Physiological Regulation of Macronutrient Balance

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BACKGROUND

For centuries the concept of energy balance has provided the bedrock for research into the mechanisms controlling body weight. However, in recent years there has been growing interest in the regulation of the individual macronutrients that combine to determine the energy status of an individual. Thus the classical energy balance equation can be more accurately represented as the integrated sum of each individual macronutrient (Figure 9.1). This chapter will discuss the evidence for the physiological regulation of macronutrient balance and the implications for the prevention and treatment of obesity.

MACRONUTRIENT METABOLISM

Digestion of food is macronutrient-specific from the moment of its ingestion. This raises the possibility that differences in the absorption, processing or storage of nutrients may provide a potential mechanism to explain a macronutrient-specific effect on body weight.

Digestion

In the first instance the efficiency of absorption of energy from individual macronutrients is variable. Approximately 96% of the energy from fat is absorbed, 91% from protein and a variable proportion from carbohydrate, depending on the relative content of ‘available’ carbohydrate and resistant starch. However, knowing the composition of the diet, the availability of energy is largely predictable (1). Moreover, except in pathological malabsorption syndromes, it is extremely consistent between individuals, which makes this an unlikely cause of individual susceptibility to weight gain.

The effect of macronutrients on diet-induced thermogenesis (DIT) is also variable. When consumed individually as the only source of nourishment, short-term experiments indicate that less energy is dissipated in the processing of fat (6%) compared to carbohydrate (12.5%) or protein (21%) (2). However, measurements made over the whole day in a whole-body calorimeter indicate very little difference in overall energy expenditure on diets with radically different ratios of fat to carbohydrate. For example, in a study in which individuals were fed isoenergetic diets with constant protein content and either 9 or 79% energy as carbohydrate, with reciprocal changes in fat intake, daily energy expenditure measured on two separate occasions in a whole-body calorimeter was not significantly different (3). Similar results have been obtained in groups of lean and obese men and women (4).

Major changes in the proportion of protein in the
diet do seem to lead to noticeable differences in diet-induced thermogenesis, but again the effect on 24-hour energy expenditure is negligible. For example, Westerterp et al. (5) showed that on a high protein/high carbohydrate/low fat diet (30:60:10% by energy) diet-induced thermogenesis represented 14.6% of the total intake and 24-hour energy expenditure was 9.2 MJ. Whilst on the low protein/low carbohydrate/high fat diet (10:60:30% by energy), diet-induced thermogenesis represented only 10.5% of total energy intake ($P = 0.01$) and while there was a trend towards a lower energy expenditure over 24 hours (8.9 MJ), the difference was not statistically significant ($P = 0.08$) (5).

### Macronutrient Oxidation

Once assimilated into the body a nutrient may be oxidized or stored. This process of nutrient partitioning is a key regulatory point in macronutrient metabolism and recent studies have shown a precise hierarchy in which macronutrients are recruited for oxidation. Since total energy expenditure is essentially constant, except for limited (and predictable) thermogenesis, the oxidation of any one nutrient will tend to suppress the oxidation of others. Alcohol dominates oxidative pathways, since it is a toxin and must be eliminated from the body as quickly as possible (6). Carbohydrate and protein also show a linkage between intake and oxidation. Numerous short-term studies have shown that the addition of carbohydrate to a meal will induce an increase in carbohydrate oxidation and likewise for protein (7,8). However, no such auto-regulatory process exists for fat oxidation. The addition of fat to a meal does not stimulate fat oxidation. Indeed the oxidation of fat is ultimately dependent on the intake of the other macronutrients, since fat oxidation accounts for the difference between the energy requirements of the individual and the combined energy content of the ingested alcohol, carbohydrate and protein (9). The addition or subtraction of carbohydrate from the diet causes a parallel increase or decrease in carbohydrate oxidation, with reciprocal changes in fat oxidation. However, when fat is added or subtracted from the diet the effect on substrate oxidation is negligible (10).

The impressive flexibility in carbohydrate oxidation rates in response to changes in intake is shown in Figure 9.2. Here, during profound overfeeding, subjects were receiving 150% of their baseline energy requirements including 539 g/day carbohydrate. Carbohydrate oxidation increased immediately and after 4–5 days carbohydrate oxidation closely matched intake so that carbohydrate balance was re-established, although at a higher level of glycogen stores. Conversely during underfeeding, when subjects received only 3.5 MJ/day, with 83 g/day carbohydrate, the oxidation of carbohydrate was suppressed and balance was again virtually re-established. The small persistent negative carbohydrate balance probably reflects a gradual depletion of muscle glycogen stores in response to this period of profound under-nutrition. Thus there is sufficient flexibility in carbohydrate oxidation to match intake over the range of about 80–540 g/day in adult men. Throughout this period the change in fat oxidation were counter-regulatory (Figure 9.3). During overfeeding the excess energy was stored primarily as fat, with a marked positive fat balance, and during underfeeding the energy deficit was met by the oxidation of endogenous fat, leading to nega-

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Figure 9.1 The oxidative hierarchy of macronutrients
tive fat balance. Changes in protein oxidation during both over- and underfeeding were modest, but with a trend towards auto-regulation (9).

Experiments investigating whether different primary sources of carbohydrate have variable effects on this carbohydrate-driven system of fuel selection have revealed no detectable differences between glucose, fructose and sucrose (11). When various energy sources are fed under controlled conditions (i.e. which exclude effects of appetite) fats and carbohydrates have a very similar effect on fat balance. This can be seen in Figure 9.4, which illustrates changes in fat balance when subjects are intentionally overfed in a whole-body calorimeter for 4 days.

The cumulative increase in fat balance did not differ significantly between treatments involving overfeeding by fat, sucrose, glucose or fructose. If individuals eat to energy balance, the pattern of macronutrient oxidation will closely match the dietary composition (i.e. respiratory quotient = food quotient). However, in conditions of energy imbalance the oxidative hierarchy predicts that fat will be the macronutrient most likely to be mobilized or stored to balance the body’s energy budget in the medium to long term.

Macronutrient Storage

The biochemical potential for the inter-conversion of macronutrients has aroused considerable interest, particularly in relation to de novo synthesis of fat from dietary carbohydrate. In energetic terms this is a very inefficient process, in which approximately 20–30% of the energy is dissipated as heat, whilst dietary fat can be stored with the loss of only 4% of its energy (12). A propensity towards de novo lipogenesis is a plausible ‘energy wasting’ strategy which may help some individuals to remain slim in the face of excess food. However, detailed studies
using stable isotopes suggest that this process is quantitatively unimportant in humans (13), except under conditions of profound overfeeding (14). This does not preclude an effect of other macronutrients on fat storage, an effect which is achieved by their suppression of the utilization of dietary fat.

MACRONUTRIENT EFFECTS ON INTAKE

Short-term studies of the effects of macronutrients on energy intake have often used a preload/test-meal paradigm. Subjects are given a ‘preload’ of known or unknown composition and after a fixed interval are offered one or more ‘test-meals’, at which they can eat *ad libitum*, but consumption is monitored. During the intervening periods they may also be asked to complete visual analogue scales indicating hunger or satiety. Similar studies have also been conducted to assess food intake over 1–3 days after a specific macronutrient manipulated meal or meals.

There are relatively few studies to address the specific effect of protein on subsequent intake. However, most data would suggest that in isoenergetic quantities, protein is probably the most satiating macronutrient (15–17). Whether this leads to differences in prospective consumption is more debatable. For example in a study of breakfasts high in protein, fat or carbohydrate followed by *ad libitum* consumption at lunch 5 hours later and thereafter, Stubbs et al. found that the high protein breakfast suppressed self-reported hunger to a greater extent over the entire 24-hour period (18). However, it was not translated into any difference in 24-hour energy intake or balance. Similarly in an extended 3-day study there was no difference in intake on days 2 and 3 following a high protein diet on day 1, relative to isoenergetic diets high in fat or carbohydrate (19). However, in most diets, protein is a much smaller constituent than fat or carbohydrate, which probably limits its overall contribution to the regulation of energy intake.

Instead most of the preload studies have focused on the relative roles of fat and carbohydrate by providing a constant proportion of protein and thus allowing reciprocal changes in fat and carbohydrate. For example, in a study where subjects were given a standard breakfast as a preload, or the same meal supplemented with 1520 kJ of fat or carbohydrate, *ad libitum* intake was measured at a subsequent test meal or snack (20). Visual analogue scores showed that the carbohydrate supplement suppressed hunger and the desire to eat, whereas the fat supplement had no effect relative to the control. By 4 hours later this difference had disappeared and there was no difference in energy intake at the test lunch consumed 4.5 hours after breakfast. In a subsequent study in which preloads were followed by an *ad libitum* snack 90 minutes later, when the difference in the hunger scores between preloads was still evident, there was a significant suppression of the snack intake after the carbohydrate-supplemented preload, whilst intake followed the fat-supplemented preload did not differ from the control.

The different results obtained by altering the interval between preload and test meal (20,21) or by varying the size or composition of foods (22) preclude total consensus in the interpretation of these studies. A further confounding factor in the analysis of these studies is the effect of the subjects’ state of knowledge. Overt manipulations of the fat to carbohydrate content of foods may produce contradictory results to covert studies. For example, Shide and Rolls showed that following a covert low fat preload, subjects consumed less at an *ad libitum* lunch than following a high fat preload. However, when information about the fat content of the preload was provided, the intake at lunch was greater following the low fat preload (23). In some cases the individual characteristics of the subjects may further distort the interpretation. Some studies have suggested that the degree of dietary restraint will influence intake at a test meal (24), although others have failed to find a difference between restrained and unrestrained eaters (23). However, it is generally agreed that dietary carbohydrate initiates a much stronger satiety signal than dietary fat and in so doing may limit prospective food consumption.

The concept that dietary carbohydrate may be more satiating than fat is consistent with the hypothesis of Flatt (7). Flatt argues that the quantity of carbohydrate oxidized each day is similar to the body’s storage capacity for carbohydrate, whereas the storage capacity for fat is considerably greater than day-to-day consumption or oxidation of this macronutrient. Thus day-to-day fluctuations in carbohydrate stores are proportionally very much
larger than for fat. This confers a much greater sensitivity to changes in the pool size for carbohydrate, than for fat, and Flatt argues that this modulates later consumption in order to restore the equilibrium. Based on this hypothesis the status of the body’s carbohydrate store is critical in determining intake and implies that individuals eat sufficient food to defend their carbohydrate stores. Thus on a diet with a low carbohydrate:fat ratio the total amount of energy consumed in order to provide sufficient carbohydrate will be greater than when consuming a diet with a high carbohydrate:fat ratio. This scenario must inevitably lead to fat deposition which will persist until such time as the substrate mixture being oxidized matches that of the habitual diet (i.e. RQ = FQ). Fat accumulation is thus interpreted as a response to a high fat diet (25).

Evidence for this theory comes from prolonged feeding trials in mice (7). Specifically there was a negative correlation between changes in carbohydrate stores and the subsequent day’s ad libitum intake, yet no association between net energy balance on one day and intake the next. However, extensive testing of this model in human studies has largely failed to support this early conjecture. This is clearly demonstrated in a study where glycogen stores were perturbed by feeding isoenergetic extremes of fat to carbohydrate intake (9 vs. 79% carbohydrate) on a ‘manipulation’ day and observing ad libitum intake on the following ‘outcome’ day (3). These studies were conducted within a whole-body calorimeter such that macronutrient balance could be ascertained relative to a nominal zero at the start of each phase of the study. Despite a difference in carbohydrate balance of 327 g between the high and low carbohydrate manipulations there was no significant difference in intake the following day. Subsequent studies have examined the impact of macronutrient manipulations which also include changes in energy balance on subsequent energy intake (26). Here an energy deficit of approximately 15% was created by the removal of either dietary fat or carbohydrate. The macronutrient manipulations produced significant differences in substrate oxidation, which were predictable from the oxidative hierarchy, but there was no evidence of any macronutrient-specific effects on subsequent intake. In each case, energy balance was restored after 1 day of ad libitum eating. These studies suggest that the net flux of all macronutrients may be better able to explain the pattern of subsequent energy intake than nutrient-specific models. In the light of this, Friedman has proposed a theoretical framework in which the stimulus to food intake is derived at the level of oxidative phosphorylation and adenosine triphosphate (ATP) production (27). However, to date there is relatively little direct experimental evidence in support of this model.

**IMPLICATIONS FOR OBESITY**

**Macronutrients and Weight Gain**

The integrated impact of the differential regulation of macronutrient intake, digestion, absorption, storage and oxidation generally supports the hypothesis that dietary fat may be particularly associated with weight gain. This has been examined in a number of studies conducted over several days or weeks. Here the period of study must be related to the precision of the measurements of changes in macronutrient balance. Tightly controlled experimental studies performed in calorimeters, where changes in fat stores can be measured to ±9 g fat/day, can be conducted over just a few days, whereas measurements made in free-living conditions, using in vivo body composition measurements require a period of several weeks or even months, since the precision is of the order of ±1 kg fat (28). Community studies, which rely solely on changes in body weight as an index of changes in fat stores, must be conducted over several months in order to provide a reliable indicator of long-term changes in fat stores, rather than acute fluctuations caused by shifts in water or carbohydrate balance.

Other studies have investigated the regulation of macronutrient balance using hour-by-hour measurements of the subjects’ self-selected intake and subsequent substrate oxidation whilst continuously confined to a whole body calorimeter. In one experiment six lean young healthy men were studied on three occasions in which each individual meal and snack was covertly manipulated to provide approximately 13% dietary energy as protein, 20, 40 or 60% energy as fat and the remainder as carbohydrate (29). Hence diets which were relatively high in fat were low in carbohydrate, with a high energy density and vice versa. On the 60% fat diet subjects were in marked positive energy and fat balance, but there was no significant change in
carbohydrate balance. Body weight increased by 0.9 kg over 7 days. On the 20% fat diet energy and fat balance was negative, although there was a modest positive carbohydrate balance. Despite the negative energy balance subjects gained 0.2 kg over 7 days, due to the increase in glycogen stores.

In a subsequent study conducted under free-living conditions absolute energy balance was lower on each dietary treatment, probably reflecting the greater energy needs of subjects outside the confines of the calorimeter. However, the inter-treatment effect was remarkably similar (30). Here the 20% fat diet elicited spontaneous weight loss of 0.74 kg in 14 days, relative to a gain of 0.09 kg on the 60% fat diet, despite eating *ad libitum*. This is consistent with a study in women, who lost 0.4 kg in 2 weeks on a 15–20% fat diet, but gained 0.32 kg over a similar period on a diet providing 45–50% fat (31).

This phenomenon of ‘high fat hyperphagia’ is a plausible explanation for the association of high fat diets with obesity (see Chapter 10). It is a robust and readily reproducible effect that is observed across different groups of subjects and in different laboratories. Given the increasing prevalence of obesity, a number of strategies have been considered to counterbalance the effect of high-fat diets. In a public health context physical activity offers an attractive option which will also provide independent health benefits. In experimental studies subjects who are confined to a calorimeter with a sedentary protocol, readily over-eat on high fat diets relative to high carbohydrate diets. However, a recent study has shown that the imposition of 3 × 40 minute periods of cycling, designed to raise the physical activity level (TEE/BMR) from 1.25 to 1.61, resulted in a significant reduction in energy balance, relative to the high fat–sedentary protocol. This was attributable to both an increase in energy needs and a reduction in intake (32) (Figure 9.5). This interaction between macronutrient and physical activity was also observed in the epidemiological analysis of the Gothenburg (Göteborg) Women’s Study where the risk of weight gain was significantly increased only in those women consuming a high fat diet who were also classified as sedentary (33).

In a clinical setting pharmacotherapy has been proposed to curb hyperphagia. In a study of six obese women offered either a 25 or 50% fat diet, along with either a centrally acting appetite suppressant (dexfenfluramine) or placebo, the drug reduced energy intake on the high fat diet relative to the placebo by 10%, but it did not significantly decrease intake on the low fat diet. It is noteworthy, however, that the effect of decreasing the fat content of the diet was more than three times greater than the impact of the drug (34) (Figure 9.6).

One of the most convincing mechanisms to explain the phenomenon of high fat hyperphagia relates to the energy density of fat (39 kJ/g), which is
disproportionately high relative to carbohydrate (16 kJ/g) or protein (23 kJ/g). In studies where the energy density of the diets was held constant in the face of macronutrient manipulations the high fat hyperphagia is frequently abolished. For example, in a crossover study using predominantly liquid diets of similar energy density but containing either 24 or 47% fat, there was no difference in energy intake over a 2-week period (35). In the studies of Stubbs and colleagues described above, it was apparent that subjects had consumed a similar bulk of food on each occasion, despite the macronutrient manipulation (29,30). Thus the hyperphagia observed on high fat diets may be viewed as 'passive over-consumption', i.e. increases in energy intake in the absence of increases in the volume of food consumed. This was investigated further in a study where the energy density of the diets was fixed, whilst still providing 20, 40 or 60% energy as fat (36). Here high fat hyperphagia was not observed, although it is notable that there was a persistent decrease in energy intake on the high carbohydrate/ low fat diet, suggesting that the suppressive effect of carbohydrate on food intake is over and above its effects on the energy density of the food.

The importance of the energy density of food as a determinant of energy intake has previously been reviewed in detail (37). Traditional high fat food-stuffs frequently have a higher energy density than low fat/high carbohydrate foods. However, the advent of new food processing methods means that an increasing number of items may be low in fat but retain an energy density comparable to the high fat variety. Their effects on body weight regulation are unclear. Likewise the role of non-caloric sweeteners (38) and fat substitutes in the relation of macronutrient balance in children (39) and adults remains controversial with conflicting results obtained using different experimental paradigms (40–42).

The primary conclusion of the experimental studies described above is that diets containing a high proportion of fat disrupt the physiological processes that regulate macronutrient balance and frequently result in positive fat balance and weight gain. In contrast, in less controlled studies, especially in the community, it is the balance between physiological processes and external and/or cognitive influences which determines the overall effect. Here the effects of macronutrients on energy intake cannot be easily segregated from other factors controlling appetite (see Chapter 8). Accordingly it does not inevitably follow that low fat diets lead to weight loss.

### Macronutrients and Weight Loss

There is currently a clear divide in scientific opinion regarding the merits of low fat/high carbohydrate diets in the context of weight loss (43,44). We conclude that although there is evidence of spontaneous weight loss associated with low fat diets relative to high fat control diets, most intervention studies have shown only a small reduction in body weight (up to 0.6 kg/month). Moreover this loss occurs mostly in the first 3–6 months, after which weight may be gradually regained. This precludes the use of low fat diets as the sole strategy for weight reduction.

Nonetheless it is pertinent to note that most ad libitum, low fat intervention studies currently in the literature were not primarily designed to examine the impact of macronutrient manipulations on body weight. Indeed most subjects were not overweight and may therefore be more likely to protect their body weight, through either physiological or cognitive processes. Some studies gave specific advice to subjects to increase carbohydrate intake to maintain body weight (45) or advised on other non-specific strategies to equalize energy intake to control values (46,47). Some studies used a low fat diet as part of a broader management plan (48,49) including advice to stop smoking, which would tend to lead to weight gain. The notable exception is the study of Ornish, in which there is a decrease of 11.5 kg in weight (relative to controls) over 1 year (48). These patients were mostly overweight and angiographic evidence of coronary artery disease, which may have provided a very significant motivational factor to enhance compliance to the comprehensive management programme.

In studies of the treatment of obese patients there is little evidence of any macronutrient-specific effects on weight loss (50–53). Here the rate of weight loss is closely related to the energy deficit that is achieved, suggesting that the macronutrient effects are more subtle than gross differences in energy intake. However, low fat diets are an effective method to decrease total energy intake and two studies have shown that subjects in the low fat group perceived the diet to be more palatable and
showed significant improvements in quality of life scores which may increase the likelihood of greater compliance in the longer term (50,51). Two studies have assessed the value of ad libitum low fat diets, relative to energy-restricted diets for weight maintenance over 1 year following acute weight loss. Schlundt found no significant difference between groups in terms of weight regain, while Toubro and Astrup demonstrated significantly enhanced weight maintenance in the low fat group (54,55).

These studies raise a number of general issues regarding the efficacy of low fat diets in community studies. Firstly, compliance to the low fat regime is obviously a prerequisite for effective weight loss. An individual's perception of their personal fat intake relative to the population average does not correlate well with actual fat intake (56). Indeed in one survey and when questioned, most people tend to believe that they eat less fat than the average person! Thus subjects who routinely incorporate some low fat products in their diet (e.g. low fat milks or spreads) may believe that they have reduced their fat intake, yet consciously or subconsciously compensate, by consuming additional fat in other items. In studies in the UK the majority of consumers report that in recent years they have reduced their personal fat intake (57), yet estimates of fat consumption from the National Food Survey have remained rather constant (58). In a study which incorporated independent estimates of compliance, using $^{13}$C-labelled glucose and subsequent measurement of $^{13}$C in expired air, there was a positive relationship between individual adherence to the low fat diet and the extent of weight loss (59). This confirms that different level of compliance is a major determinant of the success of low fat interventions.

Secondly, the actual change in dietary fat intake may be less than reported by dietary surveys. This is difficult to assess since self-reporting of food intake is notoriously unreliable and dietary education may increase any bias in the reported macronutrient intake. Attempts to educate subjects how to consume less fat may also serve to educate subjects how to report less fat. Alternatively subjects may accurately report their intake on specific measurement days, when they may closely adhere to the dietary prescription, but this may be a poor reflection of their typical eating habits (60).

Finally, there is growing concern that subjects may reduce their fat intake but not necessarily reduce their total energy intake. Even in one of the most effective of the intervention studies where there was a striking reduction in dietary fat from 31.5 to 6.8%, this was accompanied by only a 0.6 MJ/day decrease in energy intake over one year (48). Apparently three-quarters of the decrease in fat was counterbalanced by increases in energy from other dietary constituents. This compensation may represent a physiological system which recognizes the fall in energy intake and endeavours to restore the status quo by stimulating consumption (26). Even if subjects adhere to the low fat prescription, weight loss may be attenuated by increases in other macronutrients. The overt nature of a study where subjects must self-select their own food (unlike the mostly covert laboratory manipulations) may trigger unpredictable cognitive responses, as observed in the preload/test meal paradigms (23). Covert manipulations may therefore be more effective in producing spontaneous weight loss because there is no obstructive cognitive response. However, the effect of reductions in dietary energy density on innate appetite control systems are insufficient to overcome total dietary disinhibition. The emphasis on low fat foods may contribute to a perception that such foods will not cause weight gain regardless of the amount consumed, thus liberating subjects from exerting any dietary restraint (61). Low fat foods which substitute for the high fat equivalent will tend to lead to a cut in energy intake, but the addition of low fat foods to the diet will simply increase energy intake.

The rather limited impact of reductions in the proportion of fat in the diet on body weight is in contrast with the effect of increases in protein, where the community data is generally stronger than derived from the laboratory studies described previously. In observational studies of food intake over a 9-day period, dietary protein was the most efficient macronutrient at suppressing subsequent intake, independent of its contribution to net energy intake (62). In a larger study of 160 women with 16 days of weighed food records over a 1-year period the energy consumed as protein was inversely related to total energy intake (63). Most convincingly, in a dietary intervention study for the treatment of obesity two groups were randomized to a 30% fat diet. A high protein group consumed 25% energy as protein and 45% energy as carbohydrate, whilst a high carbohydrate group consumed 12% as protein and 58% as carbohydrate. Over a 6-month period the mean weight loss in the high protein group was
8.9 kg compared to only 5.1 kg in the high carbohydrate group ($P < 0.0001$) (64). The principal mechanism of this effect appeared to be a greater reduction in overall energy intake in the high protein group, which would be consistent with increased satiety reported previously following high protein preloads. However, further research is required to assess the long-term impact of high protein diets on morbidity and mortality before high protein diets can be considered as a viable public health intervention for the control of macronutrient balance and body weight.

CONCLUSIONS

There is clear evidence of physiological processes that regulate macronutrient balance in humans. However, the continuing rise in obesity suggests that these processes are also readily over-ridden. Specifically dietary fat is associated with passive over-consumption as a consequence of its relatively high energy density and weak effects on both satiation and satiety. Moreover dietary fat does not stimulate its own oxidation and its submissive position in the oxidative hierarchy ensures its preferential storage over and above carbohydrate, thus minimizing the potential for oxidative feedback signals.

The seemingly logical extension of this physiological regulation of macronutrient balance would imply that strategies to decrease dietary fat would be associated with successful weight control and possibly weight loss. However, the key question is whether the macronutrient-specific effects on appetite are sufficient to promote a decrease in energy intake in the face of other physiological mechanisms designed to maintain body weight and energy balance. The lesser effects of macronutrient manipulations seen in overt interventions, versus covert studies, suggest that potent cognitive factors are at work which are able to overcome the physiological differences between macronutrients in the control of body weight. Reductions in dietary fat may reduce the risk of passive over-consumption, but will do nothing to limit active over-consumption.

In spite of significant differences between macronutrients in digestion, oxidation, storage and appetite control the physiological regulation of macronutrient balance is at best only one aspect of the aetiology of obesity and its effective management.

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