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Invited Commentary

High-protein diets for appetite control and weight loss – the 'holy grail' of dieting?

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With the escalating global obesity problem comes the urgent need for both preventative nutrition and treatment options. While nutritionists argue about the relative roles of energy intake, energy expenditure and the interaction between genes and environment, understanding the impact of diet composition on feeding behaviour is clearly important for the development of public health strategies to encourage weight loss in the short term and weight maintenance in the longer term. In this context, isoenergetic amounts of the dietary macronutrients are not equal in terms of their effect on appetite and motivation to eat. It is now generally accepted that diet composition strongly affects *ad libitum* energy intake, with laboratory[1] and free-living studies[2] highlighting protein as the most satiating macronutrient, independent of energy density, relative to carbohydrate and fat. The role of protein-induced satiety and the ability to 'fill you up' after eating is of renewed research interest because hunger is one of the main reasons why subjects do not comply with a weight-loss regimen. Dietary strategies that can help reduce hunger and promote fullness would therefore be beneficial for weight control. Nonetheless, both the safety and efficacy of high-protein weight-loss diets have been questioned[3], particularly in combination with low-carbohydrate advice[4]. For example, recent studies have indicated greater weight loss can be achieved on high-protein diets when compared with high-carbohydrate, low-fat alternatives for periods up to 6 months[5], but by 12 months, all diets were equally effective[6]. Nonetheless, for short-term studies that encompass typical durations of weight loss, increasing the energy contribution of protein does appear effective. For example, Weigle *et al.* [7] recently indicated that increasing the percentage of dietary energy intake as protein from 15 % to 30 % over a 12-week period produced a sustained decrease in *ad libitum* intake and significant weight loss with no apparent increase in hunger. Similarly, Johnstone *et al.* [8] observed a reduction in *ad libitum* intake with subjects fed both high-protein moderate-carbohydrate and high-protein low-carbohydrate diets. Such evidence suggests that high-protein diets could be the 'holy grail' of dieting – being able to eat as much as you want (*ad libitum*) without feeling hungry and yet lose weight. Yet, despite this, nutritionists have questioned this approach because high-protein low-carbohydrate diets are high in fat, and often the contributions of fruit, vegetables and whole grains is low, which runs counter to current healthy eating advice. Indeed, there is also some recent evidence that high-protein low-carbohydrate diets may have implications for gut health[9]. Nonetheless, evidence of adverse effects in controlled situations is lacking, and, in fact, many studies report improvements in fasting lipidaemia and/or glycaemic control[10] on such diets. Any weight-loss therapy will carry health risks; for example, pharmacological and surgical approaches are usually reserved for those with elevated morbidity and mortality risk relating to their obesity. The negative impact of the excess body fat on health should be considered against the longer-term positive health benefits of weight loss. High-protein diets could be a powerful tool to promote weight loss in the short term.

There has been renewed research interest in manipulating sources of dietary protein and assessing the impact on hunger and appetite. An article in the current issue of the *British Journal of Nutrition* [11] assesses the impact of feeding diets with varying amino acid composition obtained from different protein sources. The authors compared three meals; the first contained the whey protein α-lactalbumin, a rich source of tryptophan (the precursor for the neurotransmitter serotonin), the second contained gelatin (with low amounts of tryptophan) and the third contained gelatin supplemented with tryptophan. The effect of the meals on hunger, measured by visual analogue scales, *ad libitum* food intake at lunch and amino acid and hormone profiles were monitored. The whey protein breakfast suppressed hunger only at 4 h post-ingestion, and it is of interest that the tryptophan-enriched gelatin breakfast failed to mimic the effect on appetite, despite similar plasma amino acid profiles. However, peripheral concentrations of amino acids do not always reflect absorption and sensing across the gut and liver. Correlating hunger scores with plasma amino acid values has long been a challenge[12], both from a practical point of view, because feeding mixtures of 'free' amino acids can result in nausea, and from a theoretical perspective, because protein-induced satiety probably operates via a complex system of signals arising from various sources, including the gut, liver and brain, rather than one single circuit. This is perhaps why single hunger and satiety biomarkers, such as ghrelin, peptide YY, cholecystokinin and glucagon-like peptide-1 do not always correlate well with psychometric assessments of satiety. More work is required to examine the role of feeding amino acids in 'free' form on appetite control and whether these have the same effects as when incorporated in the diet as a protein source. While no appetite-regulatory role for tryptophan was found in this study, the relationship between serotonin (5-hydroxytryptamine; 5-HT) and appetite control has been known for over 30 years[13]. It was on this basis that drugs

acting on the serotonin pathway were developed. These include D-fenfluramine, sibutramine, fluexetine and the 5-HT(2C) receptor agonist, which have been shown to modify appetite in obese subjects.

It is not clear how much protein is required to maximise protein-induced satiety or whether there is a relationship with the energy density of the diet. Normal protein intake is about 15 % of energy intake, which, for a sedentary adult male, is approximately 76–88 g/d. The high-protein diets reported for weight-loss studies often include about 30 % of energy intake as protein. This does not mean that protein intake (g) is doubled, as energy intake is reduced. Often the protein intake is increased only by 30–40 % over habitual levels[8].

Understanding the role of high-protein diets, meals and food products in feeding behaviour is another challenge. It is not clear if protein promotes satiety (inter-meal interval) or satiation (meal termination) or, indeed, both. Humans eat and overconsume energy for a variety of reasons, often not related to hunger. For example, reward aspects of food, emotional and cognitive factors all play important roles in regulating feeding behaviour. Energy homeostasis is controlled by long-term adiposity signals and short-term gastrointestinal signals. Hedonic factors may override these signals, at least in the short term. The use of functional MRI[14] and positron emission tomography (PET)[15] scan technology is giving new insights as to how feeding is regulated and will surely be a useful tool, in time, to elucidate the role of specific nutrients, including high-protein diets, on the control of appetite.

There is no conflict of interest.

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