

Protein, weight management, and satiety^{1–4}

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ABSTRACT

Obesity, with its comorbidities such as metabolic syndrome and cardiovascular diseases, is a major public health concern. To address this problem, it is imperative to identify treatment interventions that target a variety of short- and long-term mechanisms. Although any dietary or lifestyle change must be personalized, controlled energy intake in association with a moderately elevated protein intake may represent an effective and practical weight-loss strategy. Potential beneficial outcomes associated with protein ingestion include the following: 1) increased satiety—protein generally increases satiety to a greater extent than carbohydrate or fat and may facilitate a reduction in energy consumption under ad libitum dietary conditions; 2) increased thermogenesis—higher-protein diets are associated with increased thermogenesis, which also influences satiety and augments energy expenditure (in the longer term, increased thermogenesis contributes to the relatively low-energy efficiency of protein); and 3) maintenance or accretion of fat-free mass—in some individuals, a moderately higher protein diet may provide a stimulatory effect on muscle protein anabolism, favoring the retention of lean muscle mass while improving metabolic profile. Nevertheless, any potential benefits associated with a moderately elevated protein intake must be evaluated in the light of customary dietary practices and individual variability. *Am J Clin Nutr* 2008;87(suppl):1558S–61S.

INTRODUCTION

Obesity is a multifactorial disorder associated with a host of comorbidities including hypertension, type 2 diabetes, dyslipidemia, coronary heart disease, stroke, cancer (eg, endometrial, breast, and colon), osteoarthritis, sleep apnea, and respiratory problems. In the past 30 y the incidence of obesity, defined as a body mass index >30 kg/m², has increased dramatically in the United States from 15% (1976–1980) to 33% (2003–2004) (1). Although the mechanisms contributing to obesity are complex and involve the interplay of behavioral components with hormonal, genetic, and metabolic processes (2, 3), obesity is largely viewed as a lifestyle-dependent condition with 2 primary causes: excessive energy intake and insufficient physical activity. Although both factors must be considered in any individually tailored intervention, this review will focus primarily on the role of dietary protein in body weight regulation. Specifically, there is evidence that modestly increasing the proportion of protein in the diet, while controlling total energy intake, may improve body composition, facilitate fat loss, and improve body weight maintenance after weight loss (3–6). A number of recent studies have

also demonstrated that a diet with a lower proportion of carbohydrate improves glycemic control in both healthy individuals and type 2 diabetic patients and can lead to improvements in fasting triacylglycerols, HDL cholesterol, and the total cholesterol-to-HDL ratio over a 6- to 12-mo period (7, 8). However, weight loss and maintenance are possible with either a low- or high-carbohydrate diet. Prior data from the Weight Control Registry suggested that among the common features of patients who successfully maintained long-term weight loss was the adoption of a low-fat, high-carbohydrate diet (9). More recent data indicate that diets with moderate fat content may also be effective (10). Nevertheless, positive outcomes associated with increased dietary protein are thought to be due primarily to lower energy intake associated with increased satiety (8, 11–13), reduced energy efficiency and/or increased thermogenesis (14–16), positive effects on body composition, specifically lean muscle mass (4, 17, 18), and enhanced glycemic control (18, 19).

PROTEIN INGESTION AND SATIETY

It is well established that under most conditions, protein is more satiating than the isoenergetic ingestion of carbohydrate or fat (8, 11–13). This suggests that a modest increase in protein, at the expense of the other macronutrients, may promote satiety and facilitate weight loss through reduced energy consumption (20). The increased satiety from protein has been observed in a single meal (21, 22) and over 24 h (23). In one short-term study, satiety

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and metabolic rate were examined over a 24-h period in a respiration chamber. Throughout the day, satiety was greater in the high-protein group (protein/carbohydrate/fat: 30/60/10% energy) compared with the high-fat group (protein/carbohydrate/fat: 10/30/60% energy). Importantly, this effect was noted during postprandial periods as well as during meals (12). It must be noted, however, that in this instance greater satiety was observed in response to a 3-fold greater protein load, a condition unlikely to represent a normal dietary intake for most individuals. Despite some evidence that habitual exposure to a higher-protein diet may diminish its effect on satiety (24), others have suggested that the greater satiating effects of a higher-protein diet are relatively long lasting (25–27). In a 16-week study, subjects consuming a high-protein (34%)/lower-fat (29%) diet reported greater post-meal satiety than subjects consuming a standard protein (18%)/higher-fat (45%) diet (27).

In some cases, the generally higher satiating effects of protein are not evident (28). Acutely, carbohydrate is very satiating, yet protein usually has a greater prolonged satiating effect. However, under normal conditions, fiber intake, the timing of the assessment, the food form (ie, solid versus liquid), or coingestion of other macronutrients may ultimately influence reported satiety (29, 30).

There is some suggestion that different protein sources differentially affect satiety. Specifically, it has been shown that ingestion of animal (pork) protein resulted in a 2% higher energy expenditure than ingestion of a plant-based protein (soy) (31). Further, there is evidence that more rapid gastric emptying and a postprandial increase in plasma amino acid concentrations after ingestion of specific proteins (eg, whey versus casein) (32) may increase satiety because of a greater stimulatory effect on gastrointestinal hormones such as cholecystokinin and glucagon-like peptide-1 (33). For example, casein-derived peptides (casomorphins) reduce gastrointestinal motility, resulting in lower postprandial plasma amino acid concentrations, which in turn blunt the satiating effect of higher plasma amino acid concentrations. In comparison, caseinomacropeptide, a glycosylated peptide comprising 15–20% of whey products, stimulates cholecystokinin production and has been shown to increase satiety in some (34), but not all (35), studies. However, despite the suggestion of acute or transient benefits attributable to specific proteins, any such effect may be masked by the concomitant ingestion of a mixture of proteins and other macronutrients in a normal mixed diet.

Ghrelin has been shown to stimulate appetite and promote food intake and may facilitate weight gain (32). Plasma ghrelin concentrations follow a cyclical pattern, increasing before meals and decreasing shortly thereafter. The postprandial reduction is influenced by the relative proportion of macronutrients in a meal, with a greater decrease after protein and carbohydrate ingestion than after fat ingestion (36). However, increased satiety and reduced appetite associated with an increased dietary protein intake may not be mediated by ghrelin homeostasis (27).

RESTING ENERGY EXPENDITURE AND THE THERMIC EFFECT OF FOOD

Total energy expenditure is the sum of resting energy expenditure, the thermic effect of food, and energy expenditure related to activity. Whereas energy expenditure associated with physical activity offers the most flexibility and may increase several fold

above sedentary levels, resting energy expenditure is generally the largest component of total energy expenditure (65–75%) (34, 37). The energy expenditure due to muscle metabolism is the only component of resting energy expenditure that has the capacity to vary considerably. Although comparatively small relative to total energy expenditure, a small difference in the quantity of lean muscle mass could have a significant effect on energy balance (38). Nevertheless, the role of muscle mass in the prevention of obesity has seldom been examined.

There is a general consensus in the literature that protein stimulates dietary-induced thermogenesis to a greater extent than other macronutrients (14–16). The metabolic energy of protein, as defined by the Atwater factor, is 17 kJ/g. However, protein is particularly thermogenic, and the net metabolizable energy is actually 13 kJ/g, making it lower than either carbohydrate or fat (39). Several explanations have been offered for the increased thermogenic effect of protein. For example, it has been suggested that increased protein turnover accounts for most (68%) of the acute thermogenic effects of protein feeding (31). The body has no flexible storage capacity to cope with increased protein intake and therefore has to actively oxidize or otherwise eliminate excess amino acids, which subsequently increases thermogenesis (31, 40). High-protein meals may also increase thermogenesis and energy expenditure via an up-regulation of uncoupling proteins (2, 31). In animal models, increased protein intake increases uncoupling protein-2 in liver and uncoupling protein-1 in brown adipose tissue. These changes are positively correlated with energy expenditure (2).

In the literature, the definition and composition of a high-protein diet vary considerably, with intakes ranging from expression as a percentage of daily energy intake (27–68%) to an absolute amount (90.5–284 g/d). Whereas protein intake is often expressed as a percentage of total energy intake, during weight loss the absolute protein intake is more relevant (41). When weight loss occurs and energy intake is reduced, the absolute amount of protein ingested can drop below the current Recommended Dietary Allowance value of $0.8 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$, even when the percentage of calories from protein remains the same. In this instance, expressing protein intake as a percentage of calories may be misleading (6). Moreover, protein intake may be within the acceptable macronutrient distribution range, which is expressed as a percentage of energy, but still be below an amount that is optimal for health and disease prevention.

WEIGHT MANAGEMENT

Several studies have suggested that higher protein diets may increase total weight loss and increase the percentage of fat loss (18, 42, 43). In a 6-month randomized trial of 60 overweight and obese subjects, fat loss was almost twice as great in subjects receiving a high-protein diet (25% energy; 128–139 g/d) compared with a moderate-protein diet (12% energy; 76–80 g/d) (44). The benefits of a higher-protein diet have also been demonstrated in longer-term studies. In a recent 12-mo study, 50 overweight and obese subjects initially spent 6-months consuming a high-protein (25% energy) or medium-protein (12% energy) diet. Consistent with previous studies, weight loss was greater in the high-protein group (−9.4 versus −5.9 kg). During the ensuing 6-mo follow-up period, the high-protein group experienced a 10% greater reduction in intra-abdominal adipose tissue than the medium-protein group (45). As noted previously,



the negative energy balance produced by higher-protein diets is probably due to a lower spontaneous energy intake brought about by enhanced satiety (11–13) and a greater thermogenic effect (14–16).

This ability of a moderately higher-protein diet to limit weight regain after weight loss is ultimately the key determinant of efficacy. In a study of 113 moderately overweight men and women who lost 5–10% of their body weight during a 4-wk very-low-energy diet, those who consumed 18% of their energy intake as protein (101.7 g/d) during a 6-mo weight management phase regained less weight than subjects who consumed 15% of their energy intake as protein (82.7 g/d) (17). Despite only a 3% difference in protein-derived energy, the researchers noted that this effect was independent of changes in cognitive restraint, physical activity, resting or total energy expenditure, and hunger scores, as none of these parameters differed between groups. Thus, for maintenance of weight loss, it may be beneficial to modestly offset other energy sources with protein (42).

In addition to the positive outcome measures reported in controlled studies, there is a potential practical benefit associated with higher-protein diets that directly addresses one of the key areas linked to failed weight loss strategies: compliance. Groups consuming a moderate-carbohydrate, high-protein diet have an increased likelihood of maintaining weight loss at 12 mo and beyond, with improvements in cardiovascular risk factors and minimal risk of side effects (46, 47). Similarly, in a 12-mo trial overweight subjects, Due et al (45) reported substantially greater compliance in subjects consuming a higher-protein diet (25% energy) of 8% drop out, compared with subjects consuming a lower-protein diet (12% energy) of 28% drop out. Although there is general agreement that permanent weight reduction is difficult to achieve with radical diet and lifestyle changes, long-term adherence to a moderately higher-protein, energy-controlled diet may represent a feasible lifestyle adaptation and be more likely to result in improved weight loss and management.

CONCLUSION

Body weight management is a complex task involving the interplay of behavioral components with hormonal, genetic, and metabolic processes. Protein has the potential to play a key role in several aspects of body weight regulation. The mechanisms by which increased dietary protein regulate body weight are multifactorial. However, taken together, evidence suggests that a moderate increase in dietary protein in association with physical activity and an energy-controlled diet may improve the regulation of body weight by 1) favoring retention or accretion of fat-free mass at the expense of fat mass at a similar physical activity level, 2) reducing the energy efficiency with respect to the body mass regained, and 3) increasing satiety.

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