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

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ABSTRACT

Hypertriacylglycerolaemia is an important risk factor for cardiovascular disease. In men, we have shown that the effects of evening exercise on basal VLDL (very-low-density lipoprotein) metabolism are dose-dependent: a single prolonged bout of aerobic exercise [2 h at 60 % of V\textsubscript{O}\textsubscript{2 peak} (peak oxygen consumption)] reduces fasting plasma TAG [triacylglycerol (triglyceride)] concentrations, via enhanced clearance of VLDL-TAG from the circulation, whereas the same exercise performed for 1 h has no effect on VLDL-TAG metabolism and concentration. We hypothesized that women are more sensitive to the TAG-lowering effect of exercise because they reportedly use more intramuscular TAG as an energy source during exercise, and depletion of muscle TAG stores has been linked to reciprocal changes in skeletal muscle LPL (lipoprotein lipase) activity. To test our hypothesis, we measured basal VLDL-TAG and VLDL-apoB-100 (apolipoprotein B-100), and plasma NEFA [non-esterified fatty acid (‘free fatty acid’)] kinetics, by using stable isotope-labelled tracer techniques, on the morning after a single session of evening exercise of moderate duration and intensity (1 h at 60 % of V\textsubscript{O}\textsubscript{2 peak}) in eight sedentary pre-menopausal women (age, 28 ± 3 years; body mass index, 27 ± 2 kg/m\textsuperscript{2}; body fat, 34 ± 3 %; values are means ± S.E.M.). Compared with an equivalent period of evening rest, exercise had no effect on post-absorptive NEFA concentrations and the rate of appearance in plasma, VLDL-TAG and VLDL-apoB-100 concentrations, hepatic VLDL-TAG 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 hypotriacylglycerolaemia.

INTRODUCTION

High plasma TAG [triacylglycerol (triglyceride)] concentrations are an important risk factor for CVD (cardiovascular disease), particularly in women, who have a 2–3-fold greater relative risk of CVD associated with an increase in plasma TAG concentrations than men [1,2]. Therefore interventions that decrease or prevent an increase in...
plasma TAG concentrations might be important in reducing CVD, especially in women. Aerobic exercise lowers plasma TAG concentrations [3] and this might, at least in part, provide a mechanism for the cardioprotective effect of regular endurance-type physical activity.

The hypotriacylglycerolaemic effect of exercise is predominantly due to decreased TAG concentrations in the VLDL (very-low-density lipoprotein) 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 the 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 TAG concentrations and the mechanisms responsible for the hypotriacylglycerolaemic effect of exercise. Most studies (including our own) evaluating the effect of exercise on plasma TAG concentrations have investigated moderate-intensity exercise bouts \( \geq 60 \text{ min} \) 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 demonstrated previously [13] that the exercise-induced changes in basal plasma TAG metabolism leading to TAG-lowering are dose-dependent; specifically, we found that a single prolonged bout of moderate-intensity exercise \( \geq 2 \text{ h} \) of cycling at 60% of \( \dot{V}_\text{O}_2\text{peak} \) [peak \( \dot{V}_\text{O}_2 \) (oxygen consumption)] reduced fasting plasma TAG concentrations through increased efficiency of VLDL-TAG removal from the circulation with no changes in the secretion of VLDL-TAG from the liver [13], whereas 1 h of the same exercise had no effect on VLDL-TAG kinetics and plasma TAG concentrations [14]. This observation is consistent with the results from several other investigators who evaluated the effect of exercise on fasting plasma TAG concentrations in healthy untrained men and found a decrease after bouts of moderate-intensity exercise lasting for \( \geq 90 \text{ min} \) [5,6,15,16], but not \( \leq 60 \text{ min} \) [17–20].

The amount of exercise needed to bring about a decrease in fasting plasma TAG 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 \( \leq 60 \text{ min} \) in duration in women are inconsistent; some investigators observed a significant reduction (by approx. 5–10%) in fasting plasma TAG concentrations [22,23], whereas others reported no effect of the same or similar exercise on fasting plasma TAG concentrations [24,25], perhaps due to a statistical type II error. In the light of marked sexual dimorphism in VLDL-TAG metabolism [26,27] and sex differences in the exercise-induced changes in substrate flux and oxidation [28–31], it is not known whether the TAG metabolism response to exercise is the same in men and women.

In the present study, we therefore examined the effects of a single bout of exercise of moderate intensity and duration (1 h of cycling at 60% of \( \dot{V}_\text{O}_2\text{peak} \) on plasma NEFA [non-esterified fatty acid (‘free fatty acid’)], VLDL-TAG and VLDL-apoB-100 (apolipoprotein B-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-TAG metabolism leading to hypotriacylglycerolaemia.

**MATERIALS AND METHODS**

**Subjects and preliminary testing**

Eight sedentary eumenorrhoeic women participated in the present study (age, 28 \( \pm \) 3 years; body weight, 74 \( \pm \) 5 kg; fat mass, 34 \( \pm \) 3% of total body weight; body mass index, 27 \( \pm \) 2 kg/m\(^2\); values are means \( \pm \) S.E.M.). 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 TAG concentrations. None were smoking or taking medication 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 GCRC (General Clinical Research Center) Advisory Committee at Washington University School of Medicine, St. Louis, MO, U.S.A.

Approx. 2 weeks before the beginning of the experiment, body composition was assessed by dual-energy X-ray absorptiometry (Delphi-W densitometer; Hologic). \( \dot{V}_\text{O}_2\text{peak} \) was determined after subjects were familiarized with breathing through the apparatus used for metabolic measurements and warmed-up with cycling (Ergoline 800S ergometer; SensorMedics) 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 \( \dot{V}_\text{O}_2 \), despite increasing workload, and an RER (respiratory exchange ratio) \( \geq 1.1 \) over at least 1 min was achieved. \( \dot{V}_\text{O}_2 \) and \( \dot{V}_\text{CO}_2 \) (carbon dioxide production) were measured continuously by online expiratory gas exchange analysis (TrueOne 2400 Metabolic Measurement System; ParvoMedics).

**Experimental protocol**

Each subject completed two stable isotope-labelled tracer infusion studies within 4 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 shown previously that menstrual cycle phase has no effect on basal VLDL-TAG 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 on the afternoon before each isotope infusion study. For the exercise study, subjects cycled on a semi-recumbent cycle ergometer (EC-C400R Ergometer; CatEye Fitness) for 1 h starting at approx. 18:00 hours; the workload was set to elicit a $\dot{V}_{\text{O}_2}$ equivalent to 60% of $\dot{V}_{\text{O}_2\text{peak}}$. $\dot{V}_{\text{O}_2}$ was measured (TrueOne 2400 Metabolic Measurement System; ParvoMedics) for 5 min every 10 min during exercise, and the workload was adjusted as necessary to maintain the desired $\dot{V}_{\text{O}_2}$ (within ± 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 18:00 and 19:00 hours. At approx. 19:30 hours, subjects consumed a standard meal (57% of total energy from carbohydrate, 28% from fat and 15% from protein) containing approx. 63 kJ/kg of 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 05:30 hours the following morning, a catheter was inserted into a forearm vein to administer the stable isotope-labelled tracers, and a second catheter was inserted into a forearm vein to administer the stable isotope-labelled 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 a slow controlled infusion of 0.9% saline solution (30 ml/h). At 07:00 hours (time = 0), after blood samples were obtained for the determination of plasma substrate and hormone concentrations, background glycerol, palmitate and leucine TTRs (tracer-to-tracee ratios) in plasma, and VLDL-TAG and VLDL-apoB-100, a bolus of [1,1,2,3,3-2H5]glycerol (75 μmol/kg of body weight), dissolved in 0.9% saline solution, was administered through the catheter in the forearm vein and constant infusions of [2,2-2H2]palmitate (0.03 μmol · kg⁻¹ of body weight · min⁻¹), dissolved in 25% (v/v) human albumin solution, and [5,5,5-2H3]leucine (0.12 μmol · kg⁻¹ of body weight · min⁻¹; priming dose, 7.2 μmol/kg of body weight), dissolved in 0.9% saline 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 TTRs in plasma and VLDL-TAG, and the leucine TTR in plasma and VLDL-apoB-100. $\dot{V}_{\text{O}_2}$ and $\dot{V}_{\text{CO}_2}$ were measured (Deltatrac Metabolic Monitor; SensorMedics) 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 concentrations, blood was collected in tubes containing heparin; plasma was separated by centrifugation (14 000 g for 10 s at room temperature) and analysed immediately. All other blood samples were collected in chilled tubes containing EDTA. Samples were placed on ice, and plasma was separated by centrifugation at 1820 g for 15 min at 4 °C within 30 min of collection. Aliquots of plasma were kept in the refrigerator for immediate isolation of VLDL and measurement of plasma apoB-100 concentrations. The remaining plasma samples were stored at –80 °C until final analyses were performed.

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

Plasma glucose concentrations were determined on an automated glucose analyser (YSI 2300 STAT plus; Yellow Spring Instrument). Plasma insulin concentrations were measured using an RIA (Linco Research). Plasma progesterone and 17β-oestradiol concentrations were measured by ELISA (IBL Immuno-Biological Laboratories) [32]. Plasma NEFA concentrations were quantified by gas chromatography (HP 5890 Series II GC; Hewlett-Packard) after adding heptadecanoic acid to plasma as an internal standard [34]. Total plasma TAG and VLDL-TAG concentrations were determined using a colorimetric enzymatic kit (Sigma). Total plasma apoB-100 and VLDL-apoB-100 concentrations were measured using a turbidimetric immunoassay (Wako Pure Chemical Industries).

Plasma free glycerol, palmitate and leucine TTRs, the TTRs of glycerol and palmitate in VLDL-TAG, and the TTR of leucine in VLDL-apoB-100 were determined by GC/MS (Agilent Technologies/HP 6890 Series GC System with 5973 Mass Selective Detector; Hewlett-Packard) [33–35]. The heptafluorobutyrly derivative was formed for the analysis of glycerol in plasma and VLDL-TAG, the tertiary butyldimethylsilyl derivative was prepared for plasma leucine, and the N-heptafluorobutyrly n-propyl ester derivative was used for leucine in VLDL-apoB-100. Plasma free palmitate and palmitate in VLDL-TAG were analysed as methyl esters.

**Calculations**

Palmitate Ra (rate of appearance) in plasma was calculated by dividing the palmitate tracer infusion rate by the average plasma palmitate TTR value between 60 and 240 min during the physiological and isotopic steady-state; total NEFA Ra (in μmol/min) was derived by
dividing the palmitate Ra by the proportional contribution of palmitate to total plasma NEFA concentration [36]. RMR (resting metabolic rate), basal whole-body carbohydrate and fat oxidation rates, and the gross energy expenditure of the exercise session were calculated based on each subject’s VO₂ and VCO₂ measurements [37]. The HOMA-IR (homeostasis model assessment of whole-body insulin resistance) index was calculated as the product of plasma insulin (in μ-units/ml) and glucose (in mmol/l) concentrations divided by 22.5 [38].

A metabolic steady-state existed with regard to VLDL-TAG and VLDL-apoB-100 kinetics, because plasma VLDL-TAG and VLDL-apoB-100 concentrations remained constant throughout the 12-h sampling period. The FTR (fractional turnover rate) of VLDL-TAG was determined by fitting the TTR time courses of free glycerol in plasma and glycerol in VLDL-TAG to a compartmental model [39]. The absolute rate of VLDL-TAG secretion (in μmol/min), which represents the total amount of VLDL-TAG secreted by the liver, was calculated by multiplying the FTR of VLDL-TAG (in pools/min) by the concentration of VLDL-TAG in plasma (in μmol/l) and the plasma volume (in litres); plasma volume was assumed to be equal to the VLDL-TAG volume of distribution and was calculated as 0.055 l/kg of fat-free mass [13]. The plasma clearance rate of VLDL-TAG (in ml of plasma/min) was calculated as the production rate divided by the plasma concentration. The MRT (mean residence time) of VLDL-TAG (in min) was calculated as 1/FTR. MRT indicates the average time that VLDL-TAG circulates in the bloodstream; a short VLDL-TAG MRT indicates a quick removal of TAG from circulating VLDL particles, whereas a long MRT suggests that VLDL-TAG, after being secreted by the liver, remains in plasma without being hydrolysed for a considerable amount of time.

The relative contribution of systemic plasma NEFAs to VLDL-TAG fatty acids was calculated by the principle of isotopic dilution upon fitting the palmitate TTR in plasma and VLDL-TAG to a compartmental model [33,35,39]. These fatty acids represent NEFAs from the systemic circulation that are taken up by the liver and are incorporated directly into VLDL-TAG or temporarily incorporated into rapidly turning over intrahepatic and intra-peritoneal TAG stores before incorporation into VLDL-TAG. The remaining fatty acids in VLDL-TAG (non-systemic) are derived from pools of fatty acids that are not labelled 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 ml of plasma/min) and the MRT (in min) 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 concentrations and VLDL-apoB-100 FTRs as described above for VLDL-TAG. 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 the Kolmogorov–Smirnov test. A paired Student’s t test was used to compare results from the rest and exercise studies. All variables are means ± S.E.M. A P value < 0.05 was considered statistically significant.

On the basis of the results from a previous study in which we determined the day-to-day variability of total plasma TAG concentrations, and plasma NEFA, VLDL-TAG and VLDL-apoB-100 concentrations and kinetics [35], we estimated that a sample size of n = 8 would allow us to detect a ≥ 11 % change in total plasma TAG concentrations and a ≥ 20–25 % difference in NEFA Ra, VLDL-TAG and VLDL-apoB-100 concentrations and kinetics between the exercise and rest trials with a type I error rate of α = 0.05 and a type II error rate of β = 0.20 (power = 80 %).

**RESULTS**

**VO₂ peak, exercise workload and intensity**

Average VO₂ peak was 2.05 ± 0.13 l/min (i.e. 29 ± 2 ml·kg⁻¹·min⁻¹ of body weight·min⁻¹). Absolute power output (83 ± 7 Watts) and VO₂ (1.22 ± 0.06 l/min) were constant between 5 and 60 min of exercise: subjects exercised at an average of 60 ± 2 % of their VO₂ peak and at an average heart rate of 136 ± 4 beats/min. The gross energy expenditure of exercise was 1525 ± 80 kJ.

**Plasma hormone and substrate concentrations**

Plasma 17β-oestradiol and progesterone concentrations were not different on the day of the rest and exercise trials. Evening exercise had no effect on plasma glucose, NEFA, insulin, total plasma TAG and VLDL-TAG, and total plasma apoB-100 and VLDL-apoB-100 concentrations or HOMA-IR (Table 1).

**Substrate oxidation**

Average basal VO₂, VCO₂, RMR, RER and whole-body substrate oxidation rates were not affected by evening exercise compared with rest (Table 2).
Table 1 Plasma substrate and hormone concentrations after evening rest and exercise
Values are means ± S.E.M.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rest</th>
<th>Exercise</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>17β-Oestradiol (pg/ml)</td>
<td>62 ± 13</td>
<td>60 ± 17</td>
<td>0.926</td>
</tr>
<tr>
<td>Progesterone (ng/ml)</td>
<td>0.5 ± 0.2</td>
<td>0.6 ± 0.2</td>
<td>0.238</td>
</tr>
<tr>
<td>Insulin (m-units/l)</td>
<td>6.0 ± 1.5</td>
<td>5.8 ± 1.2</td>
<td>0.807</td>
</tr>
<tr>
<td>Glucose (mmol/l)</td>
<td>4.8 ± 0.1</td>
<td>4.7 ± 0.1</td>
<td>0.451</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.26 ± 0.32</td>
<td>1.23 ± 0.29</td>
<td>0.797</td>
</tr>
<tr>
<td>NEFAs (μmol/l)</td>
<td>388 ± 35</td>
<td>436 ± 34</td>
<td>0.390</td>
</tr>
<tr>
<td>Total TAG (mmol/l)</td>
<td>0.71 ± 0.11</td>
<td>0.74 ± 0.10</td>
<td>0.595</td>
</tr>
<tr>
<td>VLDL-TAG (mmol/l)</td>
<td>0.35 ± 0.06</td>
<td>0.36 ± 0.05</td>
<td>0.740</td>
</tr>
<tr>
<td>Total apoB-100 (μmol/l)</td>
<td>1.05 ± 0.10</td>
<td>1.11 ± 0.14</td>
<td>0.588</td>
</tr>
<tr>
<td>VLDL-apoB-100 (nmol/l)</td>
<td>46 ± 8</td>
<td>49 ± 8</td>
<td>0.636</td>
</tr>
</tbody>
</table>

Table 2 Respiratory gas exchange measurements, RMR and whole-body substrate oxidation rates after evening rest and exercise
Values are means ± S.E.M.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rest</th>
<th>Exercise</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\dot{V}O_2) (ml/min)</td>
<td>206 ± 7</td>
<td>206 ± 9</td>
<td>0.928</td>
</tr>
<tr>
<td>(\dot{V}CO_2) (ml/min)</td>
<td>167 ± 5</td>
<td>170 ± 9</td>
<td>0.433</td>
</tr>
<tr>
<td>RMR (kJ/min)</td>
<td>4.10 ± 0.13</td>
<td>4.14 ± 0.21</td>
<td>0.339</td>
</tr>
<tr>
<td>RER</td>
<td>0.81 ± 0.01</td>
<td>0.82 ± 0.01</td>
<td>0.824</td>
</tr>
<tr>
<td>Carbohydrate oxidation (mg/min)</td>
<td>75 ± 8</td>
<td>90 ± 10</td>
<td>0.251</td>
</tr>
<tr>
<td>Fat oxidation (mg/min)</td>
<td>51 ± 4</td>
<td>46 ± 3</td>
<td>0.379</td>
</tr>
</tbody>
</table>

Figure 1 VLDL-TAG and VLDL-apoB-100 secretion rates into plasma after evening rest and exercise
Values are means ± S.E.M.

Plasma NEFA, VLDL-TAG and VLDL-apoB-100 kinetics
Plasma NEFA Ra was not different after exercise and rest (292 ± 22 and 260 ± 20 μmol/min respectively; \(P = 0.321\)).

The FTR of VLDL-TAG 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-TAG and VLDL-apoB-100 (all \(P > 0.4\)).

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

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

DISCUSSION
The results of the present study 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 \(\dot{V}O_2\)peak) does not alter basal substrate oxidation and NEFA, VLDL-TAG and VLDL-apoB-100 flux rates in women. Although we only investigated the
effects of acute exercise, this will probably be true for chronic exercise as well, as there is no evidence that training alters the magnitude and/or duration of the hypotriacylglycerolaemic 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 of improving the plasma lipid profile, because it has been demonstrated that single bouts of moderate-intensity exercise lasting 30–60 min may lower post-prandial plasma TAG concentrations [20,24,41–43].

The results from our present study are not entirely surprising in the light of our previous work in men. We have demonstrated previously [13,14] that the exercise-induced changes in VLDL-TAG and VLDL-apoB-100 metabolism leading to TAG-lowering in men are dose-dependent. A single prolonged bout of moderate-intensity endurance exercise (2 h of cycling at 60 % of \(\dot{V}O_2\)peak) resulted in enhanced efficiency of VLDL-TAG 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-TAG 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 LPL (lipoprotein lipase) activity in muscle, and thus LPL-mediated VLDL-TAG hydrolysis, is directly linked to the exercise-induced depletion of muscle TAG stores [44]. Women use more intramuscular TAG as an energy source during moderate-intensity exercise than men [30,31], which, we expected, would render women more sensitive than men to the hypotriacylglycerolaemic effect of exercise. The results from our present study indicate that in women, as in men [14], a typical bout of exercise of moderate intensity and duration does not alter basal VLDL-TAG metabolism. Thus the exercise-induced depletion of intramuscular TAG stores was probably below the threshold needed to result in increased VLDL-TAG plasma clearance or there may in fact be no link between the post-exercise hypotriacylglycerolaemia and intramuscular TAG 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 previous studies have investigated the TAG metabolism response to single prolonged (> 90 min) bouts of exercise at moderate intensity and found significantly reduced fasting plasma TAG 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 have reported decreased plasma TAG concentrations 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], have observed no exercise-induced changes in fasting plasma TAG concentration in men and/or women. However, even in the studies that report a TAG-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 present study due to a lack of statistical power for the following reasons.

In the present study, the average differences between the exercise and rest trials were ≤5 % for total plasma TAG concentrations, all VLDL-apoB-100 kinetic parameters, VLDL-apoB-100 concentrations, VLDL-TAG concentrations and VLDL-TAG secretion rate, > 5 % but < 15 % for VLDL-TAG MRT, plasma NEFA Ra and VLDL-TAG plasma clearance rate, and 18 % for VLDL-TAG 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 min) bout of moderate-intensity endurance exercise reduces VLDL-TAG concentrations and increases VLDL-TAG FTR and VLDL-TAG plasma clearance rates, whereas in our present study the average plasma VLDL-TAG concentration increased (by 4 %) and the average VLDL-TAG FTR and VLDL-TAG 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 eight women with the data obtained in seven healthy men, who completed the same study protocol [14], to increase our sample size from \(n = 8\) to \(n = 15\), there was no statistically significant effect of 60 min of moderate-intensity endurance exercise on total plasma TAG concentrations and VLDL-TAG and VLDL-apoB-100 concentrations and kinetics (all \(P \geq 0.25\)).

Although gender does not appear to be an important parameter influencing the response of VLDL-TAG and apoB-100 metabolism to exercise, there appears to be sexual dimorphism with regard to NEFA metabolism in response to exercise. In the present study, we observed no effect of prior exercise on basal whole-body NEFA Ra and plasma NEFA concentrations. By contrast, we reported previously [14] that in men a single exercise session of the same duration and intensity (1 h at 60 % of \(\dot{V}O_2\)peak) led to an approx. 55 % increase in post-absorptive NEFA Ra and NEFA concentrations in plasma compared with rest. 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 NEFA 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 NEFA flux during recovery do not reflect differences in the acute lipolytic response to exercise, because the increase in NEFA 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 NEFA availability on the morning after exercise do not appear to depend on NEFA metabolism response during exercise, as even complete blockade of the normal lipolytic response during exercise by pharmacological means (acipimox) does not abolish the exercise-induced increase in fasting plasma NEFA concentrations approx. 15 h later [49]. Indeed, it is thought that the increase in NEFA Ra during the immediate recovery from exercise is due to augmented GH (growth hormone) secretion [50,51].

The reasons for the enhanced basal NEFA 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 been reported previously [52] that a single bout of aerobic exercise (1.5 h of cycling at moderate intensity) enhances peripheral insulin action with regard to glucose metabolism during the immediate recovery from exercise in women but not in men. 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 NEFA Ra in women, whereas we found previously an increase in men [14]. It is therefore possible that the greater GH response in men than in women during moderate-intensity exercise [29] favours the late exercise-induced increase in whole-body NEFA 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 VO₂ peak) on basal post-absorptive plasma NEFA, VLDL-TAG 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 hypotriglycerolaemia [13]. Single bouts of exercise conforming to current guidelines [21] are therefore not beneficial in terms of lowering fasting plasma TAG concentrations in healthy sedentary women.

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