Individual differences in response to regular physical activity

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ABSTRACT

BOUCHARD, C., and T. RANKINEN. Individual differences in response to regular physical activity. *Med. Sci. Sports Exerc.*, Vol. 33, No. 6, Suppl., 2001, pp. S446–S451. **Purpose:** The purpose of this review was to address the question of interindividual variation in responsiveness to regular exercise training and to define the contributions of age, sex, race, and pretraining phenotype level to this variability. **Methods:** A literature review was conducted of the studies reporting interindividual variation in responsiveness to standardized and controlled exercise-training programs, and included an analysis of the contribution of age, sex, race, and initial phenotype values to the heterogeneity in $\dot{V}O_{2max}$, high-density lipoprotein (HDL)-C and submaximal exercise, heart rate (HR), and systolic blood pressure (SBP) training responses in subjects from the HERITAGE Family Study. **Results:** Several studies have shown marked individual differences in responsiveness to exercise training. For example, $\dot{V}O_{2max}$ responses to standardized training programs have ranged from almost no gain up to 100% increase in large groups of sedentary individuals. A similar pattern of heterogeneity has been observed for other phenotypes. Data from the HERITAGE Family Study show that age, sex, and race have little impact on interindividual differences in training responses. On the other hand, the initial level of a phenotype is a major determinant of training response for some traits, such as submaximal exercise heart rate and blood pressure (BP) but has only a minor effect on others (e.g., $\dot{V}O_{2max}$, HDL-C). The contribution of familial factors (shared environment and genetic factors) is supported by data on significant familial aggregation of training response phenotypes. **Conclusions:** There is strong evidence for considerable heterogeneity in the responsiveness to regular physical activity. Age, sex, and ethnic origin are not major determinants of human responses to regular physical activity, whereas the pretraining level of a phenotype has a considerable impact in some cases. Familial factors also contribute significantly to variability in training response. **Key Words:** RESPONSE TO TRAINING, TRAINABILITY, INDIVIDUALITY, FAMILIAL AGGREGATION

We all recognize that a sedentary lifestyle is a risk factor for a number of diseases that become more prevalent with age in both genders. It is even a risk factor for premature death. In contrast, regular physical activity performed in a variety of settings is considered a behavior with favorable consequences on a large variety of health outcomes. The epidemiological, experimental, and clinical evidence for the negative effects of sedentarism and the positive influences of a physically active lifestyle will not be reviewed here. These topics have been addressed in previous consensus meetings and other relevant publications (4,10,16). The number of publications dealing with physical inactivity and activity and their effects on one or several risk factors, health outcomes, or mortality rates is already impressive and is growing. However, it is fair to say that the vast majority of the published studies have emphasized main effects and group differences while paying little attention, if any, to individual differences. It should therefore be appreciated that our present conclusions are based on the average effects observed in groups of boys and girls, men and women, or elderly subjects of both genders.

It needs to be recognized that contributions documented at the level of a group may not fully apply to each member of that group. Little is known about the individuality of the response to long-term exposure to regular exercise, to persistent sedentarism, or fluctuations with age in the level of habitual physical activity. Indeed, most of the data available have been obtained in controlled exercise studies in which subjects were exposed to regular exercise of defined mode, intensity, frequency, and duration conditions sustained for weeks or months. However, from a small body of data, we propose that there are considerable individual differences in the response to regular physical activity, at least in terms of risk factor changes, even when all members of the exercising group are exposed to the same volume of physical activity adjusted for their own tolerance level.

Because there is only a handful of studies that have specifically addressed the issue of individual differences in the response to regular exercise, an assessment of the level of evidence cannot have the same implications as for the other topics covered in the Symposium. We are of the view that, for all cases dealt with below and many others that are beyond this short review, the evidence for the presence of individual differences that are biologically meaningful is extremely strong. What is less clear is the exact nature of the mechanisms responsible for the heterogeneity in response to regular exercise. In most cases, perhaps with the exception

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of $\dot{V}O_{2max}$, the level of evidence concerning the causes of variation in responsiveness is only moderate and probably of Category B or C.

HETEROGENEITY IN RESPONSIVENESS: UBIQUITOUS AND INFORMATIVE

The first publication addressing the topic of individual differences in response to standardized exercise programs goes back only to 1983 (1). It was then emphasized that the mean response to an exercise regimen can be very misleading. For instance, a mean increase in endurance performance of, say, 25% hides the fact that some individuals may have experienced a much lower gain or no increase at all in endurance, whereas some others may have gained as much as 50% and perhaps even more. Such individual differences in trainability have been observed for any phenotype that has been investigated so far when the investigators have looked for them.

Most exercise biologists still consider the heterogeneity of scores in response to training as a nuisance. This is clearly the wrong attitude to adopt. Indeed, individual differences in the response to regular exercise are generally beyond measurement error, largely not random, and are thus informative in terms of the adaptive mechanisms involved. Individual differences for any biological phenomenon are certainly not conceived as a scourge by geneticists who have understood for a long time that biological diversity is part of the human condition and reflects in part genetic diversity.

These notions are obviously relevant to the topic of the dose-response relationship between physical activity and health. The evidence for the presence of individual differences in response to regular exercise will be reviewed with respect to four traits that relate to exercise tolerance and risk factors: maximal oxygen uptake or $\dot{V}O_{2max}$, heart rate response to a standard submaximal power output or HR 50 W, fasting level of plasma HDL cholesterol or HDL-C, and systolic blood pressure during submaximal exercise at 50 W or SBP 50 W. The review draws extensively from the HERITAGE Family Study material as it is, to the best of our knowledge, the only study to date whose goal is to address the extent and the causes of the heterogeneity in the response to regular exercise.

HETEROGENEITY OF THE $\dot{V}O_{2MAX}$ RESPONSE TO REGULAR EXERCISE

In a series of studies that we undertook 20 years ago with about 125 sedentary men and women, we were able to document the magnitude of the heterogeneity of the $\dot{V}O_{2max}$ response to standardized training programs (1,2,14). In these studies, differences in trainability could not be accounted for by age, as subjects were all young adults ranging in age from 17 to 29 yr. Sex of subjects was also not a determinant factor, as the same phenomenon was observed with the same magnitude in both young women and young men. The mean gain in $\dot{V}O_{2max}$ in these experiments was about 25% of the baseline values but with a range from no gain to a doubling of $\dot{V}O_{2max}$ (3). Similar results were subsequently reported by Kohrt et al. (9) in a group of 110 subjects, 60–71 yr of age, who trained for 9 months and more. In these older men and women, they reported a mean increase of 24%, with a range from 0 to 58%.

More extensive data on the phenomenon of individual differences in the trainability of $\dot{V}O_{2max}$ in previously sedentary men and women come from the HERITAGE Family Study (8). One should note here that considerable precautions in HERITAGE were taken to ensure that a valid and reliable measure of $\dot{V}O_{2max}$ was available before and after the exercise regimen. For instance, the baseline level is the mean of 2 $\dot{V}O_{2max}$ tests if there was less than a 5% difference between them or the highest $\dot{V}O_{2max}$ value if the difference was more than 5%. The same protocol was followed for the posttraining $\dot{V}O_{2max}$. Figure 1 depicts the enormous heterogeneity in responsiveness of $\dot{V}O_{2max}$ expressed in mL O_2 gained after being trained for 20 wk and 60 exercise sessions with a highly standardized program. The average increase reached 384 mL O_2 with an SD of 202 mL O_2. The range of response was from about zero gain to an increase of 1000 mL O_2. Figure 2 demonstrates that the same heterogeneity in response levels can be found in those who began the program with a low $\dot{V}O_{2max}$ (below the median in the left panel) and in those who were initially above the $\dot{V}O_{2max}$ median (right panel).

Table 1 (first panel) summarizes the contribution of age, sex, race, and baseline level to the trainability of $\dot{V}O_{2max}$ based on the 720 subjects who had complete data and were compliant with the training program. Age, sex, race, and baseline $\dot{V}O_{2max}$ accounted only for about 11% of the variance in the response to 20 wk of training. The sex of the subject was the largest predictor with a contribution of 5.4%, followed by age with almost 4%. In the HERITAGE Family Study, the relationship between baseline $\dot{V}O_{2max}$ and its response to the training program reached only 1% ($R^2 = 0.011$). Finally black and white differences were trivial, accounting for less than 1%. The

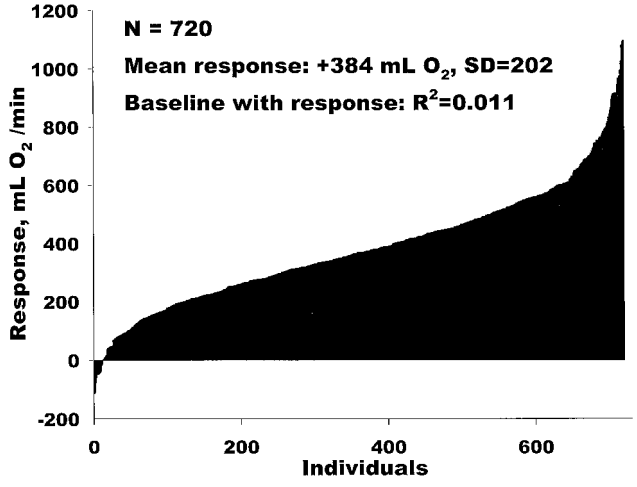

FIGURE 1—Heterogeneity of $\dot{V}O_{2max}$ training response in the HERITAGE Family Study.

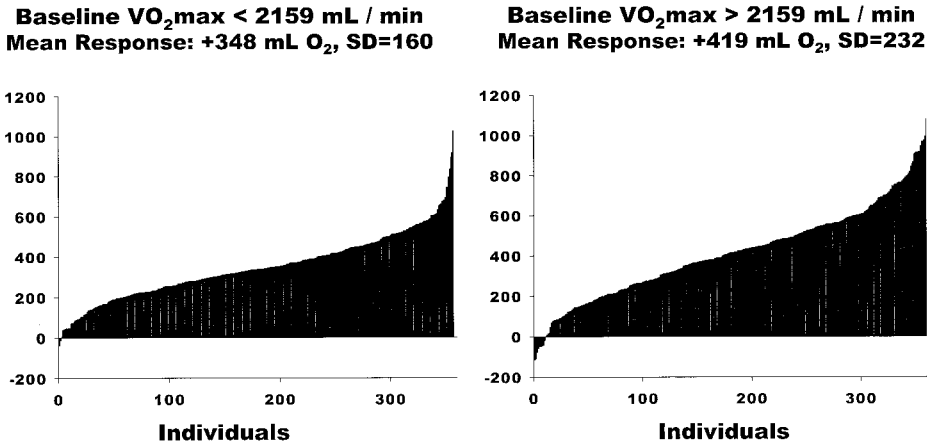

FIGURE 2—Heterogeneity of $\dot{V}O_{2max}$ training response in relation to baseline level in the HERITAGE Family Study.

reproducibility of the trait was investigated, and it was characterized by an intraclass coefficient for repeated tests of 0.97 with a coefficient of variation of 5% and no difference among the four clinical centers of the HERITAGE consortium (7,15).

In contrast, there is a strong familial aggregation for the $\dot{V}O_{2max}$ changes with regular exercise. In one study based on the HERITAGE Caucasian families, the familial aggregation was characterized by an *F*-ratio of 2.5 for the between-family variance divided by the within-family variance ($P < 0.0001$) (8).

HETEROGENEITY OF THE HEART RATE AT 50 W RESPONSE TO REGULAR EXERCISE

Figure 3 depicts individual differences in the changes in heart rate during submaximal exercise at 50 W after the 20-wk exercise program of the HERITAGE Family Study. A mean decrease of 11 beats·min^{-1} was observed among the 727 subjects with complete data. However, the SD reached 10 beats. In this particular case, the baseline level of HR 50 W was strongly and inversely related to the decrease in HR. This is exemplified in Figure 4 in which the subjects with an above-median baseline HR 50 W had a mean decrease of 16 beats·min^{-1}, SD = 10, whereas the subjects who were below the median registered a decrease of only about 7 beats·min^{-1}, SD = 8.

The contributions of sex, age, race, and baseline HR 50 W to the HR 50 W training response are summarized in Table 1 (second panel). Baseline HR 50 W levels were strongly correlated with the decrease in HR, accounting for 40% of the variance in the training-induced decreases in HR 50 W. Sex accounted for another 5%, whereas age and race were only very marginal predictors, accounting for less than 1% of the variance each. The HERITAGE reproducibility study yielded an intraclass coefficient of 0.89 with no difference across four clinical centers for the HR 50 W measurements. The coefficient of variation based on repeated tests reached 5%.

In the whole HERITAGE cohort, there was 1.8 times more variance between families than within families for the HR 50 W response to the 20-wk endurance-exercise program. The response phenotype was adjusted for age, sex, race, and baseline levels.

TABLE 1. A summary of the contributions of age, sex, race, and baseline levels to the responsiveness to regular exercise of indicators of fitness and risks in the HERITAGE Family Study.

Predictor	Partial R^2	Model R^2	F	*P*-Value
$\dot{V}O_{2max}$ training response				
Sex	0.054	0.054	40.8	0.0001
Age^3	0.016	0.069	12.0	0.0006
Age	0.007	0.077	5.6	0.018
Age^2	0.016	0.093	12.8	0.0004
Race	0.008	0.101	6.5	0.011
Baseline $\dot{V}O_{2max}$	0.011	0.112	9.2	0.003
HR 50 W training response				
Baseline HR50	0.404	0.404	490.8	0.0001
Sex	0.050	0.454	66.6	0.0001
Race	0.008	0.462	10.5	0.0012
Age	0.006	0.468	7.5	0.0062
HDL-C training response				
Baseline HDL-C	0.012	0.012	9.0	0.003
Sex	0.009	0.021	6.5	0.011
Race	0.003	0.023	2.0	0.162
Age	0.0001	—	0.1	0.791
SBP 50 W training response				
Baseline SBP50	0.317	0.317	335.3	0.0001
Sex	0.016	0.333	16.8	0.0001
Race	0.0001	—	0.1	0.709
Age	0.0000	—	0.02	0.865

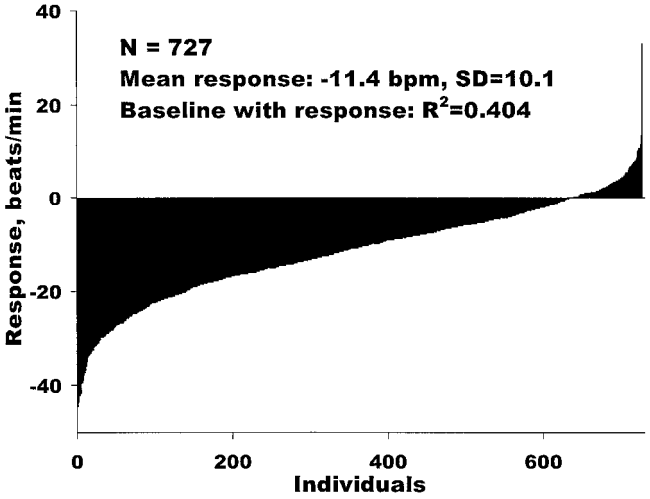

FIGURE 3—Heterogeneity of the training response of HR at 50 W in the HERITAGE Family Study.

Thus, in the aggregate, these observations indicate that there is considerable human variation in the trainability of not only maximal aerobic power but also of submaximal indicators of cardiorespiratory endurance. Even though few studies have dealt with this issue, the evidence for the presence of human heterogeneity is quite strong.

HETEROGENEITY OF THE CHANGES IN HDL-CHOLESTEROL

Surprisingly, the topic of individual differences in the response of HDL-C to regular exercise has received very little attention. Leon et al.(12), using the HERITAGE Family study data, found that heterogeneity in the responsiveness was ubiquitous among the 731 subjects who completed the training protocol and had pre- and post-training HDL-C assay results. They found that when the distribution of the percent changes in HDL-C was broken down into quartiles, the first quartile actually experienced a decrease in HDL-C of 9.3%, whereas the fourth quartile registered a mean increase of 18%. Figure 5 illustrates the extent of the HDL-C training response variation for the whole cohort. The mean increase was only 0.04 mmol·L^{-1} with SD of 0.12 (11). It is commonly accepted that HDL-C of less than 0.9 mmol·L^{-1} is clinically low. We have therefore divided the HERITAGE subjects into those with low HDL-C and those with high values. The heterogeneity in response to regular exercise within each of these two groups is depicted in Figure 6. One can observe that there were more subjects who experienced an increase in HDL-C in the clinically low group (mean increase of 0.05 mmol·L^{-1}, SD = 0.09) than in the high baseline HDL-C category (mean increase of 0.03 mmol·L^{-1}, SD = 0.13).

Table 1 (third panel) summarizes the contribution of age, sex, race, and baseline HDL-C levels to the HDL-C training response in the 731 subjects. Baseline HDL-C accounted for only 1.2% of the exercise-induced HDL-C changes, whereas sex explained almost 1%. Age and race were not significant predictors of these changes. All four variables contributed only about 2% of the variance in exercise-training-induced changes in HDL-C. Based on repeated blood samples and assays, the intraclass coefficient reached 0.94 with no difference across the four HERITAGE clinical centers. The coefficient of variation was about 6%. The *F*-ratio of the between-family variance to the within-family variance for the HDL-C changes in response to a standardized exercise regimen reached 1.8 ($P < 0.0001$) in the HERITAGE cohort.

HETEROGENEITY OF THE CHANGES IN SYSTOLIC BLOOD PRESSURE AT 50 W

To the best of our knowledge, no one has previously addressed the topic of individual differences in the regular exercise-induced changes in blood pressure. Again, we will rely on the HERITAGE Family Study data to illustrate this point. We will be using systolic blood pressure during exercise in relative steady state at 50 W as the HERITAGE subjects were generally normotensive or high normotensive in terms of resting blood pressure. We were able to retrieve a total of 723 HERITAGE subjects with valid SBP 50 W before and after training. Among these subjects, the mean decrease in SBP during cycling at 50 W was 8.2 mm Hg (SD 11.8) (Fig. 7). When the subjects were divided into two groups based on the median value of baseline SBP 50 W, those with the below-median blood pressure values

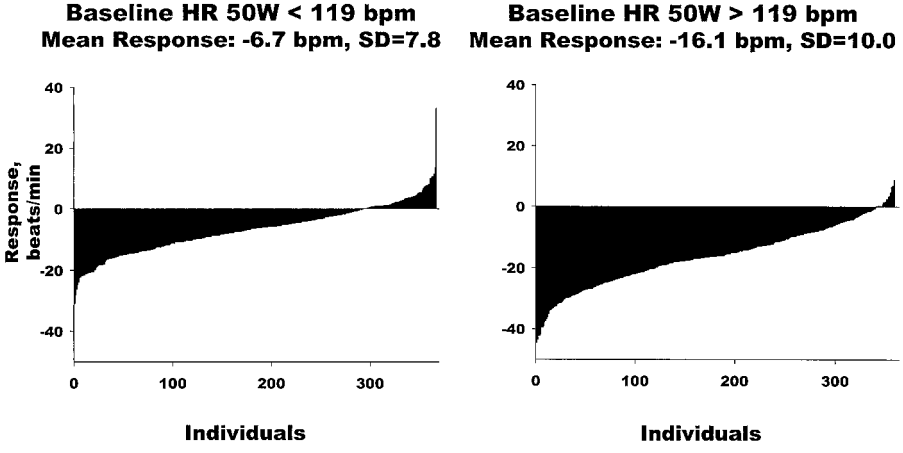

FIGURE 4—Heterogeneity of HR 50 W training response in relation to baseline in the HERITAGE Family Study.

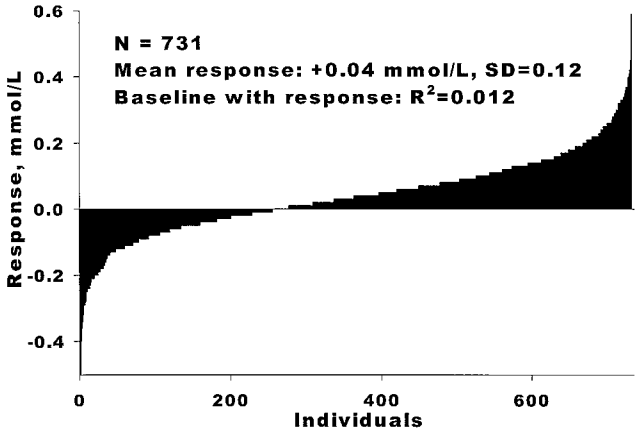

FIGURE 5—Heterogeneity of the training responses of HDL-cholesterol in the HERITAGE Family Study.

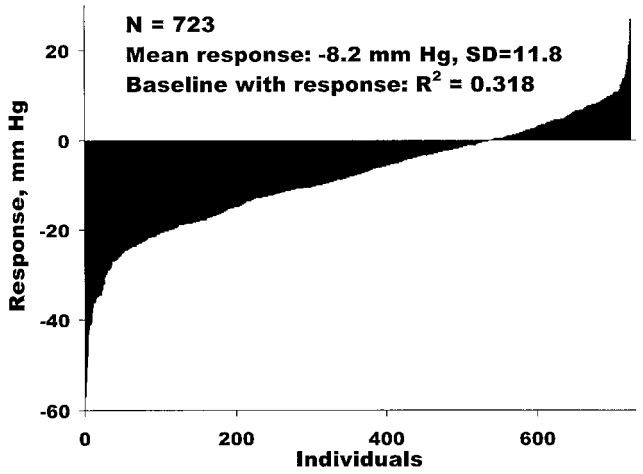

FIGURE 7—Heterogeneity of training response of SBP at 50 W in the HERITAGE Family Study.

experienced only a slight decrease of about 3 mm Hg (SD = 8.8), whereas those above median registered a decrease of 13.4 mm Hg (SD = 12.2) (Fig. 8). However, in both groups, there was considerable heterogeneity in SBP 50 W responsiveness to a standardized exercise regimen. The difference between the two groups was highly significant.

The previous results strongly suggest that the baseline level of SBP 50 W is an important determinant of its responsiveness to regular exercise. This is exactly what was found as shown in Table 1 (lower panel). Indeed, baseline SBP 50 W accounted for 32% of the variance in response, whereas sex explained 1.6%. Age and race were nonsignificant contributors to exercise SBP response to regular exercise. In HERITAGE, SBP 50 W was characterized by an intraclass coefficient for repeated assessments of 0.82 with no variation across clinical centers. The coefficient of variation reached 6%.

There was evidence of familial aggregation for the SBP 50 W response in the HERITAGE cohort with an *F*-ratio ranging from 1.2 to 1.4, depending on the adjustment procedures ($P < 0.02$).

CONCLUSION

The phenomenon described here is not limited to the four phenotypes selected to illustrate the point. It is ubiquitous and commonly observed. For instance, body weight and body composition changes in response to standardized experimental alterations of energy balance are characterized by considerable individual differences under both positive (6,13) and negative (5) energy balance conditions. Similar findings have been reported in a 1-yr randomized trial in both the diet and exercise arms of a study although compliance may have played a role in this case (17) compared with the other studies.

We conclude that there is strong evidence for the notion that there is considerable heterogeneity in the responsiveness of physiological indicators of risk factors to regular physical activity. Unfortunately, data are not available for indicators of morbidity or mortality rates. It is apparent from existing data that age, sex, and ethnic origin are not major determinants of human responses to regular physical activity, whereas the baseline level characteristic of a sedentary state has, in some cases, a considerable impact on the responsiveness. Human heterogeneity in response to regular physical activity is, however, not randomly distributed as it is characterized by familial aggregation.

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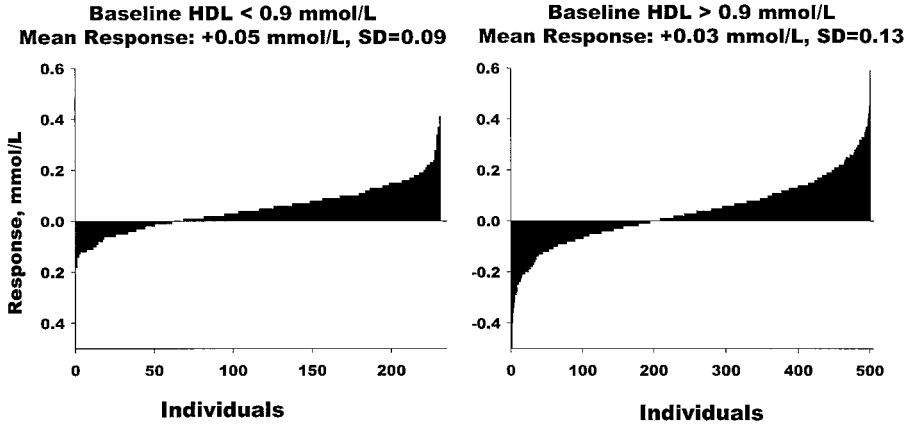

FIGURE 6—Heterogeneity of HDL-cholesterol training response in relation to baseline level in the HERITAGE Family Study.

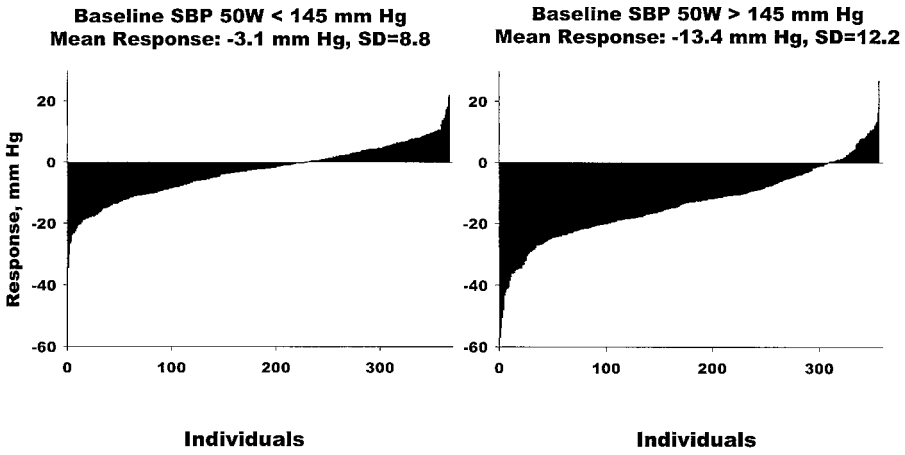

FIGURE 8—Heterogeneity of SBP 50 W training response in relation to baseline level in the HERITAGE Family Study.

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