

Role of Environmental vs. Metabolic Factors in the Etiology of Obesity: Time to Focus on the Environment

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In the obesity research literature and in the mass media, a reduced metabolic rate is probably one of the most frequently cited causes of obesity. In the current issue of *Obesity Research* (pp. 351–359), Luke et al. (1) describe the results of a fascinating study that examined this hypothesis. Specifically, they examined whether genetically related people of West African origin, living in vastly different environments with large differences in the prevalence of obesity (4% to 5% in Nigeria, 35% to 50% in the United States) had any difference in resting metabolic rate. Low metabolic rate has been observed in many cross-sectional studies that have examined subgroups of the population at high risk of obesity, including African Americans living in the U.S. (2–5), Pima Indians living in southwestern Arizona (6), and children (7) and infants (8) of overweight parents. It has even been postulated that the lower resting metabolic rate in women (9,10) may explain the higher adiposity in women compared to men. However, other more detailed studies, which have compared groups at low and high risk of obesity, have failed to find evidence to support a role for resting metabolic rate (11,12). For example, Pima Indians living in Mexico who are much thinner than their genetic relatives in Arizona have a very similar metabolic physiology, despite large differences in adiposity (13).

The comparison of African American with white people has been of recent interest because of the much higher prevalence of obesity and obesity-related health risk in the African American population. Several cross-sectional studies in children (2,4), adolescents (5), and adults (14–16) have shown that African Americans have a lower

resting metabolic rate, although this observation is not consistent across all studies (17). Several papers in the literature have extrapolated from this finding to imply that the reduced metabolic rate is the cause of the obesity. Why would this be so? Is there any reason to believe that the homeostatic regulation that finely matches energy intake to energy expenditure is less likely to perform accurately at a low level of resting metabolic rate? It seems unlikely, given that resting metabolic rate only explains about 50% of the variance in total energy expenditure (18), and in growing children, neither high or low resting energy expenditure or total energy expenditure can predict which children will gain excessive body fat during subsequent growth (12).

In terms of the lower resting metabolic rate in African Americans, the more fundamental questions may be, 1) does their lower metabolic rate influence subsequent development of obesity, and 2) what is the mechanism underlying their lower metabolic rate? Regarding question #1, sufficient data now exist to indicate that a relatively low resting metabolic rate represents an inherent, probably genetically determined, characteristic of persons of African origin that may be more of a function of body composition. However, this characteristic probably does not explain their greater likelihood of weight gain in African Americans. Our recent, still unpublished follow-up data on 52 normal-weight women (mix of weight-reduced and never-obese African Americans and whites) indicated that the African American women gained over 60% more weight after just 1 year. Greater weight gain in the women, however, was not predicted by inherent metabolic characteristics such as lower rates of sleeping or resting metabolic rate, fat oxidation, or insulin sensitivity. Rather, greater weight gain was predicted by potentially modifiable factors, including less physical strength, less daily free-living physical activity, and lower total daily (but not resting) energy expenditure. Of particular interest are other recent data suggesting that African Americans are not only more energy efficient than whites at rest but also during physical activity, resulting in

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lower total daily energy requirements relative to their body mass (15). Teleologically, this greater energy efficiency of persons of African ancestry, particularly during physical activity, must have offered a survival advantage.

Regarding question #2, differences in energy metabolism may simply reflect subtle but important differences in lean tissue composition and have no bearing on the likelihood of the regulatory system to achieve energy balance. A recent study provides evidence that the lower resting metabolic rate in African Americans may be explained by their lean body mass comprising a lower proportion of metabolically more active organ tissue relative to muscle tissue (19). Thus, a thorough comparison of metabolic rates should not only include measurements of lean and fat tissue, but also of lean tissue composition and distribution. The more frequently used body composition techniques may not have the accuracy and/or level of sophistication for such detailed assessment. Moreover, additional carefully designed prospective studies are needed to examine whether a reduced metabolic rate contributes significantly to overweight and, conversely, if a relatively high rate contributes to underweight. The latter consideration may have less public health significance, but raises an important point. If a low resting metabolic rate is predictive of weight gain, should not also a high metabolic rate predict weight loss? That is, if a homeostatic set point for body weight exists, which is driven by variations/adaptations in resting metabolic rate, can it be unidirectional, favoring regain of weight lost but not re-loss of weight gained? This seems counterintuitive, recognizing the weight-gain pattern seen almost worldwide.

The strength of the Luke study does not lie in its methods of assessing energy metabolism or body composition, but in its comparison of two groups of genetically related populations who live, literally, worlds apart. The difference in obesity of the two groups is striking: the U.S. women had an average body fat of 41.3% and a body mass index of 31.4 kg/m², whereas the Nigerian women who had an average body fat of 29.1% and a body mass index of 23.3 kg/m². Despite this large difference, the relationship between resting metabolic rate and fat free mass was identical in the two populations. This suggests that factors other than resting metabolic rate are likely to explain the greater adiposity of African Americans living in the U.S. The most evident deduction from the Luke study would be that differences in the environment must play a powerful role in contributing to the prevalence of obesity.

An interesting additional finding from this study is that vast differences in environmental factors, including diet and physical activity, do not seem to influence resting metabolic rate. This runs counter to a popular hypothesis that resting metabolic rate is typically lower in people living in tropical regions. Together with recent similar results from other groups, this finding challenges our knowledge about the relationship of ethnic/cultural dif-

ferences to resting metabolic rate. As discussed above, detailed measurements of energy expenditure components and sophisticated body composition measures may be needed to address this issue.

In summary, the recent rise of obesity prevalence and the dramatic secular trend in body weight gain are unlikely to be explained by a sudden drop in the population's resting metabolic rate. We need to focus more on what metabolic, genetic, environmental, and behavioral factors lead to a mismatch between energy expenditure and energy intake. The mismatch should be the focus of our studies and the dependent variable under investigation, rather than the components on either side of the balance. In addition, we need more comparative studies of the type conducted by Luke et al. These are challenging studies for many reasons, but must be done to learn more about the complexity of factors involved in obesity. Simple comparison studies showing a lower resting metabolic rate (or any other obesity-related phenotype) are really of little utility in determining whether that phenotype causes obesity. Unfortunately, the energy balance principal is often portrayed as a simple concept, when in fact the details of this complex homeostatic regulation are only vaguely understood. If a low resting metabolic rate relative to body composition is significantly different in any one group of people compared with another, then the Luke study clearly suggests that environmental factors may be more important in triggering the expression of an obese phenotype. To prevent and reverse the current epidemic of obesity, we must focus our efforts on identifying and modifying the most potent of these environmental factors.

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