Growth Patterns in Young Adult Monozygotic Twin Pairs Discordant and Concordant for Obesity

Kirsi H. Pietiläinen[1,2,3], Aila Rissanen[2], Maria Laamanen[1], Anna-Kaisa Lindholm[1], Harri Markkula[4], Hannele Yki-Järvinen[3], and Jaakko Kaprio[1,5]

[1] The Finnish Twin Cohort Study, Department of Public Health, University of Helsinki, Finland

[2] Obesity Research Unit, Department of Psychiatry, Helsinki University Central Hospital, Finland

[3] Department of Medicine, Division of Diabetes, Helsinki University Central Hospital, Finland

[4] Tilator Oy Ltd, Säkylä, Finland

[5] Department of Mental Health and Alcohol Research, National Public Health Institute, Helsinki, Finland

Weight discordance is very rare in monozygotic (MZ) twin pairs; when found, however, such pairs are advantageous in the search for either environmental or epigenetic causes and consequences of obesity. We analyzed the growth patterns of young adult MZ pairs discordant and concordant for obesity. Screening 5 consecutive birth cohorts (1975–1979) of 22- to 27-year-old Finnish twins (the FinnTwin16 study), we found 14 obesity discordant (Body Mass Index [BMI] difference ≥ 4 kg/m^2) MZ pairs out of 658. Ten pairs participated in clinical studies. Nine concordant pairs (BMI difference ≤ 2 kg/m^2) were examined as controls. Lifetime measured heights and weights recorded in hospitals and health centers were traced manually. Height development was similar in all the co-twins of both groups. The weight differences between the co-twins of the discordant pairs began to emerge at 18 years leading to an average discordance of 16.4 kg, 5.6 kg/m^2 (p for both = .005) at 25.7 years. The heavier co-twin weighed 221 g (p = .066), 1.0 kg/m^2 (p = .01) more already at birth than the leaner, but the differences waned by 6 months of age and reappeared only after adolescence. Both the leaner and the heavier co-twins of the discordant pairs weighed more than expected by the singleton reference values (Cole et al., 1998) after 8 years. The concordant co-twins, on the other hand, grew similarly and after 6 months, their mean growth was not distinguishable from the singleton patterns. Young adulthood represents a critical period of gaining weight irrespective of genetic background in this twin sample.

The vast majority of monozygotic (MZ) twin pairs are very similar, i.e., concordant for body size. Situations where this is not the case are extremely rare in childhood and adulthood but may arise in the perinatal period (Wilson, 1976). Nutritional imbalances between the co-twins *in utero* may lead to differences in size at birth even in MZ pairs, especially in the monochorionic twins with vascular anastomoses in the placentas (Loos et al., 2001a). Even during the first few months, however, MZ twins become progressively more concordant for body size (Ooki & Asaka, 1993; Wilson, 1979) and remain so until late adolescence (Pietiläinen et al., 1999).

After adolescence, MZ intrapair correlations for height remain high (~.90) (Silventoinen et al., 2003). Intrapair correlations of Body Mass Index (BMI, kg/m^2), on the other hand, tend to decline slightly after entering adulthood. In the Finnish twin cohorts, MZ males and females respectively have had intrapair correlations in BMI as high as .82 and .89 at 16 years (Pietiläinen et al., 1999), .74 and .78 at 20–29 years (Schousboe et al., 2003), and .73 and .66 at 30–39 years (Schousboe et al., 2003). Nevertheless, in an international sample of MZ twins reared apart after infancy (Allison et al., 1996), the co-twin correlation in BMI at the mean age of 43.4 years was .81, suggesting strong genetic control and rare discordance in BMI despite lifetime variance in environmental exposures.

The heritability of BMI is substantial: 50–90% in twin studies and 20–80% in family and adoption studies (Maes et al., 1997). However, it is well accepted that the obesity epidemic is fuelled by an environment favouring excessive calorie intake and discouraging physical activity (Hill & Peters, 1998). Although body weight is increasing worldwide in all age groups and across all BMI levels, weight-gain is most extensive among the young (Lahti-Koski et al., 2000; Lissner et al., 2000) and among those already overweight (Ball et al., 2002). Such data invites a

Kirsi H. Pietiläinen, Aila Rissanen, Maria Laamanen, Anna-Kaisa Lindholm, Harri Markkula, Hannele Yki-Järvinen, and Jaakko Kaprio

search for the environmental causes of obesity in the periods of life and groups of people associated with the highest risk.

This study was directed at identifying critical periods of weight-gain that are independent of genetic background, but can be ascribed to environmental etiology. This was approached by searching for MZ twin pairs discordant for young-adult obesity and control pairs concordant for body weight from a representative sample of Finnish twins. Studying MZ twins allows perfect paired matching for genetic factors, age, gender, and a close matching of childhood environmental factors. Thus, any differences between the co-twins are likely to arise from environmental experiences unique to a twin. Equally plausibly, epigenetic mechanisms such as DNA methylation, histone acetylation, and RNA interference may cause differences in gene function without a change in the DNA sequence and accordingly, influence growth and development. In this paper, the growth patterns in stature, weight, and BMI from birth to young adulthood (23–28 years) are explored in a rare sample of MZ twin pairs in which one has developed obesity and the other has not and in control pairs that are concordant for body weight, and they are compared with singleton referents.

Methods

Participants

The study participants were recruited from the FinnTwin16 cohort (Kaprio et al., 2002; Rose et al., 2001), a population-based, longitudinal study of 5 consecutive birth cohorts (1975–1979) of Finnish twins, their siblings and parents, identified through the national population registry of Finland. The baseline data collection of all twin pairs was initiated by mail in 1991 within 60 days of their 16th birthdays, resulting in 5561 responses (2733 full pairs). The response rates were 88% and 93% for boys and girls respectively. All respondent twins were surveyed again at 17, 18.5, and between 22 and 27 years of age. Based on responses to items on current weight and height in the latest follow-up questionnaire (response rates 83% in males and 93% in females), twin pairs were recruited to the current study. Zygosity had been earlier assigned on the basis of validated questionnaire items (Sarna et al., 1978).

After screening all monozygotic (MZ) twin pairs (N = 658), 14 healthy pairs with a reported BMI difference of at least 4 kg/m^2 were found, such that one co-twin was nonobese (BMI approximately 25 kg/m^2), while the other was obese (BMI approximately 30 kg/m^2). All 14 pairs were invited, and 10 (5 male and 5 female pairs) participated in the clinical studies. The measured differences in BMI ranged from 3.8 to 10.1 kg/m^2. As a group, the leaner co-twins were slightly overweight (mean BMI 25.7 ± SE 0.6 kg/m^2) and the heavier clearly obese (mean BMI 31.4 ± 0.5 kg/m^2; Table 1). Age- and sex-matched concordant control

MZ pairs with a reported BMI difference of less than 2 kg/m^2 were also invited. Two male and two female overweight or obese pairs (BMI ≥ 25 kg/m^2), as well as three male and two female normal-weight pairs (BMI < 25 kg/m^2) were studied. The measured differences in BMI ranged from 0.0 to 2.3 kg/m^2. The concordant twins as a group were comparable in BMI with the lean discordant co-twins. The leaner and heavier concordant co-twins had BMIs of 24.3 ± 1.2 and 25.3 ± 1.3 kg/m^2 respectively. This clinically small difference reached statistical significance (p = .008; Table 1).

All participants were healthy (except for obesity), were not on medication (except contraceptives) and were not pregnant. There was no previous history of illnesses, no hypothyroidism, and no signs of Cushing's disease or other major endocrinological disorders, based on clinical examination by a physician (K. P.). The twins were considered psychologically healthy in a structured psychiatric interview for major psychiatric disorders including depression, eating disorders and substance abuse. One obesity-discordant pair was concordant for partial deafness of unknown origin. Parity or marital status could have possibly accounted for weight-gain in single cases, but to retain the privacy of the pairs, such details were not described on a pair-to-pair basis. Further, in most cases, the obesity-discordant co-twins were concordant for parity and social relationships and not distinguishable from the concordant pairs. Differences in education or occupation did not explain differences in weight. All the concordant pairs were nonsmokers, but 4 out of 10 obesity-discordant pairs were discordant for smoking. In three pairs, the one who smoked (more) was leaner, but in one pair, the co-twin who smoked more was heavier. The mean age of the discordant twins was 25.6 ± SE 0.4 (range 23.8–27.3) years and that of the concordant twins 25.8 ± 0.4 (range 23.8–27.4) years. Both the discordant and the concordant twins resided together until the mean age of 19.6 ± 2.2 years (range 16–25 years).

Monozygosity was confirmed at the Paternity Testing laboratory, National Public Health Institute, Helsinki, Finland, by the genotyping of multiple, informative genetic markers: D3S1358 (10 alleles), vWA (12 alleles), FGA (20 alleles), AMEL (2 alleles), THO1 (7 alleles), TPOX (8 alleles), CSF1PO (10 alleles), D5S818 (11 alleles), D13S317 (9 alleles), D7S820 (11 alleles). The purpose, nature, and potential risks of the study were explained to the subjects before their written informed consent was obtained. The protocol was designed and performed according to the principles of the Helsinki Declaration and was approved by the Ethical Committee of the Helsinki University Central Hospital.

Measures

The clinical examinations were carried out in a fasting state and females were scheduled to attend during the follicular phase of their menstrual cycle.

Weight and height were measured with participants barefoot and in underwear. Weight was measured to the nearest 0.1 kg and height to the nearest 0.5 cm. The BMI (weight [kilograms] divided by height [meters] squared) was used as a measure of relative weight throughout the growth periods. In addition, the Ponderal Index (recorded birth weight [kilograms] divided by length at birth [meters] cubed) was calculated as a measure of relative birthweight.

Obstetric and delivery records were used to obtain birth lengths and weights (available for 18 pairs), head circumferences (N = 15 pairs), gestational ages (N = 16 pairs), placental weights (N = 16 pairs), chorionicity (N = 13 pairs), and Apgar scores (N = 32 individuals in 15 full pairs). Information on maternal weight gain, available in only 8 pairs, was not used in this report.

Measured heights and weights were collected from the hospitals' obstetric and neonatal units, child health centers, and health centers of elementary and high schools, colleges, vocational schools, universities and workplaces. In addition, all the other records that were available from appointments to general practitioners and specialists in public or in private health care were collected. In some cases, health cards were stored at the city archives, and the records were searched from the place of residence at each time point according to the information obtained from the twin families. In males and in one female pair, doctors' examinations at military conscription were also traced, military service being compulsory for men and voluntary for women in Finland.

Heights and weights were available from birth onwards for all the pairs except for one male discordant pair in which the first measures were recorded at 9 years due to residence abroad until that age. During the first year of life, the twins' heights and weights were measured frequently; on average 10.1 times (range 3–18). From 1 to 9.9 years, there were on average 9.5 (4–16) measurements available, and between 10–19.9 years, 7.6 (4–13) measurements. After 20 years, the twins had on average one (0–4) measurement of height and weight in addition to the ones performed during the study. Thus, a total of an average 28.4 measurements of growth from birth to early adulthood were available.

Statistics

The Pediator-program (Tilator Oy Ltd., 2004) was used in the data management of heights and weights. All calculations and statistical analyses were then performed using the Stata statistical software (release 8.0; Stata Corporation, 2003). Raw measurements of height, weight, and BMI were used at birth and at the time of the study. Other measurements were not comparable as such between the twins because of differences in ages on each measurement occasion. Therefore, height and weight measurements for each individual were linearly interpolated between two time points to obtain the measures at each birthday

from 0 to 23–25. Birthday 0 corresponds to the full-term birthday at the expected date of delivery at week 40. This corrects for differences in gestational ages between the pairs.

For comparison between these twins and singletons, the measurements at each birthday between 0 to 23 years were converted to a standardized z-score based on the 1990 British Growth Reference (Cole et al., 1998) using a recently released procedure in Stata (Vidmar et al., 2004). Creating the z-scores is gender-specific, which is why we report the results for age-specific z-scores combined, including both genders in Figure 2.

When analyzing twins as individuals, corrections for co-twin clustering and within-pair relationships were made using survey estimation procedures (SVYMEAN, SVYTEST [Wald test] for equality of means, and CORR and SVYREG for Pearson correlations). By these procedures, unbiased standard errors, regression coefficients, and p-values for twin individuals were derived. Use of nonparametric analyses in twin individuals would not permit the relevant adjustment for twin-pair clustering.

The paired Wilcoxon test was used to compare means between the leaner and the heavier co-twins in the discordant and concordant pairs. Determining the leaner and the heavier co-twin was based on BMI when studied at the metabolic ward. The Mann–Whitney U-test was applied to compare the intrapair differences in the discordant and concordant groups. The one-sample Wilcoxon test was computed to test whether the twin individuals' mean z-scores differed significantly from zero (the mean for singleton reference values). Data are shown as mean ± standard error (SE) unless indicated otherwise. A p-value of less than .05 was considered statistically significant.

Results

Heights, Weights, and Body Mass Indices from Birth to Early Adulthood

Average birth length was 46.8 ± 1.0 cm in male and 46.1 ± 0.6 cm in female subjects; birth weight was 2.65 ± 0.18 kg and 2.41 ± 0.11 kg; BMI at birth 11.9 ± 0.4 kg/m^2 and 11.3 ± 0.3 kg/m^2; and ponderal index at birth 25.5 ± 0.7 kg/m^3 and 24.1 ± 0.5 kg/m^3 respectively. Males and females did not significantly differ from each other. Compared to singletons in the above-mentioned British Growth Reference population (Cole et al., 1998), the twins in the current study were, as expected, shorter and lighter at birth. While the average measures (z-scores) for the reference population are zero, the z-scores at birth for the males and females in this study were –1.9 ± 0.4 and –2.2 ± 0.3 for lengths; –2.0 ± 0.4 and –2.3 ± 0.3 for weights; and –1.3 ± 0.4 and –1.7 ± 0.3 for BMIs respectively. All of the values in twins were significantly lower than the referents (Wald test p < .001). The adiposity rebound, the period when BMI reaches its nadir

Kirsi H. Pietiläinen, Aila Rissanen, Maria Laamanen, Anna-Kaisa Lindholm, Harri Markkula, Hannele Yki-Järvinen, and Jaakko Kaprio

Table 1

Means and Standard Errors (*SE*) of Heights, Weights, and BMIs of the Leaner and Heavier Co-twins in Twin Pairs Discordant for Adult BMI (Intrapair Difference ≥ 4 kg/m²) and Concordant for Adult BMI (Intrapair Difference ≤ 2 kg/m²)

| | | Pairs discordant for obesity as young adults | | | | Pairs concordant for obesity as young adults | | |
| | | Leaner co-twin | | Heavier co-twin | | Leaner co-twin | | Heavier co-twin |
Characteristics	N	Mean (± *SE*)	p Value*	Mean (± *SE*)	N	Mean (± *SE*)	p Value*	Mean (± *SE*)
Length at birth, cm	9	47.2 (0.6)	.90	47.1 (0.6)	9	45.8 (1.2)	.95	45.7 (1.1)
Length at full-term birthday, cm‡	9	48.8 (0.7)	.44	49.1 (0.6)	9	49.4 (0.8)	.31	48.4 (1.0)
Height at 18 years of age, cm‡	10	168.4 (3.0)	.17	169.1 (2.9)	9	171.6 (2.1)	.44	171.0 (2.5)
Height at 23 years of age, cm‡	10	168.8 (3.0)	.28	169.4 (2.8)	9	173.6 (2.3)	.14	173.1 (2.5)
Height at examination, cm§	10	169.0 (2.9)	.41	169.4 (2.9)	9	173.8 (2.4)	.48	173.0 (2.8)
Weight at birth, kg	9	2.5 (0.1)	.066	2.7 (0.1)	9	2.6 (0.2)	.59	2.4 (0.2)
Weight at full-term birthday, kg‡	9	2.8 (0.1)	.11	3.0 (0.1)	9	3.3 (0.1)	.86	3.2 (0.2)
Weight at 18 years of age, kg‡	10	67.1 (2.6)	.03	69.7 (2.2)	9	64.5 (2.3)	.37	65.5 (2.4)
Weight at 23 years of age, kg‡	10	72.9 (2.9)	.005	84.3 (2.7)	9	71.0 (3.1)	.04	72.8 (3.6)
Weight at examination, kg§	10	73.5 (2.7)	.005	89.9 (2.7)	9	73.6 (4.3)	.04	75.9 (4.8)
Ponderal index at birth, kg/m³	9	23.3 (0.7)	.02	25.5 (0.8)	9	26.0 (0.8)	.11	25.0 (0.7)
BMI at birth, kg/m²	9	11.0 (0.3)	.01	12.0 (0.4)	9	11.9 (0.5)	.26	11.5 (0.5)
BMI at full-term birthday, kg/m²‡	9	11.8 (0.3)	.04	12.5 (0.3)	9	13.5 (0.3)	.77	13.6 (0.4)
BMI at 18 years of age, kg/m²‡	10	23.7 (1.0)	.09	24.5 (1.0)	9	21.9 (0.7)	.21	22.4 (0.8)
BMI at 23 years of age, kg/m²‡	10	25.5 (0.6)	.005	29.4 (0.5)	9	23.5 (0.9)	.05	24.3 (1.0)
BMI at examination, kg/m²§	10	25.7 (0.6)	.005	31.4 (0.5)	9	24.3 (1.2)	.008	25.3 (1.3)

Note: * Leaner vs. heavier co-twin (paired Wilcoxon test).
‡ Interpolated to reflect body size at a given birthday.
§ The mean age at examination 25.6 ± 0.4 and 25.8 ± 0.4 years for the discordant and for the concordant twins, respectively.

before beginning to increase (Rolland-Cachera et al., 1984), was 6.1 ± 0.4 years in males and 4.7 ± 0.3 years in females (*p* = .008).

When examined at an average age of 25.7 ± 0.3 years, males and females respectively were 177.9 ± 0.9 cm and 163.7 ± 2.0 cm tall; weighed 83.5 ± 3.6 kg and 72.7 ± 2.7 kg; and BMIs were 26.4 ± 1.0 kg/m² and 27.2 ± 1.1 kg/m² (Wald test in BMIs between the genders, *p* = .58).

Discordant and concordant pairs. Twin growth in the discordant and in the concordant pairs is illustrated in Figure 1 (interpolated to reflect ages from full-term birthday to 25 years), and summarized for relevant details in Table 1. Figure 2 shows the twins' growth compared with singletons in the British Growth Reference population (Cole et al., 1998; *z*-scores for ages from full-term birthday to 23 years).

In the pairs that were discordant for obesity as young adults (Table 1), the leaner co-twin was 221 ± 93 g (range 270–620 g) lighter at birth (paired Wilcoxon test between the co-twins, *p* = .066). The co-twin BMI difference in the discordant pairs was 1.0 ± 0.3 kg/m² (range 0.0–2.5 kg/m²; *p* = .01) at birth, but began to diminish immediately after delivery, and was not significant (0.1 ± 0.2 kg/m²) at the age of 6 months. From then on, no weight differences were apparent until the end of puberty. The adiposity rebound was similar (*p* = .59) in the leaner (5.2 ± 0.4 years) and in the heavier (5.3 ± 0.4 years) co-twins.
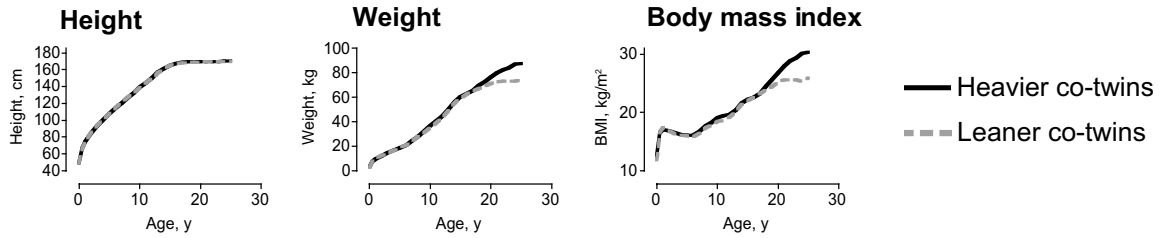
At 18 years, the heavier co-twins weighed 2.6 ± 1.0 kg more than the leaner co-twins (*p* = .03). Subsequently, the weight differences gradually increased, and when the clinical examinations were performed at an age ranging from 23.8 to 27.3 years, the discordant pairs had a 16.4 ± 1.4 kg, 5.6 ± 0.6 kg/m² difference in weight and BMI, respectively (*p* = .005). Growth in stature was very similar in both the co-twins throughout the years (Figure 1).

In the pairs that were concordant for obesity as young adults, there were no significant differences in stature, weight or BMI at birth, in childhood or in adolescence (Table 1, Figure 1). At examination (age 23.8–27.4 years), the normal-weight pairs had a 0.9 ± 1.3 kg (*p* = .35), 0.6 ± 0.3 kg/m² (*p* = .04) difference in weight and BMI, respectively, and the overweight pairs a 4.2 ± 1.0 kg (*p* = .07), 1.4 ± 0.3 kg/m² (*p* = .07) difference in weight and BMI respectively.

Between the discordant and concordant pairs, the intrapair differences in BMI and Ponderal Index at birth and those in weight and BMI in adulthood were significantly larger (*p* < .05) in the discordant pairs than in the concordant pairs.

Compared to singletons (Figure 2), the *z*-scores at birth in the discordant co-twins were –1.8 ± 0.3 for length in both the co-twins; –2.3 ± 0.2 and –1.8 ± 0.3 for weight; and –2.1 ± 0.3 and –1.1 ± 0.4 for BMI in the co-twins that were leaner and heavier, respectively, as adults. In addition to both the co-twins being

a) All discordant twins (*N* = 10 pairs)

Height   **Weight**   **Body mass index**

b) All concordant twins (*N* = 9 pairs)

Height   **Weight**   **Body mass index**
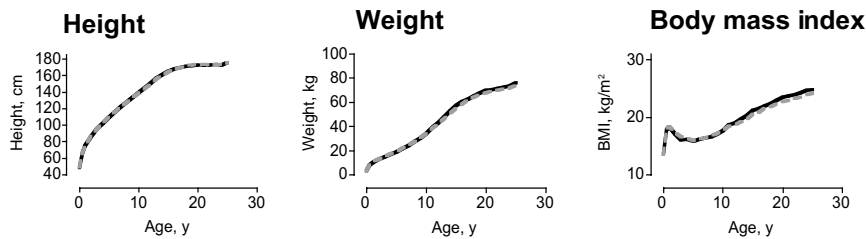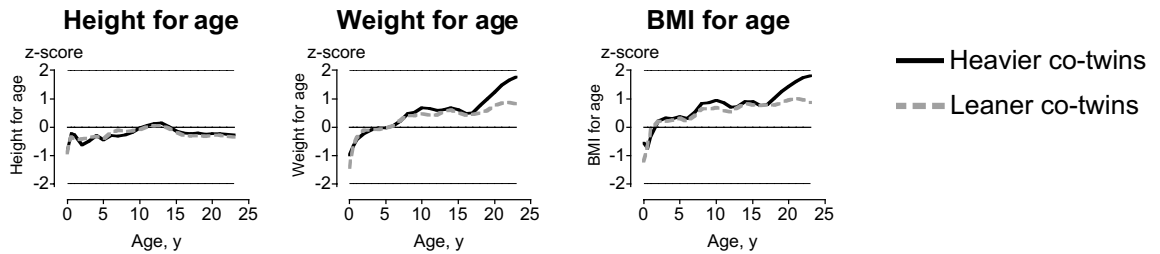
Figure 1

Growth in height, weight, and BMI in the leaner and heavier co-twins in twin pairs.
a) Discordant for adult BMI (intrapair difference ≥ 4 kg/m²), b) Concordant for adult BMI (intrapair difference ≤ 2 kg/m²). Both genders were combined because the graphs for males and females were very similar.

a) All discordant twins (*N* = 10 pairs)

Height for age   **Weight for age**   **BMI for age**

b) All concordant twins (*N* = 9 pairs)

Height for age   **Weight for age**   **BMI for age**

Figure 2

Growth in age-specific *z*-scores for height, weight, and BMI from full-term birthday to 23 years in the leaner and heavier co-twins in twin pairs.
a) Discordant for adult BMI (intrapair difference ≥ 4 kg/m²), b) Concordant for adult BMI (intrapair difference ≤ 2 kg/m²). Both genders were combined after gender-specific calculation of standardized *z*-scores based on the British Growth Reference population (Cole et al., 1998).

Kirsi H. Pietiläinen, Aila Rissanen, Maria Laamanen, Anna-Kaisa Lindholm, Harri Markkula, Hannele Yki-Järvinen, and Jaakko Kaprio

different from singletons ($p < .05$), the obese and the nonobese co-twins differed from each other for weight ($p = .066$) and BMI ($p = .01$) z-scores at birth. The concordant co-twins were comparable with each other at birth but differed from singletons ($p < .05$): the z-scores for birth length were -2.1 ± 0.5 and -2.6 ± 0.5 for the leaner and heavier (adult) co-twins, those for weight -2.1 ± 0.5 and -2.4 ± 0.5; and those for BMI -1.2 ± 0.5 and -1.7 ± 0.5. Considerable catch-up to meet the singleton values was present during the first 6 months of life in all the measures in both the discordant and the concordant pairs. In the concordant pairs as a group, the z-scores were not significantly different from the reference at any age after 6 months. However, both the co-twins of the overweight concordant pairs had the weight-for-age and BMI-for-age z-score almost one unit higher than the reference values after 1 year of age—but due to small sample size this was not significant (data not shown). The growth of discordant pairs was indistinguishable from the singleton patterns between 1–7 years, but after the age of 8 years, both obese and nonobese co-twins weighed significantly more ($p < .05$) than the singleton norms. Between the co-twins, the z-scores for weight and BMI were significantly different after 18 years, being almost one unit apart in weight-for-age ($p = .005$) and BMI-for-age ($p = .005$) at 23 years until which age the reference values were available.

Perinatal Characteristics

The twin pairs were born on average at gestational week 37 ± 2 (range 32 to 40 weeks) with no difference between the obesity discordant (38 ± 2, 35–40 weeks) and obesity concordant pairs (36 ± 2, 32–39 weeks). In twin individuals, the average Apgar scores during the first minute were 8 ± 0 with no differences between the discordant and concordant groups or co-twins within each group (data not shown). Of the 16 pairs for whom we had information, all but one concordant male pair shared a common (or fused) placenta. The average weights of the placentas were similar in discordant (1021 ± 66 g) and concordant pairs (1042 ± 96 g). The chorion-amnion status was similar in both groups: among discordant pairs, six were monochorionic (of which one was verified monoamnionic and one diamnionic) and one was dichorionic, three had missing data; among concordant pairs, five were monochorionic (of which two were verified diamnionic) and one was dichorionic, three had missing data. The gestational age correlated with twin individual's size at birth (length $r = .63$; weight $r = .65$; BMI $r = .53$; all $p < .01$), but not the first minute Apgar score ($r = .20$, $p = .14$) nor adult body size (data not shown).

Discussion

In this study, we found 14 MZ twin pairs discordant for obesity after screening a total of 658 MZ pairs from five nationally-representative birth cohorts of twins. Of these rare pairs, 10 participated in clinical studies and had an average 16.4 kg weight discordance at the age of 25.6 years. The size differences between the co-twins had begun to emerge around the age of 18 years. In all but one pair, the heavier co-twins of the discordant pairs had a slightly higher relative weight already at birth as compared to their leaner counterparts. However, the differences waned by 6 months of age and reappeared only after adolescence. Interestingly, both the leaner and the heavier co-twins of the discordant pairs weighed more than expected by the singleton norms (Cole et al., 1998) after the age of 8 years. The concordant co-twins, on the other hand, grew similarly and after 6 months, their mean growth was not distinguishable from the singleton patterns.

Dietz (1994) has introduced three critical periods for the development of obesity: the prenatal period, adiposity rebound between 5 and 7 years of age, and adolescence. Overweight could be increased in incidence, persistence or complications at these periods. Notably, in our study, the same periods could be highlighted: obese co-twins of the discordant pairs were heavier at birth, both co-twins weighed more than the referents after the age of 8 years, and the weight differences appeared after late adolescence.

Contrary to the present sample, data from previous studies in twins (Ijzerman et al., 2001; Koziel, 1998; Loos et al., 2001b; Loos et al., 2002; Wilson, 1979) and singletons (Parsons et al., 2001; Seidman et al., 1991; Sørensen et al., 1997) suggest continuous tracking of heaviness throughout the growth until adulthood. Why then were the weights of the present co-twins similar in childhood, and why did discordance only reappear after adolescence? It is possible that birth weight or factors associated with it somehow program adult weight gain after a latent period in childhood. In this small sample of discordant pairs, the association between (relative) birth weight and the subsequent weight may also be coincidental, as most probably is the rather negative (but not significant) association between birth weight and adult weight in the concordant pairs.

The large weight gain in the discordant pairs during childhood suggests that both the co-twins were predisposed to obesity. Such periodical increases in weight may be genetically regulated or reflect the effects of shared family environment on the given genotype. Even assuming that the liability to weight gain was genetic, we do not know which of the discordant co-twins was subsequently following more closely the genetic predisposition — the one remaining lean or the one gaining more weight. Further, it is not clear which lifestyle factors were more important: the efforts to prevent weight-gain in the nonobese co-twin or behaviours promoting weight-gain in the obese. Understanding this distinction may also be important on the larger public health scale in order to

implement effective strategies to encourage maintenance of healthy weight in different age groups.

Early adulthood is a time of significant environmental changes. Life-events such as getting married, having children, and starting work have been associated with decreased levels of physical activity (Brown & Trost, 2003). Combined with adopting obesity-promoting food habits (French et al., 2000), these life-events mean that young adulthood represents a critical time for weight-gain (Lahti-Koski et al., 2000; Lissner et al., 2000). In the present FinnTwin16 cohort, the prevalence of overweight (BMI $\geq$ 25 kg/m^2) increased dramatically from 18.5 years to 22–27 years: from 9.5% to 28.7% in males and from 6.7% to 15.2% in females respectively. Cross-sectional twin data (Pietiläinen et al., 1999; Schousboe et al., 2003; Schousboe et al., 2004) suggest that the relative importance of environmental effects on body-weight increases after adolescence. A longitudinal study on 5967 adult twin pairs (Korkeila et al., 1995) revealed that the weight changes during a 6-year follow-up time in adulthood were mainly determined by changing environments, as evidenced by only a modest correlation (0.50–0.67) between environmental effects at baseline and at follow-up.

MZ co-twins living together have more similar BMIs and weight changes than those living apart (Korkeila et al., 1995). In the current study, both the discordant and the concordant pairs lived together until the age of 16–25 years; thus, moving apart did not differentiate the groups from each other. Nevertheless, it is possible that gaining independence and adopting different lifestyles contributed to the development of weight differences. In a previous study of 35- to 60-year-old MZ pairs (N = 23) with more than 3 kg/m^2 weight discordance (Rissanen et al., 2002), the obese twins recalled having preferred fatty and sweet foods, alcohol, and having eaten more than their leaner co-twins at the age of 20–30 years.

MZ twin pairs discordant for obesity are obviously more dissimilar in behaviors than typical MZ pairs. Hypothetically, the discordant pairs might also differ for nonbehavioral environments such as viral exposures (Vangipuram et al., 2004) contributing to the differences in the development of obesity. Further, it cannot be excluded that such MZ twin pairs with large phenotypic differences may also be genotypically different from other MZ pairs. By this, we do not mean somatic mutations; these may arise in rare cases of MZ twins, but as the weight differences emerged only after childhood, such genetic explanations are unlikely. Rather, we propose that while sharing the same genes, the discordant pairs may have inherited a genotype that allows variation to the co-twins' phenotype more than in most MZ twins. Usually, phenotypic variation is surprisingly low despite abundant genetic variation and a range of environmental conditions (Waddington, 1942). This developmental constancy, known as canalization, may

be compromised by mutations releasing variation that are normally hidden (Siegal & Bergman, 2002), although such evidence is currently lacking in humans.

There may also be genes predisposing to variability in weight as opposed to genes determining the level of weight. Berg (1988) found that in some genotypes, the within-pair variability in MZ twins in serum-lipid levels was significantly greater than in others. The form and existence of such 'variability genes', in combination with the 'level genes' and the epigenetic mechanisms (differences in gene function without a change in the DNA sequence) behind obesity need to be clarified in the future. Studying twins may prove valuable in this approach as well (Boomsma et al., 2002). As there are few MZ twins discordant for obesity, screening and phenotyping such twins in other twin registries and pooling well-characterized MZ data is suggested for future research.

In conclusion, we document in this sample of MZ twin pairs discordant for obesity that the co-twins' weights had begun to diverge without exception in young adulthood at the mean age of 18 years. Earlier studies of twins (Rissanen et al., 2002) and singletons (Lahti-Koski et al., 2000; Lissner et al., 2000) have underscored the liability to weight gain in this particular period of life. As identifying the etiologic factors for obesity is of high importance, we continue to investigate the mechanisms behind the discordance and the reasons why young adulthood especially would be fraught with the risk of weight-gain.

References

Allison, D. B., Kaprio, J., Korkeila, M., Koskenvuo, M., Neale, M. C., & Hayakawa, K. (1996). The heritability of body mass index among an international sample of monozygotic twins reared apart. *International Journal of Obesity, 20,* 501–506.

Ball, K., Brown, W., & Crawford, D. (2002). Who does not gain weight? Prevalence and predictors of weight

maintenance in young women. *International Journal of Obesity, 26,* 1570–1578.

Berg, K. (1988). Variability gene effect on cholesterol at the Kidd blood group locus. *Clinical Genetics, 33,* 102–107.

Boomsma, D., Busjahn, A., & Peltonen, L. (2002). Classical twin studies and beyond. *Nature Review Genetics, 3,* 872–882.

Brown, W. J., & Trost, S. G. (2003). Life transitions and changing physical activity patterns in young women. *American Journal of Preventive Medicine, 25,* 140–143.

Cole, T. J., Freeman, J. V., & Preece, M. A. (1998). British 1990 growth reference centiles for weight, height, body mass index and head circumference fitted by maximum penalized likelihood. *Statistics in Medicine, 17,* 407–429.

Dietz, W. H. (1994). Critical periods in childhood for the development of obesity. *American Journal of Clinical Nutrition, 59,* 955–959.

French, S. A., Harnack, L., & Jeffery, R. W. (2000). Fast food restaurant use among women in the Pound of Prevention study: Dietary, behavioral and demographic correlates. *International Journal of Obesity, 24,* 1353–1359.

Hill, J. O., & Peters, J. C. (1998). Environmental contributions to the obesity epidemic *Science, 280,* 1371–1374.

Ijzerman, R. G., Stehouwer, C. D. A., van Weissenbruch, M. M., de Geus, E. J. & Boomsma, D. I. (2001). Intra-uterine and genetic influences on the relationship between size at birth and and height in later life: Analysis in twins. *Twin Research, 4,* 337–343.

Kaprio, J., Pulkkinen, L., & Rose, R. J. (2002). Genetic and environmental factors in health-related behaviors: Studies on Finnish twins and twin families. *Twin Research, 5,* 366–371.

Korkeila, M., Kaprio, J., Rissanen, A., & Koskenvuo, M. (1995). Consistency and change of body mass index and weight: A study on 5967 adult Finnish twin pairs. *International Journal of Obesity, 19,* 310–317.

Koziel, S. M. (1998). Effect of disparities in birth weight on differences in postnatal growth of monozygotic and dizygotic twins. *Annals of Human Biology, 25,* 159–168.

Lahti-Koski, M., Vartiainen, E., Männistö, S., & Pietinen, P. (2000). Age, education and occupation as determinants of trends in body mass index in Finland from 1982 to 1997. *International Journal of Obesity, 24,* 1669–1676.

Lissner, L., Johansson, S. E., Qvist, J., Rössner, S., & Wolk, A. (2000). Social mapping of the obesity epidemic in Sweden. *International Journal of Obesity, 24,* 801–805.

Loos, R. J., Beunen, G., Fagard, R., Derom, C., & Vlietinck, R. (2001a). The influence of zygosity and chorion type on fat distribution in young adult twins: Consequences for twin studies. *Twin Research, 4,* 356–364.

Loos, R. J., Beunen, G., Fagard, R., Derom, C., & Vlietinck, R. (2001b). Birth weight and body composition in young adult men: A prospective twin study. *International Journal of Obesity, 25,* 1537–1545.

Loos, R. J., Beunen, G., Fagard, R., Derom, C., & Vlietinck, R. (2002). Birth weight and body composition in young women: A prospective twin study. *American Journal of Clinical Nutrition, 75,* 676–682.

Maes, H. H. M., Neale, M. C., & Eaves, L. J. (1997). Genetic and environmental factors in relative body weight and human adiposity. *Behavior Genetics, 27,* 325–351.

Ooki, S., & Asaka, A. (1993). Physical growth in Japanese twins. *Acta Geneticae Medicae et Gemellologiae, 42,* 275–287.

Parsons, T. J., Power, C., & Manor, O. (2001). Fetal and early life growth and body mass index from birth to early adulthood in 1958 British cohort: Longitudinal study. *British Medical Journal, 323,* 1331–1335.

Pietiläinen, K. H., Kaprio, J., Rissanen, A., Winter, T., Rimpelä, A., Viken, R. J., & Rose, R.J. (1999). Distribution and heritability of BMI in Finnish adolescents aged 16y and 17y: A study of 4884 twins and 2509 singletons. *International Journal of Obesity, 23,* 107–115.

Rissanen, A., Hakala, P., Lissner, L., Mattlar, C. E., Koskenvuo, M., & Rönnemaa, T. (2002). Acquired preference especially for dietary fat and obesity: A study of weight-discordant monozygotic twin pairs. *International Journal of Obesity, 26,* 973–977.

Rolland-Cachera, M. F., Deheeger, M., Bellisle, F., Sempe, M., Guilloud-Bataille, M., & Patois, E. (1984). Adiposity rebound in children: A simple indicator for predicting obesity. *American Journal of Clinical Nutrition, 39,* 129–135.

Rose, R. J., Dick, D. M., Viken R. J., & Kaprio, J. (2001). Gene-environment interaction in patterns of adolescent drinking: Regional residency moderates longitudinal influences on alcohol use. *Alcoholism: Clinical & Experimental Research, 25,* 637–643.

Sarna, S., Kaprio, J., Sistonen, P., & Koskenvuo, M. (1978). Diagnosis of twin zygosity by mailed questionnaire. *Human Heredity, 28,* 241–254.

Schousboe, K., Visscher, P. M., Erbas, B., Kyvik, K. O., Hopper, J. L., Henriksen, J. E., Heitmann, B. L., & Sørensen, T. I. A. (2004). Twin study of genetic and environmental influences on adult body size, shape, and composition. *International Journal of Obesity, 28,* 39–48.

Schousboe, K., Willemsen, G., Kyvik, K. O., Mortensen, J., Boomsma, D. I., Cornes, B. K., Davis, C. J., Fagnani, C., Hjelmborg, J., Kaprio, J., de Lange, M., Luciano, M., Martin, N. G., Pedersen, N., Pietiläinen, K. H., Rissanen, A., Saarni, S., Sørensen, T. I. A., van Baal, G. C. M., & Harris, J. R. (2003). Sex differ-

ences in heritability of BMI: A comparative study of results from twin studies in eight countries. *Twin Research, 6,* 409–421.

Seidman, D. S., Laor, A., Gale, R., Stevenson, D. K., & Danon, Y. L. (1991). A longitudinal study of birth weight and being overweight in late adolescence. *American Journal of Diseases of Children, 145,* 782–785.

Siegal, M. L., & Bergman, A. (2002). Waddington's canalization revisited: Developmental stability and evolution. *Proceedings of the National Academy of Sciences of the United States of America, 99,* 10528–10532.

Silventoinen, K., Sammalisto, S., Perola, M., Boomsma, D.I., Cornes, B.K., Davis, C., Dunkel, L., de Lange, M., Harris, J.R., Hjelmborg, J.V.B., Luciano, M., Martin, N.G., Mortensen, J., Nisticò, L., Pedersen, N.L., Skytthe, A., Spector, T.D., Stazi, M.A., Willemsen, G., & Kaprio, J.(2003). Heritability of adult body height: A comparative study of twin cohorts in eight countries. *Twin Research, 6,* 399–408.

Sørensen, H. T., Sabroe, S., Rothman, K. J., Gillman, M., Fischer, P., & Sørensen, T. I. (1997). Relation between weight and length at birth and body mass index in young adulthood: Cohort study. *British Medical Journal, 315,* 1137.

StataCorp. (2003). Stata statistical software (Release 8.0) [Computer software]. College Station, TX: Stata Corporation.

Tilator Oy Ltd. (2004). Pediator software for growth data (Release 6.7.4) [Computer software]. Säkylä, Finland: Author.

Vangipuram, S. D., Sheele, J., Atkinson, R. L., Holland, T. C., & Dhurandhar, N. V. (2004). A human adenovirus enhances preadipocyte differentiation. *Obesity Research, 12,* 770–777.

Vidmar, S., Carlin, J., Hesketh, K., & Cole, T. J. (2004). Standardizing anthropometric measures in children and adolescents with new functions for egen. *The Stata Journal, 4,* 50–55.

Waddington, C. H. (1942). Canalization of development and the inheritance of acquired characters. *Nature, 150,* 563–565.

Wilson, R. S. (1976). Concordance in physical growth for monozygotic and dizygotic twins. *Annals of Human Biology, 3,* 1–10.

Wilson, R. S. (1979). Twin growth: Initial deficit, recovery, and trends in concordance from birth to nine years. *Annals of Human Biology, 6,* 205–220.