The significance of protein in food intake and body weight regulation

Margriet S. Westerterp-Plantenga

Purpose of review
To highlight the underexposed but important role of protein in food intake and body weight regulation.

Recent findings
Protein plays a key role in food intake regulation through satiety related to diet-induced thermogenesis. Protein also plays a key role in body weight regulation through its effect on thermogenesis and body composition. A high percentage of energy from dietary protein limits body weight (re)gain through its satiety and energy inefficiency related to the change in body composition.

Summary
Protein is more satiating than carbohydrate and fat in the short term, over 24 h and in the long term. Thermogenesis plays a role in this satiety effect, but the role of satiety hormones still needs to be elucidated. On the short-term 'fast' proteins are more satiating than 'slow' proteins, and animal protein induces a higher thermogenesis than vegetable protein. In the longer term the higher postabsorptive satiety and thermogenesis are sustained irrespective of the protein source. High-protein diets affect body weight loss positively only under ad-libitum energy intake conditions, implying also a decreased energy intake. Body composition and metabolic profile are improved. Additional protein consumption results in a significantly lower body weight regain after weight loss, due to body composition, satiety, thermogenesis, and energy inefficiency, while the metabolic profile improves. Implications from these findings are: for practice, recommendations for increasing the percentage of energy from protein while reducing energy intake; for clinical research, assessment of the paradox of increasing the percentage energy from a highly satiating macronutrient; of the potential roles of protein in a negative and positive energy balance; assessment of possibilities of replacing dietary protein by effective amino acids or peptides that may show a similar impact on body weight regulation.

Keywords
food intake regulation, body weight regulation, satiety, body composition, thermogenesis, energy efficiency

Curr Opin Clin Nutr Metab Care 6:635–638.

Department of Human Biology, Nutrim, Maastricht University, Maastricht, The Netherlands

Correspondence to Dr M.S. Westerterp-Plantenga, Department of Human Biology, PO Box 616, 6200 MD Maastricht, The Netherlands
Tel: +31 43 3881566; fax: +31 43 3670976; e-mail: m.westerterp@hb.unimaas.nl

Current Opinion in Clinical Nutrition and Metabolic Care 2003, 6:635–638

Abbreviation

DEE diet-induced energy expenditure

1363-1950

Introduction

Since obesity, with its comorbidities such as the metabolic syndrome and cardiovascular diseases, is one of the major biomedical problems of the last few decades, efficient, effective and satisfying treatments are necessary. The system of body weight regulation, however, shows a high degree of redundancy, that is when one pathway is modulated, another one appears at least partly as a compensator or replacer [1]. Therefore, it is of significance to find a possible treatment that affects different short and long-term mechanisms. We hypothesize that elevated protein intake may serve this purpose because of its contribution to storage of fat free mass [2], its low energy efficiency during overfeeding [3,4], and its increased satiety effect despite similar energy intake [5]. The 'Stock hypothesis' states that during overfeeding a relatively high percentage of energy as protein might have a limiting effect on body weight gain in humans through an energy inefficiency effect [3,4]. I suggest that this may also be applicable during weight regain. The low energy efficiency may be partly due to the composition of the body mass regained; fat free mass makes the cost of energy storage high [6]. The third part of the hypothesis is based upon our observation of a sustained higher satiety over 24 h during a high-protein diet without significant differences in energy intake [5], which may facilitate a low energy intake during weight maintenance.

The first part of this review deals with the relationship between the satiating and thermogenic effects of protein. The second part highlights the effect of high-protein diets on body weight loss. The third part deals with a high-protein diet and the effect on maintenance of body weight after weight loss.

Protein plays a key role in food intake regulation through satiety and diet-induced thermogenesis

Tuning energy intake to energy expenditure is realized by interaction of a variety of factors that control the actual food intake and meal pattern. Hunger, satiety and sensory signals are the main regulatory factors of meal size, meal frequency, and food selection.

On considering different satiating efficacies of the macronutrients protein, carbohydrate and fat, a hierarchy has been reported with protein as the most satiating and fat as the least satiating [5,7,8•–10•]. At the same time, a priority is shown with respect to the magnitude of the rate at which these macronutrients are metabolized [5,8•,10•]. A possible relationship between perception of satiety and metabolic rate with different macronutrient compositions was assessed in a controlled situation over 24 h in a respiration chamber. The volunteers were fed to energy balance and were provided with an activity protocol, which was the same on each day. They ingested predetermined, identical amounts of energy and volume from similar foods (with respect to organoleptic characteristics) at identical times in a fully controlled situation: a high-protein/high-carbohydrate diet (protein/carbohydrate/fat, percentage of energy 30/60/10) and a high-fat diet (protein/carbohydrate/fat, percentage of energy10/30/60). Throughout the day, in between meals, satiety and fullness were significantly higher on the high-protein/high-carbohydrate diet, than on the high-fat diet, while hunger, appetite, desire to eat, and estimated quantity to eat were significantly lower. Satiety was not only higher in the postprandial state during the high-protein/high-carbohydrate diet, it was also higher during the high-protein/high-carbohydrate meals, and hunger was lower compared with the high-fat meal. Moreover, a higher Diet-induced Energy Expenditure (DEE) was observed with a high-protein/high-carbohydrate diet compared with the DEE with a high-fat diet. Satiety was positively related to 24 h DEE. The theoretical basis of this relationship between satiety and DEE may be that increased energy expenditure at rest implies an increased oxygen consumption and an increase in body temperature which may be translated into satiety feelings [5]. This idea is derived from observations of higher satiety scores under limited oxygen availability conditions, as observed at high altitude [11] and in chronic obstructive pulmonary disease patients [11].

Thus when volunteers, in this case, lean women, ingest identical amounts of energy and volume in identical meal patterns and similar meal compositions, a difference in the satiety level due to a high-protein/high-carbohydrate diet versus a high-fat diet was related to a difference in the 24 h DEE component of energy expenditure. Higher satiety on a high-protein diet under similar energy intake conditions was also shown in the longer term during a weight maintenance/weight regain period [12,13]. This supported the improved weight maintenance in overweight to moderately obese men and women who consumed 18% of energy intake as protein after $7.5 \pm 2.0\%$ body weight loss over 4 weeks compared with their counterparts who consumed 15% of energy intake as protein [12,13].

Observations like these may be partly dependent on the source of protein, in that animal (pork meat) protein has been shown to produce a 2% higher energy expenditure than vegetable protein in soy [14]. Under longer term conditions, however, a variety of sources of protein intake are always present.

Also, in the short term, evidence for differences in short-term satiety between protein from different sources, for example whey and casein, has been presented. The digestion and absorption of whey and casein differ in that casein, unlike whey, coagulates in the stomach due to its precipitation by gastric acid [15]. As a result, overall gastric emptying time for casein appears to be longer and a smaller postprandial increase in plasma amino acids was observed compared with the noncoagulating whey protein.

Postprandial satiety appeared to be larger after a whey preload than after a casein preload, related to increased concentrations of amino acids in the blood together with stronger elevation of both cholecystokinin and glucagon-like peptide-1 [9•,16].

In rats, protein was also shown to be more potent than carbohydrate for reducing appetite, in a dose-dependent manner. The animals were more satiated by protein when the proportion was 35–50% than by carbohydrate. At least 1 day was necessary, however, before a significant decrease in the energy intake following the protein loads was observed; thus the animals had to learn the postingestive effects of the loads before the response stabilized. The authors conclude that the larger the proportion of protein in the food, the larger the satiating effect, but the quality of protein did not seem to play a significant role [17•]. The same group showed that a high-protein diet enhances satiety without conditioned taste aversion in the rat [18•]. Another effect of the high-protein diet was related to macronutrient choice, in that Wistar rats which were allowed to self-select macronutrients from weaning to maturity chose a high-protein, high-lipid diet. Moreover, insulinemia was lower in both male and female self-selecting rats. The high-protein/high-fat diet chosen by the self-selecting rats could be linked to the prevention of age-related insulin resistance [19•].

In conclusion, most of the papers show evidence for protein being more satiating than carbohydrate and fat in the short term, over 24 h and in the long term, which is unlikely to be due to taste aversion. Thermogenesis plays a role in the satiety effect, but the role of satiety hormones still needs to be elucidated more clearly. Small short-term postprandial differences were shown due to the source of the protein – ‘fast’ proteins being more satiating than ‘slow’ proteins, and animal protein inducing a higher energy expenditure than vegetable protein. In the longer term, however, the higher postabsorptive satiety and thermogenesis were sustained, with high-protein diets consisting of a variety of proteins from the usual different sources [5,12,13,20,21, 22••,23••].

Changes in body weight and body composition during a high-protein diet for weight loss

High-protein diets have been administered during weight loss as well as during body weight regain. Skov *et al.* [20] compared a high-protein diet with a control diet in order to evaluate weight loss over 27 weeks when energy intake is *ad libitum*. The effects of 25% versus 12% energy intake from protein (25% protein, 45% carbohydrate, 30% fat versus 12% protein, 58% carbohydrate, 30% fat) on weight loss in obese subjects (body mass index = 30) was examined. It was found that weight loss (8.9 versus 5.1 kg) and fat loss (7.6 versus 4.3 kg) were significantly higher in the high-protein group due to a lower energy intake (5.0 versus 6.2 MJ/day); $P < 0.05$. Also, Dumesnil *et al.* [21] found a favourable effect of a high-protein diet on body weight during *ad libitum* feeding. The low-glycemic index/low-fat/high-protein diet resulted in a spontaneous decrease in energy intake of 25% compared with a high-carbohydrate/low-fat diet (8.8 versus 11.7 MJ/day) in the ad-libitum situation, and the metabolic profile had considerably improved. Body weight loss was 2.3 kg over 6 days compared with no weight loss on the high-carbohydrate diet. In comparison with an iso-energetic high-carbohydrate diet, however, there was no significant difference in body weight loss [21]. Laymen *et al.* [22••] found an improved body composition due to a reduced ratio of dietary carbohydrate to protein and improved blood lipid profiles during weight loss in adult women. Weight loss on the high-protein diet, however, was not different from the control group, probably due to lack of difference in energy intake [22••].

In a 6-month randomized trial comparing the effects of a very low carbohydrate diet and a calorie-restricted low-fat diet on body weight and cardiovascular risk factors in healthy women [23••], it appeared that the very low carbohydrate diet group lost more weight (8.5 versus 3.9 kg; $P < 0.001$) and more body fat (4.8 versus 2.0 kg; $P < 0.01$) than the low-fat group. On closer inspection of the data, the low-carbohydrate group increased the percentage energy from protein from 16% to 28%, while the low-fat group increased this percentage from 15% to 18%. I suggest that the greater body weight loss may be due to the high-protein component in that diet. Also the lean body mass was reduced relatively less and the fat mass relatively more on the low-carbohydrate/high-protein diet [23••]. Taken together, body weight loss on a high-protein diet appears to be greater under ad-libitum energy intake conditions, leading to decreased energy intake [20,23••], suggesting that in addition to metabolic effects of protein on body weight loss, energy intake plays a role. Under iso-energetical conditions no statistically significant difference in body weight loss was shown between the high-protein and the high-carbohydrate diet. Most studies showed an improved body composition and metabolic profile on a high-protein diet.

Changes in body weight and body composition during a high-protein diet for weight maintenance

Until now, only two studies have reported observations on maintenance of body weight with a high-protein diet after body weight loss. It was shown that overweight to moderately obese men and women who consumed 18% of energy intake as protein regained less weight (1 kg) during the 3 months after $7.5 \pm 2.0\%$ body weight loss over 4 weeks compared with their counterparts who consumed 15% of energy intake as protein and regained 2 kg. The result was not due to possible differences in dietary restraint or in physical activity between the high-protein and the control group, indicating a metabolic effect of protein [12,13]. Body composition of the body mass regained was more favorable in the additional-protein group, that is there was no regain of fat mass but only of fat free mass, resulting in a lower percentage of body fat. A similar result was found after 6 months of weight maintenance [13]. Leptin concentrations from fasting blood samples increased significantly slower during weight regain in the additional-protein group, and only in the control group was the increase in leptin related to the increase in fat mass. Moreover, metabolic risk characteristics were reduced in the additional-protein group [12]. Energy efficiency (kg body mass regain/energy intake) was significantly lower in the additional-protein group. The observation with respect to energy efficiency during weight regain is comparable to the 'Stock hypothesis' described for weight gain [3,4]. Satiety was higher on the high-protein diet, while there was no indication for a difference in energy intake [12]. Taken together, evidence for our combination hypothesis for weight maintenance was shown in that increased protein intake sustained weight maintenance by (1) favoring regain of fat free mass at the cost 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 [2–5].

Thus the studies on weight maintenance after weight loss show that additional protein consumption resulted in a significantly lower body weight regain, only consisting of fat free mass, related to increased satiety and decreased energy efficiency. In addition, an improvement in the metabolic profile was shown.

Conclusion

The role of protein in body weight regulation in comparison to other macronutrients, especially in comparison to carbohydrate, consists of different aspects, including satiety, thermogenesis, energy efficiency and body composition. These aspects are partly related to each other.

First of all, protein appears to increase satiety and therefore sustains reduced energy-intake diets, preferably under ad-libitum conditions. Under such conditions in energy balance as well as in a negative energy balance, protein appears to reduce energy intake. The highly satiating effect of protein has been observed postprandially as well as postabsorptively. Postprandially the type and source of protein may be of importance, but postabsorptively the satiating effect is still present with varying types and sources. The background of the satiating effect still needs to be further elucidated. Thermogenesis as well as satiety hormones appear to play a role.

Second, high-protein diets appear to imply high thermogenesis, with satiety being related to this. Animal protein showed a higher thermogenesis than vegetable protein. In the longer term this high thermogenesis contributes to the low energy efficiency of protein.

Third, under conditions of body weight regain (while aiming for weight maintenance), a high-protein diet shows reduced energy efficiency related to a different body composition of the body weight regained in favor of fat free mass.

Fourth, during body weight loss, as well as during weight regain, a high-protein diet preserves or increases fat free mass and reduces fat mass, as well as improving the metabolic profile.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1 Westerterp-Plantenga MS. Food intake, metabolism and obesity in humans. In: Farthing MJG, Mahalanabis D, editors. The control of food and fluid intake in health and disease. Nestele Nutrition Workshop series, vol. 51; 2003. pp. 195–221.

2 Jean C, Rome S, Mathe Y, *et al.* Metabolic evidence for adaptation to a high protein diet in rats. J Nutr 2001; 131:91–98.

3 Stock MJ. Gluttony and thermogenesis revisited. Int J Obes Relat Metab Disord 1999; 23:1105–1117.

4 Dulloo AG, Jacquet J. Low-protein overfeeding: a tool to unmask susceptibility to obesity in humans. Int J Obes Relat Metab Disord 1999; 23:1118–1121.

5 Westerterp-Plantenga MS, Rolland V, Wilson SAJ, Westerterp KR. Satiety related to 24 h diet-induced thermogenesis during high protein/carbohydrate vs. high fat diets measured in a respiration chamber. Eur J Clin Nutr 1999; 53:495–502.

6 Pullar JD, Webster AJF. The energy cost of fat and protein disposition in the rat. Br J Nutr 1977; 37:355–363.

7 Latner JD, Schwartz M. The effects of a high-carbohydrate, high protein or balanced lunch upon later food intake and hunger ratings. Appetite 1999; 33:119–128.

8 • Eisenstein J, Roberts SB, Dallal G, Saltzman E. High-protein weight-loss diets: are they safe and do they work? A review of experimental and epidemiologic data. Nutr Rev 2002; 60:189–200.
A review emphasizing the modulatory effect of dietary protein on energy intake via the sensation of satiety and on energy expenditure by increasing the thermic effect of feeding in short-term studies.

9 • Hall WL, Millward DJ, Long SJ, Morgan LM. Casein and whey exert different effects on plasma amino acid profiles, gastrointestinal hormone secretion and appetite. Br J Nutr 2003; 89:239–248.
The only study until now dealing with short-term differences in satiety due to different types of protein.

10 • Raben A, Agerholm-Larsen L, Flint A, *et al.* Meals with similar energy densities but rich in protein, fat, carbohydrate, or alcohol have different effects on energy expenditure and substrate metabolism but not on appetite and energy intake. Am J Clin Nutr 2003; 77:91–100.
An elaborate study comparing appetite as well as energy metabolism effects of all different macronutrients at the same time.

11 Westerterp-Plantenga MS, Westerterp KR, Rubbens M, *et al.* Appetite at 'high altitude', operation Everest-Comex: a simulated ascent of the Mt. Everest. J Appl Physiol 1999; 87:391–399.

12 Westerterp-Plantenga MS, Lejeune MPGM, Nijs I, *et al.* High protein intake sustains weight maintenance after body weight loss in humans [abstract]. Int J Obes Relat Metab Disord 2003; 27:S127.

13 Lejeune MPGM, Kovacs EMR, Westerterp-Plantenga MS. Additional protein intake limits weight regain after weight loss in humans [abstract]. Int J Obes Relat Metab Disord 2003; 27:S25.

14 Mikkelsen PB, Toubro S, Astrup A. Effect of fat-reduced diets on 24 h energy expenditure: comparisons between animal protein, vegetable protein, and carbohydrate. Am J Clin Nutr 2000; 72:1135–1141.

15 Billeaud C, Guillet J, Sandler B. Gastric emptying in infants with or without gastro-oesophageal reflux according to the type of milk. Eur J Clin Nutr 1990; 4:577–583.

16 Boirie Y, Dangin M, Gachon P, *et al.* Slow and fast dietary proteins differently modulate postprandial protein accretion. Proc Natl Acad Sci U S A 1997; 94:14930–14935.

17 • Bensaid A, Tome D, Gietzen D, *et al.* Protein is more potent than carbohydrate for reducing appetite in rats. Physiol Behav 2002; 75:577–582.
An elegant study in rats comparing in great detail satiating effects from protein with those from carbohydrates.

18 • Bensaid A, Tome D, L'Heureux-Bourdon D, *et al.* A high-protein diet enhances satiety without conditioned taste aversion in the rat. Physiol Behav 2003; 78:311–320.
An important study in rats excluding the suspicion that reduced protein intake may be due to taste aversion.

19 • Jean C, Fromentin G, Tome D, Larue-Achagiotis C. Wistar rats allowed to self-select macronutrients from weaning to maturity choose a high-protein, high-lipid diet. Physiol Behav 2002; 76:65–73.
A study in rats suggesting that preference for protein may be related to the condition with respect to lean body mass that is present in the animal.

20 Skov AR, Toubro S, Ronn B, *et al.* Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. Int J Obes Relat Metab Disord 1999; 23:528–536.

21 Dumesnil JG, Turgeon J, Tremblay A, *et al.* Effect of a low-glycemic index–low-fat–high protein diet on the atherogenic metabolic risk profile of abdominally obese men. Br J Nutr 2001; 86:557–568.

22 •• Laymen DK, Boileau RA, Erickson DJ, *et al.* A reduced ratio of dietary carbohydrate to protein improves body-composition and blood lipid profiles during weight loss in adult women. J Nutr 2003; 133:411–417.
This study shows effects from high-protein intake under iso-energetic conditions, emphasizing the metabolic effects of a high-protein diet.

23 •• Brehm BJ, Seeley RJ, Daniels SR, *et al.* A randomized trial comparing a very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. J Clin Endocrinol Metab 2003; 88:1617–1623.
An important study that shows the effects from high-protein intake under ad-libitum conditions during a negative energy balance on body weight loss, body composition, as well as the metabolic profile.