Acute exercise-induced changes in basal VLDL-triglyceride kinetics leading to hypotriglyceridemia manifest more readily after resistance than endurance exercise

Faidon Magkos, Yiannis E. Tsekouras, Konstantinos I. Prentzas, Konstantinos N. Basioukas, Stergoula G. Matsama, Amalia E. Yanni, Stavros A. Kavouras, and Labros S. Sidossis

Department of Nutrition and Dietetics, Harokopio University, Athens, Greece

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Magkos F, Tsekouras YE, Prentzas KI, Basioukas KN, Matsama SG, Yanni AE, Kavouras SA, Sidossis LS. Acute exercise-induced changes in basal VLDL-triglyceride kinetics leading to hypotriglyceridemia manifest more readily after resistance than endurance exercise. J Appl Physiol 105: 1228–1236, 2008. First published July 31, 2008; doi:10.1152/japplphysiol.90761.2008—Resistance training is considered less effective than endurance training in lowering plasma triglyceride (TG) concentrations. Acutely, however, a single bout of strenuous exercise, whether endurance or resistance, increases the efficiency of very low-density lipoprotein (VLDL)-TG removal from the circulation and leads to hypotriglyceridemia. The comparative effects of these two types of exercise on VLDL-TG metabolism are not known. We therefore examined basal VLDL-TG kinetics by using stable isotope-labeled tracers in seven healthy, nonobese, untrained young men in the postabsorptive state, the morning after a single 90-min bout of either low-intensity endurance exercise (~30% of peak oxygen consumption) or high-intensity resistance exercise (3 sets of 10 repetitions for 12 exercises at 80% of peak torque production), matched for total energy expenditure (~400 kcal), or an equivalent period of rest on the preceding afternoon. Compared with rest, resistance exercise lowered fasting plasma VLDL-TG concentration by ~28 ± 10% (P = 0.034), increased VLDL-TG plasma clearance rate by 30 ± 8% (P = 0.003), and shortened the mean residence time (MRT) of VLDL-TG in the circulation by ~36 ± 11 min (P = 0.016), whereas endurance exercise had no effect (all P > 0.05). Basal VLDL-TG plasma clearance rate was greater (P = 0.003) and VLDL-TG MRT was shorter (P = 0.012) the morning after resistance than endurance exercise. We conclude that, for the same total energy expenditure, resistance exercise is more potent than endurance exercise in eliciting changes in VLDL-TG metabolism that have been linked with hypotriglyceridemia, and it should thus be considered as an alternative to or in addition to endurance exercise for the control of plasma TG concentrations.

Address for reprint requests and other correspondence: L. S. Sidossis, Dept. of Nutrition and Dietetics, Harokopio Univ., 70 El. Venizelou Ave., 17671 Athens, Greece (e-mail: l sodomiss@hua.gr).

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To test this hypothesis, we evaluated basal VLDL-TG kinetics in healthy men, the morning after a single bout of endurance or resistance exercise, matched for total energy expenditure, or an equivalent period of rest on the preceding afternoon.

MATERIALS AND METHODS

Subjects and preliminary testing. Subjects were recruited via advertisement in the local community. Seven young, nonobese men volunteered for the study (age: 25 ± 1 yr, body weight: 78 ± 4 kg, body mass index: 24 ± 1 kg/m², body fat: 18 ± 1%; VO₂peak: 43 ± 3 ml·kg⁻¹·min⁻¹; means ± SE). Their body weight was self-reported stable for at least 2 mo before enrollment. Subjects were healthy, as indicated by comprehensive history, physical examination, and standard blood tests, and they were recreationally active but untrained; they participated in moderate-intensity physical activities ≥2 times/wk, and none was accustomed to structured resistance or endurance exercise. None of them smoked tobacco or were taking medications known to affect lipid metabolism. The study protocol was approved by the Human Studies Committee of Harokopio University, Athens, Greece, and written informed consent was obtained from all participants.

Preliminary testing was conducted ~1–2 wk before the study. Total body fat and fat-free masses were determined by dual-energy X-ray absorptiometry (model DPX-MD, Lunar, Madison, WI). VO₂peak was determined by a submaximal incremental brisk walking test (modified Balke treadmill protocol) (2). Subjects warmed up for 5 min and were familiarized with the treadmill (Technogym Runrace, Gambettola, Italy). After warm-up, treadmill speed was kept constant, and grade was increased by 2% every 3 min. Expiratory gases were collected continuously by using a breath-by-breath gas analyzer system (Vmax229D, Sensormedics). VO₂peak was determined by the oxygen consumption (VO₂)-heart rate relationship (2). On a separate day, subjects were familiarized with the resistance exercise protocol on the isokinetic dynamometer (System 3 Pro, Biodex, Shirley, NY); three maximum intensity repetitions were performed to determine peak torque production for each exercise.

Experimental protocol. Each subject completed three time-matched trials (rest, endurance exercise, and resistance exercise) within ~4 wk; the time interval between trials was 7–10 days. To equate the energy expenditure of the two exercise sessions, and because there is no reliable way to predict the energy expenditure of resistance exercise, we used a semirandomized design in which resistance exercise was always performed before endurance exercise (48); rest and resistance exercise were randomly assigned to the first trial, and for subjects who performed resistance exercise first, rest and endurance exercise were randomly assigned to the second trial. This design is unlikely to bias our results, because there is no evidence that a single bout of exercise alters the TG concentration response to a subsequent bout of exercise performed 2 days later (5), and our two exercise trials were separated by at least 7–10 days; even chronic exercise does not have such a sustainable effect on plasma TG concentrations (25, 26).

Subjects were instructed to refrain from vigorous exercise for at least 2 wk before the first trial and until the completion of the study. For the exercise trials, they were admitted to the laboratory on the evening before the iso- fuel infusion study and performed a single 90-min bout of resistance or endurance exercise between 1700 and 1900. The resistance exercise protocol involved whole body exercise on the isokinetic dynamometer (System 3 Pro, Biodex), consisting of 3 sets of 10 repetitions at 80% of peak torque production for a total of 12 exercises, always in the same order (leg press, leg pull, shoulder press, chin-ups, knee extension, knee curl, chest press, upright row, horizontal hip flexion, horizontal hip extension, shoulder abduction, and shoulder adduction). Each exercise was performed for each limb separately and was followed by 2 min of recovery. VO₂ and carbon dioxide production (VCO₂) were measured continuously by using a gas analyzer equipped with a face mask (Vmax229D, Sensormedics). For the endurance exercise trial, each subject walked on the treadmill (Technogym Runrace) at a grade and speed that elicited slightly higher (by ~5%) VO₂ than that during resistance exercise; the higher target VO₂ was selected to compensate for the expected lower caloric equivalent due to the lower respiratory quotient (RQ) (47) during endurance compared with resistance exercise. Expiratory gases were collected and analyzed (Vmax229D, Sensormedics) at frequent intervals and speed was adjusted to maintain the desired VO₂. All subjects completed the whole resistance and endurance exercise sessions without a problem. For the time-matched resting trial, participants were requested to refrain from any form of physical activity and remain rested at home.

On entry into the study, subjects received instructions on how to record food and beverage intake and provided a detailed recording of all nutrient intake for the 3 days preceding the first trial, this included the dinner consumed after the completion of the exercise or rest session (whichever came first). They were then instructed to reproduce the exact same diet for the 3 days leading up to the subsequent two trials. None of the subjects reported any deviation from the dietary plan. Subjects abstained from alcohol and caffeine intake for 2 days before each iso- fuel infusion study, and they did not ingest any calories during the evening exercise sessions and the equivalent period of rest; dinner was consumed within the following 2 h (by 2100). Thereafter, volunteers remained fasted for ~12 h before starting the tracer infusion.

The next morning, subjects arrived at the laboratory at 0800 with minimal physical activity (i.e., did not walk or drive themselves) and after having fasted overnight. One catheter was inserted into a forearm vein to administer stable iso- labeled tracers, and a second catheter was inserted into a contralateral hand vein for blood sampling; the latter was kept warm with a heating pad. Catheters were flushed with 0.9% NaCl solution to maintain patency. Subjects were allowed to relax and get used to the catheters for an additional hour (time = 0; ~14 h after completion of the exercise or rest sessions on the previous afternoon), before a baseline blood sample was taken to determine fasting plasma metabolite and serum insulin concentrations and background tracer-to-tracee ratio (TTR) of glycerol in VLDL-TG. Immediately after, a bolus of [1,1,2,3,3-2H₅]glycerol (75 µmol/kg body weight; Goss Scientific Instruments, Essex, UK), dissolved in 0.9% NaCl solution, was administered through the catheter in the forearm vein, and blood samples were obtained at 15 min and then every hour after tracer injection for 6 h to determine glycerol TTR in VLDL-TG. VO₂ and VCO₂ were measured for 15 min by using a gas analyzer system equipped with a ventilated hood (Vmax229D, Sensormedics), once before and then hourly after tracer injection, and data were averaged. For the entire duration of the iso- fuel infusion study, subjects remained fasted in the laboratory in a sitting position. Water consumption was allowed ad libitum during the first trial and replicated in the subsequent two trials.

Sample collection and analysis. Blood samples were collected in precooled tubes containing EDTA as anticoagulant, they were placed on ice immediately, and plasma was separated by centrifugation within 30 min of collection. Aliquots of plasma (~3 ml) were transferred into plastic culture tubes and kept in the refrigerator for immediate isolation of VLDL. The remaining plasma samples were stored at ~80°C until further analyses. A separate blood sample portion was transferred into tubes with no additives for serum preparation. Serum was stored at ~80°C until further analyses.

The VLDL fraction was prepared as previously described (56). Briefly, ~2 ml of plasma was transferred into Quick Seal Centrifuge Polyalamor Tissue (Beckman Instruments, Palo Alto, CA), overlaid with a NaCl-EDTA solution (density = 1.006 g/ml) and spun for 3 h at 90,000 rpm at 4°C, in an Optima TLX ultracentrifuge equipped with the fixed-angle TLN-100 rotor (Beckman Instruments). The top
layer, containing VLDL, was removed and collected quantitatively by tube slicing (CentriTube slicer, Beckman Instruments) and was stored at −80°C until analyses. VLDL-TG were isolated by thin-layer chromatography, they were hydrolyzed, and VLDL-TG-glycerol was derivatized with heptafluorobutyric anhydride (56). The TTR of glycerol in VLDL-TG was determined by gas chromatography/mass spectrometry (MSD 5973 system, Hewlett-Packard, Palo Alto, CA), by selectively monitoring the ions at mass-to-charge ratios 467 and 472 (56). Calibration curve for standards with known isotopic enrichment was used.

The concentrations of total TG, VLDL-TG, total cholesterol, high-density lipoprotein (HDL)-cholesterol, glucose, and free fatty acids (FFA) in plasma were determined by using commercially available enzymatic kits (Alfa Wassermann Diagnostics Technologies, West Caldwell, NJ) on an automated analyzer (ACE Schiapparelli Biosystems, Fairfield, NJ). Serum insulin concentration was measured with an immunoenzymetric fluorescent method by using a commercially available kit (ST AIA-PACK IRI, Tosoh Medics). All samples for each volunteer were analyzed on the same batch with the same method.

Calculations. The gross energy expenditure of the two evening exercise sessions, and resting metabolic rate (RMR; kcal/min) and whole body substrate oxidation rates in the basal state the next morning were calculated based on respective V̇O₂ and V̇CO₂ measurements (17); net energy expenditure of exercise (i.e., above resting metabolic rate) was calculated by subtracting RMR for an equivalent period of rest from the corresponding gross energy expenditure during each exercise session. Basal whole body insulin sensitivity was assessed with the homeostasis model assessment of insulin resistance (HOMA-IR) index as the product of fasting serum insulin (mU/l) and plasma glucose (mmol/l) concentrations divided by 22.5 (42).

The fractional turnover rate (FTR) of VLDL-TG was determined by using the monoexponential approach (35). The rate of VLDL-TG secretion (μmol/min), which represents the total amount of VLDL-TG secreted by the liver, was calculated by multiplying the FTR of VLDL-TG (pools/min) by the pool size of VLDL-TG (μmol). VLDL-TG pool size equals the product of steady-state VLDL-TG concentration (μmol/ml) and plasma volume (ml); the latter was assumed to be equal to VLDL-TG volume of distribution and was calculated as 55 ml/kg fat-free mass (39, 55, 56). The plasma clearance rate of VLDL-TG (ml/min), which is an index of the efficiency of VLDL-TG removal from the circulation via all possible routes, was calculated by dividing the rate of VLDL-TG disappearance from plasma, which equals VLDL-TG secretion rate under steady-state conditions, by the concentration of VLDL-TG in plasma. This simplifies to FTR times plasma volume. The mean residence time (MRT) of VLDL-TG in the circulation (min) was calculated as 1/FTR.

Our method for evaluating VLDL-TG kinetics has been shown to provide similar results regarding VLDL-TG turnover with these obtained from multicompartmental modeling over a longer observation period (12 h), when FTR is <0.5 pools/h, but reportedly underestimates VLDL-TG turnover at higher FTRs (46). However, using either the longer modeling approach (39) or the shorter monoexponential approach (56), our laboratory has previously reported that VLDL-TG FTR is 0.45 pools/h in healthy nonobese men at rest, and we have been able to demonstrate statistically significant increases of similar magnitude (~40%) after a single prolonged bout of endurance exercise (39, 56), hence the shorter monoexponential approach (35) was considered adequate for the purposes of this study.

Statistical analysis. Analysis was carried out with SPSS version 16.0 (SPSS, Chicago, IL). All variables were normally distributed according to the Kolmogorov-Smirnov test. Data for the three trials were analyzed by using repeated-measures ANOVA and Fisher’s post hoc test for pairwise comparisons; the assumption of sphericity was satisfied in all cases. Results are presented as means ± SE. Statistical significance was set at P < 0.05. Based on a previous reproducibility study in normolipidemic nonobese men (36), a sample size of seven would allow for detecting physiologically significant differences in VLDL-TG kinetic parameters of ≥25% in magnitude, with a type I error rate of α = 5% and a type II error rate of β = 0.20 (i.e., 80% power).

RESULTS

Evening endurance and resistance exercise sessions. There were no significant differences between the resistance and endurance exercise sessions in gross and net energy expenditure; V̇O₂ tended to be lower and the RQ was significantly higher during resistance than endurance exercise (Table 1). The total work performed during resistance exercise averaged 59,606 ± 6,180 N·m (40 ± 1% from upper body exercises and 60 ± 1% from lower body exercises); the intensity of endurance exercise corresponded to 28 ± 3% of V̇O₂peak.

Metabolic rate and substrate oxidation in the basal state. Basal V̇O₂ and whole body fat oxidation rate were significantly higher the morning after resistance exercise than rest, whereas RMR tended to be higher and RQ and whole body carbohydrate oxidation rate tended to be lower; there were no significant differences between resistance and endurance exercise, or between endurance exercise and rest (Table 2).

Metabolic concentrations in the basal state. There were no significant differences between trials in fasting insulin and glucose concentrations and whole body insulin resistance (HOMA-IR index: 1.48 ± 0.12, 1.74 ± 0.24, and 1.44 ± 0.21 after rest, endurance and resistance exercise, respectively; P = 0.840) or in total and HDL-cholesterol concentrations (Table 3). Plasma VLDL-TG concentration was significantly lower after resistance exercise than rest (by −28 ± 10%; P = 0.034) but was not different between resistance and endurance exercise or between endurance exercise and rest; the average difference in VLDL-TG concentration between resistance and endurance exercise was −19 ± 14%, and this decrease failed to reach significance (P = 0.186) because one subject had lower VLDL-TG concentration after endurance than resistance exercise, contrary to the other six. Differences between treatments in total plasma TG and plasma FFA concentrations did not reach statistical significance (Table 3).

Basal VLDL-TG kinetics. There were no differences between trials in hepatic VLDL-TG secretion rate (P = 0.199; Fig. 1). The plasma clearance rate of VLDL-TG was significantly higher after resistance exercise than rest (by 30 ± 8%; P = 0.003) and endurance exercise (by 24 ± 6%; P = 0.003) (Fig. 2), and the MRT of VLDL-TG was significantly shorter (by −36 ± 11 min vs. rest; P = 0.016; and by −28 ± 8 min vs. endurance exercise; P = 0.012) (Fig. 3). Compared with the resting trial, all subjects had increased VLDL-TG plasma clearance rate and shorter MRT after resistance exercise, as opposed to only one subject after endurance exercise (Figs. 2 and 3).

Table 1. Respiratory variables and energy expenditure during evening endurance and resistance exercise

<table>
<thead>
<tr>
<th></th>
<th>Endurance</th>
<th>Resistance</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen consumption, l/min</td>
<td>0.90±0.09</td>
<td>0.87±0.10</td>
<td>0.084</td>
</tr>
<tr>
<td>Respiratory quotient</td>
<td>0.88±0.02</td>
<td>1.02±0.01</td>
<td>0.003</td>
</tr>
<tr>
<td>Gross energy expenditure, kcal</td>
<td>397±41</td>
<td>394±46</td>
<td>0.773</td>
</tr>
<tr>
<td>Net energy expenditure, kcal</td>
<td>289±38</td>
<td>287±42</td>
<td>0.773</td>
</tr>
</tbody>
</table>

Values are means ± SE.
Table 2. Respiratory variables, resting metabolic rate, and whole body substrate oxidation rates in the basal state, the morning after evening endurance or resistance exercise, or after an equivalent period of rest

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Endurance</th>
<th>Resistance</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen consumption, ml/min</td>
<td>251±11</td>
<td>255±12</td>
<td>265±14*</td>
<td>0.041</td>
</tr>
<tr>
<td>Carbon dioxide production, ml/min</td>
<td>196±9</td>
<td>194±9</td>
<td>196±8</td>
<td>0.963</td>
</tr>
<tr>
<td>Respiratory quotient</td>
<td>0.78±0.01</td>
<td>0.76±0.01</td>
<td>0.74±0.01</td>
<td>0.108</td>
</tr>
<tr>
<td>Resting metabolic rate, kcal/min</td>
<td>1.19±0.05</td>
<td>1.20±0.05</td>
<td>1.24±0.06</td>
<td>0.086</td>
</tr>
<tr>
<td>Carbohydrate oxidation, mg/min</td>
<td>58±15</td>
<td>36±13</td>
<td>21±8</td>
<td>0.120</td>
</tr>
<tr>
<td>Fat oxidation, mg/min</td>
<td>72±7</td>
<td>82±8</td>
<td>95±9*</td>
<td>0.047</td>
</tr>
</tbody>
</table>

Values are means ± SE. *Significantly different from value after rest, P < 0.05.

and 3); changes in VLDL-TG secretion rate between treatments were inconsistent (Fig. 1).

**DISCUSSION**

In this study, we examined basal VLDL-TG kinetics the morning after a single, evening bout of endurance or resistance exercise, matched for total energy expenditure, or an equivalent period of rest in healthy, nonobese, untrained young men. Our results indicate that, compared with rest, VLDL-TG concentration is reduced, VLDL-TG plasma clearance rate is increased, and the MRT of VLDL-TG in the circulation is shortened after resistance but not after endurance exercise. The effect of an evening resistance exercise bout on basal VLDL-TG kinetics manifested not only compared with evening rest (i.e., no exercise) but also compared with an evening endurance exercise bout of the same energy expenditure. These data suggest either that the exercise-induced energy deficit is not the primary mechanism mediating the effects of resistance exercise on VLDL-TG metabolism, or that resistance exercise is more potent (i.e., requires a lower energy expenditure threshold) than endurance exercise in eliciting changes in VLDL-TG metabolism that have been linked with hypotriglyceridemia.

Our findings confirm and extend previous observations regarding the effects of exercise on VLDL-TG metabolism. Our laboratory has previously demonstrated that fasting hypotriglyceridemia in response to a single, prolonged bout of moderate-intensity endurance exercise (90 min of running or 120 min of cycling at 60% of \( V_o^\text{peak} \), total energy expenditure ~900 and ~1,200 kcal, respectively) results from increased efficiency of VLDL-TG removal from plasma (by ~40% compared with rest) without any changes in hepatic VLDL-TG secretion (39, 56); however, this is not the case after less prolonged exercise (60 min of cycling at 60% of \( V_o^\text{peak} \), total energy expenditure ~600 kcal) (38). These observations are indicative of an energy expenditure threshold below which exercise-induced hypotriglyceridemia does not manifest (38), whereas once this threshold is achieved (56), more exercise does not provide additional benefit (39). In the present study, we did not detect any effect of evening endurance exercise (90 min at ~30% of \( V_o^\text{peak} \), total energy expenditure ~400 kcal) on basal VLDL-TG concentration and kinetics the next morning (~14 h after exercise cessation), in agreement with our laboratory’s previous observation (38) as well as with those of other investigators in normolipidemic subjects, reporting no changes in fasting plasma TG concentrations the day after single endurance exercise bouts of total energy expenditure ≤500 kcal (4, 44, 57, 66). The low intensity of our exercise session (~30% of \( V_o^\text{peak} \)) is not likely a key factor, because exercise-induced hypotriglyceridemia manifests after more prolonged (180 min) exercise at this intensity, and the magnitude of TG-lowering is the same as that for more intense but less prolonged exercise (90 min at ~60% of \( V_o^\text{peak} \)) of similar gross energy expenditure (~1,000 kcal) (58). Our findings therefore indicate that single sessions of typical recreational aerobic activities do not have any significant impact on basal VLDL-TG metabolism in healthy, untrained nonobese men.

Much less is known regarding the effects of resistance exercise on TG metabolism, despite that this type of exercise, at a sufficient intensity, is recommended as an alternative to or in addition to endurance exercise for maintaining and improving cardiovascular health (3). Cross-sectional reports between strength-trained athletes and sedentary subjects and longitudinal interventions in apparently healthy individuals provide conflicting information, but it is generally believed that strength training is less effective than aerobic training in lowering plasma TG concentrations (30). Results from previous studies examining the effect of a single bout of resistance exercise on fasting and postprandial plasma TG concentrations the next day (12–18 h postexercise) are inconsistent, with some reporting significant decreases (48, 65) and others not (11, 51). The reasons for these conflicting reports are

Table 3. Fasting serum insulin and plasma metabolite concentrations in the basal state, the morning after evening endurance or resistance exercise, or after an equivalent period of rest

<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>Endurance</th>
<th>Resistance</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin, pmol/l</td>
<td>37±3</td>
<td>43±6</td>
<td>35±5</td>
<td>0.669</td>
</tr>
<tr>
<td>Glucose, mmol/l</td>
<td>5.4±0.1</td>
<td>5.5±0.1</td>
<td>5.5±0.1</td>
<td>0.333</td>
</tr>
<tr>
<td>Free fatty acids, mmol/l</td>
<td>0.63±0.09</td>
<td>0.82±0.15</td>
<td>0.80±0.10</td>
<td>0.101</td>
</tr>
<tr>
<td>Total cholesterol, mmol/l</td>
<td>4.82±0.19</td>
<td>4.67±0.24</td>
<td>4.45±0.19</td>
<td>0.194</td>
</tr>
<tr>
<td>HDL-cholesterol, mmol/l</td>
<td>1.04±0.06</td>
<td>1.00±0.05</td>
<td>0.96±0.04</td>
<td>0.129</td>
</tr>
<tr>
<td>Total triglyceride, mmol/l</td>
<td>0.99±0.11</td>
<td>0.93±0.16</td>
<td>0.79±0.11</td>
<td>0.191</td>
</tr>
<tr>
<td>VLDL-triglyceride, mmol/l</td>
<td>0.37±0.07</td>
<td>0.34±0.07</td>
<td>0.24±0.05*</td>
<td>0.034</td>
</tr>
</tbody>
</table>

Values are means ± SE. HDL, high-density lipoprotein; VLDL, very low-density lipoprotein. *Significantly different from value after rest, P < 0.05.
whole VLDL particle from plasma via interaction with hepatic lipase, transfer of TG to other lipoproteins (e.g., HDL) hydrolysis by lipoprotein lipase (LPL) and possibly also by neutral lipid exchange, conversion of VLDL to lipoproteins of higher density, i.e., intermediate- and low-density lipoproteins (IDL and LDL, respectively), as well as removal of the latter (e.g., 5%) (23) has no physiologically meaningful effect on VLDL-TG plasma clearance rate (36).

Whole body VLDL-TG plasma clearance refers to all possible routes of VLDL-TG removal from plasma, including hydrolysis by lipoprotein lipase (LPL) and possibly also by hepatic lipase, transfer of TG to other lipoproteins (e.g., HDL) via neutral lipid exchange, conversion of VLDL to lipoproteins of higher density, i.e., intermediate- and low-density lipoproteins (IDL and LDL, respectively), as well as removal of the whole VLDL particle from plasma via interaction with hepatic and/or peripheral receptors (37). We cannot ascertain the opposite change in concentration and would, therefore, cancel out. Only the clearance rate is directly affected by shifts in plasma volume, but the magnitude of reported changes in the latter (e.g., 5%) (23) has no physiologically meaningful effect on VLDL-TG plasma clearance rate (36).
routes that are primarily responsible for our observation. There is some evidence suggesting that the liver after endurance exercise secretes fewer but TG-rich and therefore possibly also larger VLDL particles (39), and similar observations have been made after resistance exercise (55); in vivo studies in humans (37, 53) indicate that the removal of TG from the core of TG-rich, large VLDL particles is more efficient than that from TG-poor, small VLDL, possibly because increasing TG content and size of lipoprotein particles enhances their susceptibility to hydrolysis by LPL (18). Hence secretion of TG-richer VLDL after exercise of sufficient energy cost, whether endurance (39) or resistance (55), may underlie the augmented plasma clearance rate of VLDL-TG via enhanced whole body LPL-mediated lipolysis. This mechanism does not depend on any changes in LPL mass and activity of tissues after exercise; indeed, exercise-induced hypotriglyceridemia may manifest without any detectable increase in skeletal muscle LPL mass (39) and activity (27).

Nevertheless, LPL protein mass and activity in skeletal muscle increase transiently after strenuous exercise and remain elevated for some 16–20 h postexercise (50); this could facilitate VLDL-TG removal from the circulation, at least across the previously exercised muscles, and hence further augment whole body VLDL-TG plasma clearance rate. Other routes for accelerated VLDL-TG removal are unlikely to contribute to our observations. Enhanced transfer of TG from VLDL to HDL after exercise would result in TG enrichment of HDL particles and thus accelerated clearance of HDL, thereby lowering HDL-cholesterol concentration (34); if anything, acute exercise increases HDL-cholesterol concentrations (16). Faster removal of VLDL particles themselves from the circulation is also unlikely to explain the augmented whole body clearance of VLDL-TG, because our laboratory has reported previously that the plasma clearance rate and the mean residence time of VLDL-apolipoprotein B-100 (i.e., VLDL particles) in the circulation are not affected by single bouts of moderate-intensity endurance exercise with energy costs between 600 and 1,200 kcal (38, 39). In any case, our results indicate that the routes contributing to enhanced VLDL-TG removal after exercise are more sensitive to resistance than endurance type of activity of approximately the same energy cost. The reasons responsible for this finding are not readily apparent.

Although $\text{VO}_2$ and RMR may be higher and the RQ may be lower (increased whole body fat oxidation) the day after resistance exercise compared with resting values (21, 43), differences between evening resistance and endurance exercise of similar energy cost are small and not significant the next morning (21). Consistent with these observations, we found that basal fat oxidation rate and $\text{VO}_2$ were greater after resistance exercise than rest, but they were not different between resistance and endurance exercise. It is therefore unlikely that the greater basal fat oxidation (or $\text{VO}_2$) mediates the effects of resistance exercise on VLDL-TG plasma clearance rate, because although both were higher after resistance exercise than rest, only VLDL-TG plasma clearance rate was greater after resistance than endurance exercise, whereas fat oxidation was not. In fact, the increase in VLDL-TG plasma clearance rate leading to hypotriglyceridemia 12–24 h after exercise cessation has been observed either with (39) or without (56) exercise-induced changes in basal $\text{VO}_2$, RQ, RMR, and whole body fat oxidation rate.

Differences in substrate use during the endurance and resistance exercise sessions are also unlikely to be responsible for our findings. Resistance and endurance exercise may differ considerably in intensity and type of contraction, motor unit recruitment, muscle cell metabolism, and thus whole body substrate use (33), but many studies have demonstrated that, provided that the total energy expenditure of exercise be held constant, the intensity of exercise (low or high), and therefore the different pattern of skeletal muscle metabolism and mixture of fuels being oxidized, does not affect the TG concentration response to exercise the next day (13, 58). Even when adipose tissue lipolysis is inhibited by pharmacological means (Acipimox) during exercise, thereby causing a substantial reduction in plasma fatty acid availability and a concomitant increase in intramuscular TG and glycogen utilization (61), the plasma TG concentration response the next day is not different from that after a placebo-controlled exercise bout of similar energy expenditure (41). Although aforementioned data predominantly refer to endurance exercise, these observations strongly argue against the notion that different patterns of skeletal muscle metabolism and whole body substrate use during resistance and endurance exercise can explain their divergent effects on basal VLDL-TG metabolism.

It is not known whether a greater increase in skeletal muscle LPL activity after resistance than endurance exercise of similar energy cost could mediate our observations. After strenuous exercise, LPL activity in skeletal muscle may increase by as much as 70% late into recovery (~18 h postexercise), likely due to the depletion of intramuscular TG stores (32). There are no studies available comparing the effects of isocaloric resistance and endurance exercise bouts on skeletal muscle LPL; however, exercise-induced plasma TG-lowering 1 day after exercise does not require any significant changes in intramuscular TG stores and skeletal muscle LPL activity (27). Also, it is not clear whether and how the different intensity of the two exercise sessions may affect LPL in muscle. Results from animal studies are controversial, because some indicate that the intensity of exercise is directly related to the increase in skeletal muscle LPL activity (9), whereas others report that low-intensity exercise is more effective than high-intensity exercise in inducing skeletal muscle LPL gene transcription (28). In humans, the influence of intensity on postheparin plasma LPL activity 20–24 h after exercise cessation is minor when the total energy expenditure of exercise is maintained constant (22, 31). Therefore, different exercise-induced changes in LPL activity do not seem likely to mediate the effects of isocaloric resistance and endurance exercise on basal VLDL-TG metabolism, although this possibility warrants further investigation.

We cannot ascertain whether differences in muscle damage, inflammation, and oxidative stress following resistance and endurance exercise are related to our present findings. We previously reported that changes in basal VLDL-TG metabolism after resistance exercise compared with rest manifest with only modest elevations in creatine kinase and lactate dehydrogenase concentrations, indicative of minimal muscle damage (55). Exercise-induced cytokine production is generally lower after resistance than endurance exercise (52), but the role of cytokines and low-grade systemic inflammation in regulating basal VLDL-TG metabolism is not known. Although both types of activity acutely increase oxidative stress, the pattern of
response is very different, with lipid peroxidation being greater and protein peroxidation being lower after resistance than endurance exercise of maximal intensity (1). Limited data from in vivo and in vitro studies in animals suggest that lipid peroxidation augments the proteolysis of newly synthesized apolipoprotein B-100 in the liver, thereby reducing the secretion of VLDL particles (45, 60). Secretion of fewer but TG-richer VLDL particles after exercise is likely a key factor for the exercise-induced augmentation in basal VLDL-TG plasma clearance rate (39). Still, whether greater lipid peroxidation after resistance than endurance exercise mediates our present observations is unclear, because differences in lipid peroxidation between the two types of exercise at submaximal intensity and approximately the same VO₂ are much less pronounced, if at all (62).

In this study, dietary control ensured that our subjects were in a negative energy balance during the resistance and endurance exercise trials compared with the resting trial, by ~300 kcal (i.e., the net energy expenditure of exercise). Only a few studies have attempted to distinguish the effects of exercise from those of negative energy balance on total plasma TG concentration, and their results are controversial (20, 64); the role of energy balance and its components (exercise energy expenditure and dietary energy intake) in mediating the effects of exercise on VLDL-TG metabolism has never been investigated. Nevertheless, differences in energy balance are unlikely to explain our observations because resistance and endurance exercise induced the same energy deficit compared with the resting condition, but only resistance exercise affected basal VLDL-TG metabolism. This interpretation may be limited by the uncertainty regarding the exact quantity of the total energy deficit induced by resistance and endurance exercise. Greater excess postexercise VO₂ (EPOC) after a bout of resistance than endurance exercise of similar energy cost (21) or VO₂ (10) may have contributed to a greater cumulative energy deficit after the former treatment. However, albeit significant, differences in EPOC between these two types of exercise make up for only 20–30 kcal over 2–5 h of recovery (10, 21). Such a small difference is unlikely to mediate the vastly different VLDL-TG metabolism response ~14 h later. Therefore, the exercise-induced energy deficit (i.e., negative energy balance) is likely not the primary factor mediating the effects of resistance exercise on basal VLDL-TG metabolism.

The above points notwithstanding, the inherent inability to accurately estimate the total energy expenditure of resistance exercise should not go unmentioned. Like all previous studies that examined the effect of resistance exercise on postprandial TG metabolism (11, 12, 48, 65), we measured VO₂ throughout the resistance exercise bout (including the resting intervals, which represent postexercise EPOC during acute recovery) and used the caloric equivalent of the volume of oxygen consumed (47), despite that the short and intermittent nature of resistance exercise invalidates the typical assumptions of indirect calorimetry. Indeed, the RQ during resistance exercise in our subjects exceeded 1.0, albeit only slightly. It is unlikely that this has led to a substantial miscalculation, however, because the caloric equivalent differs by ~0.34 kcal per liter of oxygen consumed throughout the RQ range (from 0.7 to 1.0) (47), which would work out to <30 kcal for our 90-min bout at an average VO₂ of ~0.9 l/min, if indeed the error were so large. Theoretical bioenergetic considerations also suggest that the energy expenditure of weight lifting is greater than that of walking but lower than that of jogging (63), and our subjects did something intermediate between walking and jogging during their endurance exercise bout. Although we did not make any attempt to quantify the contribution of anaerobic metabolism during resistance exercise, other investigators have estimated that the anaerobic component makes a significant contribution to total energy expenditure (by an additional 15–35%) for resistance exercise involving repetitions to exhaustion at moderate intensity (60% of 1 repetition maximum) but not for that with limited number of repetitions at higher intensity (80% of 1 repetition maximum) (49), the latter more closely reflecting our resistance exercise protocol. Importantly, even if we have underestimated the total energy expenditure of resistance exercise (~400 kcal) by as much as 50%, which is unlikely, a single bout of endurance exercise of that total energy expenditure (~600 kcal) has still no effect on basal VLDL-TG kinetics the next morning (38). All these reasons reinforce our conclusion that resistance exercise is more potent than endurance exercise in eliciting changes in VLDL-TG kinetics that have been shown previously (39, 55, 56) to lead to hypotriglyceridemia.

In summary, we examined basal VLDL-TG metabolism the morning after a single, evening bout of resistance or endurance exercise matched for total energy expenditure, or an equivalent period of rest, in healthy but untrained, nonobese young men. We found that resistance exercise reduced fasting VLDL-TG concentrations by augmenting VLDL-TG removal from the circulation and shortening VLDL-TG MRT, not only compared with values after rest (i.e., no exercise) but also compared with values after endurance exercise. The latter type of activity had no effect on basal VLDL-TG concentration and kinetics despite inducing a similar total energy deficit as that of resistance exercise. Our findings in normolipidemic men need to be confirmed in other population subgroups, such as women, obese individuals, and hyperlipidemic patients; nevertheless, they suggest that resistance exercise should be considered as an alternative to or in addition to endurance exercise for the control of plasma TG concentrations.

GRANTS

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REFERENCES


