Original Research

Postprandial Thermogenesis Is Increased 100% on a High-Protein, Low-Fat Diet versus a High-Carbohydrate, Low-Fat Diet in Healthy, Young Women

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Objective: The recent literature suggests that high-protein, low-fat diets promote a greater degree of weight loss compared to high-carbohydrate, low-fat diets, but the mechanism of this enhanced weight loss is unclear. This study compared the acute, energy-cost of meal-induced thermogenesis on a high-protein, low-fat diet versus a high-carbohydrate, low-fat diet.

Methods: Ten healthy, normal weight, non-smoking female volunteers aged 19-22 years were recruited from a campus population. Using a randomized, cross-over design, subjects consumed the high-protein and the high-carbohydrate diets for one day each, and testing was separated by a 28- or 56-day interval. Control diets were consumed for two days prior to each test day. On test day, the resting energy expenditure, the non-protein respiratory quotient and body temperature were measured following a 10-hour fast and at 2.5-hour post breakfast, lunch and dinner. Fasting blood samples were collected test day and the next morning, and complete 24-hour urine samples were collected the day of testing.

Results: Postprandial thermogenesis at 2.5 hours post-meal averaged about twofold higher on the high protein diet versus the high carbohydrate diet, and differences were significant after the breakfast and the dinner meals (p < 0.05). Body temperature was slightly higher on the high protein diet (p = 0.08 after the dinner meal). Changes in the respiratory quotient post-meals did not differ by diet, and there was no difference in 24-hour glomerular filtration rates by diet. Nitrogen balance was significantly greater on the high-protein diet compared to the high-carbohydrate diet (7.6 ± 0.9 and −0.4 ± 0.5 gN/day, p < 0.05), and at 24-hour post-intervention, fasting plasma urea nitrogen concentrations were raised on the high protein diet versus the high-carbohydrate diet (13.9 ± 0.9 and 11.2 ± 1.0 mg/dL, respectively, p < 0.05).

Conclusions: These data indicate an added energy-cost associated with high-protein, low-fat diets and may help explain the efficacy of such diets for weight loss.

Counter to the current U.S. Dietary Guidelines which promote diets high in complex carbohydrates (58% of total daily energy) [1], recent clinical investigations support the efficacy of high-protein, reduced fat diets for weight loss, as well as for improved insulin sensitivity and blood lipid profiles. In a randomized trial, 65 healthy, overweight and obese subjects consumed ad libitum a high-protein (HP), reduced fat diet (24% energy from protein, 29% energy from fat) or a high-carbohydrate (HC), reduced fat diet (59% energy from carbohydrate, 29% energy from fat) for six months [2]. Subjects consuming the HP diet lost more weight compared to subjects consuming the HC diet (7.5 kg vs. 5.0 kg after three months and 8.7 kg vs. 5.0 kg after six months). Moreover, 35% of the HP subjects lost >10 kg, whereas only 9% of the HC subjects attained this degree of weight loss. In obese, hyperinsulinemic subjects, hypoenergetic (80% of calculated energy expenditure) HP diets (45% energy from protein, 30% energy from fat) induced an even more pronounced weight loss compared to an isocaloric, HC diet (58% energy from carbohydrate, 30% energy from fat), 8.3 kg vs. 6.0 kg after four weeks [3]. The frequency of a weight loss >7 kg was 71% in the HP subjects vs. 16% in HC subjects. Fasting serum insulin, triglycerides and total cholesterol concentrations decreased significantly on both diets but reductions were 20% to 50% greater on the HP diet compared to the HC diet [3].

The mechanism of enhanced weight loss on HP vs. HC diets
may be attributed to a reduced energy intake, a lesser reduction in resting energy expenditure (REE) and/or greater food-derived thermogenesis. Subjects consuming an ad libitum low fat HP diet for six months averaged 450 kcal/day less than control subjects ingesting a low fat HC diet ad libitum [2]. Under experimental conditions, subjects consumed less energy when given HP meals vs. HC meals [4]; moreover, they consumed about 20% less energy at the subsequent meal [5,6]. Various physiologic consequences of protein ingestion likely impact satiety; in particular, proteins, unlike fats, starches or glucose, are potent stimulators of cholecystokinin, the major gastrointestinal hormone inducing satiety [7].

Modest energy restriction significantly lowers REE, but relative to comparable HC diets, hypoenergetic HP diets appear to spare REE. In obese subjects adhering to a reduced-energy HC diet for four weeks (diets provided 80% of maintenance energy), REE fell 17% (−380 ± 80 kcal/day); whereas, in subjects adhering to a reduced-energy HP diet, REE fell only 6% (−130 ± 50 kcal/day)[3]. The difference in REE by diet composition appears as early as six days after the initiation of the energy restriction and may relate to improved nitrogen balance, hence reduced losses in muscle mass, on the HP diet [8].

The thermic response to protein ingestion is 50% to 100% higher than that for carbohydrate [9,10], an effect generally attributed to the metabolic costs of peptide-bond synthesis, ureogenesis and gluconeogenesis. Using 24-hour energy expenditure data, Westerterp et al. [11] estimated that the difference in diet-induced thermogenesis between a combined HP/HC diet vs. a high-fat, low protein/carbohydrate diet amounted to an extra 90 kcal over a 24-hour period. However, the metabolic cost of a HP, low-fat diet relative to the currently recommended HC, low-fat diet is not known.

Using commonly consumed foods and meal plans, we designed a low-fat, HP (30% total energy) diet based on the popular HP diet book The Zone [12] and compared postprandial thermogenesis on this diet versus a HC, low-fat diet in young, healthy, normal weight women. To characterize the daylong effect of diet composition on thermogenesis, postprandial REE was measured at 2.5 hours after the breakfast, lunch and dinner meals. Identifying the magnitude of the extra thermic effect of HP diets may help explain the demonstrated success of these diets for weight loss.

**METHODS**

**Subjects and Experimental Design**

Ten healthy female volunteers were recruited from a campus population. None had renal or hepatic disease, diabetes mellitus, heart disease, hypertension or took prescription medications. All were nonsmokers and had regular menstrual cycles. Ages ranged from 19 to 22 years, and body composition measures were in normal ranges (Table 1). Participants gave informed consent, and the study was conducted in accordance with the guidelines of the Human Subjects Institutional Review Board at Arizona State University.

Subjects consumed each of the two experimental diets for one day in a randomized crossover manner. Testing was separated by a 28 or 56 day interval to control for possible confounding effects of menstrual cycle on energy expenditure. To assure similar baseline measures, on the two days prior to all testing, subjects consumed the HC (control) diet providing 50% of energy as complex carbohydrate, 10% as simple sugar, 15% as protein and 25% as fat. This diet was formulated based on the U.S. Dietary Guidelines and the U.S.D.A. Food Guide Pyramid. Control diet meals were prepared using scales and liquid measures at the test site, packaged and taken home by subjects. The energy content of the diets were determined for individual subjects using the Harris-Benedict equation to estimate basal metabolic rate (BMR), and total energy was calculated as BMR × 1.3, an energy intake appropriate for weight maintenance in lightly active adults. Subjects were instructed to consume all the foods provided, and only these foods, on these two days.

The third day, subjects reported to the test site at 0600 hours in a rested fasted state (no food or drink other than water after 2000 hours) and weight and height were recorded. Body composition was determined in the fasting state using whole body air displacement plethysmography (Bod Pod® Body Composition Systems, Life Measurement Instruments, Concord, CA). The mean of two body composition assessments was used to calculate percent body fat using the Lohman equation [13]. Metabolic measurements were recorded using a respiratory mask and two-way, non-rebreathing valve (Hans-Rudolph, Inc., Kansas City, MO) interfaced with a MAX-1 metabolic cart (Physiodyne Instrument Corporation, Quoque, NY). Upon arrival at the laboratory, subjects were positioned in a reclining chair and habituated to the open circuit spirometry metabolic analysis apparatus for 30 minutes in a temperature controlled (25–27°C) quiet room. The respiratory mask was placed over the subject’s face and carefully checked and sealed to prevent air leakage. Subjects were instructed to remain awake and not to move, fidget or talk once the mask was in place. Body temperature was recorded during this interval. Following the 30-minute habituation period, resting REE was estimated from

| Table 1. Physical Characteristics of the Female Subjects (n = 10) |
|---------------------------|-----------------------|---------------------|
| Age (years)               | 19.0 ± 0.4            | 18–22               |
| Height (m)                | 1.66 ± 0.01           | 1.59–1.74           |
| Weight (kg)               | 64.4 ± 2.4            | 55.0–77.3           |
| BMI1                      | 23.4 ± 0.9            | 18.6–28.4           |
| Body fat (%)              | 25.2 ± 2.3            | 13.9–36.1           |

1 Body mass index, kg/m².
a mean of 20 minutes of continuous gas sampling via indirect calorimetry using the Weir formula [14]. The coefficient of variation for this procedure was 3.08%, and the between and within day correlations were 0.70 and 0.90, respectively. The non-protein respiratory quotient (RQ) was calculated (VCO₂/VO₂) to estimate fuel utilization [15]. Gas analyzers were calibrated before and after each test by nitrogen and two primary standard gases accurate to 0.01%. The pneumotachometer was calibrated using a 3L syringe to deliver fixed volumes at variable flow rates.

Following testing, a baseline fasting blood sample was collected, and subjects then ingested the breakfast meal within a 15 minute period under observation. At two hours post-meal, subjects were again positioned in the reclining chair and habituated to the metabolic cart for 30 minutes, and energy expenditure was measured for 20 minutes as described above. The lunch meal was provided four hours after the breakfast meal and consumed within a 15-minute interval. Energy expenditure was again determined at 2.5 hours post-meal. Similarly, the dinner meal was provided four hours after the lunch meal, and energy expenditure determined at 2.5 hours post-meal. Subjects remained at the test site until all measurements were completed; their activity was restricted to reading or watching TV while sitting quietly. Subjects returned to the test site the following morning in the rested, fasted state and blood collected. On the day of testing, subjects provided complete 24-hour urine collections, defined as all urine excreted following the first morning void through the initial next morning void.

Two experimental diets were tested: the control HC diet described above and the HP diet (30% of energy as complex carbohydrate, 10% as simple sugar, 30% as protein and 30% as fat). Diets were devised using the Food Processor® for Windows Nutrition Analysis Software (Version 6.11, Esha Research, Salem, OR), and menus are shown in Table 2. Only common foods and food combinations were used, and the diet plans reflected typical American meal patterns. In the HP diet, egg whites, cottage cheese, turkey, and tuna were substituted for grains. The macronutrient compositions of the test meals are shown in Table 3. Test meals were prepared using scales and consumed self-selected diets for the 25 days between feeding periods.

**Blood and Urine Measures**

Blood samples collected in EDTA-treated Vacutainer® tubes (Becton Dickinson and Co., Franklin Lakes, NJ) were immediately centrifuged for 15 minutes at 1000 × g. Aliquots of plasma were stored separately at −45° until analyses. Plasma insulin was measured by immunoradiometric assay (ICN Pharmaceuticals, Costa Mesa, CA). Plasma and urine urea nitrogen and plasma and urinary creatinine were measured colorimetrically (Procedures #555 and #640, Sigma-Aldrich, St. Louis, MO). Apparent nitrogen balance was calculated as the difference between total dietary nitrogen and total urine nitrogen (urine urea nitrogen × 1.25) with a correction of 1.8 g nitrogen loss daily to account for obligatory and fecal losses [16]. Glomerular filtration rates (GFR) were calculated as [urine creatinine (mg/dL) ÷ urine volume (mL)/plasma creatinine (mg/dL) × min].

**Statistical Analyses**

Data are reported as the mean ± SEM. Differences between blood and urine indices were analyzed using one-tailed, paired t tests. Differences between mean post-meal values for thermogenesis, non-protein RQ and body temperatures were evaluated.
using multiple analyses of variance for repeated measures and appropriate post-hoc tests. Relationships between variables were assessed by the Pearson correlation measure. The level of significance was set at $p < 0.05$. The Statistical Package for the Social Sciences (SPSS Base 7.5 for Windows, Chicago, IL) was used for all statistical calculations.

RESULTS

Body weights did not differ on the mornings of the HP and HC test days. Fasting REE was similar prior to the diet intervention, 1396 ± 53 and 1359 ± 59 kcals/24 hours for HC and HP, respectively. Postprandial REE was 8 kcals/hour higher at 2.5 hours following the breakfast meal ($p < 0.05$) and 8 kcals/hour higher at 2.5 hours following the lunch meal on the HP diet versus the HC diet (Fig. 1a). At 2.5 hours after the dinner meal, postprandial REE was 14 kcals/hour higher on the HP diet compared to the HC diet ($p < 0.05$).

Body temperature rose steadily throughout the day on both diets (Fig. 1b). The change in body temperature from the fasting baseline value was $+0.1$ and $+0.4^\circ F$ at 2.5 hours after the breakfast meal and $+0.4$ and $+0.6^\circ F$ at 2.5 hours after the lunch meal for the HC and HP diets respectively ($p > 0.05$). At 2.5 hours after the dinner meal, the change in body temperature for the HP diet was nearly 40% higher than that for the HC diet ($+0.8$ and $+0.5^\circ F$ respectively, $p = 0.08$). Body temperature was related to REE in the HP group only (HP: $r = 0.66$, $p < 0.05$; HC: $r = 0.29$, $p > 0.05$).

The fasting non-protein RQ, an indicator of substrate oxidation, was similar prior to diet intervention ($0.81 ± 0.01$ and $0.79 ± 0.02$ for HC and HP, respectively), and the change in post-meal non-protein RQ did not differ by diet (Fig. 1c). Fasting plasma insulin concentrations before and after the diet intervention did not vary by diet ($20.8 ± 2.7$ and $19.8 ± 2.2 \mu U/mL$ prior to and $22.1 ± 2.7$ and $22.7 ± 3.7 \mu U/mL$ at 24 hours post-intervention, HC and HP respectively).

Fasting plasma urea nitrogen concentrations were similar prior to diet intervention, $11.2 ± 0.8$ and $11.0 ± 0.8$ mg/dL for HC and HP, respectively. At 24 hours post-intervention, fasting plasma urea nitrogen concentrations were raised ($p < 0.05$) on the HP diet versus the HC diet, $13.9 ± 0.9$ and $11.2 ± 1.0$ mg/dL, respectively (Table 4). GFR did not vary by diet treatment ($131.6 ± 15.2$ and $129.9 ± 19.5$ mL/min, HC and HP, respectively).
The ingestion of a palatable meal (parmesan fondue, spaghetti with meatballs and chocolate éclair) increased diet-induced thermogenesis nearly 50% more than if the same meal ingredients were blended, desiccated and consumed as a tasteless biscuit.

The absence of a thermic response to the HC diet at 2.5 hours after the breakfast meal seems contradicted, but this phenomenon has been noted by others [18]. The metabolic cost of glycogen synthesis and lipogenesis is believed to account for 55% to 65% of the thermic effect of carbohydrate ingestion [22], but only for 10% to 30% of the thermic effect of protein ingestion. The breakfast meal was consumed after an overnight, 12-hour fast; hence, it is conceivable that the ingested glucose was readily utilized by body tissues and not available for glycogen synthesis. At the lunch and dinner meals, nutrient storage would be enhanced as nutrient availability increased with repeated food ingestion.

Concomitant with the thermic response to the test diets was a slight rise in body temperatures. Although the changes in body temperature were not significantly different by diet, HP feeding was associated with a greater degree of body temperature change versus HC feeding, and at the dinner meal this change was nearly significant (+0.8 °F, p = 0.082). Furthermore, body temperature was related to REE over the 12-hour testing period for the HP diet only (r = 0.66, p < 0.05), supporting the contention of Brundin and Wahren [24] that protein ingestion elicits a pyrogen-like effect.

Postabsorptive protein synthesis increases 10% to 25% for high vs. low protein meals [16,25], and the metabolic cost of

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**Table 4. Nitrogen Balance Measurements and Urine Characteristics of Young Women Fed a High-Carbohydrate (60% Total Energy), Low-Fat Diet or a High-Protein (30% Total Energy), Low-Fat Diet for One Day**

<table>
<thead>
<tr>
<th></th>
<th>High-Carbohydrate Diet</th>
<th>High-Protein Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>N intake (g)</td>
<td>12.0</td>
<td>21.8</td>
</tr>
<tr>
<td>Plasma urea N (mg/dL)</td>
<td>11.2 ± 1.0</td>
<td>13.9 ± 0.9*</td>
</tr>
<tr>
<td>Urine urea N (g)</td>
<td>8.5 ± 0.4</td>
<td>9.9 ± 0.7</td>
</tr>
<tr>
<td>Apparent N balance (gN/day)</td>
<td>−0.4 ± 0.5</td>
<td>7.6 ± 0.9*</td>
</tr>
<tr>
<td>Urine (mL)</td>
<td>2299 ± 240</td>
<td>2658 ± 306</td>
</tr>
<tr>
<td>Urine creatinine (mg/day)</td>
<td>1085.9 ± 88.9</td>
<td>1049.7 ± 70.2</td>
</tr>
<tr>
<td>Plasma creatinine (mg/dL)</td>
<td>0.52 ± 0.04</td>
<td>0.50 ± 0.07</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>131.6 ± 15.2</td>
<td>129.9 ± 19.5</td>
</tr>
</tbody>
</table>

1 Mean ± SEM, n = 10; asterisk denotes significant difference, p < 0.05.
2 Corrections of 1.8 g N/day were made for obligatory and fecal losses [16], and urine urea nitrogen was extrapolated to total urine nitrogen (× 1.25).
3 Calculated as [urine creatinine (mg/dL) × urine volume (ml)]/[plasma creatinine (mg/dL) × min].

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**DISCUSSION**

These data demonstrate that meal-induced thermogenesis at 2.5 hours post-meal averages about twofold higher on a HP, low fat diet versus a HC, low-fat diet. Generally, postprandial thermogenesis has been associated with the protein content of a meal [9,10,17–19], and our data confirm this relationship. However, the difference in the energy cost of HP versus HC diets, particularly in the context of weight loss promotion, has not been addressed by healthcare professionals. Increased diet-induced thermogenesis, in association with the preservation of REE [3,8], may contribute to the reported weight loss success of diets high in protein with moderate levels of carbohydrate, in association with the preservation of body temperature were not significantly different by diet, HP feeding was associated with a greater degree of body temperature change versus HC feeding, and at the dinner meal this change was nearly significant (+0.8 °F, p = 0.082). Furthermore, body temperature was related to REE over the 12-hour testing period for the HP diet only (r = 0.66, p < 0.05), supporting the contention of Brundin and Wahren [24] that protein ingestion elicits a pyrogen-like effect.

Postabsorptive protein synthesis increases 10% to 25% for high vs. low protein meals [16,25], and the metabolic cost of...
Metabolic Cost of High-Protein, Low-Fat Diets

this enhanced protein synthesis likely accounts for the added thermic effect of dietary protein [22, 26]. Also, there is a net retention of amino acids in the body when dietary protein is increased, and nitrogen balance is positive, as high as $+7$ to $+13$ gN/day [27,28], but more typically $+3$ gN/day, even after the HP diet is consumed for an extended period [29]. The high positive nitrogen balance noted in the present trial likely represents a transient retention of nitrogen, either as urea or free amino acids such as glutamine in muscle tissue. Pannemans et al. [16] fed ten young women (27 ± 4 years) a HP diet (21% total energy as protein) for two weeks at which time nitrogen balance was positive, $+2.1$ gN/day.

The metabolic consequences of HP diets are controversial, but most experts agree that protein intakes should not exceed 2 g · kg$^{-1}$ · day$^{-1}$, the level utilized in the present report [30,31]. Americans typically consume 15% of dietary energy as protein, corresponding to about 1 g · kg$^{-1}$ · day$^{-1}$ [32]. An often cited, adverse effect of diets high in protein is a potential effect on renal function, and individuals with impaired kidney function are advised to reduce levels of dietary protein. Experimental data, however, indicate that GFR varies little when dietary protein ranges from 10% to 30% of total energy [33–35]. The data presented here further demonstrated that an acute change in dietary protein, 15% to 30% of dietary energy, had little effect on renal function in healthy individuals. Furthermore, both plasma urea nitrogen and urine nitrogen concentrations remained within normal ranges following the HP diet intervention.

The popularity of HP diets for weight loss is unquestionable. Although this research did not assess weight loss or the long-term effects of a HP diet, results indicated that the increased thermogenesis of a HP diet may contribute to its efficacy. The recent literature suggests that diets high in protein, but with a moderate carbohydrate and low fat content, do promote a greater degree of weight loss compared to the currently recommended high-carbohydrate, low-fat diets. When considering other health issues, HP diets should be low in saturated fat and rely on low-fat milk products, egg whites, poultry and fish as protein sources. Changes in postprandial thermogenesis induced by HP diets based on non-animal products versus HC diets awaits investigation.

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