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Dietary protein – its role in satiety, energetics, weight loss and health

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Abstract

Obesity is a serious health problem because of its co-morbidities. The solution, implying weight loss and long-term weight maintenance, is conditional on: (i) sustained satiety despite negative energy balance, (ii) sustained basal energy expenditure despite BW loss due to (iii) a sparing of fat-free mass (FFM), being the main determinant of basal energy expenditure. Dietary protein has been shown to assist with meeting these conditions, since amino acids act on the relevant metabolic targets. This review deals with the effects of different protein diets during BW loss and BW maintenance thereafter. Potential risks of a high protein diet are dealt with. The required daily intake is 0·8–1·2 g/kg BW, implying sustaining the original absolute protein intake and carbohydrate and fat restriction during an energy-restricted diet. The intake of 1·2 g/kg BW is beneficial to body composition and improves blood pressure. A too low absolute protein content of the diet contributes to the risk of BW regain. The success of the so-called 'low carb' diet that is usually high in protein can be attributed to the relatively high-protein content *per se* and not to the relatively lower carbohydrate content. Metabolic syndrome parameters restore, mainly due to BW loss. With the indicated dosage, no kidney problems have been shown in healthy individuals. In conclusion, dietary protein contributes to the treatment of obesity and the metabolic syndrome, by acting on the relevant metabolic targets of satiety and energy expenditure in negative energy balance, thereby preventing a weight cycling effect.

Key words: protein-diet: satiety: energy expenditure: sparing fat-free-mass: obesity: metabolic syndrome

Introduction

Obesity is a serious health problem because of its co-morbidities[1,2]. The solution for this problem implies weight loss and long-term weight maintenance, which is difficult to achieve, since body-weight (BW) regain appears to be the pitfall[1,3]. The approach for this solution is conditional on: (i) sustained satiety despite negative energy balance, (ii) sustained basal energy expenditure despite BW loss due to (iii) a sparing of fat-free mass (FFM) (being the main determinant of basal energy expenditure)[4]. Dietary protein has been shown to assist with meeting these conditions, since amino acids act on the metabolic targets involved in satiety, energy expenditure, and the sparing of FFM[3,4]. This review, on dietary protein and its role in satiety, energetics, BW loss and health, deals with the effects of different protein diets during BW loss and BW maintenance thereafter, and on the crucial metabolic targets, namely satiety and energy expenditure. Potential risks of a high protein diet are dealt with.

Normal and high-protein diets need to be defined in both relative and absolute terms in relation to energy balance. Relatively high-protein diets for BW loss and subsequent BW maintenance have at least 25–30 % of their energy supplied from protein, implying a sustained normal-protein intake in grams of 0·8–1·2 g/kg BW, as it was before the diet. However, total energy intake is decreased. Such diets are relatively high in protein, expressed as a percentage energy (En%) from protein (20–30 En%), but since they are energy-restricted, in absolute terms (g of protein) they only contain a sufficient absolute amount of protein. The absolute amount of protein is about the same as in a relatively normal-protein diet (10–15 En% protein) in neutral energy balance (energy intake matches energy requirement set by energy expenditure).

Dietary protein and body weight management

Studies suggest that BW loss and BW maintenance thereafter, on a relatively high-protein diet, appear to be greater under conditions of *ad libitum* energy intake than under conditions of isoenergetic diets[4]. The explanation for this is that satiety is a key factor in applying relatively high-protein diets. Under *ad libitum* feeding conditions subjects eat less from the relatively high-protein diet than under iso-energetically fed conditions[5]. Such diets contain a sufficient absolute amount of protein but lead to decreased energy intake, suggesting that in addition to metabolic effects of protein on BW loss, energy intake plays an important role. This is underscored by the phenomenon that under iso-energetic conditions no

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statistically significant difference between BW loss on a high-protein or high-carbohydrate diet is shown.[3–5] However, most of the studies on protein intake in relation to BW management show an improved body composition (i.e. an increased FFM/fat mass (FM)) and metabolic profile with a relatively high-protein diet. The relatively high-protein negative energy balance diets, in general supply 20–30 % of their energy from protein and imply a required normal-protein intake in grams, while energy intake is decreased[4].

The observations with respect to energy efficiency during BW regain are comparable to the 'Stock hypothesis' described for BW gain[6]. Under conditions of slight BW regain, while aiming for weight maintenance, a required-protein diet shows reduced energy efficiency related to the body composition of the BW regained, (i.e. in favour of FFM). Here, the main issue is that building FFM requires, on average, an additional energy ingestion of 52 MJ/kg BW, whereas building a normal proportion of FM and FFM takes 30 MJ/kg BW[6]. During BW loss, as well as during weight maintenance thereafter, a relatively high (but absolutely normal) protein diet preserves or increases FFM and reduces FM, and improves the metabolic profile. Evidence shows that the required-protein intake sustains weight maintenance by: (i) favouring regain of FFM at the cost of FM at a similar physical activity level, (ii) reducing the energy efficiency with respect to the BW regained, and (iii) increasing satiety[4].

Dosage of protein during an energy-restricted diet

Studies describing assessment of effects of relatively high vs. normal-protein diets on BW management[3–5,7–15] often are assessing absolutely normal vs. low-protein diets. To answer the question as to whether diets absolutely high in protein may show a higher BW loss, improved body composition, and stronger BW maintenance after BW loss compared with protein diets at the required level of protein intake, the following study was undertaken (S Soenen, unpublished data). In 72 obese subjects BW, body composition, and metabolic parameters were assessed before and after dietary energy intakes of 100 %, 33 %, and 67 % of the individuals original daily energy requirement, for respectively 0·5, 1·5 and 4 months. The diets consisting of a required-protein diet, which met the daily protein requirement, RPD, and a high-protein diet, HPD, as protein/carbohydrate/fat at baseline, gave consistent protein intakes of 0·8 ± 0·3 g/kg BW (RPD) and 1·2 ± 0·3 g/kg BW (HPD) ($P<0·001$) throughout the study. Both diets were equally effective in supporting BW loss, the loss of body-fat, BW maintenance, and both diets showed a FFM sparing effect, which was however stronger in the high-protein diet, similar to previous observations[3–5,7–15]. This higher FFM sparing effect prevented a decrease of resting energy expenditure as a function of FFM, thereby facilitating maintenance of reduced BW, as has been shown before[3–5,7–15]. Reduction of BW was equally facilitated by the satiety capacity of protein[3–5,7–15], which contributes to compliance to the diet[3,4,8,10], as well as "attitude-toward-eating". The plasma concentrations of the peptides glucagon-like peptide-1 (GLP-1) and peptide-YY (PYY) similarly decreased over time, probably due to less nutrients being present in the gut. Physical activities, as recorded using the Baecke questionnaire, were not affected by the diets. The observation that both diets were similarly effective for (BW) loss, FM loss, and BW maintenance thereafter confirms earlier observations,[16–20] which reported no difference between two levels of protein in the diet. In those diets, the 'normal' or 'low' protein content, still provides sufficient protein (~60 g), to sustain satiety, FFM, and energy expenditure, and the diet thus shows a similar effect on BW loss as a diet higher in protein content. However, when the control diet provided an insufficient amount of protein, a rapid BW regain was shown, similar to the effect seen on most diets that, due to a limited energy content, do not provide a sufficient amount of protein[5,7,9,12–15,17]. Thus, a controlled, energy-restricted "normal-protein" diet providing at least 0·8 g Protein/kg BW is sufficient for substantial weight loss, subsequent weight maintenance, and a decrease in body fat percentage (BF%), while a controlled high-protein diet providing 1·2 g protein/kg BW is necessary for improvement of FFM and a sustained resting energy expenditure. The effect of a higher protein diet on body composition has not only been shown before during BW loss and BW maintenance thereafter[3–5,7–15,16–20], but also in a longer-term study in energy balance[21,22]. We suggest that a too low absolute protein intake contributes to the risk of BW regain. An "absolutely required" amount of protein in the diet (0·8 g/kg BW/d) is sufficient for weight loss, body fat loss, and weight maintenance; yet, an "absolutely elevated" amount of protein in the diet, thus the real high-protein diet of 1·2 g/kg BW/d, is necessary for improving FFM and resting energy expenditure (16). In further studies it was assessed whether including specific proteins, such as gelatin or alpha-lactalbumin, may improve the effect described above, due to their high satiating capacities (see below). However, this was not the case[23–25].

Effects of 'low-carb diets' in combination with 'high-protein' diets

'Low carb' diets compared with control diets have been suggested to be relatively more effective in BW management. However, these diets are relatively high in protein as well. Here the question was whether a decrease in carbohydrate or an increase in daily absolute protein intake has a stimulating effect on reducing BW and BF%.

A study with four different energy restriction diets offered parallel in a 2 × 2 factorial design, (contrasting in low vs. normal-carbohydrate intake and high vs. normal-protein intake, addressed whether it was the high-protein or low-carbohydrate factor that was crucial for the effect. The study showed irrefutably that, despite all four diets supporting weight loss, the answer is that it is the relatively high-protein content *per se* that underscores the even greater success, and not the relatively lower carbohydrate content and even that a high-protein normal-carbohydrate regimen shows relatively less regain, so better weight-maintenance.

A suggested mechanism underscoring the decrease of BW of an elevated protein, lowered carbohydrate, and relatively

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high-fat diet is the satiety effect created by the ketogenic state of the diet. The formation of ketone bodies such as β-hydroxybutyrate[26–28] is related to appetite reduction and a greater reduction of BW in humans[26–28]. Moreover, this type of diet increases energy expenditure, supporting a negative energy balance, via increased gluconeogenesis[29,30]. However, in the long-term, compliance to this type of diet is not consistent.

Dietary protein and health

One of the greatest health problems, overweightness and obesity including many co-morbidities, can be treated successfully by a high protein diet, which implies that simply BW loss and BW maintenance can reverse metabolic problems. Indeed, it has been shown convincingly that the metabolic profile including insulin sensitivity and lipid metabolism remarkably improve, mainly as an effect of BW loss, indicating that the originally inferior metabolic profile was probably the effect and not the cause of overweight. Blood pressure also decreases in relation to a decrease in FM. With respect to possible adverse events, some caution is needed when dietary protein intake is elevated in an absolute sense for a longer period of time. There may be adverse effects on the kidneys, related to elevated blood pressure. Especially individuals with sub-clinical renal malfunction, such as due to metabolic syndrome or type 2 Diabetes Mellitus, and elderly are vulnerable. However, the link between protein intake and the initiation or progression of renal disease lacks evidence in healthy individuals[4]. In those healthy individuals, high-protein diets did not affect kidney function parameters. Plasma creatinine concentrations remained between the normal values of 60–120 μmol/L. Moreover, the diets resulted in a decrease in systolic and diastolic blood pressure after BW loss.

Dietary protein and energetics

One of the metabolic targets required of high-protein diets is to sustain energy expenditure, even in negative energy balance, to prevent the BW cycling effect. The thermogenic effect of protein is clearly illustrated by the difference between the gross energy value of 22–25 kJ/g and the net metabolizable energy value of 13 kJ/g. The effect of protein intake on energy expenditure is reflected mainly in two of the four components that daily energy expenditure consists of (i.e. the sleeping metabolic rate (SMR) and the energy cost of arousal forming together the energy expenditure for maintenance or basal metabolic rate (BMR), and the thermic effect of food or diet induced energy expenditure (DEE))[4]. Reported DEE values for separate nutrients are 0 to 3 % for fat, 5 to 10 % for carbohydrate, 20 to 30 % for protein (4), and 10 to 30 % for alcohol[4]. In healthy subjects with a mixed diet, DEE represents about 10 % of the total amount of energy ingested over 24 h. When a subject is in energy balance, where intake equals expenditure, DEE is 10 % of daily energy expenditure[4]. In a few studies conducted over 24 h in a respiration chamber[31,32] healthy female volunteers were fed high-protein high/carbohydrate (En% protein/carbohydrate/fat 30/60/10) and high-fat diets (En% protein/carbohydrate/fat 10/30/60). Both diets were isoenergetic and isovolumetric, and composed of normal food items, which matched organoleptic properties (taste, smell, and appearance). Subjects each spent two 36 h periods in a respiration chamber consuming both test diets in random order. DEE was higher in all subjects when on the high-protein high-carbohydrate diet. Even when the protein type was casein alone a similar difference in energy expenditure was shown[33,34]. Effects of two diets with either 25 En% or 10 En% from casein or gelatin as the only protein sources, on energy expenditure, substrate balance, and appetite profile were studied during 36 h stays in a respiration chamber, in 24 healthy normal weight subjects (12 men and 12 women). It appeared that the high casein and gelatin diets (25 En%) resulted in a higher 24 h total energy expenditure (2·6 %) and a higher SMR (2·1 %) compared with comparable 10 En% casein or gelatin diets. Moreover, with the 25 En% diets, compared with the 10 En% diets, the subjects were in positive protein balance and negative fat balance, while satiety was 33 % higher. The 25 En% diets boosted energy expenditure, protein balance, satiety, and negative fat balance, which is beneficial to BW management[33,34]. Combining the studies on protein intake, DEE and SMR, it can be concluded that protein intake causes an acute increase in DEE and, when sustained over three days, results in an increase in SMR as well. The effects on energy expenditure and protein balance were stronger with the casein diet compared with the gelatin diet, due to the completeness of the protein. Due to the incompleteness of gelatin, the carbohydrate balance was also more positive, possibly due to gluconeogenesis.

Gluconeogenesis

A further respiratory chamber study on energy expenditure paid specific attention to gluconeogenesis and its effect on energy expenditure[29,30]. Ten healthy lean young men received an isoenergetic high-protein carbohydrate-free diet (En% protein/carbohydrate/fat 30/0/70) or a normal-protein diet (En% protein/carbohydrate/fat 12/55/33) for 1·5 d according to a randomized crossover design, and energy expenditure was measured in a respiration chamber. Endogenous glucose production (EGP) and fractional gluconeogenesis were measured via infusion of [6,6-(2)H(2)]glucose and ingestion of (2)H(2)O; absolute gluconeogenesis was calculated by multiplying fractional gluconeogenesis by EGP. Body glycogen stores were lowered at the start of the intervention with an exhaustive glycogen-lowering exercise test. EGP was lower in the carbohydrate-free condition than in the control condition, whereas fractional and absolute gluconeogenesis were higher. Resting metabolic rate was higher in the carbohydrate-free condition than in the normal-protein condition. Forty-two percent of the increase in energy expenditure after the high-protein carbohydrate-free diet was explained by the increase in gluconeogenesis[29,30]. The ATP required for the initial steps of metabolism and oxidation including urea synthesis might explain the short-term protein induced increase in DEE. The long-term protein induced increase of

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SMR might be explained by stimulation of body protein synthesis and protein turnover[35]. A well-balanced amino acid mixture produces a higher thermogenic response than does an amino acid mixture with a lower biological value (i.e. a different amino acid composition than is used for protein synthesis). This may explain why the intake of plant protein results in less protein synthesis than does the intake of animal protein.

Dietary protein and satiety

Although it has been shown repeatedly that acute high-protein meals induce satiety[4], we will focus here on relatively high-protein diets instead.

When high-protein menus are offered at each meal, lasting for one to several days, one gets into the condition of a high-protein diet once metabolic reactions have been established[32–34,36,37]. In several high-protein diet studies in normal-weight healthy subjects, a continuously higher satiety has been shown throughout the day following a high compared with a normal-protein diet; for instance in the energy balance controlled environment of a respiration chamber[32–34,36,37]. Here, a normal-protein diet given in energy balance contains 10–15 En% protein[32–34,36,37], and a high-protein diet in energy balance contains 20–30 En% protein[32–34,36,37]. A high-protein diet in the presence of carbohydrate stimulates GLP-1 release[32–34,36,37], which triggers insulin release. More importantly, only high-protein diet-induced satiety is primarily related to elevated energy expenditure[32–34,36,37], implying increased oxygen consumption and an increase in body temperature both leading to a feeling of being deprived of oxygen and thus promoting satiety[32–34,36,37]. These highly-controlled medium term studies overcome possible differences due to solid, semi-solid, or liquid foods, timing and macronutrient exchange[4], and imply the possibility of assessing satiety, energy expenditure and substrate oxidation at the same time. More of these types of studies need to be executed with different types of proteins, in overweight subjects in neutral, positive and negative energy balances.

Mechanisms behind protein-induced satiety

There appears to be a band-width in protein amount and concentration where relatively more protein is more satiating and promotes less energy intake (Figs. 1–4), supported by relatively elevated plasma amino acid concentrations, anorexigenic hormones, or energy expenditure, feeding back on the central nervous system. Mellinkoff[38] suggested already in 1956 that an elevated concentration of blood or plasma amino acids, which cannot be channeled into protein synthesis, serves as a satiety signal for a food intake regulating mechanism and thereby results in depressed food intake.

The quality or type of protein appears to be involved in hunger suppression. Protein quality is mainly determined by the amino acid composition of the protein. Some proteins are considered as 'incomplete' or 'lower quality' proteins because they are lacking one or more dietary essential amino acids or have an inadequate dietary essential amino acid balance[23,24,34,39]. Gelatin is considered as an incomplete protein because it is lacking tryptophan (TRP) and contains relatively low amounts of the other dietary essential amino acids (i.e. histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, and valine). The addition of TRP does not improve the protein quality of gelatin to a large extent. Both gelatin and gelatin with added TRP suppress hunger more than other types of protein: subsequent energy intake was decreased after a breakfast with gelatin or gelatin with added TRP compared with casein, soya, whey, or whey without glycomacropeptide (GMP)[39]. This is probably attributable to the low protein quality of gelatin and gelatin with added TRP. It has been shown that animals reject diets that lead to depletion or deficiency of dietary essential amino acids (the 'indispensable amino acid deficiency' theory). After rejection of such a diet animals begin foraging for a better dietary essential amino acid source and develop conditioned aversions to cues associated with the deficient diet[23,24]. A chemosensor for dietary essential amino acid deficiency has been found in the anterior piriform cortex[23,24]. From this area signals are projected to other brain areas that are associated with the control of food intake[23,24]. Likewise, consumption of an incomplete protein may be detected and result in a signal to stop eating in humans[38]. The observed increased gelatin-induced satiety and reduced energy intake thus may be a signal of hunger suppression rather than a satiation or satiety signal[39].

A different mechanism implies a ketogenic state contributing to appetite suppression: a high-protein, high-fat, carbohydrate-free diet induced an increased dietary fat oxidation and increased concentration of ketone bodies and suppressed

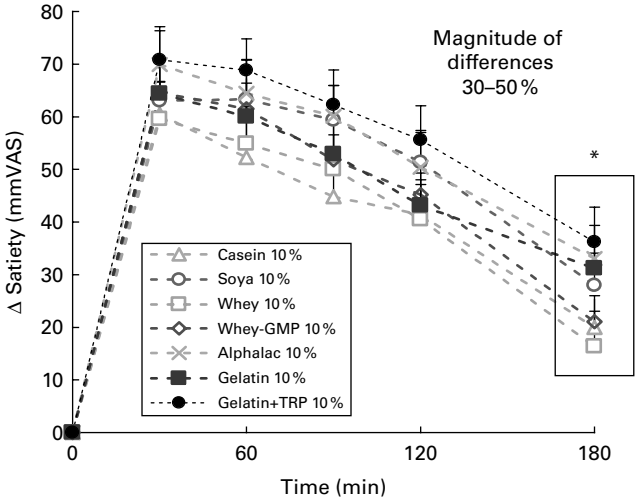

Fig. 1. Comparison of VAS-ratings of feelings of increased satiety (or fullness) between post-prandial effects of 7 different proteins, namely casein, soya, whey, whey-GMP, alpha-lactalbumin, gelatin, gelatin plus tryptophan, during 3 h after an iso-energetic, iso-volumetric semi-solid breakfast, with the same controlled appearance, taste, flavour, energy-density and viscosity, at 20 % of the energy-requirement of the individual subject, and with a single protein dosage of 10 % of energy. N = 24. After Veldhorst *et al.*, 2009[39].

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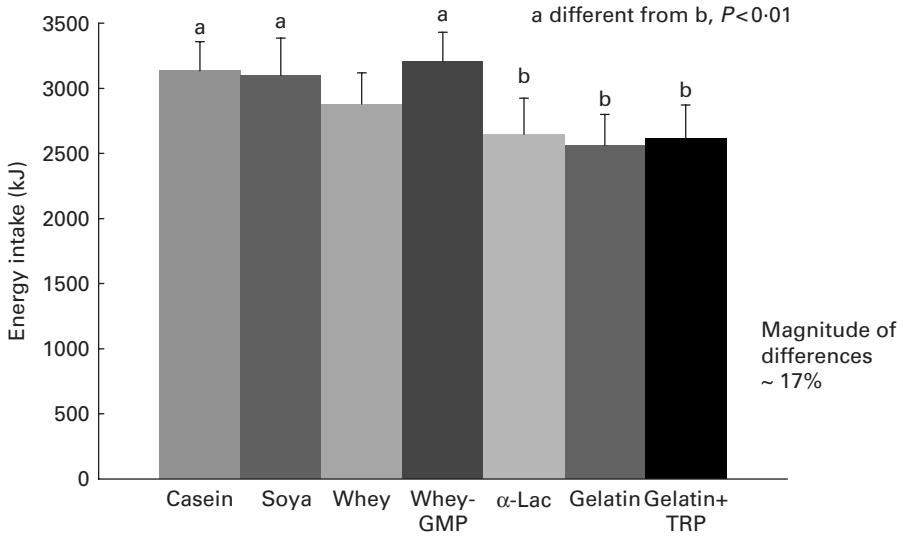

Fig. 2. Energy intake three hours after an iso-energetic, iso-volumetric semi-solid breakfast, with the same controlled appearance, taste, flavour, energy-density and viscosity, at 20 % of the energy-requirement of the individual subject, and with a single protein dosage of 10 % of energy. N = 24. Comparison between post-prandial effects of 7 different proteins, namely casein, soya, whey, whey-GMP, alpha-lactalbumin, gelatin, gelatin plus tryptophan. After Veldhorst *et al.*, 2009[39].

appetite more than a high-protein, normal-fat, normal-carbohydrate diet[26–28,30]. Increased dietary fat oxidation is suggested to reduce appetite whereas inhibition of fatty acid oxidation increases food intake[30]. The reduction of appetite with increased dietary fat oxidation may be due to stimulation of carnitine palmitoyl transferase-1 (CPT-1), a catalyst of the rate-limiting step in mitochondrial fatty acid oxidation. Increased fat oxidation with low-carbohydrate availability results in the production of ketone bodies[26–28,30]. Ketone bodies are formed from amino acids, hence consumption of a diet that is high in ketogenic amino acids results in an increased production of ketone bodies. β-Hydroxybutyrate, which is the most important ketone body in the blood[26–28,30], reduced food intake after intracerebroventricular infusion or subcutaneous injection in rats[26–28]. Leucine and lysine are the only two amino acids that are solely ketogenic amino acids; isoleucine, phenylalanine, TRP, and tyrosine are both ketogenic and glucogenic[26–28,30]. High-protein diets with proteins that predominantly consist of ketogenic amino acids may result in increased plasma ketone body concentrations, which in turn may contribute to increased satiety. Whey and alpha-lactalbumin have relatively high leucine and lysine contents which may have contributed to the increased satiety with whey compared with casein or soya, and the satiety with alpha-lactalbumin compared with casein, soya, and whey[40–42].

Changes in concentrations of gastrointestinal (an) orexigenic hormones have been hypothesized to contribute to differences in these satiating efficacies of different types of proteins[33,34,36]. Variations in concentrations of these hormones are directly recorded by the central nervous system and thereby may affect the control of food intake, but until now this lacks sufficient evidence[33,34,36].

Protein turnover and metabolism

Protein turnover and metabolism are strongly influenced by protein quality because protein synthesis requires an adequate availability of dietary essential amino acids. In other words, the intake of sufficient amounts of these amino acids is crucial for preventing negative protein turnover. A specific appetite for essential amino acids has therefore been suggested, which is supported by the observation that rats, when fed a diet deficient in one or more dietary essential amino acids, are able to recognize the presence of these amino acids in a range of diets with or without these amino acids[43,44]. Such

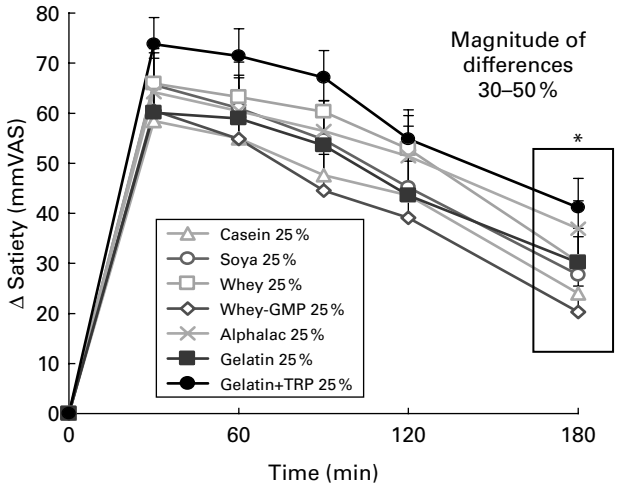

Fig. 3. Comparison of VAS-ratings of feelings of increased satiety (or fullness) between post-prandial effects of 7 different proteins, namely casein, soya, whey, whey-GMP, alpha-lactalbumin, gelatin, gelatin plus tryptophan, during 3 h after an iso-energetic, iso-volumetric semi-solid breakfast, with the same controlled appearance, taste, flavour, energy-density and viscosity, at 20 % of the energy-requirement of the individual subject, and with a single protein dosage of 25 % of energy. N = 24. After Veldhorst *et al.*, 2009[39].

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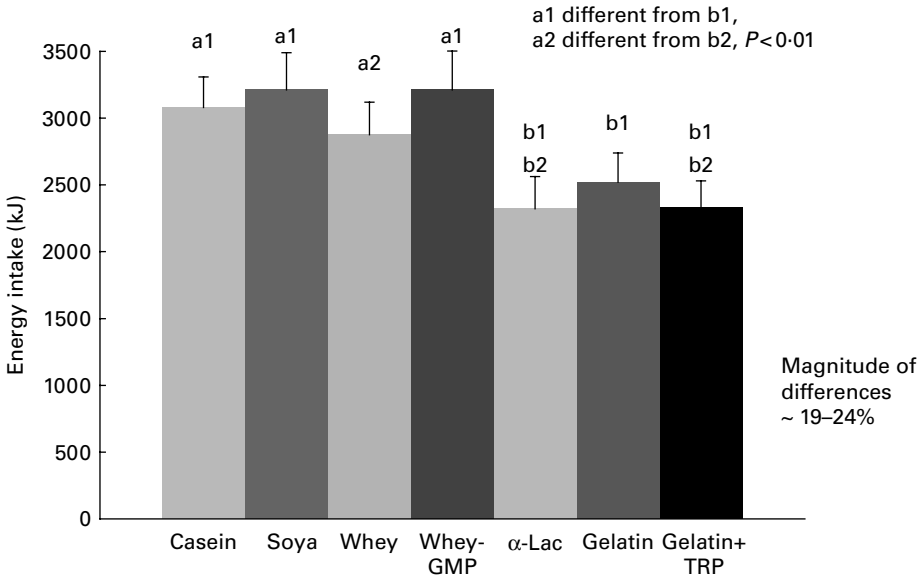

Fig. 4. Energy intake three hours after an iso-energetic, iso-volumetric semi-solid breakfast, with the same controlled appearance, taste, flavour, energy-density and viscosity, at 20 % of the energy-requirement of the individual subject, and with a single protein dosage of 25 % of energy. N = 24. Comparison between postprandial effects of 7 different proteins, namely casein, soya, whey, whey-GMP, alpha-lactalbumin, gelatin, gelatin plus tryptophan. After Veldhorst *et al.*, 2009[39].

a sensing mechanism stresses the physiological importance of maintaining an adequate rate of protein synthesis. When ingested in surplus of the needs for postprandial protein synthesis, amino acids can readily be used as a substrate for oxidation. In elderly women, increasing the amount of dietary protein from 10 to 20 En% resulted in a 63 % to 95 % increase in protein oxidation, depending on the protein source[45]. The largest increase in protein oxidation (95 %) was observed when the predominant protein source was of animal origin, whereas this increase was only 63 % when soya protein was the predominant protein source in the diet[45]. Accordingly, as mentioned in the previous section, Mikkelsen *et al.*[35] observed a higher diet-induced thermogenesis with pork meat than with soya protein. Differences in digestion rate of the various protein sources may contribute to differences in postprandial protein oxidation. Thus, in comparison with slowly digested protein, ingestion of rapidly digested protein results in a stronger increase in postprandial protein synthesis and amino acid oxidation[46,47,48]. The metabolic efficacy of protein oxidation largely depends on the amino acid composition of the protein, since large differences exist with respect to the efficacy by which amino acids are oxidized. This is due to the large variety of carbon chains and cofactors that result from amino acid catabolism[49]. For instance, the number of amino groups that undergo conversion to urea in the urea cycle (at a cost of 4 ATP) ranges from one for an amino acid such as proline or alanine to three for histidine[49,50]. Taking into account the stoichiometry of amino acid catabolism and urea synthesis, the calculated energy expenditure to produce ATP ranges from 153 kJ/ATP for cysteine to 99 kJ/ATP for glutamate (for glucose, this value is 91 kJ/ATP)[50]. Thus, even though the ATP for urea production can be derived from subsequent oxidation of the remaining carbon group itself[51], the metabolic efficacy of amino acid oxidation is relatively low (for glucose and fatty acids, the calculated energy expenditure to produce ATP is 91 and 96 kJ/ATP, respectively). This relative metabolic inefficiency may contribute to the higher diet-induced energy expenditure of a high-protein meal, which, in turn, has been shown to be related to subjective feelings of satiety.

Summary and conclusion

The solution for the co-morbidity related chronic disease, obesity implies BW loss and BW maintenance. Sustained satiety despite negative energy balance, sustained basal energy expenditure despite BW loss, a sparing of FFM (being the main determinant of basal energy expenditure) are conditional for BW management. Dietary protein acts on the metabolic targets involved in satiety, energy expenditure, and the sparing of FFM. The required daily intake needs to be 0·8–1·2 g/kg BW, implying sustaining the original absolute protein intake and only carbohydrate and fat restriction during an energy restricted diet. The intake of 1·2 g/kg BW is beneficial to body composition and improves blood pressure. A too low absolute protein content of the diet contributes to the risk of BW regain. Including specific proteins, such as gelatin or alpha-lactalbumin, because of their high satiating capacities, does not improve the effect described.

The success of the so-called 'low carb' diet that is usually high in protein can be attributed to the relatively high-protein content *per se*, which underscores the even greater success, and not to the relatively lower carbohydrate content. Lowered carbohydrate intake *per se* has no effect on decrease in BW and BF% during energy restriction, while daily elevated absolute protein intake of 1·1 vs. 0·7 g/kg BW promotes BW loss while reducing BF%.

Metabolic syndrome parameters restore, mainly due to BW loss. With the indicated dosage, no kidney problems have been shown in healthy individuals. Mechanisms behind

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sustained energy expenditure despite negative energy balance are the protein–related high diet-induced thermogenesis of 20–30 %, due to protein turn-over, urea production, and gluconeogenesis. Complete dietary proteins achieve a more positive protein balance than incomplete dietary proteins; with the latter more gluconeogenesis occurs. Mechanisms behind sustained satiety despite negative energy balance are elevated, (especially ketogenic), plasma amino acid concentrations, diet-induced thermogenesis, protein-type dependent hunger suppression, and in the case of a 'low carb'–protein diet, ketogenesis.

Evidence for the role of anorexic and orexigenic hormones is still scarce.

In conclusion, dietary protein plays an important role in health, since it contributes to the treatment of the chronic disease of obesity and the metabolic syndrome, by acting on the relevant metabolic targets of satiety and energy expenditure in negative energy balance, thereby preventing a weight cycling effect.

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