Childbirth Moderates the Genetic and Environmental Influences on BMI in Adult Twins

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We report a study of the moderating role that the number of childbirths has on the genetic and environmental influences on BMI variation. We used a classical twin design with a sample of 704 adult female twins (334 monozygotic and 370 dizygotic). A gene–environment interaction (G × E) model was applied to estimate the moderating effects of childbirth. Results show that age and number of children exert a significant positive main effect on BMI. Furthermore, we found significant moderating effects of childbirth, with a larger number of children associated with an increased sensitivity to environmental factors.

Twin studies have consistently shown significant genetic effects on the variation of BMI and related traits in both sexes and at all ages (1–4). These effects can be moderated by environmental factors like diet or physical activity (5,6). Epidemiological studies and meta-analyses have shown a clear relationship between parity and overweight (7–9), and childbirth has been suggested to act as an environmental trigger of genetic expression of BMI in women (3,10). However, to our knowledge, no study has yet looked at the relationship between childbirth and BMI within a gene–environment (G × E) interaction perspective. Analyzing possible interactions between genetic variation associated with BMI and environmental factors may provide further insight into why some individuals are more likely to become overweight. In this study, we applied a G × E moderation model to BMI data from a sample of adult female twins, incorporating number of childbirths as a moderator of genetic and environmental effects on individual differences in BMI.

METHODS

Subjects and measures
The sample comprised 200 monozygotic female pairs (134 complete and 66 incomplete) and 225 dizygotic female pairs (145 complete and 80 incomplete). Mean age was 51.46 (range: 41–67; s.d.: 7.7). The study has been approved by the Ethical Committee of the University and it follows national regulations regarding personal data protection. Zygosity was determined by questionnaire items about physical similarity and frequency of confusion of the twins by family and strangers. Height and weight were based on self-report. BMI was calculated as weight (kg)/height (m²).

Data analyses
We applied the classical twin design to estimate the contribution of genetic and environmental factors to population variation in BMI. We modeled additive genetic factors (A), shared environmental factors (C), and unique environmental factors (E). A G × E model was used to estimate the moderating effects of childbirth on the variance components A, C, and E. Main effects of age and the covariate under study were included in the model for the means, so that the genetic analysis is carried out on the residuals of this regression.

The Mx program (M.C. Neale, Richmond, VA) was used to estimate descriptive statistics and genetic models. Full Information Maximum Likelihood estimation with raw data was used for the analyses. Means, variances, twin correlations, and main effects were estimated in a saturated model. Nested models were compared with likelihood ratio tests, which has a χ²-distribution with degrees of freedom (df) equal to the difference in df between the two models.

RESULTS

Mean BMI of the sample was 25.7 (range: 16.37–48.44; s.d.: 4.4). Most of them (88.6%) had become mothers throughout their life span, with an average of 2.54 children (range: 1–10). The results of the saturated model showed no birth order or zygosity effects on mean levels or variance of BMI (P > 0.05). There was a significant positive main effect of number of childbirths (P < 0.01, β.zh = 0.21) and age (P < 0.01, β.age = 0.22) on BMI (regression coefficients were assumed to be equal for monozygotic and dizygotic twins). Thus, BMI was estimated to increase 0.21 units with every new childbirth, and 0.22 units per year. The twin correlations for BMI were 0.73 for monozygotic twins and 0.27 for dizygotic twins.

After fitting the full G × E moderator model, we proceeded to test the significance of each of the moderating effects, by fixing them to zero one by one starting with the smallest estimate. Number of childbirths showed significant moderating effects on the unique environment, but not on the genetic or shared environmental components. The contribution of the shared environment to the variance of BMI was nonsignificantly different from zero. The final model included genetic (a = 3.457) and unique environmental (e = 1.551) variance components, and a moderating effect on the later (β.e = 0.461).
Under no moderation, the heritability of BMI was estimated at 0.62. When the moderating effects were taken into account, the contribution of unique environment to the variance of BMI increased as a function of the number of childbirths. This result is depicted in Figure 1 on the unstandardized variance components.

**DISCUSSION**

Using a G × E moderation model within the classical twin design, we have investigated the effects of number of childbirths on the variation in BMI among adult women. We found that childbirth is associated with a mean increase in BMI, as well as an increase in the environmental contribution to its variation.

The analyses of main effects showed a significant increase in BMI associated with aging. A strong effect of age on BMI has been found in other adult samples (3,10) and seems to be related to both an increase in actual weight and an age-related decrease in height (4) among adult women. Additionally, this study shows that the BMI increase associated with aging is independent of parity.

Consistent with previous literature all the environmental effects were unique to the individual (1–4,9). Under no moderation, unique environmental factors explained 38% of the variance in BMI. Their influence raises with the number of childbirths, which results in an increase of the total variation in BMI, given that the absolute genetic variation remains intact. Consequently heritability decreases from 0.83 to 0.51 as the number of children increases up to four or more, whereas the relative influence of E increases from 0.17 to 0.49.

Thus, number of childbirths was associated with an increase in BMI, and a stronger effect of environmental factors. This pattern of results may be interpreted as a cumulative impact of weight retention after each delivery, which has been regarded as the main responsible for the childbirth-related increase in BMI (7,11). The much stronger relationship between childbirth and overweight among women, as compared to men, suggests the influence of sex-specific biological factors or gender-specific lifestyles. Physiological variations during pregnancy and/or breastfeeding, distribution of adipose tissue during pregnancy, physical activity in the postpartum period, or postpartum depression (12,13) may play a role in weight retention and the increase of variation in BMI among women with a larger number of childbirths.

Some methodological issues might limit the scope of our conclusions. We did not use genetic markers for zygosity assessment. Instead, zygosity was determined by a set of items based on the Dutch questionnaire, which has shown to correspond well with zygosity as determined by DNA testing, with an agreement in nearly 97% of the cases (14). Data relied on self-reports which might result in underestimation of BMI levels, and other variables which may be relevant to BMI variability among adult women, such as diet, have not been included in this study. Further research incorporating reliable measures of eating habits and other environmental factors would increase the specificity of the latent variance components estimated in this study.

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**DISCLOSURE**

The authors declared no conflict of interest.

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**REFERENCES**
