How much do we know about the heritability of BMI?

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Is obesity heritable? Like father, like son; like mother, like daughter—scientists have no doubt about it. But how great is the contribution of genetics compared with environmental influence? Many twin studies were conducted over the past decade to estimate the "heritability" of BMI, a primary measure of adiposity. The results varied from 31% to 90%, reflecting a high genetic contribution (1, 2). Almost all of the studies assumed a single constant value of heritability, occasionally sex-specific, for the study cohorts collected within short or long periods. Is this assumption true? In this issue of the Journal, Silventoinen et al. (3) conducted a study to look into the variation in heritability across age by using BMI data from a total of 87,782 twin pairs pooled from 45 twin cohorts in 4 continents (Europe, East Asia, Australia, and North America). They estimated both common environmental and additive genetic contributions to BMI at each age-year by sex and geographic-cultural region.

They discovered 3 main findings: first, the heritability of BMI was consistently high, ranging from 41% to 85%; second, there were variations in heritability during infancy, young childhood, prepuberty, puberty, and adulthood, with nadirs at preschool and midpuberty and peaks at early puberty and young adulthood; third, the heritability of BMI is different between sexes and across different geographic regions.

The first finding is not surprising, but the second may make you think. Two larger meta-analyses of twin studies (1, 2) suggested a linear increase in heritability until adulthood but did not find the intricate preschool and midpuberty decreases. The increasing role of genes on BMI over age was partially explained by the gradually more important function of appetite-regulation genes before adulthood. But why does the genetic effect decrease during the preschool and midpuberty periods? The authors explained that the relatively low heritability at 3–4 y and 13 y was due to the stronger influence of shared environmental factors, such as culture and education. In terms of modeling, I would guess that the covariance adjustment may also affect the heritability estimate and contribute to the variation in heritability found in the study. Heritability was calculated after BMI was adjusted for a linear age effect within each age-year group. However, it is well known that infants grow much faster than older children, and thus a larger age effect may be removed from the BMI variance in infants. The same is probably true for children at the onset of puberty, 10–11 y for girls and 11–12 y for boys. As a consequence, heritability may be partially underestimated during growth spurts. But this barely

explains the interesting nadirs around 3 and 13 y. So we should continue to think.

As for the third finding, other studies have compared sex differences in BMI or heritability and found results similar to this study. Although distributions of BMI are different for boys and girls, its genetic contribution seems to be more or less the same. The gap during adolescence might be explained by sex hormone–regulated genes and some unisex genes, according to the authors.

In terms of cultural-geographic differences, this study found that heritability in BMI was higher in Westerners than in Asians, which is consistent with one study (2) but contrary to another (1). All 3 studies noted that Asians have been underrepresented in twin studies (4). Particularly for this study, cohorts in poor Asian regions with more diverse environment were excluded, resulting in a small sample (<400) of Asian teens and thus larger variance in the heritability estimate. On the contrary, cohorts in Europe, North America, and Australia had consistently larger sample sizes, which gave more confidence in the trend observed in BMI heritability. Nutrition, as an important environmental factor, probably differs between 2 regions, but its influence was minimized because the authors selected homogenous samples with better nutrition. The difference in BMI across study cohorts was adjusted, which can reflect either genetic or environmental components of BMI and may also account for a small proportion of the regional differences.

As a limitation of most twin studies, only additive genetic components were considered in the heritability estimate. Although many genes are dominant or recessive (5) and may interact with one other in a nonadditive fashion, the nonadditive component cannot be separated in these studies and, unavoidably, heritability is underestimated. The so-called ADE models with a dominant genetic component but no shared environmental component tend to overestimate heritability (6–9). As a solution, combining the nonbiological same-age siblings reared together would help separate all elements (10), although such pairs are rarely available in Asia.

Finally, I want to applaud the collaborative efforts of pooling all of the data for a thorough analysis. This may offer more precise inferences than the commonly used meta-analysis approach that uses only summary statistics such as *P* values or heritability estimates. The confirmation of the high heritability of BMI and a limited

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number of genes discovered to be responsible should encourage further genetic studies to be conducted to recover the missing heritability. In addition, this study probably had a more accurate description of the age trend because it was able to use the actual age for each subject rather than the mean age of the cohort as in other meta-analyses. The unique findings here may warrant further follow-up.

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