A Genetic Analysis of Relative Weight Among 4,020 Twin Pairs, With an Emphasis on Sex Effects

David B. Allison, Stanley Heshka, Michael C. Neale, David T. Lykken, and Steven B. Heymsfield

This study replicated previous findings showing a high heritability of obesity, as measured by body mass index (kg/m²), using a measure of relative weight that does not assume a constant regression of height on weight across different populations, and evaluated whether there are sex-limited genetic effects. Subjects were 4,020 adult twin pairs. Alternative causal structural equation models were fitted to variance-covariance matrices. The ADE model (additive genetic effects, dominant/nonadditive genetic effects, and unique environment) fit best. Allowing for sex-specific effects (common sex-limitation model) significantly improved the fit, $X^2(6) = 230.5, p < .001$. The heritability of that portion of weight unrelated to height was large: .61 for men and .73 for women.

Key words: obesity, genetics, twins, sex limitation

Twin and adoption studies have established that human obesity has a genetic component (Price, Cadoret, Stunkard, & Troughton, 1987; Stunkard, Harris, Pederson, & McClearn, 1990). Twin studies suggest that 60% to 80% of the variance in relative weight is a function of genetic variation (Meyer & Stunkard, 1993). However, many questions remain unanswered. One area of ambiguity concerns sex limitation in the heritability of adiposity. Sex limitation refers to any situation in which the degree or manner in which autosomal loci affect a phenotype differs across males and females (Eaves, Eysenck, & Martin, 1989). The first purpose of this study is to test if genetic and environmental determinants of relative weight are constant across genders.

Brook, Huntley, and Slack (1975) studied 222 pairs of like-sex English twins between the ages of 3 and 15. They estimated the heritability of triceps and subscapular skinfolds. Using the traditional formula, $h^2 = 2(r_{ma} - r_{mp})$ (Eaves et al., 1989), Brook et al. obtained heritability estimates of combined skinfolds of .61 for boys and .81 for girls. Neale and Cardon (1992) studied 5,465 pairs of U.S. adult twins. Using self-reported body mass index (BMI; kg/m²), they reported significantly different heritabilities for women (.75) and for men (.74) than for women (.69). These findings were supported by an analysis of 7,245 like-sex, adult Finnish twin pairs (Korkeila, Kaprio, Rissanen, & Koskenvuo, 1991), which estimated the heritability of self-reported BMI to be .73 for men and .68 for women. Finally, using directly measured height and weight on 238 pairs of Black adolescent twins and White adolescent twins, Allison, Neale, Heshka, and Heymsfield (in press) reported that heritability of BMI did not differ by sex.

In summary, several recent studies have investigated whether females have a higher heritability for BMI than do males. Some have found evidence that indeed females have a higher heritability for BMI than do males. In contrast, others have not. Thus, sex-specific effects on the heritability of BMI remain equivocal. Some ambiguity may relate to the use of BMI as a proxy measure of body composition. The use of BMI assumes that the regression of weight on height is the same in all populations and that kg/m² is the best index of relative weight. Benn (1971). Although BMI generally performs well, some data suggest that whereas kg/m² is optimal for men, kg/m² is optimal for women (Abraham, Carroll, Najjar, & Fulwood, 1983). Clearer answers may be obtained by scaling height and weight in a way that does not assume a constant regression across sexes. Thus, the second purpose of this study is to estimate the heritability of relative weight by means of a statistical technique that does not assume a constant regression of height on weight across all populations.

Method

Subjects

Subjects were 4,020 twin pairs (699 monozygotic [MZ] men, 609 dizygotic [DZ] men, 939 MZ women, 880 DZ women, and 893 pairs of opposite-sex DZ) between 28 and 52 years of age ($M = 40.26, SD = 6.23$). Over 99%
Subjects self-reported their height and weight. Such self-reports generally correlate >.90 with direct measurements (Stewart, 1982; Stunkard & Albaum, 1981). Mean weight was 71.90 kg ($SD = 15.57$), mean height was 1.71 m ($SD = 0.10$), and mean BMI was 24.57 ($SD = 4.16$). The distribution of weight was significantly skewed and kurtotic and was therefore transformed to approximate normality through a Box–Cox transformation (Woodward, Bonett, & Brecht, 1990).

**Analyses and Results**

Data were analyzed through the use of structural equation modeling (Neale & Cardon, 1992) through MX (Neale, 1991). Hierarchically nested models were evaluated in a backward elimination fashion. Height and weight were separated using a Cholesky decomposition (Neale & Cardon, 1992). The decomposition. The latent factors influencing height (i.e., $A_h$, $D_h$, and $E_h$; see Figure 1) were also allowed to influence weight. Because the loadings characterizing the paths are estimated on the sample data, one does not need to assign these values derived in a previous population. Second, these developmental effects.

We started by fitting two alternative models. Figure 1 depicts a model in which relative weight is a function of alleles acting in an additive fashion ($A$), alleles acting in a multiplicative fashion ($D$; i.e., dominance or epistasis), and environmental influences unique to individuals ($E$). The alternative model (ACE) is one in which relative weight is a function of $A$, $E$, and $C$ (environmental influences that are common to members of a twin pair). These models were applied while allowing for sex-specific effects on the common environmental and genetic factors (i.e., a common sex-limitation model; Neale & Cardon, 1992). Models were fit to variance-covariance matrices.

In keeping with past research (Meyer & Stunkard, 1993), the ADE model fit best. The ACE $\chi^2$ was 77.88 ($df = 42$) with an Akaike information criterion (AIC; Neale & Cardon, 1992) of -6.12. The ADE $\chi^2$ was 63.89 ($df = 42$) with an AIC of -20.11. The best fitting model (ADE) was significantly better than the simpler AE model, $\chi^2 (2) = 16.18$, $p = .0003$. In contrast, the ACE model.

The best fitting model is therefore an ADE model with sex-limited genetic and environmental factors. Parameter estimates are displayed in Table 1. The total heritability of that portion of weight not related to height was .61 for males and .73 for females.

**Figure 1.** $A = $ additive genetic effects, $D = $ nonadditive (dominance) genetic effects, $E = $ unique environment. The values for the correlations among latent variables are fixed based on genetic theory (Neale & Cardon, 1992). The values outside the parentheses are for monozygotic (MZ) twins. The values inside the parentheses are for dizygotic (DZ) twins. In the ACE model, the $D$s would simply become $C$s (environmental influences that are common to members of a twin pair), and the twin–twin correlations for the $C$ factors would be fixed at 1.0 for both MZ and DZ twins.
Table 1

Parameter Estimates for Best-Fitting ADE Model

<table>
<thead>
<tr>
<th>Parameter</th>
<th>A</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raw path coefficients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>.418</td>
<td>.050</td>
<td>.337</td>
</tr>
<tr>
<td>Women</td>
<td>.686</td>
<td>.167</td>
<td>.424</td>
</tr>
<tr>
<td>Squared standardized coefficients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>.600</td>
<td>.009</td>
<td>.392</td>
</tr>
<tr>
<td>Women</td>
<td>.694</td>
<td>.041</td>
<td>.264</td>
</tr>
</tbody>
</table>

Note. A = additive genetic effects; D = nonadditive genetic effects (i.e., dominance or epistasis); E = unique environmental effects + error variance

Discussion

Approximately 60% to 70% of the variance in relative weight can be accounted for by genetic factors. An ADE model fit the data far better than an ACE model. The ADE model implies that the genetic effects are not simply additive but that some of the alleles at some of the loci that influence relative weight are dominant/recessive. These data alone cannot tell us whether the obesogenic alleles are dominant or recessive. Future studies (e.g., of the offspring of consanguineous and nonconsanguineous marriages) could be helpful in this regard. It is this nonadditivity that probably explains, in part, why many twin studies legitimately yield higher heritability estimates than one would expect simply by looking at ordinary (nontwin) familial resemblance (Meyer & Stunkard, 1993).

The ACE model was not significantly better than an AE model, suggesting that the impact of the shared common environment is of no significant consequence on adult weight. In other words, those aspects of the environment that siblings jointly experience do not appear to have a long-term influence on relative weight.

Regarding the sex-specific effects, inspection of both the standardized and raw path coefficients (Table 1) is instructive. The differences in raw parameter estimates are greater than the differences in standardized estimates. If one were to look only at the standardized estimates, one might mistakenly conclude that the environment has less influence on the relative weight of females than of males. The raw estimates show just the opposite. The environment has greater influence on females. The apparent paradox is resolved by realizing that the genetic factors also have greater influence on females than on males and that this difference is proportionately greater than the sex difference in environmental influences. These findings are consistent with those of Neale and Cardon (1992), who also reported both raw and standardized solutions. Unfortunately, many authors (e.g., Brook et al., 1975; Korkeila et al., 1991; Stunkard et al., 1990) report only standardized results. The present findings underscore the point that analysis and inspection of unstandardized solutions provide a potentially richer source of information.

Regarding the observed gender differences, several speculations can be offered. First, E taps not only environmental variance but measurement error as well. Because heights and weights were self-reported, the validity (and hence degree of error variance) may vary by gender. However, most studies show the validity to be equally high for men and women (Stunkard & Albaum, 1981). However, there is a systematic bias in reporting of weights, so that people tend to underreport their weight (Stewart, 1982). This should result in a reduced variance in weight for women and therefore cannot account for the greater variance actually observed among women.

Actual weight-relevant environmental variance may also be greater for females. For example, the desirable body image for males has been fairly constant across time and cultures compared with that for women. In addition, body image has been shown to be more psychologically central for women than for men (Hesse-Biber, Clayton-Mathews, & Downey, 1987), which may account for the greater environmental impact.

The greater genetic variance among females may be due to epistatic effects with genes located on the sex chromosomes. However, before speculating further on this, it is important to remember the nature of the phenotype being studied. Body mass, although highly correlated with body fatness, is a mixed phenotype, being composed of both fat and lean. The observed gender differences may then be due to differences in the causal structure of lean mass, fat mass, or complex combinations thereof. Genetic studies using body composition techniques that can independently partition fat and lean mass are needed to definitively resolve this issue.

These results suggest that future research in this area is likely to demand the interdisciplinary approach that characterizes the field of health psychology/behavioral medicine. First, future studies are needed that assess the genetics of obesity using rigorous body composition measurement. Second, this study and others show that there is a significant role for the environment in determining relative weight. However, these environmental influences seem to be limited to those that are not shared by siblings. Discovering what nonshared environmental factors influence some people to be in a state of chronic positive energy balance is an important task for psychologists and behavior geneticists. Finally, although genes are quite influential in determining relative weight, genes make proteins, not fat. Thus, the genotype must influence the accumulation of adiposity indirectly through energy intake and expenditure. Psychological and physiological approaches both will be needed to study the genetics of energy intake and expenditure.

References


