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Basal adipose tissue and hepatic lipid kinetics are not affected by a single exercise bout of moderate duration and intensity in sedentary women

Faidon Magkos^{*,†}, Bruce W. Patterson^{*}, B. Selma Mohammed^{*}, and Bettina Mittendorfer^{*}

^{*} Center for Human Nutrition, Washington University School of Medicine, St. Louis, MO, USA

[†] Department of Nutrition and Dietetics, Harokopio University, Athens, Greece

Abstract

Hypertriglyceridemia is an important risk factor for cardiovascular disease. In men we have shown that the effects of evening exercise on basal very low-density lipoprotein (VLDL) metabolism are dose-dependent: a single, prolonged bout of aerobic exercise (2 h at 60% of peak oxygen consumption, VO_2 peak) reduces fasting plasma triglyceride (TG) concentrations, via enhanced clearance of VLDL-TG from the circulation, whereas the same exercise performed for 1 h has no effect on VLDL-TG metabolism and concentration. We hypothesized that women are more sensitive to the TG-lowering effect of exercise because they reportedly use more intramuscular TG as energy source during exercise and depletion of muscle TG stores has been linked to reciprocal changes in skeletal muscle lipoprotein lipase (LPL) activity. To test our hypothesis we measured basal VLDL-TG and VLDL-apolipoprotein B-100 (apoB-100) and plasma free fatty acid (FFA) kinetics, by using stable isotope labeled tracer techniques, on the morning after a single session of evening exercise of moderate duration and intensity (1 h at 60% of VO_2 peak) in eight sedentary pre-menopausal women (age: 28 ± 3 yr, body mass index: 27 ± 2 kg/m², body fat: $34 \pm 3\%$; means $\pm$ SEM). Compared with an equivalent period of evening rest, exercise had no effect on post-absorptive FFA concentration and rate of appearance in plasma, VLDL-TG and VLDL-apoB-100 concentrations, hepatic VLDL-TG and VLDL-apoB-100 secretion and plasma clearance rates (all $P > 0.05$). We conclude that in women, as in men, a single session of exercise of moderate intensity and duration is not sufficient to bring about the alterations in VLDL metabolism that have been linked to post-exercise hypotriglyceridemia.

Keywords

fatty acid; tracer; triglyceride; apolipoprotein; very low-density lipoprotein

INTRODUCTION

High plasma triglyceride (TG) concentration is an important risk factor for cardiovascular disease (CVD), particularly in women, who have a two- to three-fold greater relative risk for CVD associated with an increase in plasma TG concentration than men [1,2]. Therefore, interventions that decrease or prevent an increase in plasma TG concentrations might be important in reducing CVD, especially in women. Aerobic exercise lowers plasma TG

Corresponding author: Bettina Mittendorfer, Ph.D., Washington University School of Medicine, Division of Geriatrics & Nutritional Science, 660 South Euclid Avenue; Campus Box 8031, St. Louis, MO 63110; USA, Phone: (314) 362 8450, Fax: (314) 362 8230, E-mail: Mittendb@DOM.wustl.edu.

concentration [3] and this might, at least in part, provide a mechanism for the cardioprotective effect of regular, endurance-type physical activity.

The hypotriglyceridemic effect of exercise is predominantly due to decreased TG concentration in the very low-density lipoprotein (VLDL) fraction [4–6]; it occurs within 12–24 h after exercise cessation and may last for 2–3 days [7–9], and is unlikely to result from long-term adaptations with repeated bouts of exercise (i.e., training), because both the magnitude and duration of the effect are similar in trained and untrained subjects [9–12]. However, despite a lot of research in this area, much uncertainty remains regarding the amount of exercise required to reduce plasma TG concentration and the mechanisms responsible for the hypotriglyceridemic effect of exercise. Most studies (including our own) evaluating the effect of exercise on plasma TG concentration investigated moderate-intensity exercise bouts ≥ 60 minutes in duration, which is unfeasible for sedentary individuals; moreover, most studies were conducted in men, with only few studies including women or studying women exclusively.

In healthy men, we have previously demonstrated that the exercise-induced changes in basal plasma TG metabolism leading to TG-lowering are dose-dependent; specifically, we found that a single, prolonged bout of moderate-intensity exercise (2 h of cycling at 60% of peak oxygen consumption, VO_2 peak) reduced fasting plasma TG concentration through increased efficiency of VLDL-TG removal from the circulation with no changes in the secretion of VLDL-TG from the liver [13] whereas 1 hour of the same exercise had no effect on VLDL-TG kinetics and plasma TG concentration [14]. This observation is consistent with the results from several other investigators who evaluated the effect of exercise on fasting plasma TG concentration in healthy untrained men and found a decrease after bouts of moderate-intensity exercise lasting for ≥ 90 min [5,6,15,16] but not ≤ 60 min [17–20]. The amount of exercise needed to bring about a decrease in fasting plasma TG concentrations thus exceeds, at least in healthy men, current public recommendations [21] and is actually near or above maximal effort for most sedentary individuals [9]. Results from studies that examined the effect of a single bout of moderate-intensity exercise of ≤ 60 min in duration in women are inconsistent; some investigators report a significant reduction (by ~ 5 –10%) in fasting plasma TG concentration [22,23] whereas others report no effect of the same or similar exercise on fasting plasma TG concentration [24,25], perhaps due to a statistical type II error. In the light of marked sexual dimorphism in VLDL-TG metabolism [26,27] and sex differences in the exercise-induced changes in substrate flux and oxidation [28–31], it is not known whether the TG metabolism response to exercise is the same in men and women.

In this study, we therefore examined the effects of a single bout of exercise of moderate intensity and duration (1 h of cycling at 60% of VO_2 peak) on plasma free fatty acid (FFA), VLDL-TG and VLDL-apolipoprotein B-100 (apoB-100) kinetics in sedentary women. We hypothesized that, contrary to men [14], this amount of exercise in women would be sufficient to induce changes in VLDL-TG metabolism leading to hypotriglyceridemia.

MATERIALS AND METHODS

Subjects and preliminary testing

Eight sedentary, eumenorrheic women participated in the study (age: 28 ± 3 yr, body weight: 74 ± 5 kg; fat mass: $34 \pm 3\%$ of total body weight; body mass index: 27 ± 2 kg/m²; means $\pm$ SEM). All were considered to be in good health after completing a medical evaluation, which included a history and physical examination and standard blood tests. All had normal fasting plasma glucose and TG concentrations. None were smoking or taking medications known to affect lipid metabolism. Written informed consent was obtained from all subjects before their participation in the study, which was approved by the Human Studies Committee and the

General Clinical Research Center (GCRC) Advisory Committee at Washington University School of Medicine in St. Louis, MO.

Approximately 2 weeks before the beginning of the experiment, body composition was assessed by dual-energy X-ray absorptiometry (Delphi-W densitometer, Hologic, Waltham, MA). VO_2 peak was determined after subjects were familiarized with breathing through the apparatus used for metabolic measurements and warmed up with cycling (Ergoline 800S ergometer, SensorMedics, Yorba Linda, CA) at 50 watts for 4 min. After warm-up, the work rate was increased by 20 watts/min until volitional exhaustion or a plateau in oxygen consumption (VO_2), despite increasing workload, and a respiratory exchange ratio (RER) ≥ 1.1 over at least 1 min was achieved. VO_2 and carbon dioxide production (VCO_2) were measured continuously by online expiratory gas exchange analysis (TrueOne 2400 Metabolic Measurement System, ParvoMedics, Salt Lake City, UT).

Experimental protocol

Each subject completed two stable isotope labeled tracer infusion studies within four weeks, in randomized order: once after resting and once after cycling on the preceding afternoon. To avoid potential confounding, the two trials were carried out in the same phase of the menstrual cycle. We have previously shown that menstrual cycle phase has no effect on basal VLDL-TG and VLDL-apoB-100 kinetics [32]; however, it remains uncertain whether the lipid metabolism response to exercise is also unaffected by menstrual cycle phase. Subjects were instructed to adhere to their regular diet and to refrain from exercise for a minimum of 3 days before being admitted to the GCRC, the afternoon before each isotope infusion study. For the exercise study, subjects cycled on a semi-recumbent cycle ergometer (EC-C400R Ergometer, Catye Fitness, Source Distributors, Dallas, TX) for 1 h starting at ~1800 h; the workload was set to elicit a VO_2 equivalent to 60% of VO_2 peak. VO_2 was measured (TrueOne 2400 Metabolic Measurement System, ParvoMedics, Salt Lake City, UT) for 5 min every 10 min during exercise, and the workload was adjusted as necessary to maintain the desired VO_2 (within $\pm 5\%$). After completion of the exercise, subjects took a shower and then rested in a chair. For the resting study, they sat in a chair between 1800 h and 1900 h. At ~1930 h subjects consumed a standard meal (57% of total energy from carbohydrate, 28% from fat, and 15% from protein) containing ~15 kcal per kg ideal body weight (calculated as the midpoint of the medium frame of the 1983 Metropolitan Life Insurance Company Table), and then fasted (except for water) and rested in bed until completion of the study the next day.

At 0530 h the following morning, one catheter was inserted into a forearm vein to administer stable isotope labeled tracers, and a second catheter was inserted into a vein in the contralateral hand, which was heated to 55°C with a thermostatically controlled box, to obtain arterialized blood samples. Catheters were kept open with slow, controlled infusion of 0.9% NaCl solution (30 ml/h). At 0700 h (time = 0), after blood samples for the determination of plasma substrate and hormone concentrations and background glycerol, palmitate and leucine tracer-to-tracee ratios (TTR) in plasma and VLDL-TG and apoB-100 were obtained, a bolus of $[1,1,2,3,3\text{-}^2\text{H}_5]\text{glycerol}$ (75 $\mu\text{mol/kg}$), dissolved in 0.9% NaCl solution, was administered through the catheter in the forearm vein, and constant infusions of $[2,2\text{-}^2\text{H}_2]\text{palmitate}$ (0.03 $\mu\text{mol/kg}\cdot\text{min}$), dissolved in 25% human albumin solution, and $[5,5,5\text{-}^2\text{H}_3]\text{leucine}$ (0.12 $\mu\text{mol/kg}\cdot\text{min}$; priming dose: 7.2 $\mu\text{mol/kg}$), dissolved in 0.9% NaCl solution, were started and maintained for 12 h. Blood samples were collected at 5, 15, 30, 60, 90, and 120 min and then every hour for 10 h to determine glycerol and palmitate TTR in plasma and VLDL-TG, and leucine TTR in plasma and VLDL-apoB-100. VO_2 and VCO_2 were measured (Deltatrac Metabolic Monitor, SensorMedics, Yorba Linda, CA) for 30 min from 2–2.5 h and 5.5–6 h after beginning the isotope infusion and the data were averaged.

Sample collection and analyses

To determine glucose concentration, blood was collected in tubes containing heparin; plasma was separated by centrifugation and analyzed immediately. All other blood samples were collected in chilled tubes containing sodium EDTA. Samples were placed on ice, and plasma was separated by centrifugation within 30 min of collection. Aliquots of plasma were kept in the refrigerator for immediate isolation of VLDL and measurement of plasma apoB-100 concentration. The remaining plasma samples were stored at -80°C until final analyses were performed.

The VLDL fraction was prepared as previously described [33]. Briefly, ~ 1.5 ml of plasma was transferred into OptiSeal polyallomer tubes (Beckman Instruments, Palo Alto, CA), overlaid with a NaCl/EDTA solution (1.006 g/ml) and centrifuged at $100,000 \times g$ for 16 h at 10°C in an Optima LE-80K preparative ultracentrifuge equipped with a Type 50.4 Ti rotor (Beckman Instruments, Palo Alto, CA). The top layer, containing VLDL, was removed by tube slicing (CentriTube slicer, Beckman Instruments, Palo Alto, CA). Aliquots of the VLDL fraction were set aside for measuring VLDL-apoB-100 concentration immediately after collection; the remaining samples were stored at -80°C until final analyses were performed.

Plasma glucose concentration was determined on an automated glucose analyzer (YSI 2300 STAT plus, Yellow Spring Instrument Co., Yellow Springs, OH). Plasma insulin concentration was measured by using a radioimmunoassay (Linco Research, St. Louis, MO). Plasma progesterone and 17β -estradiol concentrations were measured with ELISA (IBL Immuno-Biological Laboratories GmbH, Hamburg) [32]. Plasma FFA concentrations were quantified by gas chromatography (HP 5890 Series II GC, Hewlett-Packard, Palo Alto, CA) after adding heptadecanoic acid to plasma as an internal standard [34]. Total plasma TG and VLDL-TG concentrations were determined with a colorimetric enzymatic kit (SIGMA Chemicals, St. Louis, MO). Total plasma apoB-100 and VLDL-apoB-100 concentrations were measured with a turbidimetric immunoassay (Wako Pure Chemical Industries, Osaka, Japan).

Plasma free glycerol, palmitate and leucine TTRs, the TTRs of glycerol and palmitate in VLDL-TG, and the TTR of leucine in VLDL-apoB-100 were determined by gas chromatography – mass spectrometry (Agilent Technologies/HP 6890 Series GC System – 5973 Mass Selective Detector, Hewlett-Packard, Palo Alto, CA) [33–35]. The heptafluorobutyryl derivative was formed for the analysis of glycerol in plasma and VLDL-TG, the tertiary-butyldimethylsilyl derivative was prepared for plasma leucine, and the N-heptafluorobutyryl n-propyl ester derivative was used for leucine in VLDL-apoB-100. Plasma free palmitate and palmitate in VLDL-TG were analyzed as methyl esters.

Calculations

Palmitate rate of appearance (Ra) in plasma was calculated by dividing the palmitate tracer infusion rate by the average plasma palmitate TTR value between 60 and 240 min during physiologic and isotopic steady state; total FFA Ra (in $\mu\text{mol}/\text{min}$) was derived by dividing palmitate Ra by the proportional contribution of palmitate to total plasma FFA concentration [36]. Resting metabolic rate (RMR), basal whole-body carbohydrate and fat oxidation rates, and the gross energy expenditure of the exercise session were calculated based on each subject's VO_2 and VCO_2 measurements [37]. The homeostasis model assessment of whole-body insulin resistance (HOMA-IR) index was calculated as the product of plasma insulin (in $\mu\text{U}/\text{ml}$) and glucose (in mmol/l) concentrations divided by 22.5 [38].

A metabolic steady state existed with regard to VLDL-TG and VLDL-apoB-100 kinetics because plasma VLDL-TG and VLDL-apoB-100 concentrations remained constant throughout the 12-h sampling period. The fractional turnover rate (FTR) of VLDL-TG was determined by

fitting the TTR time-courses of free glycerol in plasma and glycerol in VLDL-TG to a compartmental model [39]. The absolute rate of VLDL-TG secretion (in $\mu\text{mol}/\text{min}$), which represents the total amount of VLDL-TG secreted by the liver, was calculated by multiplying the FTR of VLDL-TG (in pools/min) by the concentration of VLDL-TG in plasma (in $\mu\text{mol}/\text{l}$) and the plasma volume (in liters); plasma volume was assumed to be equal to VLDL-TG volume of distribution and was calculated as 0.055 l/kg fat-free mass [13]. The plasma clearance rate of VLDL-TG (in $\text{ml plasma}/\text{min}$) was calculated as the production rate divided by the plasma concentration. The mean residence time (MRT) of VLDL-TG (in minutes) was calculated as $1/\text{FTR}$. The MRT indicates the average time that VLDL-TG circulate in the bloodstream; a short VLDL-TG MRT indicates a quick removal of TG from circulating VLDL particles, whereas a long MRT suggests that VLDL-TG, after being secreted by the liver, remains in plasma without being hydrolyzed for a considerable amount of time.

The relative contribution of systemic plasma FFA to VLDL-TG fatty acids was calculated by the principle of isotopic dilution upon fitting the palmitate TTR in plasma and VLDL-TG to a compartmental model [33,35,39]. These fatty acids represent FFA from the systemic circulation that are taken up by the liver and directly incorporated into VLDL-TG or temporarily incorporated into rapidly turning over intra-hepatic and intra-peritoneal TG stores before incorporation into VLDL-TG. The remaining fatty acids in VLDL-TG (non-systemic) are derived from pools of fatty acids that are not labeled with tracer during the infusion period; this includes: i) fatty acids released from pre-existing, slowly turning over lipid stores in the liver and tissues draining directly into the portal vein, ii) fatty acids resulting from lipolysis of plasma lipoproteins that are taken up by the liver, and iii) fatty acids derived from hepatic de novo lipogenesis [40].

The FTR of VLDL-apoB-100 was calculated by fitting the TTR time-courses of free leucine in plasma and leucine in VLDL-apoB-100 to a compartmental model [26,33,35]. The rate of VLDL-apoB-100 secretion (in nmol/min), the plasma clearance rate of VLDL-apoB-100 (in $\text{ml plasma}/\text{min}$), and the MRT (in minutes) of VLDL-apoB-100 (indices of the secretion rate, plasma clearance rate, and MRT of VLDL particles) were calculated based on plasma VLDL-apoB-100 concentration and VLDL-apoB-100 FTR as described above for VLDL-TG. The MRT of VLDL-apoB-100 indicates the time the VLDL particle remains in the circulation after being secreted by the liver.

Statistical analysis

All data sets were tested for normality according to Kolmogorov-Smirnov. Student's paired t-test was used to compare results from rest and exercise studies. All variables are presented as means $\pm$ SEM. A P -value ≥ 0.05 was considered statistically significant.

Based on the results from a previous study in which we determined the day-to-day variability of total plasma TG concentration and plasma FFA, VLDL-TG, and VLDL-apoB-100 concentrations and kinetics [35], we estimated that a sample size of $n = 8$ would allow us to detect a $\geq 11\%$ change in total plasma TG concentration and a $\geq 20\text{--}25\%$ difference in FFA Ra, VLDL-TG and VLDL-apoB-100 concentrations and kinetics between the exercise and rest trials with a type I error rate of $\alpha = 0.05$ and a type II error rate of $\beta = 0.20$ (power = 80%).

RESULTS

VO₂ peak, exercise workload and intensity

Average VO₂ peak was $2.05 \pm 0.13 \text{ l}/\text{min}$ (i.e., $29 \pm 2 \text{ ml}/\text{kg}\cdot\text{min}$). Absolute power output ($83 \pm 7 \text{ watts}$) and VO₂ ($1.22 \pm 0.06 \text{ l}/\text{min}$) were constant between 5 and 60 min of exercise: subjects

exercised at an average of $60 \pm 2\%$ of their VO_2 peak, and an average heart rate of 136 ± 4 bpm. The gross energy expenditure of exercise was 363 ± 19 kcal.

Plasma hormone and substrate concentrations

Plasma estradiol and progesterone concentrations were not different on the day of the rest and exercise trials. Evening exercise had no effect on plasma glucose, FFA, insulin, total plasma TG and VLDL-TG, and total plasma apoB-100 and VLDL-apoB-100 concentrations, or HOMA-IR (Table 1).

Substrate oxidation

Average basal VO_2 , VCO_2 , RMR, RER, and whole-body substrate oxidation rates were not affected by evening exercise compared with rest (Table 2).

Plasma FFA, VLDL-TG and VLDL-apoB-100 kinetics

Plasma FFA Ra was not different after exercise and rest (292 ± 22 and 260 ± 20 $\mu\text{mol/min}$, respectively; $P = 0.321$).

The FTR of VLDL-TG was 0.75 ± 0.10 pools/h after exercise and 0.91 ± 0.25 pools/h after rest ($P = 0.407$); the FTR of VLDL-apoB-100 was 0.45 ± 0.03 and 0.43 ± 0.03 pools/h, respectively ($P = 0.649$). Exercise had no effect on the hepatic secretion rate (Figure 1), plasma clearance rate (Figure 2), and MRT (Figure 3) of VLDL-TG and VLDL-apoB-100 (all $P > 0.4$).

The relative contribution of systemic plasma FFA to total VLDL-TG production was not different after evening exercise and rest ($76 \pm 3\%$ and $71 \pm 4\%$, respectively; $P = 0.241$); accordingly, non-systemic fatty acids accounted for $24 \pm 3\%$ after exercise and $29 \pm 4\%$ after rest to total VLDL-TG production.

The molar ratio of VLDL-TG and VLDL-apoB-100 secretion rates, reflecting the average TG content of the newly secreted VLDL particles, was not different between exercise and rest trials (12649 ± 1385 and 15745 ± 3934 , respectively; $P = 0.398$).

DISCUSSION

Our results indicate that, compared with an equivalent period of rest, a single bout of aerobic exercise of moderate intensity and duration (1 h of cycling at 60% of VO_2 peak) does not alter basal substrate oxidation and FFA, VLDL-TG and VLDL-apoB-100 flux rates in women. Although we only investigated the effects of acute exercise, this will likely be true for chronic exercise as well, since there is no evidence that training alters the magnitude and/or duration of the hypotriglyceridemic effect [3,10,11], which typically manifests between 12 and 48 h after exercise [7–9]. For healthy sedentary women there are therefore no benefits with regards to basal adipose tissue and hepatic lipid metabolism from single sessions of typical recreational activities conforming to current guidelines [21], when measurements are made 12–24 h post-exercise. Nonetheless, this or similar types of exercise should not be dismissed as a means to improve the plasma lipid profile, because it has been demonstrated that single bouts of moderate intensity exercise lasting 30–60 min may lower postprandial plasma TG concentrations [20, 24,41–43].

The results from our study are not entirely surprising in the light of our earlier work in men. We have recently demonstrated that the exercise-induced changes in VLDL-TG and VLDL-apoB-100 metabolism leading to TG-lowering in men are dose-dependent. A single, prolonged bout of moderate intensity endurance exercise (2 h of cycling at 60% of VO_2 peak) resulted in

enhanced efficiency of VLDL-TG removal from the circulation and reduced hepatic VLDL-apoB-100 secretion rate [13] whereas a single 1-h bout of the same exercise had no effect of VLDL-TG and VLDL-apoB-100 concentrations and kinetics [14]. However, we hypothesized that the response in women might be different because it has been postulated that the post-exercise lipoprotein lipase (LPL) activity in muscle, and thus LPL-mediated VLDL-TG hydrolysis, is directly linked to the exercise-induced depletion of muscle TG stores [44]. Women use more intramuscular TG as energy source during moderate-intensity exercise than men [30,31] which, we expected, would render women more sensitive than men to the hypotriglyceridemic effect of exercise. The results from our study indicate that in women, as in men [14], a typical bout of exercise of moderate intensity and duration does not alter basal VLDL-TG metabolism. Thus, the exercise-induced depletion of intramuscular TG stores was likely below the threshold needed to result in increased VLDL-TG plasma clearance or there may in fact be no link between the post-exercise hypotriglyceridemia and intramuscular TG depletion.

Few studies have examined the effect of exercise exclusively in healthy women, and studies that included men and women did not evaluate potential sex differences due to the small number of subjects in each sex. In addition, most earlier studies have investigated the TG metabolism response to single, prolonged (≥ 90 min) bouts of exercise at moderate intensity and found significantly reduced fasting plasma TG concentrations 12–24 h post-exercise (by 20–40%) [12,16,22,45,46]. Inconsistent results have been reported after ≤ 60 min of moderate-intensity exercise; some investigators report decreased plasma TG concentration after such exercise bouts in women [22,23] whereas others [24,25], like us in the present study and an earlier study in men [14], report no exercise-induced changes in fasting plasma TG concentration in men and/or women. However, even in the studies that report a TG-lowering effect of exercise lasting ≤ 60 min, the magnitude of the effect was small (5–10%) [22,23]. It is unlikely that we “missed” an effect of exercise in our study due to lack of statistical power for the following reasons. In the present study, the average differences between the exercise and rest trials were $\leq 5\%$ for total plasma TG concentration, all VLDL-apoB-100 kinetic parameters, VLDL-apoB-100 concentration, VLDL-TG concentration, and VLDL-TG secretion rate, $>5\%$ but $<15\%$ for VLDL-TG MRT, plasma FFA Ra, and VLDL-TG plasma clearance rate, and 18% for VLDL-TG FTR; the magnitude of these differences is considerably smaller than the biological variability of these measurements [35]. Furthermore, the direction of the differences between exercise and rest – although small and not significant – was opposite to that of prolonged exercise [13,47]; i.e., a single, prolonged (≥ 90 minutes) bout of moderate intensity endurance exercise reduces VLDL-TG concentration and increases VLDL-TG FTR and VLDL-TG plasma clearance rate whereas in our study the average plasma VLDL-TG concentration increased (by 4%) and the average VLDL-TG FTR and VLDL-TG plasma clearance rate decreased (by 18% and 14%, respectively) in response to exercise. Lastly, even when we combined the data from our present study with the data obtained in seven healthy men, who completed the same study protocol [14] to increase our sample size from $n = 8$ to $n = 15$ (7 men from the previous study plus 8 women from the present study), there was no statistically significant effect of 60 min of moderate-intensity endurance exercise on total plasma TG concentration and VLDL-TG and VLDL-apoB-100 concentrations and kinetics (all $P \geq 0.25$).

Although sex does not appear to be an important parameter influencing the response of VLDL-TG and apoB-100 metabolism to exercise, there appears to be sexual dimorphism with regard to FFA metabolism in response to exercise. In the present study, we observed no effect of prior exercise on basal, whole-body FFA Ra and plasma FFA concentration. By contrast, we previously reported that in men a single exercise session of the same duration and intensity (1 h at 60% of VO_2 peak) led to a $\sim 55\%$ increase in post-absorptive FFA Ra and FFA concentration in plasma compared with rest [14]. This apparent sex difference in the lipolytic response to exercise is in agreement with the results from an earlier study where it was found

that enhanced lipolytic rates (whole-body FFA Ra and glycerol Ra) after exercise persist to a greater extent in men than in women during the early phase (~3 h) of recovery [29]. Interestingly, differences between men and women in FFA flux during recovery do not reflect differences in the acute lipolytic response to exercise, because the increase in FFA Ra and glycerol Ra during moderate-intensity exercise was found to be greater in women than in men or not different between the sexes [28,29,48]. Moreover, the exercise-induced changes in post-absorptive plasma FFA availability the morning after exercise do not appear to depend on FFA metabolism response during exercise, since even complete blockade of the normal lipolytic response during exercise by pharmacological means (acipimox) does not abolish the exercise-induced increase in fasting plasma FFA concentration ~15 h later [49]. Indeed, it is thought that the increase in FFA Ra during the immediate recovery from exercise is due to augmented growth hormone secretion [50,51].

The reasons for the enhanced basal FFA Ra/lipolytic rate late during the recovery from exercise in men but not in women are not clear but could be related to differences in the exercise-induced changes of adipose tissue insulin sensitivity. It has recently been reported that a single bout of aerobic exercise (1.5 h of cycling at moderate intensity) enhances peripheral insulin action with regards to glucose metabolism during the immediate recovery from exercise in women but not in men [52]. An exercise-induced increase in adipose tissue insulin action in women but not in men would be expected to result in a greater suppression of adipose tissue lipolysis after exercise than rest in women but not in men (at similar insulin concentrations, which were not altered by exercise in our men [14] or women). However, in the present study we observed no exercise-induced change in post-absorptive FFA Ra in women, whereas previously we found an increase in men [14]. It is therefore possible that the greater growth hormone response in men than in women during moderate-intensity exercise [29] favors the late exercise-induced increase in whole-body FFA Ra in men but not in women.

In conclusion, we evaluated the effects of a single bout of aerobic exercise of moderate intensity and duration (1 h of cycling at 60% of VO_2 peak) on basal, post-absorptive plasma FFA, VLDL-TG, and VLDL-apoB-100 kinetics in sedentary women. In agreement with our previous observations in men [14], we found that this amount of exercise is not sufficient to bring about the changes in basal lipid kinetics that lead to post-exercise hypotriglyceridemia [13]. Single bouts of exercise conforming to current guidelines [21] are therefore not beneficial in terms of lowering fasting plasma TG concentrations in healthy sedentary women.

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Abbreviations

ApoB-100	apolipoprotein B-100
CVD	cardiovascular disease
FFA	free fatty acid

FTR	fractional turnover rate
GCRC	General Clinical Research Center
HOMA-IR	homeostasis model assessment of whole-body insulin resistance
LPL	lipoprotein lipase
MRT	mean residence time
Ra	rate of appearance
RER	respiratory exchange ratio
RMR	resting metabolic rate
TG	triglyceride
TTR	tracer-to-tracee ratio
VCO₂	carbon dioxide production
VO₂	oxygen consumption
VLDL	very low-density lipoprotein

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Hepatic secretion rate

Figure 1. Very low-density lipoprotein (VLDL)-triglyceride (TG) and VLDL-apolipoprotein B-100 (apoB-100) secretion rates into plasma after evening rest and exercise. Data are presented as means $\pm$ SEM.

Plasma clearance rate

Figure 2. Very low-density lipoprotein (VLDL)-triglyceride (TG) and VLDL-apolipoprotein B-100 (apoB-100) plasma clearance rates after evening rest and exercise. Data are presented as means $\pm$ SEM.

Mean residence time

Figure 3. Very low-density lipoprotein (VLDL)-triglyceride (TG) and VLDL-apolipoprotein B-100 (apoB-100) mean residence times (MRT) in the circulation after evening rest and exercise. Data are presented as means $\pm$ SEM.

Table 1

Plasma substrate and hormone concentrations after evening rest and exercise

		Rest	Exercise	<i>P</i> -value
Estradiol	(pg/ml)	62 ± 13	60 ± 17	0.926
Progesterone	(ng/ml)	0.5 ± 0.2	0.6 ± 0.2	0.238
Insulin	(mU/l)	6.0 ± 1.5	5.8 ± 1.2	0.807
Glucose	(mmol/l)	4.8 ± 0.1	4.7 ± 0.1	0.451
HOMA-IR		1.26 ± 0.32	1.23 ± 0.29	0.797
Free fatty acids	(μmol/l)	388 ± 35	436 ± 34	0.390
Total triglyceride	(mmol/l)	0.71 ± 0.11	0.74 ± 0.10	0.595
VLDL-triglyceride	(mmol/l)	0.35 ± 0.06	0.36 ± 0.05	0.740
Total apolipoprotein B-100	(μmol/l)	1.05 ± 0.10	1.11 ± 0.14	0.588
VLDL-apolipoprotein B-100	(nmol/l)	46 ± 8	49 ± 8	0.636

Values are means ± SEM.

HOMA-IR, homeostasis model assessment of insulin resistance; VLDL, very low-density lipoprotein.

Table 2

Respiratory gas exchange measurements, resting metabolic rate, and whole-body substrate oxidation rates after evening rest and exercise

		Rest	Exercise	<i>P</i> -value
Oxygen consumption	(ml/min)	206 ± 7	206 ± 9	0.928
Carbon dioxide production	(ml/min)	167 ± 5	170 ± 9	0.433
Resting metabolic rate	(kcal/min)	0.98 ± 0.03	0.99 ± 0.05	0.339
Respiratory exchange ratio		0.81 ± 0.01	0.82 ± 0.01	0.824
Carbohydrate oxidation	(mg/min)	75 ± 8	90 ± 10	0.251
Fat oxidation	(mg/min)	51 ± 4	46 ± 3	0.379

Values are means ± SEM.