Ghrelin and peptide YY in postpartum lactating and nonlactating women[1–3]

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ABSTRACT

Background: Epidemiologic studies suggest that childbearing is an important contributor to the development of obesity in many women and that breastfeeding may be protective. Ghrelin and peptide YY (PYY) are gut hormones involved in appetite regulation and energy homeostasis and are biological neuroendocrine signals that potentially affect body weight and adiposity.

Objective: This study evaluated whether fasting or postprandial ghrelin or PYY is different between lactating and nonlactating postpartum women matched for age, body weight, and adiposity.

Design: Ten postpartum lactating women (mean ± SD: 28.1 ± 4.9 y of age, 69.2 ± 11.3 kg, 35.4 ± 6.6% body fat) and 8 nonlactating women (28.8 ± 7.6 y of age, 75.6 ± 13.7 kg, 37.5 ± 6.5% body fat) at 4–5 wk postpartum underwent measurements of body weight, body composition, and ghrelin and PYY responses to a standardized meal (350 kcal). Seven never-pregnant women served as control subjects (29.7 ± 4.1 y of age, 60.4 ± 4.8 kg, 25.5 ± 2.0% body fat).

Results: Ghrelin concentrations decreased, whereas PYY concentrations increased significantly ($P < 0.05$) in response to the meal, but fasting or meal-induced changes were not significantly different between lactating and nonlactating women. The fasting ghrelin concentration correlated with body mass index ($r = -0.53$, $P < 0.05$) and was significantly lower in postpartum than in control women (894.9 ± 247.7 compared with 1316.9 ± 241.0 pg/mL), even after adjustment for body mass index.

Conclusions: Our data do not support the notion that ghrelin, PYY, or both are plausible neuroendocrine signals that influence body weight regulation during lactation. They suggest, however, that ghrelin may change with increased adiposity in the postpartum state and may potentially play a role in body weight regulation after child birth. *Am J Clin Nutr* 2010;91:366–72.

INTRODUCTION

Epidemiologic studies suggest that childbearing contributes to the development of obesity in many women (1–3). It is not known, however, whether the increased risk of becoming overweight or obese after childbearing is due to lifestyle changes, biological factors, or both. Several studies have suggested that the postpartum period marks a time when a woman's physical activity level and commitment to regular exercise is likely to decline (4, 5). Such a change in regular exercise would be expected to promote weight gain unless the mother compensated by increasing physical activity through the tasks of mothering (ie, carrying and chasing a child) and/or by reducing energy intake. Furthermore, although breastfeeding is theoretically expected to promote weight loss by increasing maternal energy expenditure (≈450 kcal/d above the nonlactating state) (6), this obesity-protective effect of lactation is not evident in all women (7). This may suggest that lactation-induced neuroendocrine signals potentially increase hunger and/or energy intake to offset increased energy requirements of lactation. Indeed, Butte et al (7) speculate that changes in postpartum body weight occur in response to a sequence of complex neuroendocrine and biochemical stimuli, many of which are unknown.

Several gut hormones, including ghrelin and peptide YY (PYY), are involved in appetite regulation and energy homeostasis and may be plausible biological factors that influence weight retention (or loss) during the postpartum period and in response to lactation. Ghrelin is an orexigenic peptide released primarily from enteroendocrine cells in the stomach (8, 9), which is at its highest concentration during fasting and decreases after feeding (9). In contrast, PYY 3–36 ($PYY_{3–36}$) is an anorexigenic peptide secreted from L cells in the intestinal mucosa (8, 10, 11). PYY reaches a nadir during fasting and increases after a meal in proportion to energy intake (10, 11). Ghrelin and PYY are suppressed/stimulated maximally within 1 h and remain altered for ≤90 min postprandially before a progressive return toward fasting concentrations (9, 12, 13). Animal studies have found that postfeeding ghrelin concentrations are depressed in lactating as compared with nonlactating dam rats (14) and in lactating pigs compared with the pregnant state (15). Although a few human studies have measured ghrelin (but not PYY) in postpartum women (16–18), it is not clear whether these hormones differ in relation to lactation status. Thus, the primary purpose of this study was to evaluate fasting and postprandial ghrelin and PYY in lactating and nonlactating postpartum women. We hypothesized that ghrelin would be elevated and PYY suppressed in lactating compared with nonlactating women and that the

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meal-induced response of both peptides would be blunted in lactating women to promote energy intake to balance the cost of lactation. Additional purposes were to determine: *1*) whether fasting ghrelin and PYY differed between postpartum women and never-pregnant control subjects and *2*) whether fasting or postprandial concentrations of these peptides change in a subset of women during the first 6 mo of lactation.

SUBJECTS AND METHODS

Subject characteristics and screening

Subjects were 18 healthy, primiparous, postpartum women who were ≥18 y of age (10 lactating and 8 nonlactating) and recruited from February 2004 through July 2008. Screening for admission into the study included a medical history, a complete blood count, an evaluation of thyroid status via thyroid-stimulating hormone (TSH) measurement, a resting electrocardiogram (EKG), and a physical examination by a study physician. Subjects were excluded if they smoked; had a multiple birth; had any significant complications of pregnancy (eg, gestational diabetes); had renal, hepatic, endocrine, gastrointestinal, pulmonary, cardiac, or hematologic disease, including elevated blood pressure (>140/90 mm Hg); had low hemoglobin concentrations (<12 mg/dL); had elevated TSH concentrations; had an abnormal resting EKG; showed signs of significant depression, anxiety, eating disorders, other psychological problems, alcoholism, or other substance abuse; or used prescription or over-the-counter medications or herbal preparations that could influence metabolism. At the time of screening, the lactating group had to be exclusively breastfeeding, whereas the nonlactating group had to be exclusively feeding their infants infant formula. Women who delivered either vaginally or by cesarean delivery were included as long as they had no activity restrictions at 4–5 wk postpartum. Menstrual cycle phase was not controlled because of the uncertainty of regular cycles during the early postpartum period; however, progesterone concentrations were measured on testing days (as described below). In addition, 7 never-pregnant women who were enrolled in another study conducted over this same time period served as control subjects (19), and 5 women who agreed to continue exclusively breastfeeding (ie, not supplementing with infant formula or cow milk) until completion of the study were followed longitudinally at 12 and 24 wk postpartum. The study was approved by the Institutional Review Boards of the Pennington Biomedical Research Center, Woman's Hospital in Baton Rouge, LA, and the University of Wyoming; all procedures followed were in accordance with the ethical standards of these institutions. Volunteers were fully informed about the possible risks of all procedures before providing written informed consent.

Overview of baseline and the 12- and 24-wk visits

The postpartum women completed a 4-h test day at the Pennington Biomedical Research Center inpatient unit between 4 and 5 wk after delivery. After a 12-h overnight fast, participants reported to the metabolic unit for measurement of their resting metabolic rate (RMR), followed by fasting and postmeal blood work and anthropometric and body-composition measurements. The lactating women were asked to nurse their infants before reporting. In addition, a subset of lactating women (n = 5), completed these same measurements at 12- and 24-wk postpartum. The control women completed similar testing including RMR, fasting blood work, anthropometric and body composition but did not participate in the meal test.

Resting metabolic rate

RMR and the fasting respiratory quotient (RQ) were measured over a 30-min period by indirect calorimetry with a Deltatrac II Metabolic cart (Datex-Ohmeda, Helsinki, Finland). After resting quietly for 30 min, a transparent plastic hood connected to the cart was placed over the head of the participant. Participants remained motionless and awake during the test, and the last 20 min of the measurement were used. Calculations of oxygen consumption and carbon dioxide production were made from continuous measurements of oxygen and carbon dioxide concentrations in inspired and expired air diluted with a constant airflow (≈40 L/min) generated by the metabolic cart by using the Weir equation (20).

Fasting and postmeal blood draws

Immediately after the RMR measurement, an intravenous cannula was inserted for drawing fasting and postmeal blood samples. Blood samples were collected for the measurement of prolactin, estradiol, progesterone, leptin, adiponectin, insulin, glucose, growth hormone (GH), ghrelin, and PYY in the postpartum women and for the measurement of insulin, glucose ghrelin, and PYY in the control women. Postpartum participants were then given a standard liquid meal that consisted of 240 mL "Ensure Plus" (350 kcal, 13 g protein, 11 g fat, 50 g carbohydrate, and 3 g dietary fiber; Abbott Laboratories. Columbus, OH) which was consumed in 5 min. The participants then rested quietly until the 60-min postprandial blood draw. One nonlactating woman, however, had a clogged intravenous line during the meal test, which allowed for meal-test comparisons for 7 nonlactating and 10 lactating women. A meal test was not performed in the control women.

Blood metabolite and hormone analysis

Blood samples for the analysis of ghrelin and $PYY_{3–36}$ were collected into EDTA-containing tubes to which 150 μL aprotinin was added before centrifugation (15 min at 3000 rpm, 2–8 °C). The supernatant (plasma) was removed and stored in cryovials at −80 °C until analyzed. At study completion, ghrelin and PYY were batch-analyzed by radioimmunoassay by using human-specific kits from Phoenix Pharmaceuticals Inc (Burlingame, CA) and Linco Research Inc (St Charles, MO). Insulin, glucose, GH, prolactin, and estrogen were analyzed according to standardized procedures. Briefly, insulin was analyzed via immunoassay and GH was analyzed via immunoassay with fluorescence with the DPC Immulite 2000 (Diagnostic Product Corporation, Los Angeles, CA). Glucose was measured via glucose oxidase electrode by using the Beckman-Coulter Synchron CX7 (Brea, CA). Prolactin and estradiol were measured by automated immunoassay with chemiluminescent detection by using the Siemens 2000. The intraassay CVs for these analyses were as follows: ghrelin, 3.3–10%; PYY, 2.9–9.4%; insulin, 3.3–

TABLE 1
Physical and anthropometric characteristics and resting metabolism in postpartum lactating and nonlactating women and never-pregnant control women[1]

	Lactating women (n = 10)	Nonlactating women (n = 8)	Control women (n = 7)
Age (y)	28.1 ± 4.9	28.8 ± 7.6	29.7 ± 4.1
Height (cm)	161.7 ± 4.6	160.2 ± 3.4	162.1 ± 3.4
Weight (kg)	69.2 ± 11.3	75.6 ± 13.7	60.4 ± 4.8[2]
BMI (kg/m^2)	26.4 ± 4.0	29.5 ± 5.9	23.0 ± 1.5[2]
Body fat (%)	35.4 ± 6.6	37.5 ± 6.5	25.5 ± 2.0[2]
Fat-free mass (kg)	44.1 ± 3.8	46.7 ± 5.9	45.0 ± 4.1
Resting metabolism			
RMR (kcal/d)	1307 ± 185	1367 ± 161	1444 ± 156
RQ	0.85 ± 0.06	0.82 ± 0.06	0.85 ± 0.03

[1] All values are means ± SDs. RMR, resting metabolic rate; RQ, respiratory quotient.
[2] Significantly different from lactating and nonlactating women, $P < 0.05$ (unpaired t tests for equal or unequal variances).

5%; glucose, 0.4–2.9%; GH, 2.9–4.6% ; prolactin, 2.2–3.6; and estrogen, 4.3–9.4%.

Anthropometric and body-composition measurements

Height and body mass were measured with standard techniques by trained personnel. Body composition was assessed by using a dual-energy X-ray absorptiometry (DXA; Hologic QDR 4500a) whole-body scanner. The CVs for measurements of lean mass, fat mass, and percentage body fat were 0.8%, 1.6%, and 1.7%, respectively.

Statistical approach

Differences between body mass, body composition, resting energy expenditure, RQ, and fasting hormone concentrations between lactating (n = 10) and nonlactating (n = 8) postpartum women and between postpartum women (n = 18, lactating + nonlactating) and never-pregnant control subjects (n = 7) were analyzed by using unpaired t tests for equal or unequal variances. One-factor analysis of variance (ANOVA) with group comparisons was not used because the assumption of equal variance was not met for several key variables, including fat mass and fasting PYY concentrations. For test meal comparisons in the postpartum group, repeated-measures ANOVA was used to test for a group (lactating compared with nonlactating) by meal (fasting compared with 60-min postprandial) effect for ghrelin, PYY, insulin, and glucose. Relations between body weight, body composition, and hormone concentrations were evaluated by using Pearson product momentum correlations. When appropriate, key variables (including RMR and fasting ghrelin) were adjusted for differences in body composition by

TABLE 2
Fasting and postprandial metabolite and hormone concentrations in postpartum lactating and nonlactating women and never-pregnant control women[1]

	Lactating women (n = 10)	Nonlactating women (n = 8)	Control women (n = 7)
Glucose, fasting (mg/dL)	81.1 ± 4.1	86.6 ± 6.9[2]	90.7 ± 8.3[3]
Glucose, postprandial (mg/dL)	86.7 ± 13.5	87.4 ± 25.1	—
Insulin, fasting (μU/mL)	5.3 ± 3.4	6.3 ± 4.5	5.2 ± 2.2
Insulin, postprandial (μU/mL)[4]	26.8 ± 13.5	23.5 ± 4.8	—
Ghrelin, fasting (pg/mL)	971.8 ± 208.9	798.8 ± 271.8	1316.9 ± 241.0[3]
Ghrelin, postprandial (pg/mL)[4]	814 0 ± 129.6	739.6 ± 220.8	—
PYY, fasting (pg/mL)	65.4 ± 12.9	63.3 ± 18.3	83.3 ± 30.6
PYY, postprandial (pg/mL)[4]	91.0 ± 20.8	96.3 ± 45.4	—
Prolactin, fasting (ng/mL)	43.9 ± 33.5	11.0 ± 10.2[2]	—
Estrogen, fasting (pg/mL)	25 ± 7	66 ± 39[2]	—
GH, fasting (ng/mL)	0.41 ± 0.41	0.21 ± 0.17	—
Leptin, fasting (ng/mL)	19.3 ± 15.4	24.6 ± 14.6	—
Adiponectin, fasting (μg/L)	7.1 ± 3.0	9.0 ± 2.2	—

[1] All values are means ± SDs. GH, growth hormone; PYY, peptide YY. Postprandial responses were measured 60 min after a standard liquid meal (350 kcal) for glucose, insulin, ghrelin, and PYY in lactating and nonlactating women. No group effect (lactating compared with nonlactating women) or group × meal effect was found for ghrelin, PYY, insulin, or glucose.
[2] Significantly different from lactating women, $P < 0.05$ (unpaired t tests for equal or unequal variances).
[3] Significantly different from lactating and nonlactating women, $P < 0.05$ (unpaired t tests for equal or unequal variances).
[4] Significant meal effect, $P < 0.001$ (repeated-measures ANOVA).

using multiple-regression analysis (21). In the subset of lactating women in the longitudinal analysis, repeated-measures ANOVA was used to test for a meal (fasting compared with 60 min) by time (4, 12, and 24 wk) interaction. All statistics were computed by using PASW Statistics 17 (SPSS Inc, Chicago, IL). Data are reported as means ± SD unless otherwise specified. Significance was set at $P < 0.05$.

RESULTS

As shown in **Table 1**, the lactating and nonlactating postpartum women were closely matched for age, body mass, and body composition. The never-pregnant control subjects were matched to the postpartum group for age, height, and fat-free mass but were significantly lighter and less fat than the postpartum group. All of the women, except one in the lactating group, had progesterone concentrations indicative of the follicular phase of their menstrual cycle.

Resting metabolic rate

As shown in Table 1, there were no differences in absolute RMR and resting RQ between groups. RMR also did not differ between groups when adjusted for differences in fat-free mass, fat mass, and age (data not shown).

Fasting and postmeal blood draws

Blood concentrations of fasting metabolites and hormones, including ghrelin and PYY, are shown in **Table 2**. Not surprisingly, the lactating women had significantly higher prolactin and significantly lower estrogen concentrations than did the nonlactating postpartum women. Whereas all women had glucose concentrations within the normal limits, glucose was slightly but significantly lower in the lactating than in the nonlactating postpartum women and in the postpartum group than in the control subjects. Fasting ghrelin and PYY concentrations were not different between the lactating and nonlactating women, but fasting ghrelin was statistically lower in the postpartum women than in the control women (Table 2). These differences remained after adjustment for body mass index (BMI; in kg/m^2). No statistical differences in fasting PYY concentrations were found between postpartum and control women ($P = 0.16$).

Glucose, insulin, ghrelin, and PYY responses to the standardized meal for the lactating and nonlactating women are presented in Table 2. A significant meal effect ($P > 0.001$) was found for ghrelin, which fell significantly after the meal, and for PYY and insulin, which rose significantly after the meal. The meal response for ghrelin and PYY, however, was not different between groups ($P > 0.05$, time × group interaction).

Relations between hormone concentrations and body mass and energy expenditure

As shown in **Figure 1**, BMI was significantly correlated with fasting ghrelin and leptin but not with PYY or the other hormones (**Table 3**). Fat mass and percentage body fat were significantly correlated with fasting leptin concentrations but only fat mass (and not percentage body fat) tended to correlate with fasting ghrelin. BMI, fat mass, and percentage body fat were also significantly correlated with fasting ghrelin ($r = -0.62$, -0.62, and -0.56, respectively; $P < 0.01$) but not with PYY when the control subjects were included in the analysis. Fasting ghrelin was positively correlated with fasting insulin ($r = 0.52$, $P = 0.03$) and tended to be negatively correlated with fasting leptin ($r = -0.46$, $P = 0.06$) and adiponectin ($r = -0.42$, $P = 0.08$) but not with PYY or GH.

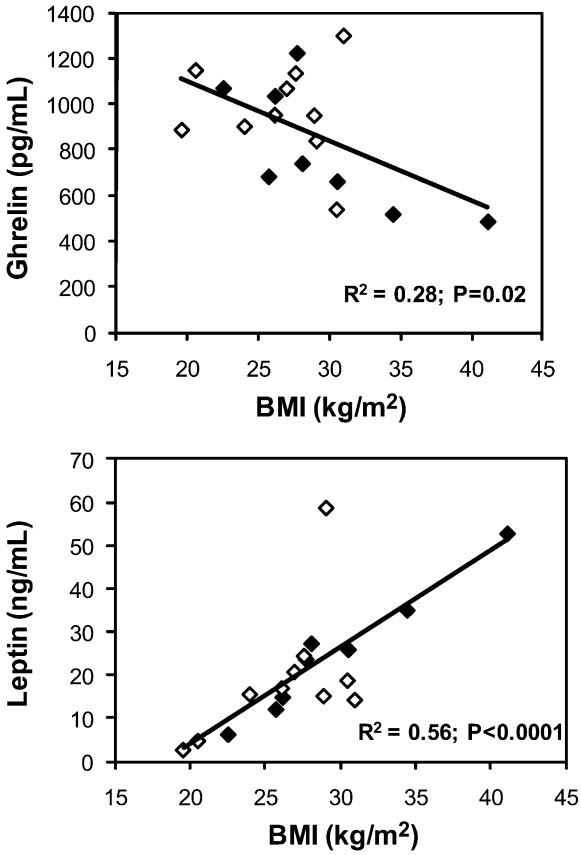

FIGURE 1. Relations between BMI and fasting ghrelin and leptin concentrations in lactating (◇) and nonlactating (♦) postpartum women ($n = 18$).

Change in ghrelin and PYY with increasing duration of lactation

Body mass and body fat decreased significantly ($P < 0.05$ for time) in the subset of women ($n = 5$) who continued to lactate for 6 mo and were 68.6 ± 5.3, 67.4 ± 5.0, and 65.0 ± 5.2 kg and 37.1 ± 1.9%, 36.4 ± 2.1%, and 35.3 ± 3.1% at 4-, 12-, and 24-wk postpartum, respectively. Despite changes in adiposity, however, fasting ghrelin, PYY, leptin, and adiponectin concentrations (**Table 4**),; RMR; RQ; and the meal-induced responses of ghrelin and PYY (data not shown) did not differ significantly over time.

DISCUSSION

This was the first study to simultaneously investigate fasting and meal-induced responses of the hunger-stimulating hormone ghrelin and the appetite-suppressing hormone PYY in postpartum lactating and nonlactating women. We found that both fasting and meal-induced changes in these hormones were not different between lactating and nonlactating women at 4 wk postpartum,

TABLE 3
Pearson product moment correlation coefficients (r) between body mass and adiposity and fasting hormone concentrations in postpartum lactating and nonlactating women (n = 18)[1]

	BMI (kg/m^2)	Fat mass (kg)	Body fat (%)
Insulin (μU/mL)	0.11	0.1	−0.12
GH (ng/mL)	−0.40[2]	−0.45[2]	−0.36
Leptin (ng/mL)	0.75[3]	0.79[3]	0.72[3]
Adiponectin (μg/L)	0.16	0.16	0.31
Ghrelin (pg/mL)	−0.53[3]	−0.45[2]	−0.32
PYY (pg/mL)	−0.15	0.04	0.26

[1] GH, growth hormone; PYY, peptide YY.
[2] $P < 0.07$.
[3] $P < 0.05$.

but that the fasting ghrelin concentration was significantly lower in postpartum than in never-pregnant control women, even after adjustment for adiposity. In a small subgroup (n = 5), we also found that fasting and meal-induced responses of these peptides were not altered across 6 mo of lactation despite significant reductions in body weight and adiposity.

Given the role of ghrelin and PYY in appetite regulation and energy balance (8, 22, 23), we were surprised that the fasting concentrations or postmeal response of either of these gut peptides were not altered during lactation. Substantial evidence indicates that ghrelin infusion at physiologic doses stimulates hunger and food intake (24, 25) and promotes adiposity by reducing fat oxidation (26) and altering adipocyte metabolism (24). Overall, ghrelin is thought to participate in meal initiation and signal the hypothalamus when increased metabolic efficiency is needed (27). Ghrelin is also present in human milk (16, 18, 28), and its concentration is correlated with circulating maternal blood concentrations (16). Whereas less is known overall about PYY and body weight regulation, PYY administration at physiologic doses reduces food intake and adiposity in rodents (24, 29, 30), but this may be a result of taste aversion, nausea, and vomiting (31). PYY is also present in human milk (32) and stimulates oxytocin secretion in lactating rats (33), which suggests that this peptide may also be important during lactation. How these gut peptides affect hunger and food intake is not completely understood but is thought to be via central circulation, where the peptides cross the blood-brain barrier and directly interact with neurons located in the arcuate nucleus of the hypothalamus (8, 23).

Whereas our data do not support that ghrelin, PYY, or even leptin is a likely neuroendocrine signal that assists in driving changes in food intake or body mass in response to lactation, they do suggest that ghrelin may be altered in the postpartum state and may thereby be a potential signal that affects appetite or body weight after childbirth. As previously shown in other populations (9, 12, 34, 35), we found that basal ghrelin but not PYY is downregulated with increasing adiposity in postpartum women, regardless of lactation status. The 33% lower ghrelin concentration relative to never-pregnant control subjects, however, was lower than predicted based on body fat and/or BMI. Aydin et al (16) also found that fasting ghrelin was 15% lower in lactating women than in control women at 15 d postpartum. In this study, the postpartum group also had a significantly higher BMI (29.0 ± 1.4) than the control subjects (23.2 ± 2.1), but the authors did not adjust for these differences. It has been speculated that a reduced ghrelin concentration may be a consequence of elevated leptin (34), which was directly correlated with BMI in the current study and tended to be indirectly correlated with ghrelin. Reduced ghrelin secretion during a state of energy excess (ie, excess adiposity or obesity) that occurs in the postpartum period in most women may provide a feedback signal to reduce orexigenic stimulation (22). Whereas we hypothesized that lactating women would have less suppressed ghrelin because of the elevated energy cost of lactation, we found that ghrelin concentrations were statistically indistinguishable between the lactating and nonlactating women. Although sleep deprivation, common in postpartum women, may have altered fasting ghrelin in individual women to various degrees (36), it is unlikely that differences in sleep cycles contributed to differences between lactating, nonlactating, and control women because short sleep cycles are typically associated with elevated (rather than suppressed) ghrelin (36). Only future longitudinal studies can determine whether lowered postpartum ghrelin is important in long-term body weight regulation after childbirth.

The physiologic relevance of circulating ghrelin and PYY within the normal physiologic range in humans is not well understood. The best evidence that physiologic concentrations of ghrelin affect feeding was derived from studies of lactating dairy cows, which found that higher circulating ghrelin concentrations predicted greater pasture intake (37). Whereas the current study was not designed to investigate hunger or food intake in relation to fasting concentrations of gut peptide, we did evaluate fasting

TABLE 4
Fasting glucose and hormone concentrations with increasing duration of lactation in a subset of postpartum lactating women (n = 5)[1]

	Baseline	12 wk	24 wk
Glucose (mg/dL)	82.4 ± 4.4	79.2 ± 4.4	81.6 ± 3.1
Insulin (μU/mL)	4.5 ± 1.0	3.9 ± 1.1	5.2 ± 2.6
Ghrelin (pg/mL)	919.0 ± 232.1	847.0 ± 175.3	819.0 ± 198.1
PYY (pg/mL)	70.8 ± 15.1	74.6 ± 15.5	78.2 ± 16.6
Prolactin (ng/mL)	59.8 ± 38.9	24.3 ± 8.5	20.2 ± 6.4
Estrogen (pg/mL)	21.6 ± 3.6	26.8 ± 7.8	49.2 ± 16.3
GH (ng/mL)	0.63 ± 0.44	0.94 ± 0.11	1.37 ± 1.57
Leptin (ng/mL)	19.3 ± 3.5	15.9 ± 6.1	16.4 ± 6.1
Adiponectin (μg/L)	9.1 ± 2.2	12.7 ± 5.3	12.0 ± 6.6

[1] All values are means ± SDs. GH, growth hormone; PYY, peptide YY. No time effect (duration of lactation) was found for glucose or any of the hormones by repeated-measures ANOVA.

ghrelin and PYY in relation to resting metabolism and macronutrient oxidation. As opposed to what could be expected from previous ghrelin infusion studies in rodents (26), we did not find that higher circulating ghrelin was associated with a higher RQ. We also did not find that RQ or REE was higher in lactating women, as has been noted in some (38) but not all studies (39). Quite intriguingly, however, we did find that postpartum women, particularly those who were lactating, had slightly but significantly lower fasting blood glucose concentrations. This may be a normal physiologic response related to improved postpartum insulin sensitivity after normal pregnancy-induced insulin resistance (40) or may be reflective of recent shunting of glucose into breast milk.

Also of interest in our preliminary longitudinal analysis was that resting metabolism, ghrelin, and PYY concentrations were not significantly altered from 6 to 24 wk postpartum in the 5 women who continued to breastfeed, despite significant decreases in body weight and adiposity. The results for ghrelin are in contrast with those of a previous longitudinal study that found that postprandial total ghrelin concentrations (measured 3 h after breakfast) increased and that acylated ghrelin decreased with prolonged lactation (18). Indeed, these results are also intriguing given that ghrelin typically increases after calorie-restricted weight loss (9, 41).

Whereas our data serve as important preliminary data for how ghrelin and PYY are altered after childbirth, they have some limitations. In particular, our sample size was relatively small (n = 18), our postmeal analysis had only one collection point (at 60 min), and our control group did not undergo measurement of postprandial gut peptides and was not matched to the postpartum group for body mass and adiposity. Concerning sample size, our enrollment of 18 women (8–10 per group) may have limited the power to detect differences, for example, in fasting ghrelin, which was slightly higher in lactating than in nonlactating women and tended to be lower in postpartum than in control women. Whereas we purposely selected the 60-min postprandial point to reflect the nadir ghrelin (9) and peak PYY (12) concentrations, collection of additional time points in future studies will allow for calculation of area under/above the curve and/or time postprandial ghrelin and/or PYY remain depressed or elevated, respectively, which may be more important physiologic measures. Finally, our study focused only on ghrelin and PYY and did not measure acylated ghrelin (42) or other potentially important peptides, including glucagon-like peptide 1 (GLP-1) or oxyntomodulin (8, 42). GLP-1, in particular, is synthesized by the same cells as PYY, suppresses appetite similar to PYY, and also stimulates pancreatic insulin release. GLP-1 may be of importance in future studies because it may affect appetite as well as gestational and postgestational diabetes.

In conclusion, the results of this study do not support the hypothesis that ghrelin and PYY are plausible biological neuroendocrine signals that influence appetite and body weight regulation during lactation. They do, however, suggest that ghrelin may be altered with increased adiposity after childbirth and that further studies of these hormones in well-designed longitudinal studies would be of interest for understanding the pathogenesis of obesity associated with child bearing.

The authors' responsibilities were as follows—DEL-M, ER, and LD: study design; DEL-M and LD: data collection; DEL-M and LH: data analysis; DEL-M: manuscript preparation; and DEL-M, ER, LH, and LD: manuscript review. None of the authors had a personal or financial conflict of interest.

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