Birth weight and body composition in young women: a prospective twin study

Ruth JF Loos, Gaston Beunen, Robert Fagard, Catherine Derom, and Robert Vlietinck

ABSTRACT

Background: The intrauterine environment may be critical for the development of obesity. Alternatively, the same genetic factors may influence both birth weight and adult body composition.

Objective: We evaluated the association between birth weight and adult body composition in female twins, which allowed us to control for maternal and genetic influences.

Design: Of 447 twin pairs randomly selected from the East Flanders Prospective Twin Survey, 238 pairs, aged 18–34 y, participated. Adult body mass, height, and lean body mass were measured, and the body mass index (BMI), waist-to-hip ratio, and sum of skinfold thicknesses were calculated. The twins were considered as individuals and pairs.

Results: When the twins were considered as individuals, twins who were heavier at birth were taller (3.3 cm/kg greater birth weight) and slightly heavier (1.13 kg/kg greater birth weight) as adults than were lighter twins. They also had more lean body mass and less subcutaneous and abdominal fat at birth. Pairwise comparison showed that for every level of intrapair birth weight difference (≥5%, ≥10%, and ≥15%), the twin who was heavier at birth was taller in adult life (0.8, 1.2, and 2.0 cm, respectively). When the intrapair birth weight difference exceeded 15%, the heavier twin was also heavier (3.1 ± 6.08 kg) as an adult than her much lighter sister.

Conclusion: Birth weight accounts for some of the differences in adult body composition between twins. 

INTRODUCTION

The intrauterine environment may be critical for the development of obesity (1). Several studies showed that birth weight or weight at 1 y of age is positively associated with the risk of obesity as an adult, defined as being heavy in relation to height (2, 3). Furthermore, persons who were lighter at birth tended to have more abdominal or truncal fat later in life (4–9), which is a major risk factor for many health-related complications (10–12). An alternative explanation is that the same genetic factors influence both birth weight and adult body composition. Stern et al (13) suggested that genes that cause a higher birth weight also increase the risk of developing the so-called metabolic syndrome, a clustering of dyslipidemia, hypertension, insulin resistance, and cardiovascular disease in adulthood (10, 11, 14, 15). Twin studies can help in distinguishing between genetic and environmental causes. Twins share a maternal environment and gestational age, and monozygotic twins are genetically identical. Comparing the members of a twin pair allows control for potentially confounding maternal and genetic characteristics. So far, only Allison et al (16) and Baird et al (17) have applied the twin approach to study the fetal origins of adult body composition. They found that the monozygotic twin who was heavier at birth was taller in later life, whereas adult body mass and body mass index (BMI) were similar for both twins. The main shortcomings of these studies are that zygosity was inaccurately determined (16, 17), adult height and body mass were self-reported (16), and no measures for body fatness and fat distribution were included (16).

In the present study we examined the association between birth weight and adult body composition, in particular lean body mass, subcutaneous fatness, and fat distribution, in female twins. The study used twins of the East Flanders Prospective Twin Survey (EFPTS), a population-based register known for its prospectively collected perinatal data and accurate zygosity determination (18).

SUBJECTS AND METHODS

Participants

The subjects were randomly selected from the EFPTS, a register of all twins born in the Belgian province of East Flanders...
since 1964. The register is characterized by its extensive collection of perinatal data at birth and placental examination within 24 h after delivery. Zygosity is determined through sequential analysis based on sex, fetal membranes, umbilical cord blood groups, placental alkaline phosphatase, and DNA fingerprints. A detailed description of the EFPTS was given by Loos et al (18).

Between July 1964 and May 1982 the EFPTS registered 2141 twin pairs with a birth weight of ≥500 g or a gestational age of ≥22 wk. Pairs in which one or both members were stillborn, died during the neonatal period or later in life, or had major congenital malformation were excluded, resulting in 1780 twin pairs, of whom 95 could not be traced because they moved abroad or changed address. After separating the remaining twins into male, female, and unlike-sex pairs, we randomly contacted 447 pairs from the female and unlike-sex groups. To ensure equally distributed groups, we stratified for birth year and zygosity. Eventually, 238 pairs (overall response: 53.2%) aged 18–34 y agreed to participate in the Prenatal Programming Twin Study, of whom 188 pairs were female same sex and 50 pairs were unlike sex (Figure 1).

Because only female twins were eligible for the present study, only the female members of the 50 unlike-sex pairs were included. In 11 cases, only one member of a same-sex pair participated. Eventually, 415 subjects participated in the examinations. They gave informed consent, and the project was approved by the local committee of medical ethics.

FIGURE 1. Allocation of subjects.

Measures

Birth weights were obtained from the obstetric records. Gestational age was reported by the obstetrician and was calculated as the number of completed weeks of pregnancy. Birth weights were also expressed as SD scores of the respective means/wk of gestation (z scores) to estimate the relative position of birth weight for a given gestation. The reported relative difference in birth weight (%) was calculated between the heavier and lighter sibling: [(heavier/1000 - lighter)/heaver] × 100.

Between February 1997 and April 2000, all twins visited our research center for a 2-h examination, which took place in the morning. Two trained researchers performed the anthropometric measurements according to standardized procedures. The intraclass correlation for interobserver reliability reached 0.93–0.99. Subjects were measured barefoot and lightly clothed. Standing height was measured with a Harpenden fixed stadiometer (Holtain Ltd, Crosswell, United Kingdom) to the nearest 0.1 cm and body mass on a balance scale (SECA, Hamburg, Germany) to the nearest 0.1 kg. Waist and hip circumferences were measured with a flexible steel tape to 1-mm accuracy. Waist circumference was taken between the costal margin and the iliac crest, and hip circumference at the widest part of the hips, generally at the level of the greater trochanters. Five skinfold thicknesses were taken, in duplicate, to 0.1-mm accuracy with a Harpenden skinfold caliper (British Indicators Ltd, St Albans, United Kingdom) at
the biceps, triceps, subcapular, suprailliac, and calf sites. Lean body mass (kg) was estimated with the use of the bioelectrical impedance analyzer BIA310 (Biodynamics, Seattle). BMI (in kg/m²), as a measure of overall body composition, was calculated as body weight divided by the square of height. Waist-to-hip ratio, as a measure of abdominal fat distribution, was expressed as a percentage. The 5 skinfold thicknesses were summed to evaluate the overall subcutaneous fatness.

Statistical analysis

Twins were considered both as individuals and as members of twin pairs for particular analyses. First, we performed multiple regression and analysis of variance to evaluate the relation between birth weight and body composition. Means and SDs were presented according to 4 birth weight classes, both adjusted and unadjusted for body mass. Adjustment was performed by linear regression. We excluded 3 subjects with a body mass <100 kg because of nonlinearity above this point. Because the inclusion of both members of a twin pair may violate the assumption of independence of the observations, the regression analysis in parallel with body mass, lean body mass, adjusted and unadjusted, was positively associated with standardized birth weight. Because of the high correlation between body mass and adult height, and the association with height increased (r = 0.90), sum of skinfold thicknesses and waist-to-hip ratio showed a negative association with birth weight. Because of the high correlation between body mass, on the one hand, and lean body mass (r = 0.90), sum of skinfold thicknesses (r = 0.78), and waist-to-hip ratio (r = 0.45), on the other hand, we adjusted these anthropometric measures for body mass. When adjusted for body mass, birth weight remained positively associated with lean body mass, and the negative relation with the sum of skinfold thicknesses and waist-to-hip ratio increased. Birth weight explained 6.4% of the variance in height. For other anthropometric characteristics, the contribution of birth weight did not exceed 3%.

RESULTS

Birth weight, gestational age, and unadjusted anthropometric characteristics are given in Table 1. At birth, monozygotic twins weighed 112 g less (P = 0.02) than did dizygotic twins. At the time of the examinations, monozygotic twins were slightly younger (P = 0.045) than were dizygotic twins. Adult body composition was not significantly different between the groups.

Birth weight and adult body composition

Birth weight was positively related to adult height (Table 2), ie, adult height increased 3.26 cm/kg increase in birth weight, resulting in a difference of 4.8 cm between the means of the 2 extreme birth weight classes. Greater adult body mass was associated with higher birth weight, but this trend was not significant. The other anthropometric characteristics also differed with differing birth weights. Lean body mass was positively associated with birth weight, and the sum of the skinfold thicknesses and waist-to-hip ratio showed a negative association with birth weight. Because of the high correlation between body mass, on the one hand, and lean body mass (r = 0.90), sum of skinfold thicknesses (r = 0.78), and waist-to-hip ratio (r = 0.45), on the other hand, we adjusted these anthropometric measures for body mass. When adjusted for body mass, birth weight remained positively associated with lean body mass, and the negative relation with the sum of skinfold thicknesses and waist-to-hip ratio increased. Birth weight explained 6.4% of the variance in height. For other anthropometric characteristics, the contribution of birth weight did not exceed 3%.

When birth weight was expressed as an SD score for gestational age, a positive association with body mass was apparent and the association with height increased (Table 3). Twins in the highest standardized birth weight class were on average 6.3 cm taller and 5.8 kg heavier than twins in the lowest birth weight class. In parallel with body mass, lean body mass, adjusted and unadjusted, was positively associated with standardized birth weight. The negative association with the sum of skinfold thicknesses and...
waist-to-hip ratio became apparent when these measures were adjusted for body mass. As with the absolute birth weight classes, the body compositions of the intermediate classes of standardized birth weight (−1 to <0 and 0 to <1) were not significantly different. Standardized birth weight explained a substantial part of the variance in adult height (10.5%) and in lean body mass (5.4%), but much less of the variance in body mass, sum of skinfold thicknesses, and waist-to-hip ratio. Gestational age was not significantly associated with adult body composition, and it was therefore not introduced in the regression models.

Birth weight in relation to healthy and unhealthy body composition

Twins with a healthy body composition weighed on average 434 g more than did twins with an unhealthy body composition (Figure 2). The more unhealthy anthropometric characteristics a person had, the lower her birth weight was. The same significant trend was apparent when birth weight was standardized for gestational age. For every additional unhealthy characteristic, a stepwise decrease in standardized birth weight was observed.

Pairwise analysis: the heavier compared with the lighter twin

An intrapair birth weight difference of ≥5% resulted in an intrapair difference in adult height, with the heavier twin being on average 0.8–2 cm taller than her lighter sister (Table 4). The association between the intrapair birth weight difference and the intrapair difference in height was positive. A positive association was also found with the intrapair differences in other anthropometric measures. However, only when intrapair differences were extreme, ie, exceeding 15%, did body mass and the sum

### Table 2

<table>
<thead>
<tr>
<th>Birth weight</th>
<th>Body mass (kg)</th>
<th>Height (cm)</th>
<th>BMI (kg/m²)</th>
<th>Lean body mass (kg)</th>
<th>Sum of skinfold thicknesses (mm)</th>
<th>Waist-to-hip ratio (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2000 g</td>
<td>59.5 ± 9.74</td>
<td>162.8 ± 5.44</td>
<td>22.5 ± 5.55</td>
<td>41.5 ± 5.12</td>
<td>76.7 ± 22.67</td>
<td>41.1</td>
</tr>
<tr>
<td>&lt;2000 g</td>
<td>61.1 ± 11.88</td>
<td>165.3 ± 6.18</td>
<td>22.4 ± 4.12</td>
<td>43.2 ± 6.06</td>
<td>72.2 ± 31.19</td>
<td>41.5</td>
</tr>
<tr>
<td>Regression analysis</td>
<td>Slope:</td>
<td>Pr:</td>
<td>r²:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slope:</td>
<td>1.13</td>
<td>0.30</td>
<td>0.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pr:</td>
<td>&lt;0.001</td>
<td>6.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r²:</td>
<td>0.46</td>
<td>0.23</td>
<td>0.4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 ± SD. The slope of relation, estimated by multiple regression, gives the change in anthropometric characteristics/kg increase in birth weight; r² gives the percentage of variance explained by birth weight.

2 Three missing values.

3 Geometric z per birth weight class.

4 Six missing values.

5 Standardized slope: indicates the number of SD changes in sum of skinfold thicknesses with a 1-SD change in birth weight.

6 One missing value.

### Table 3

<table>
<thead>
<tr>
<th>Standardized birth weight (z scores)</th>
<th>Body mass (kg)</th>
<th>Height (cm)</th>
<th>BMI (kg/m²)</th>
<th>Lean body mass (kg)</th>
<th>Sum of skinfold thicknesses (mm)</th>
<th>Waist-to-hip ratio (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;−1</td>
<td>58.2 ± 9.20</td>
<td>162.2 ± 5.51</td>
<td>22.2 ± 3.61</td>
<td>41.1 ± 4.90</td>
<td>73.0 ± 30.71</td>
<td>73.8 ± 4.30</td>
</tr>
<tr>
<td>−1 to &lt;0</td>
<td>61.2 ± 9.58</td>
<td>165.3 ± 5.81</td>
<td>22.4 ± 3.31</td>
<td>43.3 ± 5.24</td>
<td>75.2 ± 29.27</td>
<td>72.8 ± 4.45</td>
</tr>
<tr>
<td>0 to &lt;1</td>
<td>64.0 ± 9.19</td>
<td>166.5 ± 6.20</td>
<td>21.8 ± 3.22</td>
<td>43.3 ± 5.26</td>
<td>70.8 ± 26.44</td>
<td>73.1 ± 4.48</td>
</tr>
<tr>
<td>≥1</td>
<td>64.0 ± 12.35</td>
<td>168.5 ± 6.58</td>
<td>22.6 ± 4.31</td>
<td>45.5 ± 6.01</td>
<td>70.1 ± 28.48</td>
<td>73.2 ± 4.68</td>
</tr>
</tbody>
</table>

1 ± SD. The slope of relation, estimated by multiple regression, gives the change in anthropometric characteristics/SD increase in birth weight; r² gives the percentage of variance explained by birth weight (z score).

2 One missing value.

3 Geometric z per birth weight class.

4 Four missing values.

5 Standardized slope: indicates the number of SD changes in sum of skinfold thicknesses with a 1-SD change in birth weight.

6 One missing value.
who weighed only 2032 g at birth. The greater body mass of the heavier twin was accompanied by more lean body mass (1.7 kg) but also more subcutaneous (6.9 mm) and abdominal fat (1.1%). When the intrapair birth weight difference was <15% (heavier and lighter weighing, respectively, 2564 and 2377 g), no significant intrapair differences emerged, except for adult height. When body composition was adjusted for adult body mass, the lean body mass, sum of skinfold thicknesses, and waist-to-hip ratio were not significantly different between siblings, irrespective of the intrapair birth weight difference. Intrapair birth weight differences of <5% did not result in any intrapair difference in adult body composition.

D I S C U S S I O N

In the present study we investigated the association between birth weight and adult body composition in female twins. By investigating the association between the intrapair difference in birth weight and adult body composition in monozygotic twins, we eliminated maternal and genetic influences that could confound this association.

Our findings support the association between birth weight and adult body composition found by previous studies (2–9). When considered as individuals, twins with a very low birth weight (<2000 g) had a significantly different adult body composition than did twins with a high birth weight (≥3000 g). Twins who were heavier at birth were not only taller and slightly heavier as adults but also had more lean body mass and less subcutaneous and abdominal fat than did twins who were lighter at birth. However, the results were different when the twins were considered as a pair, i.e., one twin having a very low birth weight and her sister a high birth weight. Pairwise comparison showed that for every level of intrapair birth weight difference, the monozygotic twin who was heavier at birth was taller in adult life. Only when the intrapair birth weight difference exceeded 15% was the heavier twin also heavier as an adult than her much lighter sister. Smaller intrapair birth weight differences did not result in significant intrapair differences in adulthood.

I N D I V I D U A L  B I R T H  W E I G H T  A N D  B O D Y  C O M P O S I T I O N

Birth weight was positively associated with adult height, explaining 6.4–10.5% of its variance, and to a lesser extent with

### TABLE 4

Intrapair differences in anthropometric characteristics, unadjusted and adjusted for body mass, according to intrapair birth weight differences in monozygotic twins

<table>
<thead>
<tr>
<th>Anthropometric characteristic and intrapair birth weight difference</th>
<th>Unadjusted difference</th>
<th>Adjusted difference 1</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass (kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0% to &lt;5% (&lt; n = 35)</td>
<td>0.0 ± 2.1</td>
<td>0.0 ± 2.1</td>
<td>0.99</td>
</tr>
<tr>
<td>5% to &lt;10% (&lt; n = 36)</td>
<td>0.0 ± 2.3</td>
<td>0.0 ± 2.3</td>
<td>0.67</td>
</tr>
<tr>
<td>10% to &lt;15% (&lt; n = 22)</td>
<td>0.0 ± 2.0</td>
<td>0.0 ± 2.0</td>
<td>0.78</td>
</tr>
<tr>
<td>≥15% (&lt; n = 35)</td>
<td>0.0 ± 2.1</td>
<td>0.0 ± 2.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Height (cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0% to &lt;5% (&lt; n = 35)</td>
<td>0.0 ± 2.1</td>
<td>0.0 ± 2.1</td>
<td>0.99</td>
</tr>
<tr>
<td>5% to &lt;10% (&lt; n = 36)</td>
<td>0.0 ± 2.3</td>
<td>0.0 ± 2.3</td>
<td>0.67</td>
</tr>
<tr>
<td>10% to &lt;15% (&lt; n = 22)</td>
<td>0.0 ± 2.0</td>
<td>0.0 ± 2.0</td>
<td>0.78</td>
</tr>
<tr>
<td>≥15% (&lt; n = 35)</td>
<td>0.0 ± 2.1</td>
<td>0.0 ± 2.1</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0% to &lt;5% (&lt; n = 35)</td>
<td>0.0 ± 2.1</td>
<td>0.0 ± 2.1</td>
<td>0.99</td>
</tr>
<tr>
<td>5% to &lt;10% (&lt; n = 36)</td>
<td>0.0 ± 2.3</td>
<td>0.0 ± 2.3</td>
<td>0.67</td>
</tr>
<tr>
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<td>0.0 ± 2.0</td>
<td>0.0 ± 2.0</td>
<td>0.78</td>
</tr>
<tr>
<td>≥15% (&lt; n = 35)</td>
<td>0.0 ± 2.1</td>
<td>0.0 ± 2.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0% to &lt;5% (&lt; n = 35)</td>
<td>0.0 ± 2.1</td>
<td>0.0 ± 2.1</td>
<td>0.99</td>
</tr>
<tr>
<td>5% to &lt;10% (&lt; n = 36)</td>
<td>0.0 ± 2.3</td>
<td>0.0 ± 2.3</td>
<td>0.67</td>
</tr>
<tr>
<td>10% to &lt;15% (&lt; n = 22)</td>
<td>0.0 ± 2.0</td>
<td>0.0 ± 2.0</td>
<td>0.78</td>
</tr>
<tr>
<td>≥15% (&lt; n = 35)</td>
<td>0.0 ± 2.1</td>
<td>0.0 ± 2.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Sum of skinfold thicknesses (mm)</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0% to &lt;5% (&lt; n = 34)</td>
<td>-2.6 ± 3.0</td>
<td>-2.6 ± 3.0</td>
<td>0.67</td>
</tr>
<tr>
<td>5% to &lt;10% (&lt; n = 34)</td>
<td>-1.0 ± 2.1</td>
<td>-1.0 ± 2.1</td>
<td>0.63</td>
</tr>
<tr>
<td>10% to &lt;15% (&lt; n = 22)</td>
<td>-2.7 ± 1.8</td>
<td>-2.7 ± 1.8</td>
<td>0.81</td>
</tr>
<tr>
<td>≥15% (&lt; n = 34)</td>
<td>6.9 ± 17.1</td>
<td>6.9 ± 17.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Waist-to-hip ratio (%)</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0% to &lt;5% (&lt; n = 35)</td>
<td>-0.6 ± 3.0</td>
<td>-0.6 ± 3.0</td>
<td>0.44</td>
</tr>
<tr>
<td>5% to &lt;10% (&lt; n = 36)</td>
<td>-0.4 ± 2.7</td>
<td>-0.4 ± 2.7</td>
<td>0.72</td>
</tr>
<tr>
<td>10% to &lt;15% (&lt; n = 22)</td>
<td>0.5 ± 2.7</td>
<td>0.5 ± 2.7</td>
<td>0.40</td>
</tr>
<tr>
<td>≥15% (&lt; n = 35)</td>
<td>1.1 ± 3.0</td>
<td>1.1 ± 3.0</td>
<td>0.07</td>
</tr>
</tbody>
</table>

1 ± SD. The Wilcoxon matched-pairs signed-rank test was used to test the intrapair differences in anthropometry, according to 4 levels of intrapair birth weight difference. Regression analysis was performed to test for a trend between the intrapair birth weight difference, considered as a continuous variable, and the intrapair difference in adult body composition.

2 Two missing values.

3 Three missing values.
adult body mass. Consequently, we found no significant relation between birth weight and BMI. This is in agreement with many others, who examined this relation in children (7, 19, 20), adolescents (8, 20, 21), and adults (14, 23–26). Only 2 studies (16, 17) previously used twins to examine the relation between birth weight and adult body composition. Only Allison et al (16) considered twins as individuals as well as performing a pairwise analysis. In agreement with our study, they found a positive relation between birth weight and height (r = 0.24) but no significant relation for BMI (r = 0.08). They concluded that the intrauterine period is critical for the development of height but not for relative weight, as measured by BMI. Some studies reported a small but significant positive relation between birth weight and adult BMI in men (2, 3, 24).

Because BMI is more an indicator of heaviness than of body fatness (27), these findings do not allow the drawing of conclusions about body composition and fat distribution. Nevertheless, central fat deposition, more than overall obesity, is known to be associated with the metabolic syndrome (10, 11, 14, 15). In parallel with the small increase in adult body mass, we found that higher birth weights were associated with more lean body mass. This was accompanied by lower values for subcutaneous and abdominal fat. When we adjusted for adult body mass, the relation between birth weight and subcutaneous and abdominal fat was even more pronounced. Our findings agree with those of others who found an inverse relation between birth weight and subcutaneous fat and abdominal or truncal fat in adolescents (7–9) and adults (4–6) when allowance was made for body mass or BMI. The contribution of birth weight to the variance of adult body composition was small, not exceeding 3%, except for height (6.4–10.5%) and lean body mass (5.4%). In addition, when we combined unhealthy body-composition characteristics, we found a stepwise decrease in birth weight for every additional unhealthy characteristic. We suggest, on the basis of our individual data, that the intrauterine period may be important for the development of adult body composition, in favor of those who experience an advantageous prenatal environment, as indicated by a high birth weight.

The mechanisms underlying the association between an adverse intrauterine environment and adult body composition are unknown, but several plausible explanations have been proposed. Undernutrition in twins, which may result from limited maternal-placental supply, seems to affect intrauterine growth mainly in the last trimester of pregnancy, a period that is marked by a considerable weight gain (28). Undernutrition in this period may lead to a slowing down in metabolic rate and in intrauterine growth, which enhances the fetus’s ability to survive (29). The fetus may reduce its metabolic dependence on glucose and increase the oxidation of other substrates, including amino acids. This not only may result in a reduced muscle mass but may also affect muscle structure and impair metabolism (30). Another possibility is that nutritional deprivation may cause abnormalities intrinsic to the adipocyte and result in excessive accumulation of fat (12). Human (4, 31, 32) and animal (12) studies have suggested that nutritional deprivation early in pregnancy alters the central regulatory mechanisms of the hypothalamic-pituitary-adrenal axis. Hypersensitivity of this axis seems to be related to abdominal obesity (11). This is consistent with the findings of the Dutch famine study that undernutrition during early gestation results in higher body mass, BMI, and waist circumference (31, 32). This mechanism may not seem to be responsible for the association in twins, because intrauterine growth in twins slows down in the last trimester of pregnancy. However, Luke et al (33) found that maternal weight gain early in pregnancy contributed significantly to birth weight in twins. Also, genetic factors may underlie the association between birth weight and adult body composition. Stern et al (13) concluded on the basis of a large family study that genes that cause a higher birth weight also worsen the metabolic syndrome in adulthood. Also, molecular genetic studies point in this direction, with promising candidate genes that may influence growth in prenatal and postnatal life (34, 35).

Intrapair birth weight difference and intrapair difference in body composition

With a pairwise analysis of monozygotic twins we could control for potential genetic and maternal influences. Although family and twin studies indicate that height is under strong genetic control (36–38), we found that a small intrapair birth weight difference (≥ 5%) resulted in a small but significant intrapair difference in adult height and that the larger the intrapair birth weight difference, the more pronounced the intrapair difference in adult height. This confirms the results of our individual analyses that the intrauterine environment influences adult height more than it does the other anthropometric characteristics. As long as the intrapair birth weight difference did not exceed 15%, body mass, lean body mass, subcutaneous fat, and abdominal fat were not significantly different between the twins. These findings agree with those of Allison et al (16) and Baird et al (17), who found that the monozygotic twin who was heavier at birth was also taller in adulthood than the sibling who was lighter at birth. In these studies, body mass and BMI were not significantly different between the siblings.

Our findings suggest that, when birth weights do not differ markedly, genetic and postnatal influences may compensate for the adverse prenatal environment of the lighter twin, except for adult height. Average birth weights were amply within the intermediate birth weight classes (2000 to <3000 g), a range in which our individual data did not show any differences in body composition. However, when the intrapair birth weight difference was extreme, ie, ≥ 15%, adult body mass of the lighter twin at birth (2032 g on average) was significantly less than that of her heavier sibling (2611 g on average). This indicates that extremely adverse intrauterine conditions will have enduring consequences for adult body mass. The intrapair difference amounted to 3.1 kg, given an intrapair birth weight difference of <600 g, which is more than we would expect from our individual data, ie, 1.13 kg body mass increase/kilogram increase in birth weight. This is in line with the findings of 2 studies that applied the twin model to examine the fetal programming hypothesis and blood pressure. Dwyer et al (39) and Poultet et al (40) found an inverse relation between the intrapair birth weight difference and the intrapair difference in systolic blood pressure in 2 independent samples of monozygotic twins. Both studies showed a reduction in systolic blood pressure of > 5 mm Hg/kg increase in birth weight, whereas in singletons this is on average 2 mm Hg. The comparatively large effect seen in pairwise analyses relative to individual data suggests that discordance in birth weight within pairs may be more closely related to the underlying mechanisms of fetal programming than is birth weight variation between unrelated singletons.

We would expect, on the basis of our individual data, that the heavier twin at birth would have a more favorable body
composition than her sister. However, when we adjusted for body mass, adult body composition was not significantly different between siblings. This may be due to the small contribution of birth weight to adult body mass and subcutaneous and abdominal fatness.

In conclusion, our data suggest that the intrauterine environment is critical for adult height. Lower birth weight is associated with greater subcutaneous and abdominal fatness and with reduced lean body mass. In analyses of pairs, however, the enduring prenatal effects on adult body mass became apparent only in twins with marked intrapair birth weight differences.

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REFERENCES