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Twin study of genetic and environmental influences on adult body size, shape, and composition

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OBJECTIVE: To investigate the genetic and environmental influences on adult body size, shape, and composition in women and men, and to assess the impact of age.
MATERIALS AND METHODS: In this cross-sectional study of 325 female and 299 male like-sex healthy twin pairs, on average 38 y old (18–67 y), we determined zygosity by DNA similarity, and performed anthropometry and bioelectrical impedance analysis of body composition. The contribution to the total phenotypic variance of genetic, common environment, and individual environment was estimated in multivariate analysis using the FISHER program. Further, these variance components were analysed as linear functions of age.
RESULTS: In both women and men genetic contributions were significant for all phenotypes. Heritability for body mass index was 0.58 and 0.63; for body fat%, 0.59 and 0.63; for total skinfolds, 0.61 and 0.65; for extremity skinfolds 0.65 and 0.62; for truncal skinfolds, 0.50 and 0.69; for suprailiac skinfolds, 0.49 and 0.48; for waist circumference, 0.48 and 0.61; for hip, 0.52 and 0.58; for lean body mass/height^2, 0.61 and 0.56; and for height, 0.81 and 0.69, respectively. There was no strong evidence of common environmental effects under the assumptions of no nonadditive effect. The pattern of age trends was inconsistent. However, when significant there was a decrease in heritability with advancing age.
DISCUSSION: These findings suggest that adult body size, shape, and composition are highly heritable in both women and men, although a decreasing tendency is seen with advancing age.
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Introduction

Large family studies in different populations have consistently demonstrated a familial correlation in adult body mass index (BMI), at about 0.2 between parents and offspring and at about 0.3 between siblings.[1] According to many twin and adoption studies, these correlations are attributable mainly to genetic influences rather than to effects of the shared environment.[1] Fewer studies have addressed the genetic and environmental influences on body shape, assessed by body circumferences and skinfold measurements,[2–5] and on body composition of fat and lean mass.[6–10] However, there is a considerable variation in results across the studies and they may be biased for several reasons.

The large studies are generally based on reported instead of measured height and weight, implying various types of errors that may tend to either reduce or inflate the estimated genetic influence. The smaller studies, although using measured phenotypic traits, are usually based on select groups of subjects with an unclear relation to the background population.

The family studies, including the adoption studies, have shown much weaker genetic influences than the twin studies. The proportions of phenotypic variance ascribed to genetic variance (the heritability) are about 0.4 in the family studies and about 0.7 in the twin studies, which conversely implies that the family studies suggest much greater

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influence of the environment.[1] Generational differences between parents and their offspring as well as age differences between family members may contribute to increased variation in the apparent environmental influences. On the other hand, the estimate of the genetic influence in twin studies, which essentially is derived from a comparison of the phenotypic resemblance of monozygotic twin pairs with that of dizygotic twin pairs, may be inflated if the monozygotic twin pairs have been exposed to more similar environment than the dizygotic twin pairs. Obviously, correct zygosity classification of each twin pair is crucial. Since it usually is based on resemblance of the appearance, there is the possibility that dizygotic twin pairs who resemble each other in body size and shape may have been misclassified as monozygotic twins, which also would inflate the estimate of genetic influence and reduce the estimated effects of the shared environment.

In the present study, we have assessed the genetic and environmental influences on BMI, waist and hip circumferences, thickness of truncal and extremity skinfolds and size of the fat and lean body mass as measured in a large population-based sample of adult twin pairs, whose zygosity was determined by polymorphic DNA markers.

Materials and methods

Sample

This study is part of a twin study of the metabolic syndrome and related components (GEMINAKAR), for which subjects were identified through the population-based Danish Twin Registry. [11] A mailed questionnaire was sent to a total of 2099 like-sex twin pairs, who in a previous mailed survey had accepted to be contacted again, and who were alive and living in Denmark according to civil registry records. The questionnaire included information about the exclusion criteria of the study, that is, pregnancy, breastfeeding, known diabetes or cardiovascular disease, and the twins were informed that both twins in a pair were needed for the examination. Pairwise, in 465 pairs at least one of the twins did not want to participate, and in 754 twin pairs at least one of the twins did not answer the questionnaire. If one twin partner in a pair was a nonresponder or not willing to participate the pair as such was excluded. In 880 pairs, both twins answered positively to the questionnaire, which corresponds to a pairwise response rate of 42%. Either based on their written replies or at the following telephone interviews, 116 pairs were excluded due to the above-mentioned exclusion criteria, to various other diseases, or conditions preventing them from completing a bicycle test, which was part of the examination. A remaining group of 386 monozygotic (MZ) and 378 dizygotic (DZ) pairs were willing and able to participate. In order to get an equal distribution of twin pairs across the age span in the different zygosity groups, sampling from this group was stratified according to age and sex. Examination was carried out on a total of 624 twin pairs aged 18–67 y with a distribution of 225, 293, and 106 pairs in three consecutive age groups (18–34, 35–50, and 51–67 y).

Of the 2099 invited twin pairs, data on self-reported BMI obtained in 1994 were available on 3212 individuals (916 participants and 2296 nonparticipants). In this subgroup of the invited twins, the mean was not significantly different between participants and nonparticipants. However, the variance was significantly smaller in the group of participants (8.3) compared to the group of nonparticipants (11.0) with BMI ranges being 14.7–51.5 and 13.6–59.9 kg/m^2, respectively. This slight difference in variances could be due to the more extreme individuals in the population (obese/anorexics) having a higher threshold for participation, and hence probably not an indication that our study population is unrepresentative of the true population. No significant differences were found in MZ and DZ correlation between the participants and nonparticipants (MZ correlations were 0.75 (s.e. 0.03) among participants and 0.68 (0.02) among nonparticipants, and DZ correlations were 0.39 (0.05) and 0.40 (0.03), respectively).

Zygosity of twins was established using nine polymorphic DNA-based microsatellite markers with the PE Applied Biosystems AmpFISTR Profiler Plus Kit.

Anthropometry

Height was measured to the nearest cm using a vertical scale with a horizontal moving headboard. Weight was measured to the nearest 0.1 kg using a standing beam scale. BMI was calculated as weight (kg)/height $(m)^2$. Skinfold thicknesses were measured to the nearest 0.1 mm thrice at each of four different sites (biceps, triceps, subscapular and suprailiac) using a Harpenden calliper. All skinfold measurements were made on the right side of the body. The mean of each site was used to calculate the sum of the biceps and triceps skinfolds (extremity skinfolds), the sum of the subscapular and suprailiac skinfolds (truncal skinfolds), and the sum of the four skinfolds (total skinfolds). Waist circumference (waist) was measured midway between the lowest rib and the iliac crest. Hip circumference was measured over the widest part of the gluteal region. Generally, intra- and interobserver variations, represented as coefficients of variation, are quite low for height, weight, and waist and hip circumference (0.4–1.3 and 0.2–1.4, respectively), whereas these are somewhat higher for skinfolds (7.2–10.3 and 6.4–24.5, respectively).[12] Both intra- and interobserver variation was attempted minimised by the use of these standard procedures carried out by only two well-trained observers. Measurements of BMI, waist and hip were carried out on all twins. Measurements of skinfolds were carried out in 491 twin pairs.

Bioelectrical impedance analysis

The bioelectrical impedance was measured using a BIA-103 RJL-system analyser (RJL-systems Detroit) with a 50 kHz,

800 μA device, following the instructions given by the manufacturer. The measurement was taken with the subject lying comfortably on a coach with the limbs abducted from the body. A tetrapolar electrode placement was used following standard procedures.[13] The electrodes were placed on the dorsal surface of the right hand and foot, at the distal metacarpals and metatarsals, respectively, and between the distal prominences of the radius and the ulna at the wrist and the medial and lateral malleoli at the ankle. Measurements were taken at room temperature in the morning following an overnight fast and after intake of only 75 g glucose solution as part of a subsequent oral glucose tolerance test. Body fat% assessed by bioelectrical impedance was estimated for women and men using the following equation, where impr50 is the electrical impedance with a 50 kHz, 800 μA device, and where sex is 0 for women and 1 for men: Fat% = (0.819 weight −0.064 sex weight −0.279 (height^2/impr50)−0.231 height + 0.077 age + 14.941) 100/ weight.[14]

A cross-validation study, also conducted in adult Danish subjects, using a four-compartment model based on measurements of total body water and potassium as a reference method has shown that this method gives a reliable average estimate of body fat%.[14] Impedance readings are affected by a number of conditions, that is, phase of menstrual cycle in women, skin temperature, and physical activity before measurement, but the contribution to these variations in the readings are fairly small.[15] The impedance method has been found to have an excellent reproducibility of resistance readings over a wide span in body composition and age, variations of 1–3% on the same day, day to day or even week to week for successive readings have been reported by several, for review see Heitmann.[15] The additional information for calculation of body composition is based on age, height, and weight. Measures that all have a very high reproducibility. Lean body mass was assessed by subtracting body fat in kg from body weight in kg. Analogous to BMI, lean body mass in kg was divided by height^2 in m^2. Owing to technical device problems, measurements of bioelectrical impedance were carried out on only 384 twin pairs.

Statistical methods

Analyses of twin studies assume that intrapair variance of MZ twins is due to environmental factors and measurement errors, while intrapair variance in DZ twins is additionally affected by genetic factors. It is also assumed that common environmental factors are shared to a similar extent by MZ and DZ twins. Comparison of the correlation of the trait of interest in MZ twin pairs with that in DZ twin pairs can therefore provide a means of determining the genetic contribution to observed variation in the trait. Simultaneous estimation of additive genetic, nonadditive genetic (ie dominance and epistasis), and common environmental variance is not possible because of confounding.[16] In this study, the tendency for DZ correlations to be about half or more than half of the MZ correlations lead to the consistent use of a model partitioning the total phenotypic variance (V_p) as additive genetic (V_a), common environmental (V_c), and individual environmental variance (V_e), the latter including variance due to measurement errors. Although we have modelled and estimated variances under the assumption of no nonadditive genetic effects, our results do not rule out such effects.

The covariance between the observations on a pair of twins (Y_1,Y_2) was modelled as

$$\mathrm{cov}(Y_1, Y_2) = kV_a + V_c$$

where $k = 1$ for MZ pairs and $k = \frac{1}{2}$ for DZ pairs. For any trait, demonstration of a significant difference in covariance, and hence in correlation, between MZ twin pairs and DZ pairs is consistent with a significant genetic determination of variation in the trait.

Models were fitted by maximum likelihood under the assumptions of the multivariate model,[16] using the software FISHER.[17] This allows simultaneous modelling of the mean effects, the variances, covariances, and variance components as functions of measured covariates and the selection of parsimonious models by reference to the likelihood ratio criterion.[16] For all traits, an overall mean and a linear regression on age were fitted. Tests of assumptions and outliers were performed.[18,19] To yield approximately normal distributions with reasonable size of variances logarithmical transformation and multiplication by 10 or 100 were performed. Under asymptotic likelihood theory, standard errors were estimated. Statistical significance was defined by a nominal P-value of 0.05 or less.

Differences in parameter estimates between the genders were tested using the estimates and their asymptotic standard errors. The test statistic was the ratio of the difference between the estimates and the standard error of that difference, which is asymptotically distributed as a normal distribution under the null hypothesis that the parameters are the same in males and females.

In addition to the standard partitioning of variation, total variation and (co)variance components were modelled as linear functions of age using FISHER.[17,19] If t is the age of a particular twin pair, then the complete model for the (co)variances was modelled as

$$V_p(t) = V_a(t) + V_c(t) + V_e(t)$$

and

$$\mathrm{cov}(Y_1, Y_2|t) = kV_a(t) + V_c(t)$$

For each of the variance component x ($x = a$, c, e), the variance was modelled as

$$V_x(t) = V_x(t = 18) + b_x(t - 18)$$

The intercept was arbitrarily chosen at the age of the youngest twin pairs in the data (18 y).

For the total and each of the three variance components, an age-dependent variance model was selected if: (1) b_x was significant and (2) the maximum likelihood of the model

was significantly different (twice difference in log-likelihood >3.84) from a model without age dependence. A linear function is likely to be robust to outliers and is expected to detect an increasing or decreasing trend.

Results

The average age of both women and men were 38 y, and the average BMI was slightly greater in men than in women (Table 1). As expected, the women had thicker skinfolds at all sites and smaller waists than the men, whereas hip circumferences were about the same. In women, the body fat% was also greater and the lean body mass/height^2 smaller than in men. There were high correlations between the various phenotypic traits except for height, which was weakly correlated with all other traits (Table 2). In both women and men, the waist circumference, body fat%, and lean body mass/height^2 were highly correlated with BMI.

In this study, DZ correlations tended to be greater than half the MZ correlations, which implied that we consistently used models estimating additive genetic (V_a), common environmental (V_c), and individual environmental variance components (V_e) (Table 3). The MZ correlations ranged from 0.61 through 0.93, and the DZ correlations from 0.27 through 0.59, and all were highly significantly different from zero. There were highly significant additive genetic and individual environmental components for all traits, whereas the common environmental components were not significantly different from zero in any trait except for hip circumference in women and height in men (Table 3). There were no significant differences between women and men in the extent of additive genetic and common environmental influences.

The results of the analyses of the age trends did not reveal a clear and consistent pattern (Table 3). Total phenotypic variance in women generally showed an unexpected declining trend with advancing age except for the variance of BMI, lean body mass/height^2, and height (data not shown). Total phenotypic variance in men showed an increasing tendency with age except for the hip circumference, which showed a decreasing trend (data not shown). The age trends of total phenotypic variance were significant only for total and extremity skinfolds in women. For some of the traits (BMI, body fat%, waist circumference and height in men; body fat% and lean body mass/height^2 in women) the MZ correlations declined significantly with advancing age, which for BMI, body fat% and waist circumference in men led to significant increases in the individual environmental variance component. For some traits (BMI, body fat%, and waist circumference in women) the DZ correlations increased significantly with age, but this did not lead to significant age trends in any of the variance components. The additive genetic component declined significantly with age for some traits (total and extremity skinfolds in women; hip circumference in men) even though there were no significant age trends in the MZ and DZ correlations.

In view of the inconsistent pattern of age trends, we have calculated the proportions (with confidence intervals) of the total phenotypic variance contributed by the additive genetic (V_a) (heritability), the common environmental (V_c), and the individual environmental variance components (V_e) under the assumption of no age effects (Table 4). If age effects were included, both a decrease in the additive genetic component as well as an increase in the individual environmental component would result in a decrease in heritability with advancing age.

Table 1 Descriptive statistics of the twin sample

	Women		*Men*	
Phenotype	*Number*	*Mean (s.d.)*	*Number*	*Mean (s.d.)*
Age (y)	650	37.5 (10.5)	598	38.1 (11.0)
BMI (kg/m^2)	650	24.0 (3.9)	598	24.9 (3.1)
Fat%	432	29.7 (7.1)	336	21.1 (5.7)
Total skinfolds (mm)	504	65.6 (23.9)	478	45.4 (17.5)
Extremity skinfolds (mm)	504	31.1 (11.0)	478	16.1 (6.4)
Truncal skinfolds (mm)	504	34.6 (14.7)	478	29.4 (12.3)
Suprailiac skinfolds (mm)	504	15.4 (7.9)	478	13.2 (6.7)
Waist (cm)	650	78.5 (9.7)	598	89.3 (8.9)
Hip (cm)	650	96.7 (9.5)	598	96.2 (6.9)
Lean body mass/height^2 (kg/m^2)	432	16.6 (1.1)	336	19.3 (1.2)
Height (cm)	650	166.6 (6.2)	598	179.7 (6.8)

Table 2 Phenotypic correlations for fat variables, lean body mass/height^2 and height among 1248 twins, in women in the lower left and in men in the upper right half of the table

	BMI	*Fat%*	*Total skinfolds*	*Extremity skinfolds*	*Trunc skinfolds*	*Suprailiacskinfolds*	*Waist*	*Hip*	*Lean body mass/height^2*	*Height*
BMI (kg/m^2)	—	0.90	0.72	0.60	0.71	0.60	0.87	0.03	0.86	−0.16
Fat%	0.95	—	0.81	0.67	0.80	0.70	0.89	0.74	0.56	−0.15
Total skinfolds (mm)	0.80	0.86	—	0.88	0.97	0.90	0.71	0.63	0.43	−0.20
Extremity skinfolds (mm)	0.72	0.77	0.90	—	0.70	0.68	0.58	0.52	0.34	−0.14
Trunc skinfolds (mm)	0.75	0.81	0.94	0.74	—	0.93	0.70	0.63	0.43	−0.21
Suprailiac skinfolds (mm)	0.70	0.76	0.88	0.64	0.94	—	0.58	0.59	0.36	−0.21
Waist (cm)	0.87	0.87	0.74	0.64	0.71	0.66	—	0.70	0.61	0.06
Hip (cm)	0.84	0.88	0.79	0.69	0.70	0.71	0.82	—	0.47	0.22
Lean body mass/height^2 (kg/m^2)	0.89	0.70	0.60	0.55	0.56	0.53	0.73	0.67	—	−0.10
Height (cm)	−0.09	−0.01	−0.03	−0.00	−0.05	−0.05	0.17	0.21	−0.11	—

Table 3 Correlations and variance components of age adjusted anthropometric variables as well as body fat % and height adjusted lean body mass assessed by bioelectrical impedance in women and men

	Correlations(s.e.)		*Variance components (s.e.)*		
Phenotype	*MZ*	*DZ*	V_a^2	V_c^2	V_e^2
BMI ($log_e \times 10$)					
Women	0.76	0.47[a]	1.31	0.42	0.54
	(0.03)	(0.06)	(0.28)	(0.26)	(0.06)
Men	0.70[b]	0.39	0.84	0.09	0.39[a]
	(0.04)	(0.06)	(0.19)	(0.17)	(0.05)
Fat%					
Women	0.72[b]	0.42[a]	26.33	5.60	12.67
	(0.04)	(0.08)	(7.56)	(6.96)	(1.69)
Men	0.65[b]	0.33	16.20	0.33	9.01[a]
	(0.06)	(0.09)	(5.45)	(4.54)	(1.45)
Total skinfolds ($log_e \times 10$)					
Women	0.69	0.38	7.61[b]	0.96	3.88
	(0.04)	(0.07)	(2.03)	(1.77)	(0.50)
Men	0.69	0.37	8.09	0.56	3.88
	(0.04)	(0.07)	(2.15)	(1.90)	(0.50)
Extr. skinfolds (($log_e \times 10$)					
Women	0.66	0.27	7.68[b]	0	4.15
	(0.05)	(0.08)	(0.93)		(0.50)
Men	0.70	0.39	8.28	1.06	3.93
	(0.04)	(0.08)	(2.24)	(2.05)	(0.50)
Truncal skinfolds ($log_e \times 10$)					
Women	0.70	0.46	8.99	3.78	5.35
	(0.04)	(0.06)	(2.66)	(2.37)	(0.69)
Men	0.69	0.34	10.14	0	4.60
	(0.04)	(0.07)	(1.18)		(0.58)
Suprailiac skinfolds ($log_e \times 100$)					
Women	0.69	0.45	1280	514	795
	(0.04)	(0.06)	(389)	(343)	(102)
Men	0.70	0.46	1120	493	698
	(0.04)	(0.07)	(354)	(322)	(91)
Waist ($log_e \times 10$)					
Women	0.68	0.44[a]	0.64	0.26	0.43
	(0.04)	(0.06)	(0.18)	(0.16)	(0.05)
Men	0.61[b]	0.30	0.48	0	0.31[a]
	(0.05)	(0.07)	(0.06)		(0.03)
Hip ($log_e \times 100$)					
Women	0.76	0.50	0.46	0.21	0.22
	(0.03)	(0.05)	(0.10)	(0.10)	(0.02)
Men	0.79	0.51	0.29[b]	0.11	0.10
	(0.03)	(0.06)	(0.06)	(0.06)	(0.01)
Lean Body Mass/height^2					
Women	0.78[b]	0.47	0.76	0.21	0.28
	(0.03)	(0.07)	(0.19)	(0.18)	(0.04)
Men	0.81	0.53	0.78	0.35	0.26
	(0.03)	(0.07)	(0.21)	(0.21)	(0.04)
Height ($log_e \times 100$)					
Women	0.93	0.53	11.05	1.71	0.91
	(0.01)	(0.05)	(1.42)	(1.51)	(0.10)
Men	0.93[b]	0.59	9.17	3.17	0.90
	(0.01)	(0.05)	(1.27)	(1.42)	(0.10)

[a]Increasing with age. [b]Decreasing with age.

Table 4 Proportions of variance components in women and men, presented with approximate 95% confidence intervals

	Proportion of variance components (CI_{95})		
Phenotype	*Additive genetic component*	*Common environmental component*	*Individual environmental component*
BMI ($log_e \times 10$)			
Women	0.58 (0.34–0.82)	0.19 (0.00–0.41)	0.23 (0.17–0.29)
Men	0.63 (0.36–0.90)	0.07 (0.00–0.32)	0.30 (0.22–0.38)
Fat%			
Women	0.59 (0.26–0.92)	0.13 (0.00–0.42)	0.28 (0.20–0.36)
Men	0.63 (0.24–1.00)	0.01 (0.00–0.36)	0.36 (0.24–0.48)
Total skinfolds ($log_e \times 10$)			
Women	0.61 (0.30–0.92)	0.08 (0.00–0.35)	0.21 (0.23–0.39)
Men	0.65 (0.32–0.98)	0.05 (0.00–0.34)	0.30 (0.22–0.38)
Extr. skinfolds ($log_e \times 10$)			
Women	0.65 (0.55–0.75)	0	0.35 (0.25–0.45)
Men	0.62 (0.31–0.93)	0.08 (0.00–0.37)	0.30 (0.22–0.38)
Truncal skinfolds ($log_e \times 10$)			
Women	0.50 (0.23–0.77)	0.21 (0.00–0.46)	0.29 (0.21–0.37)
Men	0.69 (0.61–0.77)	0	0.31 (0.23–0.39)
Suprailiac skinfolds ($log_e \times 100$)			
Women	0.49 (0.20–0.78)	0.20 (0.00–0.45)	0.31 (0.23–0.39)
Men	0.48 (0.19–0.77)	0.21 (0.00–0.48)	0.31 (0.23–0.39)
Waist ($log_e \times 10$)			
Women	0.48 (0.23–0.73)	0.20 (0.00–0.44)	0.32 (0.24–0.40)
Men	0.61 (0.51–0.71)	0	0.39 (0.29–0.49)
Hip ($log_e \times 100$)			
Women	0.52 (0.28–0.76)	0.24 (0.02–0.46)	0.24 (0.18–0.30)
Men	0.58 (0.35–0.81)	0.22 (0.00–0.44)	0.20 (0.14–0.26)
Lean body mass/height^2			
Women	0.61 (0.32–0.90)	0.17 (0.00–0.44)	0.22 (0.16–0.28)
Men	0.56 (0.27–0.85)	0.25 (0.00–0.52)	0.19 (0.13–0.25)
Height ($log_e \times 100$)			
Women	0.81 (0.59–1.00)	0.13 (0.00–0.35)	0.06 (0.04–0.08)
Men	0.69 (0.49–0.89)	0.24 (0.04–0.44)	0.07 (0.05–0.09)

The proportion of genetic variance (the heritability) for BMI and body fat% was in the narrow range of 0.58–0.63. The common environment component ranged from 0.01 through 0.19 (all nonsignificant), whereas the individual environment component ranged from 0.23 through 0.36. The genetic component for the skinfolds ranged from 0.48 through 0.69, the common environment component from 0 through 0.21 (all nonsignificant) and the individual environment from 0.29 through 0.35. The genetic component for waist circumference was 0.61 in men and 0.48 in women, with a correspondingly higher, although nonsignificant, common environmental component in women. The component proportions for the hip circumference were almost the same in women and men, with genetic components at 0.52–0.58 and common environment components at 0.24–0.22, respectively. The genetic component for lean body mass/height^2 was 0.61 in women and 0.56 in men, and the common environment components were 0.17 and 0.25, respectively.

For BMI, body fat%, total and truncal skinfolds, and waist and hip circumference the proportions due to the genetic component were slightly greater in men than in women, in whom the common environment appeared to have a somewhat stronger influence. The opposite was seen for height, where heritability was greater in women due to a greater though not significant influence of common environment in men. For suprailiac skinfolds, hip circumference and lean body mass/height^2 there was a considerable effect of the common environment in both genders though only significant for hip circumference in women. However, the confidence intervals were rather broad and showed a considerable overlap for most estimates.

Discussion

All traits exhibited high heritability estimates ranging from 0.5 through 0.8. For fat measures, the heritability estimates were generally at the same level in both genders, although slightly higher in men than in women, who appeared to be somewhat more influenced by the common environment. The opposite was seen for height adjusted lean body mass and height. However, there was no strong evidence of common environmental effects under the assumption of no nonadditive genetic effects.

The strength of the study is also making its limitations. It was based on a detailed physical assessment and DNA-based zygosity determination of the twin pairs, and the sample was relatively large, which although still implies some uncertainties in twin analysis as reflected in the confidence limits of the variance components. The precision of direct measurement is phenotype dependant. In the existing literature, several studies have shown lower repeatability for skinfold measures than for other anthropometric measurements and bioelectrical impedance, which may lead to overestimation of the nonshared environment, and conversely, underestimation of the heritability estimates for skinfolds.[12,20,21] Furthermore, for skinfolds and waist and hip circumferences repeatability was better in lean than in obese subjects.[21] In attempt to remove the confounding of disease status and/or medical treatment on the intraclass correlations, we excluded subjects having diagnosed diabetes or cardiovascular disease.

A number of previous twin studies have addressed the possible age effects on the genetic and environmental influences on adult BMI, whereas no twin study apparently has addressed age effects on other traits related to fatness. The previous cross-sectional studies of the effect of age on the variation of BMI were all based on self-reported data, and their results were inconsistent. Korkeila *et al*[22] estimated the heritability for BMI in different age groups. They found a decrease in heritability with increasing age, but whether this was due to a decrease in the additive genetic variance or an increase in the individual environmental variance was not described. Herskind *et al*[23] also addressed the age effects and used a model with additive genetic and individual environmental components only, which gave the best fit. In men, they found a surprisingly low heritability in middle-aged men (0.46) compared to older men (0.61), and no age effects in women (0.77 and 0.75, respectively). However, judged from the pattern of stable MZ-correlations and increasing DZ-correlations with increasing age in men an increase in common environmental variance with age may have contributed to the result. Carmichael and McGue[24] carried out a combined analysis of women and men. They found an increase in the individual environmental variance of BMI, whereas the additive genetic variance remained stable. A large longitudinal study of male veterans, combining earlier measured data with self-reported follow-up data, found that heritability increased with increasing age,[25] which, however, may be a spurious result due to the method of analysis.[26] In a 6-y follow-up study Korkeila *et al*.[27] reported stability of the genetic component in BMI over time with a large genetic correlation between genetic effects at baseline and at follow-up. In a period of 28 y between baseline at second examination, Fabsitz *et al*[28] also found stable heritability estimates over time, but with a much lower genetic correlation between the two measurements (0.38), suggesting that a different subset of genes was active during that time.

We found some significant age effects on various variance components, but also these results were inconsistent. They were either due to a decrease in the additive genetic variance or an increase in the individual environmental variance, both resulting in a decrease in the heritability estimate. A decrease in the additive genetic variance could indicate that some genes for a given phenotype are switched off in later life, whereas an increase in the individual environmental component may reflect an accumulation of effects of various environmental exposures. On the other hand, absence of age effects does not exclude that different genes or different environmental exposures may be active at different ages with the same net effect on the phenotype.[28] In spite of its size, our study may lack statistical power for proper assessment of more subtle age effects. In addition, as repeatability for skinfolds and waist and hip circumferences decreases with increasing obesity, and as obesity is increasing with advancing age in the present age range, these measures may exhibit artificial decreasing tendencies in heritability with increasing age. Moreover, owing to the cross-sectional design of the study, care must be taken when interpreting significant influences of age, because both cohort effects and age-dependent recruitment bias may have played a role. The inconsistency of the results of both the previous and the present studies of age effects justified the presentation of our results independent of age within the adult age range studied here.

We assumed that both BMI and body fat% as measured by bioimpedance technique were appropriate indicators of general fatness. The two measures were highly correlated within each sex. Heritability estimates of BMI in large twin studies have been in the range of 0.5–0.8.[22–24,27,29–33] Most of these studies are based on self-reported data, which adds a random error to the total phenotypic variation, but which may also be biased.[34] Lower accuracy of data would lead to an overestimation of individual environmental effects, resulting in lower heritability estimates, and zygosity-dependent correlated errors could increase the heritability estimates. BMI based on direct measurements was obtained in one large population of male twins who had served the military (US National Academy of Sciences—National Research Council). Heritability estimates of BMI from various analyses of these data ranged from 0.5 to 0.8.[25,35,36] Austin *et al*[37] measured BMI on 434 pairs of female twins and estimated a heritability of 0.6 after adjusting for the MZ twins being more similar to their cotwin with respect to common environmental and shared behavioural influences, such as exercise and diet. However, common environmental

effects were found in neither the former studies nor in the latter study. This is in accordance with findings on BMI in adoption studies, which by including both biologic and adoptive relatives allow separate assessment of genetic and common environmental effects.[38–41] In contrast, family studies tend to show influences from the common environment.[1]

One family study, including a limited number of twins, analysed body fat by underwater weighing, and estimated a genetic effect at 0.25 and a cultural transmission (corresponding to shared environmental effects on parents and offspring) at 0.30.[6] A smaller family study (without twins or adoptees) of body fat, also measured by underwater weighing, estimated a 'heritability' of 0.62.[7]

One previous study of subscapular and triceps skinfolds has performed classic twin analysis on 351 pairs of middle-aged male twins, in whom the heritability estimates were of the same magnitude as in the males of the present study.[5] In the present study, the overall picture in both genders for total as well as truncal and extremity skinfolds was that there was the same contribution of additive genetic and environmental variance as for BMI and body fat%, with heritabilities ranging from 0.48 through 0.69.

Waist circumferences and waist-to-hip ratios have been used as measures of abdominal fatness. Heritability estimates of waist-to-hip ratio in previous studies were lower and more discrepant (0.06–0.61)[2–4] than heritability estimates of waist circumference (0.46–0.90).[3,4] Several problems have been recognised in the analysis of ratios like the waist-to-hip ratio.[42] In addition, studies that have compared the two measures with the results of computed X-ray tomography suggest that waist is the best predictor of both abdominal visceral fat and the related cardiovascular risk factors.[43,44] We therefore chose to analyse waist and hip separately. We found heritabilities for waist circumference that were in agreement with the previous studies, 0.48 in women and 0.61 in men, and for hip circumference (for which we have not found previous studies), 0.52 in women and 0.58 in men. Abdominal fat assessed by waist circumference does not discriminate between intraabdominal visceral fat and subcutaneous fat. Suprailiac skinfolds in both genders were influenced by common environmental factors to the same extend as waist circumference in women, whereas no evidence for common environment was found for waist circumference in men.

A few small studies have used more direct measures of abdominal fatness. Abdominal fat assessed by dual-energy X-ray absorptiometry (DXA) showed a heritability of 0.50,[8] and abdominal subcutaneous and visceral fat assessed by computed tomography (CT) showed heritability estimates of 0.42 and 0.56, respectively.[9] Our analysis of the genetic and environmental influences on the abdominal subcutaneous fat, assessed by the supra-iliac skinfold thickness, gave the same results as the latter study. One family study (without twins or adoptees) measured fat mass by underwater weighing technique and abdominal visceral fat using CT, and suggested that there are complex interactions with age and sex.[45] In the present study, waist circumference was more influenced by genes in men than in women, who in contrast were under more influence of common environment than men.

The height-adjusted lean body mass was also under genetic control, with heritability estimates of about 0.60 in both genders and considerable, though not significant, effect of the common environment. A previous study including 227 female twin pairs[10] estimated a heritability of 0.56 for lean body mass (by the Falconer method). In a family study including twins and adoptees, Bouchard *et al*[6] estimated a heritability of 0.30. Height, which can be regarded as an indirect measure of lean body mass, exhibited high heritability estimates, greater for women than for men, who, in contrast, were under more influence of the common environment than women. The sex difference found in this study contrasts the findings in a Finnish study, which for self-reported height found lower heritability in women than in men,[46] but favours the hypothesis of male growth being more affected by nutritional,[47] climatic[48] and psychosocial factors[49] than female growth.

In our analysis, we have assumed the absence of any nonadditive genetic variance, that is, variation due to dominance and epistasis, which arise from intra- and interlocus genetic interactions.[30] However, a number of studies of BMI have clearly suggested that there may be nonadditive genetic effects.[1,32,50] None of the traits examined in our study suggested that there could be such effects, which usually are suspected in the standard twin studies if the MZ correlations exceed twice the DZ correlations. Even though demonstration of the effects may require greater sample size and extended sampling designs, it should also be considered that the difference between MZ and DZ correlations in such visible traits as body size and shape could be upwardly biased by zygosity misclassification, selective recruitment and correlated errors in self-reported height and weight. Moreover, possible sex- and age-dependency of these sources of bias may confound sex and age effects in the genetic and environmental influences.

The joint distributions of BMI and of the other related traits among the members of the families, and also among the twins, indicate that the genetic influence is based on polygenic effects. However, segregation analysis applied to data from several family studies has suggested that major genes may influence BMI,[51] general body fat,[52] subcutaneous fat distribution,[53,54] and abdominal visceral fat.[55,56] There has been only little success in identifying the specific genes constituting the polygenic background of obesity.[57,58] So far, only mutations in the melanocortin 4 receptor gene, occurring in 2–4% of the population, have been consistently associated with common obesity.[59,60]

In conclusion, twin studies, including our study, confirm that the measures applied for general body fat, shape, and composition in adults are strongly influenced by genetic factors, but that there is a tendency for decreasing genetic

influence with increasing age. There are also clear individual environmental effects, but only weak evidence for common environmental effects, which generally appear to be somewhat stronger in women than in men except for height-adjusted lean body mass and height, for which men were more influenced by the common environment than women. This conclusion is drawn under the assumption of no nonadditive genetic effects. None of the studies have demonstrated clear and consistent age effects on the genetic and environmental influences. Future studies should address to what extent the various traits are influenced by the same genetic and environmental factors and whether they are the same in women and men.

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