Evidence for Genetic Influences on Human Energy Intake: Results from a Twin Study Using Measured Observations

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Human obesity is associated with greater-than-average energy intake, although relatively few studies have tested the heritability of food intake. The present study examined the genetic architecture of measured caloric intake during laboratory test meals in 36 monozygotic and 18 dizygotic twin pairs. A series of analyses tested the hypotheses that (1) there would be a genetic influence on total caloric intake, (2) there would be genes influencing total caloric intake above and beyond those influencing body composition, (3) there would be a phenotypic association between total caloric intake and fat mass above and beyond any genetic influences, and (4) there would be genetic influences on macronutrient intake (i.e., fat, carbohydrate, and protein intake) above and beyond total caloric intake. Results suggested genetic influences on age- and sex-adjusted total caloric intake (24–33% of the variance), although 95% confidence intervals were wide and suggested that "true" heritability estimates might be considerably lower or higher. Caloric intake was influenced by both common and unique environmental factors. Greater-than-average caloric intake was associated with increased adiposity, despite probable genetic influences on both phenotypes. Finally, there was evidence for macronutrient-specific familial influences, although the extent to which they were genetic or environmental in origin could not be teased apart. Results suggest that human obesity may be influenced by behaviors that are themselves genetically regulated. However, further studies are needed to obtain more precise heritability estimates and a better understanding of the conditions under which genetic influences on energy intake emerge.

KEY WORDS: Obesity; eating; common environment; unique environment; heritability; twins; gene–environment interaction; behavior.

INTRODUCTION

Obesity is a complex phenotype influenced by both genetic and environmental factors (Crowne and Allison, 1998; Maes et al., 1997), the nature of which is not completely understood. Obesity appears to result, at least partially, from behaviors including hyperphagia (i.e., greater-than-average energy intake) and reduced physical activity. These behaviors most likely contribute to a positive energy balance, thus promoting obesity development. However, few studies have examined the genetics of behaviors that might link the predisposing genotype to the ultimate obesity phenotype (Faith et al., 1997; Pi-Sunyer, 1997). In particular, the genetic architecture of human energy intake has not been characterized in much detail.

The primary aim of this study was to test the hypothesis that there are genetic influences on measured total and macronutrient-specific caloric intake in adults. This question is of importance given the role of eating to obesity onset. However, few studies have examined the genetic architecture of eating-related phenotypes in humans (Reed et al., 1997). Some studies have examined the heritability of self-reported energy intake (DeCastro, 1993; Fabsitz et al., 1978; Heller et al., 1988), although this method has questionable validity (Lichtman et al., 1992; Schoeller and Fjeld, 1991). Other studies examined the
heritability of taste preferences for individual food items (Greene et al., 1975; Kronfeld et al., 1983; Falciglia and Norton, 1994; Faust, 1974) rather than ad libitum energy intake at a multitemal meal. The present twin study extends previous research by testing the heritability of measured caloric intake at a buffet-style meal served in the laboratory and measuring percentage body fat for multivariate analyses.

The following hypotheses were tested. First, we hypothesized significant genetic influences on total caloric intake. This hypothesis was tested through a series of analyses of increasing complexity, ranging from test-retest stability and among-twin correlations to structural equation modeling. Second, we hypothesized that there would be genes influencing total caloric intake above and beyond those influencing fat mass, although some genes were hypothesized to influence both phenotypes (i.e., a genetic correlation). Third, we hypothesized that increased total caloric intake at test meals would be associated with increased body mass index (BMI; kg/m²) and percentage body fat, even after allowing for genetic influences on these phenotypes. Fourth, we hypothesized genetic influences on each of the macronutrients (i.e., fat, carbohydrate, and protein) above and beyond genetic influences on total caloric intake.

METHODS

Subjects

Subject characteristics are presented in Table I. Fifty-four pairs of same-sex twins were recruited from the tri-state area (New York, New Jersey, Connecticut) using newspaper advertisements and the New York Obesity Research Center twin registry. Thirty-six monozygotic (MZ) and 18 dizygotic (DZ) pairs participated in the study. All subjects were screened for a history of eating disorders, food allergies, and other factors that may induce dietary restriction (e.g., diabetes, medication, kosher diet, vegetarian diet). Eligible subjects (1) had to be at least 18 years of age; (2) were not lactose intolerant by self-report and had no relevant food allergies; and (3) were willing to undergo simple body composition testing, eat foods, and spend two half-day sessions at our laboratory. Each subject was compensated $150 in total for his/her participation.

Zygosity was determined through antigen profile of five markers, with an accuracy rate of >95%. In addition, all subjects indicated their zygosity through self-report. In seven cases, there was a discrepancy between subjects' self-report and maker analyses. For these subjects, additional markers were analyzed by the Coriell Repositories (Coriell, Camden, NJ) to reconcile the discrepancy.

Buffet Lunch

On each visit to the laboratory (two visits in total for each twin), a buffet lunch was served to each twin individually. Although twins came to the laboratory on the same days and times, they never ate in the presence of one another. At the appropriate time (see Procedures, below), each twin was seated at a table containing a variety of foods (see Table II). Subjects were instructed to consume whichever foods and drinks

<table>
<thead>
<tr>
<th>Variable</th>
<th>MZ</th>
<th>DZ</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pairs</td>
<td>36</td>
<td>18</td>
<td>54</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>77.8</td>
<td>77.8</td>
<td>77.8</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Caucasian</td>
<td>44.4</td>
<td>33.3</td>
<td>40.7</td>
</tr>
<tr>
<td>% African-American</td>
<td>47.2</td>
<td>55.6</td>
<td>50.0</td>
</tr>
<tr>
<td>% Hispanic</td>
<td>5.6</td>
<td>5.6</td>
<td>5.6</td>
</tr>
<tr>
<td>% Asian</td>
<td>2.8</td>
<td>5.6</td>
<td>3.7</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.66 ± 0.08</td>
<td>1.67 ± 0.09</td>
<td>1.67 ± 0.08</td>
</tr>
<tr>
<td>BMI*</td>
<td>25.9 ± 6.05</td>
<td>27.0 ± 6.02</td>
<td>26.3 ± 6.04</td>
</tr>
<tr>
<td>Total caloric intake#</td>
<td>401.7 ± 297.5</td>
<td>461.7 ± 316.2</td>
<td>421.7 ± 292.1</td>
</tr>
<tr>
<td>Fat intake#</td>
<td>166.08 ± 141.03</td>
<td>175.6 ± 130.8</td>
<td>169.3 ± 137.2</td>
</tr>
<tr>
<td>Carbohydrate intake#</td>
<td>185.07 ± 119.08</td>
<td>228.4 ± 161.7</td>
<td>199.5 ± 135.6</td>
</tr>
<tr>
<td>Protein intake#</td>
<td>51.03 ± 39.95</td>
<td>57.6 ± 38.8</td>
<td>53.2 ± 39.5</td>
</tr>
</tbody>
</table>

* Data presented are mean ± SD.
# Calories unadjusted for age and sex.
they wanted and as much as they wanted. After eating lunch, subjects answered several questions about the food served to them (e.g., “Was the food itself tasty?” “Did the food look right?” “What did you like the least about the meal?”). Each twin pair was randomly assigned to a “food serving” condition to establish which twin within a given pair, Sibling A or Sibling B, would first be served lunch on the given laboratory visit.

**Measures**

**Body Mass Index (BMI; kg/m²).** Subjects’ heights and weight were measured by standard stadiometer and balance-beam scale, respectively, and converted to BMI. Subjects were weighed while clothed and with shoes off. BMI is very reliable and a reasonably valid index of adiposity when compared with more sophisticated laboratory methods (Heymsfield et al., 1995).

**Bioimpedance Analysis (BIA).** Subjects’ percent body fat was measured by an RJL bioimpedance analyzer (RJL Systems, Detroit, MI). The validity of BIA as a measure of fatness has been demonstrated in several studies (Heymsfield et al., 1995). BIA measures the body’s resistance to an introduced electrical current of known frequency, which can then be converted to percentage body fat through validated equations. BIA estimates of fat mass correlate with adiposity estimates from laboratory methods such as total body electrical conductivity. BIA estimates are also reliable (test-retest r > .92) (Heymsfield et al., 1995).

**Total Caloric Intake.** Each food container was weighed before and after the Test Meal was eaten, without the subject present. Using nutrient information from food labels, total gram intake was converted to total caloric intake. Measures were taken for each twin on each of the two visits. The average total caloric intake was reliable (r = .86) using the Spearman-Brown prophecy equation (Rosenthal and Rosnow, 1991) and was used in all statistical analyses.

**Macronutrient-Specific Intake.** As with total caloric intake, we used nutrient information to measure the calories consumed from fat, carbohydrate, and protein at each lunch meal. Again, these calculations were done for each twin on each of the two visits and we used the mean score for each subject for all analyses.

### Table II. Macronutrient Contents of Foods Served at the Test Meal

<table>
<thead>
<tr>
<th>Food item</th>
<th>Amount (g)</th>
<th>kcal/g</th>
<th>Fat (g per typical serving)</th>
<th>Carbohydrate (g per typical serving)</th>
<th>Protein (g per typical serving)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chocolate candy</td>
<td>52</td>
<td>5.0</td>
<td>9.0</td>
<td>30.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Sandwich cookies</td>
<td>158</td>
<td>4.9</td>
<td>7.0</td>
<td>23.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Glazed donuts</td>
<td>95</td>
<td>4.1</td>
<td>11.0</td>
<td>26.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Apple</td>
<td>244</td>
<td>0.6</td>
<td>1.3</td>
<td>30.7</td>
<td>0.4</td>
</tr>
<tr>
<td>Tomato</td>
<td>226</td>
<td>0.2</td>
<td>0.2</td>
<td>5.8</td>
<td>1.4</td>
</tr>
<tr>
<td>Grapes</td>
<td>110</td>
<td>0.7</td>
<td>0.2</td>
<td>8.7</td>
<td>0.3</td>
</tr>
<tr>
<td>Dip</td>
<td>245</td>
<td>1.6</td>
<td>4.0</td>
<td>2.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Pretzel rods</td>
<td>110</td>
<td>3.7</td>
<td>0.5</td>
<td>24.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Wheat thins</td>
<td>110</td>
<td>4.8</td>
<td>6.0</td>
<td>19.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Hot dog rolls</td>
<td>98</td>
<td>2.6</td>
<td>2.0</td>
<td>21.0</td>
<td>4.0</td>
</tr>
<tr>
<td>White bread</td>
<td>53</td>
<td>2.3</td>
<td>1.5</td>
<td>21.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Whole wheat</td>
<td>75</td>
<td>2.4</td>
<td>1.5</td>
<td>14.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Carrot sticks</td>
<td>110</td>
<td>0.4</td>
<td>1.0</td>
<td>48.9</td>
<td>5.6</td>
</tr>
<tr>
<td>Broccoli</td>
<td>110</td>
<td>0.3</td>
<td>1.4</td>
<td>26.8</td>
<td>16.3</td>
</tr>
<tr>
<td>Turkey breast</td>
<td>35</td>
<td>1.1</td>
<td>1.5</td>
<td>3.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Mustard</td>
<td>339</td>
<td>0.0</td>
<td>0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Mayonnaise</td>
<td>220</td>
<td>7.1</td>
<td>11.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Ketchup</td>
<td>387</td>
<td>0.9</td>
<td>0</td>
<td>4.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Shef’s spread</td>
<td>234</td>
<td>4.3</td>
<td>7.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Swiss cheese</td>
<td>90</td>
<td>4.0</td>
<td>14.0</td>
<td>1.0</td>
<td>12.0</td>
</tr>
<tr>
<td>Muenster cheese</td>
<td>88</td>
<td>3.7</td>
<td>13.0</td>
<td>1.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Chicken nuggets</td>
<td>90</td>
<td>2.2</td>
<td>12.0</td>
<td>15.0</td>
<td>9.0</td>
</tr>
<tr>
<td>Wiener</td>
<td>160</td>
<td>3.1</td>
<td>13.0</td>
<td>1.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Orange juice</td>
<td>500</td>
<td>0.6</td>
<td>0.0</td>
<td>26.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Regular cola</td>
<td>382</td>
<td>0.4</td>
<td>0.0</td>
<td>39.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Diet cola</td>
<td>373</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Water</td>
<td>500</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>
Procedures

Twin pairs aged 18 and older were recruited for a study on "twins' taste preferences." Potential subjects were screened over the phone and those meeting study inclusion criteria were scheduled to come to the laboratory for participation. Subjects were not instructed to fast prior to their appointment. Figure 1 summarizes the study protocol for hypothetical Siblings A and B, respectively, within a given twin pair on each visit to the Obesity Research Center (ORC). All subjects were scheduled to arrive at the ORC at 1000 hr, at which point they signed the Consent Form. Next, during min 0–30, body composition measurements were taken on both twins. During min 30–60, Sibling A was served a small snack consisting of a pound cake slice, jam, and milk, as part of a separate research question (not discussed herein). Following the snack, during min 60–75, Sibling A watched a brief video on keeping a food diary. This video was presented because all subjects were required to keep a 3-day food diary upon leaving the laboratory. The diaries were kept for other purposes and are not discussed herein.

In contrast to Sibling A, Sibling B first watched the video during min 30–45 and then was served the snack during min 45–75. We counterbalanced snacks and video presentations within twin pairs for logistical reasons, that is, so the experimenter did not have to feed the two twins simultaneously.

During min 75–90, both siblings had their blood drawn (for zygosity testing). During min 90–120, Sibling A completed the Test Meal. Afterward, during min 120–150, Twin A completed a questionnaire packet for exploratory analyses (the results of which are not presented in this paper). Sibling B completed the Test Meal and questionnaire packet in the opposite order of Sibling A. Thus, during min 90–120 he/she completed the questionnaire packet. During min 120–150 Sibling B was served the Test Meal. At approximately 150 min after arrival, twins completed the protocol for the day and left the laboratory.

Statistical Analyses

Sample characteristics are presented as means and standard deviations. Test–retest stability, between-twin correlation analyses, and structural equation modeling (Neale and Cardon, 1992) were used to test the hypothesis of genetic influences on total caloric intake. For structural equation modeling, we tested the relative fit of competing genetic-environmental models. These models differed in the extent to which they posited additive genetic (A), common environmental (C), or unique environmental (E) influences on the phenotypes. Goodness of fit was assessed by the Akaike (1987) information criterion (AIC) and other standard indexes (Neale and Cardon, 1992). Multivariate structural equation modeling using the "Cholesky decomposition" (Neale and Cardon, 1992, Chap. 12) tested the hypothesis that there are genetic influences on total caloric intake above and beyond fat mass. These analyses also allowed for estimation of the genetic correlation (Neale and Cardon, 1992) between caloric intake and body composition phenotypes. Structural equation modeling using "phenotypic-cause" models (Neale and Cardon, 1992, Chap. 13) tested the hypothesized phenotypic association between caloric intake and body fat. Finally, structural equation modeling using the "common pathways" model (Neale and Cardon, 1992, Chap. 12) tested the hypothesis that there are macronutrient-specific genetic influences.

Across all structural equation modeling analyses, the difference in fit between competing models was tested by a chi-square test. Hypotheses were formally tested by comparing the fit of a "full" versus "reduced" model, which allowed us to test the effects of specific genetic and/or environmental parameters.

RESULTS

Evidence for Genetic Influences on Total Caloric Intake

Stability of Total Caloric Intake. Behaviors that are genetically influenced should be at least somewhat stable over brief time periods. Thus, at minimum, total caloric intake should be relatively consistent across
meals if there is a genetic influence on this phenotype. To test the stability of total caloric intake, we computed its test-retest correlation among the 108 individuals in our sample. Results indicated that total caloric intake was highly consistent when measured twice, approximately 1 week apart (test-retest \( r = .76, p < .0001 \)). The mean (±SD) caloric intake on visits 1 and 2 was 454.4 ± 327.9 and 389.0 ± 337.6, respectively. Adjusting for the effects of age and sex via multiple regression analysis, the association between caloric intake on the two visits was significant (\( r = .71, p < .0001 \)).

**Similarity of Total Caloric Intake Among Twins.** Adjusting for age and sex, total caloric intake was highly similar among all 54 twin pairs (\( r = .76, p < .0001 \)). Consistent with the hypothesis of a genetic influence, associations were stronger among MZ (\( r = .80 \)) than DZ (\( r = .68 \)) twin pairs. Figure 2 presents a scatterplot of adjusted total caloric intake among MZ and DZ twin pairs. Falconer’s (1990) formula yields a heritability estimate of almost one-quarter (\( h^2 = .24 \)), indicating that by this simple formula approximately one fourth of the variance in caloric intake was due to genetic variations.

**Structural Equation Modeling.** Table III presents heritability estimates and their 95% confidence intervals (CIs) estimated by Neale and Miller’s (1997) method. The data were best fit by a model positing additive genetic (A), common environmental (C), and unique environmental (E) influences (AIC = −3.361, \( \chi^2 = 2.693, df = 3, p = .45 \)). The root mean squared error approximation (RMSEA), a chi-square goodness-of-fit statistic that is relatively independent of sample size (Neale, 1997), also supported the ACE model. Only the ACE model had a RMSEA <.05, which is indicative of a very good fit (RMSEA = 0.041). Additive genetic, common environmental, and unique environmental influences accounted for 33, 48, and 19% of the variance, respectively, in adjusted caloric intake. At the same time, the 95% CIs for parameter estimates were quite wide and, for additive genetic influences, ranged from 0 to 81%. Although reduced models provided reasonable fits to the data, there was a decrement in overall fit in relation to the ACE model which approached significance for both the AE (\( \chi^2 = 2.167, p = .14 \)) and the CE (\( \chi^2 = 2.45, p = .11 \)) models.

**Evidence for Genetic Influences on Total Caloric Intake Above and Beyond Body Composition**

The second hypothesis predicted genetic influences on total caloric intake above and beyond those influencing BMI or percent body fat. This hypothesis was tested by comparing the fit of a reduced versus full model and can be pictorially represented with the aid of Fig. 3. The reduced model posited that genetic influences on caloric intake were attributable solely to genes influencing BMI (i.e., pleiotropy). That is, it posits that pathway \( a_5 \) is fixed to zero, while all other pathways are free to vary. The full model, in contrast, posited genetic influences directly on caloric intake above and beyond genes influencing BMI. That is, all pathways including \( a_2 \) were free to vary. To the extent that a distinct set of genes influences caloric intake, the full model should fit the data better. A 1-df chi-square test comparing the two models approached significance (\( \chi^2 = 3.09, p = .08 \)), suggesting that there may be genetic influences on total caloric intake that were not simply a function of those influencing BMI.

A comparable analysis tested whether the effects of BMI influence total caloric intake above and beyond BMI. Looking at Fig. 3, the reduced model posited that pathway \( c_7 \) was fixed to zero, with all other pathways (i.e., \( a_1, c_1, e_1, a_2, e_2 \)) free to vary. In contrast, the full model posited common environmental influences on total caloric intake above and beyond BMI. Thus, all pathways including \( c_7 \) were free to vary. The 1-df chi-square test testing the reduced and full models was significant (\( \chi^2 = 4.39, p = .04 \)), suggesting that there are common environmental influences specific to caloric intake.

Finally, a 2-df chi-square test assessed whether there are familial (i.e., joint environmental and genetic) influences on caloric intake above and BMI. Here, pathways \( a_2 \) and \( c_2 \) were jointly fixed to zero in the reduced model, whereas no parameters were fixed in the full model. Results indicated that the full model provided a significantly
better fit to the data ($\chi^2 = 48.49$, $p < .0001$), providing evidence for an overall familial influence.

When replicating these analyses with measures of percentage body fat, similar findings emerged. Specifically, 1-df chi-square tests suggested significant genetic ($\chi^2 = 4.99$, $p = .03$) and common environmental ($\chi^2 = 7.47$, $p = .06$) influences on total caloric intake when their respective effects were tested in separate models. The 2-df test evaluating overall familiality was also significant ($\chi^2 = 51.70$, $df = 2$, $p < .0001$).

**Evidence for Phenotypic Associations of Total Caloric Intake with BMI and Fat Mass**

Hypothesis 3 predicted that, despite independent genetic influences on caloric intake and body composition, there would be a phenotypic association between caloric intake and BMI (or fat mass). Indeed, across all 108 subjects, adjusted total caloric correlated positively with BMI ($r = .42$, $p < .001$) and percentage body fat ($r = .42$, $p < .001$). This hypothesis was formally tested by comparing the fit of two competing models using SEM. The analysis is pictorially represented in Fig. 4. The reduced model posited genetic influences on caloric intake and BMI but no association between the phenotypes. Thus, parameter $p$ was constrained to zero, with all other parameters free to vary. This model was compared against a full model that included a phenotypic correlation (i.e., parameter $p$ was also free to vary). The difference between the full and the reduced models was compared by a 1-df chi-square test.4

![Fig. 3](image1.png)

**Fig. 3.** Pictorial representation of structural equation models used to test Hypothesis 2 and related analyses. A, additive genetic influence; C, common environmental influence; E, unique environmental influence. In the full model, all parameters were free to vary. In the reduced model used to test for genetic influences on total caloric intake, parameter $a_1$ was fixed to zero. In the reduced model used to test for common environmental influences on total caloric intake, parameter $c_1$ was fixed to zero. In the reduced model used to test for overall familial influences on total caloric intake, both parameter $a_2$ and parameter $c_2$ were jointly fixed to zero. These models were constructed as a Cholesky model (Neale and Cardon, 1992, p. 248).

![Fig. 4](image2.png)

**Fig. 4.** Pictorial representation of structural equation models used to test Hypothesis 3 and related analyses. A, additive genetic influence; C, common environmental influence; E, unique environmental influence. In the full model, all parameters were free to vary. For the reduced model, parameter $p$ was fixed to zero. This model was constructed as a “phenotypic causation” model (Neale and Cardon, 1992, p. 265).

4 Our study did not have enough statistical power to test competing phenotypic causal models, that is, whether increased caloric intake caused increased BMI, or vice versa. Thus, our analyses only speak to phenotypic associations. Analyses were conducted according to pathways depicted in Fig. 4 (i.e., with the causal pathway from caloric intake to BMI) given the plausibility of this model from experimental animal models of diet-induced obesity (e.g., Boozer et al., 1995).
Multivariate analyses indicated that the full model fit the data well ($\chi^2 = 14.41, df = 13, p = .35, AIC = -11.60$). Moreover, the difference between the models was significant ($\chi^2 = 12.92, p = .0003$), suggesting a phenotypic association between caloric intake and BMI. When replicating these analyses using percentage body fat instead of BMI, similar findings emerged. The overall fit of the full model was very good ($\chi^2 = 15.91, df = 13, p = .25, AIC = -10.08$) and significantly worsened when a phenotypic correlation was not modeled ($\chi^2 = 8.03, df = 1, p < .001$).

There was evidence for a genetic correlation ($r_g$) between total caloric intake and BMI ($r_g = .37$), as well as total caloric intake and percentage body fat ($r_g = .43$), in the models tested. Thus, certain genes may have a joint (i.e., pleiotropic) influence on energy intake and body composition.

**Evidence for Macronutrient-Specific Genetic Influences**

The fourth hypothesis predicted genetic influences on fat, carbohydrate, and protein intake above and beyond total caloric intake. This hypothesis was testing by comparing the relative fit of two competing models and is pictorially represented in Fig. 5. The reduced model posited common and unique environmental influences, but no genetic influences, on each of the macronutrients. Thus, parameters $a_1$, $a_2$, and $a_3$ were fixed to zero, with all other parameters free to vary. The full model posited environmental plus additive genetic influences on each of the macronutrients, and so all parameters were free to vary. To the extent that there are macronutrient-specific genetic influences, the full model should better fit the data. The difference in fit between the models was tested by a 3-df chi-square test and was not significant ($\chi^2 = 1.49, p = .68$). Thus, analyses did not support the hypothesis of macronutrient-specific genetic influences.

A similar 3-df chi-square test was conducted to test for macronutrient-specific common environmental influences. For the reduced model, parameters $c_1$, $c_2$, and $c_3$ were fixed to zero, with other parameters in Fig. 5 free to vary. For the full model, all parameters were free to vary. The difference between the models was not significant ($\chi^2 = 1.67, p = .64$), suggesting that there may not be macronutrient-specific common environmental influences.

Finally, because additive genetic and common environmental influences can be highly correlated and the present sample size may have been insufficient to tease apart their respective effects, we tested the overall familiality of macronutrient-specific intake. That is, we tested for joint additive genetic and common environmental influences on the macronutrients. For the reduced model, parameters $a_1$, $c_1$, $a_2$, $c_2$, $a_3$, and $c_3$ were fixed to zero with all other parameters free to vary. For the full model, all parameters were free to vary. A 6-df test comparing the models was significant ($\chi^2 = 23.15, p < .0001$), suggesting overall familial influences on macronutrient-specific intake.

**DISCUSSION**

Insight into the genetics of obesity has increased dramatically in recent years. There is now emerging evidence of possible genetic contributions to putative causes of obesity, including energy expenditure and substrate utilization (Goran, 1997). Preliminary studies using self-report methods suggested a genetic contribution to energy intake (e.g., DeCastro, 1993). Building upon these studies, the present research suggests a probable genetic basis for ad libitum food intake, measured under controlled conditions. Across the different models tested, genes appeared to explain 24 to 33% of the variability in age- and sex-adjusted total caloric intake. One tentative conclusion from these data is that measured caloric eating might be worth measuring in...
studies searching for obesity-promoting genes. Existent linkage studies for obesity have tended to concentrate on physiologic and metabolic variables but not necessarily energy intake measures (Comuzzie et al., 1997; Norman et al., 1998). A critical issue would be whether the additional power conferred by obtaining such measurements would outweigh practical phenotyping costs.

While documenting evidence for genetic influences on caloric intake, an equally important finding from this study was the wide confidence intervals (CIs) around the heritability estimates. For example, the 95% CIs suggested that additive genetic influences could account for between 0 and 81% of the variance in caloric intake. This implies that genetic influences on caloric intake could conceivably be very small in an absolute sense and much smaller than those seen for BMI and body fat (Comuzzie and Allison, 1998). These findings underscore the need for additional research, perhaps with larger samples, to derive more precise heritability estimates or to better understand the conditions under which genetic influences on eating behavior emerge. With few exceptions (e.g., Bouchard et al., 1990), there are limited data on gene–environment interactions involving human ingestive behavior. Until such studies are conducted, the nature and magnitude of genetic influences on human energy intake remain somewhat unclear.

A noteworthy finding was the significant influence of common environmental factors on energy intake. This is in contrast with the almost-universal finding that the common environment does not influence BMI. This discrepancy suggests that the common environment’s influence on obesity may be an indirect one—that is, mediated through its impact on eating behavior. This finding also raises the question “What are the common environmental factors affecting food intake?” Although socioeconomic status and parental education are prototypic examples of common environmental factors, our study implicates a class of more transient, “day-to-day” variables that impact on eating behavior. Inherent in our protocol, twins arrived to the laboratory together on the same days, experienced the same conditions external to the laboratory (e.g., outdoor climate), encountered the same idiosyncrasies of the experimenter on a given day, etc. By capturing the broader eating context (including coming to the laboratory and eating) (Meiselman, 1996), our protocol may have been particularly sensitive to detect such common environmental influences. Designs such as the present, where subjects come to the laboratory and undergo a common protocol, may be well suited for detecting such environmental influences on behavioral phenotypes when they exist.

These findings might also reflect the effects of a gene–environment correlation on food intake (Rutter et al., 1997). Because twins generally traveled to the laboratory together, our design inherently afforded subjects the opportunity to create their own idiosyncratic environments prior to eating in the laboratory. To the extent that MZ twins “constructed” more similar experiences or environments than DZ twins (e.g., through breakfast selection), and this influenced subsequent food intake in the laboratory, such a scenario would implicate a gene–environment correlation. The protocol used herein, thus, might offer a useful research design for testing possible gene–environment correlations as they occur in the “natural” environment. Future studies using this sort of design might incorporate more focused microlevel environmental measures, prior to laboratory arrival, to test more powerfully for gene–environment correlations on the ultimate behavioral phenotype.

The present results may help clarify two seemingly contradictory findings from the literature: first, that obesity is strongly genetically influenced and, second, that increased energy intake is correlated with increased adiposity. Consistent with previous studies, the findings suggest that one pathway by which genes influence obesity might be through increased food intake. That disease-promoting behaviors are partially genetically influenced is receiving increasing recognition (Plomin, 1998; Rimer, 1997).

The tradeoff between sample size and rigorous behavioral measurement in genetic studies has been discussed elsewhere (Wachs, 1983) and is a common challenge for behavioral investigators. The present sample size was relatively small for testing more complex genetic–environmental models (Martin et al., 1983). For example, the present study provided evidence for macronutrient-specific familial influences, although the power was insufficient to disentangle clearly additive genetic from common environmental effects. On the other hand, even the largest samples might not adequately compensate for the measurement error inherent in self-reported food intake, and therefore, smaller samples with more precise behavioral measurements might be preferable for testing certain genetic models.

The interface between two subdisciplines, i.e., experimental ingestive behavior and gene mapping, has remained somewhat untapped in the human obesity field. Rigorous feeding studies have generally not incorporated genetically informative designs (Kissileff
et al., 1980, 1984; Rolls et al., 1994), whereas human linkage studies have typically not measured eating behavior. Genetic studies using animal studies have made much greater use of controlled food intake measures (Bray, 1996; Campfield et al., 1995; Pellymounther et al., 1995). The present study underscores the potential advantage of measuring ingestive behavior in human genetic studies. However, the results presented herein also suggest the possibility of strong environmental influences on caloric intake. Studies designed to estimate better the heritability of energy intake and the conditions under which such predispositions emerge may be especially informative.

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