International Journal of Obesity (1997) 21, 1024–1031
 0307–0565/97 $12.00

Familial resemblance for abdominal visceral fat: the HERITAGE family study

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OBJECTIVES: Abdominal visceral fat (AVF) is considered a risk factor for diabetes, atherogenic lipid profiles and hypertension. However, little is known about the genetic contribution to AVF as compared to total body fat.
DESIGN: AVF was assessed by computerized tomography, and total body fat (fat mass) was assessed by underwater weighing in 86 families participating in the Heritage Family Study. All family members were sedentary at baseline examination. The familial factors underlying the variability in age-adjusted AVF, age-fat mass-adjusted AVF and age-adjusted fat mass, were assessed using a familial correlation model.
RESULTS: The maximal heritability (including genetic and familial environmental effects) for AVF was comparable before (47%) and after (48%) adjusting for fat mass, and was 55% for fat mass itself in these sedentary families. Spouse correlations were significant for fat mass and for AVF prior to, but not after, adjustment for fat mass.
CONCLUSIONS: These results confirm the only previous study which investigated the familial aggregation of AVF (both in pattern and magnitude), suggesting that the factors underlying AVF in these sedentary families may be similar to those in the population at large. Although both genetic and familial environmental factors probably influence each of fat mass and AVF, there appears to be a predominantly genetic etiology for the visceral component which is independent of total body fat. These findings imply that some individuals are more at risk than others because of an inherited tendency to store abdominal fat viscerally rather than subcutaneously.

Keywords: total fat mass; sedentary; heritability

Introduction

In obese subjects, upper body or central obesity is correlated with various metabolic disturbances and is believed to be associated with (i) greater susceptibility to glucose intolerance, insulin resistance and compensatory hyperinsulinaemia,[1,2,3] (ii) an atherogenic plasma lipoprotein profile,[4,5] and (iii) elevated blood pressure.[6] Abdominal visceral obesity may be an important component in this cluster of complications known as the metabolic syndrome.[7] Cross-sectional population studies suggest that abdominal visceral fat (AVF) increases with age in both sexes,[8] usually with higher levels observed in males.[9]

The genetic contributions to several common measures of upper body or central obesity, as measured by subcutaneous skinfold sums and ratios, have been well characterized.[10] However, less is known about the familiality of the AVF level. The first suggestion of a genetic component for AVF variability came from intervention studies conducted with identical twins. The within-pair variability for changes in AVF level in response to an extended period of overfeeding[11] or negative energy balance,[12] was significantly lower than the among-pair variability, suggesting a genetic basis for the propensity to store or mobilize fat in the visceral area. More direct evidence for a role of familial factors in AVF level came from a study of French Canadian families. The maximal heritability for AVF, unadjusted and adjusted for total fat mass, was 58% and 56%, respectively, in the Québec Family Study.[13] Also in these families, evidence consistent with a major gene accounting for 51% of the variance and additional familial multifactorial effects accounting for 21% of the variance was found.[14] However, the major gene evidence for AVF was reduced after adjusting for total fat mass, suggesting some degree of common genetic influence on both.

The HERITAGE Family Study is a study of the genetic and nongenetic determinants of the response to endurance exercise training for several cardiovascular risk factors in sedentary families.[15] A battery of measures relating to cardiovascular and diabetes risk was collected both prior to (baseline), and after a 20-week endurance exercise training regimen. Here, we investigate the familial resemblance for AVF measured at baseline in order to: (1) determine whether there is evidence of familial factors; (2) if so, infer the

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Received 28 January 1997; revised 30 June 1997; accepted 3 July 1997

potential contribution of genetic factors in the familial aggregation and (3) discuss how these familial and genetic effects may relate to the population at large.

Methods

Sample

The HERITAGE Family Study sample and study protocol are more thoroughly outlined in Bouchard *et al*.[15] In summary, 98 nuclear families of Caucasian descent were recruited, each with both biological parents and at least two biological children and are scheduled to complete the protocol. The current study includes 86 families with complete data. Exact sample sizes for fathers, mothers, sons and daughters are given in Table 1. Families of African-American descent were also recruited, but are not reported here. Recruitment of families was based on extensive publicity and advertisements from four clinical centers.

Several criteria were used to screen subjects for participation. First, individuals were required to be between the ages of 16–65 y (16–40 y for children and ≤ 65 y for parents) in order to avoid maturation (low end) and aging (high end) complications. Second, families were required to be sedentary, defined at baseline as engaging in no regular physical activity over the previous 6 months, for example, any activity lasting 30 min or more and involving an energy expenditure of at least 7 METS (one MET is 3.5 ml O_2 uptake per kg body wt per min) for individuals ≥ 50 y or 8 METS for younger individuals, and occurring more than once a week. Sedentary status was assessed by a physician at the screening interview. Families with some nonsedentary members were included provided that the nonsedentary individual(s) remained inactive for at least 6 months. Only 6 individuals were in this latter group. Verification of sedentary state after 6 months was also monitored by the physician. A third criterion was that individuals with a body mass index (BMI) greater than 40 kg/m^2 were usually excluded because of metabolic abnormalities and exercise difficulties associated with extreme obesity, unless certified by a physician. Fourth, individuals with blood pressure greater than 159 mm Hg for systolic and/or greater than 99 mm Hg for diastolic were also excluded. Finally, individuals were required to be in good health in order to complete the exercise training, and individuals with any condition or disease that is life-threatening or that could be aggravated by cycle exercise were excluded. For example, definite or possible coronary heart disease and chronic or recurrent respiratory problems were bases for exclusion, as were uncontrolled endocrine and metabolic disorders, including diabetes or use of lipid-lowering drugs. See Bouchard *et al*[15] for a more detailed list of exclusionary criteria.

Measures

Each individual was examined on a battery of measures both prior to, and after completing, the 20-week standardized training program. Only the baseline measures are investigated here. AVF level was assessed by computerized tomography (CT) scan. Subjects were examined in a supine position with their arms stretched above the head,[16] and the abdominal scan was obtained between the fourth and fifth lumbar (L4–L5) vertebrae. The attenuation interval used in the quantification of the areas of adipose tissue was from -190 to -30 Hounsfield units. The AVF area was defined by drawing a line within the muscle wall surrounding the abdominal cavity. This area is primarily located in the adipose tissue of the abdominal cavity and is referred to in this paper as the AVF area. Underwater weighing was performed to determine body composition and estimate total body fat mass (FM).[17] A correction was made for residual lung volume by the oxygen dilution method.[18,19]

Means and s.d.s for the raw (unadjusted) AVF area at L4–L5 (cm^2), fat mass (kg) and age (y) are given in Table 1, separately in four sex by generation groups (fathers, mother, sons and daughters). Based on a

Table 1 Sample statistics

Variable	*n*	*Mean*	*s.d.*	*n*	*Mean*	*s.d.*
	Fathers			*Mothers*		
Age (y)	86	52.9	5.2	85	51.7	5.2
Abdominal visceral fat (cm^2)	86	159.2	57.2	85	121.0	59.9
Fat mass (kg)	84	25.0	9.0	82	27.5	10.4
BMI (kg/m^2)	86	28.4	4.3	86	27.5	4.9
Percent body fat (%BF)	84	27.7	6.3	82	36.9	7.8
	Sons			*Daughters*		
Age (y)	128	24.7	5.9	138	24.3	5.9
Abdominal visceral fat (cm^2)	127	74.9	41.7	135	48.5	26.3
Fat mass (kg)	123	16.6	10.6	138	17.1	9.1
BMI (kg/m^2)	127	25.5	4.7	138	23.1	4.1
Percent body fat (%BF)	123	19.1	8.9	138	25.8	8.7

BMI = body mass index.

comparison of standard errors, there appeared to be generation differences in the means within each sex for each of AVF and FM, with higher levels in parents than offspring. The mean levels of AVF were also higher in fathers than mothers, and higher in sons than daughters. FM mean levels were higher in mothers than fathers, with approximately equal levels in sons and daughters. For comparison purposes, Table 1 also gives the sample statistics for BMI and percent body fat (%BF, derived from the underwater weighing).

Age adjustments

Each of AVF and FM was adjusted for the effects of baseline age using a stepwise multiple regression procedure. Since there appeared to be mean differences based on sex and generation, the age adjustments were carried out separately in each of the four sex by generation groups. In summary, a given measure was regressed on a polynomial in age in a stepwise manner, retaining only those terms which were significant at the 5% level. The variable used in the familial analysis was the age (within sex and generation)-adjusted and standardized residual score from the regression analysis, referred to here as the phenotype. Significant age terms and percentages of variance accounted for in each of the sex by generation groups are given in Table 2. Age was a significant predictor in each sex by generation group and in general accounted for more variance in offspring than parents.

A separate set of stepwise regressions (by sex and generation) was performed on the AVF area by using a polynomial in age (age, age^2, age^3) and a polynomial in fat mass (FM, FM^2, FM^3), with the same procedure described for the age adjustments. Significant age and FM terms and percentages of variance accounted for in each of the sex by generation groups, are given in Table 2. As shown, FM accounted for a much larger percentage of the variance in AVF level than did age. As expected given these regression results, AVF and FM were significantly correlated within individuals (0.71 for the complete sample, 0.53 for fathers, 0.72 for mothers, 0.81 for sons and 0.74 for daughters).

Familial correlation model

A sex-specific familial correlation model was used to investigate whether there was evidence of familial factors underlying the variation in each of the age-adjusted AVF and FM, and age-FM-adjusted AVF phenotypes. The general procedure was to determine which of the familial correlations (spouse, parent-offspring and sibling) were significant and whether there were any sex and/or generation differences. The assumptions underlying the model were that parent-offspring and sibling pairs shared about half of their genes in common, as well as some familial environmental effects and that spouse pairs shared only familial environmental effects provided mating was at random with regards to the trait. A pattern of significant correlations among siblings and between parents and offspring, but not between spouses, would suggest a primarily genetic etiology for the familial resemblance. Significant spouse correlations, in addition to the sibling and parent-offspring correlations, would suggest that at least some of the familial effect may be due to shared environments. However, if mating is not random with regards to the trait, then significant spouse correlations may reflect genetic factors as well.

The computer program SEGPATH[20] fitted the model directly to the family data using the method of maximum likelihood under the assumption that the phenotypes within a family, jointly follow a multivariate normal distribution. The general model was based on four groups of individuals (fathers (f), mothers (m), sons (s) and daughters (d)) giving rise to 8 correlations in 3 classes (1 spouse (fm), 4 parent-offspring (fs, fd, ms, md) and 3 sibling (ss, dd, sd)). Null hypotheses (for example, equating some correlations or fixing others to zero) were also evaluated. For example, the test for no spouse correlation involved a model in which $fm = 0$ and the remaining 7 correlations were estimated. Each null hypothesis was tested by a comparison to the general model using the likelihood ratio test, which is the difference in minus twice the log-likelihoods (-2 Ln L) obtained under the two nested models. The likelihood ratio is approximately distributed as a χ^2, with the degrees of freedom being equal to the difference in the number of parameters estimated in the two competing hypotheses. In addition to the likelihood ratio test, Akaike's[21] Information Criterion (AIC) (which is -2 ln L plus twice the number of estimated parameters) was used to judge the fit of the nonnested models. The 'best' model by the AIC, is the one with the smallest value.

Two general series of null hypotheses were tested. Sex and/or generation differences were tested in the first series, including no sex differences in the offspring (model 2: $fs = fd$, $ms = md$, $ss = dd = sd$, d.f.

Table 2 Data adjustments – the percentage accounted for by the significant terms* is given in parentheses

Variable	*Fathers*	*Mothers*	*Sons*	*Daughters*
Fat mass (FM)	age^3 (1.96%)	age^3 (3.52%)	age, age^3 (21.77%)	age (6.44%)
AVF area				
adjusted for age	age (6.83%)	age^3 (5.74%)	age, age^3 (29.81%)	age^3 (15.03%)
adjusted for age and FM	age, FM, FM^2 (42.61%)	age, FM (48.04%)	age^3, FM (68.22%)	age^3, FM (62.62%)

*$P < 0.05$
AVF = abdominal visceral fat

Table 3 Model-fitting summary

		AVF			*FM-adjusted AVF*			*FM*		
Model	*d.f.*	χ^2	*P*	*AIC*	χ^2	*P*	*AIC*	χ^2	*P*	*AIC*
(1) General model				16.00			16.00			16.00
(2) $fs=fd$, $ms=md$, $ss=dd=sd$	4	5.76	0.218	13.76	2.77	0.598	10.77	2.77	0.686	10.27
(3) $fs=fd=ms=md$, $ss=dd=sd$	5	6.77	0.239	12.77	5.44	0.365	11.44	2.30	0.806	8.30
(4) $fs=fd=ms=md=ss=dd=sd$	6	7.09	0.312	11.09	5.44	0.489	9.44	3.80	0.704	7.80
(5) $ss=dd=sd=0$	3	16.68	<0.001	26.68	18.25	<0.001	28.25	33.93	<0.001	43.93
(6) $fs=fd=ms=md=0$	4	22.33	<0.001	30.33	24.81	<0.001	32.81	24.09	$<0,001$	28.09
(7) $fm=0$	1	8.83	0.003	22.83	0.38	0.540	14.38	7.13	0.008	21.13
(8) $fm=fs=fd=ms=md=ss=dd=sd=0$	8	49.62	<0.001	49.61	42.71	<0.001	42.71	66.61	<0.001	66.61
(9) $fm=fs=fd=ms=md=ss=dd=sd$	7	7.35	0.394	9.35	8.29	0.308	10.29	3.83	0.800	5.83
Parsimonious models										
All eight correlations equal	7	7.35	0.394	9.35				3.83	0.800	5.83
Combine (4) and (7): $fm=0$, and remaining seven correlations equal	7				5.80	0.563	7.80			

AVF = abdominal visceral fat; FM = fat mass; d.f. = degrees of freedom; AIC = Akaike's[21] Information Criterion; *f* = father; *m* = mother; *s* = son; *d* = daughter.

Table 4 Parameter estimates

	AVF		*FM-adjusted AVF* [a]		*FM*	
Parameters	*General*	*Most Parsimonious*	*General*	*Most Parsimonious*	*General*	*Most Parsimonious*
fm	0.31 ± 0.09	0.26 ± 0.05	0.07 ± 0.12	[0]	0.28 ± 0.10	0.32 ± 0.05
fs	0.29 ± 0.09	[0.26]	0.17 ± 0.10	0.24 ± 0.04	0.33 ± 0.09	[0.32]
fd	0.15 ± 0.10	[0.26]	0.18 ± 0.09	[0.24]	0.29 ± 0.09	[0.32]
ms	0.36 ± 0.08	[0.26]	0.35 ± 0.09	[0.24]	0.33 ± 0.08	[0.32]
md	0.22 ± 0.10	[0.26]	0.31 ± 0.08	[0.24]	0.26 ± 0.10	[0.32]
ss	0.38 ± 0.12	[0.26]	0.38 ± 0.10	[0.24]	0.46 ± 0.12	[0.32]
dd	0.36 ± 0.14	[0.26]	0.24 ± 0.14	[0.24]	0.45 ± 0.11	[0.32]
sd	0.14 ± 0.09	[0.26]	0.19 ± 0.09	[0.24]	0.33 ± 0.09	[0.32]
Maximal heritability[b]		47%		48%		55%

[a] When all eight correlations are equal, the correlation is 0.23, with a corresponding maximal heritability (see footnote**) of 42%.
[b] Maximal heritability computed as $[(r_{sibling}+r_{parent\text{-}offspring})\ (1+r_{spouse})/(1+r_{spouse}+2r_{spouse}r_{parent\text{-}offspring})]$, includes both genetic and familial environmental (if significant) sources of variance, and is adjusted for degree of spouse resemblance.
AVF = abdominal visceral fat; FM = Fat mass.

$=4$), no sex differences in parents or offspring (model 3: $fs=fd=ms=md$, $ss=dd=sd$, d.f. $=5$), and neither sex nor generation differences (model 4: $fs=fd=ms=md=ss=dd=sd$, d.f. $=6$). Additional null hypotheses tested the significance of the familial resemblance by familial class, including no sibling resemblance (model 5: $ss=dd=sd=0$, d.f. $=3$), no parent-offspring resemblance (model 6: $fs=fd=ms=md=0$, d.f. $=4$), no spouse resemblance (model 7: $fm=0$, d.f. $=1$), and no familial resemblance at all (model 8: $fm=fs=fd=ms=md=ss=dd=sd=0$, d.f. $=8$). Finally, in model 9 all eight correlations were equated ($fm=fs=fd=ms=md=ss=dd=sd$, d.f. $=7$). A parsimonious model was derived by combining all non-rejected hypotheses using likelihood ratio and AIC tests. Maximal heritability was computed using the equation shown in the footnote to Table 4 and the familial correlations from the most parsimonious model. This estimate included both genetic and familial environmental (if significant) sources of variance, and was adjusted for the degree of spouse resemblance (if significant).

Results

The model-fitting results are given in Table 3 for each of: AVF area, FM-adjusted AVF and FM. For AVF, none of the tests for no sex or generation differences in the correlations were rejected (models 2 through 4, all *P* values >0.05). The significance tests suggested that each of the sibling (model 5: $\chi^2_3=16.68$, $P<0.001$), parent-offspring (model 6: $\chi^2_4=22.33$, $P<0.001$), and spouse correlations (model 7: $\chi^2_1=8.83$, $P=0.003$) were greater than zero. In model 8 the test for no familial resemblance was rejected ($\chi^2_8=49.66$, $P<0.001$), and all correlations could be equated in model 9 ($\chi^2_7=7.35$, $P=0.394$, AIC $=9.35$). Either of models 4 or 9 fit the data by likelihood ratio, and the AIC suggests that model 9 (all 8 correlations equal) provides the 'best' fit.

For FM-adjusted AVF, there were no sex or generation differences in the correlations (models 2–4), the sibling (model 5: $\chi^2_3=18.25$, $P<0.001$) and parent-offspring correlations (model 6: $\chi^2_4=24.81$, $P<0.001$) were significant, but the spouse correlation was not (model 7: $\chi^2_1=0.38$, $P=0.540$). All eight

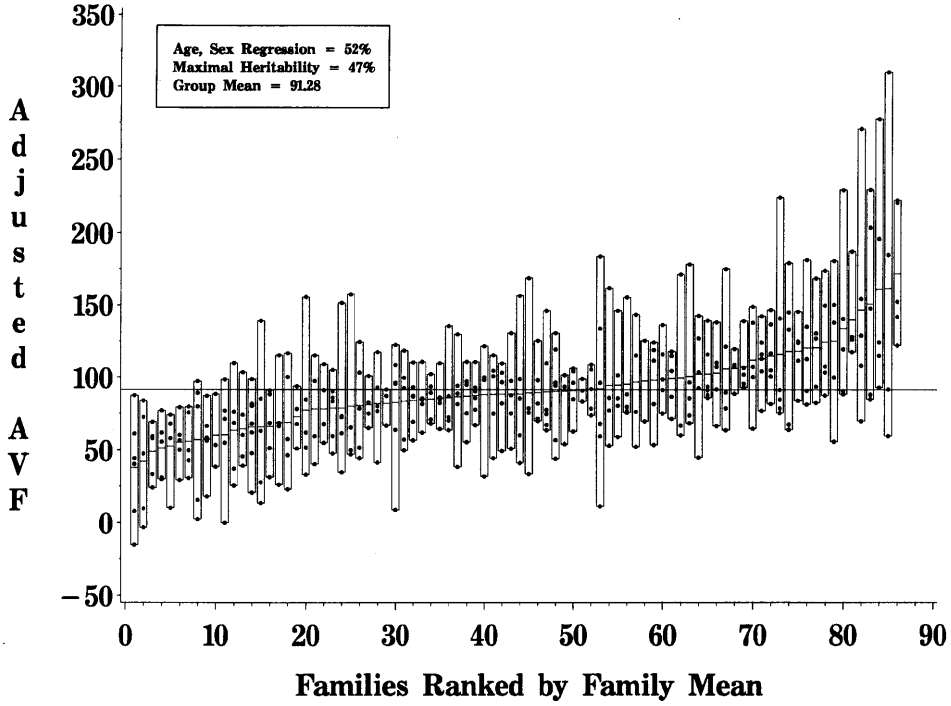

Figure 1 Age-sex-adjusted abdominal visceral fat (AVF) phenotype (Y-axis) plotted against family rank (for example, families ranked by family mean). The adjusted AVF value for each individual was calculated as the residual from the regression model shown in the insert (with percent variance accounted for noted), plus the group mean. Each family is enclosed within a box, with individual data points plotted as dots and each family mean as a dash. The horizontal line is the group mean (value noted in the insert). The maximal heritability shown in the insert is taken from Table 4.

correlations could be equated in model 9. The most parsimonious model, obtained by combining models 4 (no sex or generation differences) and 7 (no spouse resemblance), fit the data by likelihood ratio ($\chi^2_7 = 5.80$, $P = 0.563$) and was the 'best' model by AIC (7.80).

The results for FM are similar to those for AVF. There were no sex or generation differences (models 2–4), all of the familial correlations were significantly different from zero (sibling correlations in model 5, parent-offspring correlations in model 6 and spouse correlations in model 7) and all eight correlations could be equated (model 9). Therefore, the most parsimonious hypothesis was for a single correlation representing all eight correlations (model 9: $\chi^2_7 = 3.83$, $P = 0.800$, AIC = 5.83).

Parameter estimates (correlations ± s.e.m.s) are given in Table 4 under both the general and the most parsimonious models. There were no sex or generation differences in the correlations and spouse correlations were significant for FM and for AVF prior to but not after FM adjustment. The maximal heritability is shown in the last row of Table 4. The maximal heritability was highest for FM (55%) and approximately equal for the two AVF variables (47–48%).

A graphical representation of the results are given in Figure 1 (AVF), Figure 2 (FM-adjusted AVF) and Figure 3 (FM), as originally proposed by Bogardus *et al*.[22] In each of these figures, each family is enclosed within a vertical box with individual scores plotted as dots, each family mean given with a dash and the families ranked by family mean. The adjusted values were derived using the regression model shown in the insert (for example, in Figure 1 and Figure 3, the dependent variables were age and sex, and in Figure 2 they were age, sex and FM). The individual plotted values were computed as the residual from the regression, plus the family mean, thus scaling to the raw measurement units. The percent of variance accounted for by the regression is also shown in the insert. The maximal heritabilities noted in the inserts were taken from Table 4.

Discussion

There were three issues of interest in this investigation of baseline AVF level in the HERITAGE Family Study. First, we wished to understand if, and to what extent, AVF area phenotypes aggregate in sedentary families. Second, we wanted to verify whether genetic effects were potentialy involved in AVF area familiality. Third, we wished to gain a better understanding of how these inactive families compare to the population at large.

Our results suggest that there is a familial resemblance for AVF area and total body fat in sedentary families (maximal heritabilities of 47% and 55%, respectively), as well as for AVF area adjusted for total body fat (maximal heritabilities of 48%). Furthermore, for each of AVF and FM, there appears to be a significant familial environmental component, as evidenced by the significant spouse correlation, assuming random mating. However, this environmen-

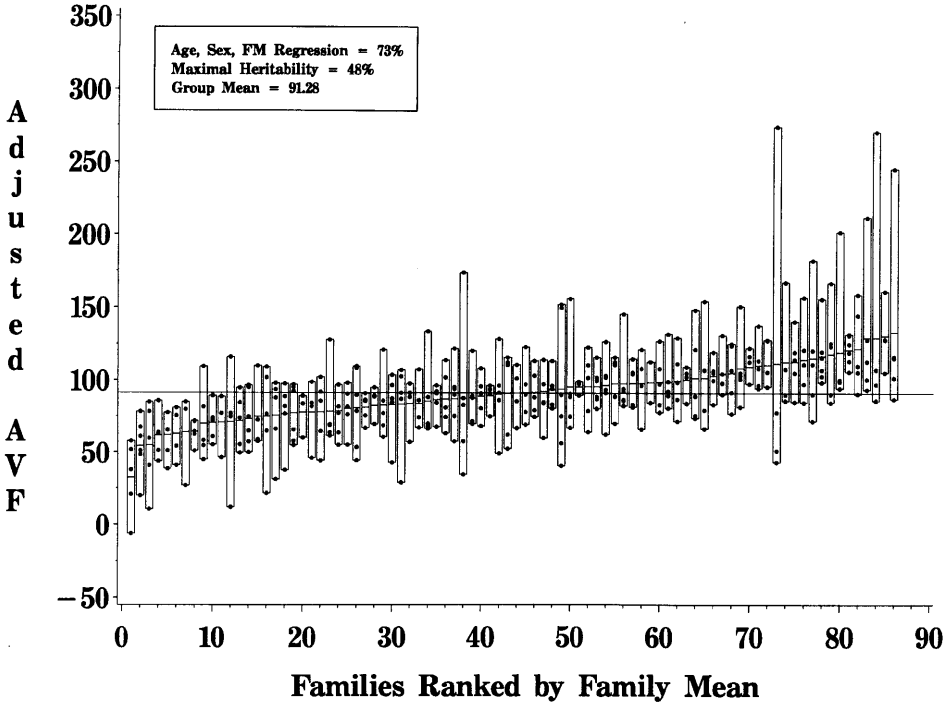

Figure 2 Age-sex-FM-adjusted abdominal visceral fat (AVF) phenotype (Y-axis) plotted against family rank. See Figure 1 for further details.

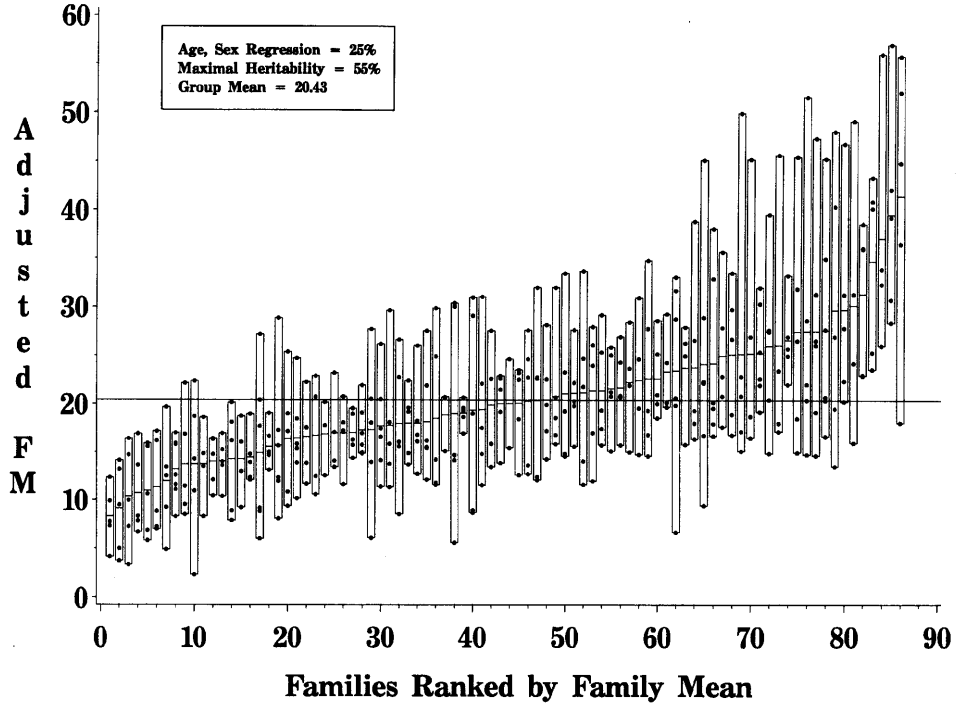

Figure 3 Age-sex-adjusted FM phenotype (Y-axis) plotted against family rank. See Figure 1 for further details.

tal effect may be on fat mass *per se*, as the spouse correlation is no longer significant after adjusting AVF for FM. In support of this argument is the observation that the spouse correlation was also significant in the analysis of FM *per se*. We also note, however, that if mating is not random with regards to FM, then this effect may be a function of genetic factors as well. Therefore, the equation shown in the footnote to Table 4 includes an adjustment for the effects of spousal resemblance. Regardless of the source of the common determinants of FM and AVF, however, the tendency to store and use fat specifically in the abdominal visceral depot appears to be a trait which may be influenced predominantly by genetic factors. Moreover, while there are sex and generation differences in mean levels of AVF in the population,

there are none in the familial correlations in these inactive families.

The only other data on the familiality of AVF area come from the Québec Family Study (QFS), which comprises a random sample of French Canadian families, and potentially from a twin study of Caucasian females from Australia. Similar methodologies were used in the present study and in the QSF, both as regards measurement and familial analysis. The sample statistics for the HERITAGE were compared to those of the QFS as reported by Pérusse *et al*.[13] The samples were similar in mean ages (56, 53, 26 and 25 y for fathers, mothers, sons and daughters, respectively in the QFS, and 53, 52, 25 and 24 y, respectively in the HERITAGE). However, as compared to the HERITAGE, the means in the QFS fathers, mothers, and sons appeared to be lower for each of BMI (27.8 ± 0.47, 26.0 ± 0.53 and 24.6 ± 0.43, respectively) and FM (22.8 ± 0.93, 24.7 ± 0.91 and 15.1 ± 1.0, respectively), with the reverse pattern in daughters. In other words, the QFS sample tended to be somewhat more lean than the HERITAGE sample.

In the QFS, Pérusse *et al*[13] reported a significant heritability for AVF, both prior to (58% using the maximal heritability equation shown in Table 4 of the present study) and after (56%) adjusting for fat mass. While these estimates are somewhat higher than the corresponding estimates of 47% and 48% found in the present study, they do not appear to be significantly different on the basis of the standard errors. Also consistent with the QFS findings, the spouse correlation in HERITAGE study was significant only prior to adjustment for total FM, suggesting a primarily genetic etiology for the AVF level which is independent of total body fat levels.

The Australian twin study[23] measured central abdominal fat using a DEXA scan. Their central abdominal fat phenotype included both visceral and subcutaneous fat, as well as the total area of L2, L3 and L4, and not the visceral space between L4 and L5 as in the HERITAGE. The female twins were on average 5 y younger and had somewhat lower BMI values (24.5 ± 0.9 for MZ and 23.8 ± 0.7 for DZ) than the HERITAGE mothers. Nevertheless, after adjusting central abdominal fat for total FM, a genetic heritability of 73% was obtained, with little or no contribution from the common environment. While comparison of these twin results to the current study is complicated by the fact that different methodologies were used, both in measurement of phenotype and in type of family data, they suggest that the etiology of AVF variability is primarily genetic. Also, the two intervention studies conducted with pairs of young adult male identical twins,[11,12] which showed that the AVF area changes with chronic overfeeding or long term negative energy balance, were much more similar within pairs than between pairs, also support the conclusion that the AVF area has a strong genetic component.

The results in the sedentary HERITAGE families are particularly interesting because variation due to a factor known to affect AVF, physical activity, is controlled for in this design. This control over level of habitual physical activity was less stringent in the QFS data. Together, these comparisons suggest that the pattern of familial aggregation for AVF is similar in the sedentary HERITAGE families, and in randomly ascertained French Canadian families. The familial variance in these sedentary families for each of FM and AVF probably include both genetic and familial environmental factors. But, when AVF is made independent of total body fat there appears to be a predominantly genetic etiology. The magnitudes of the familial estimates are also similar in the HERITAGE and QFS. These results imply that some individuals may have an inborn predisposition to store fat in the abdominal visceral depot. Given the association between AVF and various metabolic disturbances leading to cardiovascular disease and noninsulin-dependent diabetes mellitus, it is important to identify the biological mechanisms and the genes responsible for these differences.

Acknowledgements

The HERITAGE study is supported by the NHLBI through the following grants: HL45670 (C Bouchard, PI), HL47323 (AS Leon, PI), HL47317 (DC Rao, PI), HL47327 (JS Skinner, PI), and HL47321 (JH Wilmore, PI). Thanks are expressed to all the co-principal investigators, investigators, co-investigators, local project coordinators, research assistants, laboratory technicians, and secretaries who are contributing to the study. Finally, the entire HERITAGE consortium is very thankful to those hard-working participating families whose involvement alone demonstrates the feasibility of this study.

References

1 Kissebah AH, Freedman DS, Peiris AN. Health risks of obesity. *Med Clin North Am* 1989; **73**: 111–138.
2 Park KS, Rhee BD, Lee KU, Kim SY, Lee HK, Koh CS, Min HK. Intra-abdominal fat is associated with decreased insulin sensitivity in healthy young men. *Metabolism* 1991; **40**: 600–603.
3 Després JP, Nadeau A, Tremblay A, Ferland M, Moorjani S, Lupien PJ, Thériault G, Pinault S, Bouchard C. Role of deep abdominal fat in the association between regional adipose tissue distribution and glucose tolerance in obese women. *Diabetes* 1989a; **38**: 304–309.
4 Després JP, Moorjani S, Ferland M, Tremblay A, Lupien PJ, Nadeau A, Pinault S, Thériault G, Bouchard C. Adipose tissue distribution and plasma lipoprotein levels in obese women: Importance of intra-abdominal fat. *Arteriosclerosis* 1989b; **9**: 203–210.
5 Després JP, Moorjani S, Lupien PJ, Tremblay A, Nadeau A, Bouchard C. Regional distribution of body fat, plasma lipoproteins, and cardiovascular disease. *Arteriosclerosis* 1990; **10**: 497–511.
6 Johnson D, Prud'homme D, Després JP, Nadeau A, Tremblay A, Bouchard C. Relation of abdominal obesity to hyperinsu-

linemia and high blood pressure in men. *Int J Obes* 1992; **16**: 881–890.
7 Björntorp P. Visceral obesity: A 'Civilization syndrome'. *Obes Res* 1993; **1**: 206–222.
8 Enzi G, Gasparo M, Biondetti PR, Fiore D, Semisa M, Zurlo F. Subcutaneous and visceral fat distribution according to sex, age and overweight, evaluated by computed tomography. *Am J Clin Nutr* 1986; **44**: 739–746.
9 Lemieux S, Prud'homme D, Bouchard C, Tremblay A, Després JP. Sex differences in the relation of visceral adipose tissue accumulation to total body fatness. *Am J Clin Nutr* 1993; **58**: 463–467.
10 Bouchard C, Després JP, Mauriège P. Genetic and nongenetic determinants of regional fat distribution. *Endocrine Rev* 1993; **14**: 72–93.
11 Bouchard C, Tremblay A, Després JP, Nadeau A, Lupien PJ, Thériault G, Dussalt J, Moorjani S, Pinault S. Fournier G. The response to long-term overfeeding in identical twins. *New Engl J Med* 1990; **322**: 1477–1482.
12 Bouchard C, Thériault, G, Nadeau A, Lupien PJ, Moorjani S, Prud'homme D, Fournier G. The response to exercise with constant energy intake in identical twins. *Obes Res* 1994; **2**: 400–410.
13 Pérusse L, Després JP, Lemieux S, Rice T, Rao DC, Bouchard C. Familial aggregation of abdominal visceral fat level: Results from the Québec Family Study. *Metabolism* 1996; **45**: 378–382.
14 Bouchard C, Rice T, Lemieux S, Després JP, Pérusse L, Rao DC. Major gene for abdominal visceral fat area in the Québec Family Study. *Int J Obes* 1996; **20**: 420–427.
15 Bouchard C, Leon AS, Rao DC, Skinner JS, Wilmore JH, Gagnon J. The HERITAGE family study: Aims, design and measurement protocol. *Med Sci Sports Exerc* 1995; **27**: 721–729.
16 Sjöström L, Kvist H, Cederblad, A, Tylén U. Determination of total adipose tissue and body fat in women by computed tomography, 40K and tritium. *Am J Physiol* 1986; **250**: E736–E745.
17 Behnke AR, Wilmore JH. *Evaluation and regulation of body build and composition.* Prentice-Hall: Englewood Cliffs, 1974, pp 21–27.
18 Wilmore JH. A simplified method for determination of residual lung volume. *J Appl Physiol* 1969; **27**: 96–100.
19 Wilmore JH, Vodak PA, Parr RB, Girandola RM, Billing JE. Further simplification of a method for determining residual lung volume. *Med Sci Sports* 1980; **12**: 216–218.
20 Province MA, Rao DC. 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* 1995; **12**: 203–219.
21 Akaike H A new look at the statistical model identification. *IEEE Trans Automat Control* 1974; **19**: 716–723.
22 Bogardus C, Lillioja S, Ravussin E, Abbott W, Zawadzki JK, Young A, Knowler WC, Jacobowitz R, Moll PP. Familial dependence of the reseting metabolic rate. *N Engl J Med* 1986; **315**: 96–100.
23 Carey DGP, Nguyen TV,Campbell LV, Chisholm DJ, Kelly P Genetic influences on central abdominal fat: A twin study. *Int J Obes* 1996; **20**: 722–726.