AMERICAN JOURNAL OF HUMAN BIOLOGY 12:32–41 (2000)

Cross-Trait Familial Resemblance for Resting Blood Pressure and Body Composition and Fat Distribution: The HERITAGE Family Study

PING AN,[1]* TREVA RICE,[1] JACQUES GAGNON,[2] ARTHUR S. LEON,[3] JAMES S. SKINNER,[4] JACK H. WILMORE,[5] CLAUDE BOUCHARD,[2] AND D.C. RAO[1,6]
[1]*Division of Biostatistics, Washington University School of Medicine, St. Louis, Missouri*
[2]*Physical Activity Sciences Laboratory, Laval University, Québec, Canada*
[3]*School of Kinesiology and Leisure Studies, University of Minnesota, Minneapolis, Minnesota*
[4]*Department of Kinesiology, Indiana University, Bloomington, Indiana*
[5]*Department of Health and Kinesiology, Texas A&M University, College Station, Texas*
[6]*Department of Genetics and Psychiatry, Washington University School of Medicine, St. Louis, Missouri*

ABSTRACT Cross-trait familial resemblance between resting blood pressure (BP) and body composition and fat distribution was examined in 98 Caucasian families participating in the HERITAGE Family Study by using a multivariate familial correlation model assessing both intraindividual and interindividual cross-trait correlations. The 520 family members were sedentary at baseline examination, and both resting systolic (SBP) and diastolic (DBP) BP were cross-analyzed with each of the following 10 indications of body composition and fat distribution: percent body fat (%BF), abdominal visceral fat (AVF), body mass index (BMI), fat-free mass (FFM), fat mass (FM), sum of eight skinfolds (SF), total abdominal fat (TAF), ratio of trunk-to-extremity skinfolds (TER), waist circumference (WAIST), ratio of waist-to-hip circumferences (WHR). Five of the variables were also corrected for fat mass (AVFf, TAFf, TERf, WAISTf, WHRf) to index these measures independent of total degree of adiposity. In general, the results suggested strictly intraindividual cross-trait resemblance, with occasional spouse cross-trait resemblance, but few or no sibling or parent–offspring cross-trait correlations. This pattern is largely consistent with nongenetic specific environmental determinants for the BP–body composition and fat distribution covariation, with possibly some common environmental influence between spouses and negligible genetic effects. The only findings suggesting any familial cross-trait resemblance were significant sibling correlations for DBP-FFM and DBP-WHR, although the parent–offspring correlation was not significant. These findings suggest that the observed BP–body composition and fat distribution cross-trait correlations in these sedentary families are probably not due to multifactorial effects such as polygenic and/or common familial environmental effects. Whether or not other factors such as nonadditive effects are involved warrants further investigation using other methods. Am. J. Hum. Biol. 12:32–41, 2000.

Contract grant sponsor: NHLBI; Contract grant numbers: HL45670, HL47323, HL47317, HL47327, HL47321.
*Correspondence to: Ping An, M.D., Division of Biostatistics, Washington University School of Medicine, 600 S. Euclid Ave., Campus Box 8067, St. Louis, MO 63110. E-mail: anping@wubios.wustl.edu
Received 15 September 1998; Revision received 30 November 1998; Accepted 7 December 1998

It is generally recognized that blood pressure (BP) and body composition and fat distribution are correlated within an individual (e.g., Després et al., 1988), and they are determined in part by familial factors (see Ward, 1990; Bouchard et al., 1998). It is also recognized that level of fatness is a complex trait that can be characterized more specifically in terms of total fat, fat distribution, and abdominal visceral fat (Bouchard et al., 1998). Although several studies suggest that BP and body composition and fat distribution may share some of the same genetic (i.e., pleiotropic) and/or common environmental determinants (Schork et al., 1994; Cheng et al., 1998), only one study (Rice et al., 1994) examined the relationship between BP and alternative measures of body composition and fat distribution. That study suggested that BP (specifically diastolic BP) shared more of the same familial determinants with measures of fat distribution than with other body composition indices.

The present study was intended as a replication and extension of a similar study using the results of the Québec Family Study (Rice et al., 1994). In the current investigation, we systematically examined the pleiotropy hypothesis (Rice et al., 1994) for BP and 15 body composition and fat distribution variables using data from 98 sedentary families of Caucasian descent who participated in the HERITAGE Family Study, and who were normotensive and generally nonobese. Using a multivariate familial correlation model, both systolic (SBP) and diastolic (SBP) BP were cross-examined with each of the 10 body composition and fat distribution variables, including percent body fat (%BF), abdominal visceral fat (AVF), body mass index (BMI), fat-free mass (FFM), fat mass (FM), sum of eight skinfolds (SF), total abdominal fat (TAF), ratio of trunk-to-extremity skinfolds (TER), waist circumference (WAIST), and ratio of waist-to-hip circumferences (WHR). Each of the variables was adjusted for the effects of age and sex. In addition, in order to index AVF, TAF, TER, WAIST, and WHR independent of total level of adiposity, these five measures was adjusted for the effects of age, sex, and fat mass (AVFf, TAFf, TERf, WAISTf, and WHRf). Each of these five variables was also cross-examined with SBP and DBP, respectively.

METHODS

Sample

A total of 520 individuals in 98 families of Caucasian descent (256 males, 264 females) were analyzed in this study. Subjects with incomplete resting BP (n = 2) or body composition values (n = 4) were excluded from the analysis, as was one member of a monozygotic twin pair and a family consisting of only a single offspring. Families of African-American descent were also recruited and tested, but are not reported here. Recruitment of families was based on extensive media publicity and advertisements from four participating clinical centers.

Several criteria were applied to screen subjects for participation (Bouchard et al., 1995). For example, subjects were 17–40 years of age for children and ≤65 years for parents, sedentary at baseline, and had a BMI ≤40 kg/m^2 (except 40.1–47.5 for seven individuals) and resting SBP ≤159 mm Hg and DBP ≤99 mm Hg. In addition, use of anti-hypertension medication was a cause for exclusion. In general, participants were required to be in good physical health in order to complete the 20-week exercise program.

Measures

Multiple resting BP measurements were made on two separate days. Resting BP measurements were obtained before 11:00 AM with subjects in a 4-hour fasted state, and with no caffeine-containing beverages and tobacco products for at least 2 hours prior to assessments. Measurements were performed in a quiet room at a neutral ambient temperature (24–25°C) with the lights dimmed after participants rested for at least 5 min in a reclining chair with legs slightly elevated and the chair's back support reclined at about 45° from the ground. BP was determined using a properly fitted cuff connected to a Colin STBP-780 automated unit. At least four BP readings were taken following an initial 5-min rest period, with 2-min intervals between readings. Although recorded on the paper form, the first measurement was discarded. The three valid measurements taken on each of the two days were averaged for further analyses (Wilmore et al., 1997).

Underwater weighing was performed to estimate fat mass (FM) (Behnke and Wilmore, 1974) and a correction was made

for residual lung volume assessed by the oxygen dilution method (Wilmore, 1969; Wilmore et al., 1980), or the helium dilution technique (Menelly and Kaltreider, 1949; Motley, 1957). %BF and FFM were calculated. AVF was assessed by computerized tomography (CT) scan. Subjects were examined in a supine position with their arms stretched above the head (Sjöstrom et al., 1986); the abdominal scan was obtained between the L4–L5 vertebrae. The attenuation interval used in the quantification of the areas of adipose tissue was from −190 to −30 Hounsfield units. AVF area was defined by drawing a line within the muscle wall surrounding the abdominal cavity. TAF was also assessed by CT scan. Skinfold thickness was measured at eight sites with Harpenden calipers (Harrison et al., 1988) and each was based on the mean of two trials. A third trial was administered if the difference between the first two was not within 1.0 mm. SF was the sum of all eight skinfolds and TER was calculated as the sum of trunk skinfolds (subscapular + suprailiac + abdominal + midaxillary) divided by the sum of extremity skinfolds (triceps + biceps + medial calf + thigh). BMI and WHR were calculated from anthropometric measurements of height and weight, and waist and hip circumferences, respectively (Wilmore et al., 1997).

Data adjustments

Resting SBP, DBP, %BF, AVF, BMI, FFM, FM, SF, TAF, TER, WAIST, and WHR were adjusted for age using a stepwise multiple regression procedure. AVF, TAF, TER, WAIST, and WHR were further adjusted for FM using the same procedure. Briefly, each phenotype was regressed on up to a cubic polynomial in age (and FM for AVFf, TAFf, TERf, WAISTf and WHRf) within four sex–generation groups (fathers, mothers, sons, and daughters). The resulting squared residuals were similarly adjusted for age and FM effects on the variance, i.e., heteroscedasticity (Rice et al., 1997a). The final adjusted phenotypes were standardized to a mean of zero and a standard deviation of one.

Familial correlation model

A multivariate familial correlation model may be conceptualized as a simple extension of the univariate case using matrix notation. In the univariate case (one phenotype per individual), there are four types of individuals (f: father, m: mother, s: son, d: daughter), leading to eight correlations within three familial classes: one spouse (fm), four parent–offspring (fs, fd, ms, md), and three sibling (ss, sd, dd). In the "bivariate" case (two phenotypes on an individual), each of the eight correlations becomes a 2×2 matrix (see Appendix A). For example, the spouse matrix (FM) contains four elements (f_1m_1, f_1m_2, f_2m_1, and f_2m_2), where subscript 1 denotes a BP measure, and subscript 2 is a body composition measure. In addition, there are four extra correlations indexing the intraindividual (within-person) cross-trait resemblance. The total number of estimated correlations is 34 for a bivariate case. However, only the 18 cross-trait correlations are discussed in this study. See Rice et al. (1994) for details.

The computer program SEGPATH (Province and Rao, 1995) was used to estimate the familial correlations by maximum likelihood methods. In this study, the statistical method of analysis fits the model directly to the family data, under the assumption that the phenotypes in a family follow jointly a multivariate normal distribution. The total log-likelihood function for the entire sample of families is expressed as a function of the 34 correlations and the 16 means and variances.

In order to test certain sex-specific and cross-trait hypotheses, a general model and several reduced models were estimated for each of the 30 pairs of variables. Hypotheses were tested using the likelihood-ratio test, which is distributed as a χ^2, with the df being the difference in the number of parameters estimated in the two competing hypotheses (i.e., general model vs. reduced model). A summary of the hypotheses tested is given in Appendix B. Model 1 is the general model. Models 2–4 test sex-specific hypotheses and Models 5–8 test cross-trait hypotheses. For example, Model 5 tests whether there are cross-trait correlations in the sibling matrices by fixing all cross-trait sibling correlations to zero, Model 6 tests whether there are cross-trait correlations in the parent–offspring matrices (all parent–offspring cross-trait correlations fixed to zero), and Model 7 tests if there are cross-trait correlations in the spouse matrices (spouse cross-trait correlations fixed to zero). In addition to the likelihood ratio test, Akaike's information criterion (AIC), which

TABLE 1. Means and SD for unadjusted measures

Variables	No.	Mean	SD	Variables	No.	Mean	SD
		Fathers				Mothers	
SBP (mm Hg)	98	122.0[2]	13.1	SBP (mm Hg)[1]	94	116.9[2]	11.9
DBP (mm Hg)[1]	98	72.9[2]	8.6	DBP (mm Hg)[1]	94	67.7[2]	6.8
Age (years)[1]	98	53.3	5.3	Age (years)[1]	94	42.1	5.0
%BF (%)[1]	92	27.4[2]	6.3	%BF (%)[1]	85	36.6[2]	7.9
AVF (cm^2)[1]	98	158.1[2]	61.8	AVF (cm^2)[1]	93	120.1[2]	59.0
BMI (kg/m^2)[1]	97	28.4	4.4	BMI (kg/m^2)[1]	93	27.5	4.8
FFM (kg)	92	62.5[2]	7.4	FFM (kg)[1]	85	44.5[2]	5.0
FM (kg)[1]	92	24.5	9.0	FM(kg)[1]	85	27.0	10.4
SF (mm)[1]	85	146.5[2]	48.9	SF (mm)[1]	81	196.5[2]	52.0
TAF (cm^2)[1]	98	427.9[2]	147.3	TAF (cm^2)[1]	93	483.4[2]	164.4
TER (mm)[1]	85	1.9[2]	0.5	TER (mm)	81	0.9[2]	0.2
WAIST (cm)[1]	98	101.2[2]	11.2	WAIST (cm)[1]	94	95.0[2]	14.3
WHR (cm)[1]	98	1.0[2]	0.1	WHR (cm)[1]	94	0.9[2]	0.1
		Sons				Daughters	
SBP (mm Hg)	158	119.3[2]	8.8	SBP (mm Hg)[1]	170	110.5[2]	7.8
DBP (mm Hg)[1]	158	65.6[2]	8.4	DBP (mm Hg)[1]	170	61.8[2]	6.3
Age (years)[1]	158	25.3	6.0	Age (years)[1]	170	25.3	6.2
%BF (%)[1]	148	19.7[2]	9.3	%BF (%)[1]	169	26.6[2]	8.9
AVF (cm^2)[1]	157	78.5[2]	43.5	AVF (cm^2)[1]	168	51.8[2]	28.1
BMI (kg/m^2)[1]	157	25.7[2]	4.9	BMI (kg/m^2)[1]	169	23.7[2]	4.4
FFM (kg)	148	64.2[2]	8.0	FFM (kg)[1]	169	46.1[2]	5.2
FM (kg)[1]	148	17.1	11.0	FM (kg)[1]	169	18.0	9.7
SF (mm)[1]	150	121.8[2]	54.1	SF (mm)[1]	167	147.5[2]	51.1
TAF (cm^2)[1]	157	284.0	184.4	TAF (cm^2)[1]	168	302.8	166.1
TER (mm)[1]	150	1.6[2]	0.5	TER (mm)	167	0.9[2]	0.2
WAIST (cm)[1]	158	90.7[2]	14.0	WAIST (cm)[1]	170	81.1[2]	12.1
WHR (cm)[1]	158	0.9[2]	0.1	WHR (cm)[1]	170	0.8[2]	0.1

[1]Significant ($P < 0.05$) mean differences for father-son, mother-daughter (within-sex) comparisons.
[2]Significant ($P < 0.05$) mean differences for father-mother, son-daughter (within-generation) comparisons.

is −2 ln L plus twice the number of estimated parameters, was used to compare nonnested models; the "best" model is the one with the smallest AIC (Akaike, 1974). The most parsimonious model is obtained by combining nonrejected hypotheses into a single test. If the combined test fails to fit the data, then the hypothesis having the smallest *P*-value is added back into the parsimonious model until an acceptable fit is reached.

RESULTS

Coefficients of variations (CV) for repeated measures were 4% and 6% for resting SBP and DBP, respectively. The intraclass correlations (ICCs) for repeated measures are 0.84 and 0.79 for resting SBP and DBP, respectively. Reproducibility of anthropometric and body composition and fat distribution measures is very high, with ICCs ranging from 0.95–1.00 (Wilmore et al., 1997).

Means and SDs of the unadjusted resting variables are presented in Table 1. In both generations, there were no sex differences in the means for age and FM within each generation. BP, AVF, BMI (not significant in fathers vs. mothers), FFM, TER, WAIST, and WHR were greater in males, whereas, %BF, SF, and TAF were higher in females. In both sexes, parents tended to have higher BP and body composition and fat distribution measures than offspring, except no significant differences in SBP and FFM were noted for fathers vs. sons, and in TER for mothers vs. daughters.

Data adjustment results for resting SBP and DBP can be found in An et al. (1999), for %BF and SF in Rice et al. (1997a), and for AVF and AVFf in Rice et al. (1997b). In general, age accounted for little to moderate variance (ranging from zero to 25%), with more variance accounted for in offspring (especially sons) than in parents. As expected, FM accounted for an appreciable percentage of the variance in AVFf (from 43.0% in fathers to 76.2% in sons, $P < 0.05$), in TAFf (from 85.3% in fathers to 94.4% in sons, $P < 0.05$), in WAISTf (from 69.7% in mothers to 90.9% in sons, $P < 0.05$), and in WHRf (from 20.7% in mothers to 75.2% in sons, $P < 0.05$), although relatively little was accounted for in TERf (zero to less than 10%, $P < 0.05$).

The intraindividual cross-trait correlations among %BF, AVF, BMI, FM, SF, TAF,

and WAIST are generally high (0.58–0.97), except 0.37 for AVF-SF in fathers. WHR and the remaining variables are significantly correlated (0.20–0.90), except for a nonsignificant intraindividual correlation with TER in fathers. Correlations of FFM with the remaining variables except TER range from 0.17 to 0.72, or are nonsignificant with %BF, WHR in mothers. Correlations of TER with the remaining variables are nonsignificant in fathers, and are generally low (0.17–0.42) or nonsignificant in mothers and offspring.

Table 2 gives the *P* values for each of the models described in Appendix B for each of the 30 sets of bivariate analyses. In general, there were no cross-trait correlations in the sibling (Model 5) or parent–offspring matrices (Model 6), since most *P*-values were greater than 0.05. Three exceptions were for significant parent–offspring correlations between SBP and AVFf, and sibling correlations for DBP-FFM and DBP-WHR. In contrast, most of the cross-trait spouse (Model 8) and intraindividual (Model 8) correlations were significant. Table 3 gives the maximum likelihood estimates for the significant intraindividual and spouse matrices under the most parsimonious models. The cross-trait parameter estimates and standard errors (SEs) under both the general and the most parsimonious models for SBP-AVFf, DBP-FFM, and DBP-WHR are presented in Table 4. There is little suggestive evidence of significant interindividual cross-trait familial resemblance in each of the 30 BP and body composition and fat distribution pairs. However, there is a noticeable spouse cross-trait and intraindividual cross-trait resemblance.

DISCUSSION

In the current investigation, we examined the cross-trait familial resemblance between BP and body composition and fat distribution measures in the HERITAGE Family Study. This investigation was intended as both a replication and an extension of a similar one based on the results of the Québec Family Study data. In that study (Rice et al., 1994), both SBP and DBP were cross-examined with %BF, BMI, SF, and TER; measures of abdominal visceral adiposity were not available. Rice et al. (1994) reported a heritable association between BP and fat distribution measures (specifically DBP and TER), but not with BMI or measures of total fat. In contrast to Rice et al. (1994) and others who reported heritable links between SBP and BMI (Schork et al., 1994; Schieken et al., 1992), the current study found no evidence to support a pleiotropic hypothesis between BP and any of the body composition measures. Rather, the majority of the analyses suggested either strictly intraindividual cross-trait resemblance, or significant spouse and intraindividual correlations, with no sibling or parent–offspring resemblance. These patterns are consistent with nongenetic specific environmental determinants for the covariation, with possibly some common environmental influence between spouses. The failure of the current study to detect evidence of pleitropy between measures of resting BP and body composition is in part likely due to reduced power (small sample size), and in part due to a possible underestimation of the cross-trait correlations in this sedentary sample. That is, physical exercise may be a potentially important environmental factor influencing cross-trait resemblance. If it is the major source of the covariance, then we would expect the correlations to be reduced, or even eliminated. In addition, we note that the methods used here were designed to detect additive familial effects (i.e., polygenic and/or common familial environment), and therefore the possibility of nonadditive effects cannot be ruled out.

Thus, an alternative explanation for our findings involves a pleiotropic hypothesis in the major gene component. Putative major gene effects have been reported for BP (Pérusse et al., 1991), BMI (Borecki et al., 1993), total fat (Rice et al., 1993), fat distribution (Borecki et al., 1995), and AVF (Rice et al., 1997b). Most recently, Cheng et al. (1998) and Rice et al. (in press) found evidence for major locus pleiotropy between SBP and BMI using bivariate segregation analysis. Cheng et al. (1998) suggested only major locus (no multifactorial) pleiotropy, while Rice et al. (in press) reported larger pleiotropic effects due to a major locus than to multifactorial factors. Together, these studies suggest that the familial factors leading to covariation between SBP and BMI may be primarily due to a major locus. The multifactorial model used in the current study would not necessarily detect this source of covariation, especially if the major locus effect is nonadditive.

It is interesting to note that the only find-

*TABLE 2. Summary of P-values for each sex and cross-trait hypothesis test**

Model	nc	df	%BF	AVF	AVFf	BMI	FFM	FM	SF	TAF	TAFf	TER	TERf	W	Wf	WHR	WHRf
SBP:																	
1. General	34	—															
2. No sex differences in offspring	18	16	.923	.218	.090	.208	.185	.749	.786	.747	.425	.929	.920	.611	.070	.297	.237
3. No sex differences in offspring or parents	12	22	.918	.299	.173[a]	.120	.369	.748	.671	.720	.648[a]	.945	.959	.725	.196	.602	.515
4. No sex, no generation differences	7	27	.927[a]	.151[a]	.071	.134[a]	.314[a]	.810[a]	.699[a]	.583[a]	<.001	.843[a]	.918[a]	.628[a]	.224[a]	.304[a]	.416[a]
5. No cross-trait in siblings	30	4	.955[a]	.910[a]	.931[a]	.992[a]	.135[a]	.991[a]	.708[a]	.968[a]	.231[a]	.769[a]	.791[a]	.878[a]	.227[a]	.215[a]	.205[a]
6. No cross-trait in parent–offspring	26	8	.995[a]	.291[a]	.035	.975[a]	.999[a]	.992[a]	.490[a]	.965[a]	.922[a]	.840[a]	.918[a]	.943[a]	.410[a]	.575[a]	.408[a]
7. No cross-trait in spouse	32	2	<.001	.001	.067	.003	.592[a]	<.001	.024	.003	.415[a]	.373[a]	.262[a]	.018	.763[a]	.044	.386[a]
8. No cross-trait in intraindividual	30	4	.198	<.001	.017	.003	.016	.028	.398	.010	.401[a]	.038	.012	.007	.287[a]	.185	.588[a]
9. Parsimonious			.554		.081				.428							.070	
10. Most parsimonious			.943	.146	.185	.160	.335	.846	.733	.632	.619	.866	.915	.678	.133	.343	.384
DBP:																	
1. General	34	—															
2. No sex differences in offspring	18	16	.328	.130[a]	.104	.072	.063	.357	.147	.473	.061	.423	.492	.524	.055	.173	.227
3. No sex differences in offspring or parents	12	22	.556	.061	.128	.043	.139[a]	.587	.243	.594	.213	.308	.430	.456	.061	.096[a]	.323
4. No sex, no generation differences	7	27	.528[a]	.023	.108[a]	.054[a]	.043	.559[a]	.343[a]	.381[a]	.266[a]	.487[a]	.640[a]	.228[a]	.051[a]	.020	.324[a]
5. No cross-trait in siblings	30	4	.278[a]	.451[a]	.712[a]	.250[a]	.015	.257[a]	.729[a]	.670[a]	.242[a]	.790[a]	.724[a]	.156[a]	.065[a]	.028	.410[a]
6. No cross-trait in parent–offspring	26	8	.815[a]	.124	.192[a]	.701[a]	.943[a]	.925[a]	.708[a]	.589[a]	.604[a]	.125[a]	.236[a]	.921[a]	.721[a]	.370[a]	.589[a]
7. No cross-trait in spouse	32	2	<.001	.002	.343[a]	.023	.745[a]	<.001	.064	.004	.966[a]	.746[a]	.390[a]	.004	.413[a]	.014	.618[a]
8. No cross-trait in intraindividual	30	4	.014	<.001	<.001	<.001	.033	.005	.035	<.001	.237[a]	.165	.129	<.001	.044	<.001	.203[a]
9. Parsimonious				.044 .038					.227			.303	.400				
10. Most parsimonious			.567	.169	.078	.070	.180	.613	.370	.417	.246	.505	.582	.269	.067	.116	.438

*nc, number of estimated correlations; df, number of reduced correlations; %BF, percent body fat; AVF, abdominal visceral fat; BMI, body mass index; FFM, fat free mass; FM, fat mass; SF, sum of eight skinfolds; TAF, total abdominal fat; TER, ratio of trunk-to-extremity skinfolds; W, waist circumference; WHR, ratio of waist-to-hip circumfrence; AVFf, TAFf, TERf, WHRf, adjusted for fat mass.

[a]Combinations for most parsimonious models.

*TABLE 3. Maximum likelihood estimates (±SE) of significant intraindividual and interindividual correlations under the most parsimonious model**

	Spouse f_1m_2	Spouse f_2m_1	Intraindividual f_{12}	Intraindividual m_{12}	Intraindividual s_{12}	Intraindividual d_{12}
SBP:						
%BF	0.29 ± 0.06	[0.29][a]	0.11 ± 0.04	[0.11]	[0.11]	[.11]
AVF	0.20 ± 0.06	[0.20]	0.15 ± 0.04	[0.15]	[0.15]	[.15]
BMI	0.14 ± 0.06	[0.14]	0.17 ± 0.04	[0.17]	[0.17]	[.17]
FFM	[0]	[0]	0.16 ± 0.03	[0.16]	[0.16]	[.16]
FM	0.27 ± 0.06	[0.27]	0.15 ± 0.04	[0.15]	[0.15]	[.15]
SF	0.15 ± 0.07	[0.15]	0.10 ± 0.04	[0.10]	[0.10]	[.10]
TAF	0.17 ± 0.06	[0.17]	0.16 ± 0.04	[0.16]	[0.16]	[.16]
TAFf	[0]	[0]	[0]	[0]	[0]	[0]
TER	[0]	[0]	0.10 ± 0.04	[0.10]	[0.10]	[.10]
TERf	[0]	[0]	0.11 ± 0.04	[0.11]	[0.11]	[.11]
WAIST	0.15 ± 0.06	[0.15]	0.17 ± 0.03	[0.17]	[0.17]	[.17]
WAISTf	[0]	[0]	[0]	[0]	[0]	[0]
WHR	0.15 ± 0.06	[0.15]	0.12 ± 0.04	[0.12]	[0.12]	[.12]
WHRf	[0]	[0]	[0]	[0]	[0]	[0]
DBP:						
%BF	0.27 ± 0.06	[0.27]	0.12 ± 0.04	[0.12]	[0.12]	[.12]
AVF	0.26 ± 0.09	0.25 ± 0.09	0.50 ± 0.07	0.20 ± 0.10	0.10 ± 0.05	[.10]
AVFf	[0]	[0]	0.08 ± 0.04	[0.08]	[0.08]	[.08]
BMI	0.13 ± 0.06	[0.13]	0.16 ± 0.04	[0.16]	[0.16]	[.16]
FM	0.25 ± 0.06	[0.25]	0.16 ± 0.04	[0.16]	[0.16]	[.16]
SF	0.15 ± 0.07	[0.15]	0.08 ± 0.04	[0.08]	[0.08]	[.08]
TAF	0.17 ± 0.06	[0.17]	0.15 ± 0.04	[0.15]	[0.15]	[.15]
TAFf	[0]	[0]	[0]	[0]	[0]	[0]
TER	[0]	[0]	0.09 ± 0.04	[0.09]	[0.09]	[.09]
TERf	[0]	[0]	0.08 ± 0.04	[0.08]	[0.08]	[.08]
WAIST	0.17 ± 0.06	[0.17]	0.14 ± 0.04	[0.14]	[0.14]	[.14]
WAISTf	[0]	[0]	0.07 ± 0.03	[0.07]	[0.07]	[.07]
WHRf	[0]	[0]	[0]	[0]	[0]	[0]

*See Table 1.
[a]Parameters in square brackets were equated to a preceding parameter, or were fixed at zero.

ings in this study suggesting any familial cross-trait resemblance in the multifactorial component were significant sibling correlations for DBP-FFM and DBP-WHR (see Table 4). The latter is a fat distribution measure, and may support at least in part the findings by Rice et al. (1994). It is also interesting to note that FFM and WHR are the only two variables whose correlations with the remaining body composition and fat distribution measures are either low or nonsignificant. A pattern of significant sibling but nonsignificant parent–offspring resemblance may suggest dominance effects in the genetic components or developmental (age-specific) effects. For example, the genetic effect may be relatively greater in young adulthood than middle age, decreasing as individuals mature and are affected by various environmental exposures. Alternatively, it could be due to the fact that siblings may share more similar environments than do parents and offspring. However, the aggregate sibling correlation is negative, influenced primarily by the cross-sex sibling resemblance.

It was interesting to note the changes in the intraindividual and spouse cross-trait correlations for TAF and WAIST after adjusting for FM. Prior to FM adjustment, the cross-trait correlations were significant, but after adjustment, they were either nonsignificant or reduced. This pattern suggested that the cross-trait resemblance between BP with TAF and WAIST may be a function of total fat.

We also note that there were significant parent–offspring (but not sibling) correlations for SBP and AVFf. This perplexing pattern is not easily explained. However, examination of the parameter estimates and associated SEs under the parsimonious model suggested that the correlations were not significantly different from zero, even though that hypothesis was rejected by the likelihood ratio test. In fact, estimates under the general model show that only two of the eight parent–offspring correlations were significant (f_1d_2 and m_2s_1) and opposite in sign, yielding an aggregate estimate of about zero.

In summary, findings from the present

*TABLE 4. Maximum likelihood estimates (±SE) under the general and most parsimonious models for selected traits**

Correlations	SBP-AVFf General	SBP-AVFf Parsimonious	DBP-FFM General	DBP-FFM Parsimonious	DBP-WHR General	DBP-WHR Parsimonious
Spouse						
f_1m_2	0.17 ± 0.11	0.19 ± 0.08	0.02 ± 0.11	[0]	0.16 ± 0.10	0.18 ± 0.07
f_2m_1	0.20 ± 0.10	[0.19]	0.08 ± 0.10	[0]	0.26 ± 0.09	[0.18]
Parent–offspring						
f_1s_2	0.03 ± 0.09	0.07 ± 0.06	−0.06 ± 0.10	[0]	0.06 ± 0.09	[0]
f_2s_1	−0.06 ± 0.10	−0.05 ± 0.05	0.02 ± 0.10	[0]	0.20 ± 0.09	[0]
f_1d_2	0.23 ± 0.10	[0.07]	−0.09 ± 0.10	[0]	0.06 ± 0.09	[0]
f_2d_1	0.09 ± 0.10	[−0.05]	−0.06 ± 0.08	[0]	0.07 ± 0.08	[0]
m_1s_2	−0.02 ± 0.10	[0.07]	−0.05 ± 0.10	[0]	−0.01 ± 0.09	[0]
m_2s_1	−0.27 ± 0.09	[−0.05]	−0.09 ± 0.10	[0]	−0.09 ± 0.09	[0]
m_1d_2	0.15 ± 0.09	[0.07]	0.02 ± 0.10	[0]	0.06 ± 0.09	[0]
m_2d_1	−0.01 ± 0.10	[−0.05]	−0.02 ± 0.09	[0]	0.05 ± 0.08	[0]
Siblings						
s_1s_2	0.00 ± 0.09	[0]	−0.21 ± 0.09	−0.08 ± 0.04	−0.06 ± 0.08	−0.10 ± 0.04
d_1d_2	0.03 ± 0.09	[0]	0.09 ± 0.08	[−0.08]	0.07 ± 0.08	[−0.10]
s_1d_2	0.06 ± 0.08	[0]	−0.19 ± 0.09	[−0.08]	−0.16 ± 0.08	[−0.10]
s_2d_1	0.05 ± 0.09	[0]	−0.10 ± 0.08	[−0.08]	−0.15 ± 0.07	[−0.10]
Intraindividual						
f_{12}	0.23 ± 0.10	0.21 ± 0.07	0.27 ± 0.09	0.23 ± 0.06	0.42 ± 0.08	0.21 ± 0.06
m_{12}	0.21 ± 0.10	[0.21]	0.16 ± 0.10	[0.23]	0.07 ± 0.10	[0.21]
s_{12}	−0.08 ± 0.09	0.01 ± 0.05	−0.07 ± 0.09	0.02 ± 0.05	−0.04 ± 0.08	−0.01 ± 0.06
d_{12}	0.13 ± 0.08	[0.01]	0.06 ± 0.08	[0.02]	0.07 ± 0.08	[−0.01]

*SBP, systolic blood pressure; AVFf, abdominal visceral fat corrected for fat mass; DBP, diastolic blood pressure; FFM, fat free mass, WHR, ratio of waist-to-hip circumferences.

study suggest that the commonly noted BP and body composition and fat distribution correlation is probably not due to additive multifactorial effects such as polygenic and common familial environmental effects in these sedentary families. Rather, this association may be a function of specific environmental factors that are unique to each individual and, thus, not heritable, or a function of other heritable factors not assessed here such as major gene pleiotropy. Further analyses of these data using bivariate segregation methods is warranted in order to address this suggestion.

ACKNOWLEDGMENTS

The HERITAGE family study is supported by the National Heart, Lung and Blood Institute through the following grants: HL45670 (C. Bouchard, PI), HL47323 (A.S. Leon, PI), HL47317 (D.C. Rao, PI), HL47327 (J.S. Skinner, PI), and HL47321 (J.H. Wilmore, PI). We thank all the investigators, local project coordinators, research assistants, laboratory technicians, and secretaries who are contributing to the study.

LITERATURE CITED

Akaike H. 1974. A new look at the statistical model identification. IEEE Trans Automat Control 19:716–723.

An P, Rice T, Gagnon J, Borecki IB, Pérusse L, Leon AS, Skinner JS, Wilmore JH, Bouchard C, Rao DC. 1999. Familial aggregation of resting blood pressure and heart rate in a sedentary population: the HERITAGE Family Study. Am J Hypertens (in press).

Behnke AR, Wilmore JH. 1974. Evaluation and regulation of body build and composition. Englewood Cliffs, NJ: Prentice Hall.

Borecki IB, Bonney GE, Rice T, Bouchard C, Rao DC. 1993. Influence of genotype-dependent effects of covariates on the outcome of segregation analysis of the body mass index. Am J Hum Genet 53:676–687.

Borecki IB, Rice T, Pérusse L, Bouchard C, Rao DC. 1995. Major gene influence on the propensity to store fat in trunk versus extremity depots: evidence from the Québec Family Study. Obes Res 3:1–8.

Bouchard C, Leon AS, Rao DC, Skinner JS, Wilmore JH, Gagnon J. 1995. The HERITAGE Family Study: aims, design and measurement protocol. Med Sci Sports Exerc 27:721–729.

Bouchard C, Pérusse L, Rice T, Rao DC. 1998. The genetics of human obesity. In: Bray GA, Bouchard C, James WPT, editors. Handbook of obesity. New York: Marcel Dekker. p 157–190.

Cheng LSC, Livshits G, Carmelli D, Wahrendorf J, Brunner D. 1998. Segregation analysis reveals a major gene effect controlling systolic blood pressure and BMI in an Israeli population. Hum Biol 70:59–75.

Després JP, Tremblay A, Thériault G, Pérusse L, Leblanc C, Bouchard C. 1988. Relationships between body fatness, adipose tissue distribution and blood pressure in men and women. J Clin Epidemiol 41: 889–897.

Harrison GG, Buskirk ER, Lindsay-Carter JE. 1988. Skinfold thicknesses and measurement techniques. In: Lohman TG, Roche AF, editors. Anthropometric standardization reference manual. Champaign, IL: Human Kinetics. p 55–80.

Menelly GR, Kaltreider NL. 1949. The volume of the lung determined by helium dilution: description of the method and comparison with other procedures. J Clin Invest 28:129–139.

Motley HL. 1957. Comparison of simple helium closed with the oxygen open-circuit method for measuring residual air. Am Rev Tuberc Pulm Dis 76:601–615.

Pérusse L, Moll PP, Sing CF. 1991. Evidence that a single gene with gender- and age-dependent effects influences systolic blood pressure determination in a population-based sample. Am J Hum Genet 49:94–105.

Province MA, Rao DC. 1995. General purpose model and a computer program for combined segregation and path analysis (SEGPATH): automatically creating computer programs from symbolic language model specifications. Genet Epidemiol 12:203–219.

Rice T, Borecki IB, Bouchard C, Rao DC. 1993. Segregation analysis of fat mass and other body composition measures derived from underwater weighting. Am J Hum Genet 52:967–973.

Rice T, Province M, Pérusse L, Bouchard C, Rao DC. 1994. Cross-trait familial resemblance for body fat and blood pressure: familial correlations in the Québec Family Study. Am J Hum Genet 55:1019–1029.

Rice T, Daw EW, Gagnon J, Bouchard C, Leon AS, Skinner JS, Wilmore JH, Rao DC. 1997a. Familial resemblance for body composition measures: the HERITAGE Family Study. Obes Res 5:557–562.

Rice T, Després JP, Pérusse L, Gagnon J, Leon AS, Skinner JS, Wilmore JH, Rao DC, Bouchard C. 1997b. Segregation analysis of abdominal visceral fat: the HERITAGE Family Study. Obes Res 5:417–424.

Rice T, Blangero J, Pérusse L, Bouchard C, Rao DC, Borecki IB. 1999. Genetic pleiotropy for body mass index and systolic blood pressure: the Québec Family Study. Am J Hum Genet (in press).

Schieken RM, Mosteller M, Goble MM, Moskowitz WB, Hewitt JK, Eaves LJ, Nance WE. 1992. Multivariate genetic analysis of blood pressure and body size: the Medical College of Virginia twin study. Circulation 86:1780–1788.

Schork NJ, Weder AB, Trevisan M, Laurenzi M. 1994. The contribution of pleiotropy to blood pressure and body mass index variation: the Gubbio Study. Am J Hum Genet 54:361–373.

Sjöstrom L, Kvist H, Cederblad A, Tylen U. 1986. Determination of the total adipose tissue volume in women by computed tomography: comparison with 40K and tritium techniques. Am J Physiol 250:736–745.

Ward RH. 1990. Familial aggregation and genetic epidemiology of blood pressure. In: Laragh JH, Brenner BM, editors. Hypertension: pathophysiology, diagnosis and management. New York: Raven Press. p 81–100.

Wilmore JH. 1969. A simplified method for determination of residual lung volume. J Appl Physiol 27:96–100.

Wilmore JH, Vodak PA, Parr RB, Girandola RM, Billing JE. 1980. Further simplification of a method for determining residual lung volume. Med Sci Sports 12: 216–218.

Wilmore JH, Stanforth PR, Domenick MA, Gagnon J, Daw EW, Leon AS, Rao DC, Skinner JS, Bouchard C. 1997. Reproducibility of anthropometric and body composition measurements: the HERITAGE Family Study. Int J Obes 21:297–303.

APPENDIX A. Bivariate familial correlation model

	F	M	S	D
F	R_F	FM	FS	FD
M		R_M	MS	MD
S			R_S and SS	SD
D				R_D and DD

Note: In element notation the matrices are defined as follows, where subscript 1 denotes a BP measure and subscript 2 reflects a body composition measure.

Interindividual–intergroup (full rank) matrices:

$$FM = \begin{matrix} f_1m_1 & f_1m_2 \\ f_2m_1 & f_2m_2 \end{matrix} \qquad FS = \begin{matrix} f_1s_1 & f_1s_2 \\ f_2s_1 & f_2s_2 \end{matrix}$$

$$FD = \begin{matrix} f_1d_1 & f_1d_2 \\ f_2d_1 & f_2d_2 \end{matrix} \qquad MS = \begin{matrix} m_1s_1 & m_1s_2 \\ m_2s_1 & m_2s_2 \end{matrix}$$

$$MD = \begin{matrix} m_1d_1 & m_1d_2 \\ m_2d_1 & m_2d_2 \end{matrix} \qquad SD = \begin{matrix} s_1d_1 & s_1d_2 \\ s_2d_1 & s_2d_2 \end{matrix}$$

Interindividual–intragroup (diagonal) matrices:

$$SS = \begin{matrix} s_1s_1 & s_1s_2 \\ & s_2s_2 \end{matrix} \qquad DD = \begin{matrix} d_1d_1 & d_1d_2 \\ & d_2d_2 \end{matrix}$$

Intraindividual (correlational) matrices:

$$R_F = \begin{matrix} 1 & f_{12} \\ & 1 \end{matrix} \qquad R_M = \begin{matrix} 1 & m_{12} \\ & 1 \end{matrix} \qquad R_S = \begin{matrix} 1 & s_{12} \\ & 1 \end{matrix} \qquad R_D = \begin{matrix} 1 & d_{12} \\ & 1 \end{matrix}$$

The blank elements (lower off-diagonals in the latter six matrices) are equated with their respective upper off-diagonal elements (e.g., $s_2s_1 = s_1s_2$). The number of cross-trait correlations (all off-diagonal elements) is 18 and constitutes the primary focus of this study.

APPENDIX B. Summary of sex and cross-trait hypotheses

Model	df	Parameter reductions
1. General	—	All 34 correlations estimated
2. No sex differences in offspring	16	$s_1s_2 = d_1d_2 = s_1d_1$, $s_1s_2 = d_1d_2 = s_1d_2 = s_2d_1$, $s_2s_2 = d_2d_2 = s_2d_2$, $f_1s_1 = f_1d_1$, $f_1s_2 = f_1d_2$, $f_2s_1 = f_2d_1$, $f_2s_2 = f_2d_2$, $m_1s_1 = m_1d_1$, $m_1s_2 = m_1d_2$, $m_2s_1 = m_2d_1$, $m_2s_2 = m_2d_2$, $s_{12} = d_{12}$
4. No sex differences in offspring or parents	22	$s_1s_1 = d_1d_1 = s_1d_1$, $s_1s_2 = d_1d_2 = s_1d_2 = s_2d_1$, $s_2s_2 = d_2d_2 = s_2d_2$, f_1s_1 $f_1d_1 = m_1s_1 = m_1d_1$, $f_1s_2 = f_1d_2 = m_1s_2 = m_1d_2$, $f_2s_1 = f_2d_1 = m_2s_1 = m_2d_1$, $f_2s_2 = f_2d_2 = m_2s_2 = m_2d_2$, $f_1m_2 = f_2m_1$, $f_{12} = m_{12}$, $s_{12} = d_{12}$
4. No sex, no generation differences	27	$f_1s_1 = f_1d_1 = m_1s_1 = m_1d_1 = s_1s_1 = d_1d_1 = s_1d_1$, $f_1s_2 = f_1d_2 = m_1s_2 = m_1d_2 = f_2s_1 = f_2d_1 = m_2s_1 = m_2d_1 = s_1s_2 = d_1d_2 = s_1d_2 = s_2d_1$, $f_2s_2 = f_2d_2 = m_2s_2 = m_2d_2 = s_2s_2 = d_2d_2 = s_2d_2$, $f_1m_2 = f_2m_1$, $f_{12} = m_{12} = s_{12} = d_{12}$
5. No cross-trait in siblings	4	$s_1s_2 = d_1d_2 = s_1d_2 = s_2d_1 = 0$
6. No cross-trait in parent–offspring	8	$f_1s_2 = f_2s_1 = f_1d_2 = f_2d_1 = m_1s_2 = m_2s_1 = m_1d_2 = m_2d_1 = 0$
7. No cross-trait in spouse	2	$f_1m_2 = f_2m_1 = 0$
8. No cross-trait in intraindividual	4	$f_{12} = m_{12} = s_{12} = d_{12} = 0$
9. Most parsimonious		Combination of all non-rejected hypotheses above