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ScienceDirect
Metabolism Clinical and Experimental 57 (2008) 757–765
Metabolism
Clinical and Experimental
www.metabolismjournal.com

Moderate protein intake improves total and regional body composition and insulin sensitivity in overweight adults

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Received 18 July 2007; accepted 17 January 2008

Abstract

A high protein intake (~40% of energy intake) combined with aerobic and resistance exercise training is more closely associated with improved body composition and cardiovascular risk profile than a traditional protein intake (~15% of intake) combined with moderate-intensity aerobic exercise. However, there is concern that such high-protein diets may adversely affect health. We therefore tested the hypothesis that moderate protein intake (~25% of energy intake) would elicit similar benefits on body composition and metabolic profile as high protein intake. Twenty-four overweight/obese men and women (body mass index [BMI] = 32.2 ± 3.4, percentage of body fat [%BF] = 37.3 ± 8.0) were matched for BMI and %BF and randomly assigned to one of 3 groups for a 3-month nutrition/exercise training intervention: (1) high-protein diet (~40% of energy intake) and combined high-intensity resistance and cardiovascular training (HPEx, n = 8, 5 female and 3 male), (2) moderate-protein diet (~25% of energy intake) and combined high-intensity resistance and cardiovascular training (MPEx, n = 8, 5 female and 3 male), or (3) high-protein diet only (HPNx, n = 8, 5 female and 3 male). Total and regional body composition (dual-energy x-ray absorptiometry), insulin sensitivity (insulin sensitivity index to the oral glucose tolerance test), insulin-like growth factor–1 (IGF-1), IGF binding protein–1 (IGFBP-1), IGF binding protein–3 (IGFBP-3), and blood lipids were measured at baseline and after the intervention. All groups experienced significant ($P < .05$) and similar losses of body weight, BMI, and total and abdominal %BF, and similar improvements in insulin sensitivity (HPEx, 6.3 ± 1.2 vs 9.5 ± 0.98; MPEx, 6.2 ± 1.4 vs 8.4 ± 1.6; HPNx, 3.7 ± 1.1 vs 7.0 ± 1.1; insulin sensitivity index to the oral glucose tolerance test; $P < .05$) and leptin levels. Furthermore, the HPEx group demonstrated decreases in total cholesterol (TC) and triglycerides, and increases in IGF-1 and IGFBP-1. The MPEx group experienced decreases in TC, whereas the HPNx group had increases in high-density lipoprotein cholesterol, TC to high-density lipoprotein, IGF-1, and IGFBP-1. In conclusion, moderate protein intake elicits similar benefits in body composition and insulin sensitivity as a high-protein diet. These findings may have practical implications for individuals interested in diets containing elevated dietary protein.

1. Introduction

The recognition of obesity as a major public health concern has prompted an abundance of research focused on developing pharmacologic agents to prevent weight gain and promote weight loss [1]. Although significant progress has been made in elucidating the pathways that control energy homeostasis [2,3], this progress has thus far failed to thwart the worldwide spread of obesity. Consequently, lifestyle intervention programs involving exercise training and healthy nutritional practices are still the cornerstone of obesity treatment and prevention.

Although it is generally accepted that healthy nutrition and increased physical activity are essential components of

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doi:10.1016/j.metabol.2008.01.015

all lifestyle intervention programs, there is still controversy regarding the specific combination of diet and exercise that is most efficacious for combating obesity and its associated complications. In addition to efficacy, the practicality and feasibility of varying programs are of considerable concern given the high rate of weight recidivism [4].

Current recommendations advocate a high-carbohydrate (55%-65% of energy intake), low-fat (<30%), and low-protein (10%-15%) diet in conjunction with moderate-intensity aerobic exercise (50%-70% heart rate maximum) [5-7]. However, epidemiologic data from the Nurses' Health Study indicate that a higher protein intake (>15%) significantly reduces the risk for cardiovascular disease in women [8]. Furthermore, several intervention studies have reported that high-protein diets are as, if not more, effective than high-carbohydrate diets in reducing body weight and disease risk [9-11].

High-protein diets may be particularly beneficial for physically active individuals given the elevated protein turnover and requirements with regular physical activity [12,13]. Unfortunately, most of the available studies have examined the effects of a high-protein diet in sedentary individuals and/or have not adequately controlled for physical activity. We recently reported that, compared with a low-protein diet (15%) combined with moderate-intensity exercise, a lifestyle intervention program consisting of a high-protein diet (40%) consumed as 6 smaller meals per day and high-intensity exercise training resulted in greater reductions in total and abdominal body fat and several disease risk factors [14]. Despite the greater benefits of a high-protein diet, participant adherence and long-term efficacy of diets containing 40% to 50% of energy intake as protein have been questioned [15,16]. Furthermore, despite research to the contrary [17], there is concern among many health professionals that consuming 40% to 50% of energy intake as protein may have adverse effects on renal function and bone turnover, and may increase cardiovascular disease risk because of the high saturated fat and cholesterol content of protein-rich foods [18,19]. More modest elevations in protein intake (eg, 25% of energy intake) may minimize these potential adverse effects and reduce the weight recidivism seen with higher-protein diets. Therefore, it is important to determine if modest increases in protein intake, evenly distributed throughout the day, elicit similar beneficial effects as higher-protein diets on body composition and cardiometabolic disease risk factors. In this context, the purpose of the present study was to extend our previous findings [14] by comparing the effects of high vs moderate protein intake (40% vs 25%, respectively; consumed in 6 meals per day) in combination with high-intensity exercise training on body composition and cardiometabolic disease risk factors in a group of overweight, middle-aged men and women over a 3-month period. We hypothesize that a moderate protein intake would elicit similar benefits in total and regional adiposity and insulin sensitivity as a high protein intake.

2. Methods

2.1. Subjects

Twenty-four overweight or obese (body mass index [BMI] = 32.2 ± 3.4; percentage of body fat [%BF] = 37.3 ± 8.0) persons (15 female and 9 male) between the ages of 31 and 59 years were recruited using newspaper advertisements and e-mail distribution within the Saratoga Springs, NY, area. All subjects were healthy, nonsmokers, and free of overt metabolic and cardiovascular disease as assessed by a medical history and a comprehensive medical examination. All subjects were sedentary (<30 minutes, 2 d/wk of structured physical activity) and weight stable (±2 kg) for at least 6 months before the beginning of the study. Each participant provided informed written consent in adherence with the Skidmore College Human Subjects review board before participation.

2.2. Experimental design

Subjects were matched for BMI and %BF and randomly assigned to one of 3 groups for a 3-month nutrition and exercise training intervention: (1) high-protein diet (~40% of energy intake) and combined high-intensity resistance and cardiovascular training (HPEx, n = 8, 5 female and 3 male, age = 42 ± 8 years), (2) moderate-protein diet (~25% of energy intake) and combined high-intensity resistance and cardiovascular training (MPEx, n = 8, 5 female and 3 male, age = 47 ± 10 years), or (3) high-protein diet only (HPNx, n = 8, 5 female and 3 male, age = 54 ± 2 years). All testing procedures were measured at baseline and after the 3-month intervention period. It is important to note that we recently published a similar 3-month intervention study that included an inactive, nonexercising, age-matched control group (mean daily protein intake of ~18% of total energy) of 17 subjects (5 female and 12 male, age = 43 ± 11 years) who experienced no changes in any of the variables measured from pre- to posttesting [14]. As a result, we felt that inclusion of another control group for this study would not be appropriate or ethical given the lack of improvement in any of the variables measured in the first study. Instead, we incorporated a third group, who consumed the high-protein diet but did not perform any exercise, so we could assess the independent effects of the high-protein diet alone on our variables of interest.

2.3. Laboratory testing procedures

All laboratory procedures were conducted between 6:00 AM and 10:00 AM after a 12-hour fast and a 48-hour restriction of exercise, caffeine, and alcohol intake. Upon arrival to the laboratory, height and body weight (model number FS0900; Befour, Saukville, WI) were measured with subjects clothed in shorts and a T-shirt.

2.3.1. Total body and regional body composition

Total and regional body composition was determined by dual-energy x-ray absorptiometry (software version 4.1,

model DPX-IQ; Lunar, Madison, WI) with subjects in the supine position as previously described [20]. Total body adiposity is expressed as %BF. Regional adiposity was determined by creating regions of interest for the abdomen (region 1) and hip (region 2) using the region of interest option (with ruler) within the manual analysis menu of the Lunar software. Abdominal adiposity is expressed as percentage of abdominal fat, and body fat distribution is expressed as abdomen-hip ratio as previously described [21].

2.3.2. Oral glucose tolerance test, insulin sensitivity, blood lipids, insulin-like growth factor–1 system, and leptin

After a 12-hour overnight fast, a 75-g oral glucose tolerance test (OGTT) was administered to establish the level of glucose tolerance, plasma insulin response, and insulin sensitivity index to the oral glucose load (ISI_{OGTT}). The ISI_{OGTT} was calculated to assess whole-body insulin sensitivity using the validated formula by Matsuda and DeFronzo [22]:

$$ISI_{OGTT} = \frac{10\,000}{\sqrt{glucose_{fasting} \times insulin_{fasting} \times glucose_{mean,\ OGTT} \times insulin_{mean,\ OGTT}}}$$

The OGTT procedure performed in our laboratory has been previously described [23]. Resting heart rate was obtained in the supine position via telemetry using a Polar Heart Rate monitor (Polar a_3; Polar Electro, Warminster, PA) after 20 to 30 minutes of quiet resting before the OGTT procedure. Blood samples (~10 mL) from an antecubital vein were collected at times 0 (pre–glucose load), 30, 60, 90, 120, and 180 minutes after glucose ingestion and analyzed for the following parameters: plasma glucose (glucose oxidase method), insulin using a radioimmunoassay (Diagnostic Systems Laboratories, Webster, TX), serum free fatty acids (enzymatic colorimetric technique; Wako Chemicals, Richmond, VA), total cholesterol (TC) (enzymatic colorimetric method, COD-PAP, microtiter application; WAKO Chemicals), high-density lipoprotein cholesterol (HDL-C) (phosphotungstate-magnesium salt precipitation method), triglyceride levels (spectrophotometric microplate procedure), and serum leptin (immunoradiometric assay, Diagnostic Systems Laboratories). Circulating concentrations of total insulin-like growth factor–1 (IGF-I), IGF binding protein–1 (IGFBP-1), and IGF binding protein–3 (IGFBP-3) were quantified using a 2-site immunoradiometric assay. Total IGF-I required an acid-ethanol extraction procedure to extract IGFBPs. All analytes quantified by immunoradiometric assay and radioimmunoassay were counted on a gamma counter using 1-minute counts (Cobra gamma counter; Packard Instruments, Downers Groove, IL).

2.3.3. Three-day food diary

For 3 days before beginning the study and at 1-month intervals, each subject was asked to record daily the amount and time of day each food and beverage were ingested. The food logs were analyzed using the Food Processor SQL Edition (version 9.3; ESHA Research, Salem, OR) for each subject's 3-day food diary (2 week days and 1 weekend day). All dietary analyses were performed by the same laboratory technicians.

2.3.4. Exercise training

All training sessions were monitored by a member of the research team and a certified strength and conditional specialist. Exercise compliance was reinforced through weekly inspection of exercise journals, monthly group meetings, and daily exercise monitoring and subject-researcher contact. In the event that a subject missed a scheduled exercise session, it was made up on an alternate day that week so that all exercise sessions were fully completed for each week. The exercise training program consisted of alternating days of high-intensity resistance (RT) and cardiovascular training (CT) 6 d/wk for 20 and 40 minutes (CT and RT, respectively). The RT sessions alternated between upper body (chest, back, shoulders, biceps, and triceps) and lower body (quadriceps, hamstrings, calves, and abdominals) workouts performed on both free weight and weight machines (Paramount Fitness, Los Angeles, CA) in the specific order listed above. Sessions were designed to target larger muscle groups first, followed by smaller muscle groups. Two exercises were performed for each muscle group: subjects performed 4 sets of the first exercise, increasing the resistance (kilograms) and decreasing the repetitions (12-10-8-6). Subjects completed a fifth set of 12 repetitions of the first exercise at the same weight as the third set. A final (sixth) set of 12 repetitions of the second exercise was performed to complete the exercises for the respective muscle group. The total time for each resistance exercise session ranged between 35 and 40 minutes.

Cardiovascular training sessions were based on a high-intensity interval program in which participants rated their perceived exertion on a scale of 1 to 10 (1 = resting quietly, 5 = a warm-up level, 10 = an all-out exertion). Participants began with a 2-minute warm-up at level 5, increased their exertion each minute for 3 minutes until level 9 was perceived, and then recovered at level 6 for 1 minute. This same pattern was performed a total of 4 times. However, on the fourth cycle, participants increased their last minute of exertion to 10, followed by a 1-minute recovery at their initial warm-up level 5. The total time for the session was 20 minutes.

Caloric cost of exercise training was calculated for all participants in the HPEx and MPEx groups, as previously described [14]. Participants recorded the repetitions, weight lifted, and duration (minutes) for all RT sessions and the intensity level achieved for all CT sessions (see Methods above). Total exercise performed at baseline and week 12 was obtained from each subjects' daily exercise journal and subsequently analyzed for the calories expended using the

Table 1
Sample menus from the HPEx, HPNx, and MPEx 3-month dietary intervention plans (~2000 kcal)

	HPEx (n = 8) and HPNx (n = 8)	MPEx (n = 8)
Breakfast	Egg whites scrambled (5) 1 Slice whole-wheat bread 1 Teaspoon extravirgin olive oil Cottage cheese, 1/4 cup Red grapes, 1/4 cup Decaffeinated coffee, 1 cup Skim milk, 1 cup	Egg whites scrambled (4) 1 Whole-wheat tortilla Peach salsa, 2 tablespoons Orange juice, 1 cup
Midmorning snack	CarbSense protein bar (260 kcal) 27 g carbohydrate, 25 g protein, 8 g fat	AdvantEdge protein bar (240 kcal) 28 g carbohydrate, 17 g protein, 8 g fat
Lunch	Spinach, sautéed with olive oil 1 cup/1 teaspoon Sardines in oil, 6 oz 1 Slice whole-wheat bread Cottage cheese, 0.5 cup Skim milk, 1 cup Apple, 1 small	Spinach salad, 1.5 cup Baby carrots, 2 Red bell pepper, 1/3 cup Dried cranberries, 1/4 cup Red grapes, 1/4 cup 1 Whole-wheat bagel Balsamic vinegar dressing, 2 tablespoons Atlantic pollock fish, 4 oz
Midafternoon snack	CarbSense protein bar	AdvantEdge protein bar
Dinner	Chicken breast, broiled, 10 oz in teriyaki marinade, 2 tablespoons Asparagus sautéed in olive oil, 12/1 tablespoon Pineapple, 1/4 cup Barley, 0.5 cup Walnuts, 0.25 cup Skim milk, 1 cup	Broccoli, raw, 3/4 cup Mushrooms, raw, 2 Whole-wheat pasta, 1 cup Chicken, grilled, 4.5 oz Walnuts, 3 oz Peach, 1 medium
Evening snack	CarbSense protein shake (150 kcal) 5 g carbohydrate, 25 g protein, 3.5 g fat	AdvantEdge protein shake (180 kcal) 28 g carbohydrate, 13g protein; 3g fat

American College of Sports Medicine guidelines. Specifically, the resistance and cardiovascular exercises were assigned metabolic equivalent values of 10.0 and 12.5, respectively. The caloric cost of the exercise was then calculated from the following formula: caloric cost (kilocalories per week) = metabolic equivalent value (of given exercise) × body weight (kilograms) × time spent exercising per week (hours).

To assess the level of physical activity among the participants, the previously validated Aerobics Center Longitudinal Study Physical Activity Questionnaire was used to quantify physical activity over the previous 3 months (kilocalories per week and day) [24].

2.3.5. Nutritional intervention

Both experimental diets were similar in fat (~30% total energy) and low in refined sugar (<10% total energy) and saturated fat (<9% total energy). Diets were devised using the Food Processor SQL Edition (version 9.3, ESHA Research), which included common foods (see sample menus, Table 1). A 7-day menu cycle was provided for all participants and included breakfast, lunch, and dinner meal plans. All participants were provided verbal and written instructions regarding the meal frequency, appropriate portion sizes, and specific foods that met their respective dietary guidelines. Participants were instructed to consume foods according to their respective programs but were encouraged to eat until satisfied (ad libitum). The HPEx and HPNx meal plans consisted of 6 small protein (40%), carbohydrate (30%), and fat (30%) balanced meals. Participants were responsible for providing themselves with 3 of the 6 daily meals using the formulated 7-day meal plan menus consistent with the macronutrient composition and portion size. The remaining 3 daily meals were provided for them in the form of supplemental powder shakes they mixed with water, ready-to-drink shakes, or bars (CarbSense, EAS; Abbott Laboratories, Abbott Park, IL). The MPEx diet consisted of 6 small protein (~25%), carbohydrate (~45%), and fat (~30%) balanced meals; and participants were also provided 3 supplemental meals (AdvantEdge, EAS, Abbott Laboratories). It is important to highlight that the composition of both diets emphasized unprocessed, unrefined, natural whole foods and were thus high in fruits, vegetables, healthy oils, and lean sources of protein. To decrease boredom and increase compliance with the diets, subjects were allowed 1 "free day" and 2 to 3 servings of alcoholic beverages in a 7-day period. A registered dietician met weekly with study participants on an individual basis to answer questions and clarify dietary guidelines. Dietary compliance was further reinforced and monitored through daily subject-researcher contact, weekly inspection of nutrition journals, weekly return of empty supplement packets, and monthly group meetings.

2.3.6. Statistical analysis

The statistical evaluation of the data was accomplished by a 3 × 2 repeated-measures analysis of variance with group (HPEx, MPEx, and HPNx) and time (baseline, 12 weeks) as the factors using SPSS Statistical Analysis Software (version 14.0; SPSS, Chicago, IL). Where significant main effects were identified by repeated-measures analysis of variance, post hoc comparisons (Tukey test) were performed to locate differences. The total areas under the glucose and insulin curves were determined by computer analysis with a trapezoidal model that summated only the areas above the fasting baseline level. A Pearson product correlation coefficient was used to estimate associations between variables. Statistical power for the major outcome variables (total and regional body composition, ISI_{OGTT}, leptin, IGF-1 system, and blood lipids) ranged from 0.70 to 0.90 assuming a P value equal to .05 and N = 24 participants (8 per treatment group). The significance was set at $P < .05$. All values

Table 2
Subject characteristics at baseline and after lifestyle intervention in HPEx, MPEx, and HPNx

Variable	HPEx (n= 8)			MPEx (n= 8)			HPNx (n= 8)		
	Pre	Post	% Change	Pre	Post	% Change	Pre	Post	% Change
Age (y)	42 ± 3	–	–	44 ± 3	–	–	54 ± 2[b]	–	–
Body weight (kg)	88.2 ± 5.7	82.0 ± 5.3	−7.0 ± 0.8[a]	90.8 ± 4.9	85.3 ± 4.7	−6.3 ± 0.8[a]	94.5 ± 6.5	89.3 ± 5.9	−5.3 ± 1.0[a]
BMI	31.9 ± 1.3	29.7 ± 1.3	−6.9 ± 0.8[a]	32.1 ± 1.0	30.1 ± 1.1	−6.4 ± 0.8[a]	33.3 ± 2.2	31.5 ± 2.2	−5.4 ± 1.0[a]
Body fat (%)	38.2 ± 2.7	34.1 ± 3.1	−11.8 ± 2.2[a]	36.8 ± 3.0	33.2 ± 3.2	−11.0 ± 2.9[a]	40.3 ± 2.4	38.3 ± 2.6	−5.4 ± 1.3[a]
Total fat mass (kg)	31.4 ± 2.2	26.1 ± 2.3	−17.4 ± 2.3[a]	31.0 ± 2.6	26.7 ± 2.6	−15.1 ± 3.2[a]	35.7 ± 2.6	32.3 ± 2.8	−9.6 ± 1.8[a]
Lean body mass (kg)	51.8 ± 4.6	51.7 ± 4.7	−0.3 ± 0.7	54.6 ± 4.5	54.8 ± 4.5	0.7 ± 0.8	53.6 ± 4.9	52.9 ± 4.8	−1.1 ± 1.0
Lean body mass/body weight (%)	58.3 ± 2.6	62.6 ± 2.9	7.3 ± 1.1[a]	59.6 ± 2.8	63.9 ± 3.0	7.6 ± 1.3[a]	56.4 ± 2.1	59.0 ± 2.5	4.5 ± 0.9[a]
Waist circumference (cm)	101.6 ± 5.4	92.1 ± 4.9	−9.3 ± 0.7[a]	103.0 ± 3.9	94.6 ± 3.7	−8.5 ± 0.8[a]	102.2 ± 5.8	94.3 ± 4.8	−7.5 ± 0.8[a]
Abdominal fat (%)	40.7 ± 2.3	37.1 ± 2.7	−9.2 ± 2.4[a]	39.4 ± 2.8	36.6 ± 3.0	−6.2 ± 3.6[a]	42.0 ± 2.2	40.3 ± 2.3	−4.0 ± 1.2[a]
Abdominal fat (kg)	4.0 ± 0.4	3.3 ± 0.4	−18.7 ± 3.3[a]	4.1 ± 0.3	3.6 ± 0.3	−12.6 ± 3.3[a]	4.6 ± 0.4	4.3 ± 0.5	−7.2 ± 2.5[a]

Values are mean ± SE; significant effect of [a]time and [b]group by time interaction. Significance set at $P < .05$.

are reported as means ± standard errors (SEs) unless otherwise noted.

3. Results

3.1. Baseline characteristics

Men and women had similar patterns of response for all variables measured; and thus, the data were analyzed together for each group. Of the 15 women participants, 7 were postmenopausal; however, statistical analysis showed that they did not differ in response from premenopausal women for any of the measured variables. All premenopausal women were tested during the follicular phase (1 to 4 days) of the menstrual cycle based on the date of menstruation. Subject characteristics and selected outcome variables at baseline did not differ between groups and are shown in Table 2.

3.2. Assessment of energy intake and expenditure

Self-reported dietary energy and macronutrient intakes are shown in Table 3. The HP groups experienced reductions in self-reported total energy intake over the 3-month intervention despite being instructed to consume food ad libitum. All groups significantly increased dietary protein intake and decreased carbohydrate intake as intended; and the magnitude of change was significantly greater ($P < .05$) in HPEx and HPNx compared with MPEx, as designed. The percentage of dietary fat intake was unchanged from baseline in all groups, although the saturated fat intake declined significantly ($P < .05$) in all groups. Thus, these differences imply that when instructed to consume a particular macronutrient ratio intake ad libitum, energy intake among participants is approximately equal, despite significant differences in macronutrient composition (Table 3).

The level of physical activity during the preceding 3 months, estimated via questionnaire, among the groups at baseline was not different (HPEx, 273 ± 72; MPEx, 292 ± 67; HPNx, 213 ± 40 kcal/d). The estimated caloric cost of the exercise sessions was significantly increased ($P < .01$) from baseline to 12 weeks in both the HPEx and MPEx groups, as expected (HPEx, 1098 ± 90 vs 1450 ± 118; MPEx, 1132 ± 82 vs 1507 ± 115 kcal/wk), although not different from each other (data not shown in table form).

3.3. Body weight, composition, and fat distribution

Mean changes in body weight and total and regional body composition during the 12-week study interventions are shown in Table 2. Within all intervention groups, significant losses of body weight, BMI, and %BF were observed from baseline to 12 weeks; and the magnitude of change was similar among groups. However, it is important to note that a

Table 3
Dietary intake factors at baseline and after lifestyle intervention in HPEx, MPEx, and HPNx

Variable	HPEx (n = 8)			MPEx (n = 8)			HPNx (n = 8)		
	Pre	Post	% Change	Pre	Post	% Change	Pre	Post	% Change
Energy intake (kcal/d)	2180 ± 172	1855 ± 148	−15 ± 6[a]	2043 ± 213	1890 ± 222	−7.5 ± 7	2136 ± 267	1739 ± 152	−20 ± 7.5[a]
Protein (%)	14.7 ± 0.8	43.5 ± 1.6	202.1 ± 21.8[a,b]	16.7 ± 1.1	26.9 ± 0.8	70.0 ± 12.9[a]	17.1 ± 1.5	42.6 ± 1.2	136.6 ± 24[a,b]
Protein (g)	80.2 ± 5.6	187.0 ± 12.2	137.0 ± 14.3[a,b]	86.8 ± 8.6	109.8 ± 9.1	31.1 ± 15.8[a]	88.5 ± 6.5	153.8 ± 11.5	80.2 ± 10.5[a,b]
Carbohydrate (%)	48.0 ± 2.1	25.3 ± 1.6	−46.3 ± 5.0[a,b]	52.0 ± 4.0	41.9 ± 2.6	−7.1 ± 10.4[a]	50.6 ± 2.3	27.2 ± 1.5	−44.6 ± 5.5[a,b]
Carbohydrate (g)	266.2 ± 24.0	113.5 ± 12.4	−56.8 ± 5.1[a,b]	242.6 ± 23.6	183.1 ± 16.8	−19.3 ± 14.9[a]	280.3 ± 44.2	109.3 ± 6.5	−55.6 ± 5.4[a,b]
Fat (%)	35.1 ± 2.3	31.3 ± 0.8	−7.7 ± 7.9	33.1 ± 3.4	28.8 ± 2.3	−2.0 ± 17.8	29.2 ± 1.8	30.5 ± 2.7	11.6 ± 11.0
Fat (g)	85.6 ± 8.4	59.6 ± 2.8	−26.5 ± 6.8[a]	80.3 ± 11.9	53.0 ± 7.9	−16.6 ± 19.7[a]	70.7 ± 9.7	58.1 ± 6.5	−9.7 ± 11.7
Saturated fat (g)	29.5 ± 3.8	17.9 ± 1.3	−32 ± 9.6[a]	29.7 ± 4.4	13.6 ± 2.2	−41.8 ± 15.0[a]	23.6 ± 3.6	16.9 ± 2.8	−22.3 ± 14.8[a]
Fiber (g)	19.2 ± 3.1	16.3 ± 1.5	−1.0 ± 15.7	17.5 ± 2.5	20.5 ± 3.1	29.0 ± 26.3	22.4 ± 2.6	17.3 ± 1.3	−16.9 ± 10.5[a]

Values are mean ± SE; significant effect of [a]time and [b]group by time interaction. Significance set at $P < .05$.

Table 4
Cardiometabolic factors at baseline and after lifestyle intervention in HPEx, MPEx, and HPNx

Variable	HPEx (n = 8)			MPEx (n = 8)			HPNx (n = 8)		
	Pre	Post	% Change	Pre	Post	% Change	Pre	Post	% Change
TC (mg/dL)	206.9 ± 10.5	169.0 ± 13.5	−17 ± .2 8.0[a]	212.4 ± 10.5	193.6 ± 13.5	−9.7 ± 3.7[a]	208.0 ± 15.7	192.1 ± 10.8	−6.3 ± 4.8
HDL-C (mg/dL)	33.8 ± 4.9	33.2 ± 3.4	3.7 ± 8.2	29.3 ± 1.7	34.1 ± 3.7	13.3 ± 12.3	27.5 ± 1.5	31.6 ± 2.0	15.0 ± 4.3[a]
TC/HDL	7.1 ± 1.0	6.3 ± 1.0	−10.2 ± 8.7	7.7 ± 0.6	6.7 ± 0.6	−13.5 ± 7.7	8.0 ± 0.7	6.5 ± 0.8	−18.4 ± 7.6[a]
Triglycerides (mg/dL)	100.1 ± 16.1	75.2 ± 6.7	−36.5 ± 13.1[a]	101.1 ± 16.6	86.2 ± 6.7	−20.6 ± 22.9	69.1 ± 7.1	83.2 ± 18.3	17.4 ± 18.5
Fasting insulin (μU/mL)	4.4 ± 1.3	2.0 ± 0.1	−28.1 ± 13.4[a]	8.7 ± 3.8	4.0 ± 1.0	−14.9 ± 24.2	15.9 ± 5.8	2.0 ± 0.02	−61.1 ± 16.1[a]
Fasting glucose (mg/dL)	92.1 ± 3.7	88.4 ± 2.9	−3.1 ± 4.7	92.0 ± 4.4	86.8 ± 2.9	−5.8 ± 6.6	103.3 ± 7.3	93.3 ± 5.0	8.4 ± 4.9
FFA (mmol/L)	0.6 ± 0.07	0.6 ± 0.06	0.0 ± 0.00	0.6 ± 0.09	0.6 ± 0.06	0.0 ± 0.0	0.7 ± 0.1	0.8 ± 0.07	12.7 ± 11.9
Leptin (ng/mL)	67.0 ± 10.9	26.1 ± 8.8	−64.8 ± 7.1[a,b]	51.6 ± 12.2	34.4 ± 6.5	−19.2 ± 18.0 [a]	74.2 ± 17.3	26.9 ± 6.2	−58.3 ± 8.0[a,b]
IGF-1	396.6 ± 79.3	444.9 ± 79.7	16.0 ± 7.5[a]	264.5 ± 26.7	284.4 ± 21.4	10.2 ± 8.4	252.0 ± 14.9	306.9 ± 18.9	22.9 ± 7.0[a]
IGFBP-1	8.6 ± 2.9	16.1 ± 4.7	189.2 ± 90[a]	13.2 ± 4.2	16.5 ± 4.3	75.7 ± 42.1	10.0 ± 2.3	14.1 ± 3.0	79.5 ± 60.5[a]
IGFBP-3	4327.0 ± 359.2	4418.8 ± 310.1	7.5 ± 11.8	3795.8 ± 300.4	3859.8 ± 231.3	3.8 ± 6.2	4052.6 ± 262.4	3909.9 ± 175.3	−2.0 ± 4.8

Values are mean ± SE; significant effect of [a]time and [b]group by time interaction. Significance set at $P < .05$. FFA indicates free fatty acids.

strong trend ($P = .09$) existed for a greater loss of %BF in the 2 exercise groups compared with HPNx, highlighting the importance of exercise in combination with nutritional intervention on body composition. Furthermore, all groups displayed similar decreases in abdominal fat percentage and waist circumference. Despite the significant decreases in total body weight, BMI, waist circumference, and total and regional %BF, the ratio of total lean body mass to body weight percentage increased significantly in all groups, reflecting a significant reduction of total body fat mass over the 3-month lifestyle interventions.

3.4. Cardiovascular and metabolic parameters

The effects of the 12-week interventions on cardiometabolic risk factors are shown in Table 4. Total cholesterol and triglycerides decreased significantly only in HPEx, whereas TC decreased in MPEx; HPNx increased HDL-C and decreased TC/HDL-C.

Fasting insulin decreased to a similar extent only in the HP groups. Serum leptin decreased significantly in all groups, although the magnitude of decline was greater in HPEx and HPNx. Of particular interest, IGF-1 and IGFBP-1 increased in all groups; but the increase was significant only in HPEx and HPNx.

3.5. Glucose tolerance and insulin sensitivity

Both the plasma glucose (HPEx, 23 336 ± 1930 vs 20 404 ± 1795; MPEx, 23 080 ± 1554 vs 20 492 ± 1871; HPNx, 28 103 ± 3119 vs 22 935 ± 2329 mg/dL) and insulin (HPEx, 2485 ± 457 vs 1766 ± 262; MPEx, 2691 ± 476 vs 2727 ± 858; HPNx, 3306 ± 454 vs 2683 ± 545 μU/mL) responses (area under the curve, total) after the OGTT improved similarly ($P < .05$) only in the HP groups after the 3-month intervention (Figs. 1 and 2). In addition, there was a significant improvement in insulin sensitivity in all groups over the 3-month period (HPEx, 6.3 ± 1.2 vs 9.5 ± 0.98; MPEx, 6.2 ± 1.4 vs 8.4 ± 1.6; HPNx, 3.7 ± 1.1 vs 7.0 ± 1.1; ISI_{OGTT}; $P < .05$) (Fig. 3). In the pooled sample, the improvement in insulin sensitivity was positively related to the reduction in both abdominal body fat ($r = -0.40$, $P < .05$) and total %BF ($r = -0.62$, $P < .01$).

4. Discussion

We [14] and others [9,10,11,25] have previously shown that replacing a portion of dietary carbohydrate with protein elicits beneficial changes in body composition and cardiometabolic risk factors. Specifically, we previously reported that a lifestyle intervention program consisting of a high-protein diet (~40%) and high-intensity exercise training resulted in greater reductions in total and abdominal body fat and several disease risk factors compared with a low-protein diet (15%) and more moderate-intensity exercise. Given the high recidivism rate and poor compliance of high-protein diets [16], we examined whether similar health benefits could be derived from a more moderate protein intake (25%).

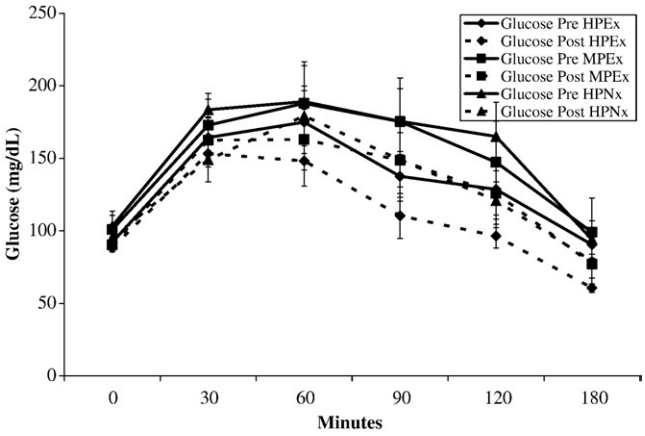

Fig. 1. The time course of change in plasma glucose during an OGTT in HPEx, MPEx, and HPNx before and after the 3-month interventions. Each value is mean ± SE.

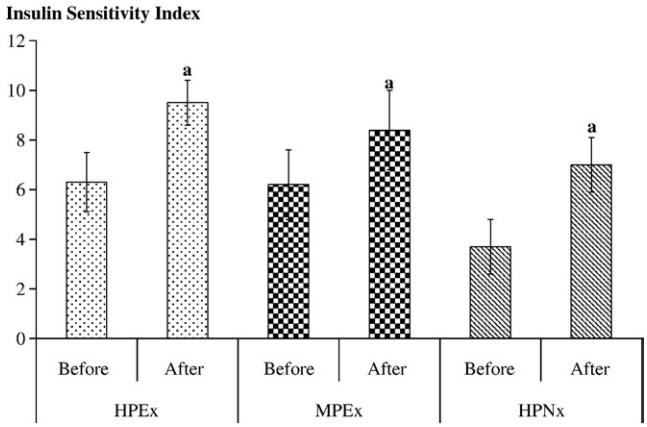

Fig. 3. The insulin sensitivity index after the OGTT in HPEx, MPEx, and HPNx before and after the 3-month interventions. Each value is mean ± SE. [a] $P < .05$.

The primary finding of the current study was that a lifestyle intervention program consisting of moderate protein intake and high-intensity exercise training was as effective as a program with an identical training component but higher protein intake (~40%) in improving body composition and insulin sensitivity. Furthermore, the beneficial effects observed in the study appear to be specific to the dietary intervention, as similar benefits were derived in groups with and without exercise. This finding may have important implications for individuals who are unable and/or unwilling to consume 40% of their daily calories as protein.

All groups lost significant amounts of body weight and total body fat, although there was a tendency for the 2 exercise groups (MPEx and HPEx) to decrease %BF to a greater degree ($P = .09$), suggesting an added benefit of combining the 2 lifestyle strategies. Perhaps more importantly, waist circumference and abdominal body fat significantly decreased to a similar extent in all groups. Given the close association between central adiposity and cardiometabolic disease [26,27], reductions in abdominal fat may directly translate into reduced cardiovascular and metabolic risk. Indeed, the reduction in abdominal adiposity (as well as total %BF) observed in the current study was directly related to the improvements in insulin sensitivity.

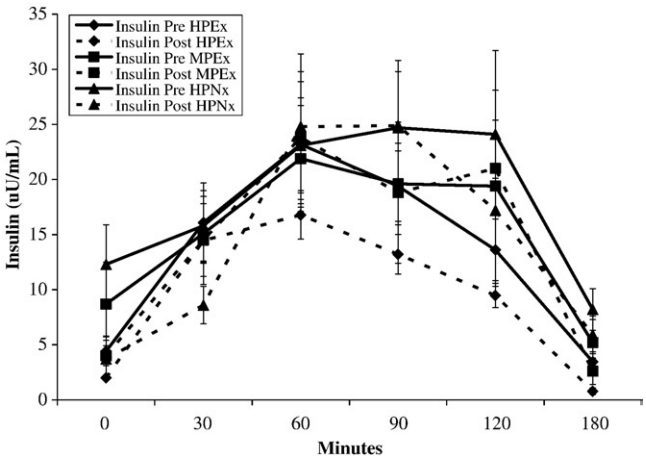

Fig. 2. The time course of change in plasma insulin during the OGTT in HPEx, MPEx, and HPNx before and after the 3-month interventions. Each value is mean ± SE.

Previous studies have reported that high-protein diets mitigate the reductions in lean body mass typically observed with dietary weight loss. For example, Layman et al [10] found that a reduced ratio of dietary carbohydrate to protein preserved lean body mass and promoted fat loss after 10 weeks of caloric restriction. In the current study, we found that lean body mass was maintained at both protein levels. In fact, when fat-free mass was expressed as a ratio of total body weight, groups experienced significant increases. One possible mechanism contributing to the maintenance of lean mass within the context of an overall body mass loss may lie in the observed increase in IGF-I. Insulin-like growth factor–I contributes to a positive nitrogen balance and is thought to modulate many of the beneficial aspects of physical activity in terms of muscle adaptation and remodeling [28]. Although the increase in IGF-I was surprising given that several studies have shown that IGF-I decreases after short-term training (<3 months) and caloric restriction, there is increasing evidence that illustrates the importance of dietary protein content in influencing IGF-I concentrations [29,30] and supports our finding in the HPNx group. It is important to note that weight training has also been shown to attenuate the reduction in lean body mass with caloric restriction [31]; and thus, we cannot differentiate the relative contributions of the exercise and dietary components to the maintenance of lean body mass. Still, these findings stress the importance of a lifestyle intervention program that incorporates both an RT program and a protein intake comprising at least 25% of total calories. This suggestion may be particularly important for older individuals given the accelerated reduction in lean body mass with advancing age.

We previously reported that 2 lifestyle intervention programs differing in protein intake and exercise intensity

had no effect on fasting plasma glucose levels [14], which is contrary to numerous studies indicating an improvement in insulin sensitivity after weight reduction [32,33]. The discrepancy is likely due to the lack of a direct measure of insulin sensitivity in our previous study. In light of that limitation and the conflicting data regarding the effects of a high-protein vs high-carbohydrate diet on insulin sensitivity [34], we included a more robust measure of insulin sensitivity in the current study. Indeed, our data showed a significant improvement in insulin sensitivity and a reduction in total areas under the curve for glucose and insulin in all intervention groups after the 3-month intervention, but no differential effects of high vs moderate protein consumption. Our results are concordant with some [10,35,36] but not all [29] studies reporting an improvement in insulin sensitivity with increased dietary protein intake and/or exercise training. Given the significant improvement in insulin sensitivity in our subjects, it is likely that a shift in substrate partitioning favoring increased fat oxidation occurred [37], contributing to the maintenance of lean body mass and improved total and abdominal fat loss observed in our subjects.

Triglycerides decreased significantly in HPEx but not in MPEx, which is in agreement with some [25,38] but not all [11] previous studies showing a greater reduction in triglycerides with high- vs low-protein diets. The lack of an effect in MPEx may be due to the higher carbohydrate intake in this group given the reduction in triglyceride clearance that has been observed after high-carbohydrate diets [39]. Both groups displayed improvements in cholesterol, although improvements differed slightly. Specifically, HPEx displayed a significant reduction in TC and a nonsignificant reduction in cholesterol to HDL ratio, whereas MPEx displayed a significant reduction in cholesterol to HDL ratio but no change in TC. In HPNx, only HDL-C and TC/HDL-C were increased. It is possible that a longer treatment program would have elicited more consistent changes in the groups; but nonetheless, the data demonstrate that both moderate and high protein intakes beneficially affect cholesterol levels.

Protein has been suggested to increase satiety and suppress food intake more than fat or carbohydrate [40,41]. Weigle et al [41] recently found that increasing dietary protein from 15% to 30% produced a significant reduction in food intake despite significantly decreased leptin levels, thus suggesting an increase in central nervous system leptin sensitivity. In the current study, plasma leptin levels dropped significantly in all groups; but the magnitude of change was greater in HPEx and HPNx compared with MPEx. It is unclear whether the greater reduction reflects an enhanced leptin sensitivity because the difference did not translate into greater weight loss in the 2 high-protein groups.

There are several limitations to the current study that should be noted. First, although we did not include a nonintervention control group, we have previously documented that a similar intervention using age-matched controls over a 12-week period (within a year time frame) elicited no changes in any of the variables measured and, therefore, did not feel it was appropriate or ethical to include such a group again. Similarly, we did not include a low-protein (eg, 15% of total kilocalories) comparison group, primarily because the effects of high- and low-protein diets have been previously compared and such a comparison was not the intent of the present study. Second, our cohort was primarily white; and thus, the results cannot be extrapolated to other ethnicities. Finally, in an attempt to minimize the internal variability, we chose to provide subjects with 3 meals per day of the total 6 meals per day they consumed. As a result, our findings may not be applicable to free-living conditions.

In conclusion, the study shows that 2 lifestyle intervention programs with identical training regimens but differing levels of protein intake (moderate and high) resulted in similar improvements in body weight, body composition, and insulin sensitivity. These findings suggest that the health benefits previously observed with high-protein diets can be derived from a much more modest and manageable level of protein intake. These results may have important and widespread application given the popularity of high-protein diets among the general public. Subsequent research is necessary to determine if the long-term efficacy and adherence of moderate-protein diets are greater than those of high-protein diets. Finally, health recommendations should consider advocating lifestyle modification programs consisting of a moderate protein intake in conjunction with CT and RT given the increasing body of literature demonstrating the widespread health benefits of such programs.

Acknowledgment

This study was supported by a grant from Abbott Laboratories, EAS division, to PJ Arciero. We would like to thank Thomas Spinella; Colleen Grossner, MSc, RD; and Monica Bracken, RD, for their excellent dietary counseling support and Tasha Ballard, PhD, for lipid assays. We are grateful to Debra Nichols and Anita Miczek for the timely ordering of all equipment and supplies throughout the study. We are especially thankful to the highly motivated subjects who completed this study with enthusiasm and dedication.

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