Effect of weight loss by a low-fat diet and a low-carbohydrate diet on peptide YY levels

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Abstract

Objective—To compare the effects of weight loss by an energy-restricted low-fat diet versus low-carbohydrate diet on serum peptide YY (PYY) levels.

Design—8-week prospective study of 30 obese adults (mean age: 42.8 ± 2.0 years, mean BMI 35.5 ± 0.6 kg/m²).

Results—After 8 weeks, subjects on the low-carbohydrate diet lost substantially more weight than those on the low-fat diet (5.8 kg vs. 0.99 kg, p<0.001). Weight loss by either diet resulted in a 9% reduction in both mean fasting serum PYY levels (baseline: 103.5 ± 8.8 pg/ml, after weight loss: 94.1 ± 6.5 pg/ml, p<0.01) and postprandial AUC PYY (baseline: (20.5 ± 1.5) × 10³ pg·hr⁻¹·ml⁻¹, after weight loss: mean AUC PYY (18.8 ± 1.4) × 10³ pg·hr⁻¹·ml⁻¹ p<0.001). There was a trend towards lower levels of PYY with greater degrees of weight loss.

Conclusions—Reduced PYY levels after weight loss by an energy-restricted low-fat or low-carbohydrate diet likely represents a compensatory response to maintain energy homeostasis and contributes to difficulty in weight loss during energy-restricted diets.

Keywords
PYY; weight loss; low-fat diet; low-carbohydrate diet

Introduction

Nearly 45% of women and 30% of men in the United States are attempting to lose weight at any given time (1). Although energy-restricted diets and low-fat diets are the most commonly recommended diets for weight loss, low-carbohydrate diets are a popular alternative (2,3). A recent meta-analysis reported that low-carbohydrate diets are as effective as low-fat diets in inducing weight loss for up to one year (4).
Peptide YY (PYY) plays a role in appetite and food intake regulation. Enteroendocrine cells lining the distal small bowel and colon secrete PYY\textsubscript{1–36} and the truncated isoform PYY\textsubscript{3–36} in response to a meal (5). The effect of various dietary interventions on PYY remains unclear. In a previous study, we reported that one-week of a low-carbohydrate, high-fat diet led to 55% higher levels of postprandial serum PYY levels compared with a low-fat, high-carbohydrate diet (6).

In this study, we aimed to compare the effects of weight loss by an energy-restricted low-fat versus low-carbohydrate diet on serum PYY levels. We hypothesized that weight loss by a low-carbohydrate diet would lead to higher PYY levels. To test this hypothesis, we compared fasting and postprandial PYY levels in obese individuals at baseline and after 8 weeks of weight loss with a low-fat (<30% of total calories derived from fat) or a low-carbohydrate diet (<30gm of carbohydrate/day, with <10% of total calories derived from carbohydrates).

**Materials/Subjects and Methods**

Subjects were recruited to this prospective study by advertisement in the Richmond, Virginia area. Inclusion criteria included body mass index (BMI) 30 kg/m\textsuperscript{2} – 40 kg/m\textsuperscript{2}, age 18–60 years, and stable weight for ≥3 months. Exclusion criteria included clinically significant pulmonary, cardiac, renal, hepatic, or infectious disease; blood pressure > 170/100 mmHg; diabetes mellitus with HbA1C ≥7.9%; and pregnancy or lactation. Three diabetic persons participated, and all had HbA1C <7%. Subjects provided informed, signed consent. Procedures took place at the General Clinical Research Center (GCRC), and the protocol was approved by the Institutional Review Board of Virginia Commonwealth University.

After enrollment, subjects presented for a screening visit and instruction on maintenance of a 3-day food diary. The subjects’ energy requirements were estimated with the equation: total energy expenditure = fasting metabolic rate (calculated with the Harris-Benedict equation) \times activity factor (sedentary = 1.3, some regular exercise = 1.5, and regular exercise = 1.7). From these estimates, daily caloric intake needed to achieve an energy deficit of 500 kcal/day was estimated for each individual.

After randomization to an energy-restricted low-fat or low-carbohydrate diet, subjects presented to the GCRC at 0800 after a 10-hour overnight fast. Baseline serum PYY, glucose, insulin, leptin, and adiponectin levels were drawn at −15 min and 0 min. Subjects consumed a low-fat or low-carbohydrate test meal (mean 540 kcal), and serum samples were subsequently drawn at 30-minute intervals over the next 2.5 hours. Subjects received counseling from a study dietitian on maintenance of an energy-restricted low-fat diet or low-carbohydrate diet and were instructed to avoid modifying physical activity.

Subjects were responsible for preparing their own meals. They presented to the GCRC weekly for a weight determination. Compliance was assessed by interview and degree of weight loss, with less than 1 kg loss over a 3-week defined as noncompliance. Noncompliant individuals were required to meet individually with a dietitian. After 8 weeks, subjects
presented again to the GCRC and underwent similar procedures to those performed at baseline.

Serum glucose concentrations were measured on a glucose analyzer using oxidative methodology, and serum insulin using a double-antibody RIA. For PYY determinations, aprotinin (Sigma-Aldrich, Inc., St. Louis, MO) at a concentration of 1 μg/ml and dipeptidyl peptidase IV (DPP-IV) inhibitor (Linco, Research, Inc., St. Louis, MO) at a final concentration of 100 μM were added to the serum, and the samples were stored at −70°C until assays were performed. Total PYY was measured using a sensitive and specific RIA (Linco Research, Inc., St. Louis, MO). The lower limit of detection was 10 pg/ml, and the coefficients of variation were 9.4% within and 8.5% between assays. Serum leptin and adiponectin were measured with ELISA kits (Diagnostic System Laboratories, Inc., Webster, TX).

Areas under the curve (AUC) for insulin, glucose, and PYY were calculated with the trapezoidal method. The primary variable of interest was postprandial AUC PYY. In order to detect a 35% difference between the groups with a standard deviation of 154.5, based on a published study (7), 10 subjects per group were needed to achieve a power of 80% with α=0.05. Estimating a potential 20% noncompliance rate, the sample size increased to 16 subjects per group.

All data are presented as means ± SEM. Baseline measurements were assessed with unpaired t-tests, and comparisons between groups analyzed using repeated-measures ANOVA with time and diet as main effects. Linear relationships were tested by Pearson’s correlation coefficient. The macronutrient composition of the diets was calculated using the Nutrition Data System for Research (version 4.04, Nutrition Coordinating Center, University of Minnesota). All statistical analysis were made using JMP Version 8.0 (SAS Institute Inc., Cary, NC), with p<0.05 statistically significant.

Results

Two subjects dropped out, one from each group. Baseline characteristics for the remaining 30 participants are summarized in Table 1. The mean age was 42.8 ± 2.0 years, and the mean BMI 35.5 ± 0.6 kg/m². There were no significant differences in baseline characteristics. Furthermore, analysis with inclusion of the 2 eliminated subjects demonstrated no differences in any baseline variables between groups.

After 8 weeks, weight loss for the entire study group (n=30) was −3.7 ± 0.7 kg (95% CI [−5.2, −2.3]). Subjects on the low-carbohydrate diet lost significantly more weight than those on the low-fat diet (−5.8 ± 0.75 kg, 95% CI [−7.3, −4.3] vs. 0.99 ± 0.86, 95% CI [−2.8, 0.8] respectively, p<0.001). No difference in weight loss was observed by gender or race, and there were no significant associations between weight loss and baseline weight, BMI, or levels of fasting insulin, glucose, leptin, or adiponectin.

Fasting serum PYY levels (Figure 1A) decreased by 9% over 8 weeks (103.5 ± 8.8 pg/ml, 95% CI [85.4, 121.5] vs. 94.1 ± 6.5 pg/ml, 95% CI [80.8, 107.4], p<0.01). Similarly, postprandial serum PYY levels (Figure 1B) decreased by 9% [(20.5 ± 1.5) × 10⁻³]
pg·hr\(^{-1}\)ml\(^{-1}\), 95% CI (17.5, 23.5)] and [(18.8 ± 1.4) \times 10^3 \text{ pg·hr}^{-1}\]ml\(^{-1}\), 95% CI (15.9, 21.7), p<0.001]. There was a trend towards an inverse relationship between weight loss and fasting PYY level such that greater extent of weight loss correlated with lower fasting PYY levels (r=−0.32, p=0.09). No significant correlations were observed between PYY and glucose, insulin, leptin, or adiponectin.

**Discussion**

Contrary to our hypothesis that weight loss with a low-carbohydrate diet would increase PYY levels, serum fasting and postprandial AUC PYY decreased by nearly 10% after weight loss by either diet. Subjects randomized to the low-carbohydrate diet lost 6-fold more weight than those randomized to the low fat-diet. However, change in AUC PYY occurred independently of dietary intervention and degree of weight loss.

Few studies to date have evaluated the effects of dietary composition on PYY expression in humans. Unlike our previous study (6), this study showed no difference in postprandial PYY levels between low-fat and low-carbohydrate diets, likely because subjects prepared their own meals and were not as adherent to their assigned diets as subjects in the previous study. The fact that some subjects did not achieve weight loss as expected with a 500 kcal/day deficit suggests noncompliance. Sloth et al. (8) reported no difference in PYY levels with a high monounsaturated fat, low glycemic index diet versus a low-fat diet. Likewise, Brownley et al. (9) reported that postprandial PYY levels were not affected by glycemic load in obese women.

An interesting finding of this study is that postprandial PYY decreased significantly after weight loss regardless of low-fat or low-carbohydrate diet. Similarly, Sloth et al. (8) reported that 8 weeks of a low energy diet resulted in lower PYY levels and increased appetite scores. In addition, Chan et al. (10) reported that short-term fasting over 48–72 hours reduced fasting PYY levels. Since lower PYY levels are associated with increased appetite (5,7), we speculate that reduced PYY levels following diet-induced weight loss represents a physiological homeostatic mechanism to preserve baseline body weight. Reduced PYY levels would indirectly stimulate hypothalamic neurons containing neuropeptide Y and agouti-related protein, which in turn would stimulate appetite and food intake.

Limitations of this study include measurement of total PYY rather than PYY\(_{3-36}\). However, total PYY levels correlate closely with PYY\(_{3-36}\) levels (11). Furthermore, subjects did not keep weekly food diaries. Therefore, verification of compliance with the prescribed diets was not entirely achievable. Lastly, measures of hunger, appetite, and satiety were not evaluated.

In summary, this study demonstrates that weight loss by either a low-fat or low-carbohydrate diet reduces postprandial serum PYY levels. This finding suggests that low PYY levels may contribute to the high recidivism and weight regain with energy-restricted diets. Further investigation is needed to determine whether diets comprised of various...
macronutrient compositions may increase PYY levels and promote weight loss in obese individuals.

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Figure 1.
A) Fasting serum PYY level before a test meal at baseline and after 8 weeks of weight loss for all subjects. B) Postprandial serum AUC PYY at baseline and after 8 weeks of weight loss for all subjects.

*p < 0.01 vs. baseline

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Table 1
Baseline Characteristics
No baseline differences were present between groups.

|                      | Low-Fat Diet Group (n=13) | Low-Carbohydrate Diet Group (n=17) |
|----------------------|---------------------------|------------------------------------|
| Age (years)          | 45.4 ± 2.3                | 40.9 ± 3.0                          |
| Sex                  | 10F/3M                    | 15F/2M                              |
| Race                 | 6B/7W                     | 9B/8W                               |
| Weight (kg)          | 96.9 ± 2.8                | 100.9 ± 3.5                         |
| BMI (kg/m²)          | 34.9 ± 0.8                | 36.0 ± 0.9                          |
| Waist (cm)           | 105.9 ± 5.3               | 103.6 ± 2.4                         |
| Waist-to-hip ratio   | 0.88 ± 0.06               | 0.84 ± 0.01                         |
| Systolic BP (mmHg)   | 123.6 ± 3.7               | 133.9 ± 4.5                         |
| Diastolic BP (mmHg)  | 74.7 ± 2.6                | 78.8 ± 3.1                          |
| Mean arterial pressure| 91.0 ± 2.8                | 97.1 ± 3.5                          |
| Fasting glucose (mg/dl)| 94.0 ± 3.1                | 98.4 ± 4.2                          |
| Fasting insulin (mU/l)| 9.0 ± 1.2                 | 9.9 ± 1.1                           |
| Fasting PYY (pg/ml)  | 118.9 ± 13.3              | 91.7 ± 11.3                         |
| AUC PYY (pg·hr⁻¹·ml⁻¹)| 18336.7 ± 1633.4          | 22169.5 ± 2257.6                    |
| Leptin (ng/ml)       | 32.8 ± 4.5                | 35.9 ± 3.9                          |
| Adiponectin (ug/ml)  | 7.5 ± 0.9                 | 8.0 ± 0.8                           |

F=female, M=male, B=black, W=white.

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