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Obesity—still highly heritable after all these years[1,2]

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In this issue of the Journal, Wardle et al (1) have published—and should be commended for—a careful statistical analysis of data from a population-based cohort of childhood twins that has advanced the understanding of pediatric obesity and placed that understanding in the context of the modern obesity epidemic. As one of the first twin studies to focus on body mass index (BMI) and abdominal adiposity in children born since the increase in pediatric obesity rates began accelerating 2–3 decades ago, its findings are important in ≥2 ways. First, the study confirms the substantial broad-sense heritability of obesity in a younger sample during this time interval. Broad-sense heritability is the proportion of within-population phenotypic variation that is due to within-population genotypic variations. This is in contrast to narrow-sense heritability, which refers only to the additive genetic influences and tends to be much lower (2). With broad-sense heritability estimated at 77% and a total (ie, shared and nonshared) environmental effect of <25%, we have evidence that the basic genetic architecture of obesity has not changed substantially. This implies that the lessons we have learned from 2 decades of careful study of the genetics of obesity since the seminal study by Stunkard et al (3) remain applicable. Second, Wardle et al were able to estimate broad-sense heritability for waist circumference in children for the first time. The fact that mean height, weight, and BMI in study subjects were quite close to 1990 levels, whereas mean waist circumference exceeded 1990 levels by 0.8 SDs, suggests that this measurement may explain the observed increase in adiposity with greater sensitivity and is consistent with recent evidence indicating that waist circumference levels seem to be increasing even beyond that which would be expected from increases in BMI (4, 5).

The statistical analysis appears sound and uses widely accepted methods and models. Heritability estimates from a simple method based on intraclass correlations (*see* Table 2 in reference 1) agree with estimates from the more elaborate statistical models (*see* Table 3 in reference 1), which speaks to the reasonableness of the models. We wish, however, that certain features in the data were given more attention in the body of their report. For example, Table 1 in Wardle et al shows that the proportions of overweight and obese subjects among dizygotic females (4.0% and 15.4%, respectively) exceeds the proportions among the entire sample (2.9% and 11.4%) and even those among monozygotic females (3.2% and 11.6%). In a similar vein, the intraclass correlation of BMI and waist circumference between dizygotic female twins (0.55 and 0.57, respectively) exceeds the correlation between dizygotic male twins (0.45 and 0.42). These 2 observations suggest that dizygotic females are perhaps a unique subpopulation deserving more attention.

Weight, height, and waist circumference measurements were made by the subjects' parents. Although researchers verified these measurements with in-home visits among a subsample of 228 children and observed high correlation between parent-measured and researcher-measured figures, it does not appear that the authors have considered the possibility of twin pair–correlated measurement error. If such a correlation existed and were similar among monozygotic and dizygotic pairs, it would tend to inflate the estimate of common (shared within household) environmental variance (ie, Σ_c^2).

Beyond these methodologic issues, we hesitate to concur with some of the inferences the authors drew from the modest (10%) shared-environment effect for both BMI and waist circumference. Although relatively low compared with the genetic effect, the shared-environment effect represents >40% of the entire environmental effect. Because public health interventions target environments and not genes, it seems somewhat odd to suggest that home-targeted interventions should be reduced on the basis of this finding. Nor does this suggestion jibe with the fact that most school-based prevention programs have failed to reduce obesity levels (6), and arguably the most successful childhood obesity treatment program to date has been family-based (7). It is also important to note that the shared-environment effect is the result of the degree of variability of environments that were observed in the sample, and, therefore, it cannot be used to infer the possible effects of altering the environment in which we all live and that may vary only modestly among families. If all homes, for example, had the same poor dietary and exercise practices, the shared-environment effect would be estimated as zero, and yet it would be entirely appropriate to attribute much of the obesity to parental behaviors. Even more speculatively, it has been conjectured that environmental contaminants may be contributing to the obesity epidemic (8). To the extent that this is true and that such environmental factors are ubiquitous, they are common to us all and therefore may not show up as common environmental variance.

The report by Wardle et al opens with a rather sweeping statement that the obesity epidemic is "clearly due to changes in the environment, because genes have not altered." Evidence in the

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literature to the contrary suggests the possibility of changes in the genetic background of contemporary populations by factors such as assortative mating, selection (eg, increased fecundity of moderately overweight persons), demographic changes (9), and epigenetic effects (10, 11) and that these changes could be relevant in humans as well. These changes should not be dismissed out of hand.

In conclusion, the research by Wardle et al adds to our body of research on the genetics of BMI in children by confirming that prior findings of a high heritability remain valid, even in the face of the current obesity epidemic, and by extending that research to show that the same general conclusions apply to waist circumference. With the power of the genome-wide association analyses finally in our hands, specific genetic variations influencing human obesity now are beginning to be found. As these measured genotype approaches finally begin to fulfill their promise, the tried-and-true unmeasured genotype approaches continue to help inform us about the overall effects of genotypic variation and its interaction with the environment.

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