Low resting energy expenditure in constitutionally lean children: may a high energy efficiency be a factor maintenance of a low body weight?

The prevalence of obesity in adults and children has increased markedly over the past decades to such an extent that it has reached what many people call epidemic levels (1). The pool of genes present in the various populations affected is unlikely to have changed very significantly over such a short time span, which means that changes in environmental factors are involved in first line. Among these, changes in dietary habits and a low level of physical activity are prime suspects. However, many individuals remain lean even though they are exposed basically to the same environmental factors as those who developed obesity. This can be held as evidence for significant gene–environment interactions in the control of body weight, although differences in physical activity may also be at hand.

In an interesting paper published in this issue of Clinical Nutrition, Tounian et al. (2) studied a subgroup of children with so-called ‘constitutional leanness’. Contrarily to the unfortunate children who gain fat mass when exposed to our fat-rich, sedentary environment, these children gain medical attention because of a degree of leanness judged abnormal. Although this medical condition has been little studied, there is some evidence for familial clustering, which suggests that genetic factors might be at hand (3). Tounian et al. hypothesized that leanness in these children could be due to any or a combination of three factors: (1) high energy expenditure; (2) high physical activity; (3) low energy intake. They therefore measured resting energy expenditure and found it significantly lower than predicted from their body composition. Given the fact that physical activity accounts for a relatively small portion (about 30% in adults) of 24 h energy expenditure (4), it is unlikely that an increased physical activity able to compensate for the low resting energy expenditure and to produce additional weight loss would have passed unnoticed. Tounian et al. concluded therefore that a low energy intake was responsible for the leanness of these children. This conclusion is fully supported by the observation of a low urinary nitrogen excretion, consistent with a low protein intake.

From an energetic point of view, these observations clearly challenge the frequently proposed hypothesis, i.e. that energetic inefficiency may confer a resistance to weight gain. According to this hypothesis, a low energy efficiency would allow to oxidize excess substrates to produce heat, thus avoiding an undue increase in fat mass. Based on the report by Tounian et al., this hypothesis does not hold true for children with constitutional leanness. In the absence of such energy wasting, what can explain the maintenance of such a low body weight in otherwise normal children? It is quite possible, as proposed by Tounian et al., that the affected children have for some reason, such as alterations of food intake control, a low spontaneous drive to ingest food. Energy restriction would then in turn lead to a low energy expenditure through adaptative mechanisms. Alternatively, it could be hypothesized that energy efficiency is by itself involved in the control of food intake. Over the past few years, several cellular systems have been shown to potentially modulate metabolic pathways according to the intracellular energy, or substrate status. AMP activated protein kinase, acetyl-CoA carboxylase, or even UCPs (of which some isoforms are expressed in the brain) may play such roles (5–7). Is it therefore possible that a high energy efficiency in specialized central nervous cells might actually help maintain a low food intake? If that were the case, then one should perhaps search for abnormal reduction in energy expenditure during starvation in obesity-prone individuals rather than for low increases in energy expenditure during overfeeding.

However, the above considerations remain, not even speculative, but a mere questioning in an attempt to fit these surprising observations in a more general perspective. Little is known on ‘constitutional leanness’, however. Given the facts that these children bear some features reminding of children born small for gestational age (who are characterized by low weight and height for age, together with an increased relative fat mass) (8), and that intrauterine metabolism might condition metabolism in subsequent life (9), a careful assessment of the ‘intrauterine history’ of constitutionally lean children should certainly be a major point for future investigations. It may turn out that intrauterine undernutrition may permanently alter not only the metabolism of peripheral tissues, but also perhaps only in some individuals, the function of cells constituting the food intake control center in the central nervous system. The data presented by Tounian et al. do not allow to further evaluate the mechanisms underlying constitutional leanness. Their observation of a low unexplained resting
metabolic rate in these children should nonetheless encourage basic and clinical researchers to explore novel possible avenues to explain the variations in energy intake and expenditure leading eventually to the development of obesity.

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References