Familial resemblance in ventilatory threshold: the HERITAGE Family Study

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ABSTRACT

GASKILL, S. E., T. RICE, C. BOUCHARD, J. GAGNON, D. C. RAO, J. S. SKINNER, J. H. WILMORE, and A. S. LEON. Familial resemblance in ventilatory threshold: the HERITAGE Family Study. *Med. Sci. Sports Exerc.*, Vol. 33, No. 11, 2001, pp. 1832–1840. **Purpose:** This study investigates the familial resemblance of $\dot{V}O_2$ at the ventilatory threshold ($\dot{V}O_{2vt}$) from 199 nuclear families (100 White and 99 Black) participating in the HERITAGE Family Study. **Methods:** $\dot{V}O_{2vt}$ ($mL \cdot min^{-1}$) was determined in the sedentary state and again after 20 wk of aerobic cycle ergometer exercise training in 339 individuals (131 parents and 228 of their offspring), aged between 17 and 65 yr. $\dot{V}O_{2vt}$ was adjusted for weight, age, fat mass, and fat-free mass by using regression methods. **Results:** There was evidence for significant familial resemblance in the sedentary state for $\dot{V}O_{2vt}$ (maximal heritability = 58% in White and 54% in Black families) and $\dot{V}O_{2vt}/\dot{V}O_{2max}$ (maximal heritability = 38% in White and 39% in Black families). Spouse, sibling, and parent-offspring relationships for $\dot{V}O_{2vt}$ were significant at baseline, suggesting that both genetic and shared environmental factors may contribute to the familial resemblance in the sedentary state. There was a moderate familial component in the response of $\dot{V}O_{2vt}$ to aerobic exercise training in Whites (22%) and a larger component in Blacks (51%). In Blacks, the familial effect for $\dot{V}O_{2vt}/\dot{V}O_{2max}$ appeared to be accounted for by fat and fat-free mass. **Conclusion:** These results show a strong familial contribution to $\dot{V}O_{2vt}$ in the sedentary state and to the response of $\dot{V}O_{2vt}$ to aerobic exercise training. **Key Words:** SEDENTARY, HERITABILITY, EXERCISE TRAINING

It has been shown that there is familial resemblance for $\dot{V}O_{2max}$. Bouchard et al. (6), using familial data from the HERITAGE Family Study (HERITAGE), estimated maximal heritability in 429 White sedentary subjects from 86 nuclear families to be at least 50%. Previous studies estimated that familial resemblance, which includes both genetic and shared environmental factors, accounts for 30–67% of $\dot{V}O_{2max}$ (3,4,6,7,10,11,13–17,24).

Although $\dot{V}O_{2max}$ is a measure of maximal aerobic power, most daily activities are performed at submaximal exercise intensities. However, few prior studies (5,9,16,18,19) have looked at the baseline heritability of markers of submaximal fitness. Results from these previous studies have found maximal heritability estimates of 28–48%.

Pérusse et al. (20) investigated the contribution of genetic factors to baseline and response to HERITAGE training in several submaximal performance phenotypes including oxygen consumption ($\dot{V}O_2$) at power outputs (PO) of 50 W, 60% and 80% $\dot{V}O_{2max}$ and PO at 60% and 80% $\dot{V}O_{2max}$. The maximal heritability of the baseline phenotypes varied from 48–74%, whereas the maximal heritability for the training response phenotypes tended to be lower (23–57%). Studies with monozygotic (MZ) twins exercise trained for periods of 15 or 20 wk on a standardized cycle ergometer found that there were significant within-MZ twin pair resemblances for submaximal measures of $\dot{V}O_2$, suggesting that genetic factors are involved in the trainability of these phenotypes (4).

In the present study, familial resemblance for submaximal aerobic fitness, both in the sedentary state before starting exercise training and in its response to training, are investigated

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using HERITAGE data. $\dot{V}O_2$ ($mL \cdot min^{-1}$) at the ventilatory threshold ($\dot{V}O_{2vt}$) adjusted for body weight is used to estimate submaximal sustainable aerobic fitness. This is justified by the work of many prior investigators who have shown that $\dot{V}O_{2vt}$ and the associated variable of $\dot{V}O_2$ at the lactate threshold (LT) is related to sustainable aerobic work capacity and aerobic fitness. Londeree has summarized many of these studies in a meta-analysis evaluating training at intensities relative to ventilatory threshold (VT) and LT (12). In addition to $\dot{V}O_{2vt}$, we investigated the familial resemblance of VT as a percentage of $\dot{V}O_{2max}$ (VT%$\dot{V}O_{2max}$) and the response of $\dot{V}O_{2vt}$ ($mL \cdot min^{-1}$) to aerobic exercise training. These results represent the first reported estimates of familial influences on baseline measures and the response to training of $\dot{V}O_{2vt}$ and VT%$\dot{V}O_{2max}$.

METHODS

Familial resemblance in nuclear two-generation families is estimated using a simple familial correlation model. Since parent-offspring and sibling pairs share half of the same genes, twice the average parent-offspring and sibling correlations represents the maximal familial effect (i.e., maximal heritability). This estimate is considered maximal, since it represents effects attributable to all sources of familial variance, including genetic and shared family environment. On the other hand, the correlation between spouses usually represents effects attributable to familial environments, since spouses share few genes in common, assuming that there is random mating. The familial correlation model was applied to measures of $\dot{V}O_{2vt}$ and VT%$\dot{V}O_{2max}$ for both baseline and the response to training, separately in Black and White families participating in the HERITAGE Family Study.

Sample. A total of 339 individuals from 100 White families and 172 individuals from 99 Black families had satisfactory baseline data for both $\dot{V}O_{2vt}$ and $\dot{V}O_{2max}$. Recruitment of families was derived from extensive media publicity and advertisements at the four participating clinical centers (Arizona State University [later moved to Indiana University], Laval University, University of Minnesota, and the University of Texas at Austin). Several inclusion criteria were used for screening. White families were required to have both biological parents and at least three offspring, whereas Black families could participate in units as small as two first-degree members (i.e., parent-child or two siblings) (5). Parents had to be 65 yr or younger and offspring were between the ages of 17 and 40 yr. With a few exceptions approved by a physician, subjects had a body mass index (BMI) less than 40 $kg \cdot m^{-2}$. Resting BP did not exceed 159 mm Hg for systolic blood pressure or 99 mm Hg for diastolic blood pressure. In addition, antihypertensive and lipid drug therapy were causes for exclusion. Most importantly, subjects were required to be sedentary at baseline; this was defined as no regular vigorous activity in the previous 6 months. In general, subjects were required to be in good health. Details of subject screening and methodology in HERITAGE have been previously published (5). Approval was obtained from the institutional review boards for the protection of human subjects in research projects at each of the four participating HERITAGE clinical centers, and written informed consent was obtained from each participant.

Exercise training. After baseline assessments, each subject was trained on a cycle ergometer 3 times$\cdot wk^{-1}$ for 20 wk. The intensity and/or duration was automatically adjusted for each individual every 2 wk, starting at the heart rate (HR) associated with 55% of baseline $\dot{V}O_{2max}$ for 30 min per session and increasing incrementally until each subject was working at the HR associated with 75% of baseline $\dot{V}O_{2max}$ for 50 min during the last 6 wk. The PO was adjusted automatically to maintain the appropriate HR response during all training sessions by a built-in computer program. Each session was supervised on site and adherence to the protocol was strictly monitored (23).

Measurements. A battery of measurements was administered to each individual both before (baseline) and after (posttraining) engaging in the 20-wk standardized exercise-training program. Each participant at baseline performed two maximal exercise tests, separated by at least 48 h, and again posttraining using a SensorMedics ergometrics 800S (Yorba Linda, CA) cycle ergometer. Heart rate was monitored by an electrocardiogram. Gas exchange variables ($\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}E$, and RER) were recorded as a rolling average of three 20-s intervals. Criteria for reaching $\dot{V}O_{2max}$ included meeting two of the three following criteria: 1) RER > 1.1, 2) plateau in $\dot{V}O_2$ (change of less than 100 $mL \cdot min^{-1}$ in the last three consecutive 20-s points) or 3) a HR within 10 beats of age-predicted maximal HR (6,23). All subjects met at least two of these criteria both at baseline and at posttraining. Details of the exercise tests have been described elsewhere (5,6,23).

VT was determined by concurrently evaluating graphs of V-slope (change in slope of the $\dot{V}O_2$ vs $\dot{V}CO_2$ plot from less than 1 to greater than 1), ventilatory equivalents (first sustained rise in $\dot{V}E/\dot{V}O_2$ without a concurrent rise in $\dot{V}E/\dot{V}CO_2$), and excess CO_2 (first sustained rise in excess CO_2 as calculated by the formula $(\dot{V}CO_2^2/\dot{V}O_2) - \dot{V}CO_2$) plots. The methods used followed a tight protocol requiring independent investigators to determine VT within 3% of one another for the data to be accepted. Gaskill et al. (8) have previously described details of the combined VT determination method used in this study. The combined method was shown in that study to greatly reduce the standard deviation of the LT − VT difference (70–140% reduction over using individual VT determination methods). Because of the rigid VT determination criteria, VT was adequately determined in only about 60% of the HERITAGE population.

Data adjustments. Data were adjusted for several covariates before the familial analyses using stepwise (and/or forced) multiple regression. In summary, a variable was regressed on a set of covariates, separately in eight race by sex by generation groups (fathers, mothers, sons, and daughters in each of the White and Black gender samples). In the stepwise regressions, only those terms that were significant at the 5% level were retained. The resulting squared residuals from this mean regression were similarly adjusted for

covariate effects in the variance (i.e., heteroscedasticity) using another stepwise regression. The final adjusted variable was the residual from the mean regression, divided by the square root of the predicted score from the second regression. A final standardization step was taken to ensure zero mean and unit variance.

For baseline $\dot{V}O_{2vt}$ ($mL \cdot min^{-1}$), a two-step regression procedure was used. In the first step, $\dot{V}O_{2vt}$ was adjusted for weight (kg) using a forced regression, and in the second step was further adjusted for a polynomial in age (age, age^2, age^3) using stepwise regression. The two-step procedure that forced weight into the equation was necessary, since weight was not significant ($\alpha > 5\%$) in one of the race by sex by generation groups (Black fathers). A second baseline $\dot{V}O_{2vt}$ phenotype was constructed similarly to the first, except that in the second regression the stepwise covariates included a polynomial in age, fat mass (FM), and fat-free mass (FFM). Thus, the two analysis variables represent $\dot{V}O_{2vt}$ adjusted for weight and age ($B1\dot{V}O_{2vt}$), and adjusted for weight, age, FM, and FFM ($B2\dot{V}O_{2vt}$). With few exceptions, the additional adjustments for FM and FFM had little or no impact on the weight and age analysis and the data are not further presented. $VT\%\dot{V}O_{2max}$ was computed as $\dot{V}O_{2vt}$ ($mL \cdot min^{-1}$) $\times$ $100/\dot{V}O_{2max}$ ($mL \cdot min^{-1}$) and then adjusted for covariates. Two adjusted variables were constructed for $VT\%\dot{V}O_{2max}$ using stepwise regression. The first was adjusted for a polynomial in age ($B1\%\dot{V}O_{2max}$), and the second adjusted for age, FM, and FFM ($B2\%\dot{V}O_{2max}$). With few exceptions, the additional adjustments for FM and FFM had little or no impact on the weight and age analysis, and the data are not further presented except where differences between the two models were noted. The response $\dot{V}O_{2vt}$ was first computed as posttraining ($mL \cdot min^{-1}$) − baseline ($mL \cdot min^{-1}$) values, and then adjusted for a polynomial in age and the baseline value ($mL \cdot min^{-1}$) using stepwise regression ($D1\dot{V}O_{2vt}$).

Familial aggregation. Familial aggregation was tested with an sex-specific familial correlation model using the computer program SEGPATH (21). The program fits the model directly to the family data using maximum likelihood methods under the assumption that the phenotypes within a family jointly follow a multivariate normal distribution. The general model was derived from four types of family members (fathers (f), mothers (m), sons (s), daughters (d)), leading to eight correlations within three familial classes (1 spouse (fm), four parent-offspring (fs, fd, ms, md), and three sibling (ss, dd, sd)). The general model (i.e., all eight correlations estimated) was fit to the data, as were several reduced (alternative) models examining sex and/or generation differences and the significance of the correlations. Reduced hypotheses were tested using the likelihood ratio test (LRT), which is the difference in minus twice the log-likelihoods ($-2 \ln L$) obtained under the general model and a reduced hypothesis. The LRT is distributed as a χ^2, with the degrees of freedom equal to the difference in the number of parameters estimated in the two nested models. In addition, Akaike's information criterion (AIC), which 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 (1).

Several reduced hypotheses tested for sex and generation differences. First, the hypothesis of no sex differences in offspring was tested (fs = fd, ms = md, ss = dd = sd, $df = 4$). Other models included tests for no sex differences in parents and offspring (fs = fd = ms = md, ss = dd = sd, $df = 5$), and no sex or generation differences (fs = fd = ms = md = ss = dd = sd, $df = 6$). In addition, models positing same versus opposite sex correlations (fs = ss = md = dd, fd = ms = sd, $df = 5$) and sex-specific correlations (fs = ss, md = dd, fd = ms = sd, $df = 4$) were examined. A maternal or mitochondrial hypothesis (ms = md = ss = dd = sd, $df = 4$), and an environmental hypothesis consisting of a single correlation (fm = fs = fd = ms = md = ss = dd = sd, $df = 7$) were also tested. Finally, the hypotheses of no sibling correlations (ss = dd = sd = 0, $df = 3$), no parent-offspring correlations (fs = fd = ms = md = 0, $df = 4$), no spouse correlation (fm = 0, $df = 1$), and no familial resemblance at all (fm = fs = fd = ms = md = ss = dd = sd = 0, $df = 8$) were tested. Nonrejected hypotheses were combined in order to form the most parsimonious model, from which the familial effects (maximum heritabilities) were derived. Maximal heritability was computed as follows: $(r_{sib} + r_{po})(1 + r_{spouse})/[1 + r_{spouse} + (2)(r_{spouse})(r_{po})]$, where r_{sib} is the average sibling correlation, r_{po} is the average parent-offspring correlation, and r_{spouse} is the spouse correlation (22). This equation adjusts the familial effect for spouse resemblance, and when the spouse correlation is zero the equation reduces to twice the average sibling and parent-offspring correlation.

RESULTS

Sample statistics and covariate adjustments. Table 1 gives the sample sizes, means, and standard deviations for each of the measures, separately in eight race by sex by generation groups. Mean group differences were judged by a comparison of standard errors. Race differences were noted for every variable in the offspring (sons and daughters). In the parents, there were race differences for age and mass variables but not $\dot{V}O_2$ variables in the fathers and few race differences in the mothers (age and baseline $\dot{V}O_{2vt}$). There were both sex and generation differences for most variables in all groups, except for fewer sex differences across Black females (mothers vs daughters).

Because the $\dot{V}O_{2vt}$ was significantly skewed (1.0) and leptokurtotic (1.74), a log-transformation was performed before covariate adjustments, which resulted in a more normally distributed variable (0.29 and −0.002, respectively). Covariate adjustment results are given in Tables 2–4. The adjustment of $\dot{V}O_{2vt}$ ($mL \cdot min^{-1}$) for weight (Table 2) generally accounts for more variance in Blacks than in Whites except for fathers, where the inverse was seen. Further adjustments for age (Table 3), FFM, and FM (Table 4) generally account for additional variance across offspring (Black and White son and White daughter) groups but not for parents for $\dot{V}O_{2vt}$. Age is a better predictor of $VT\%\dot{V}O_{2max}$

TABLE 1. Means and standard deviations (SD) by race and family position.

Variables	White			Black		
	N	Mean	SD	*N*	Mean	SD
Fathers						
Age (yr)	70	53.1	5.0[a,c]	11	49.9	7.3[a,b]
$\dot{V}O_{2max}$ baseline[d]	70	30.8	5.2[b,c]	11	29.6	3.0[b]
$\dot{V}O_{2vt}$ baseline[d]	70	16.5	2.8[c]	11	15.8	1.8[b]
$\dot{V}O_{2vt}$ response[d]	66	4.9	3.1[c]	11	4.2	2.2
VT%VO_{2max} (%)	70	54.2	7.3[b,c]	11	53.8	5.9[b]
Mothers						
Age (yr)	41	51.9	5.1[a,c]	24	45.4	5.4[a,b,c]
$\dot{V}O_{2max}$ baseline[d]	41	24.2	5.3[b,c]	24	22.0	3.4[b,c]
$\dot{V}O_{2vt}$ baseline[d]	41	15.3	3.0[a,c]	24	13.6	1.7[a,b,c]
$\dot{V}O_{2vt}$ response[d]	38	4.2	2.7	20	3.4	2.7
VT%VO_{2max} (%)	41	63.8	8.7[b,c]	24	62.2	6.2[b]
Sons						
Age (yr)	123	25.4	6.0[a,c]	64	27.5	7.1[a,c]
$\dot{V}O_{2max}$ baseline[d]	123	40.9	7.8[a,b,c]	64	35.5	6.4[a,b,c]
$\dot{V}O_{2vt}$ baseline[d]	123	19.8	5.0[a,b,c]	64	17.8	3.4[a,b,c]
$\dot{V}O_{2vt}$ response[d]	109	7.6	4.8[a,b,c]	47	6.1	3.7[a,b,c]
VT%VO_{2max} (%)	123	48.6	7.7[a,b,c]	64	51.5	6.8[a,b]
Daughters						
Age (yr)	105	25.4	6.4[a,c]	73	28.5	8.3[a,c]
$\dot{V}O_{2max}$ baseline[d]	105	32.7	5.1[a,b,c]	73	26.0	6.0[a,b,c]
$\dot{V}O_{2vt}$ baseline[d]	105	18.4	3.5[a,b,c]	73	15.3	3.1[a,b,c]
$\dot{V}O_{2vt}$ response[d]	99	5.4	3.6[a,b]	63	3.6	2.1[a,b]
VT%VO_{2max} (%)	105	57.3	8.2[a,b,c]	73	60.1	8.3[a,b]

[a] Race differences (within sex and generation, $P < 0.05$).
[b] Sex differences (within generation and race, $P < 0.05$).
[c] Generation differences (within sex and race, $P < 0.05$).
[d] $\dot{V}O_2$ units are expressed as $mL \cdot kg^{-1} \cdot min^{-1}$ to allow comparisons across groups.

in White parents and Black daughters than is FM or FFM. For the response of $\dot{V}O_{2vt}$, baseline $\dot{V}O_{2vt}$ levels account for 4–12% of the variance in the White mothers and offspring.

Familial aggregation. The SEGPATH model-fitting results are given in Tables 5 (White sample) and 6 (Black sample). For the age-adjusted $\dot{V}O_{2vt}$ at baseline (B1$\dot{V}O_{2vt}$) in the White sample, none of the sex or generation tests were significant. For example, there were no sex differences in the offspring ($\chi^2_4 = 7.08$, $P = 0.1316$) or the offspring and parents ($\chi^2_5 = 7.45$, $P = 0.1894$), nor were there any generation differences ($\chi^2_6 = 7.74$, $P = 0.2580$). Same versus opposite sex correlations were not ruled out ($\chi^2_5 = 6.27$, $P = 0.2808$), nor were sex-specific correlations ($\chi^2_4 = 4.97$, $P = 0.2900$). Moreover, a single correlation model fit the data ($\chi^2_7 = 8.73$, $P = 0.2726$), as did the maternal transmission (or mitochondrial) model ($\chi^2_4 = 5.76$, $P = 0.2177$). Although the sibling ($\chi^2_3 = 17.38$, $P = 0.0006$) and parent-offspring correlations ($\chi^2_4 = 30.27$, $P < 0.0001$) were significantly different from zero, the spouse correlation ($\chi^2_1 = 2.56$, $P = 0.1093$) was not. The hypothesis of no familial effects (model 12) was rejected ($\chi^2_8 = 46.35$, $P < 0.0001$). The AIC was used to determine the best sex-differences hypothesis, which was model 4 (no sex or generation differences). The combined test of no sex or generation difference and no spouse correlation (models 4 + 9) fit the data by likelihood ratio criterion ($\chi^2_7 = 9.99$, $P = 0.1891$). However, the AIC for that model (11.99) was larger than that for the single correlation hypothesis (model 10, AIC = 10.73). Therefore, although either model adequately fits the data, the single correlation model provides the "best" fit and was chosen as the most parsimonious.

For age-adjusted VT%$\dot{V}O_{2max}$ (B1%$\dot{V}O_{2vt}$) in Whites, the parent-offspring correlations were significant ($\chi^2_4 =$

TABLE 2. Percent of variance accounted for in baseline $\dot{V}O_{2vt}$ by weight.

Race	Fathers	Mothers	Sons	Daughters
Black	7.5	46.7	33.8	39.6
White	25.5	10.3	5.1	14.1

TABLE 3. Age adjustments.

Group/Variance	Mean		Variance (Heteroscedasticity)	
	Terms	R^2	Terms	R^2
$\dot{V}O_{2vt}$ baseline				
Black				
Fathers	None	—	None	—
Mothers	None	—	None	—
Sons	None	—	None	—
Daughters	None	—	None	—
White				
Fathers	None	—	None	—
Mothers	None	—	None	—
Sons	None	—	None	—
Daughters	None	—	None	—
VT%$\dot{V}O_{2max}$ baseline				
Black				
Fathers	None	—	Age	53.3
Mothers	None	—	None	—
Sons	None	—	None	—
Daughters	Age^3	7.0	None	—
White				
Fathers	Age	9.3	None	—
Mothers	Age	24.1	None	—
Sons	None	—	None	—
Daughters	None	—	None	—
$\dot{V}O_{2vt}$ response				
Black				
Fathers	None	—	None	—
Mothers	None	—	None	—
Sons	None	—	None	—
Daughters	None	—	Baseline	7.5
White				
Fathers	None	—	None	—
Mothers	Baseline	10.7	None	—
Sons	Baseline	4.5	None	—
Daughters	Baseline	11.9	None	—

TABLE 4. Age, FM, and FFM adjustments.

Group/Variance	Mean		Variance (Heteroscedasticity)	
	Terms	R^2	Terms	R^2
$\dot{V}O_{2vt}$ baseline				
Black				
Fathers	None	—	None	—
Mothers	None	—	FM	54.9
Sons	FFM, age, FM	35.4	FM	10.0
Daughters	None	—	None	—
White				
Fathers	None	—	FFM	1.07
Mothers	None	—	None	—
Sons	FFM, FM	12.6	None	—
Daughters	FM, FFM	11.0	None	—
VT%$\dot{V}O_{2max}$ baseline				
Black				
Fathers	None	—	Age	53.3
Mothers	None	—	FFM	29.1
Sons	FM, age	16.9	None	—
Daughters	Age^3	7.3	None	—
White				
Fathers	Age	11.0	None	—
Mothers	Age	24.7	None	—
Sons	None	—	None	—
Daughters	None	—	None	—

10.86, $P = 0.0282$), although the sibling ($\chi^2_3 = 5.32$, $P = 0.1499$) and spouse ($\chi^2_1 = 2.84$, $P = 0.921$) correlations were not. In general, there was a significant familial effect ($\chi^2_8 = 18.95$, $P = 0.0256$). These separate tests suggest a model for no sex or generation differences, and no sibling and no spouse correlations (models 4 + 7 + 9). Although this hypothesis fit the data by likelihood ratio test ($\chi^2_7 = 10.91$, $P = 0.1426$, AIC = 12.91), the most parsimonious model by AIC was for a single correlation (AIC = 6.97).

Finally, for the age-baseline $\dot{V}O_{2vt}$ adjusted $\dot{V}O_{2vt}$ response to training ($D1\dot{V}O_{2vt}$) in Whites, any of the models fit by likelihood ratio (i.e., no hypotheses were rejected). Although several alternative models were tested, the most parsimonious model by AIC was for a single correlation (AIC = 6.59).

The model-fitting results for the Black sample were quite different (Table 6). Because of the small sample sizes, there was not enough power to test for sex differences, so the correlations were tested for significance by familial class (i.e., assuming no sex differences). For the age-adjusted $\dot{V}O_{2vt}$ ($B1\dot{V}O_{2vt}$), there was significant familial resemblance between sibling pairs but there was no parent-offspring or spouse resemblance. The separate tests suggest a model for no parent-offspring and no spouse correlations (models 3 and 4). However, the best model by likelihood ratio test and by AIC was for a single familial correlation (where sib = parent-offspring) and with no spouse correlation (AIC = 2.31). After $\dot{V}O_{2vt}$ was adjusted for FM and FFM ($B2\dot{V}0_{2vt}$), only the sibling correlations were significant by likelihood ratio. However, the most parsimonious model by AIC was for no spouse correlation and a single correlation model where parent-offspring = siblings (models 4 + 6, AIC = 2.11).

For the age-adjusted VT%$\dot{V}O_{2max}$ ($B1\%\dot{V}O_{2max}$) in Whites, the best model by AIC was for a single correlation (i.e., spouse = parent-offspring = sibling), although none of the correlations were strictly significant by likelihood ratio test. After VT%$\dot{V}O_{2max}$ was adjusted for FM and FFM ($B2\%\dot{V}O_{2max}$), the "best" model was for only a spouse correlation (i.e., parent-offspring = sibling = 0). The most parsimonious model (AIC = 3.14) for the $\dot{V}O_{2vt}$ ($mL \cdot kg^{-1} \cdot min^{-1}$) response to training ($D1\dot{V}O_{2vt}$) was for a single correlation (model 5).

The parameter estimates under both the general and the most parsimonious models are given in Tables 7 (White) and 8 (Black). In the White sample, the maximal heritability estimates at baseline were 58% for $\dot{V}O_{2vt}$ and 38% for VT%$\dot{V}O_{2max}$. Adjustments for FM and FFM were similar. For Whites, the maximal heritability estimate for the response of $\dot{V}O_{2vt}$ to aerobic training was 22%.

In the Black sample, the maximal heritability estimates for baseline $\dot{V}O_{2vt}$ (54%) were similar to those of the White sample regardless of adjustments for FM or FFM. The estimates were similar to those of the White sample for VT%$\dot{V}O_{2max}$ before adjustment for FM and FFM (39%) but not after FM and FFM adjustments, where there was no longer evidence to suggest a nonzero heritability, perhaps because of the small sample size in the Black sample. The response of $\dot{V}O_{2vt}$ to aerobic training in Blacks has a larger estimate of maximal heritability than in the White sample (51%).

DISCUSSION

Significant familial contributions were found for both baseline $\dot{V}O_{2vt}$ and baseline VT%$\dot{V}O_{2max}$ ($\dot{V}O_{2vt}/\dot{V}O_{2max}$), as well as for the response to training. Other important findings were that familial factors accounted for more variance in $\dot{V}O_{2vt}$ (over 50%) than in VT%$\dot{V}O_{2max}$ (less than 40%). Also, adjustments for FM and FFM only affected the heritability for VT%$\dot{V}O_{2max}$ in the Black sample. The only Black versus White differences in the familial effects were for VT%$\dot{V}O_{2max}$ after FM and FFM adjustment (greater

TABLE 5. Goodness of fit tests: White sample.

Model	*df*	χ^2	*P*	AIC
B1$\dot{V}O_{2vt}$ [baseline $\dot{V}O_{2vt}$ (weight, age adjusted)]				
1. General				16.00
2. No sex difference: Off	4	7.08	0.1316	15.08
3. No sex difference: Off or Par	5	7.45	0.1894	13.45
4. No sex or generation difference	6	7.74	0.2580	11.74
5. Same vs opposite sex	5	6.27	0.2808	12.27
6. Sex-specific	4	4.97	0.2900	12.97
7. No sib correlations	3	17.38	0.0006	27.38
8. No PO correlations	4	30.27	<0.0001	38.27
9. No spouse correlation	1	2.56	0.1093	16.56
10. Single correlation	7	8.73	0.2726	10.73*
11. Maternal (mitochondrial)	4	5.76	0.2177	14.76
12. No correlations	8	46.35	<0.0001	46.35
4 + 9	7	9.99	0.1891	11.99
B1%$\dot{V}O_{2max}$ [baseline $\dot{V}O_{2vt}/\dot{V}O_{2max}$ (age adjusted)]				
1. General				16.00
2. No sex difference: Off	4	3.60	0.4629	11.60
3. No sex difference: Off or Par	5	3.78	0.5821	9.78
4. No sex or generation difference	6	4.21	0.6477	8.21
5. Same vs opposite sex	5	3.49	0.6243	9.49
6. Sex-specific	4	3.40	0.4937	12.40
7. No sib correlations	3	5.32	0.1499	15.32
8. No PO correlations	4	10.86	0.0282	18.86
9. No spouse correlation	1	2.84	0.0921	16.84
10. Single correlation	7	4.97	0.6642	6.97*
11. Maternal (mitochondrial)	4	1.56	0.8153	9.56
12. No correlations	8	18.95	0.0151	18.95
4 + 7 + 9	7	10.91	0.1426	12.91
4 + 7	6	7.71	0.2601	11.71
D1$\dot{V}O_{2vt}$ [training response of $\dot{V}O_{2vt}$ (age, baseline adjusted)]				
1. General				16.00
2. No sex difference: Off	4	3.03	0.5535	11.03
3. No sex difference: Off or Par	5	3.65	0.6013	9.65
4. No sex or generation difference	6	3.79	0.7044	7.79
5. Same vs opposite sex	5	3.55	0.6159	9.55
6. Sex-specific	4	2.59	0.6290	10.59
7. No sib correlations	3	2.37	0.5001	12.37
8. No PO correlations	4	5.14	0.2734	13.14
9. No spouse correlation	1	2.19	0.1389	16.19
10. Single correlation	7	4.59	0.7102	6.59*
11. Maternal (mitochondrial)	4	3.35	0.5017	11.35
12. No correlations	8	9.08	0.3356	9.08
9 + 10	7	5.44	0.6064	7.44
7 + 8	7	7.13	0.4155	9.13

* Most parsimonious model.

effect in Whites) and for the $\dot{V}O_{2vt}$ response (greater effect in Blacks).

For baseline $\dot{V}O_{2vt}$, there was no difference in the familial effect between the White and Black samples, respectively, either before (58% and 54%) or after (47% and 46%) the combined adjustments for FM and FFM. For the response to training in $\dot{V}O_{2vt}$, there was evidence of significant familial/genetic influences in both races, with the familial influence for the training response in the Black sample (51%) being greater than and about double that of the familial influence in the White sample (22%).

There was a strong familial component for $\dot{V}O_{2vt}$ in the sedentary state. Although the contributions of genetics and familial environment cannot be separately quantified, inspecting the correlation patterns can lead to inferences about their relative contributions to the variation in the phenotype. The significant spouse correlations for baseline $\dot{V}O_{2vt}$, at least in the White sample, suggest an environmental component as well as a genetic component. Thus, in the sedentary state some individuals will have varying submaximal fitness levels on the basis of genetics and shared familial environment. A β path analysis of the Quebec Family Study sample (17) suggested that nongenetic factors could explain 100% of the transmission of steady-state work rate at a fixed HR of 150 (PWC_{150}) from parents to offspring. In the present study, it is not possible to differentiate genetic versus environmental effects, but it cannot be ruled out that shared environment contributes substantially to the maximal heritability effects though, generally, the parent-offspring and sibling correlations are stronger than the spousal correlations.

These baseline data are similar to submaximal aerobic power results reported by Bouchard et al. (2). In that study, an evaluation of the familial relationship of PWC_{150}, adjusted for body mass, found estimates of the total genetic effect to be about 30–48%. The slightly higher values (47–58%) found in this study may be a result of the controlled heterogeneous sedentary nature of the individuals in the current study or a result of the different variables used to evaluate submaximal fitness. Pérusse et al. (18) and Katzmarzyk et al. (9), using data from the Canadian Fitness Study (11,680 participants from 4,144 nuclear families)

TABLE 6. Goodness of fit tests: Black sample.

Model	*df*	χ^2	*P*	AIC
B1$\dot{V}O_{2vt}$ [baseline $\dot{V}O_{2vt}$ (weight, age adjusted)]				
1. General				6.00
2. No sib correlations	1	6.00	0.0143	10.00
3. No PO correlations	1	3.00	0.0833	7.00
4. No spouse correlation	1	0.18	0.6714	4.18
5. Single correlation	2	0.31	0.8564	2.31*
6. PO = sib	1	0.05	0.8231	4.05
7. No correlations	3	8.99	0.0294	8.99
3 + 4	2	3.11	0.2112	5.11
4 + 6	2	0.31	0.8564	2.31*
B1%$\dot{V}O_{2max}$ [baseline $\dot{V}O_{2vt}/\dot{V}O_{2max}$ (age adjusted)]				
1. General				6.00
2. No sib correlations	1	1.20	0.2733	5.20
3. No PO correlations	1	2.76	0.0967	6.76
4. No spouse correlation	1	1.56	0.2117	5.56
5. Single correlation	2	1.08	0.5827	3.08*
6. PO = sib	1	0.43	0.5120	4.43
7. No correlations	3	4.79	0.1878	4.79
4 + 6	2	1.64	0.4404	3.64
2 + 4	2	2.80	0.2466	4.80
B2$\dot{V}O_{2vt}$ [baseline $\dot{V}O_{2vt}$ (weight, age, FM, and FFM adjusted)]				
1. General				6.00
2. No sib correlations	1	4.02	0.0450	8.02
3. No PO correlations	1	2.59	0.1075	6.59
4. No spouse correlation	1	0.04	0.8415	4.04
5. Single correlation	2	0.33	0.8479	2.33
6. PO = sib	1	0.05	0.8231	4.05
7. No correlations	3	6.74	0.0807	6.74
3 + 4	2	2.71	0.2579	4.71
4 + 6	2	0.11	0.9465	2.11*
B2%$\dot{V}O_{2max}$ [baseline $\dot{V}O_{2vt}/\dot{V}O_{2max}$ (age, FM, and FFM adjusted)]				
1. General				6.00
2. No sib correlations	1	0.83	0.3623	4.83
3. No PO correlations	1	0.00	>0.9999	4.00
4. No spouse correlation	1	2.90	0.0886	6.90
5. Single correlation	2	2.95	0.2288	4.95
6. PO = sib	1	0.20	0.6547	4.20
7. No correlations	3	3.74	0.2909	3.74
4 + 6	2	3.19	0.2029	5.19
2 + 3	2	0.84	0.6570	2.84*
D1$\dot{V}O_{2vt}$ [training response of $\dot{V}O_{2vt}$ (age, baseline adjusted)]				
1. General				6.00
2. No sib correlations	1	1.90	0.1681	5.90
3. No PO correlations	1	1.16	0.2815	5.16
4. No spouse correlation	1	2.33	0.1269	6.33
5. Single correlation	2	1.14	0.5655	3.14*
6. PO = sib	1	0.00	>0.9999	4.00
7. No correlations	3	4.57	0.2061	4.57
4 + 6	2	2.46	0.2923	4.46

* Most parsimonious model.

estimated general heritability of 28% for PCW_{150} but, like the current study, could not differentiate between genetic and environmental transmission. The results from the Canadian Fitness Study are similar, though of lesser magnitude, to the results from the current analyses. Most recently, using data for White HERITAGE participants, Pérusse et al. (20) reported that the maximal heritability of several measures of submaximal fitness corrected for weight, age, and sex ($\dot{V}O_2$ at PO of 50 W, 60%$\dot{V}O_{2max}$, 80%$\dot{V}O_{2max}$ and PO at 60%$\dot{V}O_{2max}$, 80%$\dot{V}O_{2max}$) reached values ranging from 48–74%. In the current study, baseline $\dot{V}O_{2vt}$ averaged 55% of $\dot{V}O_{2max}$ and had a maximal, weight-, and age-adjusted heritability for Whites of 58%. This compares favorably with the 50% maximal heritability for 60%$\dot{V}O_{2max}$ determined by Pérusse et al.

For VT%$\dot{V}O_{2max}$, the pattern of results was quite similar to those for $\dot{V}O_{2vt}$, except that the magnitude of the effect was lower (38% and 39% for Whites and Blacks, respectively) than for $\dot{V}O_{2vt}$. However, in the Black sample, the familial effects appeared to be entirely explained by FM and FFM. In an analysis of the HERITAGE data, we have found that $\dot{V}O_{2vt}$ declines at a slower average rate of -0.113 $mL \cdot min^{-1} \cdot kg^{-1} \cdot yr^{-1}$ between ages 17 and 65 in our study population, than does $\dot{V}O_{2max}$ (-0.465 $mL \cdot min^{-1} \cdot kg^{-1} \cdot yr^{-1}$). These differences in the age-related loss in submaximal versus maximal cardiorespiratory fitness account for 43% of the variance in VT%$\dot{V}O_{2max}$ with age. Furthermore, the $\dot{V}O_{2vt}$ heritability data presented in the present study and the heritability in HERITAGE of $\dot{V}O_{2max}$ reported by Bouchard et al. (6) probably contribute significantly to the reported familial component of VT%$\dot{V}O_{2max}$, at least in the White sample.

Finally, the maximal heritability in the response to training of $\dot{V}O_{2vt}$ in the current study is similar to results found by others. Pérusse et al. (22) found maximal heritability in the

TABLE 7. Parameter estimates (± SE) under general and parsimonious models: White subsample.[a]

	Parameter	General	Parsimonious
B1$\dot{V}O_{2vt}$ [baseline $\dot{V}O_{2vt}$ (weight, age adjusted)]	FM	0.25 + 0.15	0.34 + 0.06
	FS	0.43 + 0.08	0.34
	FD	0.37 + 0.12	0.34
	MS	0.21 + 0.12	0.34
	MD	0.50 + 0.11	0.34
	SS	0.18 + 0.14	0.34
	DD	0.52 + 0.13	0.34
	SD	0.35 + 0.09	0.34
	h^2	58%	
B1%$\dot{V}O_{2max}$ [baseline $\dot{V}O_{2vt}$/$\dot{V}O_{2max}$ (age adjusted)]	FM	0.40 ± 0.18	0.20 ± 0.06
	FS	0.31 ± 0.09	0.20
	FD	0.13 ± 0.13	0.20
	MS	0.17 ± 0.20	0.20
	MD	0.23 ± 0.13	0.20
	SS	0.06 ± 0.13	0.20
	DD	0.35 ± 0.18	0.20
	SD	0.17 ± 0.11	0.20
	h^2	38%	
D1$\dot{V}O_{2vt}$ [training response of $\dot{V}O_{2vt}$ (age, baseline adjusted)]	FM	0.35 ± 0.19	0.11 ± 0.06
	FS	0.14 ± 0.12	0.11
	FD	–0.01 ± 0.13	0.11
	MS	0.29 ± 0.12	0.11
	MD	–0.05 ± 0.21	0.11
	SS	0.14 ± 0.13	0.11
	DD	–0.09 ± 0.18	0.11
	SD	0.13 ± 0.11	0.11
	h^2	22%	

[a] Values without standard errors were either fixed to zero or equated with a preceding parameter.

TABLE 8. Parameter estimates (± SE) under general and parsimonious models: Black subsample.[a]

	Parameter	General	Parsimonious
B1$\dot{V}O_{2vt}$ [baseline $\dot{V}O_{2vt}$ (weight, age adjusted)]	FM	0.13 + 0.31	0
	PO	0.27 + 0.14	0.27 + 0.09
	SIB	0.31 + 0.13	0.27
	h^2	54%	
B1%$\dot{V}O_{2max}$ [baseline $\dot{V}O_{2vt}$/$\dot{V}O_{2max}$ (age adjusted)]	FM	0.59 ± 0.27	0.21 ± 0.11
	PO	0.29 ± 0.14	0.21
	SIB	0.15 ± 0.14	0.21
	h^2	39%	
B2%$\dot{V}O_{2max}$ [baseline $\dot{V}O_{2vt}$/$\dot{V}O_{2max}$ (age, FM, and FFM adjusted)]	FM	0.86 ± 0.12	0.86 ± 0.12
	PO	0.01 ± 0.22	0
	SIB	0.13 ± 0.14	0
	h^2	0%	
D1$\dot{V}O_{2vt}$ [training response of $\dot{V}O_{2vt}$ (age, baseline adjusted)]	FM	0.63 ± 0.22	0.29 ± 0.14
	PO	0.26 ± 0.21	0.29
	SIB	0.27 ± 0.18	0.29
	h^2	51%	

[a] Values without standard errors were either fixed to zero or equated with a preceding parameter.

response to HERITAGE training in several submaximal phenotypes ($\dot{V}O_2$ at PO of 50 W, 60%$\dot{V}O_{2max}$, 80%$\dot{V}O_{2max}$ and PO at 60%$\dot{V}O_{2max}$, 80%$\dot{V}O_{2max}$) to range from 23–57% in White families. The intensity of training studied by Pérusse et al. that best corresponds to the intensity of exercise at VT for this population is the training response for $\dot{V}O_2$ at 60%$\dot{V}O_{2max}$. The maximal heritability in White families of 23% for the 60%$\dot{V}O_{2max}$ phenotype compares favorably with maximal heritability of 22% for White families in the current study.

The evidence for a genetic influence in the $\dot{V}O_{2vt}$ response to a standardized aerobic training program suggests that there are genetic factors, as well as the shared exercise program, influencing the training response. Gaskill et al. (8) previously reported that the absolute intensity of exercise training during the final 6 wk of the HERITAGE exercise program was responsible for about 28% and 35% (Black and White families, respectively) of the $\dot{V}O_{2vt}$ aerobic exercise training response. Combining the familial and training intensity data would suggest that a maximum of 50% of the $\dot{V}O_{2vt}$ response variability in Whites and 90% in the Black sample could be accounted for by these two variables.

In summary, $\dot{V}O_{2vt}$ has similar maximal heritabilities of 58% and 54% for the White and Black samples, respectively, in the sedentary state after adjustments for age and body mass. In contrast, the $\dot{V}O_{2vt}$ response to training is characterized by apparently divergent familial components (22% and 51%) in Whites and Blacks, respectively.

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