Invited commentary

Adaptive thermogenesis during over- and underfeeding in man

Changes in body energy stores, reflected by changes in body mass, are the result of variations in the balance between energy intake and energy expenditure. Energy expenditure can be divided in to three components: obligatory energy expenditure, which is the energy expenditure required for the performance of cellular and organ functions, energy expenditure for physical activity, and adaptive thermogenesis, a variable regulated component of energy expenditure responding to changes in temperature and diet (Lowell & Spiegelman, 2000; Fig. 1). From an evolutionary point of view it makes sense that the body energy stores are defended during times of famine by reducing energy expenditure and that in times of food surplus the essential requirements of the body can be met rapidly and energy stores are refilled. Whilst a reduction in adaptive thermogenesis plays an obvious role in defending the body against excessive weight loss in times of food scarcity, the role of an increase in adaptive thermogenesis during times of feast is less clear. Stock (1999) has argued that the diet-induced adaptive thermogenesis under these conditions will allow an adequate supply of essential nutrients while avoiding the risks to survival of excessive fat gains. Our current Western diet, which is higher in fat and lower in protein content than that of our early ancestors, may be regarded as unbalanced in an evolutionary sense (Simopoulos, 1999). Overfeeding on a low-protein diet elicits a more pronounced thermogenic response, reflected as an increased energy cost of weight gain, than overfeeding on a normal-protein diet (Stock, 1999). It is important to be aware of the fact that diet-induced adaptive thermogenesis is used here in a broader sense than what is often regarded as diet-induced thermogenesis, i.e. the increase in energy expenditure above resting levels during the first hours after a meal, because it also includes changes in the adaptive component of RMR due to variations in dietary intake.

The capacity for cold-induced adaptive thermogenesis may differ between individuals (van Marken Lichtenbelt & Daanen, 2003). Studies in monozygotic twins, in which the energy intake and level of physical activity were carefully controlled, show large interindividual variation in the body-weight changes in response to an energy deficit or energy surplus. However, the between-pair variation was always larger than the within-pair variation, suggesting a genetic component in the capacity for adaptive thermogenesis (Bouchard *et al.* 1990; Hainer *et al.* 2001). Adaptive thermogenesis is a regulated phenomenon, in which the sympathetic nervous system is involved. Mice lacking all three β-adrenoceptor subtypes have lost their ability for diet-induced adaptive thermogenesis (Lowell & Bachman, 2003). In man the thermogenic response to catecholaminergic stimulation is lowered in obese subjects, suggesting a diminished capacity to resist weight increases under conditions of excess energy intake (Schiffelers *et al.* 2001). Food-related signals for changes in the level of activation of the sympathetic nervous system may come from cellular nutrient sensors, such as the hexosamine pathway. The hexosamine pathway may be linked to the energy expenditure response to changes in food intake through adaptations in mitochondrial efficiency and activation of leptin-mediated neuroendocrine responses such as a reduced food intake and increased energy expenditure through activation of the sympathetic nervous system (Obici *et al.* 2002; Ravussin, 2002).

Careful studies by Leibel *et al.* (1995) have already shown that the human body is capable of adapting its energy expenditure to changes in dietary intake and thus diminish diet-induced weight fluctuations. The study by Macias (2004), published in this issue of the *British Journal of Nutrition*, reports similar findings using a different, indirect, methodology to estimate changes in energy expenditure. Macias (2004) has measured the changes in overnight body-weight reduction under conditions of under- and overfeeding and found that overnight weight loss was reduced by 8–15 % during a 3·8 MJ/d energy deficit period and increased by 15 % during a 3·7 MJ/d energy surplus period. Although this is a quite simple and straightforward method, it also has certain disadvantages such as the number of times overnight body-weight loss has to be determined in order to obtain an accurate measure and the fact that a change in overnight reduction of body weight cannot be directly converted to a change in energy expenditure (Macias, 2004).

The reduction of overnight weight loss of 22·3–40·2 g/d on the energy-restricted diet in Macias' (2004) study would result in a body-mass saving of 0·78–1·41 kg over 35 d. If the overnight reduction of weight loss was also present during the remainder of the 24 h, an even greater body-mass saving may have occurred. The theoretical weight loss (without adaptive changes in energy expenditure) on the energy-restricted diet in Macias' (2004) study can be calculated to be 4·4 kg, based on an energy content of 30 MJ/kg fat mass and 100 % fat mass loss. The latter is probably an incorrect assumption, which results in an underestimation of theoretical weight loss. The actual weight loss varied between 3·2 and 4·0 kg. Both the change in overnight weight loss and the difference between theoretical and actual weight loss support a reduction of adaptive thermogenesis during the underfeeding period.

Based on a 35 d energy surplus of 3·7 MJ/d and a weight gain of approximately 3 kg, the energy cost of weight gain was 43 MJ/kg in Macias' (2004) study. According to Stock's (1999) estimations this would not support an
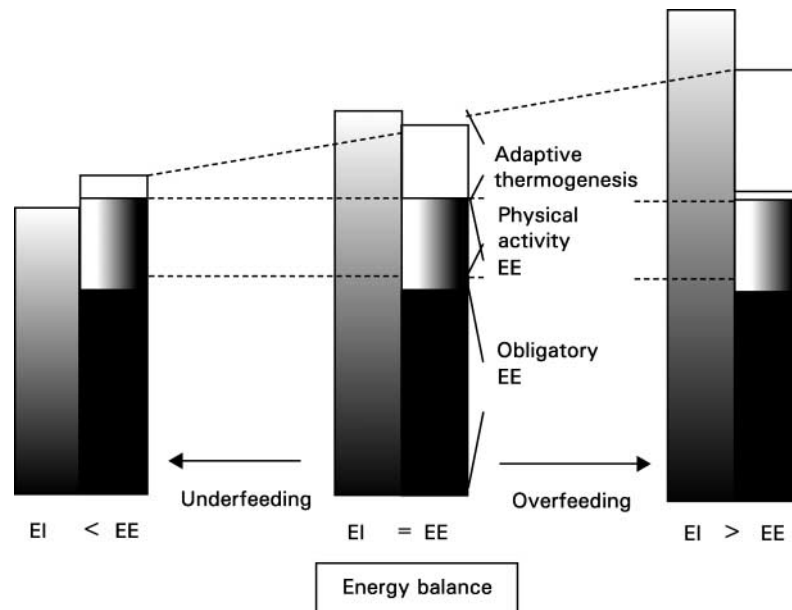
Fig. 1. Changes in energy balance resulting from changes in energy intake (EI). Adaptive thermogenesis, the regulated component of energy expenditure (EE), which responds to changes in temperature and diet, will increase during overfeeding and decrease during underfeeding, thus reducing the energy imbalance created by overfeeding or underfeeding. Over time, body-mass changes that result from the energy imbalance will result in changes in obligatory EE, required for the maintenance of cellular and organ functions, and EE for physical activity and a new energy balance at a lower or higher body weight will be attained.

increase in adaptive thermogenesis if 100 % of the weight gain were gain of fat, since the energy cost of increasing fat mass is 45 MJ/kg. However, as argued by Stock (1999), it is more realistic to assume that approximately 60 % of the weight gain is fat gain. In that case the energy cost of weight gain is only 30 MJ/kg (Stock, 1999). The theoretical weight gain during the overfeeding period would therefore be about 4·3 kg, while the actual weight gain was 3 kg. The increase in overnight body-weight loss would lead to an approximately 1·5 kg lower body-weight increase. Both would support an increase in adaptive thermogenesis during overfeeding in Macias' (2004) study.

Thus Macias' (2004) data on changes in overnight weight loss indeed support adaptive changes in energy expenditure which diminish variations in body weight and body energy stores in both dietary conditions, as has been shown in a more direct way before (Leibel *et al.* 1995). Interindividual variations in the responsiveness of adaptive thermogenesis to under- and overfeeding may help explain why some individuals are more susceptible to weight gain under conditions of excess energy intake or more resistant to weight loss under conditions of energy restriction. Future studies will undoubtedly reveal which genes are involved in adaptive thermogenesis and may help to predict individual susceptibility to weight changes.

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