men</th>
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<tbody>
<tr>
<td></td>
<td>(n = 5)</td>
<td>(n = 6)</td>
<td>(n = 12)</td>
<td></td>
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<tr>
<td><strong>Test meal</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>843 ± 23</td>
<td>755 ± 35</td>
<td>23 ± 755</td>
<td>28.3 ± 1.0</td>
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<tr>
<td>Fat (g)</td>
<td>28.4 ± 0.8</td>
<td>25.4 ± 1.2</td>
<td>3.0 ± 0.9</td>
<td>25.2 ± 1.1</td>
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<tr>
<td><strong>Plasma FFAs and insulin</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Postabsorptive FFA (μmol/L)</td>
<td>631 ± 45</td>
<td>447 ± 52b</td>
<td>184 ± 37</td>
<td>447 ± 52b</td>
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<tr>
<td>Postabsorptive insulin (pmol/L)</td>
<td>42 ± 7</td>
<td>28 ± 5</td>
<td>14 ± 5</td>
<td>74 ± 23</td>
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<tr>
<td>Postprandial insulin (pmol/L)</td>
<td>269 ± 37</td>
<td>136 ± 11</td>
<td>133 ± 60</td>
<td>256 ± 77</td>
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<td><strong>Whole-body 5-h substrate utilization (g)</strong></td>
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<tr>
<td>Carbohydrate</td>
<td>22.4 ± 1.6</td>
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<td>Fat</td>
<td>14.8 ± 1.2</td>
<td>10.4 ± 2.9</td>
<td>14.6 ± 2.3</td>
<td>25.3 ± 2.5</td>
</tr>
<tr>
<td>Meal 24-h FA oxidation (g)</td>
<td>5.14 ± 1.62</td>
<td>8.94 ± 2.45</td>
<td>3.80 ± 3.29</td>
<td>8.94 ± 0.81</td>
</tr>
<tr>
<td><strong>Meal FA storage (mg meal fat/g lipid)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal SAT</td>
<td>0.42 ± 0.06</td>
<td>0.53 ± 0.19</td>
<td>0.11 ± 0.17</td>
<td>0.17 ± 0.02</td>
</tr>
<tr>
<td>Gluteal SAT</td>
<td>0.73 ± 0.10</td>
<td>0.84 ± 0.18</td>
<td>0.10 ± 0.17</td>
<td>0.20 ± 0.03</td>
</tr>
<tr>
<td><strong>Meal FA storage/utilization (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper-body SAT</td>
<td>19.6 ± 0.5</td>
<td>21.6 ± 4.1</td>
<td>20.2 ± 3.5</td>
<td>22.0 ± 0.8</td>
</tr>
<tr>
<td>Lower-body SAT</td>
<td>21.4 ± 4.3</td>
<td>28.4 ± 4.3a</td>
<td>7.0 ± 6.2</td>
<td>5.5 ± 0.8</td>
</tr>
<tr>
<td>Oxidation</td>
<td>18.4 ± 5.9</td>
<td>35.6 ± 10.0</td>
<td>17.2 ± 13.2</td>
<td>35.8 ± 3.4</td>
</tr>
<tr>
<td>Unaccounted for</td>
<td>40.4 ± 5.3</td>
<td>14.4 ± 9.2a</td>
<td>−26.0 ± 30.7</td>
<td>14.4 ± 9.2a</td>
</tr>
</tbody>
</table>

All values are mean ± SEM. SAT, subcutaneous adipose tissue; FA, fatty acid. Means with different superscript letters are significantly different, \( P < 0.05 \) (ANCOVA with baseline values used as a covariate and post hoc Tukey tests).

1 Significant change after weight loss, \( P < 0.05 \) (paired t test).
2 Significant change from gluteal SAT, \( P < 0.05 \) (paired t tests).

\( n = 4 \) for lower-body obese women, \( n = 5 \) for upper-body obese women, and \( n = 10 \) for upper-body obese men.

\( n = 11 \) for upper-body obese men. Test meal composition for energy and fat intakes, respectively: before, 758 ± 33 kcal and 25.5 ± 1.1 g; after: 616 ± 19 kcal and 20.7 ± 0.6 g.

\( n = 11 \) for upper-body obese men. Test meal composition for energy and fat intakes, respectively: before, 758 ± 33 kcal and 25.5 ± 1.1 g; after: 616 ± 19 kcal and 20.7 ± 0.6 g.
is greater in upper-body than in lower-body subcutaneous fat in normal-weight men and women (9–11, 17). A recent study of meal FA uptake in obese women did not detect any differences in lower- and upper-body meal FA storage (13), although there was a significant trend for meal FA storage in leg fat to increase in relation to leg fat mass in women receiving a normal-fat meal. Our finding that LOb women stored significantly more meal fat in lower-body than in upper-body adipose tissue is consistent with that trend. This implies that, in some individuals, lower-body adipose tissue has a competitive advantage relative to upper-body adipose tissue, and that this advantage works to create and/or maintain a lower-body obesity phenotype. Although another possibility is that accelerated lipolysis in lower-body fat cells in LOb women is offset by preferential uptake of meal FA, in vivo measures of leg FFA release have consistently shown that lower-body fat is “hypo-lipolytic” relative to upper-body fat (4, 6, 29). The corollary to this meal fat storage hypothesis is that individuals in whom upper-body fat is more efficient in storing dietary fat will develop an upper-body fat distribution along with the associated health risks.

We also found evidence in favor of the role that meal FA storage may have in maintaining the sexual dimorphism of fat distribution. Much less meal FA storage was found in subcutaneous fat in UOb men, both lower- and upper-body, than in obese women. This pattern in obese individuals was more pronounced than that observed in normal-weight men and women (10, 11).

For the groups combined, we observed an increase in the 24-h dietary fat oxidation after weight loss, despite a slight reduction in total fat oxidation for the 5 h after the experimental meal. This suggests that, after a diet and exercise program resulting in weight loss, more dietary fat is used for immediate energy needs, which seems to be more than offset by a reduction in the oxidation of endogenous FAs. The difference in 5-h and 24-h fat oxidation could be due to enhanced insulin-mediated suppression of FFA availability (30), which in turn may contribute to the improved tissue sensitivity to insulin after weight loss (31–33).

Although changes (or lack thereof) in postabsorptive and postprandial insulin concentrations may not be accurate indicators of insulin sensitivity, there was a significant overall decrease in postabsorptive plasma FFA concentrations after weight loss. The changes in FFA concentrations with weight loss may indicate that the reduced total FA oxidation despite overall increases in 24-h meal fat oxidation are a reflection of a better regulation of adipose tissue lipolysis.

After the loss of significant amounts of body fat, there was an expected pattern of increasing meal fat uptake (mg meal FA/g adipose lipid), especially in upper-body fat in UOb women and men. This suggests that abdominal fat cells in these individuals may respond to losses in intracellular triglyceride by enhancing the storage of dietary fat in this region and would likely contribute to a preferential regain of upper-body fat after dieting. Similarly, after weight loss, there was a significant difference in the changes in the percentage of lower-body meal fat uptake between LOb women and men, where a lower percentage of body meal fat storage increased in women and slightly decreased in UOb men. The preferential sequestering of fat into lower-body depots in the LOb women further supports a role of dietary fat in maintaining regional body fat distribution.

There are a number of potential explanations for the regional differences in meal FA storage in LOb women and for the sex differences in meal FA storage. These range from differences in regional postprandial adipose tissue blood flow (10, 34, 35), LPL activity (15, 36, 37), cellular FA transport (38), or efficiency of adipocyte TG synthesis (39). Previous studies that compare regional LPL concentrations in men and women have generally found higher concentrations of LPL in women than in men (15, 36, 37). Furthermore, LOb women have been reported to have higher LPL activity in gluteal and femoral fat, which implies a greater potential for FA uptake in these regions (40). However, LPL activity cannot completely account for sex differences in regional fat uptake (41, 42). Contrary to what might be expected, 10 kg of weight loss was shown to reduce LPL activity in upper- and lower-body fat in women, but not in men (15). Little is known about the relative contributions of blood flow, FA transport, or triglyceride synthesis steps as regulators of regional meal FA storage. Unfortunately, beyond describing the relation between meal FA storage and body fat distribution in this study, we were not able to measure processes related to these steps.

The present study sampled gluteal subcutaneous fat to examine lower-body meal fat uptake. Fat metabolism in gluteal subcutaneous fat has previously been observed to be intermediate between abdominal and thigh subcutaneous fat (10). In contrast, Uranga et al (11) found no differences between meal FA uptake in gluteal and femoral subcutaneous fat regions. Despite the fact that thigh subcutaneous fat metabolism was not measured in the present study, abdominal and gluteal subcutaneous fat metabolism differed in a manner consistent to variations in upper- and lower-body obesity seen in the literature. Thus, although we generally prefer thigh subcutaneous fat when examining differences between lower- and upper-body fat (10), gluteal subcutaneous fat appears to be acceptable in representing the metabolism of lower-body fat (11).

In summary, we studied how dietary FAs are stored in different subcutaneous fat depots in obese men and women with different distributions of body fat. The observation that LOb women are more efficient at storing meal FA in gluteal than in abdominal fat suggests that the trafficking of dietary triglycerides may play a role in determining fat distribution. In addition, UOb men store a much lower proportion of dietary fat in subcutaneous regions, which also hints at a role for this process in the sex differences in fat distribution. Finally, fat loss via diet and exercise modified meal FA storage in such a way as to favor the maintenance of regional body fat distribution. Understanding the potential role of dietary fat trafficking in determining fat distribution will help focus future studies on more mechanistic processes.

The authors’ responsibilities were as follows—SS and SBV: analyzed the data, wrote the manuscript, and provided significant advice; DDH: collected and analyzed the data, and wrote the manuscript, and MDJ: designed the experiment, collected and analyzed the data, and wrote the manuscript. None of the authors declared a conflict of interest.

REFERENCES


