

Nature versus nurture in childhood obesity: a familiar old conundrum^{1,2}

Sue YS Kimm

Childhood obesity is an emerging pandemic of the new millennium, and thus we urgently need to understand its causal web. During the past decade, the identification of an obesity gene and the development of new insights into the physiology of appetite regulation and energy metabolism led to great promise and excitement. Despite these advances, we have yet to uncover the complex dynamics of energy intake and energy expenditure (EE) in the context of a person's environment, behavior, and genes.

One plausible pathway for nature to manifest itself is via modulation of thermogenesis, which in turn affects energy balance. A perennial question is whether obesity-prone persons have lower resting metabolic rates than do lean people, because this endogenous trait could be genetically modulated. Thus far, there is no consistent evidence directly linking lower metabolic rates to obesity, perhaps because the published information comes mostly from cross-sectional studies of obese subjects. The association between body mass index or fat mass and resting metabolic rate is paradoxical: heavy persons generally have high metabolic rates. This is counter to the expectation that excess energy storage in heavy persons is the result of parsimonious EE.

In this regard, the prospective design of the study by Treuth et al (1) in this issue of the Journal is a welcome addition to current information. The study population of 8-y-old prepubertal girls is an interesting group to examine because girls of that age are at the threshold of the major dynamic shifts in body composition that take place with the onset of puberty. Although the girls were all lean at the outset, they were stratified by the presence of parental obesity as a marker of risk. Despite the commendable aims of this study, we are left with several tantalizing questions that could serve as fuel for future studies.

Implicit in the study's premise is that a high risk of obesity conferred by parental obesity status is related to differential EE, with high-risk children having lower EE than do low-risk children. Yet, no differences in EE at baseline according to parental obesity status were found. However, although the study subjects were all lean (< 90th percentile for weight-for-height), the daughters of obese parents were actually heavier than were the daughters of lean parents. In this study, EE was not adjusted for body composition. Thus, a valid comparison of EE between the daughters of lean parents and those of obese parents cannot be made. It is possible that if the EE of the high-risk group were adjusted for their higher body mass, their adjusted EE would actually be lower than the adjusted EE of

the daughters of lean parents. On the whole, conflicting evidence still exists as to whether a predisposition to obesity is manifested as a low resting EE (REE) in childhood (2). The study by Treuth et al fails to resolve this controversy because several models for the components of EE were examined separately without adjustment for multiple comparisons. Hence, the statistical significance of these analyses remains in question.

Puberty appears to increase REE (3), but the effect of puberty is inconsistent. Bandini et al (4) observed no change in REE with pubertal maturation. In contrast, other researchers found a decrease in REE from the early to the mid stages of puberty (5, 6). Although Bandini et al (4) found no differences in REE among prepubertal children according to parental overweight status, pubertal children of lean parents had lower REE than did those who had at least one overweight parent.

Puberty is also a time of great vulnerability to body fat gain (7). Treuth et al found a significant interaction between time and parental obesity status for the relations of several variables with fat mass, ie, the effect of familial predisposition to obesity emerged during early pubertal maturation. The observed interaction between parental obesity and age of the child may be a reflection of parental obesity status becoming manifest only after the initiation of puberty via differential fat gain in high-risk children. We may also conjecture that the effect of puberty on EE differs by parental obesity status at puberty. However, pubertal development occurs in different stages, and thus we may wish to know at which stage this time interaction takes place. Despite the longitudinal information on outcome measures, the time-independent nature (ie, baseline) of all the predictor variables yields information only on the average change over the 2 y of follow-up. The interaction between parental obesity status and time tells us only that there were differences in gains in fat mass or percentage body fat over time according to parental obesity status but does not provide us with the timing of this interaction. The examination of interactions between EE and time, between EE and pubertal stage, or even between EE, time, and parental obesity status

¹ From the Department of Family Medicine, University of Pittsburgh School of Medicine, Pittsburgh.


² Reprints not available. Address correspondence to SYS Kimm, University of Pittsburgh School of Medicine, Department of Family Medicine, 3518 Fifth Avenue, Pittsburgh, PA 15261. E-mail: kimm@pitt.edu.

might have shed some interesting light on when the differential effect of EE by parental obesity status becomes manifest.

Finally, assuming that parental obesity status is a marker of a genetic propensity for obesity, Treuth et al state, "Heritability of adiposity may then be an important factor contributing to increase in body fatness." Yet, we must not lose sight of another type of heritability, which is cultural transmission of learned "obesogenic" behaviors passed from parents to daughters. A report from the Quebec Family Study indicates that if the definition of obesity phenotype were narrowed from overall body fatness to specific body fat distribution, parental body-composition measures would offer less predictive value than would childhood and adolescent body-composition measures (8). Parental measures explained only an additional 2–9% of the variance in adult adiposity phenotypes beyond that explained by childhood and adolescent values, which together explained > 50% of the variance. Whitaker et al (9) reported that the odds of childhood obesity leading to later obesity in young adulthood increased exponentially from infancy to adolescence. However, parental obesity more than doubled the risk of adult obesity among all children aged < 10 y. In addition, the odds ratios for obesity associated with maternal obesity were slightly higher than those associated with paternal obesity. Does this finding suggest that the contribution made by the mother reflects nurture because she is the traditional caretaker of the family lifestyle, including diet? The doubling of risk with the presence of parental obesity may also be due to the compound effect of genetic and cultural heritability. The interaction between parental obesity and age of the child in the study by Treuth et al does not rule out the combined effect of nature and nurture.

Whether it is an expression of nature or the end result of nurture, the causal web of obesity is complex, and we may never be able to uncover the intricate pattern of interlinking threads. As MacMahon and Pugh (10) used to exhort, it is not necessary to understand causal mechanisms in their entirety to effect preventive measures. Knowledge of even one small component may allow significant degrees of prevention (10). Because nature can be viewed as an unbreakable thread in this causal web, efforts also must be made toward identification of a breakable nurture thread in the web. We do not need to wait for the unraveling of the entire web to begin to make progress against the rising tide of obesity.

In an ideal world, it would be optimal to start a longitudinal study at birth. It would be desirable to have serial (and even annual) longitudinal measures of body fatness and predictor

variables of interest including EE, as an intermediate phenotype of obesity-susceptibility genes, and measures of the environment such as energy intake and physical activity. We can move forward by borrowing strategies from clinical epidemiologists, who accrue large sample sizes in their clinical trials by using many different clinical centers, all with common protocols. As we plan our individual studies in this area, perhaps we should devise a consensus approach to the collection of standardized information on key variables of relevance, such as body fatness and pubertal maturation stages. These data from individual studies could be pooled with greater reliability to construct a "synthetic cohort," whose ages would span the entirety of childhood and adolescence. By gathering information on the effect of genetics and the environment in the context of the natural history of growth, we may yet have an opportunity to solve this conundrum of nature versus nurture in obesity. 

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