No effect of menstrual cycle phase on basal very-low-density lipoprotein triglyceride and apolipoprotein B-100 kinetics

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Magkos, Faidon, Bruce W. Patterson, and Bettina Mittendorfer. No effect of menstrual cycle phase on basal very-low-density lipoprotein triglyceride and apolipoprotein B-100 kinetics. Am J Physiol Endocrinol Metab 291: E1243–E1249, 2006. First published July 11, 2006; doi:10.1152/ajpendo.00246.2006.—Dyslipidemia, manifested by increased plasma triglyceride (TG), increased total and LDL-cholesterol concentrations and decreased HDL-cholesterol concentration, is an important risk factor for cardiovascular disease. Premenopausal women have a less atherogenic plasma lipid profile and a lower risk of cardiovascular disease than men, but this female advantage disappears after menopause. This suggests that female sex steroids affect lipoprotein metabolism. The impact of variations in the availability of ovarian hormones during the menstrual cycle on lipoprotein metabolism is not known. We therefore investigated whether very-low-density lipoprotein (VLDL)-TG and VLDL-apolipoprotein B-100 (apoB-100) kinetics are different during the follicular (FP) and luteal phases (LP) of the menstrual cycle. We studied seven healthy, premenopausal women (age 27 ± 2 yr, BMI 25 ± 2 kg/m²) once during FP and once during LP. We measured VLDL-TG, VLDL-apolipoprotein B-100, and plasma free fatty acid (FFA) kinetics by using stable isotope-labeled tracers, VLDL subclass profile by nuclear magnetic resonance spectroscopy, whole body fat oxidation by indirect calorimetry, and the plasma concentrations of lipoprotein lipase (LPL) and hepatic lipase (HL) by ELISA. VLDL-TG and VLDL-apolipoprotein B-100 concentrations varied markedly within the FP and LP. We conclude that VLDL-TG and VLDL-apolipoprotein B-100 metabolism is not affected by menstrual cycle phase.

DYSLPIDEMIA, characterized by increased plasma triglyceride (TG), increased total and LDL-cholesterol, and reduced HDL-cholesterol concentrations, is a major risk factor for cardiovascular disease (41). Premenopausal women have a lesser risk of developing cardiovascular disease than age-matched men, but the “female advantage” disappears after menopause (26). Differences in plasma lipid concentrations, particularly plasma TG concentration, between men and women and pre- and postmenopausal women are likely responsible for this phenomenon. The increase in cardiovascular disease risk resulting from a given rise in plasma TG concentration is more than twofold higher for women than for men (23). Premenopausal women have lower plasma TG concentration than men (55); this difference between the sexes is abolished after menopause because of an increase in plasma TG concentration that coincides with the onset of menopause (10). This suggests a beneficial effect of ovarian hormones on plasma TG metabolism. Findings from studies in postmenopausal women receiving hormone replacement therapy and premenopausal women taking hormonal contraceptives indicate that this is likely due to the lack of progestosterone rather than estradiol.

Hormone replacement therapy providing progestins alone to postmenopausal women decreases fasting plasma TG concentration, whereas estrogens increase fasting plasma TG concentration (19). Also, estrogen-rich oral contraceptives induce hypertriglyceridemia, whereas those containing both estrogens and progestins do not (15). The mechanisms responsible for these hormone-induced changes in fasting plasma TG concentration are not entirely clear but are likely mediated via direct effects of female sex steroids on very-low-density lipoprotein (VLDL) metabolism. In the postabsorptive state, most of the TG in plasma circulate in the core of VLDL, which are produced and secreted by the liver. Circulating VLDL-TG are progressively hydrolyzed by lipoprotein lipase (LPL) present in muscle and adipose tissue capillary endothelia (12). Estrogens have been found to increase VLDL-TG secretion (18, 52); however, only one study investigated the effect of progestins on TG kinetics and found no differences in TG secretion into plasma in women who received compared with those who did not receive progestins (28).

The impact of physiological fluctuations in the secretion of endogenous ovarian steroids during a normal menstrual cycle on plasma TG concentration is unclear. Several studies report no significant differences in plasma TG concentration at various time points during a menstrual cycle (8, 32, 33), whereas in other studies plasma TG concentration was found to be lower during the luteal phase (LP) than during the follicular phase (FP) (13, 42). Some of the discrepancy between findings from different studies may be due to differences in timing within each cycle phase; both plasma estradiol and progestosterone concentrations vary markedly within the FP and LP. The influence of normal cyclic variations in ovarian sex hormone availability during the menstrual cycle on TG metabolism has never been studied.

The purpose of the present study was to examine the effect of menstrual cycle phase on VLDL-TG and VLDL-apolipoprotein B-100 (apoB-100) metabolism. We hypothesized that VLDL-TG and VLDL-apolipoprotein B-100 secretion rates would be greater during the FP than during the LP. We therefore measured VLDL-TG, VLDL-apolipoprotein B-100, and plasma free fatty acid concentrations by magnetic resonance spectroscopy, whole body fat oxidation by indirect calorimetry, and the plasma concentrations of lipoprotein lipase (LPL) and hepatic lipase (HL) by ELISA. VLDL-TG and VLDL-apolipoprotein B-100, and plasma free fatty acid concentrations varied markedly within the FP and LP.

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(FFA) kinetics by using stable isotope-labeled tracers, VLDL subclass distribution by nuclear magnetic resonance (NMR) spectroscopy, whole body fat oxidation by indirect calorimetry, and the plasma concentration of LPL and hepatic lipase (HL), the key enzymes involved in VLDL-TG metabolism, by ELISA in healthy, premenopausal women once during mid-FP and once during the LP of a menstrual cycle. FP labeled tracer infusion studies within 2–6 wk, in randomized order: subjects before their participation in the study, which was approved by the Human Studies Committee and the GCRC Advisory Committee at Washington University School of Medicine in St. Louis, MO.

Experimental protocol. Each subject completed two stable isotope-labeled tracer infusion studies within 2–6 wk, in randomized order: one during the FP and one during the LP of a menstrual cycle. FP studies were carried out between 5 and 9 days after the onset of menstruation; LP studies were carried out between 6 and 2 days before the onset of menstruation.

Participants were instructed to maintain their normal lifestyle between the FP and LP studies and to adhere to their regular diet and refrain from exercise for 3 days before being admitted to the GCRC the afternoon before each isotope infusion study. At 1930, they refrain from exercise for 3 days before being admitted to the GCRC before the onset of menstruation. Studies were carried out between 5 and 9 days after the onset of menstruation.

To determine glucose concentration, blood was collected in tubes containing heparin, and 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.

Sample preparation and analyses. The VLDL fraction was prepared as previously described (37). 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 g for 16 h at 10°C in an Optima LE-80K preparative ultracentrifuge equipped with a 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 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 progesterone and 17β-estradiol concentrations were measured with ELISA kits (IBL Immuno-Biological Laboratories, Hamburg, Germany). Plasma glucose concentration was determined on an automated glucose analyzer (YSI 2300 STAT plus; Yellow Spring Instrument, Yellow Springs, OH). Plasma insulin concentration was measured by RIA (Linco Research, St. Charles, MO). Plasma FFA concentrations were quantified by gas chromatography (Hewlett-Packard 5890-II, Palo Alto, CA) after heptadecanoic acid was added to plasma as an internal standard (44). Total plasma TG and VLDL-TG concentrations were determined using a colorimetric enzymatic kit (Sigma Chemicals, St. Louis, MO). Total plasma and VLDL-apoB-100 concentrations were measured with a turbidimetric immunoassay (Wako Pure Chemical Industries, Osaka, Japan). Plasma immunoreactive protein masses of LPL (29) and HL (6) were determined using sandwich ELISAs that do not cross-react with HL and LPL, respectively.

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 (GC-MS; MSD 5973 system; Hewlett-Packard, Palo Alto, CA) (37, 44). Heptafluorobutyric (HFB) anhydride was used to form an HFB derivative of glycerol in plasma and VLDL-TG. The tert-butyldimethylsilyl derivative was prepared for the analysis of plasma leucine, and the N-heptafluorobutyril 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.

Plasma VLDL subclass distribution was determined by proton NMR spectroscopy (LipoScience, Raleigh, NC) using an AVANCE INCA NMR Chemical Analyzer equipped with an UltraShield superconducting magnet (Bruker BioSpin, Billerica, MA), as described previously (34). Briefly, plasma samples were diluted twofold, and 600 μl of the diluted sample was used on the automated NMR spectrometer system set at 400.13 MHz and 47°C. Each sample was run once, and multiple scans were obtained and averaged. Total VLDL particle number (in nmol/l), the number of individual VLDL subclasses (diameters: large >60 nm, medium 35–60 nm, and small 27–35 nm), and average VLDL particle size (diameter in nm) were calculated from the NMR spectra (16).

Calculations. Palmitate rate of appearance (Rn) in plasma was calculated by dividing the palmitate tracer infusion rate by the average plasma palmitate TTR value between 60 and 240 min during physiological and isotopic steady state; total FFA Rn was derived by dividing palmitate Rn by the proportional contribution of palmitate to

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Table 1. Plasma hormone, metabolite, and lipase concentrations during follicular and luteal phases of the menstrual cycle.

<table>
<thead>
<tr>
<th></th>
<th>Follicular Phase</th>
<th>Luteal Phase</th>
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<tbody>
<tr>
<td>Progesterone, nmol/l</td>
<td>1.3 (0.6, 1.4)</td>
<td>40.9 (10.2, 46.4)*</td>
</tr>
<tr>
<td>Estradiol, pmol/l</td>
<td>234 (103, 246)</td>
<td>257 (184, 332)</td>
</tr>
<tr>
<td>Insulin, pmol/l</td>
<td>24 ± 4</td>
<td>24 ± 4</td>
</tr>
<tr>
<td>Glucose, mmol/l</td>
<td>4.8 ± 0.1</td>
<td>4.6 ± 0.1</td>
</tr>
<tr>
<td>Free fatty acids, µmol/l</td>
<td>366 ± 45</td>
<td>352 ± 31</td>
</tr>
<tr>
<td>Total TG, mmol/l</td>
<td>0.57 ± 0.05</td>
<td>0.58 ± 0.05</td>
</tr>
<tr>
<td>VLDL-TG, nmol/l</td>
<td>0.28 ± 0.03</td>
<td>0.29 ± 0.03</td>
</tr>
<tr>
<td>Total apoB-100, mg/l</td>
<td>485 ± 43</td>
<td>534 ± 40</td>
</tr>
<tr>
<td>VLDL-apoB-100, mg/l</td>
<td>18 ± 3</td>
<td>18 ± 3</td>
</tr>
<tr>
<td>LPL, µg/l</td>
<td>44.4 (40.9, 54.8)</td>
<td>36.9 (34.4, 52.7)</td>
</tr>
<tr>
<td>HL, µg/l</td>
<td>5.9 ± 0.7</td>
<td>5.7 ± 0.4</td>
</tr>
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</table>

Values for progesterone, estradiol, and LPL are medians and quartiles; all other values are means ± SE. TG, triglyceride; VLDL, very-low-density lipoprotein; apoB-100, apolipoprotein B-100; LPL, lipoprotein lipase; HL, hepatic lipase. *Value during LP is significantly different from corresponding value during FP; *P = 0.02. †Group values are derived from 6 subjects, due to plasma limitations in 1 subject.

calculated on the basis of plasma VLDL-apoB-100 concentration and VLDL-apoB-100 FTR as described above for VLDL-TG.

**Statistical analysis.** All data sets were tested for normality. Normally distributed variables are presented as means ± SE; paired Student’s t-test was used to compare results from FP and LP studies. Not normally distributed variables (plasma estradiol and progesterone concentrations, VLDL-TG secretion rate, the molar ratio of VLDL-TG to VLDL-apoB-100 secretion, LPL concentration, and large VLDL particle number) are presented as medians and quartiles in parentheses; Wilcoxon’s signed ranks test was used to compare results from FP and LP studies. A *P* value ≤0.05 was considered statistically significant.

**RESULTS**

**Plasma hormone, metabolite and lipase concentrations.** Plasma progesterone concentration was ~30 times higher during LP than FP (*P* = 0.02), whereas plasma estradiol concentration was not different (*P* = 0.31; Table 1). Plasma insulin, glucose, FFA, total and VLDL-TG, total and VLDL-apoB-100, and HL and LPL concentrations were not different during FP and LP (Table 1).

**Resting metabolic rate, respiratory quotiend and substrate oxidation.** Resting metabolic rate (FP 0.93 ± 0.03 and LP 0.94 ± 0.02 kcal/min, *P* = 0.44), respiratory quotient (FP 0.81 ± 0.01 and LP 0.82 ± 0.02, *P* = 0.51) and whole-body fat (FP 45 ± 3 and LP 42 ± 6 mg/min, *P* = 0.63) and carbohydrate (FP 63 ± 9 and LP 76 ± 17 mg/min, *P* = 0.40) oxidation rates were not different between FP and LP.

**FFA Ra and VLDL-TG and apoB-100 kinetics.** FFA Ra was 242 ± 29 µmol/min during FP and 226 ± 19 µmol/min during LP (*P* = 0.54). The rate of VLDL-TG secretion (Fig. 1) and VLDL-TG mean residence time (Fig. 2) were not different between FP and LP (*P* = 0.30 and *P* = 0.69, respectively). The relative contribution of systemic fatty acid sources to total VLDL-TG production was 71 ± 3% during FP and 75 ± 4% during LP (*P* = 0.12). Accordingly, nonsystemic fatty acids contributed 29 ± 3% during FP and 25 ± 4% during LP to total VLDL-TG production.

The rate of VLDL-apoB-100 secretion (Fig. 3) and VLDL-apoB-100 mean residence time (Fig. 4) were not different between FP and LP (*P* = 0.92 and *P* = 0.37, respectively.

The molar ratio of VLDL-TG to VLDL-apoB-100 secretion, an index of the TG content of newly secreted VLDL particles, did not differ significantly between FP [11671 (10497, 31723)] and LP [13798 (11862, 14043); *P* = 0.40].
VLDL particle number and size. There were no significant differences between the two menstrual cycle phases in the total number of VLDL particles in plasma ($P = 0.62$) and VLDL subclass distribution ($P \geq 0.25$; Table 2). Average VLDL particle size was 45.3 ± 0.8 nm during FP and 46.0 ± 1.2 nm during LP ($P = 0.65$).

**DISCUSSION**

We measured whole body substrate oxidation and FFA, VLDL-TG, and VLDL-apoB-100 concentrations and kinetics during mid-FP and mid-LP in healthy, premenopausal women who did not take oral contraceptives. We found no differences between FP and LP in whole body substrate oxidation and plasma substrate concentrations, FFA $R_a$, VLDL-TG and VLDL-apoB-100 secretion by the liver, and VLDL-TG and VLDL-apoB-100 mean residence times in the circulation. It is therefore unlikely that results from studies investigating basal lipid kinetics in this population would be confounded by obtaining data on different days of the menstrual cycle.

Our finding that plasma FFA concentration and $R_a$ were not different between FP and LP is consistent with previous reports on the effect of menstrual cycle phase on basal, postabsorptive plasma FFA concentration and FFA $R_a$ (20, 24). It is unlikely that this consistent lack of difference was due to insufficient statistical power of the studies or the variation in sex hormone concentrations within each cycle phase. Also, studies in which hormone replacement therapy was administered to postmenopausal women report no effect of estrogens and progestins, given alone or in combination, on basal plasma FFA concentration and flux (28). Furthermore, no differences were observed in basal lipolytic rate, measured in vitro, in adipocytes collected from healthy, premenopausal women during the FP or LP (45). Systemic plasma FFA availability is therefore most likely not affected by variations in female sex hormone availability.

The lack of differences in VLDL-TG and VLDL-apoB-100 concentrations and kinetics between FP and LP in our study appears to be somewhat unexpected on the basis of results from studies administering exogenous hormones in pre- and postmenopausal women (reviewed in Refs. 15 and 48). Oral estrogen administration increases VLDL-TG and VLDL-apoB-100 secretion and concentration in plasma (9, 15, 48), whereas oral administration of progestins elicits the opposite effect and lowers VLDL-TG and VLDL-apoB-100 concentrations and VLDL-apoB-100 secretion (15, 48, 60), although it apparently has no effect on VLDL-TG secretion (28). The difference between these findings and ours may be due to differences in the amount of sex hormones available: exogenous hormone administration in the earlier published studies resulted in relatively high, steady hormone concentrations in the systemic circulation that were maintained for several weeks. The route of delivery, however, is probably the most important factor. Unlike oral estrogen therapy, transdermal estrogen therapy is not associated with changes in plasma VLDL-TG and VLDL-apoB-100 concentrations and VLDL-apoB-100 kinetics (57), most likely because it reduces the amount of estradiol delivered to the liver. The effect of transdermal progestins on plasma TG metabolism is not known, and the effect of menstrual cycle

**Table 2. VLDL subclass distribution during the follicular and luteal phases of the menstrual cycle**

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<thead>
<tr>
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<th>Follicular Phase</th>
<th>Luteal Phase</th>
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<tr>
<td></td>
<td>mmol/l %Total</td>
<td>mmol/l %Total</td>
</tr>
<tr>
<td>Total VLDL</td>
<td>41±7</td>
<td>43±7</td>
</tr>
<tr>
<td>Small VLDL (27–35 nm)</td>
<td>24±5</td>
<td>58±5</td>
</tr>
<tr>
<td>Medium VLDL (35–60 nm)</td>
<td>16±3</td>
<td>41±5</td>
</tr>
<tr>
<td>Large VLDL (&gt;60 nm)</td>
<td>0.26 (0.17, 0.53)</td>
<td>0.8±0.2 (0.19, 0.76)</td>
</tr>
<tr>
<td></td>
<td>0.27 (0.19, 0.76)</td>
<td>0.9±0.2</td>
</tr>
</tbody>
</table>

Values for large VLDL particle number are medians and quartiles; all other values are means ± SE. Group values are derived from 6 subjects, due to plasma limitations in 1 subject.
Further support for our findings comes from our plasma FFA and insulin concentrations and FFA $R_e$ data, which were not different between FP and LP. Insulin and plasma FFA availability are thought to be the main regulators of VLDL-TG and VLDL-apoB-100 secretion (reviewed in Ref. 30). Approximately two-thirds of fatty acids in VLDL-TG are derived from plasma (this study and Refs. 5, 34, and 37). The remaining fatty acids in VLDL-TG (i.e., nonsystemic plasma fatty acids) are derived from pools of fatty acids that are not labeled with tracer during the infusion period; this includes fatty acids released from preexisting, slowly turning-over lipid stores in the liver and tissues draining directly into the portal vein, fatty acids resulting from lipolysis of plasma lipoproteins that are taken up by the liver, and fatty acids derived from hepatic de novo lipogenesis (30). Results from studies in animals and isolated hepatocytes investigating the effect of female sex steroids on the fatty acid synthesis pathway in the liver are inconclusive: both estrogens and progestins have been shown to exert inhibitory or stimulatory as well as no effects (e.g., Refs. 22, 25, and 47). The only study that investigated the effect of variations in female sex hormone availability on hepatic de novo lipogenesis in human subjects in vivo used a cross-sectional design and suggests that the fraction of VLDL-TG derived from de novo synthesized fatty acids is greater during FP than during LP (14); however, the absolute rate of VLDL-TG secretion was not measured in that study. In any case, de novo lipogenesis contributes little (<5%) to total basal hepatic VLDL-TG production (1, 5, 21). Potential differences in the availability of this source of fatty acids are therefore difficult to detect, and we may have missed them. It is unlikely, however, that such small differences are physiologically relevant compared with the magnitude of changes in VLDL-TG secretion that occur in response to physiological intervention, such as high-carbohydrate diet (39) and weight loss (37), or in response to experimental manipulation of substrate and hormone availability (30, 38, 51).

We also observed no differences in the mean residence time for VLDL-TG or VLDL-apoB-100 during FP and LP. Therefore, the efficiency of removal was not affected by menstrual cycle phase. This is in general agreement with earlier studies measuring the effect of female sex hormones or menstrual cycle phase on HL and LPL activity, although the findings are somewhat confusing. Postheparin HL activity was found to be lower during LP than during FP, but postheparin LPL activity was not different (53). Also, oral estrogen administration suppresses postheparin HL but not LPL activity (e.g., Refs. 3 and 54), whereas exogenous progestins increase postheparin HL activity (e.g., Refs. 11 and 54); their effect on LPL is unclear. Furthermore, when postmenopausal women were treated with oral estrogen, addition of progestins abolished the estrogen-induced increase in femoral adipose tissue LPL activity and decreased abdominal adipose tissue LPL activity (31). However, no differences were observed in either fat depot following transdermal estrogen administration, whether alone or combined with progestins (31). Differences in HL activity are unlikely to affect VLDL-TG removal and concentration because HL, compared with LPL, contributes little to VLDL-TG hydrolysis (62). Only one study examined the effect of menstrual cycle phase on LPL activity in subcutaneous adipose tissue samples from healthy, premenopausal women; no differences were observed between FP and LP (45). No information is currently available with respect to female sex steroids and skeletal muscle LPL.

Although the effect of menstrual cycle phase on VLDL-TG and VLDL-apoB-100 kinetics has never been investigated, there are a few studies that assessed the effects of exogenous estrogens and progestins on VLDL-TG and VLDL-apoB-100 removal from the circulation; the findings from these studies are conflicting. In one, progesterin had no effect on the efficiency of VLDL-apoB-100 removal in postmenopausal women (60). In another, cross-sectional study, oral contraceptives, containing progestins only or estrogens plus progestins, were associated with higher endogenous and exogenous TG removal from plasma compared with no treatment or estrogens alone (28). Most other studies are difficult to interpret, because they assessed the effect of estrogens combined with progestins compared with no treatment but not to estrogens or progestins alone (27, 56, 59).

There are some limitations to our study. First, we studied our women during mid-FP and mid-LP, and (by design) plasma estradiol concentrations were not different between the two trials. Therefore, we cannot exclude differences in lipid kinetics between mid-FP or mid-LP and other time points during the menstrual cycle (e.g., time of menses or ovulation). However, it is unlikely that major differences exist: studies that measured VLDL-TG (2, 49, 53), total plasma TG (8, 32, 33), and total plasma apoB-100 (4, 32, 40) concentrations (no data available for VLDL-apoB-100) at various time points during a menstrual cycle found no significant differences between study days, although some studies reported lower total plasma and VLDL-TG (35, 61) concentrations during the LP than at the time of ovulation; this, however, could be related to other factors (e.g., the surge in LH and FSH). Second, we studied a small number of subjects, which could have made it difficult to detect very small differences in VLDL-TG and VLDL-apoB-100 kinetics between menstrual cycle phases. However, we are confident in the conclusions from our study for several reasons. First, our data set indicated no trend for differences in lipid kinetics between menstrual cycle phases. Second, the intrindividual variability of the major outcome variables between the two menstrual cycle phases, calculated as the coefficient of variation between FP and LP, was on average 25%. This degree of variability, albeit relatively high, is very similar to the intrindividual coefficient of variation of 23% for VLDL-apoB-100 kinetics when healthy premenopausal women were studied on the same day of two consecutive menstrual cycles (57). Third, we assessed the reproducibility of lipid kinetic measurements in eight healthy men and found that the day-to-day variability in VLDL-TG and VLDL-apoB-100 secretion rates was ~15% (F. Magkos and B. Mittendorfer, unpublished observation). On the basis of this and our published data (34, 37, 38), we performed a power analysis and found that we should have detected a difference in the magnitude of $\pm 20\%$ in VLDL-TG and VLDL-apoB-100 kinetics between menstrual cycle phases with $n = 7$, assuming a $\beta$-value of $\pm 0.2$ and a level of significance $\alpha = 0.05$. In light of the normal biological variability for plasma TG concentration (50) and VLDL-TG and VLDL-apoB-100 kinetics (F. Magkos and B. Mittendorfer, unpublished observation), differences between
menstrual cycle phases that are <20% are likely of minor physiological significance.

In summary, basal postabsorptive rates of whole body substrate oxidation, FFA concentration and $R_n$ and VLDL-TG and VLDL-apoB-100 kinetics are not different between FP and LP. Our findings confirm previous investigations on the effect of menstrual cycle phase on FFA kinetics and complement them by providing evidence that VLDL-TG and VLDL-apoB-100 kinetics are not different during FP and LP. We conclude that studying premenopausal women who are not taking oral contraceptives, on different days of their menstrual cycle, will likely not confound basal postabsorptive lipid kinetic measurements.

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