

# Controlling food intake and energy balance: which macronutrient should we select?

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## Controlling food intake and energy balance: which macronutrient should we select?

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### Introduction

'Count genes, not calories' was the title of a nutrition article in the *Financial Times* of Friday, 13 June 2003. It referred to the results of the Human Genome Project and the discovery of our 35 000 genes, whose functions are currently both known and unknown. It also mentioned the study that painstakingly and systematically analysed all 17 000 genes of the *Caenorhabditis elegans* worm to see which ones were involved in fat storage [1]. The result was 305 genes whose inactivation reduced body fat and 112 whose loss led to extra fat. As the titles of these articles indicate, it is clear that more emphasis should and will be focused on the importance of genetic background in body weight regulation. Putting on weight is the end result of a highly complex and still largely unknown system, almost every step of which can be modified according to our genes.

In spite of all of the advances in the understanding of the genetic basis of weight regulation, genes cannot explain the explosive increase in the prevalence of obesity in the past three decades. For example, it is impossible for genes to mutate adaptively (evolution) in a population over such a very short period of time. This axiom, and the fact that we still cannot manipulate genetic material in humans, means that we still have to count our calories and exercise in order to impart lifestyle and behaviour changes.

### Lifestyle changes and food intake

Obesity is generally accepted as resulting from an imbalance between food intake and daily physical activity. Obesity is thus the largest nutrition-related problem in the developed world. Despite the overwhelming amount of research and statistical analysis, no clear explanation can be given for the relationship

between changes in behaviour and the rapid increase in the prevalence of obesity in the past three decades.

Health guidelines have been focused on three particular lifestyle factors: increased levels of daily physical activity and reduction of the intake of fat and sugars, particularly added sugars. The urgency to take public action regarding physical activity is generally accepted, but there is much debate about dietary macronutrients such as total fat intake and the intake of sugars and rapidly digested carbohydrates. In the 1970s some nutritionists considered sucrose, particularly added sucrose, as perhaps the most important dietary factor predisposing to weight gain [2]. Since then, attention has shifted towards fat as the major nutritional component promoting excess energy intake and weight gain [3]. Furthermore, data from national food surveys indicated a pronounced shift in the fat:carbohydrate ratio towards a diet more rich in fats [4].

Despite the controversy about the particular role of sugars, the message that fat in the diet is responsible for excess energy intake and weight gain became stronger. As a consequence of the recommendations to reduce fat intake, the market for low-fat food expanded rapidly in the 1990s [5]. The actual intake of fat expressed as a percentage of energy (En%), based on individuals' self-recordings, has decreased significantly over the past decade [6]. Although a number of meta-analyses on the relationship between freely available low-fat diets and body weight control showed that dietary fat intake is directly associated with obesity, the scientific evidence for the relationship between dietary fat content and the prevalence of obesity has been seriously challenged in recent years [7]. For example, Katan *et al.* [8] questioned the importance of low-fat, high-carbohydrate diets in the prevention and treatment of obesity. A reduction in fat intake resulted in only a very limited weight reduction of a few kilograms body weight.

Another important argument concerns the so-called fat paradox [9]. With the increasing popularity of lower-fat products, food intake statistics have shown a decrease in dietary fat intake although the prevalence of obesity is increasing. In fact, they blamed the nutrition community contributing to the obesity problem by conveying the notion that only fat calories lead to weight gain and that grains and other starches can be eaten with impunity.

However, we should consider this with great caution because we now know that there is a systematic underreporting of energy and fat, most probably in the whole population but certainly in the obese [10]. The message that we need to reduce fat has its impact on food recordings despite all efforts to validate food intake data. This massive systematic underreporting can also be concluded from the production figures, as recently presented in the draft report on Diet, Nutrition and the Prevention of Chronic Diseases from the WHO FAO (Food and Agriculture Organisation), in which edible fat production and available food energy steadily rose over the past decades [11]. For example, the available fat per capita per day rose in the United States from 117 to 143 g between 1967 and 1997. Although the waste of food has increased substantially, it probably did not do so at the same rate as the increase in production. Consequently, there appears to be a discrepancy between an increase in food production per capita, and underreporting is a likely explanation.

A direct relationship between dietary fat and energy density was also questioned because of the observation that many lower-fat foods currently available are based on sugars, leading to energy density values similar to those of their high-fat counterparts [9]. This argument can not be true based on simple facts in physics. Energy density is mainly determined by energy content per gram of ingredients and the water content of the food product. Therefore, a very close correlation can be found between the energy content and fat content of a random selection of food items in the supermarket [12]. This type of message has renewed interest in implicating carbohydrates as being the primary nutritional factor behind the increase in obesity. Many refined carbohydrate foods produce a high glycemic response, thereby promoting postprandial carbohydrate oxidation at the expense of fat oxidation, thus altering fuel partitioning in a way that may be conducive to body fat gain [13]. This concept is in contrast with foods that produce a low glycemic response and lower postprandial insulin secretion.

The reduced capacity of obese individuals to mobilize and subsequently oxidize fat has been mentioned as a consequence of long-term hyperinsulinemia, but whether a direct link exists between both is questionable. Hyperglycemia and hyperinsulinemia are often accompanied by a decreased circulation of free fatty acids and a reduction in lipid oxidation [14]. Postprandial increases in glucose will indeed reduce blood free fatty acids and fat oxidation in the short term because of the effect of the subsequent insulin increase. The question that remains in relation to body weight control is whether these physiological effects persist or whether compensation occurs over 24 h.

The well-controlled study by Kiens and Richter [15], who provided high or low-glycemic index foods to lean volunteers freely for 30 days in a crossover design, did not find any differences in body weight between the two interventions in spite of significant differences in insulin profile during the day being observed between both diets on days 3 and 30.

Many animal studies have demonstrated an overeating effect with glucose, sucrose, and high-glycemic index diets [13]. As was demonstrated decades ago with cafeteria food diets, palatability is a major determinant of feeding behaviour in animals [16]. This is also true in humans, but the availability of tasty food in the supermarket or elsewhere is not specifically restricted to high-fat and sweet high-glycemic index products. Many products with a broad variety of macronutrients are very palatable. Therefore, the outcome of animal freely available food studies regarding the role of carbohydrates in the diet is not an accurate indication of the role of refined carbohydrates in the human diet.

### **Should we recommend low fat or low carbohydrate diets?**

Because body weight changes are mostly related to differences in energy intake, one should study the relationship between the type of macronutrient and body weight when individuals have free access to food. Studies comparing different diets under energy restriction or iso-energetic conditions are less valuable for providing information about the effects on body weight regulation than are overfeeding or freely available food studies.

A number of meta-analyses on the relationship between freely available low-fat diets and body weight control showed that a reduction in dietary fat intake is directly associated with weight loss [7]. Medium ( $\leq 3$  months) and long-term ( $\geq 6$  months) human intervention studies looking at the effect of the type of carbohydrate on body weight are, however, very limited.

Raben *et al.* [17] investigated the effect of a high-sucrose diet versus a high-starch and a high-fat diet on 14-day freely available energy intake, body weight, and energy expenditure in normal-weight and post-obese women. On average, energy intake was 13 and 12% lower on the starch diet than on the sucrose and fat diets, respectively. In both post-obese and normal-weight individuals, body weight and fatness decreased significantly on the starch diet. The authors mentioned three reasons for the low-energy intake in the high-starch diet: an increased satiating power because of the high fibre content and volume and a reduced palatability compared with the sucrose and fat diets. The higher energy intake with the sucrose diet was explained by the large amount of

sucrose-containing drinks in this diet. Fluids in general are less efficient at increasing satiety and suppressing food intake than are solid foods. This physiological difference between solid and liquid food is one of the basic principles on which carbohydrate sports drinks were developed to provide maximal levels of energy to the muscles of athletes. This potential weight-gaining effect of carbohydrate drinks was recently confirmed in a randomized 10-week study of overweight individuals who used dietary supplements containing sucrose or artificial sweeteners [18]. This is in line with prospective observational data on the risk of weight gain in children and the use of sugar-sweetened drinks [19]. Such studies indicated that the form of carbohydrate intake, liquid versus solid, may lead to extra energy intake before adequate feedback from satiety signals occurs.

The only large-scale, long-term, randomized controlled trial on the role of the carbohydrate:fat ratio in the diet as well as the simple versus complex carbohydrate issue is the CARMEN Multi-centre Trial [20], which involved 398 moderately overweight individuals in five different countries. That study investigated the effect on energy intake, body weight, and blood lipids of over 6 months of the freely available intake of low-fat diets (a reduction of ~10 En%) rich in either simple or complex carbohydrates. The results showed that both low-fat, high-carbohydrate diets reduced body weight significantly by 1.6 kg (for high simple carbohydrates) and 2.4 kg (for high complex) compared with a control normal-fat, normal-carbohydrate diet (Figure 1).

The energy density of both carbohydrate diets was significantly reduced [−0.10 (high simple) and −0.18 (high complex) kcal/g, respectively], although a large number of the low-fat alternatives contained higher levels of carbohydrates, particularly sucrose.

The findings from the CARMEN Study underline the importance of the public measure to reduce fat intake. A decrease in body weight of 2–3 kg by means of a general reduction in fat intake of approximately 10 En% in the general population could reduce the prevalence of obesity from 25 to 15% [7].

Very recently, the public debate received new input with the publication in *The New England Journal of Medicine* of two studies on the effects of the Atkins diet (high fat/low carbohydrate). Foster *et al.* [21] followed 63 obese individuals in a randomized controlled diet for 12 months. One group was given a copy of the popular book ‘Dr Atkins’ New Diet Revolution’ and the other group was asked to follow an energy-restricted low-fat diet. Although the initial weight loss was higher in the high-fat diet, no significant difference could be observed after 12 months. However, the dropout rate was high in both

groups (~40%). The study of Samaha *et al.* [22], randomly assigned 132 severely obese individuals to a low-carbohydrate diet (restriction to <30 g per day) or a low-fat and energy-restricted diet (500 kcal and <30 En% from fat). Weight loss in the low-carbohydrate group was significantly less (1.8 kg) than in the high-fat group (5.7 kg) after 6 months. Interestingly, macronutrient composition changes over the 6 months showed an increase in protein intake from 17 to 22 En% in addition to the increase in fat intake (33–41 En%). In the low-fat diet it turned out that the macronutrient composition of the diet did not change from habitual eating patterns (fat: 33 En%, carbohydrate: 51 En% and protein: 16 En%).

What can we learn from such studies? First of all, there are few other areas in which the frontiers of science are so confused by such a multitude of conflicting opinions. Nevertheless, a better understanding of what is going on is desperately needed because the epidemic of obesity is growing at rate that urgently needs valid intervention strategies at a population level. However, our understanding of the mechanisms of hunger and food intake are still not at a comprehensive level despite the enormous research input in the past few decades.

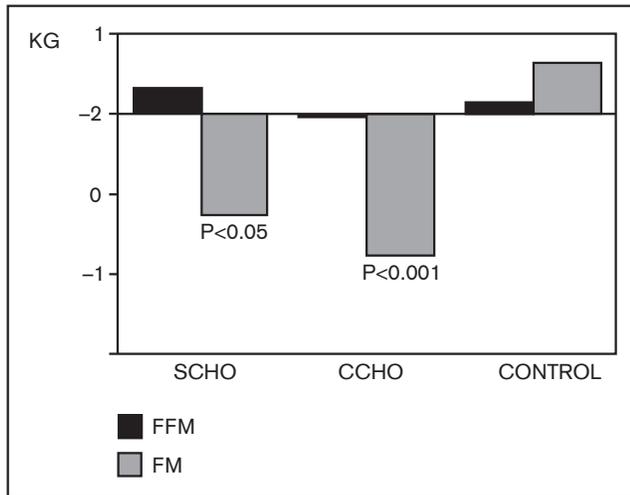
### In search of factors regulating body weight

The title of our editorial comment in 1998 would be an appropriate title again this year [23]. At that time we began to understand the role of the central neural system in the control of food intake. The first wave in leptin publications after its discovery in 1995 showed clearly that the system was much more complicated than just a satiety and feeding centre in the hypothalamus. Consequently, we invited Hans-Rudolf Berthoud to review the existing knowledge on the neural systems controlling food intake and energy balance (pp. 615–620). He presents a brief overview of the molecular mechanisms involved in the neural circuits regulating food intake and weight balance. A focus is on the pivotal role of the medial hypothalamus in the integration of metabolic signals coming from the peripheral organs such as the gut and liver to various brain regions. Here also is the link with the environmental factors influencing final eating behaviour, which are so strong in the modern world. He proposed that the switch between the instinctive control of food intake to a more cognitive control is necessary to stop the obesity epidemic.

The next paper by Drazen and Woods (pp. 621–628) discussed the equally important topic of peripheral signals of the gastrointestinal tract in the control of hunger and satiety.

In particular, this is of importance in relation to the problem of all the positive food signals in the modern

**Figure 1. Changes (kg) in fat free mass and fat mass during a 6-month intervention trial with 398 moderately obese adults on a low-fat, high simple carbohydrate diet, low-fat, high complex carbohydrate or normal fat, carbohydrate diet**



CCHO, Low-fat, high complex carbohydrate diet; CONTROL, normal fat, carbohydrate diet; FFM, fat-free mass; FM, fat mass; SCHO, low-fat, high simple carbohydrate diet.

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world during eating. These meal-related signals arise from many sources including the gastrointestinal tract, attractive food cues and the higher brain centres. An understanding of these types of processes are of utmost importance because most of the current problems are related to the direct effect of overeating during meals as well as starting too early with the next meal. Important known gastrointestinal hormones such as cholecystokinin and glucagon-like peptide 1 are discussed, but also lesser known peptides such as apolipoprotein A-IV, peptide YY, and the recently discovered ghrelin. The authors concluded that intervention should be directed at multiple targets simultaneously to be effective. The natural biology of body weight regulation is so fundamental for survival that it has an abundance of different pathways to control hunger and satiety both at a central and a peripheral level.

These two reviews can also be considered as basic introductions in the mechanisms of hunger and satiety in relation to the next papers dealing with the different macronutrients.

Unfortunately, the review on carbohydrates is not present in this issue as a result of unforeseen circumstances. Anderson and Woodend [24] recently published an excellent review on short-term satiety and food intake, which could serve as an alternative source of information about the role of carbohydrates and food intake.

French and Robinson (pp. 629–634) discusses in a very comprehensive review several items related to fat as a macronutrient in the diet and food intake. Short-term studies demonstrate a poor compensation for manipulating fat content, leading to passive overconsumption. Fat makes food palatable, which can certainly override the satiety effects of covertly manipulated macronutrient loads. The author also emphasized the importance of the structure of fats in relation to satiety signals, which could be of importance for the development of fats with a higher satiating effect.

Perhaps the most promising macronutrient in relation to body weight regulation is protein. Westerterp-Plantenga (pp. 635–638) highlights the potentials of protein as a macronutrient in the diet in relation to body weight regulation and especially weight management after weight loss. Protein has all the positive effects to function as an ideal macronutrient in the diet. It gives the highest satiating signals during and after the meal to reduce overall food intake. It increases diet-induced thermogenesis to lift energy expenditure in balance with energy intake, and finally, not well recognized so far, it can help in the additional formation of active energy-demanding tissues (only with exercise), such as muscle to increase thermogenesis further. This is of particular interest in relation to the problem of weight regain after weight loss. The studies reviewed clearly demonstrated a positive effect on long-term weight control. The author also summarized some of the problems we have to solve in the near future to come up with practical solutions. One of these is the problem of how to increase the portion of highly satiating ingredients in the diet.

Finally, Yeomans *et al.* (pp. 639–644) has reviewed the ‘forgotten’ energy-containing macronutrient alcohol. With an energy density of 7 kcal per gram and the current intake levels we cannot ignore this macronutrient in the search for important risk factors for weight gain. In contrast to the other macronutrients, in particular protein, there is minimal evidence for any reduction in food intake to compensate for the potential energy in alcohol. This stimulatory effect of alcohol is not only on short-term food intake but also over extended periods of time. On a metabolic level, alcohol suppresses fatty-acid oxidation, increases short-term thermogenesis, and stimulates a number of neurochemical and peripheral systems implicated in appetite control, including inhibitory effects on leptin, glucagon-like peptide 1, and serotonin and the enhancement of gamma-aminobutyric acid and neuropeptide Y. All of these effects could lead to over-eating, which marks this macronutrient as perhaps the most prominent obesity-inducing macronutrient.

In summary, as we highlighted 5 years ago in the editorial, the black box of weight regulation is slowly opening, and regulatory mechanisms are being discovered. The different roles that macronutrients play in our diet in this complex neurochemical system of hunger and satiety is becoming more clear. The reviews in this issue indicate that we are on our way to a better understanding of these issues, but that much remains to be learned.

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