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Original article

Maintenance of energy expenditure on high-protein vs. high-carbohydrate diets at a constant body weight may prevent a positive energy balance

E.A. Martens [a,*], H.K. Gonnissen [a], B. Gatta-Cherifi [b], P.L. Janssens [a], M.S. Westerterp-Plantenga [a]

[a] Department of Human Biology, Maastricht University, Maastricht, The Netherlands
[b] Group Energy Balance and Obesity, INSERM U862, Neurocentre Magendie, Bordeaux, France

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SUMMARY

Background & aims: Relatively high-protein diets are effective for body weight loss, and subsequent weight maintenance, yet it remains to be shown whether these diets would prevent a positive energy balance. Therefore, high-protein diet studies at a constant body weight are necessary. The objective was to determine fullness, energy expenditure, and macronutrient balances on a high-protein low-carbohydrate (HPLC) diet compared with a high-carbohydrate low-protein (HCLP) diet at a constant body weight, and to assess whether effects are transient or sustained after 12 weeks.
Methods: A randomized parallel study was performed in 14 men and 18 women [mean ± SD age: 24 ± 5 y; BMI (in kg/m^2): 22.8 ± 2.0] on diets containing 30/35/35 (HPLC) or 5/60/35 (HCLP) % of energy from protein/carbohydrate/fat.
Results: Significant interactions between dietary intervention and time on total energy expenditure (TEE) ($P = 0.013$), sleeping metabolic rate (SMR) ($P = 0.040$), and diet-induced thermogenesis (DIT) ($P = 0.027$) appeared from baseline to wk 12. TEE was maintained in the HPLC diet group, while it significantly decreased throughout the intervention period in the HCLP diet group (wk 1: $P = 0.002$; wk 12: $P = 0.001$). Energy balance was maintained in the HPLC diet group, and became positive in the HCLP diet group at wk 12 ($P = 0.008$). Protein balance varied directly according to the amount of protein in the diet, and diverged significantly between the diets ($P = 0.001$). Fullness ratings were significantly higher in the HPLC vs. the HCLP diet group at wk 1 ($P = 0.034$), but not at wk 12.
Conclusions: Maintenance of energy expenditure on HPLC vs. HCLP diets at a constant body weight may prevent development of a positive energy balance, despite transiently higher fullness. The study was registered on clinicaltrials.gov with Identifier: NCT01551238.

1. Introduction

High-protein diets appear to show different effects in relation to energy balance. Considering the increasing prevalence of overweight and obesity, energy-restricted and ad libitum high-protein diets have come into focus as being beneficial strategies for body weight loss, and weight maintenance thereafter [1–4]. Most remarkable long-term effects are shown when relatively high-protein diets are consumed in negative energy balance achieved by restriction of carbohydrate and fat intake, but not of protein intake. The potential of these diets to maintain a negative energy balance, to induce body weight loss, and to maintain the lower body weight, can be explained by a sustained satiety at the level of the original diet [5,6], and a sustained energy expenditure, which is underscored by preservation of fat-free mass (FFM)[c] [7,8]. However, the question remains whether these effects, observed for high-protein diets in negative energy balance, can be translated into preventive measures for body weight gain when consumed in

Abbreviations: AEE, activity energy expenditure; DIT, diet-induced thermogenesis; En%, % of energy; FFM, fat-free mass; HCLP, high-carbohydrate low-protein; HPLC, high-protein low-carbohydrate; RQ, respiratory quotient; SMR, sleeping metabolic rate; VAS, visual analog scale.

* Corresponding author. Department of Human Biology, Maastricht University, PO Box 616, 6200 MD Maastricht, The Netherlands. Tel.: +31 433884596.
E-mail address: eap.martens@maastrichtuniversity.nl (E.A. Martens).

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neutral, or even in positive energy balance. A positive energy balance induced by overfeeding with a high-protein diet was shown to result in a significant body weight gain. In a situation with low physical activity, fat mass as well as FFM were increased, together with an increase in resting energy expenditure [9]. Resistance training combined with a high-protein diet in positive energy balance showed an apparent effect on FFM accretion [10]. The acute effects of high protein intake combined with resistance training on muscle protein synthesis are assumed to be predictive for high-protein diets stimulating muscle hypertrophy in the longer-term [11–13].

At a constant body weight, energy balance can be neutral in principle, but may fluctuate between days [14]. Studies performed at a constant body weight can be used to predict whether protein intake plays a role in the development of overweight and obesity. The results of a systematic review of epidemiological studies suggest that protein intake was neither associated with body weight gain or obesity, nor with body weight loss; moreover, the observations are inconsistent [15]. Recently, it was suggested that the differential effects of protein intake are due to differences in protein source [16]. Furthermore, it has been observed that protein intake is maintained within a small range across populations and over time [17].

Short-term intervention studies using energy-balanced diets with large contrasts in relative protein content have shown that high-protein diets induce increased satiety compared with diets lower in protein, at least over 24 h [5,18–23]. Furthermore, higher rates of energy expenditure [24,25], a positive protein balance [21,24,26] and an initial negative energy balance [24] were observed in response to these energy-balanced high-protein diets. However, it is unclear whether the observed effects from these acute studies are transient or sustained, thus implying prevention of body weight gain. In order to assess whether a high-protein diet would be a concept for prevention of a positive energy balance, we carried out a dietary intervention study to determine fullness, energy expenditure, and macronutrient balances on a high-protein low-carbohydrate (HPLC) diet compared with a high-carbohydrate low-protein (HCLP) diet at a constant body weight, and assessed whether effects are transient or sustained after 12 weeks.

2. Materials and methods

The Medical Ethical Committee of Maastricht University approved the study, and all subjects gave written informed consent. The study was registered on clinicaltrials.gov with Identifier: NCT01551238.

2.1. Study subjects

Sensitivity analysis on data from a respiration chamber study by Westerterp et al. [27] for the difference in 24-h diet-induced thermogenesis (DIT) between 29 En% and 9 En%-protein diets showed that the effect size was 0.391. Based on this effect size, with an α of 0.05 and a β of 0.10, sample size calculation showed that at least 16 subjects per group were needed to show an interaction effect of dietary intervention and time on 24-h DIT in this study.

Forty-two subjects were recruited by advertisements in local newspapers and on notice boards at the university, of whom five dropped out due to lack of time. Five subjects had to be excluded from the data analysis because of non-compliance with the designated protein intake, as shown by the urinary nitrogen biomarker. Metabolic parameters of one subject were missing. Thus, 32 subjects (14 men and 18 women) were included in the final data analysis, and 31 subjects (14 men and 17 women) in the analysis of metabolic parameters.

Subjects underwent a screening that included anthropometric measurements and the completion of questionnaires eliciting information about health, smoking behavior, use of medications, alcohol consumption, physical activity, eating behavior and palatability of the study foods. Subjects were normal weight or slightly overweight [BMI range (in kg/m^2): 19.2-26.1 and aged between 19 and 34 years. BMI and age were equally divided between males and females. Waist circumference was measured at the smallest circumference between the rib cage and iliac crest, and hip circumference at the level of the spina iliaca anterior superior. Subjects were non-smoking, not using more than moderate amounts of alcohol (>10 drinks/wk), were weight stable (body weight change <3 kg during the last 6 months and had no planned weight change during the study period), and were not using medication or supplements except for oral contraceptives in women.

The validated Dutch translation of the Baecke Activity Questionnaire was used to measure habitual physical activity scores, which were subsequently converted into a standardized individual physical activity level [28,29]. Eating behavior was analyzed using a validated Dutch translation of the Three-Factor Eating Questionnaire, which measures the 3 factors involved in eating behavior, namely 'cognitive restraint of eating, 'disinhibition of restraint', and 'hunger' [30,31].

Protein and carbohydrate shakes were served and tested on palatability by 100-mm visual analog scales (VAS) anchored with 'not at all' at one end and 'extremely' at the other end. Only subjects who rated the shakes as sufficiently palatable (VAS score $\geq$50 mm), and who were confident of being able to consume these daily during the study period were included in the study.

2.2. Dietary intervention

This study used a single-blind parallel design comprising short- and longer-term intervention periods with diets differing in relative protein content. Two days before the baseline measurement in a respiration chamber, all subjects were provided with an energy-balanced diet containing a normal relative protein content (15/50/35% of energy (En%) from protein/carbohydrate/fat). Individual daily energy requirements were calculated as the basal metabolic rate determined with the formula of Harris and Benedict [32] times the individual physical activity level. During the 48-h baseline measurement, a diet with a similar macronutrient composition was served, whereby the physical activity level was estimated to be 1.35 for subjects being in energy balance. Subsequently, subjects were randomly allocated to the HPLC (30/35/35 En% from protein/carbohydrate/fat) or the HCLP (5/60/35 En%) diet group following stratification on sex, age and BMI. Protein was completely exchanged with carbohydrate, resulting in a relative fat content being similar in the baseline-, the HPLC- and the HCLP diets. Subjects were instructed to maintain a stable body weight and physical activity level throughout the complete period of 12 weeks. Therefore, they received detailed dietary guidelines based on individual daily energy requirement, calculated as the basal metabolic rate times the individual physical activity level. The dietary guidelines consisted of a variety of recipes for breakfasts, lunches, dinners and snacks, including the food items and the amounts that had to be consumed. The HPLC and HCLP diets were comparable, and consisted of commercially available food items. The guidelines included the prescription to consume additional protein [HPLC: whey with α-lactalbumin (Hiprotal Whey Protein Alpha, FrieslandCampina Domo EMEA, Amersfoort, The Netherlands)] or carbohydrate [HCLP: maltodextrin (Fantomalt, Nutricia, Zoetermeer,

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