

Influence of human obesity on the metabolic fate of dietary long- and medium-chain triacylglycerols¹⁻³

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ABSTRACT The metabolic fate of an oral long-chain-triacylglycerol (LCT) load and of a mixed oral LCT and medium-chain-triacylglycerol (MCT) load was followed for 6 h in eight control and eight obese subjects with normal postabsorptive triacylglycerol concentrations. Labeled triacylglycerol and indirect calorimetry were used. Results showed that LCTs were less oxidized in obese than in control subjects (3.2 ± 0.5 compared with 6.0 ± 0.4 g, $P < 0.01$). Moreover, the amount of LCT oxidized was negatively correlated with fat mass ($r = -0.77$, $P < 0.01$). Appearance in plasma of dietary triacylglycerol-derived long-chain fatty acids was blunted in obese subjects and it was negatively related to fat mass ($r = -0.84$, $P < 0.01$) and positively to LCT oxidation ($r = 0.70$, $P < 0.01$). On the contrary, MCT oxidation was not altered in obese subjects compared with control subjects. Furthermore, the proportion of MCTs oxidized was higher in both groups compared with LCTs ($\bar{x} \pm \text{SEM}$: $57.5 \pm 2.6\%$ compared with $15.2 \pm 1.6\%$, $P < 0.01$, $n = 16$). Our conclusion is that obesity is associated with a defect in the oxidation of dietary LCTs probably related to an excessive uptake by the adipose tissue of meal-derived long-chain fatty acids. MCTs, the oxidation of which is not altered in obesity, could therefore be of interest in the dietary treatment of obesity. *Am J Clin Nutr* 1998;67:595-601.

KEY WORDS Oral lipid load, fatty acid oxidation, medium-chain triacylglycerol, obesity, long-chain triacylglycerol, women

INTRODUCTION

Obesity is characterized by an increase in lipid stores. It is generally associated with enhanced lipid consumption, which contributes to its development (1). Thus, the study of the metabolic fate of dietary lipids in obese subjects is crucial in the understanding of this disease. However, few studies have been concerned with dietary fat metabolism during obesity. Moreover, in most of these studies, patients had hypertriglyceridemia, a condition that does not allow for testing the effect of obesity per se (2-4). Many of these studies reported the evolution of postprandial lipid concentrations, but this approach did not allow exogenous lipids to be distinguished from endogenous ones. This information could only be obtained by using labeled triacylglycerol. Moreover, with use of breath carbon dioxide tests and indirect calorimetry measurements, exogenous and total lipid oxidation can be calculated. Using [¹³C]triolein, we recently showed that large amounts of triacylglycerol-derived fatty acids appeared in the blood of control subjects, and that only 19% of a

long-chain triacylglycerol (LCT) load was oxidized in 6 h (5). Roust and Jensen (6), using [¹⁴C]trioleate included in a mixed meal, showed that meal-derived fatty acids contributed significantly to postprandial fatty acid flux and obtained similar results in obese and control subjects. Nevertheless, in obese subjects, no study has reported the different steps involved in the metabolism of orally ingested fat from intravascular release to oxidation.

Medium-chain triacylglycerols (MCTs) are metabolized differently from LCTs. After absorption by enterocytes, medium-chain fatty acids are released in the portal blood and taken up by the liver (7), where they are largely oxidized. Their intramitochondrial transport does not require carnitine palmitoyltransferase (8) and therefore does not represent a limiting step. Consequently, MCTs are oxidized more than are LCTs (9). For these reasons, MCTs could be useful in the dietary treatment of obesity.

Therefore, our aim was to determine the effect of obesity on the different steps of dietary fat metabolism. Subjects were chosen so that they had large differences in fat mass, but no lipid disorders, to test the effect of obesity per se. Triacylglycerol labeled with stable isotopes was used in combination with indirect calorimetry measurements. The metabolism of LCTs was compared with that of a mixture of MCTs and LCTs (1:1) to evaluate the influence of a substitution of LCTs by MCTs. Some data from the control subjects presented in this paper were already reported (5).

SUBJECTS AND METHODS

Materials

[1,1,1-¹³C₃]Triolein [99 atom % (AP) ¹³C] and [1,1,1-¹³C₃]triolein (99 AP ¹³C) were purchased from Eurisotop (Saint Aubin,

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France). MCTs were composed of trioctanoin and tridecanoin (2:1; Arkopharma, Carros, France). Thin-layer chromatography was performed on 60 G silica gel plates (Merck, Darmstadt, Germany). Triheptadecanoic acid and heptadecanoic acid were from Sigma (St Louis). All solvents were from Merck. Boron trifluoride methanol (Sigma) was used for fatty acid methyl ester preparation.

The labeled oil was prepared by adding 200 mg [1,1,1-¹³C₃]triolein to 30 g olive oil; 150 mg [1,1,1-¹³C₃]trioctanoin was added to a 30-g mixture of 50% (by wt) olive oil and 50% MCTs (2:1, trioctanoate and tridecanoate). Tracers were carefully homogenized. An aliquot of the labeled oil was collected to assess the isotopic enrichment.

Subjects

Eight obese [body mass index (BMI; in kg/m²) > 26] and eight normal-weight control women participated in this study. The characteristics of the subjects are presented in **Table 1**. None of the control subjects had a familial or personal history of dyslipidemia, obesity, or diabetes, or was taking any medication except for oral contraceptives. Three of the obese subjects had a familial history of obesity, one was taking an antihypertensive drug, and none was diabetic. Obese subjects were chosen to have normal postabsorptive concentrations of triacylglycerols and fatty acids. All subjects gave their written consent to the study after being informed of its nature, purpose, and possible risks. The experimental protocol was approved by the ethics committee of Hospices Civils de Lyon according to the Huriot law.

Total lean body mass and total fat mass were evaluated by using a dual-energy X-ray absorptiometer (Hologic QDR 2000; Hologic Inc, Waltham, MA). The in vivo, short-term reproducibility of these measurements was assessed in control and obese subjects. The CV between two measures was determined for fat mass and for fat-free mass. For fat mass, the CVs were 1.9 ± 2.1% and 1.8 ± 1.6% for obese and control subjects, respectively (NS, Student's *t* test). For fat-free mass, CVs were 1.9 ± 2.0% and 1.6 ± 1.7% for obese and control subjects, respectively (NS, Student's *t* test). These results are comparable with those reported in the literature (10).

Experimental protocols

Each subject underwent the LCT and MCT-LCT experiments, which were done in random order and separated by an interval ≥ 1 wk. All experiments were performed with subjects in the postabsorptive state after an overnight fast. An indwelling, nonheparin-containing catheter was placed into one forearm vein for blood sampling. After a basal period of 60 min, either 30 g labeled olive oil for the LCT experiment or 30 g labeled MCT-LCT mixture was ingested in < 5 min. Lemon juice was added to the oil to improve its taste. Blood samples were collected at baseline (two samples)

TABLE 1
Characteristics of subjects¹

Characteristic	Control (n = 8)	Obese (n = 8)
Age (y)	22 (21–25)	32.5 (23–47) ²
Fat mass (kg)	15.4 (11.2–25)	46.3 (26–54.9) ²
Fat-free mass (kg)	38.3 (35.9–43.2)	43.5 (39.8–48.2) ²
BMI (kg/m ²)	20.4 (18.7–25.2)	35.5 (26.5–43.1) ²

¹ Median; range in parentheses.

² Significantly different from control, *P* < 0.01 (nonparametric Mann-Whitney *U* test).

and every 30 min for 360 min in tubes with heparin and centrifuged immediately at 4 °C. Plasma was then stored at –20 °C until the determination of metabolite and insulin concentrations. In the LCT experiment, additional blood samples were collected at each sample time in tubes with EDTA and kept at 4 °C to prepare chylomicrons and VLDL by ultracentrifugation as described previously (5). Respiratory exchange measurements (Deltatrac metabolic monitor; Datex, Helsinki) were used to estimate total lipid oxidation rate and energy expenditure rate as described previously (5). Urine was collected in the basal state and from 0 to 360 min after the start of the experiments to determine nitrogen excretion. Two samples of expired gases were obtained in the basal state to determine basal ¹³CO₂ abundance, then expired gas samples were collected each 30 min as described previously (11).

Analytic procedures

Plasma glucose, triacylglycerol, β-hydroxybutyric acid (12), and fatty acid (13) concentrations were measured by enzymatic methods. Plasma insulin was measured by radioimmunoassay (14). Urinary nitrogen was determined by chemiluminescence (Antek 703C; Sopares, Paris). Because MCTs are mostly oxidized in the liver, plasma medium-chain fatty acids were not extracted. In the LCT experiments, lipids were extracted from chylomicrons, VLDL, or plasma according to the method of Bligh and Dyer (15) by using chloroform:methanol (1:2, vol:vol). Triheptadecanoic acid and heptadecanoic acid were added as internal standards. Fatty acids [retardation factor (Rf) = 0.22] and triacylglycerol (Rf = 0.5) were separated by thin-layer chromatography on 60 G silica gel plates with hexane:diethyl ether:acetic acid (80:20:1, by vol) as the mobile phase (16). Fatty acids and triacylglycerol were scraped off the plate and then treated with heptane:methanol (250 μL) (20:80, vol:vol) and 14% boron trifluoride in methanol (250 μL) at 100 °C for 30 min for fatty acid methyl ester preparation (17).

Gas chromatography–isotope ratio mass spectrometry analysis

During the LCT experiment, analysis of the isotopic enrichments of oleic acid from plasma fatty acids and from triacylglycerol in chylomicrons and VLDL was performed by using an isotope ratio mass spectrometer (IRMS, SIRA 12; VG Isogas, Middlewich, United Kingdom) interfaced with a gas chromatograph (5890A; Hewlett Packard, Evry, France) equipped with a Ross injector (230 °C) and a capillary column (SP2380, 0.25 mm internal diameter × 30 m; Supelco, Bellefonte, PA) as described previously (5). Oven temperature was maintained at 170 °C for 3 min, then raised 15 °C/min to 200 °C and then raised 30 °C/min to 250 °C, at which it was maintained for 5 min. Oleate concentrations were measured by gas chromatography with an internal standard. In both experiments, the ¹³C enrichment of expired carbon dioxide was determined on a dual-inlet IRMS (VG Isogas) as described previously (18).

Calculations

The ¹³C-¹²C ratio of the sample and of the reference were used to calculate the δ¹³C‰ of the sample. The measured δ¹³C‰ values were transformed to ¹³C AP and mole percent excess (MPE) as described previously (18). The quantity of [¹³C]oleate in chylomicron-triacylglycerol, VLDL-triacylglycerol, and fatty acids was determined at each point as the product of oleate concentration measured by gas chromatography and MPE [¹³C]oleate.

For the LCT experiment, the oxidation of the triacylglycerol load was calculated by using a formula described previously (5). For the MCT-LCT experiment, this formula was adapted to MCT oxidation as follows:

$$\text{Exogenous lipid oxidized (g/min)} = \quad (1)$$

$$\frac{\{[\text{AP CO}_2(t) + \text{AP CO}_2(t_{-30})]/2\} - \text{AP CO}_2(t_0)/100\} \times \dot{V}\text{CO}_2}{\{[\text{AP TG}_{\text{load}} - \text{AP CO}_2(t_0)]/100\} \times [(15.15/499) \times 29] \times 22.4 \times 0.8}$$

where $\text{AP CO}_2(t)$ is the AP value of the expired CO_2 at time t (the end of each 30-min period), $\text{AP CO}_2(t_0)$ is the AP value of the expired CO_2 at time t_0 , $\text{AP TG}_{\text{load}}$ is the AP value of the labeled oil load analyzed by IRMS, and $\dot{V}\text{CO}_2$ is the production rate of carbon dioxide. Four hundred ninety-nine is the mean molecular weight of ingested MCT composed of two-thirds trioctanoate and one-third tridecanoate. Twenty-nine is the mean number of carbons in MCT. The mass in grams of the labeled MCT moiety of the MCT-LCT mixture is 15.15, 22.4 is the volume (L) of a mole of carbon dioxide, and 0.8 is a correction factor for incomplete recovery of ^{13}C bicarbonate used for obese and control subjects (19).

Equations for glycogen oxidation were used. Corrections for ketogenesis were made by using β -hydroxybutyrate concentrations in blood and urine as described (20). For the MCT-LCT experiment, oxidation of MCTs and LCTs was calculated separately. Oxidation of MCTs was determined according to equation 1. The oxygen consumption rate ($\dot{V}\text{O}_2$) and $\dot{V}\text{CO}_2$ involved in MCT oxidation were determined by using a stoichiometric equation for the ingested medium-chain fatty acid mixture, which was composed of two-thirds trioctanoate and one-third tridecanoate: $\text{C}_{29}\text{H}_{54}\text{O}_6 + 79/2\text{O}_2 \rightarrow 29\text{CO}_2 + 27\text{H}_2\text{O}$. These $\dot{V}\text{O}_2$ and $\dot{V}\text{CO}_2$ values were subtracted from total $\dot{V}\text{O}_2$ and $\dot{V}\text{CO}_2$ to calculate LCT oxidation (endogenous and exogenous LCT oxidation, which could not be differentiated) during the MCT-LCT experiment by using the usual formula. Total lipid oxidation was calculated as the sum of LCT and MCT oxidation.

Diet-induced thermogenesis (DIT) was calculated as follows:

$$\text{DIT (\%)} = \{[(\text{postprandial EE} - \text{BMR})/\text{min} \times 360 \text{ min}] / \text{energy (kJ) of the load}\} \times 100 \quad (2)$$

where EE is energy expenditure and BMR is basal metabolic rate.

Statistical analysis

Correlations and incremental areas under the curve (AUC_i , area under the curve above basal values) were calculated with Microsoft EXCEL 5.0 (by using the trapezoidal method for the AUC calculation; Microsoft, les Ullis, France). Results are expressed as means \pm SEMs. Comparison of values was done by nonparametric tests. When necessary, the respective effects of diet and subject were analyzed by a two-factor analysis of variance (ANOVA).

RESULTS

Basal state

Hormonal and metabolic measures

In the basal state, only insulinemia was greater in obese subjects than in control subjects: 95 ± 17 compared with 47 ± 3

pmol/L, ($P < 0.01$). Glycemia (4.66 ± 0.25 compared with 4.56 ± 0.10 mmol/L), fatty acids (450 ± 56 compared with 405 ± 47 $\mu\text{mol/L}$), triacylglycerol (920 ± 110 compared with 752 ± 71 $\mu\text{mol/L}$), and β -hydroxybutyrate (61 ± 10 compared with 68 ± 8 $\mu\text{mol/L}$) between obese and control subjects, respectively, were not significantly different. Energy expenditure was greater in the obese subjects (276 ± 17 compared with 226 ± 8 kJ/h, $P < 0.05$).

LCT experiment

Hormonal and metabolic measures

After the LCT load, triacylglycerol increased in both groups (**Figure 1**) and no significant difference in triacylglycerol AUC_i was observed between groups. After an early peak, fatty acids increased progressively during the test to reach concentrations of 651 ± 99 and 731 ± 79 $\mu\text{mol/L}$ at 360 min in the control and obese groups, respectively. Glycemia was not increased by the lipid load. A slight but significant insulin peak (69 ± 6 pmol/L at 60 min compared with 47 ± 3 pmol/L in the basal state, $P < 0.05$) was observed in the control group but not in the obese group. Then, insulin decreased in both obese and control groups (66 ± 10 and 46 ± 6 pmol/L at 360 min, respectively).

Appearance of label in chylomicron-triacylglycerol, fatty acids, and VLDL-triacylglycerol

The evolution of the ^{13}C enrichment of oleate in chylomicron-triacylglycerol, fatty acids, and VLDL-triacylglycerol in the control and the obese groups is shown in **Figure 2**. The appearance of the label in chylomicron-triacylglycerol was similar in both groups, as shown by the lack of difference of AUC_i of ^{13}C oleate in chylomicron-triacylglycerol between groups (1192 ± 177 and 927 ± 121 $\mu\text{mol} \cdot 6 \text{ h/L}$ for control and obese groups, respectively; NS). The appearance of ^{13}C oleate in VLDL-triacylglycerol was not different in control and obese subjects as measured by the AUC_i of ^{13}C oleate in VLDL-triacylglycerol (328 ± 59 and 282 ± 78 $\mu\text{mol} \cdot 6 \text{ h/L}$ for the control and obese groups, respectively). On the contrary, the appearance of ^{13}C oleate in fatty acids was dramatically reduced in the obese group compared with the control group: AUC_i of ^{13}C oleate in fatty acids, 1.8 ± 0.4 compared with 4.4 ± 0.4 $\mu\text{mol} \cdot 6 \text{ h/L}$ ($P < 0.01$). At the plateau, the ratio of enrichment between fatty acids and chylomicron-triacylglycerol was largely decreased in the obese

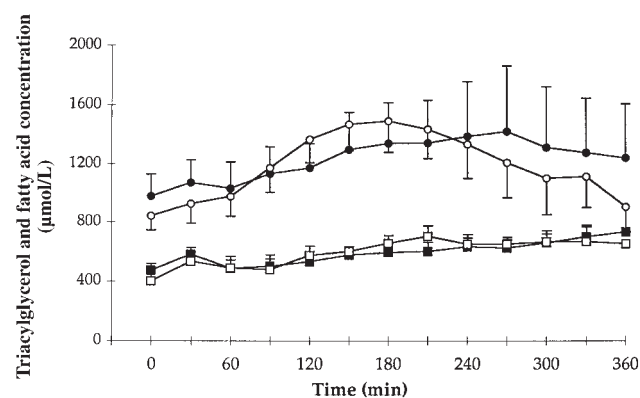


FIGURE 1. Changes in triacylglycerol and fatty acid concentrations during the long-chain triacylglycerol experiment in the control ($n = 8$) and the obese ($n = 8$) subjects. \circ , triacylglycerol control; \bullet , triacylglycerol obese; \square , fatty acids control; \blacksquare , fatty acids obese. $\bar{x} \pm \text{SEM}$.

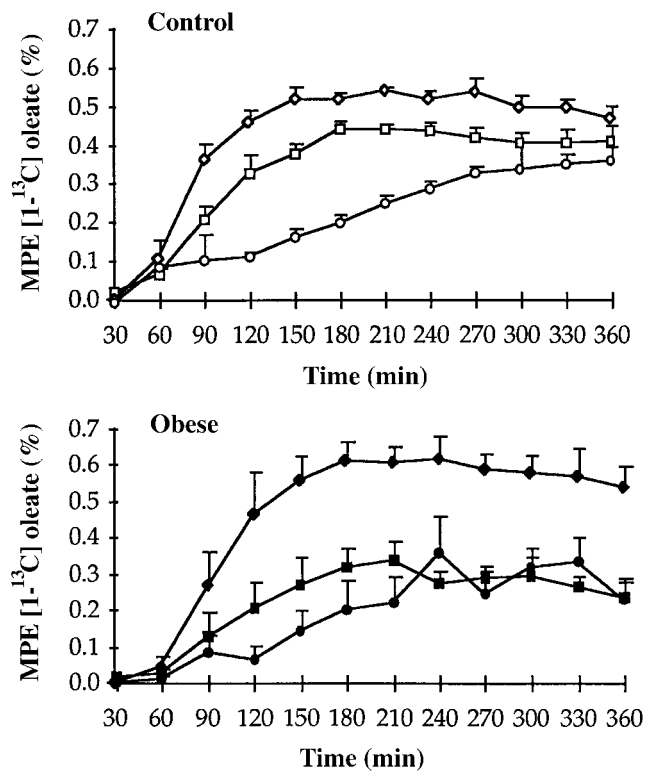


FIGURE 2. Appearance of $[1-^{13}\text{C}]$ oleate in chylomicron-triacylglycerol (\diamond), fatty acids (\square), and VLDL-triacylglycerol (\circ), in control (open symbols) and obese (filled symbols) subjects during the long-chain triacylglycerol experiment. $\bar{x} \pm \text{SEM}$.

compared with the control subjects ($53 \pm 7\%$ compared with $81 \pm 4\%$, $P < 0.01$).

Exogenous lipid oxidation, total lipid oxidation, and DIT

Cumulative values of exogenous lipid oxidized for 6 h are shown in **Figure 3**. Exogenous lipid oxidation was dramatically reduced in the obese compared with the control subjects (3.2 ± 0.5 compared with 6.0 ± 0.1 g, $P < 0.01$). Despite this effect, total lipid oxidation measured for 6 h was greater in the obese subjects (18.4 ± 1.1 compared with 14.0 ± 1.4 g, $P < 0.05$). However, total lipid oxidation expressed according to fat-free mass was not significantly different between groups (0.36 ± 0.04 and 0.42 ± 0.03 g/kg fat-free mass for the control and obese groups, respectively). DIT (expressed as a percentage of energy ingested) was lower in obese subjects than in control subjects: $5.6 \pm 1.2\%$ compared with $9.8 \pm 0.9\%$ ($P < 0.05$).

Relation to fat mass

To test the influence of fat mass on the metabolism of the lipid load, we analyzed the results obtained in the whole population ($n = 16$) according to fat mass. A negative correlation was found between fat mass and exogenous lipid oxidation ($r = -0.74$, $P < 0.01$; **Figure 4**) and the AUC_i of $[^{13}\text{C}]$ oleate in fatty acids ($r = -0.84$, $P < 0.01$; **Figure 5**). Moreover, this last correlation persisted even when the AUC_i of $[^{13}\text{C}]$ oleate was expressed per kilogram fat mass ($r = -0.94$, $P < 0.01$), suggesting that this relation was not due only to the quantity of fat mass. A correlation was also found between the AUC_i of $[^{13}\text{C}]$ oleate in fatty acids and exogenous lipid oxidation ($r = 0.70$, $P < 0.01$), thus arguing for

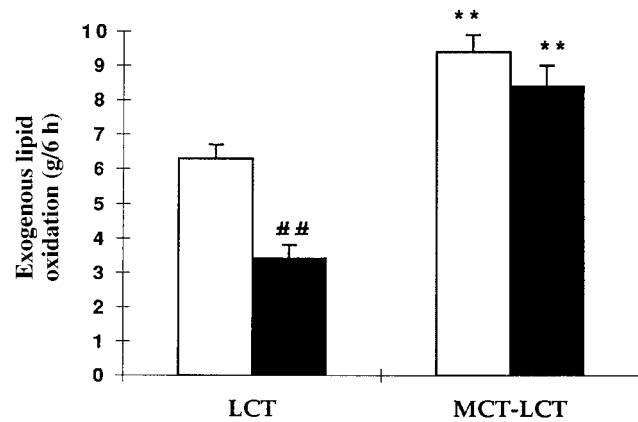


FIGURE 3. Cumulative exogenous lipid oxidation for 6 h during the long-chain triacylglycerol (LCT) and the medium-chain triacylglycerol (MCT) and LCT experiments in control (\square) and obese (\blacksquare) subjects. ## Significantly different from control subjects, $P < 0.01$; ** Significantly different from the LCT experiment, $P < 0.01$. $\bar{x} \pm \text{SEM}$.

a relation between lipid oxidation and the appearance in the blood of dietary fatty acids.

MCT-LCT experiment

Hormonal and metabolic measures

No change in triacylglycerol concentrations was observed after the MCT-LCT load in either group (**Figure 6**). Fatty acids increased progressively during the test and reached values of 573 ± 43 $\mu\text{mol/L}$ in control subjects and 843 ± 33 $\mu\text{mol/L}$ in obese subjects at 360 min ($P < 0.02$ and $P < 0.05$ compared with basal values for control and obese subjects, respectively). β -Hydroxybutyrate concentrations increased as soon as 60 min to 252 ± 61 and 190 ± 47 $\mu\text{mol/L}$ in the control and the obese groups, respectively, and then plateaued. A small but significant insulin peak was observed at 60 min in the control subjects (70 ± 6 compared with 47 ± 3 pmol/L in the basal state, $P < 0.05$) but not in the obese subjects (105 ± 5 compared with 95 ± 17 pmol/L, NS).

Exogenous lipid oxidation, total lipid oxidation, and DIT

Cumulative values of MCT oxidation for 6 h were not significantly different between groups: 9.2 ± 0.4 and 8.1 ± 0.6 g for control and obese subjects, respectively (**Figure 3**). Total lipid oxidation for 6 h was also not significantly different between groups: 17.8 ± 1.6 and 21.6 ± 2.2 g for the control and obese subjects, respectively. DIT was slightly lower in the obese group: $7.0 \pm 2.1\%$ compared with $8.3 \pm 1.6\%$ ($P < 0.05$).

Comparison between LCT and MCT-LCT experiments

Metabolites

AUC_i values of fatty acids and triacylglycerol were not different between groups nor between the LCT and the MCT-LCT experiments. On the other hand, the AUC_i of β -hydroxybutyrate was greater during the MCT-LCT experiment in both groups ($P < 0.005$).

Lipid oxidation

As shown in **Figure 7**, MCTs were oxidized more rapidly than LCTs. Indeed, the maximum of MCT oxidation occurred 195

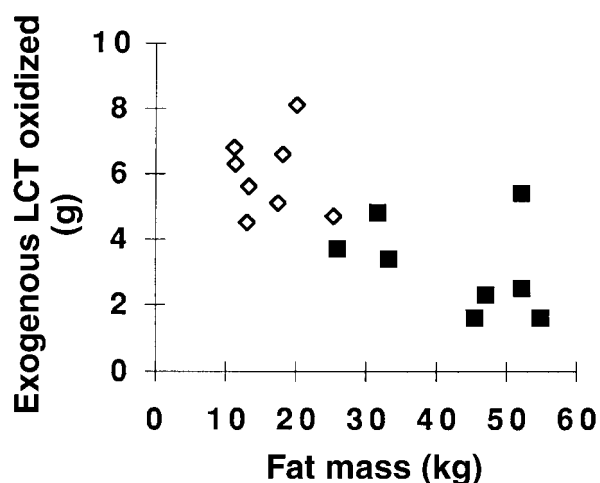


FIGURE 4. Correlation between fat mass and the cumulative amount of long-chain triacylglycerol (LCT) oxidized in control (◇) and obese (■) subjects. $y = -0.003x + 0.19$; $r = -0.74$.

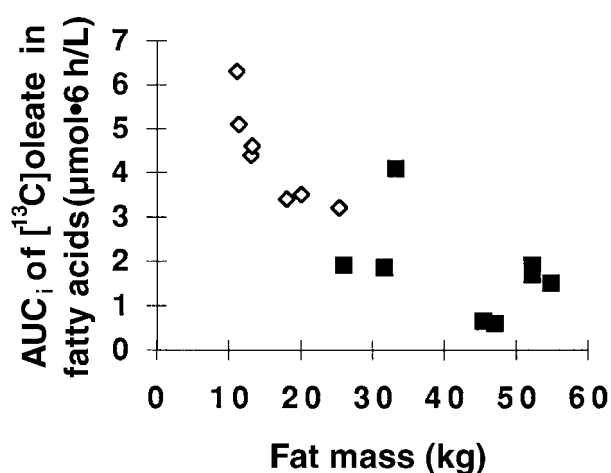


FIGURE 5. Correlation between fat mass and the incremental area under the curve (AUC_i) of [¹³C]oleate in fatty acids in control (◇) and obese (■) subjects. $y = -0.09x + 7.2$; $r = -0.84$.

min after ingestion whereas for the LCT experiment the maximum was reached at 360 min. Moreover, MCTs were oxidized more completely than LCTs: $61 \pm 0.4\%$ compared with $20 \pm 0.4\%$ ($P < 0.01$) in the control group and $54 \pm 0.6\%$ compared with $11 \pm 0.5\%$ ($P < 0.01$) in the obese group 6 h after ingestion.

Total lipid oxidation in control subjects was greater after the MCT-LCT experiment than after the LCT experiment: 17.8 ± 1.6 compared with 14.0 ± 0.4 g ($P < 0.05$). In the obese group, we observed the same trend although it was not significant: 21.2 ± 2.2 compared with 18.4 ± 1.1 g (MCT-LCT and LCT experiments, respectively). The decrease in DIT was observed in both groups but was more pronounced after the LCT load.

DISCUSSION

Our study was designed to determine the influence of obesity on the metabolic fate of dietary lipids. We showed the occurrence, in obese women, of a defect in the oxidation of exogenous LCT, a defect that was proportional to fat mass. On the contrary, we showed that the oxidation of medium-chain fatty acids was not altered in obese subjects and that total lipid oxidation tended to be higher after an MCT-LCT load than after LCT given alone. During both experiments, no abnormality of postprandial lipemia was observed in obese subjects, who had only an increase in basal insulinemia and basal lipid oxidation rate, as is usually found (21). Thus, the effect of obesity per se could be studied independently from lipid metabolism disorders.

In this study, we found that the appearance of dietary triacylglycerol-derived fatty acids (represented by AUC_i of [¹³C]oleate) was reduced in the obese group, and that this defect was related to fat mass. It could not have been due to a dilution phenomenon by endogenous fatty acids because the calculation of [¹³C]oleate takes this into account. The appearance of label in fatty acid is due to the hydrolysis of chylomicron-triacylglycerol by lipoprotein lipase. Thus, the lack of appearance of [¹³C]oleate observed in the obese subjects could have been related to a defect in chylomicron-triacylglycerol clearance. This was unlikely in our study, given the absence of a difference between groups for both triacylglycerol AUC_i and [¹³C]oleate in chylomicron AUC_i.

These results are different from those of Potts et al (4), who showed a decreased removal of chylomicron-triacylglycerol in obese subjects. This could be explained by differences between the subjects in metabolic profile. Indeed, in our study, obese subjects were chosen to have normal postabsorptive triacylglycerol concentrations, whereas in the Potts et al study postabsorptive triacylglycerol concentrations were almost twofold higher in obese than in control subjects, suggesting that obese subjects already had abnormal lipid metabolism.

Our results are also different from those of Roust and Jensen (6), who found similar meal-derived fatty acid concentrations in control and obese subjects 14 h after ingestion of a mixed meal. This discrepancy may be explained by differences in protocol. In Roust and Jensen's study, the mixed meal induced an insulin release that could have interfered with lipid metabolism. Moreover, in Roust and Jensen's study postabsorptive oleate turnover rates were twice as high in obese as in control subjects, as were postabsorptive fatty acid concentrations. In our study, obese and control subjects had similar postabsorptive and postprandial fatty acid concentrations. Because a dissociation between fatty acid concentration and fatty acid turnover rate has never been shown, we supposed that fatty acid fluxes were also similar between obese and control subjects in our study.

Therefore, our data strongly suggest that the release of exogenous fatty acids in plasma is altered in obese subjects. Because no difference in chylomicron-triacylglycerol clearance was observed, the major hypothesis to explain this phenomenon is that it is related to an increase in tissue fatty acid uptake. However, it is not known whether this uptake occurs mostly in white adipose tissue or in muscles or liver.

Because the appearance of labeled fatty acids was negatively correlated with fat mass, it could be speculated that this defect was due to an enhanced uptake of fatty acids by hypertrophic adipose tissue. However, a relation with fat mass persisted even when data are expressed per fat mass, suggesting that an increased uptake per unit of fat occurred. Because it has been shown that lipoprotein lipase activity is greater in adipose tissue of obese people than in nonobese people (22), enhanced lipoprotein lipase activity could play a role in triacylglycerol-derived fatty acid uptake, explaining the differences

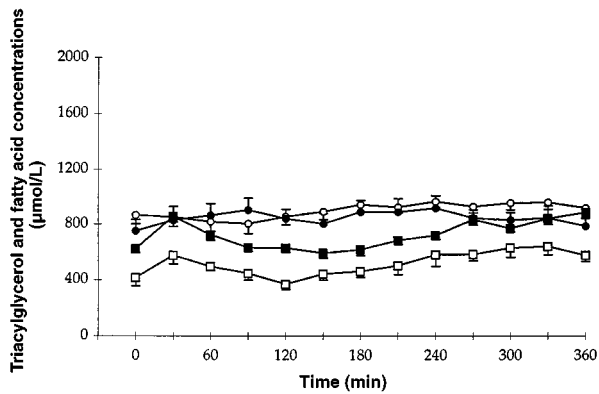


FIGURE 6. Changes in triacylglycerol and fatty acid concentrations during the medium-chain triacylglycerol, long-chain triacylglycerol experiment in the control ($n = 8$) and obese subjects ($n = 8$). \circ , triacylglycerol control; \bullet , triacylglycerol obese; \square , fatty acids control; \blacksquare , fatty acids obese. $\bar{x} \pm \text{SEM}$.

between obese and control subjects. However, lipoprotein lipase may not be the only mechanism responsible for fatty acid uptake, as suggested by Mårin et al (23). The acylation-stimulating protein appears to also be involved in fatty acid uptake and in adipocyte esterification of fatty acid into triacylglycerol, as suggested by Cianflone et al (24). Moreover, this protein's plasma concentration was greater in control subjects during a high-fat meal than during a glucose load. Nevertheless, its role in this increase in fatty acid uptake during obesity remains to be determined.

Muscle may have been a site of increased uptake of fatty acids. However, muscle fatty acid uptake has been shown to be reduced with obesity in the postabsorptive state (25). Moreover, an important finding of our study was the defect of dietary triacylglycerol oxidation. Thus, if muscle was the site of the increase in fatty acid uptake, taking into account the decrease in fatty acid oxidation, a significant increase in the reesterification process should have occurred. Although this cannot be totally excluded, it is more likely that the decrease in exogenous lipid oxidation during obesity is due to a lack of supply of long-chain fatty acids for muscle. This hypothesis is supported by the strong correlation between exogenous lipid oxidation and the appearance of exogenous fatty acid ($r = 0.70$, $P < 0.01$).

Finally, enhanced reesterification by liver must be discussed because this phenomenon has been shown in obese subjects (26). However, in our study the appearance of labeled VLDL was sim-

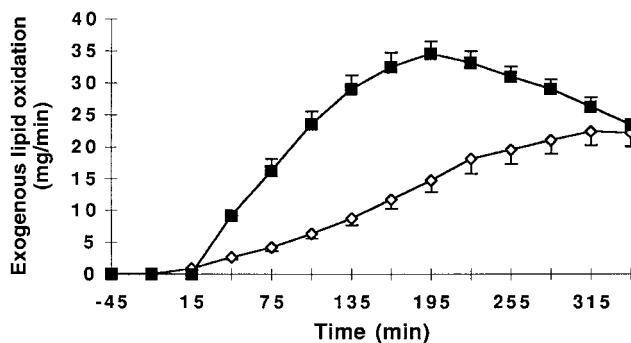


FIGURE 7. Comparison of the kinetics of exogenous lipid oxidation during the long-chain triacylglycerol (LCT) experiment (\diamond) and of medium-chain triacylglycerols (MCT) during the MCT-LCT experiment (\blacksquare). $\bar{x} \pm \text{SEM}$; $n = 16$.

ilar in obese and control subjects both kinetically and by the AUC of [^{13}C]oleate in VLDL.

Oxidation of the LCT load was dramatically reduced in the obese subjects (by 47%) and this defect was related to the appearance of the fat load-derived fatty acids. These results agree with those of Raben et al (27), which showed that the decrease in fat oxidation after a high-fat load was associated with low fatty acid concentrations. They also agree with our previous results in normal subjects, suggesting that dietary lipid oxidation was related to the intravascular release of dietary fatty acids (5). The defect in lipid oxidation could also have been due to an alteration of muscle oxidation. However, no relation was found between fat mass and total lipid oxidation expressed according to fat-free mass after the fat load, thus arguing for normal lipid oxidation by muscle in obesity.

We also showed that MCT oxidation, in contrast with LCT oxidation, was not altered in obese subjects. Because MCT metabolism shows large differences from that of LCT, such as portal release of fatty acids and oxidation in the liver, abnormalities observed in LCT metabolism were not seen. As already shown by Metges and Wolfram (9), MCT oxidation values over 6 h were dramatically higher than LCT values: 57% of the 15 g MCT ingested was oxidized compared with only 15% in the LCT experiment (means of the control and obese subjects). Like these authors, we also found large differences in oxidation kinetics between MCTs and LCTs. Although the AUC₀₋₆ values of β -hydroxybutyrate concentrations during the MCT-LCT experiment were higher than during the LCT experiment, β -hydroxybutyrate concentrations did not reach supraphysiologic values.

Total lipid oxidation during the MCT-LCT experiment was higher than during the LCT experiment in both groups (although in the obese group it was not significantly so). Thus, fat balance was therefore less positive after the MCT-LCT experiment than after the LCT experiment. DIT during the MCT-LCT experiment was lower than in Seaton et al's study (28), probably because of the smaller amount of MCT ingested (15 compared with 45 g). On the contrary, DIT after the LCT experiment was lower in obese than in control subjects. Blunted DIT in obese subjects has been shown after a glucose load (29), a mixed diet (30), and a high-protein diet (31), but to our knowledge only one study has reported blunted DIT after a pure fat load (32).

In conclusion, we report here the occurrence of a defect in dietary LCT oxidation during obesity. This defect appears to be related to an enhanced uptake of diet-derived fatty acids, probably in adipose tissue. On the other hand, MCT oxidation was unaltered in obese subjects. Thus, MCTs may be of interest in the dietary treatment of obesity. However, our study was brief and used a pure fat load. Long-term studies including mixed diets will precisely determine the role of MCTs in nutritional recommendations for obese people. \blacksquare

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