Familial aggregation of submaximal aerobic performance in the HERITAGE Family study

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Division of Kinesiology, School of Medicine, Laval University, Québec, CANADA; Laboratory of Molecular Endocrinology, Laval Hospital Research Center, Ste-Foy, CANADA; Division of Biostatistics and Departments of Genetics and Psychiatry, Washington University Medical School, St. Louis, MO; Department of Health and Kinesiology, Texas A&M University, College Station TX; School of Kinesiology and Leisure Studies, University of Minnesota, Minneapolis, MN; Pennington Biomedical Research Center, Louisiana State University, Baton Rouge, LA; and Department of Kinesiology, Indiana University, Bloomington, IN

ABSTRACT

PÉRUSSE, L., J. GAGNON, M. A. PROVINCE, D. C. RAO, J. H. WILMORE, A. S. LEON, C. BOUCHARD, and J. S. SKINNER. Familial aggregation of submaximal aerobic performance in the HERITAGE Family study. *Med. Sci. Sports Exerc.*, Vol. 33, No. 4, 2001, pp. 597–604. **Purpose:** This study examines the contribution of genetic factors to submaximal aerobic performance phenotypes measured before and after 20 wk of endurance training. **Methods:** Submaximal oxygen consumption ($\dot{V}O_2$) at three power outputs, 50 W ($\dot{V}O_2$50W), 60% ($\dot{V}O_2$60%) and 80% ($\dot{V}O_2$80%) of $\dot{V}O_{2max}$ and power outputs at 60% (PO60%) and 80% (PO80%) of $\dot{V}O_{2max}$ were measured during cycle ergometer exercise tests in 483 subjects from 99 white families participating in the HERITAGE Family study. The baseline phenotypes were adjusted for the effects of age, sex, and body mass using stepwise multiple regression procedures. The response phenotypes, computed as the difference (Δ) between the posttraining and baseline measures, were adjusted for age, sex, and the baseline value. **Results:** All submaximal exercise phenotypes measured at baseline and in response to training were characterized by a significant familial resemblance. Maximal heritabilities of the baseline phenotypes range from 48% to 74% with significant spouse, sibling, and parent-offspring correlations. The hypothesis of maternal inheritance where mother-offspring and sibling correlations were forced to be equal was found to fit the data for $\dot{V}O_2$60%, $\dot{V}O_2$80% and PO80%. For the response phenotypes, the maximal heritabilities tended to be lower (23–57%) with a significant maternal inheritance for $\Delta\dot{V}O_2$60%, ΔPO60%, and ΔPO80%. **Conclusion:** These results suggest that the submaximal working capacities of sedentary subjects and their responses to endurance training are influenced by familial/genetic factors with a significant contribution of maternal inheritance. **Key Words:** OXYGEN UPTAKE, POWER OUTPUT, EXERCISE TRAINING, GENETICS, HERITABILITY

Cardiorespiratory fitness and its response to regular exercise are characterized by marked interindividual differences (2,12,20). Results from twin and family studies suggest that genetic factors are important in determining this variability (5). Most studies on the heritability of cardiorespiratory fitness were based on twin data and used maximal oxygen uptake ($\dot{V}O_{2max}$) as a phenotype. One of the studies with the largest sample size and comprising 436 pairs of monozygotic (MZ) and 622 pairs of dizygotic (DZ) twins reported an MZ intraclass correlation of 0.62 for predicted $\dot{V}O_{2max}$ compared with 0.29 for DZ twins (21), suggesting an heritability of more than 60% for $\dot{V}O_{2max}$. Another twin study based on smaller number of pairs (29 MZ pairs and 19 DZ pairs) but with a direct measure of $\dot{V}O_{2max}$ and after adjustment for body weight, body fat, and sports participation reported an heritability of 66% (8). The most recent twin study was based on a sample of 105 10-yr-old twins, and their parents reported a heritability above 65% for $\dot{V}O_{2max}$ (13), but this estimate is difficult to interpret as $\dot{V}O_{2max}$ was not adjusted for body mass. The first genetic studies of $\dot{V}O_{2max}$ based on family data (11,14) suggested that about 40% of the variance in $\dot{V}O_{2max}$ could be accounted for by genetic factors. More recently, HERITAGE Family study reports have shown that $\dot{V}O_{2max}$ in the sedentary state (4) and in response to a standardized endurance training program (3) were characterized by a significant familial resemblance with estimates of heritability reaching about 50% of the phenotypic variance.

Compared with $\dot{V}O_{2max}$, relatively few studies have investigated the role of genetic factors in submaximal aerobic performance and its response to exercise training. Some family data from the Quebec Family Study (16,17) and from a nationally representative sample of the Canadian population (10,15) suggested that physical working capacity measured at a heart rate of 150 beats·min^{-1} was characterized by a significant familial resemblance that was mainly accounted for by shared familial environmental factors. Studies with monozygotic (MZ) twins trained under standardized endurance cycle exercise programs for periods of 15 or 20 wk revealed that O_2 consumption changes measured at a given submaximal power output was characterized by a significant within MZ twin pair resemblance (5), suggesting

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that genetic factors are involved in the trainability of these phenotypes. To our knowledge, the role of genetic factors in determining the response of submaximal aerobic performance to exercise training was not investigated in any population-based family study. Thus, the purpose of the present study was to determine whether or not submaximal exercise capacities and their responses to 20 wk of endurance training were characterized by a significant familial resemblance and assess the heritability of the corresponding phenotypes using data from the HERITAGE Family study.

METHODS

Sample. Subjects of the HERITAGE Family study were used for the purpose of this study. The HERITAGE study is a multicenter study designed to investigate the effects of regular exercise on several cardiovascular disease and diabetes risk factors and to determine the role of genetic factors in the cardiovascular, metabolic, and hormonal adaptations to exercise training. The specific aims, design, and measurements of the study have been described in detail elsewhere (6).

For the present study, a total of 483 whites from two-generation families (184 parents and 299 biological offspring) and ranging in age from 17 to 65 yr were available. Subjects were required to be sedentary at baseline, defined as engaging in no regular physical activities over the previous 6 months, and to be free of any condition or disease that could be aggravated by exercise training. Obese individuals (BMI $>$ 40 $kg \cdot m^{-2}$) were excluded because of potential metabolic abnormalities and exercise difficulties, unless they were able to meet the demands of the training program as judged by a physician. Individuals with resting blood pressure greater than 159 mm Hg for systolic and/or greater than 99 mm Hg for diastolic or those on antihypertensive medications were also excluded. More details about exclusion criteria can be found in Bouchard et al. (6).

Training protocol. Subjects trained on cycle ergometers three times a week for 20 wk using a standardized protocol. Subjects worked at a heart rate (HR) corresponding to 55% of their baseline maximal $\dot{V}O_2$ ($\dot{V}O_{2max}$) for 30 min per session at the beginning. The intensity or duration of the training program were adjusted every 2 wk until the 14th week, at which time subjects trained at a HR associated with 75% of their baseline $\dot{V}O_{2max}$ for 50 min during the remaining of the training protocol. Training intensities were adjusted individually by a computer system recording training data and automatically adjusting the power output (PO) of the cycle ergometer to keep each subject's heart rate within 5 beats of the programmed heart rate during the training sessions. Details about the training program can be found elsewhere (20).

Exercise tests. Three exercise tests were conducted on separate days, before and after training, on SensorMedics ErgoMetrics 800S cycle ergometers (Yorba Linda, CA). These tests, described in detail elsewhere (20), were done at about the same time of the day and with at least 48 h between two tests. First, subjects completed a maximal exercise test. The subjects started pedaling at a PO of 50 W for 3 min with increases of 25 W every 2 min thereafter until volitional exhaustion. Second, subjects performed a submaximal exercise test during which they exercised 8–12 min at an absolute PO of 50 W and for 8–12 min at a relative PO equivalent to 60% of their initial $\dot{V}O_{2max}$. Finally, a submaximal/maximal exercise test was performed, starting with the same protocol as in the submaximal test and then followed by 3 min of exercise at 80% of the subject's initial $\dot{V}O_{2max}$. The resistance was then increased to the highest PO attained in the first test and by 25 W every 2 min thereafter until exhaustion.

Gas exchange variables ($\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}E$, and RER) were recorded using a SensorMedics 2900 metabolic measurement cart throughout each exercise test and reported as the rolling average of the last three 20-s intervals of each exercise stage. The criteria for $\dot{V}O_{2max}$ were: RER $>$ 1.1, plateau in $\dot{V}O_2$ (changes of $<$ 100 $mL \cdot min$ in the last three 20-s intervals) and an HR within 10 $beats \cdot min^{-1}$ of the maximal HR predicted by age. HR was monitored with an electrocardiogram and values were recorded during the last 15 s of each exercise stage of the maximal test and once steady state was achieved at each of the submaximal work rates during the submaximal and submaximal-maximal tests. All subjects achieved a $\dot{V}O_{2max}$ by one of these criteria in at least one of the two maximal exercise tests, both pre- and post-training. The submaximal exercise phenotypes that were used in the present study were $\dot{V}O_2$ at 50 W ($\dot{V}O_2$50W), 60% ($\dot{V}O_2$60%), and 80% ($\dot{V}O_2$80%) of $\dot{V}O_{2max}$ and power outputs (W) at 60% (PO60%) and 80% (PO80%) of $\dot{V}O_{2max}$. Because duplicate measures were available at 50 W and at 60% of $\dot{V}O_{2max}$, the average of the two measures were taken as values for $\dot{V}O_2$50W, $\dot{V}O_2$60%, and PO60%. These submaximal power output levels were selected because we wanted both a measure of O_2 consumption in a 10- to 12-min steady state at an absolute power output level (50 W) that could be sustained by all participants and also higher intensity power output levels which, in this case, were defined in terms of percentages of $\dot{V}O_{2max}$. The response to training was computed as the difference (Δ) between the posttraining and baseline measurements of the same measures. A paired *t*-test on the response scores was used to test for the effects of endurance training.

Data adjustments. Baseline phenotypes were adjusted for the effects of age, sex, and body mass, whereas response phenotypes were adjusted for the effects of age, sex, and baseline value. These adjustments were performed within each of the four sex by generation groups by using a stepwise multiple regression procedure retaining only those terms that were significant at the 5% level. The phenotypes used in the genetic analysis were the residuals from the regression standardized to a 0 mean and a standard deviation of 1. In general, the effects of age and body mass were significant in all groups for submaximal oxygen consumption ($\dot{V}O_2$50W, $\dot{V}O_2$60%, and $\dot{V}O_2$80%) measured at baseline, with about 14–54% of the variance accounted for, whereas for PO60% and PO80% only the age effects were significant (9–21%). For the response phenotypes, age terms were generally not significant, whereas baseline values accounted for 16–23% of the variance in $\dot{V}O_2$50W and 3–12% for the other response phenotypes.

Familial correlation model. Familial aggregation in the baseline and response phenotypes was investigated by computing familial correlations. An ANOVA comparing the between- and the within-family variances was first performed to test whether or not the phenotypes aggregate in families. The familial correlation model was based on four groups of individuals {fathers (*f*), mothers (*m*), sons (*s*), and daughters (*d*)}, giving rise to eight interindividual correlations in three familial classes {1 spouse (*fm*), 4 parent-offspring (*fs*, *fd*, *ms*, *md*), and 3 sibling (*ss*, *dd*, *sd*)}. The maximum likelihood computer program SEGPATH (18) fitted the model directly to the family data under the assumption that the phenotypes within a family jointly follow a multivariate normal distribution. A general model with all eight familial correlations and several reduced models (see Appendix A) testing specific null hypotheses were fitted to the data. Three broad classes of reduced models were considered. First, null hypotheses on sex and/or generation differences in the familial correlations were tested, including no sex differences in the offspring, no sex differences in parents or offspring, and no sex nor generation differences. Second, null hypotheses testing the nature and strength of the familial resemblance were also conducted by familial class, including no sibling resemblance (model 5: ss = dd = sd = 0), no parent-offspring resemblance (model 6: fs = fd = ms = md = 0), no spouse resemblance (model 7: fm = 0), and a environmental model where all eight correlations were equated. Third, five models of maternal inheritance (where mother-offspring and sibling correlations are expected to be equal, i.e., ms = md = sd = ss = dd), with or without restrictions about the father's contribution, were tested. In model 9, the hypothesis of maternal inheritance without any assumption about the father's contribution was tested. Maternal inheritance was also tested under the constraint that the father-offspring correlations were independent of sex (fs = fd, ms = md = sd = ss = dd), that the father's contribution is environmental rather than genetic (fm = fs = fd, ms = md = sd = ss = dd), that the father's contribution is not significant (fm = fs = fd = 0, ms = md = sd = ss = dd), and that the father-mother correlation is not significant (fm = 0, fs = fd, ms = md = sd = ss = dd). These reduced models were tested against the general model using the likelihood ratio test, which is approximately distributed as a χ^2, with the degrees of freedom being the difference in the number of parameters estimated in the two competing hypotheses. The most parsimonious model was derived by combining all nonrejected null hypotheses. In addition to the likelihood ratio test, Akaike's (1) Information Criterion (AIC), which is -2 ln L plus twice the number of estimated parameters, was used to judge the fit of nonnested models. The most parsimonious model by AIC is the one with the smallest value. Maximal heritabilities were computed from the maximum-likelihood estimates of the familial correlations obtained under the most parsimonious model as follows (19):

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

TABLE 1. Descriptive statistics of the sample at baseline and after training in each of the sex and generation groups.[a]

Variable	*N*	Baseline	Posttraining
Fathers			
Age (years)	93	53.6 ± 5.3	
Body weight (kg)	92	87.4 ± 15.4	87.1 ± 15.5
VO_2 50W (ml)	91	1083 ± 130	1047 ± 120
VO_2 60% (ml)	92	1578 ± 282	1776 ± 319
VO_2 80% (ml)	89	2098 ± 367	2380 ± 398
PO 60% (W)	92	96 ± 25	121 ± 27
PO 80% (W)	90	144 ± 32	177 ± 36
Sons			
Age (years)	140	25.4 ± 6.1	
Body weight (kg)	139	82.6 ± 16.8	82.3 ± 16.6
VO_2 50W	138	1091 ± 105	1046 ± 107
VO_2 60%	139	2004 ± 314	2264 ± 328
VO_2 80%	134	2646 ± 391	3003 ± 427
PO 60% (W)	139	134 ± 30	167 ± 32
PO 80% (W)	135	190 ± 38	239 ± 42
Mothers			
Age (years)	91	52.1 ± 5.1	
Body weight (kg)	91	72.4 ± 13.4	72.1 ± 13.3
VO_2 50W (ml)	90	991 ± 108	955 ± 97
VO_2 60% (ml)	89	1020 ± 165	1132 ± 186
VO_2 80% (ml)	82	1358 ± 204	1575 ± 265
PO 60% (W)	88	54 ± 16	69 ± 18
PO 80% (W)	84	85 ± 19	109 ± 23
Daughters			
Age (years)	159	25.5 ± 6.4	
Body weight (kg)	159	64.1 ± 13.3	64.1 ± 13.2
VO_2 50W	154	953 ± 104	919 ± 96
VO_2 60%	159	1254 ± 196	1447 ± 234
VO_2 80%	150	1677 ± 265	1974 ± 300
PO 60% (W)	159	79 ± 17	102 ± 20
PO 80% (W)	150	117 ± 23	151 ± 26

[a] Significant ($P < 0.0001$) effects of endurance training were observed for all submaximal exercise phenotypes.

This heritability estimate includes both genetic and nongenetic sources of variance and is adjusted for the degree of spouse resemblance. For the maternal inheritance models, the maximal maternal heritability was based on the common mother-offspring and sibling correlations.

RESULTS

Table 1 presents the sample sizes, means, and standard deviations for age, body mass, and submaximal exercise capacity before and after training, separately in each of the sex and generation groups (fathers, mothers, sons, and daughters). Endurance training resulted in significant ($P < 0.0001$) improvements of all indicators of submaximal exercise capacity in parents and offspring of both sexes.

The results of the ANOVA performed to test the significance of the familial aggregation indicated significant familial resemblance for all indicators of submaximal exercise capacity and their responses to endurance training (results not shown). There were about 2–5 times more variance between families than within families for the baseline phenotypes, with 38–56% of the variance accounted for by family lines. The response to exercise training was also characterized by a significant familial resemblance which accounted for 30–43% of the variance in the response phenotypes, independent of the baseline values.

The model fitting results for the baseline and the response phenotypes are presented in appendix B. The results for indicators of submaximal $\dot{V}O_2$ and POs at baseline indicate

TABLE 2. Maximum likelihood estimates of familial correlations (± standard error) under the general and most parsimonious models for baseline phenotypes.[a]

Parameter	$\dot{V}O_2$ 50W	$\dot{V}O_2$ 60%	$\dot{V}O_2$ 80%	PO 60%	PO 80%
General model					
fm	0.45 ± 0.08	0.20 ± 0.10	0.14 ± 0.11	0.33 ± 0.09	0.25 ± 0.10
fs	0.39 ± 0.07	0.20 ± 0.09	0.19 ± 0.09	0.22 ± 0.09	0.21 ± 0.09
fd	0.39 ± 0.09	0.14 ± 0.08	0.06 ± 0.07	0.21 ± 0.08	0.17 ± 0.08
ms	0.41 ± 0.08	0.35 ± 0.08	0.36 ± 0.08	0.44 ± 0.08	0.50 ± 0.07
md	0.52 ± 0.06	0.26 ± 0.08	0.28 ± 0.07	0.32 ± 0.07	0.41 ± 0.06
sd	0.42 ± 0.08	0.37 ± 0.07	0.31 ± 0.06	0.46 ± 0.06	0.49 ± 0.06
ss	0.31 ± 0.11	0.41 ± 0.11	0.26 ± 0.12	0.49 ± 0.10	0.52 ± 0.09
dd	0.65 ± 0.07	0.09 ± 0.11	0.003 ± 0.11	0.15 ± 0.11	0.23 ± 0.11
Most parsimonious model					
fm	0.45 ± 0.08	0.17 ± 0.07	0.12 ± 0.07	0.24 ± 0.07	0.20 ± 0.07
fs	{0.45}	{0.17}	{0.12}	{0.24}	{0.20}
fd	{0.45}	{0.17}	{0.12}	{0.24}	{0.20}
ms	{0.45}	0.30 ± 0.05	0.29 ± 0.06	0.38 ± 0.05	0.44 ± 0.05
md	{0.45}	{0.30}	{0.29}	{0.38}	{0.44}
sd	{0.45}	{0.30}	{0.29}	{0.38}	{0.44}
ss	{0.45}	{0.30}	{0.29}	{0.38}	{0.44}
dd	{0.45}	{0.30}	{0.29}	{0.38}	{0.44}
Best maternal inheritance model[b]					
fm	0.41 ± 0.06	0.17 ± 0.07	0.12 ± 0.07	0.24 ± 0.07	0.20 ± 0.07
fs	{0.41}	{0.17}	{0.12}	{0.24}	{0.20}
fd	{0.41}	{0.17}	{0.12}	{0.24}	{0.20}
ms	0.48 ± 0.05	0.30 ± 0.05	0.29 ± 0.06	0.38 ± 0.05	0.44 ± 0.05
md	{0.48}	{0.30}	{0.29}	{0.38}	{0.44}
sd	{0.48}	{0.30}	{0.29}	{0.38}	{0.44}
ss	{0.48}	{0.30}	{0.29}	{0.38}	{0.44}
dd	{0.48}	{0.30}	{0.29}	{0.38}	{0.44}

[a] Values in brackets are fixed or equal to a preceding value; h^2 = maximal heritability computed as described in the methods.
[b] The best maternal model is the most parsimonious model for VO_2 60%, VO_2 80%, PO 60%, and PO 80%.

significant parent-offspring and sibling correlations for all indicators of submaximal working capacity, whereas the spouse correlation was significant only for $\dot{V}O_2$50W, PO60% and PO80%. Except for $\Delta\dot{V}O_2$50W and $\Delta\dot{V}O_2$80%, the model testing maternal inheritance (model 8) could not be rejected, suggesting that familial resemblance could be partly attributable to specific maternal genetic and/or environmental factors.

The familial correlations under the general, the most parsimonious and the best maternal inheritance models (when significant and different from the most parsimonious model) are presented in Tables 2 and 3 for baseline and response phenotypes, respectively. The maximal heritabilities derived from the most parsimonious model and the best maternal inheritance model (where ms = md = sd = ss =dd) are presented in Figure 1. For all baseline phenotypes except $\dot{V}O_2$50W, the best maternal inheritance model was the most parsimonious model. Heritability estimates were 70% and 48% for $\dot{V}O_2$50W; 52% and 30% for $\dot{V}O_2$60%; 48% and 29% for $\dot{V}O_2$80%; 68% and 38% for PO60%; and 74% and 44% for PO80%, under the most parsimonious and the best maternal inheritance models,

TABLE 3. Maximum likelihood estimates of familial correlations (± standard error) under the general and most parsimonious models for the response phenotypes.[a]

Parameter	$\dot{V}O_2$ 50W	$\Delta\dot{V}O_2$ 60%	$\Delta\dot{V}O_2$ 80%	ΔPO 60%	ΔPO 80%
General model					
fm	0.28 ± 0.10	0.14 ± 0.10	0.18 ± 0.11	0.15 ± 0.10	0.16 ± 0.12
fs	0.31 ± 0.09	0.02 ± 0.10	−0.05 ± 0.09	0.14 ± 0.09	0.15 ± 0.10
fd	0.06 ± 0.09	0.09 ± 0.09	0.008 ± 0.10	0.07 ± 0.09	0.18 ± 0.09
ms	0.35 ± 0.08	0.09 ± 0.10	0.09 ± 0.10	0.08 ± 0.10	0.21 ± 0.10
md	0.10 ± 0.09	0.19 ± 0.09	0.22 ± 0.10	0.06 ± 0.10	0.13 ± 0.10
sd	0.40 ± 0.08	0.02 ± 0.09	0.12 ± 0.10	0.19 ± 0.09	0.27 ± 0.09
ss	0.45 ± 0.11	0.19 ± 0.13	0.20 ± 0.12	0.36 ± 0.11	0.48 ± 0.10
dd	0.36 ± 0.09	0.28 ± 0.11	0.35 ± 0.11	0.40 ± 0.11	0.31 ± 0.11
Most parsimonious model					
fm	0.27 ± 0.10	0.12 ± 0.04		0.15 ± 0.10	
fs	0.21 ± 0.06	{0.12}	{0}	0.10 ± 0.06	0.15 ± 0.05
fd	{0.21}	{0.12}	{0}	{0.10}	{0.15}
ms	{0.21}	{0.12}	{0}	{0.10}	{0.15}
md	{0.21}	{0.12}	{0}	{0.10}	{0.15}
sd	0.41 ± 0.06	{0.12}	0.22 ± 0.07	0.27 ± 0.07	0.33 ± 0.07
ss	{0.41}	{0.12}	{0.22}	{0.27}	{0.33}
dd	{0.41}	{0.12}	{0.22}	{0.27}	{0.33}
Best maternal inheritance model					
fm	NS	{0.03}	NS	0.12 ± 0.06	0.16 ± 0.07
fs	NS	{0.03}	NS	{0.12}	{0.16}
fd	NS	{0.03}	NS	{0.12}	{0.16}
ms	NS	0.15 ± 0.05	NS	0.19 ± 0.05	0.26 ± 0.05
md	NS	{0.15}	NS	{0.19}	{0.26}
sd	NS	{0.15}	NS	{0.19}	{0.26}
ss	NS	{0.15}	NS	{0.19}	{0.26}
dd	NS	{0.15}	NS	{0.19}	{0.26}

[a] Values in brackets are fixed or equal to a preceding value; h^2 = maximal heritability computed as described in the methods.
NS, the maternal inheritance was not significant.

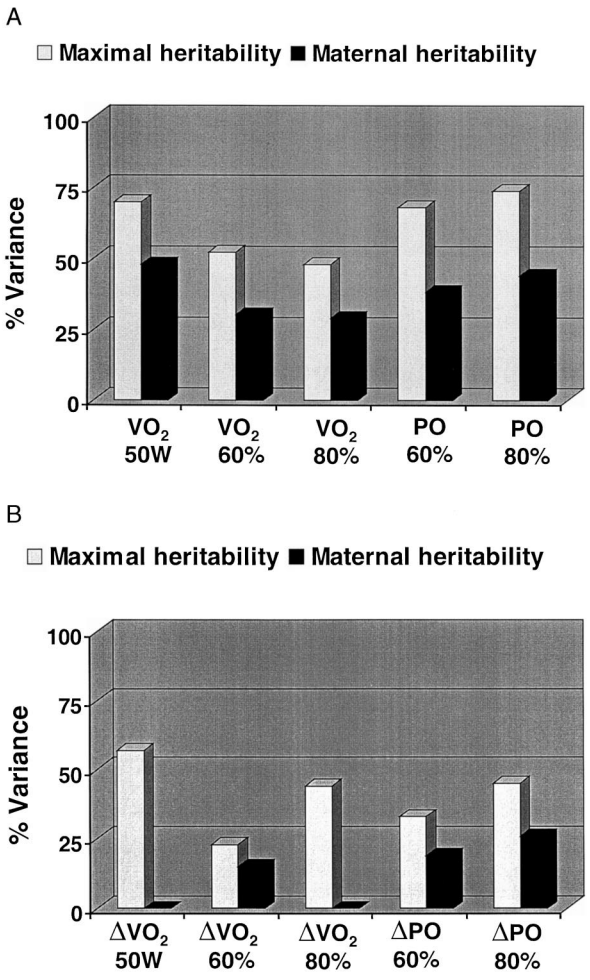

FIGURE 1—Maximal and maternal heritabilities of submaximal oxygen consumption and power outputs in baseline (top) and in response to endurance training (bottom) derived from the most parsimonious and the best maternal inheritance models, respectively.

respectively. The response phenotypes were characterized by lower heritabilities (bottom panel, Fig. 1) than the baseline values. Heritability estimates were 57% and 0% for $\dot{V}O_2$50W; 23% and 15% for $\dot{V}O_2$60%; 44% and 0% for $\dot{V}O_2$80%; 33% and 19% for PO60%; and 45% and 26% for PO80%, under the most parsimonious and the best maternal inheritance models, respectively.

DISCUSSION

The results of the present study suggest that submaximal exercise $\dot{V}O_2$ and PO in sedentary subjects strongly aggregate in families. The changes in the same phenotypes brought about by 20 wk of endurance training, after adjustment for pretraining levels, were also characterized by significant familial resemblance. The heritability estimates derived from the familial correlations computed from spouses, parent-offspring, and siblings ranged from 48% to 74% for the baseline phenotypes and from 23% to 57% for the response phenotypes. These estimates reflect the contribution of both genetic and shared familial environmental factors as, in most cases, the spouse correlations were significant.

The familial correlation model used in the present study cannot distinguish between the contributions of genetic and familial environmental factors in the familial resemblance. For this reason, the heritability estimates presented in Figure 1 are considered as "maximal heritabilities" because they could result from the transmission of both genetic and familial environmental factors. However, the pattern of correlations observed among spouses, parent-offspring, and siblings can be used to make inferences about the relative importance of genetic versus nongenetic factors in the heritabilities. Thus, a pattern of significant parent-offspring and sibling correlations with no spouse correlation would suggest that the familial resemblance is primarily attributable to genetic factors, whereas the presence of significant spouse correlations in addition to the parent-offspring and sibling correlations would suggest the contribution of shared family environment in addition to genetic factors. The latter pattern of familial correlations was observed for all baseline phenotypes. Indeed, we found that the spouse correlations were significant and equal to the parent-offspring correlations, ranging from 0.12 for $\dot{V}O_2$80% to 0.45 for $\dot{V}O_2$50W. The sibling correlations were higher than the spouse and parent-offspring correlations (except for $\dot{V}O_2$50W), ranging from 0.29 to 0.44.

This pattern of familial correlations is similar to the one reported in two other family studies. In the Quebec Family Study (QFS), the PO measured at a heart rate of 150 beats·min^{-1} and expressed per kg of body weight (PWC150/kg) exhibited significant familial resemblance with significant spouse (0.21), parent-offspring (0.14), and sibling (0.25) correlations (16). In another study performed with the same population, maximal heritability, which included the transmission of both genetic and nongenetic factors, reached 22% (17). Familial aggregation of submaximal PO derived from a step test was also investigated in a large sample of the Canadian population involving 13,804 subjects who participated in the 1981 Canada Fitness Survey (15). Familial correlations computed for PWC150·kg^{-1} reached 0.17, 0.17, and 0.26 for spouses, parent-offspring, and sibling pairs, respectively. Analysis of these correlations with a path model, assuming the transmission of both genetic and environmental factors from parent to offspring (without the possibility to distinguish between them), translated into a maximal heritability of 28% (15).

The endurance training program resulted in significant improvements in submaximal performance. The $\dot{V}O_2$ at 50 W was reduced by 10–15% on average, whereas it was significantly increased at the relative POs of 60% (12–16%) and 80% (14–18%). Changes induced by endurance training and adjusted for pretraining values were also characterized by a significant familial resemblance, with maximal heritabilities ranging from 23% to 57% (Fig. 1, bottom panel). These findings suggest that trainability of submaximal working capacities is strongly influenced by familial and/or genetic factors. For $\dot{V}O_2$80% and PO80%, the spouse correlation was not significant, suggesting that genetic factors may be more important than familial environmental factors in determining the trainability of submaximal exercise performed at a high intensity. Other evidence that genetic factors could be involved in

determining the trainability of submaximal aerobic performance comes from twin studies. In a study of six pairs of monozygotic (MZ) twins, total PO during a 90-min ergocycle exercise test was measured before and after 15 wk of endurance training. A highly significant within-pair resemblance was observed for the training gains, with the intraclass coefficient for twin resemblance reaching 0.83 (9). In another study, seven pairs of male MZ twins exercised twice daily while being kept on a constant daily energy intake for 3 months (7). The exercise training protocol resulted in significant improvements in submaximal $\dot{V}O_2$ and in the heart rate measured at fixed POs. Again, changes were characterized by a significant within-pair resemblance. For the changes in $\dot{V}O_2$ measured at 50 W in the latter study, there were 15 times more variance between pairs than within pairs and the intraclass correlation for the resemblance in the response reached 0.87 (7). The results of these twin studies, along with those of the present family study, strongly suggest that the trainability of submaximal exercise capacities is influenced by genetic factors.

Despite similar trends in the familial correlations, the maximal heritabilities reported in this study are higher than those reported in the few other family studies of submaximal working capacities. Besides differences in the analytical strategies used in these studies that could account for some of the differences in the heritability estimates, it is important to keep in mind that the subjects of the present study had to be sedentary. A stringent control over initial physical activity, an important environmental determinant of interindividual differences in submaximal aerobic performances, probably contributed to a reduction of the phenotypic variance and thus to an increase in the heritabilities.

The analytical approach used to investigate the familial resemblance of submaximal aerobic performance in the present study allowed us to specifically test different models of maternal inheritance in which the mother-offspring and sibling correlations were forced to be equal. Our results showed that all submaximal aerobic performance phenotypes measured at baseline could be characterized by a significant maternal component, with the best maternal inheritance model assuming that the father's contribution is environmental rather than genetic (model 10 in Appendix B). To the best of our knowledge, this is the first study to show a significant contribution of maternal inheritance for submaximal aerobic performance phenotypes, as such evidence was not found in the other two family studies for $PWC150 \cdot kg^{-1}$ (15,16). However, a study undertaken in the same cohort of families found a significant maternal heritability for $\dot{V}O_{2max}$ (4). Although the molecular basis of this maternal inheritance is not known, possible mechanisms include 1) contribution of genes from mitochondrial DNA (which are transmitted from the mother only because all mitochondria in a fertilized egg come from the egg only); 2) *in utero* maternal effects not driven primarily by mitochondrial DNA; 3) a genetic effect expressed only when the gene is inherited from the mother; or 4) a maternal cultural transmission.

Heritabilities reported in the present study for submaximal working capacities and their responses to training are slightly higher than those reported recently for $\dot{V}O_{2max}$ in the same population (4). Using the same familial correlation model as the one used here, the maximal heritability of $\dot{V}O_{2max}$ adjusted for age and body mass was 52%. As shown in Figure 1 (top panel), the heritability of $\dot{V}O_2$ measured at a relative PO of 60% and 80% of $\dot{V}O_{2max}$ is very similar to the one reported for $\dot{V}O_{2max}$ in the study of Bouchard et al. (4) and accounts for about 50% of the phenotypic variance after adjustment for age and body mass. However, $\dot{V}O_2$ measured at low intensity exercise appears to be characterized by a stronger genetic effect with a maximal heritability reaching 70% for $\dot{V}O_2$50W. The smaller phenotypic variance of $\dot{V}O_2$50W, which was found to be more influenced by age, sex, and body mass differences than the other baseline phenotypes, could explain the higher heritability of this phenotype.

In summary, results of the present study reveal that submaximal exercise capacities measured in sedentary subjects before and in response to endurance training aggregate in families and that genetic and other familial factors contribute to this familial resemblance. We estimated the maximal heritabilities of the phenotypes to range from about 50–70%. Moreover, we showed the contribution of specific maternal effects in the heritability of these traits, with maternal heritabilities ranging from about 15–48%. Finally, we showed that the trainability of submaximal aerobic performance, independent of the pretraining value, is influenced by genetic factors, confirming the results reported for $\dot{V}O_{2max}$ in the same cohort of families.

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APPENDIX A

Summary of hypotheses testing

MODELS	FM	FS	FD	MS	MD	SD	SS	DD
General								
No sex differences in offspring		FS = FD		MS = MD		SD = SS = DD		
No sex differences in parents or offspring		FS = FD = MS = MD				SD = SS = DD		
No sex nor generation differences		FS = FD = MS = MD = SD = SS = DD						
Environmental model	FM = FS = FD = MS = MD = SD = SS = DD							
No spouse resemblance								
No parent-offspring resemblance								
No sibling resemblance								
No familial resemblance								
Maternal inheritance models								
Without any assumption on father's effect				MS = MD = SD = SS = DD				
No sex differences in father-offspring		FS = FD		MS = MD = SD = SS = DD				
No sex differences in F-O and no spouse		FS = FD		MS = MD = SD = SS = DD				
Father's contribution is environmental	FM = FS = FD			MS = MD = SD = SS = DD				
No other source of familial resemblance				MS = MD = SD = SS = DD				

Gray boxes indicate that the parameter equals zero.

APPENDIX B

Results for Hypothesis Testing for VO_2 50W

PHENOTYPE / MODEL	BASELINE		RESPONSE	
	P-Value	AIC	P-Value	AIC
VO_2 50W				
1. No sex differences in offspring (fs=fd, ms=md, sd=ss=dd, df=4)	0.071	16.62	0.035	18.36
2. No sex differences in parents or offspring (fs=fd=ms=md, sd=ss=dd, df=5)	0.073	16.08	0.060	16.59
3. No sex nor generation differences (fs=fd=ms=md=sd=ss=dd, df=6)	0.091	14.93	0.035	23.41
4. No sibling resemblance (ss=dd=sd=0, df=3)	< .0001	78.30	< .0001	54.00
5. No parent-offspring resemblance (fs=fd=ms=md=0, df=4)	< .0001	58.07	0.0003	28.96
6. No spouse resemblance (fm=0, df=1)	< .0001	33.48	0.823	20.98
7. Environmental model (fm=fs=fd=ms=md=sd=ss=dd, df=7)	0.141	12.95	0.006	21.78
8. Maternal inheritance: Without any assumption on father's effect (ms=md=sd=ss-dd, df=4)	0.084	16.21	0.023	19.33
9. Maternal inheritance: No sex differences in father-offspring (fs=fd, ms=md=sd=ss=dd, df=5)	0.125	14.63	0.008	21.48
10. Maternal inheritance: Father's contribution is environmental (fm=fs=fd, ms=md=sd=ss=dd, df=6)	0.168	13.10	0.010	20.70
11. Maternal inheritance: No other source of familial resemblance (fm=fs=fd=0, ms=md=sd=ss=dd, df=7)	< .0001	40.20	0.0006	27.56
12. Maternal inheritance: No sex differences in F-O and no spouse (fm=0, fs=fd, ms=md=sd=ss=dd, df=6)	< .0001	32.79	0.0007	27.20
Parsimonious: Model 10 (df=6)	0.168	13.10		
Parsimonious: Model 7 (df=7)	**0.141**	**12.95**		
Parsimonious: Models 2 + 6 (df=6)			0.008	21.20
Parsimonious: Model 2 (df=5)			**0.06**	**16.59**

Results for Hypothesis Testing for VO_2 60%

PHENOTYPE / MODEL	BASELINE		RESPONSE	
	P-Value	AIC	P-Value	AIC
VO_2 60%				
1. No sex differences in offspring (fs=fd, ms=md, sd=ss=dd, df=4)	0.192	14.10	0.351	12.43
2. No sex differences in parents or offspring (fs=fd=ms=md, sd=ss=dd, df=5)	0.104	15.12	0.349	11.58
3. No sex nor generation differences (fs=fd=ms=md=sd=ss=dd, df=6)	0.129	13.90	0.456	9.71
4. No sibling resemblance (ss=dd=sd=0, df=3)	< .0001	38.50	0.035	18.62
5. No parent-offspring resemblance (fs=fd=ms=md=0, df=4)	0.0005	28.13	0.239	13.51
6. No spouse resemblance (fm=0, df=1)	0.624	17.47	0.174	15.85
7. Environmental model (fm=fs=fd=ms=md=sd=ss=dd, df=7)	0.189	11.99	0.562	7.81
8. Maternal inheritance: Without any assumption on father's effect (ms=md=sd=ss-dd, df=4)	0.191	14.12	0.354	12.40
9. Maternal inheritance: No sex differences in father-offspring (fs=fd, ms=md=sd=ss=dd, df=5)	0.291	12.16	0.478	10.51
10. Maternal inheritance: Father's contribution is environmental (fm=fs=fd, ms=md=sd=ss=dd, df=6)	0.391	10.29	0.542	9.02
11. Maternal inheritance: No other source of familial resemblance (fm=fs=fd=0, ms=md=sd=ss=dd, df=7)	0.091	14.29	0.450	8.80
12. Maternal inheritance: No sex differences in F-O and no spouse (fm=0, fs=fd, ms=md=sd=ss=dd, df=6)	0.142	13.62	0.383	10.36
Parsimonious: Model 10 (df=6)	**0.391**	**10.29**	0.450	8.80
Parsimonious: Models 2 + 5 + 6 (df=7)			0.099	14.03
Parsimonious: Model 7 (df=7)			**0.562**	**7.81**

Results for Hypothesis Testing for PO 60%

PHENOTYPE / MODEL	BASELINE		RESPONSE	
	P-Value	AIC	P-Value	AIC
PO 60%				
1. No sex differences in offspring (fs=fd, ms=md, sd=ss=dd, df=4)	0.115	15.43	0.387	12.15
2. No sex differences in parents or offspring (fs=fd=ms=md, sd=ss=dd, df=5)	0.047	17.20	0.515	10.24
3. No sex nor generation differences (fs=fd=ms=md=sd=ss=dd, df=6)	0.033	17.69	0.120	14.12
4. No sibling resemblance (ss=dd=sd=0, df=3)	< .0001	56.30	< .0001	32.79
5. No parent-offspring resemblance (fs=fd=ms=md=0, df=4)	< .0001	35.36	0.575	10.90
6. No spouse resemblance (fm=0, df=1)	0.002	23.38	0.169	15.89
7. Environmental model (fm=fs=fd=ms=md=sd=ss=dd, df=7)	0.051	16.02	0.177	12.21
8. Maternal inheritance: Without any assumption on father's effect (ms=md=sd=ss-dd, df=4)	0.141	14.90	0.067	16.78
9. Maternal inheritance: No sex differences in father-offspring (fs=fd, ms=md=sd=ss=dd, df=5)	0.187	13.48	0.106	15.07
10. Maternal inheritance: Father's contribution is environmental (fm=fs=fd, ms=md=sd=ss=dd, df=6)	0.166	13.14	0.156	13.33
11. Maternal inheritance: No other source of familial resemblance (fm=fs=fd=0, ms=md=sd=ss=dd, df=7)	0.007	21.34	0.078	14.78
12. Maternal inheritance: No sex differences in F-O and no spouse (fm=0, fs=fd, ms=md=sd=ss=dd, df=6)	0.009	21.13	0.077	15.41
Parsimonious: Model 10 (df=6)	**0.166**	**13.14**	0.156	13.33
Parsimonious: Models 2 + 5 + 6 (df=7)			0.236	11.24
Parsimonious: Model 2 (df=5)			**0.515**	**10.24**

Results for Hypothesis Testing for VO_2 80%

PHENOTYPE / MODEL	BASELINE		RESPONSE	
	P-Value	AIC	P-Value	AIC
VO_2 80%				
1. No sex differences in offspring (fs=fd, ms=md, sd=ss=dd, df=4)	0.116	15.41	0.120	15.31
2. No sex differences in parents or offspring (fs=fd=ms=md, sd=ss=dd, df=5)	0.013	20.45	0.157	13.98
3. No sex nor generation differences (fs=fd=ms=md=sd=ss=dd, df=6)	0.025	18.49	0.029	18.07
4. No sibling resemblance (ss=dd=sd=0, df=3)	0.0002	30.00	0.004	23.34
5. No parent-offspring resemblance (fs=fd=ms=md=0, df=4)	< .0001	33.60	0.230	13.62
6. No spouse resemblance (fm=0, df=1)	0.215	15.64	0.110	16.55
7. Environmental model (fm=fs=fd=ms=md=sd=ss=dd, df=7)	0.034	17.12	0.033	17.26
8. Maternal inheritance: Without any assumption on father's effect (ms=md=sd=ss-dd, df=4)	0.098	15.82	0.039	18.08
9. Maternal inheritance: No sex differences in father-offspring (fs=fd, ms=md=sd=ss=dd, df=5)	0.091	15.49	0.072	16.10
10. Maternal inheritance: Father's contribution is environmental (fm=fs=fd, ms=md=sd=ss=dd, df=6)	0.147	13.51	0.045	16.87
11. Maternal inheritance: No other source of familial resemblance (fm=fs=fd=0, ms=md=sd=ss=dd, df=7)	0.098	14.08	0.070	15.08
12. Maternal inheritance: No sex differences in F-O and no spouse (fm=0, fs=fd, ms=md=sd=ss=dd, df=6)	0.096	14.76	0.048	16.72
Parsimonious: Model 10 (df=6)	**0.147**	**13.51**		
Parsimonious: Models 2 + 5 + 6 (df=7)			**0.168**	**12.38**

Results for Hypothesis Testing for PO 80%

PHENOTYPE / MODEL	BASELINE		RESPONSE	
	P-Value	AIC	P-Value	AIC
PO 80%				
1. No sex differences in offspring (fs=fd, ms=md, sd=ss=dd, df=4)	0.264	13.23	0.472	11.54
2. No sex differences in parents or offspring (fs=fd=ms=md, sd=ss=dd, df=5)	0.013	20.48	0.617	9.54
3. No sex nor generation differences (fs=fd=ms=md=sd=ss=dd, df=6)	0.006	22.04	0.185	12.80
4. No sibling resemblance (ss=dd=sd=0, df=3)	< .0001	63.92	< .0001	39.27
5. No parent-offspring resemblance (fs=fd=ms=md=0, df=4)	< .0001	44.26	0.070	16.68
6. No spouse resemblance (fm=0, df=1)	0.026	18.94	0.185	15.75
7. Environmental model (fm=fs=fd=ms=md=sd=ss=dd, df=7)	0.009	20.55	0.267	10.81
8. Maternal inheritance: Without any assumption on father's effect (ms=md=sd=ss-dd, df=4)	0.249	13.39	0.149	14.76
9. Maternal inheritance: No sex differences in father-offspring (fs=fd, ms=md=sd=ss=dd, df=5)	0.366	11.42	0.217	13.05
10. Maternal inheritance: Father's contribution is environmental (fm=fs=fd, ms=md=sd=ss=dd, df=6)	0.462	9.66	0.311	11.11
11. Maternal inheritance: No other source of familial resemblance (fm=fs=fd=0, ms=md=sd=ss=dd, df=7)	0.093	14.21	0.079	14.72
12. Maternal inheritance: No sex differences in F-O and no spouse (fm=0, fs=fd, ms=md=sd=ss=dd, df=6)	0.122	14.06	0.141	13.64
Parsimonious: Models 2 + 6 (df=6)			**0.493**	**9.41**
Parsimonious: Models 2 + 5 + 6 (df=7)			0.053	15.90
Parsimonious: Model 10 (df=6)	**0.462**	**9.66**	0.311	11.11