Macronutrients and Energy Balance in Obesity

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Energy balance is the difference between metabolizable energy intake and total energy expenditure. Energy intake is difficult to measure accurately; changes in body weight, for example, are not a good measure of the adequacy of energy intake, because fluctuations in body weight are common even if the overall trend is toward weight loss. It is now customary to assess energy requirements indirectly from total energy expenditure. Total energy expenditure consists of basal metabolism, postprandial thermogenesis, and physical activity. Energy expenditure is related to both body weight and body composition. A reduction in total energy expenditure accompanies weight loss, because basal metabolic rate decreases with the loss of lean tissue mass. Similarly, with weight gain, there is an increase in basal metabolic rate, because lean tissue mass grows to support the increase in fat tissue mass. Excess energy intake over energy expenditure causes weight gain and an accompanying increase in total energy expenditure. Following a period of adaptation, total energy expenditure will match energy intake and body weight will stabilize at a higher level. This same relationship holds for weight loss. Respiratory quotient (measured in steady state) is an indication of the proportion of energy expenditure derived from fat and carbohydrate oxidation. Over long periods of time, fat balance is equivalent to energy balance, as an excess of fat intake over fat oxidation causes fat storage.

THE MAINTENANCE of a stable body weight and body composition over the years results from a precise balance between energy intake and energy expenditure, as well as macronutrient intake and macronutrient oxidation. A daily excess of 5% (~100 kcal/d) of energy intake over total energy expenditure leads to approximately 6 to 7-kg weight gain in a period of 5 years. About half of the weight gain occurs during the first year.[1] After this period, weight gain levels out as a new steady state is reached. On average, about 75% of this weight gain is composed of fat and 25% of associated lean tissue. The initial body composition of the individual subjected to this energy excess, as well as the nature of the tissue retained, influences the magnitude of weight gain. Obese people gain more weight for a given excess energy than lean people.[1]

The variation in day-to-day energy intake within the same individual is much larger than the variation in total energy expenditure. The true habitual energy intake is difficult to assess, particularly in obese individuals who tend to underestimate true food intake.[2,3] Consequently, many clinicians now assess energy requirement from estimates of total energy expenditure, rather than estimates of energy intake.

COMPONENTS OF TOTAL ENERGY EXPENDITURE

Total energy expenditure can be partitioned into three components: basal energy expenditure, diet-induced thermogenesis, and total spontaneous physical activity.[4] Basal energy expenditure is measured under standardized resting conditions early in the morning before any activity. This component is essentially dependent on the amount and activity of the fat-free mass. Diet-induced thermogenesis is the increase in energy expenditure following the ingestion of food. This depends primarily on food composition but the state of energy balance also contributes to the level of diet-induced thermogenesis. The physical activity component is highly variable and depends on behavior, body weight and body composition, intensity of exercise, duration of exercise, and net work efficiency.

BODY WEIGHT

Early studies performed using a respiration chamber have shown that 24-hour energy expenditure is related to body weight.[5] In obese women subjected to a low-calorie diet, weight loss is accompanied by a decrease in total energy expenditure.[6] In addition, in absolute terms, total energy expenditure in obese patients has consistently been found to be significantly greater than that of lean controls.[7] The effect of body weight change on the three components of energy expenditure (basal metabolic rate, postprandial thermogenesis, and physical activity) was assessed in a separate study.[8] All components of energy expenditure decreased with weight loss and increased again with body weight gain.

ACTIVITY-RELATED ENERGY EXPENDITURE

Activity-related energy expenditure mainly depends on body weight and the type, intensity, and duration of exercise, as well as on the mechanical efficiency with which the individuals perform the work. Controversy still exists about the role of low activity levels in the etiology of obesity, both in adolescence and adulthood. A number of experimental studies based on indirect assessment of physical activity using pedometers, accelerometers, cinematography, and heart rate have demonstrated a significant reduction in spontaneous physical activity in certain obese groups compared with lean matched controls.

However, measurements of energy expenditure (by indirect calorimetry) have shown a linear relationship between body weight and 24-hour (or activity-related) energy expenditure.[5] It appears, therefore, that despite the greater placidity characterizing some grossly obese people, the absolute rate of energy expenditure—particularly in weight-bearing activities—is not lower than in lean people, as the blunted activity levels do not fully compensate for the greater gross energy cost of a given activity.

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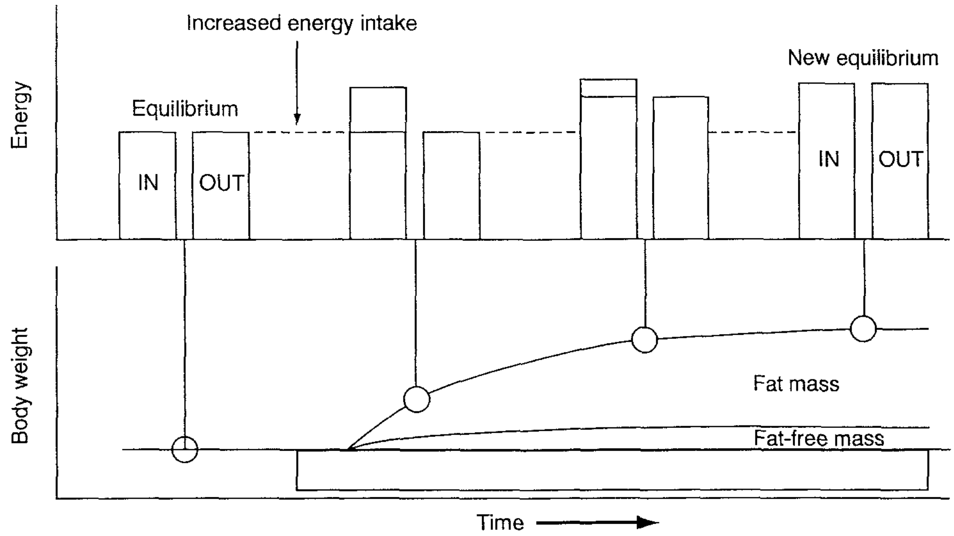

Fig 1. Following an acute overfeeding period, the energy balance can be reestablished as a result of heavier body weight and other factors shown in Fig 2. This figure exemplifies the time factor necessary for establishing a new energy equilibrium. Since over a long period of time, the change in energy balance is mostly explained by a change in fat balance (the fat-free mass storage is a proportionally small component of the total gain and represents a limited energy storage) the same concept of dynamic change can be applied to fat balance: an increased fat mass engenders a progressive rise in fat oxidation, so that after a period of time fat balance is reestablished.

THE DEVELOPMENT OF OBESITY

In simple terms, there are three distinct phases in the development of obesity. The static phase in pre-obese individuals, when weight is essentially constant, is followed by the dynamic phase during which weight increases (Fig 1). Eventually, a new static phase is reached. In practice, it is sometimes difficult to identify each distinct phase. Once body weight begins to increase, energy expenditure will also rise (Fig 2), so that the gap between energy intake and energy expenditure will diminish progressively (Fig 1). Over time, a new equilibrium is reached where the new energy expenditure matches energy intake and body weight stabilizes (static phase).

When weight is maintained at a constant level, energy intake matches energy expenditure (Fig 3). During short periods of overfeeding with mixed diets, energy is initially stored mostly as glycogen and fat. When overfeeding persists for long periods, excess energy is stored primarily as fat, with some increase in supporting lean tissue mass.

Small persistent increases in energy intake have a different impact on lean and obese patients. In response to the same amount of overfeeding, the weight of lean individuals

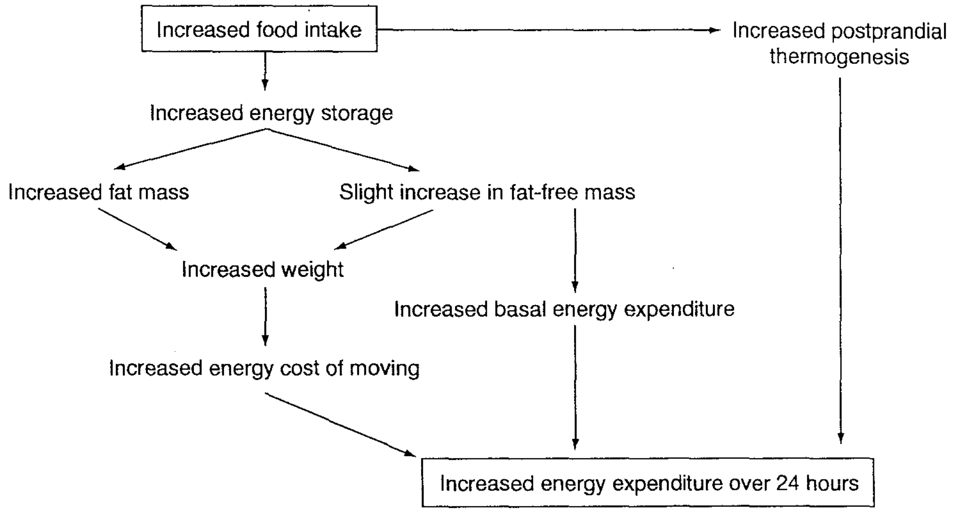

Fig 2. Acute overfeeding results not only in an increase substrate storage, but also in a rise in energy expenditure. This is explained by three factors:
(1) Increased food intake. This leads to an absolute rise (expressed in kcal/d) in postprandial (or dietary-induced) thermogenesis.
(2) Increased body weight. This is the consequence of an increased fat mass (resulting from positive fat balance), as well as a small rise in fat-free mass (due to positive protein balance), the latter contributing to enhance resting energy expenditure.
(3) Heavier body weight. This means that for a given physical activity, the cost of moving the heavier body is greater.

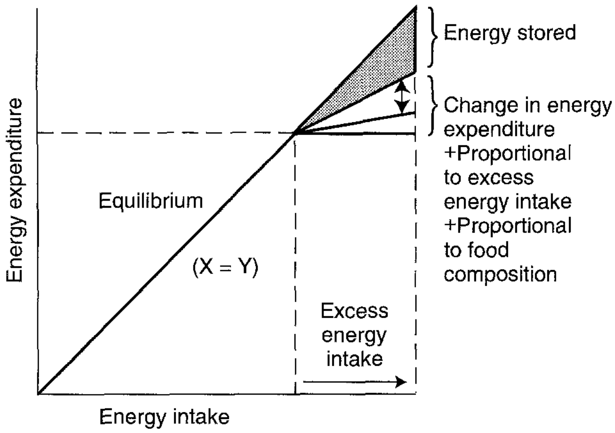

Fig 3. If a subject would remain in energy balance at any level of food intake, he would progress along the 45-degree line (X = Y) and a state of energy equilibrium would be reached at any level of energy intake. In practice, a step increase in energy intake induced by overfeeding is not able to reestablish the energy balance immediately since most of the energy surfeit is stored in the body as fat. The rise in energy expenditure accompanying the excess energy intake varies according to many factors, including the magnitude of energy dislocation, the composition of food taken in excess, and other factors related to the host. For example, an excess protein intake would lead to a lower net efficiency of energy retention—as evidenced by a higher thermogenesis (ie, a steeper line)—rather than a high-carbohydrate or a high-fat diet.

stabilizes after gaining fewer kilograms than that of obese individuals.[1]

WEIGHT MAINTENANCE: ENERGY BALANCE VERSUS SUBSTRATE BALANCE

Macronutrient intake and the level of physical activity vary spontaneously from day to day in a manner that is not necessarily synchronized. Substrate storage and mobilization therefore naturally fluctuate from day to day in a healthy individual. However, the fact that long-term stability of body weight and body composition is observed in many non-obese individuals despite these short-term fluctuations of substrate balance implies that compensatory changes occur. These adaptive changes include a change in substrate oxidation resulting from a change in energy expenditure and/or respiratory quotient (RQ), a change in body composition, and a change in food intake. The first two factors will be discussed here.

The percentage of energy derived from the different macronutrients (fat, carbohydrate, and protein) can be calculated from oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), and nitrogen excretion rates. The RQ ($\dot{V}CO_2/\dot{V}O_2$) provides an indication of the proportion of energy expenditure covered by fat and carbohydrate oxidation; protein oxidation is independently estimated from the rate of urinary nitrogen excretion over 24 hours.

The RQ is very sensitive to the composition of the diet,[9] and especially carbohydrate intake: acute ingestion of carbohydrates rapidly increases the RQ[10] and vice versa. This indicates that changes in the composition of the fuel mix oxidized occur rapidly in response to a change in the nature of macronutrient intake.[11]

Even if energy balance is close to equilibrium on a day-to-day basis, this may not necessarily be the case for the substrate balance. However, this lack of equilibrium of the substrate balance is only a transitory phenomenon, which occurs, for example, after changing the proportion of macronutrients in the diet without changing the total energy intake (isocaloric diet). As a result of this phenomenon, there is a larger deviation in substrate balance than energy balance on a day-to-day basis.

Flatt[11-14] was the first investigator who focused on macronutrient balance rather than energy balance, and clearly established that, in contrast to fat balance, carbohydrate and protein balances are accurately regulated.

CARBOHYDRATE VERSUS FAT BALANCE

In steady-state conditions, carbohydrate balance is usually reached over a 1 to 3-day period. Acute changes in carbohydrate intake from day to day are not immediately accompanied by a change in carbohydrate oxidation, as shown by the time required for the RQ to adjust to a new steady state.[9] As the body glycogen storage capacity is limited to 0.4 to 0.8 kg, an average daily carbohydrate intake of 250 g corresponds to 30% to 60% of the glycogen storage capacity.

The largest energy stores in the body are fat stores in adipose tissue, which represent 15 kg of body fat in a lean woman of 60 kg. This corresponds to 135,000 kcal. The daily fat intake constitutes, therefore, a small proportion (<1%) of the energy content of fat stores. Although protein and carbohydrate oxidation spontaneously adjust to protein and carbohydrate intakes, this is not the case for fat oxidation.[15] As a result, over a period of time longer than a few days, the gap between energy intake and total energy expenditure is primarily accommodated by changes in the body's fat content. Due to the high density of body fat (9 kcal/g), these variations are usually imperceptible from day to day and they are relatively minor compared with the size of the body's fat stores.

Lipid balance is poorly regulated, as it is rather insensitive to a large change in lipid intake,[15,16] and consumption of a mixed meal is followed by a decrease in fat oxidation, and an increase in carbohydrate oxidation. Recent studies have shown that within 1 week of either a high-carbohydrate or a high-fat diet, protein and carbohydrate equilibrium is usually achieved.[17] This is not the case for fat balance, indicating that there is no short-term metabolic response stimulating fat oxidation to correct the deviation from fat equilibrium. Low-fat diets must therefore be recommended when strategies for the prevention of obesity are designed.

OVERFEEDING SITUATIONS

Weight gain occurs when energy intake chronically exceeds energy expenditure. A new steady state is progressively reached after body weight has increased (Fig 1). On a day-to-day basis over a short period of time, weight gain or weight loss can transiently occur without a consistent effect on energy balance: changes in water balance constitute a powerful confounding factor and are also influenced by the state of carbohydrate balance, as glycogen storage is associated with an increase in water retention and vice versa.

The few human studies performed under conditions of short-term overfeeding have consistently shown an increase in resting and 24-hour energy expenditure. In a study of overfeeding with a mixed diet for more than 1 week, 75% of the excess energy intake was stored and 25% of the excess energy intake above the maintenance requirement was dissipated by thermogenesis.[18] The various factors explaining the increase in total energy expenditure and its components are represented in Fig 2. The energy stored in the body is composed of fat storage in adipose tissue and a small fraction by lean tissue gain. The thermogenic capacity of the human during overfeeding is not constant and depends on the nature of excess food eaten (excess protein is more thermogenic than excess carbohydrate or excess fat), as well as on the magnitude of overfeeding (large energy intake excess leads to a higher thermogenic effect than small energy surfeit) (Fig 3). The thermogenic effect of overfeeding is explained by the fact that exogenous substrates are not stored with 100% efficiency. The net efficiency of nutrient storage is substantially lower than the net efficiency of substrate mobilization, as the former requires the resynthesis of macromolecules, which involves extra adenosine triphosphate cost.

RQ OF THE BODY VERSUS RQ OF THE DIET (FOOD QUOTIENT)

RQ is defined as the ratio between the amount of carbon dioxide produced for a given amount of oxygen consumed by the body (V_{CO_2}/V_{O_2}). It is a useful indicator of the type of nutrients being metabolized by the body. The RQ of carbohydrate oxidation is 1.0, while fatty acid oxidation gives a value of approximately 0.7 depending on the composition of fatty acids oxidized. A resting postabsorptive RQ in a non-obese individual ranges between 0.8 and 0.85,[9] indicating that approximately 50% of the body's energy needs are met by fat oxidation and 40% by carbohydrate utilization. The energy supplied by protein oxidation is generally small, totaling about 10% to 15% of total energy expenditure.

Measurements of the RQ provide an index of the relative proportion of carbohydrate and fat oxidized. It is convenient to compare the RQ of the individual to the RQ of the diet (food quotient [FQ]) to assess the extent to which the relative proportions of carbohydrate and fat in the fuel mix oxidized by the body is different from that provided by the diet. In steady-state conditions, if the relative proportion of substrate oxidized is equivalent to that contained in the diet, the RQ will be equal to the FQ. If this is not the case, some changes in the body's glycogen store or fat reserve (or both) must occur.

RQs measured over 24 hours are influenced by the composition of the diet (ie, the FQ), as well as by the magnitude of the energy imbalance. During overfeeding, RQ will be greater than FQ, an indication that fat oxidation is inhibited; during underfeeding, RQ will be lower than FQ, indicating that fat oxidation is stimulated. The relationship between RQ, FQ, and energy balance is not simple, as situations can arise in which a high FQ is given under submaintenance conditions, the former potentially increasing the RQ and the latter decreasing it. When the individual has a RQ that is greater than the FQ, the fuel mix oxidized by the body has a greater proportion of carbohydrate than that contained in the diet, indicating a transient state in which the total amount of carbohydrate in the diet (not the percentage) is greater than that oxidized (overfeeding situation). In contrast, if the average RQ is lower than the FQ, the fuel mix oxidized has a greater proportion of fat than that contained in the diet.

Fat storage occurs when fat intake exceeds fat oxidation. This results in weight gain. The greatest fat gain occurs when a low-fat oxidation rate is combined with a high fat intake. Studies have shown that the total carbohydrate oxidation rate over 24 hours is similar in obese and non-obese individuals. However, fat oxidation was found to be greater in obese patients than in lean controls.[16-17] Protein oxidation rates were similar, but this depends also on the absolute amount of protein in the diet.

CONCLUSIONS

Weight gain occurs when energy intake exceeds energy expenditure. As energy expenditure increases with weight gain, a new equilibrium will eventually be reached and weight will stabilize. An imbalance between fat intake and oxidation may be one of the main contributors to the development of obesity in susceptible individuals.

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