Characterization of the diurnal rhythm of peptide YY and its association with energy balance parameters in normal-weight premenopausal women

Brenna R. Hill, Mary Jane De Souza, and Nancy I. Williams

Women’s Health and Exercise Laboratory and the Department of Kinesiology, Pennsylvania State University, University Park, Pennsylvania

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Hill BR, De Souza MJ, Williams NI. Characterization of the diurnal rhythm of peptide YY and its association with energy balance parameters in normal-weight premenopausal women. Am J Physiol Endocrinol Metab 301: E409–E415, 2011. First published May 31, 2011; doi:10.1152/ajpendo.00171.2011.—PYY may play a role in modulating satiety and energy expenditure; increasing PYY postprandially has been studied largely in single-meal responses. The diurnal rhythm of PYY and its role in energy balance have not been fully characterized. The purpose of our study was to characterize features of the diurnal rhythm of PYY and determine its role in regulating energy balance. This study was a cross-sectional analysis of 11 subjects in whom 24-h repeated blood sampling was conducted at baseline of a larger prospective study. Breakfast (B), lunch (L), dinner (D), and a snack (S) occurred between 0900 and 1900. Total PYY was assayed every hour from 0800 to 1000, every 20 min from 1000 to 2000, and every hour from 2000 to 0800. PYY variables included total AUC, postprandial peaks, and 24-h mean. Energy balance variables included energy intake, RMR, RQ, and NEAT. PYY postprandial peaks were significantly higher than fasting (r = 0.01). Twenty-four-hour peak PYY occurred after L and was significantly higher than all other peaks (P < 0.01). A cubic curve function accounted for most of the variance in PYY (r² = 69.9%, P < 0.01). Fasting PYY (0800) correlated with postprandial peaks at B (r = 0.77, P = 0.01), L (r = 0.71, P = 0.01), and D (r = 0.65, P = 0.03). The only significant association between PYY and energy expenditure was that RMR (kcal/24 h) correlated with 24-h mean PYY (r = 0.71, P = 0.013) and total AUC (r = 0.69, P = 0.019). We conclude that PYY displays a meal-driven diurnal rhythm and is correlated to RMR, a major contributor to energy expenditure. Thus, PYY varies in accordance with energy content and RMR, supporting a role for PYY in energy balance modulation.

Body weight regulation; energy homeostasis

PEPTIDE YY (PYY) is secreted from L cells in the gut, where it slows digestion, acting as an “ileal brake” to increase absorption of nutrients (16). PYY1–36, cleaved to PYY3–36 via dipeptidyl peptidase, is secreted in proportion to energy and macronutrient content, where high-fat or high-protein meals stimulate greater PYY secretion than high-carbohydrate meals (1, 5, 15). PYY reaches peak concentrations 1–2 h postprandially and aids in meal cessation (1) and has thus been identified as a satiety hormone.

Fasting as well as postprandial PYY concentrations have been shown to be depressed in obese and elevated in energy-deficient women (3, 13, 20, 31). Findings regarding the effect of weight loss/gain on PYY are conflicting as well as its role in energy balance (10, 14, 19, 24, 29–31). To date, much of the work in humans has been observations of single-meal responses in pathophysiological conditions (3, 13, 15, 19, 20) where normal physiological responses have been perturbed. Thus, studies in individuals without chronic disease may aid in our understanding of the role of PYY in the etiology of disease.

The diurnal rhythms of hormones like ghrelin and leptin have been characterized in terms of responses to meal timing (8, 21, 32), energy content of meals (22), and the impact of energy deficiency (18, 22). The diurnal rhythm of PYY has yet to be fully characterized under normal physiological conditions or in relation to meal timing and meal energy or macronutrient content of meals. Studies of single-meal responses do not address whether PYY responses change across the day due to time of day or as nutrient intake accumulates.

Studies have also suggested a potential role for PYY in the modulation of energy expenditure (EE) (9, 34). In the hypothalamus, PYY binds to inhibitory Y2 receptors (Y2R) in the arcuate nucleus, where neuropeptide Y (NPY) and proopiomelanocortin (POMC) neurons are located. PYY binds to Y2R on NPY neurons, inhibiting orexigenic NPY secretion. This inhibition releases inhibition of POMC neurons, resulting in greater POMC activation and thus secretion of anorexigenic hormones (α-MSH) and increasing EE (26, 27, 36). Guo et al. (14) found a negative correlation between fasting PYY and resting metabolic rate as well as respiratory quotient (RQ) and postprandial peak PYY. Additionally, Sloth and colleagues (33, 34) peripherally infused PYY and showed increases in EE (kJ/day) as well as fat oxidation (lowered RQ) in lean and obese men.

The purpose of this study was to characterize features of the diurnal rhythm of PYY and to explore the role of PYY in energy balance in normal-weight premenopausal women. We hypothesized that meal energy content and timing would be key components in eliciting the 24-h profile of PYY and that PYY would correlate positively to indices of EE.

SUBJECTS AND METHODS

Experimental Design and Subjects

This study was part of a larger prospective study designed to assess the effects of energy restriction on metabolism and reproductive function. We examined the 24-h profile of total PYY and energy balance parameters in subjects during the baseline period. PYY was measured in blood samples from 11 subjects who completed 24-h blood sampling and anthropometric and energy balance measurements on days 2–7 of the follicular phase. Nonsmoking, healthy, nonexercising (<1 h/wk purposeful exercise) women aged 18–30 yr with body weights of 48–73 kg, 15–30% body fat, and BMI between 18 and 25 kg/m² were included. Exclusion criteria included any evidence of disordered eating or history of an eating disorder, loss/gain of a significant amount of weight (± 2.3 kg) in the past year, or use of hormonal contraceptives or medication that may have altered metabolic hormones. Each subject signed an informed consent form.

Address for reprint requests and other correspondence: N. I. Williams, 108 Noll Laboratory, Penn State University, University Park, PA 16802 (e-mail: niw1@psu.edu).

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approved by the Biomedical Institutional Review Board of Pennsylvania State University.

Screening

Subjects provided information regarding demographics, medical history, menstrual history, and physical activity along with eating attitude questionnaires. A fasting blood sample was obtained between 0600 and 1000 for analysis of a complete blood count and basic chemistry panel and to rule out abnormal pituitary function or metabolic diseases. Psychological stability and the absence/risk of eating disorders were established in an interview under the supervision of a clinical psychologist. Subjects met with a General Clinical Research Center (GCRC) registered dietician to ensure absence of aberrant dietary habits and suitability for a controlled feeding study. Documentation of two to three ovulatory menstrual cycles prior to the study was performed with measurements of midluteal phase serum progesterone and the midcycle urinary LH surge (First Response, Tambrands).

Anthropometrics

Hydrostatic weighing was performed after correcting for residual lung volume to determine body composition. Body density was used to calculate body composition using the Brozek equation (7). Body weight was measured on the same day, with subjects wearing shorts and a t-shirt (without shoes), and recorded to the nearest 0.01 kg.

Energy Balance Parameters

Resting metabolic rate. Resting metabolic rate (RMR) was measured using a ventilated hood system between 0600 and 1000 following an overnight fast. Subjects lay in the supine position for 20–30 min to acclimate to the room temperature and testing procedures; the hood was placed over each subject’s head for 30 min. Expired air was measured every minute for carbon dioxide and oxygen concentration, using a carbon dioxide analyzer (URAS4; Hartmann & Braun, Frankfurt, Germany) and a paramagnetic oxygen analyzer (Magnos 4G, Hartmann & Braun). The values for minutes in which steady state was achieved were averaged to calculate RMR (kcal/day), determined using the Weir equation (40), and RQ.

Physical activity expenditure. To determine 24-h EE, subjects wore a triaxial activity monitor (AM; RT3 accelerometer; Stayhealthy, Monrovia, CA) 24 h/day for one 7-day period to assess the energy cost of all nonpurposeful exercise EE (kcal). The AM was worn on the left hip for 3 wk of baseline and was not worn during showering/bathing. Subjects recorded weekly AM logs that identified all types of activity and when the monitor was taken off. Because all subjects were free-living dietary intake. Three-day diet logs were completed by each subject and consisted of records from two weekdays and one weekend day. Subjects recorded any and all energy intake from food and beverage for the entire day. Data were analyzed in Nutritionist Pro (First Data Bank, Indianapolis, IN) by GCRC registered dieticians.

Determination of Baseline Energy Needs

Caloric intake required to maintain weight for each subject (baseline energy needs) was calculated based on the sum of EE from the measurement of 24-h RMR and AM kcals. The prescribed diet was prepared by the GCRC metabolic kitchen and then provided for a 7-day calibration period during baseline where subjects were weighed daily, and ≥ 100-kcal adjustments were made if body weight fluctuated by more than ±1 kg. The 7-day diet was comprised of 55% carbohydrates, 30% fat, and 15% protein and totaled the amount of calories that represented one’s individual energy needs.

Twenty-Four-Hour Assessment of PYY Diurnal Rhythm

All subjects were tested in the follicular phase (days 2–7) ≥1 wk after the calibration period. Subjects were instructed to abstain from exercise or caffeine ingestion 24 h prior to the test and to fast as of 2000 the night prior. Subjects arrived at the GCRC at 0730 on the day of testing, where they remained in a supine position with their upper bodies slightly elevated. An intravenous catheter was inserted in a forearm vein whereafter blood samples were obtained every 10 min for 24 h. A total of 488 ml (33 tablespoons) of blood was drawn over the 24-h period. Each sample was allowed to clot at room temperature and subsequently spun in a centrifuge for 15 min at 2,500 rpm. Serum aliquots were transferred to storage tubes and stored in a −80°C freezer until analysis.

All meals for the 24-h sampling protocol were prepared in the GCRC metabolic kitchen. Food items were measured to the nearest gram to achieve the prescribed calorie level. The diet was comprised of 55% carbohydrate, 30% fat, and 15% protein and consisted of three meals and a snack prepared for 0900 (breakfast), 1200 (lunch), 1800 (dinner), and 2100 (snack). Dinner consisted of 503 ± 0.4 kcal, the remainder of which was distributed between breakfast (416 ± 30 kcal), lunch (486 ± 26 kcal), and the snack (66 ± 4 kcal). Subjects knew when meals were to be administered and were required to eat all/only the food provided. The caloric prescription for the 24-h blood sampling period provided subjects with 85% of their calculated baseline energy needs to account for reductions in EE due to inactivity associated with bed rest. Meal composition was as follows: breakfast: 48% carbohydrate, 32% fat, and 20% protein; lunch: 54% carbohydrate, 32% fat, and 14% protein; and dinner: 55% carbohydrate, 30% fat, and 15% protein. A snack comprised of 95% carbohydrate, 2% fat, and 4% protein was provided at 2100. Meals provided were reflective of what subjects typically consumed throughout baseline and consisted of foods like English muffins, orange juice, turkey lunchmeat sandwiches, grapes, and pork stir-fry.

PYY Radioimmunoassay Analysis

Serum samples were assayed for total circulating PYY hourly from 0800 to 1000, every 20 min from 1000 to 2000, and hourly from 2000 to 0800. PYY was assayed using a radioimmunoassay (Millipore, Billerica, MA). The sensitivity of the assay was 10 pg/ml, and the intra- and interassay coefficients of variation were 2.9 and 7.1%, respectively.

Data Analysis

Fasting PYY was designated as 0800. Postprandial peak PYY was defined as the highest PYY concentration (pg/ml) obtained after meal administration and prior to subsequent meal administration (1–2 h postprandially). PYY nadirs were determined to be the lowest PYY preprandial concentration before each meal. Twenty-four-hour mean PYY was the average of all PYY concentrations (pg/ml) observed in the 24-h analysis. Total area under the curve (AUC) was calculated by the trapezoidal rule. Four-hour-blocked AUC was defined as meal response AUC for the time between 0800 and 1200, 1200 and 1600, 1600 and 2000, and 2000 and 0000 to capture the breakfast, lunch, dinner, and snack responses, respectively, and 0000 and 0400 and 0400 and 0800 to capture the nocturnal AUCs. Meal rises were defined as the change in PYY that occurred from meal administration to the peak postprandial PYY concentration (pg/ml). Last, 24-h peak PYY was considered the highest concentration of PYY (pg/ml) obtained in the entire 24-h sampling period.

Statistical Analyses

To determine the presence of a diurnal rhythm, 24-h PYY profiles were analyzed using ANOVA with repeated measurements to determine differences in meal-related postprandial peaks across the day. When main effects were detected, post hoc analyses were performed...
by means of paired sample \( t \)-tests employing the Bonferroni correction factor. Regression curve-fit analysis was also employed to determine what, if any, curvilinear function best fit the 24-h profile of PYY.

To determine the relationship between fasting PYY and meal-related PYY features, Pearson correlations were performed to assess the relationship between fasting PYY (pg/ml) and 24-h mean PYY, AUC variables, and meal peaks/nadir. Pearson correlations were calculated to determine the association between PYY and energy balance parameters such as body composition variables, 24-h sampling meal energy and macronutrient content, 3-day dietary intake and macronutrient composition, RMR, and RQ. A \( P \) value of \(<0.05\) was considered statistically significant. Data are reported as means ± SE, and all analyses were performed using SPSS software (version 18.0; SPSS, Chicago, IL).

RESULTS

Subjects

Subject demographics are shown in Table 1. Subjects were healthy, normal-weight, premenopausal women. Subjects were sedentary at baseline (<1 h purposeful exercise/wk) and had remained weight stable (no significant weight loss/gain ± 2.3 kg) for ≥1 year prior to the study.

PYY Diurnal Rhythm

Figure 1 illustrates the 24-h profile of total circulating PYY. PYY exhibits a meal-driven diurnal rhythm characterized by elevated postprandial concentrations after every meal that were significantly higher than fasting PYY. The 24-h peak PYY concentration, observed after lunch, was significantly higher than fasting PYY and all other postprandial peaks across the day (Fig. 1B). This was likely due to an additive effect of breakfast and lunch calories combined, which was correlated to the lunch postprandial peak PYY concentration (\( r = 0.64, P = 0.04 \)). Presumably, the between-meal duration of 3 h between breakfast and lunch allowed for a greater lunch postprandial PYY peak than the 6 h between lunch and dinner, although the energy content of lunch and dinner was not significantly different (\( P = 0.52 \)). Additionally, despite the difference in absolute PYY concentrations between lunch and dinner, the meal rises at lunch and dinner were not significantly different (\( P = 0.90 \)).

To further characterize the diurnal rhythm of PYY, total AUC was partitioned into 4-h blocks of time to illustrate meal-related AUC. The lunch response AUC from 1200 to 1600 was significantly higher than the breakfast response AUC from 0800 to 1200 (\( P = 0.001 \)). Also, the nocturnal AUC blocks (0000–0400, \( P = 0.003 \); and 0400–0800, \( P = 0.006 \)) were significantly lower than the 0800–1200 AUC block. No significant difference was found when the dinner response AUC (1600–2000, \( P = 0.54 \)) was compared with the breakfast response. Figure 1C displays the result of a regression curve-fit analysis, where a cubic curvilinear function accounted for a significant amount of the variance in 24-h PYY (\( r^2 = 69.9\% \), \( P < 0.01 \)).

Table 1. Subject characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Means ± SE</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>20 ± 0.6</td>
<td>18–24</td>
</tr>
<tr>
<td>Height, cm</td>
<td>166.7 ± 1.4</td>
<td>159.4–175.3</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>58.5 ± 1.4</td>
<td>51.1–66.5</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>21.1 ± 0.6</td>
<td>18.4–23.9</td>
</tr>
<tr>
<td>%Body fat</td>
<td>27.0 ± 1.6</td>
<td>19.7–36.8</td>
</tr>
<tr>
<td>Fat mass, kg</td>
<td>15.9 ± 1.2</td>
<td>10.7–22.2</td>
</tr>
<tr>
<td>FFM, kg</td>
<td>42.6 ± 1.2</td>
<td>37.4–49.6</td>
</tr>
</tbody>
</table>

BMI, body mass index; FFM, fat-free mass.

AUC (1600–2000, \( P = 0.54 \)) was compared with the breakfast response. Figure 1C displays the result of a regression curve-fit analysis, where a cubic curvilinear function accounted for a significant amount of the variance in 24-h PYY (\( r^2 = 69.9\% \), \( P < 0.01 \)).
Fasting PYY and 24-h Diurnal Rhythm

Fasting PYY (pg/ml; 0800) correlated with postprandial meal peaks at breakfast ($r = 0.77$, $P = 0.01$), lunch ($r = 0.71$, $P = 0.01$), and dinner ($r = 0.65$, $P = 0.03$) as well as total AUC ($r = 0.86$, $P = 0.001$) and 24-h mean PYY ($r = 0.83$, $P = 0.002$). Figure 2A depicts the relationship between fasting PYY and total AUC and the 24-h mean PYY. Additionally, fasting PYY correlated significantly with total energy intake (kcal/day; $r = 0.63$, $P = 0.04$) provided on the day of 24-h blood sampling as well as combined energy intake from breakfast and lunch (kcal; $r = 0.64$, $P = 0.03$) and total energy intake from carbohydrate (g; $r = 0.63$, $P = 0.04$), fat (g; $r = 0.64$, $P = 0.03$), and protein (g; $r = 0.60$, $P = 0.05$). These same meal energy content variables also showed significant positive correlation with total AUC and 24-h mean PYY (Table 2).

Day of 24-h Sampling

PYY concentrations expressed in a variety of ways were significantly correlated with the energy content from all meals across the day. Table 2 illustrates correlations between total kilocalories, macronutrient and meal energy content, and PYY peaks and nadirs, fasting PYY, AUC, and 24-h mean concentrations across the day.

PYY and Energy Balance

Table 3 depicts energy balance parameters for both energy intake and expenditure. Energy intake is reported from 3-day diet logs in terms of average total daily intake (kcal) as well as macronutrient content (g). EE variables include total daily caloric expenditure (kcal/24 h), RMR (kcal/24 h and kcal·kg fat-free mass$^{-1}$·24 h$^{-1}$), RQ, and EE from AM (kcal/24h).

Body Weight and Body Composition

Table 4 illustrates Pearson correlations between PYY, body composition, and energy balance parameters. No significant correlation was found between fasting PYY, 24-h mean PYY, or AUC and any measurement of body composition.
Dietary Intake from 3-Day Diet Logs

Average daily energy intake obtained from 3-day diet logs is shown as total energy intake (1,806 ± 124 kcal/day) and divided into macronutrient content per gram and percentage of carbohydrate, fat, protein, and alcohol (Table 3). To determine the role of PYY in chronic energy intake, PYY variables were correlated to variables obtained from the 3-day diet logs; however, no significant correlations were found (Table 4).

EE

Table 4 also exemplifies that significant correlations were found between RMR (kcal/24 h) and 24-h mean PYY (r = 0.71, P < 0.013) as well as total AUC (r = 0.69, P = 0.019). Figure 2B depicts the relationship between RMR and PYY 24-h mean and total AUC. Breakfast (r = 0.65, P = 0.03), lunch (r = 0.69, P = 0.02), and dinner (r = 0.66, P = 0.03) postprandial peaks were also positively correlated with RMR (kcal/24 h). No other significant correlations were found among any characteristics of PYY and body composition, chronic energy intake, or EE.

DISCUSSION

Diurnal Rhythm of PYY

To our knowledge, we are the first to report that PYY displays features of an energy-driven diurnal rhythm entrained by meal timing in healthy premenopausal women. Several groups have reported the 24-h profile of PYY; however, these studies were in reference to pathophysiological conditions and obtained samples at time intervals where capturing meal responses may be compromised (12, 13, 28, 37). Total energy intake and macronutrient content of the 24-h sampling period were positively correlated to fasting PYY and all meal-related PYY parameters, suggesting a meal-driven PYY response. In contrast to our data, Guo et al. (14) found no correlation between fasting PYY and 24-h intake in obese and lean individuals. Additionally, postprandial peaks are all significantly elevated above fasting, which demonstrates that the diurnal rhythm of PYY is driven by meal timing as well.

Fasting PYY Correlates

Positive correlations between fasting PYY and postprandial peaks as well as total AUC and 24-h mean PYY provide evidence that higher fasting PYY concentrations are associated with a greater PYY response over the entire 24-h period. This suggests that higher fasting PYY may be associated with enhanced satiety and subsequent weight regulation and thus serves as a proxy indicator of PYY across the day. In support of our findings, a study by le Roux et al. (20) suggests that declines in fasting and postprandial PYY concentrations were

Table 3. Energy balance parameters

<table>
<thead>
<tr>
<th>Variable Fasting kcal 24-h Mean kcal</th>
<th>Peak B</th>
<th>Peak L</th>
<th>Peak D</th>
<th>Nadir B</th>
<th>Nadir L</th>
<th>Nadir D</th>
<th>Nadir N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total 24-h, kcal 0.63* 0.72* 0.69*</td>
<td>0.68*</td>
<td>0.64*</td>
<td>0.67*</td>
<td>0.69* 0.72* 0.64*</td>
<td>0.70*</td>
<td>0.72*</td>
<td>0.62*</td>
</tr>
<tr>
<td>Total fat, g 0.64* 0.69* 0.69*</td>
<td>0.68*</td>
<td>0.61*</td>
<td>0.69*</td>
<td>0.65* 0.69* 0.64*</td>
<td>0.68*</td>
<td>0.69*</td>
<td>0.61*</td>
</tr>
<tr>
<td>Total CHO, g 0.63* 0.62* 0.61*</td>
<td>0.54*</td>
<td>0.43</td>
<td>0.65*</td>
<td>0.49 0.65* 0.49</td>
<td>0.49 0.58 0.35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total 24-h, kcal</td>
<td>0.63* 0.70* 0.71*</td>
<td>0.68* 0.64* 0.67*</td>
<td>0.69* 0.72* 0.64*</td>
<td>0.70* 0.72* 0.62*</td>
<td>0.69* 0.72* 0.62*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PYY, peptide YY; AUC, area under the curve; B, breakfast; L, lunch; D, dinner; N, nocturnal; CHO carbohydrate. *P < 0.05.
associated with decreased satiety in obese compared with lean subjects, whereas Batterham et al. (4) has shown that infusions of PYY lead to enhanced satiety in humans.

**PYY and Energy Intake**

Our data demonstrate that there was one PYY peak that is significantly higher than all other postprandial peaks even when there was no significant difference in meal energy content between lunch and dinner. Our finding that the meal rise is not significantly different between lunch and dinner thus indicates that the meal-induced PYY rise is dependent on the caloric content of the meal. Presumably, PYY was highest after lunch because the time between breakfast and lunch was relatively short (3 h), and thus PYY concentrations remained elevated from the breakfast meal. This may suggest that allowing more time between meals permits more time for digestion/absorption and diminished PYY secretion. Additionally, our data best fit (highest r² and lowest P values) a cubic curvilinear function illustrating that PYY response is significantly altered across the day, highest at lunch and lowest after an overnight fast.

Several studies suggest that more frequent meals across the day may allow for beneficial metabolic effects as well as greater 24-h satiety (6, 11, 35). Because the PYY response is meal driven, more frequent meals across the day may allow for the maintenance of higher circulating PYY and perhaps greater 24-h satiety. Whether changing meal timing would affect peak PYY concentrations is unknown; however, we speculate that this would modify the 24-h pattern we observed. Little is known about the diurnal rhythm of PYY; therefore, it may be advantageous to explore other modulators of PYY beyond what we have investigated.

PYY is considered a satiety hormone among others that displays similar meal response patterns. Glucagon-like peptide-1 (GLP-1) and cholecystokinin (CCK) also act in concert in response to nutrient ingestion to comprise the satiety response. GLP-1 is cosecreted with PYY from L cells in the gut, and thus it is possible that these two hormones share a similar diurnal rhythm. It has been shown that both PYY and GLP-1 concentrations rise 5–30 min postprandially, which is likely due to vagal stimulation before nutrients reach the gut. Additionally, the effects of these peptides act as an “ileal brake” (17). GLP-1, like PYY, has been shown to be reduced in obesity (39). However, GLP-1 has been shown to be reduced, whereas PYY has been shown to be elevated, in young anorexic females (38).

CCK is secreted from I cells and acts similarly to PYY and GLP-1. It rises 10–30 min postprandially and, like PYY, responds more robustly to fat and protein ingestion more so than carbohydrate (23). Additionally, the release of PYY has been demonstrated in dogs to be dependent upon CCK (25). Last, unlike PYY, fasting CCK has been shown to be elevated in obese women and decreased in anorexia nervosa compared with lean control subjects (2).

**PYY and Energy Balance**

The role of PYY in energy balance is unclear, as evidenced by several disparities in the current literature that may be the result of varying populations being studied (14, 19, 20, 31). Contrary to our finding, one study showed a negative correlation between fasting PYY and indices of EE like RMR (kcal/24 h) and RQ in obese individuals in response to a single meal (14). However, our subjects were normal-weight sedentary women, and our results reflect the complete 24-h profile of PYY in response to three meals. This discrepancy may suggest a mechanistic disparity in pathophysiological conditions where the positive correlation seen in our study is lost in obesity, where blunted fasting and circulating PYY occur (20), or in energy deficiency or gastric bypass patients, where PYY is elevated (19, 31). This correlation may exemplify a role for PYY in EE under normal physiological conditions, where higher circulating PYY may be driving metabolism throughout the entire 24-h period and/or vice versa. It is possible that greater circulating concentrations of PYY may be acting due to activation of hypothalamic receptors where PYY binds to the Y2R and inhibits NPY secretion and its orexigenic effects. Y2R binding also activates POMC neurons, enhancing anorexigenic effects and increasing EE (26, 27). To the contrary, higher resting metabolisms may be driving a greater secretion of PYY; however, a mechanism by which metabolism may stimulate PYY secretion has yet to be elucidated.

Although PYY correlated with dietary intake from the day of the 24-h blood sampling, no correlations were found in relation to 3-day diet logs, suggesting that PYY plays a role in short-term satiety and meal cessation as opposed to chronic energy intake. Additionally, there were no correlations found between any PYY parameter and any measurement of body composition, and thus PYY may not play a role in long-term energy storage.

**Limitations**

This study was originally designed to measure physiological responses to meals occurring at known times of the day. Measurements of satiety like visual analog scales were not utilized, and thus this study can only speculate as to the effect of greater responses in PYY on satiety. Additionally, total PYY was assayed, which includes both PYY1–36 and PYY3–36; however, when measuring 24-h PYY it may be beneficial to capture both forms of PYY since both forms may be physiologically relevant (34).

**Conclusions**

PYY can be characterized as having a meal-driven diurnal rhythm, as illustrated by significant correlations between PYY and numerous meal-related parameters exemplifying that meal timing as well as caloric load of a meal elicit postprandial responses, contributing to the 24-h profile. PYY’s role in EE is correlated to absolute resting metabolism; however, a defining role in this area needs further attention. Our data further support the hypothesis that PYY plays a significant role in energy balance as a satiety hormone and correlate of EE.

**ACKNOWLEDGMENTS**

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DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the authors.

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