Familial Aggregation of Amount and Distribution of Subcutaneous Fat and Their Responses to Exercise Training in the HERITAGE Family Study

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Abstract

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Objective: Investigate the familial aggregation of amount and distribution of subcutaneous fat and their changes in response to endurance training.

Research Methods and Procedures: A total of 483 sedentary subjects from 99 nuclear families were recruited, trained for 20 weeks of exercising on cycle ergometers, and measured before and after training for the following indicators of subcutaneous fat and fat distribution: trunk fat (TRUNK = sum of abdominal, subscapular, suprailiac, and midaxillary skinfolds), extremity fat (EXTREM = sum of biceps, triceps, thigh, and calf skinfolds), subcutaneous fat (SF8 = sum of the eight skinfolds), the trunk to extremity skinfolds ratio adjusted for SF8 (TER) and waist girth adjusted for body mass index (WAIST). The familial aggregation of the age- and sex-adjusted baseline phenotypes and their responses to training (Δ) after adjustment for the baseline values was investigated using a familial correlation model.

Results: Significant familial aggregation was observed for all the phenotypes measured at baseline and for ΔTRUNK and ΔWAIST. Transmissibility estimates reached about 30% to 35% for TRUNK, EXTREM, and SF8 and 50% for TER and WAIST. The transmissibilities of the response phenotypes were lower, ranging from 0% for ΔWAIST to 21% for ΔTRUNK and the pattern of familial correlations suggested a greater within- than between-generation resemblance in the response.

Discussion: This study suggests that the amount and distribution of subcutaneous fat strongly aggregates in families, whereas the response to exercise training is characterized by a moderate and more complex pattern of familial resemblance. We conclude that familial/genetic factors are more important in determining the amount and distribution of subcutaneous fat than their responses to exercise training.

Key words: heritability, familial resemblance, fat distribution, exercise training

Introduction

Data from several prospective studies suggest that obesity and regional fat distribution are associated with increased risk of several chronic diseases, including type 2 diabetes (1,2), hypertension (3,4), and cardiovascular disease (5–8). Several family studies have reported that body fat and fat distribution exhibit familial resemblance (9,10). Measurement of body fat distribution in family studies is most often based on anthropometric measurements such as skinfold thicknesses or waist and hip circumferences and simple

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indices or ratios derived from these measurements. Studies based on these anthropometric measures (11–17) reveal that genes and shared family environment contribute to the familial aggregation of subcutaneous fat. In general, the pattern of body fat distribution is characterized by slightly higher heritability estimates than the total amount of body fatness. Heritability estimates ranging from about 30% to 85% have been reported for indicators of subcutaneous fat distribution (9,10,18–20). A few studies have also reported evidence for the segregation of a major gene effect for measures of subcutaneous fat distribution (21,22)

Relatively few studies have investigated the role of genetic factors in the response of body fat and fat distribution phenotypes to alterations in energy balance, despite evidence that there are interindividual differences in the susceptibility to gain or lose weight in response to such alterations. In a series of intervention studies conducted in pairs of monozygotic twins subjected either to positive energy balance induced by overfeeding (23,24) or negative energy balance induced by exercise training (25,26), it was shown that there were considerable differences in the way individuals respond to chronic alterations in energy balance. These twin studies revealed a significant intrapair resemblance in the response of body weight, body composition, adiposity, subcutaneous fat distribution, and abdominal visceral fat to the experimental overfeeding or negative energy balance induced by exercise training (27). For instance, the intraclass correlation coefficient used to assess the within-pair resemblance reached 0.47 and 0.84 for the changes in the amount of subcutaneous fat in response to the overfeeding and negative energy balance protocols, respectively. The within-pair similarity observed in the response to the standardized caloric surplus or the energy deficit suggests that the genotype plays a significant role in determining the body fat and fat distribution responses.

Although results from these twin studies suggest that changes in fat distribution in response to overfeeding or negative energy balance are genotype-dependent, the extent of familial resemblance and the heritability of such changes have never been investigated. The objective of the present study was to determine if there was familial resemblance in the response of subcutaneous fat distribution to exercise training using data from the HERITAGE Family Study. The transmissibility of the phenotypes measured before training in sedentary subjects and their responses to 20 weeks of endurance training was assessed from maximum likelihood estimates of familial correlations.

Research Methods and Procedures

Sample

Subjects of the HERITAGE Family Study were used for the purpose of this study. The HERITAGE study is a multicenter (four clinical centers and a Data coordinating center) study designed to investigate the effects of regular exercise on several cardiovascular disease and diabetes risk factors and to determine the role of genetic factors in the cardiovascular, metabolic, and hormonal adaptations to exercise training. The specific aims, design, and measurements of the study have been described in detail elsewhere (28).

For the present study, a total of 483 white subjects from 99 nuclear families (184 parents and 299 biological offspring) ranging in age from 17 to 65 years were available. Data on both parents were available in all families, and the number of offspring per family ranged from one (two families) to five (two families). Most families ($n = 61$) included three offspring. All subjects were required to be sedentary at baseline, defined as engaging in no regular physical activities over the previous 6 months, and to be free of any condition or disease that could be aggravated with exercise training. Moreover, obese individuals (body mass index [BMI] $>$ 40 kg/m^2) were excluded because of potential metabolic abnormalities and exercise difficulties associated with extreme obesity, unless they were able to meet the demands of the training program. The average BMI of the subjects involved in the present study was 25.9 kg/m^2, and there were six subjects with BMI values over 40 kg/m^2 (four parents and two offspring). More details about exclusion criteria can be found in Bouchard et al. (28).

Training Program

The subjects trained on cycle ergometers, three times a week, for 20 weeks using the same standardized protocol. The subjects exercised at a heart rate corresponding to 55% of their baseline maximal oxygen consumption ($\dot{V}O_2$ max) for 30 minutes per session at the beginning, increasing progressively toward a heart rate associated with 75% of their baseline $\dot{V}O_2$ max for 50 minutes, which they maintained during the last 6 weeks of the training protocol. The intensity and duration of the training program were adjusted every 2 weeks. Training intensities were adjusted individually by a computer system recording all training data and adjusting automatically the power output of the cycle ergometer to keep the heart rate response of the subject within five beats of the programmed heart rate at all times during all training sessions. Details about the training program and the measure of $\dot{V}O_2$ max can be found elsewhere (29,30).

Measurements

A series of anthropometric and girth measurements were obtained on each subject before and after training, as described in detail elsewhere (31). Height and weight were measured to the nearest 0.1 kg and 0.1 cm, respectively, using a stadiometer and a balance beam scale. The BMI (weight in kg/height in m^2) was derived from height and weight measurements. Skinfold thicknesses were measured twice at eight different sites (biceps, triceps, medial calf,

thigh, subscapular, suprailiac, abdominal, and midaxillary) with Harpenden calipers following the procedures recommended by Lohman et al. (32). A third measurement was taken if the first two differed by more than 1.0 mm. The two measurements (the two closest when three measures were taken) were averaged and used as the final value. The sum of the four trunk skinfolds (TRUNK = subscapular + suprailiac + abdominal + midaxillary) and the sum of the four extremity skinfolds (EXTREM = biceps + triceps + medial calf + thigh) were used as indicators of truncal and extremity subcutaneous fat, respectively. The sum of the eight skinfolds (SF8) was used as an indicator of the amount of subcutaneous fat. The trunk-to-extremity skinfolds ratio (TER = TRUNK/EXTREM) was used as an indicator of the propensity to store fat in the truncal abdominal area relative to the extremities. Waist circumference was measured to the nearest 1.0 cm using a Fiberglas anthropometric tape. The reproducibility of these anthropometric measurements, measured on three separate days within a 3-week period, was found to be high with intraclass correlations greater than or equal to 0.97 for the skinfolds and girth measurements (31). The training-induced changes in fat distribution were computed as the difference between the post-training and baseline measurements. A paired *t* test on the response scores was used to test for the effects of endurance training.

Data Adjustments

All fat distribution variables were adjusted for the effects of age on the mean and the variance as described in detail elsewhere (33). Briefly, within each of the four sex-by-generation groups, each phenotype was regressed on up to a cubic polynomial in age using a stepwise multiple regression procedure, retaining only those terms that were significant at the 5% level (mean regression). The squared residuals derived from this regression were regressed on another polynomial in age to adjust for age effects on the variance (variance regression). The phenotype used in the genetic analysis was the residual from the mean regression divided by the square root of the predicted score from the variance regression and standardized to a zero mean and a standard deviation of one. This adjustment corrects for age effects in the means and variances of the phenotypes and does not affect the covariances among relatives, which are used to derive the estimates of transmissibility. In addition to age, the variables TER and WAIST were also adjusted for subcutaneous fat (SF8) and BMI, respectively. All response phenotypes were also further adjusted for baseline values.

Familial Correlation Model

The familial correlation model was based on four groups of individuals—fathers (*f*), mothers (*m*), sons (*s*), and daughters (*d*)—giving rise to eight interindividual correlations in three familial classes as follows: one spouse (*fm*), four parent-offspring (*fs*, *fd*, *ms*, *md*), and three sibling (*ss*, *dd*, *sd*). The maximum likelihood computer program SEGPATH (34) fitted the model directly to the family data under the assumption that the phenotypes within a family jointly follow a multivariate normal distribution. Null hypotheses were tested using the likelihood ratio test, which is the difference in minus twice the log-likelihoods (-2 ln L) obtained under the two different nested models. The likelihood ratio is approximately distributed as a value of χ^2, with the degrees of freedom being the difference in the number of parameters estimated in the two competing hypotheses. In addition to the likelihood ratio test, Akaike's (35) Information Criterion (AIC), which is -2 ln L plus twice the number of estimated parameters, was used to judge the fit of non-nested models. The most parsimonious model by AIC is the one with the smallest value.

A general model with all eight familial correlations (Model 1) and several reduced models (Models 2 through 9) testing specific null hypotheses were fitted to the data. Two broad classes of reduced models were considered. First, null hypotheses relating to sex and/or generation differences in the familial correlations were tested, including no sex differences in the offspring (Model 2: $fs = fd$, $ms = md$, $ss = dd = sd$ [$df = 4$]), no sex differences in parents or offspring (Model 3: $fs = fd = ms = md$, $ss = dd = sd$ [$df = 5$]) and no sex nor generation differences (Model 4: $fs = fd = ms = md = ss = dd = sd$ [$df = 6$]). Second, null hypotheses testing the strength of the familial resemblance were also conducted by familial class, including no sibling resemblance (Model 5: $ss = dd = sd = 0$ [$df = 3$]), no parent-offspring resemblance (Model 6: $fs = fd = ms = md = 0$ [$df = 4$]) and no spouse resemblance (Model 7: fm = 0 [$df = 1$]). Finally, in Model 8, all eight correlations were equated ($fm = fs = fd = ms = md = ss = dd = sd$ [$df = 7$]), whereas the hypothesis of no familial resemblance at all ($fm = fs = fd = ms = md = ss = dd = sd = 0$ [$df = 8$]) was tested in Model 9. Models were then combined with the aim of finding the most parsimonious model. Although there is no single rule to determine which combination of models leads to the most parsimonious model, we started by combining all nonrejected null hypotheses. This was done by combining the best sex/generation differences models with the best model testing the strength of the familial correlations (Models 5 through 7), given constraints across models. If the AIC from this combined model is smaller than any other models, this becomes the most parsimonious model. The heritabilities were computed from the maximum likelihood estimates of the familial correlations obtained under the most parsimonious model as follows:

$$h^2 = (r_{\text{sibling}} + r_{\text{parent-offspring}})(1 + r_{\text{spouse}})/(1 + r_{\text{spouse}} + 2r_{\text{spouse}}r_{\text{parent-offspring}})$$

This heritability estimate includes both genetic and nongenetic sources of variance and is adjusted for the degree of

spouse resemblance. To indicate that this heritability estimate includes the contribution of both genetic and familial environmental factors transmitted from parents to offspring, we will refer to it as a "transmissibility" estimate. The confidence intervals associated with these estimates were also calculated using the same equation as above by substituting the standard errors obtained from the estimates of the familial correlations.

Results

Table 1 presents the sample sizes, means, and standard deviations for age and for each of the fat distribution phenotypes before and after training, separately in each of the sex-by-generation groups (fathers, mothers, sons, and daughters). The values observed at baseline reveal that, within each generation, females have a higher amount of subcutaneous fat (SF8) than males, whereas parents have higher values than their offspring within each sex. Moreover, sex differences are moderate for trunk skinfolds, with males having slightly higher values than females, but are important for extremity skinfolds with females having a much higher amount of subcutaneous fat on the extremities compared to males. Except for TER in fathers, mothers, and daughters, endurance training resulted in significant reductions in all indicators of the amount and distribution of subcutaneous fat (unadjusted data) within each group.

There was considerable variation in the response of subcutaneous fat phenotypes to exercise training. Figure 1 illustrates the extent of this variation for the changes in trunk fat within each of the four groups. The figure clearly shows that in parents and offspring of both sexes there was considerable variation in the response of trunk fat to endurance training. Although most individuals exhibited a reduction in trunk fat, there were some individuals who gained fat following exercise training.

Table 2 presents a summary of the covariate adjustments for baseline and response phenotypes in each of the four sex-by-generation groups. For trunk and extremity skinfolds, significant effects of age in the mean were observed in sons (26% and 9%) and daughters (6% for EXTREM), whereas no significant effects of age in the variance were noted, except for trunk skinfolds in fathers (14%). For TER, significant effects of subcutaneous fat (SF8) in the mean (7%) and the variance (13%) were observed in mothers. A linear effect of age accounted for 13% of the variance in sons, whereas a quadratic effect of age and SF8 accounted for 15% of the variance in daughters. Age and BMI were found to explain between 73% and 93% of the mean variation in WAIST, whereas significant effects of BMI were noted in the variance of WAIST in fathers (5%) and daughters (4%). For the changes in trunk (ΔTRUNK) and extremity (ΔEXTREM) skinfolds, significant effects of the baseline value in the mean and in the variance were generally noted in all

Table 1. Descriptive statistics of the sample at baseline and after training in each of the sex and generation groups

	Fathers			Mothers			Sons			Daughters		
Variable	***N***	**Baseline**	**Post-training**	***N***	**Baseline**	**Post-training**	***N***	**Baseline**	**Post-training**	***N***	**Baseline**	**Post-training**
Age (years)	93	53.6 ± 5.3		91	52.1 ± 5.1		140	25.4 ± 6.1		159	25.5 ± 6.4	
SF8 (mm)	79	146.7 ± 50.0	140.8 ± 49.0*	75	194.3 ± 50.3	187.3 ± 49.9*	129	121.0 ± 54.2	113.1 ± 52.0†	153	147.4 ± 50.6	141.0 ± 49.9†
TRUNK (mm)	81	94.6 ± 29.8	90.5 ± 29.4†	79	93.5 ± 29.1	90.7 ± 30.1‡	131	74.7 ± 35.5	69.1 ± 33.6†	155	70.4 ± 29.2	67.3 ± 29.3†
EXTREM (mm)	90	53.3 ± 23.5	51.4 ± 22.7*	80	103.0 ± 26.6	98.8 ± 25.5†	135	48.4 ± 23.1	46.3 ± 22.6†	155	78.2 ± 25.1	74.9 ± 24.7†
TER	79	1.88 ± 0.52	1.85 ± 0.52	75	0.91 ± 0.21	0.92 ± 0.24	129	1.60 ± 0.47	1.55 ± 0.43*	153	0.90 ± 0.25	0.89 ± 0.24
WAIST (cm)	92	101.0 ± 11.3	100.2 ± 11.7*	90	95.2 ± 14.3	94.0 ± 14.6*	139	90.8 ± 14.2	89.8 ± 14.1†	157	81.0 ± 12.1	79.9 ± 11.7†

Effects of endurance training based on unadjusted data: ‡ $p < 0.05$; * $p < 0.001$; † $p < 0.0001$.

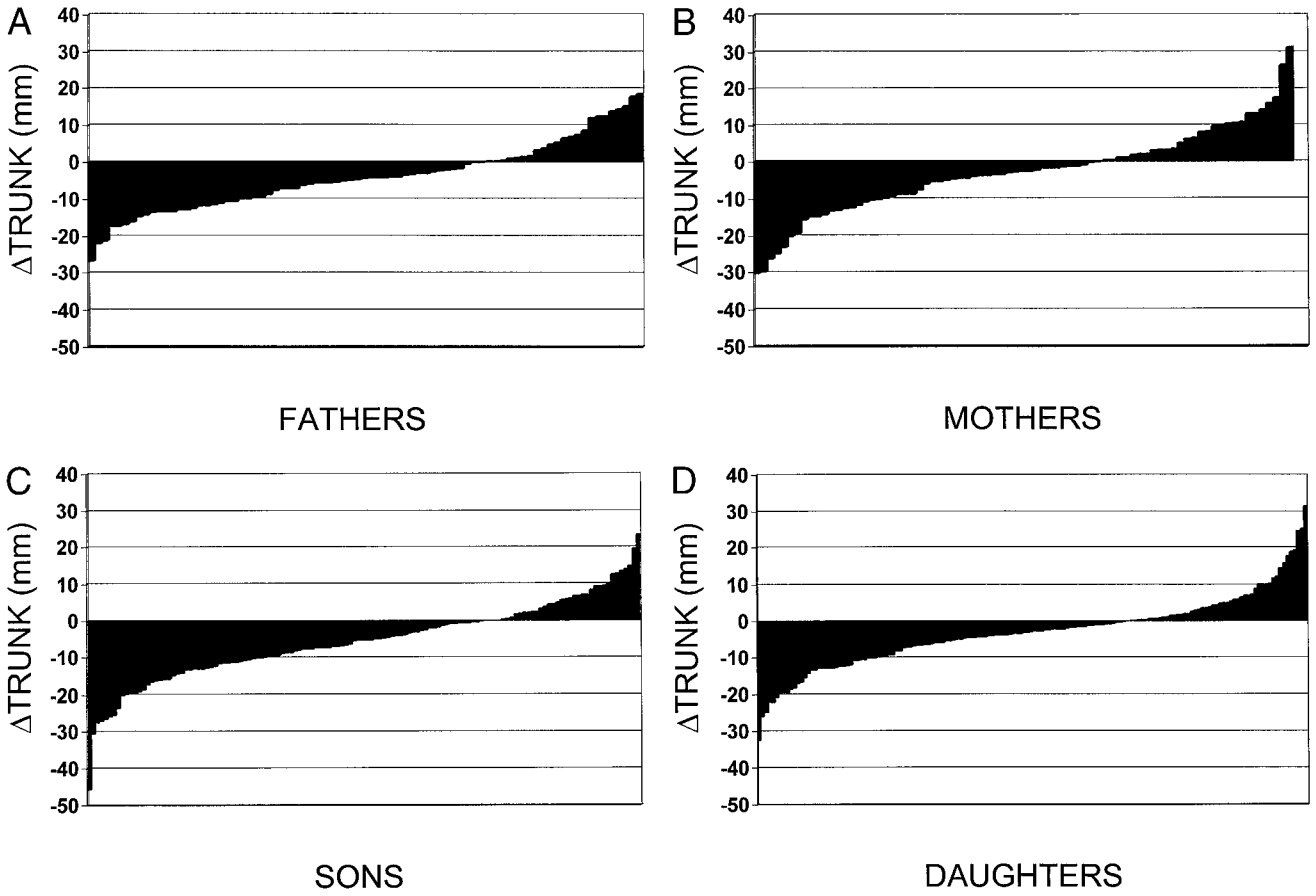

Figure 1. Individual changes in trunk skinfolds (ΔTRUNK) following 20 weeks of endurance training in fathers (A), mothers (B), sons (C), and daughters (D).

groups. These effects accounted for between 3% and 18% of the variance. For ΔTER, the baseline value contributed significantly to the mean variation in sons (11%) and daughters (8%) and to the variance in fathers (10%) and daughters (4%). Finally, baseline waist circumference was found to contribute significantly to the mean (8%) and to the variance of ΔWAIST (3%) only in daughters.

A summary of the model-fitting results for the baseline and the response phenotypes are presented in Tables 3 and 4, respectively. For each model, the *p* values and the AIC of the likelihood ratio tests are presented. The results for the baseline phenotypes (Table 3) indicate that the hypothesis of no sex nor generation differences cannot be rejected. On the other hand, the sibling and the parent-offspring correlations were significant for each phenotype, whereas the hypothesis of no spouse correlation was rejected for EXTREM and WAIST. Finally, the hypothesis of no familial resemblance (Model 9) was strongly rejected for all phenotypes. The parsimonious model combining the hypotheses of no sex nor generation differences in the correlations (Model 4: $fs = fd = ms = md = ss = dd = sd$) and the hypothesis of no spouse correlation (Model 7: $fm = 0$) could not be rejected based on the likelihood ratio tests. However, based on the AIC, the most parsimonious hypothesis (the one with the lowest AIC value) was Model 8 in which all eight correlations were equated.

The results for the response phenotypes are shown in Table 4. As observed for the baseline phenotypes, there are no sex nor generation differences for the responses (Model 4: $fs = fd = ms = md = ss = dd = sd$). However, unlike the results observed for baseline phenotypes, when all eight correlations are tested together (Model 9), there is little evidence for familial resemblance for ΔSF8 ($p = 0.15$), ΔEXTREM ($p = 0.15$), or ΔTER ($p = 0.09$). Tests of individual parameters suggest that only sibling correlations (Model 5) for ΔTRUNK and only the spouse correlation (Model 7) for ΔSF8, ΔEXTREM, and ΔWAIST were significant. For ΔSF8, the combined test of no sibling and no parent-offspring correlation (a model with only the spouse correlation) could not be rejected ($p = 0.35$, AIC = 9.83), but the combined test of Models 2 and 6 (adding back the sibling correlations) provided a better fit (AIC = 5.88) and was therefore chosen as the most parsimonious model.

Table 2. Summary of covariate adjustments for baseline and response phenotypes in the four sex-by-generation groups

Variable	Fathers	Mothers	Sons	Daughters
Baseline				
TRUNK				
Means	None	None	Age (26.0%)	None
Variance	Age^2, age^3 (13.8%)	None	None	None
EXTREM				
Means	None	None	Age (9.0%)	Age^3 (5.6%)
Variance	None	None	None	None
TER				
Means	None	SF8 (7.3%)	Age (13.3%)	Age^2, SF8 (15.2%)
Variance	None	SF8 (13.4%)	None	None
WAIST				
Means	Age, BMI (86.7%)	BMI (73.5%)	Age, BMI (93.4%)	Age, BMI (74.6%)
Variance	BMI (5.5%)	None	None	BMI (3.8%)
Response				
ΔTRUNK				
Means	None	TRUNK (7.9%)	TRUNK (8.4%)	TRUNK (2.8%)
Variance	TRUNK (5.0%)	TRUNK (9.3%)	TRUNK (8.4%)	Age^3, TRUNK (9.6%)
ΔEXTREM				
Means	None	EXTREM (8.8%)	EXTREM (4.4%)	EXTREM (5.1%)
Variance	EXTREM (5.2%)	EXTREM (10.4%)	EXTREM (17.9%)	EXTREM (8.7%)
ΔTER				
Means	None	None	TER (10.6%)	TER (8.0%)
Variance	TER (10.3%)	None	Age (8.2%)	TER (4.2%)
ΔWAIST				
Means	None	None	None	WAIST (8.8%)
Variance	None	None	None	WAIST (2.5%)

For ΔTRUNK, the test (not shown) combining the nonrejected models (Models 2, 6, and 7, thus a model estimating only a single sibling correlation) could not be rejected ($p = 0.27$) but provided a slightly worse fit (AIC = 10.82) than Model 2 (AIC = 10.6). Because the hypothesis of no spouse correlation was of low significance ($p = 0.09$), we tested the hypothesis of combined Models 2 and 6, i.e., a model with only spouse and equal sibling correlations. This hypothesis could not be rejected and was retained as the best Model (AIC = 9.50). For ΔEXTREM, spouse resemblance was the only significant correlation ($p = 0.02$). Thus a model combining Models 5 and 6 with only a spouse correlation could not be rejected but did not provide the lowest AIC. The combination of Models 2 and 6 estimating only a spouse correlation with a single sibling correlation could not be rejected ($p = 0.48$, AIC = 9.51), but Model 6, with no parent-offspring correlations but allowing for sibling and spouse resemblance, provided the best fit (AIC = 9.10) and was therefore considered as the most parsimonious model.

For ΔTER, none of the hypotheses were formally rejected, although the hypotheses of no sex differences in offspring (Model 2) and no parent-offspring correlations were almost nonsignificant. The combination of Models 5 and 7 (no sibling and no spouse correlations) was also tested both with and without sex differences in the parent-offspring correlations. Thus, a model with only the four sex-specific parent-offspring correlations (Models 5 + 7) could not be rejected ($p = 0.20$, AIC = 13.96) and provided a better fit than a combination of Models 3, 5, and 7 with equal parent-offspring correlations ($p = 0.07$, AIC = 15.15) or Models 2, 5, and 7 with father-offspring and mother-offspring correlations ($p = 0.04$, AIC = 17.11). However, based on AIC, Model 8 (AIC = 12.61) was preferred over the combination of Models 5 and 7 (AIC = 13.96) and

Table 3. Summary of results from fitting reduced models for baseline phenotypes

		SF8		TRUNK		EXTREM		TER		WAIST	
Models	***df***	***p****	**AIC†**	***p***	**AIC**	***p***	**AIC**	***p***	**AIC**	***p***	**AIC**
1. General			16.00		16.00		16.00		16.00		16.00
2. No sex differences, offspring	4	0.48	11.45	0.50	11.35	0.76	9.87	0.71	10.13	0.24	13.48
3. No sex differences, parents or offspring	5	0.39	11.21	0.64	9.39	0.84	8.05	0.79	8.39	0.32	11.85
4. No sex nor generation differences	6	0.50	9.32	0.76	7.39	0.90	6.24	0.88	6.39	0.41	10.08
5. No sibling	3	0.027	19.19	0.01	20.70	0.003	23.78	<0.001	32.16	<0.001	43.63
6. No parent-offspring	4	0.026	19.07	0.01	22.39	0.033	18.48	<0.001	32.35	<0.001	33.82
7. No spouse	1	0.09	16.94	0.19	15.71	0.045	18.03	0.08	17.02	0.015	19.94
8. Equal correlations	7	0.60	7.47	0.84	5.44	0.94	4.32	0.91	4.70	0.53	8.10
9. All correlations = 0	8	0.003	23.26	<0.001	27.15	<0.001	29.14	<0.001	50.55	<0.001	61.40
Parsimonious models											
Models 4 and 7	7	0.29	11.53	0.59	7.54	0.52	8.16	0.55	7.90		
Model 8	7	**0.60**	**7.47**	**0.84**	**5.44**	**0.94**	**4.32**	**0.91**	**4.70**	**0.53**	**8.10**

* p = p values from the likelihood ratio χ^2 test; a significant value ($p < 0.05$) indicates rejection of the null hypothesis.
† AIC = Akaike's Information Criterion; the most parsimonious model is the one with the smallest AIC and is shown in bold.

remained as the most parsimonious model for ΔTER. In the model with the lowest AIC for ΔWAIST, Model 8, the sibling and parent-offspring correlations were not significant, whereas the spouse correlation was significant (p = 0.04). The combination of Models 5 and 6, in which the familial resemblance is explained by the spouse correlation, provided the best fit (AIC = 9.22) and was considered as the most parsimonious model.

Table 4. Summary of results from fitting reduced models for the response phenotypes

		ΔSF8		ΔTRUNK		ΔEXTREM		ΔTER		ΔWAIST	
Models	***df***	***p****	**AIC†**	***p***	**AIC**	***p***	**AIC**	***p***	**AIC**	***p***	**AIC**
1. General			16.00		16.00		16.00		16.00		16.00
2. No sex differences, offspring	4	0.91	8.99	0.63	10.60	0.30	12.86	0.05	17.48	0.82	9.56
3. No sex differences, parents or offspring	5	0.90	7.62	0.36	11.46	0.36	11.45	0.09	15.48	0.44	10.79
4. No sex nor generation differences	6	0.37	10.49	0.06	16.15	0.39	10.27	0.14	13.72	0.33	10.91
5. No siblings	3	0.11	25.95	0.009	21.53	0.11	16.05	0.33	13.40	0.33	13.41
6. No parent-offspring	4	0.81	9.61	0.42	11.90	**0.89**	**9.10**	0.07	16.56	0.40	12.02
7. No spouse	1	0.05	17.75	0.09	16.87	0.02	19.20	0.1	16.69	0.037	22.39
8. Equal correlations	7	0.21	11.55	0.055	15.81	0.22	11.52	**0.16**	**12.61**	0.043	16.46
9. All correlations = 0	8	0.15	12.03	0.015	18.92	0.15	12.04	0.09	13.73	0.04	16.14
Parsimonious models											
Models 2 and 6 ($fm + sd = ss = dd$)	6	**0.93**	**5.88**	**0.48**	**9.50**	0.48	9.51	0.12	14.02		
Models 5 and 6 (only fm)	7	0.35	9.83			0.39	9.35			**0.41**	**9.22**
Models 5 + 7 (fs, ms, fd, md)	4							0.20	13.96		
Models 3 + 5 + 7 ($fs = ms = fd = md$)	7							0.07	15.15		

* p = p values from the likelihood ratio χ^2 test; a significant value ($p < 0.05$) indicates rejection of the null hypothesis.
† AIC = Akaike's Information Criterion; the most parsimonious model is the one with the smallest AIC and is shown in bold.

Table 5. Maximum likelihood estimates of familial correlations (±SE) under the general and most parsimonious models for baseline phenotypes

Parameter	SF8	TRUNK	EXTREM	TER	WAIST
General model					
fm	0.19 ± 0.11	0.15 ± 0.11	0.22 ± 0.10	0.22 ± 0.12	0.27 ± 0.10
fs	0.14 ± 0.09	0.24 ± 0.09	0.18 ± 0.08	0.33 ± 0.08	0.20 ± 0.09
ms	0.14 ± 0.10	0.11 ± 0.10	0.15 ± 0.10	0.30 ± 0.09	0.23 ± 0.09
fd	0.02 ± 0.11	0.13 ± 0.09	0.10 ± 0.09	0.18 ± 0.09	0.28 ± 0.09
md	0.26 ± 0.08	0.27 ± 0.08	0.22 ± 0.08	0.34 ± 0.09	0.38 ± 0.08
sd	0.21 ± 0.09	0.20 ± 0.09	0.26 ± 0.08	0.29 ± 0.08	0.23 ± 0.09
ss	0.23 ± 0.13	0.25 ± 0.12	0.21 ± 0.13	0.31 ± 0.10	0.20 ± 0.11
dd	0.08 ± 0.11	0.14 ± 0.11	0.13 ± 0.11	0.24 ± 0.12	0.47 ± 0.09
Most parsimonious model					
fm	0.16 ± 0.04	0.19 ± 0.05	0.18 ± 0.04	0.28 ± 0.05	0.29 ± 0.05
fs	[0.16]*	[0.19]	[0.18]	[0.28]	[0.29]
ms	[0.16]	[0.19]	[0.18]	[0.28]	[0.29]
fd	[0.16]	[0.19]	[0.18]	[0.28]	[0.29]
md	[0.16]	[0.19]	[0.18]	[0.28]	[0.29]
sd	[0.16]	[0.19]	[0.18]	[0.28]	[0.29]
ss	[0.16]	[0.19]	[0.18]	[0.28]	[0.29]
dd	[0.16]	[0.19]	[0.18]	[0.28]	[0.29]
Transmissibility (CI)†	31% (23%–39%)	36% (26%–46%)	34% (26%–42%)	50% (40%–60%)	51% (41%–61%)

* Values in brackets are fixed or equal to the preceding value.

† CI = 95% confidence intervals calculated as described in the Methods section.

Maximum likelihood estimates of the familial correlations under the general and most parsimonious models are presented in Tables 5 and 6 for the baseline and response phenotypes, respectively. These tables also present the transmissibility estimates calculated from the most parsimonious models. For the baseline phenotypes, the transmissibilities range from 31% for SF8 to 51% for WAIST. In all cases, the most parsimonious model was a model in which the familial correlations were all equal, suggesting that both genetic and shared environmental factors contribute to the familial aggregation of these phenotypes. For the response phenotypes, the transmissibilities range from 14% for ΔTER to 21% for ΔTRUNK and could be attributed to both genetic and environmental factors. Only the spouse correlation was significant for ΔWAIST, suggesting that the transmissibility of this phenotype is zero.

Discussion

In the present study, we used a familial correlation model to determine whether there is evidence of familial resemblance in the amount and distribution of subcutaneous fat measured in sedentary subjects before and in response to 20 weeks of endurance exercise. The results indicate a strong familial aggregation of the baseline phenotypes. The transmissibilities of the amount and distribution of subcutaneous fat ranged from 31% to 51%. Although correlations derived from nuclear family data alone do not allow a distinction to be made between genetic and cultural transmission, the pattern of correlations observed among spouses, parent-offspring, and siblings can be used to make inferences about the relative contribution of genetic vs. environmental factors. For example, significant correlations between parent-offspring and siblings, but not between spouses, would suggest that the familial aggregation is primarily attributable to genetic factors. The presence of a significant spouse correlation, in addition to parent-offspring and sibling correlations, might suggest that shared familial environment also contributes to the familial resemblance, provided that there is neither phenotypic assortative mating nor social homogamy.

Despite differences across studies arising from the use of different skinfolds, the estimates reported in the present study are comparable to those previously reported. A transmissibility of 31% was found in the present study for total amount of subcutaneous fat (SF8). Results from other fam-

Table 6. Maximum likelihood estimates of familial correlations (±SE) under the general and most parsimonious models for the response phenotypes

Parameter	ΔSF8	ΔTRUNK	ΔEXTREM	ΔTER	ΔWAIST
General model					
fm	0.25 ± 0.12	0.19 ± 0.11	0.27 ± 0.11	0.20 ± 0.11	0.33 ± 0.10
fs	−0.12 ± 0.09	−0.15 ± 0.09	0.04 ± 0.10	−0.03 ± 0.09	−0.06 ± 0.08
ms	−0.01 ± 0.13	−0.05 ± 0.13	−0.06 ± 0.11	−0.14 ± 0.09	0.08 ± 0.10
fd	−0.02 ± 0.09	−0.04 ± 0.09	0.07 ± 0.090	0.11 ± 0.09	−0.13 ± 0.09
md	−0.02 ± 0.09	0.10 ± 0.10	0.01 ± 0.08	0.25 ± 0.09	0.03 ± 0.09
sd	0.11 ± 0.10	0.22 ± 0.09	0.02 ± 0.08	0.04 ± 0.10	0.07 ± 0.09
ss	0.17 ± 0.12	0.09 ± 0.12	0.31 ± 0.12	0.00 ± 0.09	−0.02 ± 0.13
dd	0.18 ± 0.12	0.28 ± 0.10	−0.02 ± 0.10	0.16 ± 0.09	0.17 ± 0.11
Most parsimonious model					
fm	0.25 ± 0.12	0.21 ± 0.11	0.25 ± 0.11	0.07 ± 0.02	0.33 ± 0.10
fs	[0]*	[0]	[0]	[0.07]	[0]
ms	[0]	[0]	[0]	[0.07]	[0]
fd	[0]	[0]	[0]	[0.07]	[0]
md	[0]	[0]	[0]	[0.07]	[0]
sd	0.15 ± 0.07	0.20 ± 0.07	0.03 ± 0.08	[0.07]	[0]
ss	[0.15]	[0.20]	0.32 ± 0.12	[0.07]	[0]
dd	[0.15]	[0.20]	−0.02 ± 0.11	[0.07]	[0]
Transmissibility (CI)†	15% (8%–22%)	21% (14%–28%)	15% (5%–25%)	14% (10%–18%)	0%

* Values in brackets are fixed or equal to the preceding value.
† CI = 95% confidence intervals calculated as described in the Methods section.

ily studies found similar results for subcutaneous fat. In the Quebec Family Study (QFS), we found that the transmissibility of subcutaneous fat assessed from the sum of six skinfolds reached 40% (36). More recently, we studied the familial aggregation of subcutaneous fat by computing familial correlations of principal components arising from the six skinfolds measured in the QFS (17). The transmissibility of the first component, which loaded equally on the six skinfolds, reached 46%. The familial aggregation of subcutaneous adiposity was also investigated in a large sample of the Canadian population involving 13,804 subjects who participated in the 1981 Canada Fitness Survey (37). Measurements of trunk fat (sum of suprailiac and subscapular skinfolds), extremity fat (sum of triceps, biceps, and calf skinfolds), and subcutaneous fat (sum of five skinfolds) were used as indicators of the amount of subcutaneous fat. Transmissibilities of 35%, 39%, and 37% were obtained for trunk, extremity, and subcutaneous fat, respectively. The estimates of 36%, 34%, and 31% obtained in the present study are very similar to those obtained in the general Canadian population. Comuzzie et al. (14) reported heritabilities ranging from 26% for the abdominal skinfold to 58% for the biceps skinfold based on genetic and environmental correlations computed in 408 subjects from 24 pedigrees.

The transmissibilities of TER (adjusted for total subcutaneous fat) and WAIST (adjusted for BMI) reached 50%, which suggests that subcutaneous fat distribution may be more influenced by familial/genetic factors than by the amount of subcutaneous fat itself. These results suggest that genetic and/or environmental factors play a role in determining the propensity to store fat in the abdominal area, independent of total amount of body fatness. Similar estimates were also obtained for these two phenotypes after adjustment for age and sex effects alone (results not shown). The similarity of the results with and without adjustment for the covariates suggests that there is probably little pleiotropy in the additive effects between these particular traits. A transmissibility of 37% has been reported for TER based on the five skinfold measures taken in participants of the Canada Fitness Survey (37). Transmissibilities ranging from about 50% to 60% have been reported for various indicators of fat distribution in the QFS (36). The familial aggregation study of the principal components derived from

the analysis of skinfold thicknesses in QFS revealed that the second principal component, which contrasted the trunk and extremity skinfolds, had a transmissibility of 52%. A recent study based on 105 monozygotic and dizygotic twin pairs aged from 10 to 14 years and using a model-fitting approach found that 85% of the variance in TER based on five skinfold measures were accounted for by genetic factors (19). Another twin study based on 340 female monozygotic and dizygotic twin pairs reported heritabilities of 32% to 48% and 72% to 82% for age- and BMI-adjusted waist-to-hip ratio and waist circumference, respectively (20). Although heritability estimates derived from twin studies tend to be higher than those reported in family studies, most of the family studies (11,15,16) and some twin studies (13) suggest that at least 40% to 50% of the variance in the pattern of fat distribution is accounted for by genetic and common familial environmental factors, which is similar to the results reported in the present study.

The endurance training program resulted in significant reductions in total adiposity as well as in the amount of abdominal fat (trunk fat and waist circumference). However, the changes induced by exercise training were moderate. For example, the average reduction in trunk fat was 3% in mothers, 4% in fathers and daughters, and 7% in sons. Similar reductions were observed for the other fat distribution phenotypes. A review of intervention studies of changes in body composition following exercise training suggests that exercise training does not result in substantial changes in body weight and body composition (38). In the present study, the average weight lost was 0.3 kg in fathers, mothers, and sons, whereas no weight was lost in daughters. These small changes suggest that the energy deficit induced by exercise training was probably compensated for by increased energy intake.

The training-induced changes in amount and distribution of subcutaneous fat were heterogeneous and characterized by moderate levels of familial aggregation. The pattern of familial correlations obtained for ΔSF8, ΔTRUNK, and ΔEXTREM reveals the absence of parent-offspring resemblance (except for ΔTER) and the presence of significant spouse correlations that are generally at least as high as the sibling correlations. This pattern of correlations indicates cohort effects in the response of subcutaneous fat to training. That is, a more similar response among subjects of the same generation than in subjects of different generations that could arise from familial genetic and/or environmental factors that are age-dependent. The estimates of transmissibility for the response phenotypes were in the range of 15% to 20%. For ΔTER, the transmissibility reached 14%, whereas for ΔWAIST no transmissible effect was found because only the spouse correlation was significant.

In summary, the results of this study reveal that the amount and distribution of subcutaneous fat, assessed from skinfold thicknesses, strongly aggregates in families with transmissibility estimates ranging from about 30% to 35% for the amount of subcutaneous fat and reaching 50% for the fat distribution phenotypes adjusted for total adiposity. Although endurance training resulted in statistically significant reductions in subcutaneous fat and waist circumference, on average the changes were small and characterized by a low level of familial aggregation. The transmissibilities of the response phenotypes adjusted for the pretraining values ranged from 0% to 20%. We conclude that familial/genetic factors are more important in determining the amount and the distribution of subcutaneous fat in the sedentary state than their responses to exercise training.

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