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Heredity and Health-Related Fitness

A Note From the Editors

In the February Issue of the Physical Activity and Fitness Research Digest we noted the importance of heredity as a factor affecting the development of the health-related physical fitness. We cited the research of Claude Bouchard and colleagues and indicated that a forthcoming issue for the Digest would deal with the influences of heredity on physical fitness in greater detail.

In this issue of the Digest readers have the opportunity to read a synthesis paper on "Heredity and Health-Related Fitness" written by the most prominent scholar in the area. While we have known for some time that heredity was a factor affecting fitness performances, it was not until Dr. Bouchard and his colleagues began their in-depth studies in the area that we began to really know the extent of hereditary influences.

Dr. Bouchard has studied families, especially families with twins, to learn how heredity affects fitness. Heredity (genotypes) affects different fitness components (phenotypes) in different ways. For example two people of the same age and sex with similar lifestyles could vary in health-related fitness just because of the genes they inherited. As noted later in this paper, the heritability for body fatness is 25%+, muscle fitness 20-40%, and CV fitness 10 to 25%.

But Heritability only accounts for differences that heredity might make when comparing two people who have not trained. Bouchard and colleagues have been the pioneers who have demonstrated that not only do people differ in fitness based on heredity, but people of different genetic backgrounds respond differently to training. In other words, two people of different genetic background could do the exact same exercise program and get quite different benefits (see Figure 1). Some people get as much as 10 times as much benefit from activity as others who do the same program.

Though quite technical in some places, the following paper has many practical implications for teachers and professionals in physical activity and fitness. Some of these are listed below:

- Recognizing individual differences is critical in helping students, clients, and patients with fitness achievement. People do not enter our programs with similar backgrounds, nor do they respond similarly to training.
- Assumptions about a person's fitness cannot always be indicative of their current activity levels. The conclusion that the lower fitness of one person compared to another is a result of inactivity is a dangerous one. Those who do not adapt quickly to physical activity need encouragement to keep them involved, no discouragement associated with conclusions about their level of activity and effort.
- Different people (genotypes) respond differently to each part of fitness (phenotype). A person who has less hereditary predisposition to one type of fitness may respond well to another. For this reason we should be careful not to expect people to perform well on all health-related fitness tests just because they score well on one test.

Even those with little technical background can benefit from the paper that follows. Read on!

INTRODUCTION

Health is the culmination of many interacting factors, including the genetic constitution. Humans are genetically quite diverse. Current estimates are that each human being has about one variable DNA base for every 300 bases out of a total of about 3 billion base pairs. Variations in DNA sequence constitute the molecular basis of genetic individuality. Given genetic individuality, an equal state of health and of physical and mental well-being is unlikely to be achieved for all individuals even under similar environmental and lifestyle conditions. Some will thrive better than others and will remain free from disabilities for a longer period of time. Allowing for such individuality, it should thus come as no surprise that there is a minority of adults who remain relatively fit in spite of a sedentary lifestyle.

Genetic differences do not operate in a vacuum. They constantly interact with existing cellular and tissue conditions to provide a biological response commensurate with environmental demands. Genes are constantly interacting with everything in the physical environment as well as with lifestyle characteristics of the individual that translate into signals capable of affecting the cells of the body. For instance, overfeeding, a high fat diet, smoking, and regular endurance exercise are all powerful stimuli that may elicit strong biological responses. However, because of inherited differences at specific genes, the amplitude of adaptive responses varies from one individual to another. Inheritance is one of the important reasons why we are not equally prone to become diabetic or hypertensive or to die from a heart attack. It is also one major explanation for individual difference in the response to dietary intervention or regular physical activity.

HEALTH-RELATED FITNESS

There is no universally agreed upon definition of fitness and of its components. In the present context, we are particularly interested in what is now referred to as health-related fitness, i.e. in the physical and physiological components of fitness that impact more directly on health status. Health-related fitness refers to the state of physical and physiological characteristics that define the risk levels for the premature development of diseases or morbid conditions presenting a relationship with a sedentary mode of life (Bouchard and Shepard, 1993). Important determinants of health-related fitness include such factors as body mass for height, body composition, subcutaneous fat distribution, abdominal visceral fat, bone density, strength and endurance of the abdominal and dorso-lumbar musculature, heart and lung

functions, blood pressure, maximal aerobic power and tolerance to submaximal exercise glucose and insulin metabolism, blood lipid and lipoprotein profile, and the ratio of lipid to carbohydrate oxidized in a variety of situations. A favorable profile for these various factors presents a clear advantage in terms of health outcomes as assessed by morbidity and mortality statistics. The components of health-related fitness are numerous and are determined by several variables, including the individual's pattern and level of habitual activity, diet and heredity.

THE GENETIC PERSPECTIVE

In general, genetic issues can be considered from two different perspectives. The first is from the genetic epidemiology perspective. Here the evidence is derived from samples of human subjects, particularly families, large pedigrees, relatives by adoption or twins. The data can be epidemiological in nature or be enriched by molecular studies. The second perspective is frankly molecular and pertains to transcription, translation, and regulatory mechanisms and how the genes adapt or come into play in response to various forms of acute exercise and of training. In this case, the tissue (generally heart muscle or skeletal muscle) is perturbed by an acute or a chronic stress and the changes are monitored. The emphasis is therefore on the molecular mechanisms involved in the adaptation.

Both approaches are very useful in delineating how important genes are for a given phenotype. However, they differ considerably in the type of information they can provide. The first approach is asking whether individual differences for a given phenotype are caused by DNA sequence variation, gene-environment interactions and gene-gene interactions seen among human beings and, ultimately, what are the genes involved and the specific DNA variants accounting for human heterogeneity. The second approach relies heavily on animal models with a focus on the role of various DNA sequences on regulatory mechanisms with no particular interest for the differences that may exist among members of the species.

The genetic epidemiology approach is of particular interest to us here because it deals with individual differences caused by inherited DNA sequence differences. Results available from the genetic epidemiology perspective will therefore constitute the essential of this review.

HEREDITY AND HEALTH-RELATED FITNESS

Although the literature presents evidence for a role of genetic factors in most of the health-related fitness phenotypes, the quality of the evidence varies according to the phenotype considered. Four major components of health-related fitness will be considered here.

Morphological component

Obesity (body fat content) and regional fat distribution are the phenotypes or morphological fitness that have been studied most by geneticists. Table 1 summarizes the trends emerging from several reviews regarding the contribution of genetic factors to obesity, regional subcutaneous fat distribution, abdominal visceral fat and bone density. The body mass index (BMI), subcutaneous fat (sum of skinfold thicknesses) and percent body fat derived from underwater weighing are among the most commonly used phenotypes in genetic studies of obesity. They are characterized by heritability levels reaching about 25% and at times higher. Results from a few studies suggest that BMI and percent body fat may be influenced by variation at a single or a few genes, although there are conflicting results. The phenotypes associated with regional fat distribution are generally characterized by slightly higher heritability levels with values reaching about 30% to 50% of the phenotypic variance. The trunk to extremity skinfolds ratio as a marker of regional subcutaneous fat distribution has been found to be influenced by major effects, possibly associated with variation at a single gene, suggesting that the pattern of fat deposition between the trunk and the limbs is significantly conditioned by genetic factors.

TABLE 1. An overview of trends in heritability data for selected factors of morphological fitness

Phenotype	Heritability ^a	Familial environment ^b
Body fat Content	~25%	Weak
Distribution of Subcutaneous fat	30-50%	Weak
Visceral fat	30-60%	Unknown
Bone density	30-60%	Weak

- a) Approximate proportion of the variation in the phenotype compatible with a genetic transmission after removing the effects of age and sex.
b) Conditions shared by individuals living together.

Muscular component

This fitness component is probably the one for which the evidence for a contribution of genetic factors is the least abundant. Two studies used family data to study familial transmission of muscular fitness. In one study (Pérusse et al., 1988), muscular endurance and muscular strength measurements were obtained in 13,804 subjects who participated in the 1981 Canada Fitness Survey. The results showed that about 40% of the phenotypic variance in muscular endurance and muscular strength could be accounted for by factors transmitted from parents to offspring. In the Quebec Family Study (Pérusse et al., 1987), we found a genetic effect of 21% for muscular endurance and 30% for muscular strength. These results suggest that the heritability of muscular fitness is significant and ranges from low to moderate.

Cardiorespiratory component

Cardiorespiratory fitness is a major component of health-related fitness and depends on a large number of phenotypes associated primarily with cardiac, vascular and respiratory functions. Measurements of submaximal exercise capacity and maximal aerobic power are generally performed to assess cardiorespiratory fitness. The contribution of genetic factors to these two phenotypes has been recently reviewed (Bouchard et al, 1992) and estimates of heritability were found to be lower for submaximal exercise capacity (about 10%) than for maximal aerobic power (about 25%). These inherited differences in cardiorespiratory fitness may be partly explained by interindividual differences in heart structures and functions, but relatively little is known about the role of heredity on these determinants despite evidence for significant familial aggregation.

Because of the high prevalence of hypertension in most developed countries and its association with an increased risk of death from myocardial infarction or stroke, the genetic and non-genetic determinants of blood pressure have been extensively studied in various populations. Overall, it is clearly established that blood pressure aggregates in families and heritability estimates reported from various populations are remarkably similar, accounting for about 30% of the interindividual differences. More recently, several specific genes have been implicated in the determination of the susceptibility to hypertension.

Metabolic component

There is increasing evidence that the metabolic component of health-related fitness should be considered as an important element of the relationship between physical activity and health. The metabolic component refers to normal blood and tissue carbohydrate and lipid metabolisms and adequate hormonal actions, particularly insulin. A large number of studies have been reported on the genetics of blood lipids and lipoproteins, because of their predominant role in the etiology of cardiovascular disease. Briefly, genetic factors contribute to interindividual difference in blood lipids and lipoproteins with heritability estimates generally accounting for about 25% to as much as 98% of the phenotypic variance, depending on the trait considered with an average value of 50%. Major gene effects have been reported for most of the phenotypes including total cholesterol, LDL-cholesterol, HDL-cholesterol, various apolipoprotein concentrations and Lpa. Highly significant genetic effects have also been reported for fasting glucose and insulin values as well as for plasma fibrinogen, a protein involved in blood clotting. The glucose and be characterized by lower heritability estimates (<25%) than for fasting values.

The contribution of heredity to the various health-related fitness components thus ranges from low to moderate and, except for some phenotypes pertaining to muscular fitness and metabolic fitness, it rarely exceeds 50% of the phenotypic variance and is often below 25%. These low to moderate heritabilities should not be interpreted as an indication that genes are not important in the determination of these phenotypes. These highly complex phenotypes are undoubtedly influenced by a variety of interactions. There is increasing evidence to the effect that interactions between genes and environmental factors or between various genes are common and contribute to interindividual differences in health-related fitness phenotypes and, consequently, cannot be any longer ignored in the field of physical activity, fitness and health.

HEREDITY AND RESPONSE TO EXERCISE

Research has amply demonstrated that aerobic performance, stroke volume, skeletal muscle oxidative capacity and lipid oxidation rates are phenotypes that can adapt to training. For instance, the VO₂max of sedentary persons increases, on the average, by about 20 to 25 percent after a few months of training. The skeletal muscle oxidative potential can easily increase by 50 percent with training and, at times, it may even double. However, if one is to consider a role for the

genotype in such responses to training, there must be evidence of individual differences in trainability. There is now considerable support for this concept (Bouchard, 1986; Lortie et al, 1984). Some indications about the extent of individual differences in the response of maximal oxygen uptake to training are shown in Figure 1. Following exposure to training programs lasting from 15 to 20 weeks in 47 young men, some exhibited almost no change in VO₂max, while others gained as much as on liter of O₂ uptake. Such differences in trainability could not be accounted for by age (all subjects were young adults, 17 to 29 years of age) or gender (all young men). The initial (pre-training) level accounted for about 25 percent of the variance in the response of VO₂max; the lower the initial level the greater the increase with training. Thus about 75% of the heterogeneity in response to regular exercise was not explained.

Similar individual differences were observed for other relevant phenotypes such as indicators of endurance, markers of skeletal muscle oxidative metabolism, markers of adipose tissue metabolism, relative ratio of lipid and carbohydrate oxidized, fasting glucose and insulin levels as well as in their response to a glucose challenge, and fasting plasma lipids and lipoproteins (Bouchard et al, 1992). All these phenotypes respond to regular exercise in the young adults of both sexes. However, there are considerable individual differences in the response of these biological markers to exercise-training, some exhibiting a high responder pattern, while others are almost non-responders and with a whole range of response phenotypes between these two extremes.

What is the main cause of the individuality in the response to training? We believe that it has to do with as yet unidentified genetic characteristics (Bouchard, 1986). To test this hypothesis, we have no performed several different training studies with pairs of identical (MZ) twins, the rationale being that the response pattern can be observed for being that the response pattern can be observed for individuals having the same genotype (within pairs) and for subjects with differing genetic characteristics (between pairs). We have concluded from these studies that the individuality in trainability of cardiovascular fitness phenotypes and in response to exercise- training of cardiovascular risk factors is highly familial and most likely genetically determined. The data are expressed in terms of the ratio of the variance between genotypes to that within genotypes in the response to standardized training conditions. The similarity of the training response among members of the same MZ pair is illustrated in Figure 1 for the VO₂max phenotype based on the result of our first study on this issue (Prud'homme et al, 1984). In this case, 10 pairs of MZ twins were subjected to a fully standardized and laboratory

controlled- training program for 20 weeks and gains of absolute $\dot{V}O_{2\max}$ showed almost 8 times more variance between pairs than within pairs.

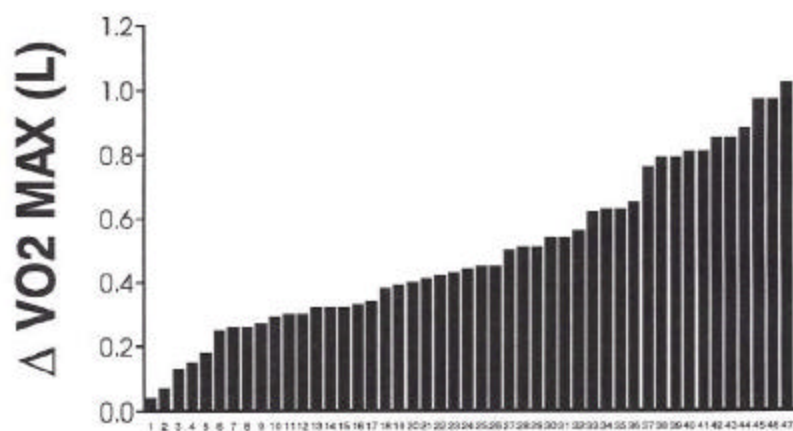


Figure 1. Individual differences in the response of 47 young men to training programs lasting from 15 to 20 weeks. Results are expressed as gains of $\dot{V}O_{2\max}$ in litres of O_2 per minute.

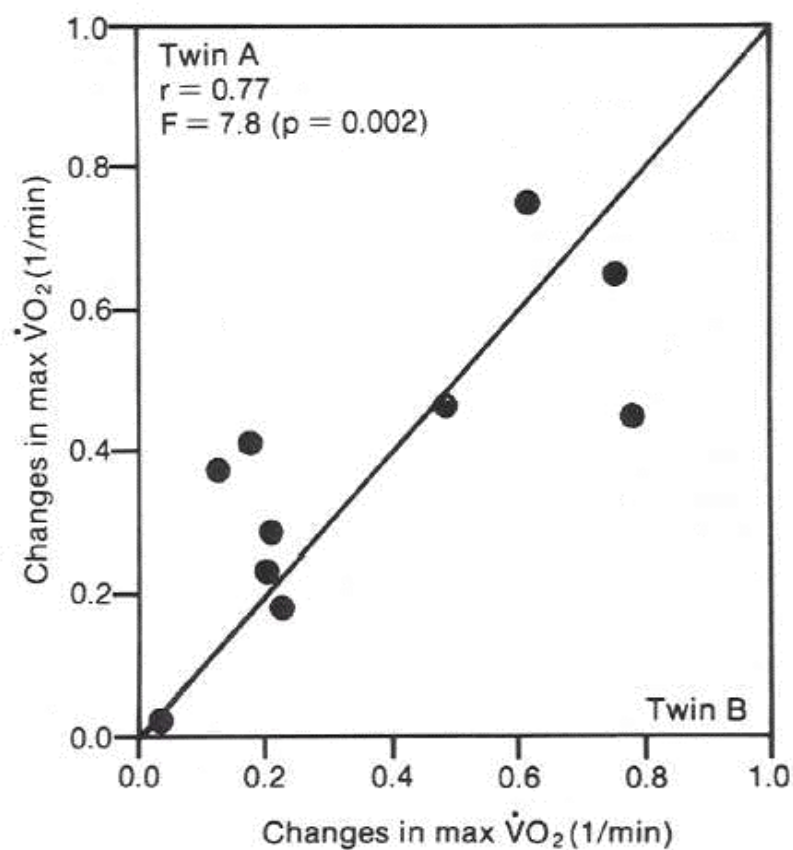


Figure 2. Intrapair resemblance in 10 pairs of monozygotic twins for training changes in $\dot{V}O_{2\max}$ (liters of O_2 per min) after 20 weeks of endurance training. Adapted from Prud'homme et al, *Medicine and Science in Sports and Exercise*, 1984.

Over a period of several years, 26 pairs of MZ twins were trained in our laboratory with standardized endurance and high intensity cycle exercise programs

for periods of 15 or 20 weeks (Bouchard et al, 1992). After 10 weeks of training, the twins were exercising 5 times per week, 45 min. Per session at the same relative intensity in each program. These training programs caused significant increases in $\dot{V}O_{2\max}$ and other indicators of aerobic performance. They were also associated with a decrease in the intensity of the cardiovascular and metabolic responses at a given submaximal power output. For instance, when exercising in relative steady state at 50 watts, there were decreases in heart rate, oxygen uptake, pulmonary ventilation, ventilatory equivalent of oxygen and with an increase in the oxygen pulse. These various metabolic improvements were, however, all characterized by a significant within-pair resemblance (Bouchard et al, 1992). We have made the same observation for the alterations seen in skeletal muscle metabolism following training studies performed on skeletal muscle biopsies obtained before and after the training program in a good number of MZ twin pairs (Simoneau et al, 1986).

Nonpharmacological interventions designed to improve the cardiovascular risk profile center around the cessation of smoking, weight loss by means of dietary restriction and at times regular physical activity, dietary modifications aimed at fat, sodium and fiber intake, and regular exercise in order to improve health-related fitness. Among the expected changes associated with a regular exercise regimen, one finds in a group of sedentary and unfit adults a decrease in resting heart rate and blood pressure, a reduction in fasting plasma insulin level and its response to a glucose load, a decrease in plasma triglycerides and, occasionally, in LDL-cholesterol and total cholesterol, and an increase in plasma HDL-cholesterol. Little is known about the individual differences in the response of these important clinical markers to regular exercise and about the role of genetic variation. We have used the MZ twin design to explore these issues in two studies. In one experiment, 6 pairs of young adult male MZ twins exercised on the cycle ergometer 2 hours per day for 22 consecutive days (Poehlman et al, 1986). The mean intensity of training reached 58 percent of $\dot{V}O_{2\max}$ and the program was designed to induce an energy deficit of about 1,000 kcal per day. Baseline energy intake was assessed and prescribed for the 22 days of the training program. The diet prescription was fully enforced for each subject in the metabolic ward where they lived for the duration of the experiment. The second study was performed on 7 pairs of MZ twins who followed the same regimen for 100 days. The results of both studies are quite concordant. The program induced a significant increase in $\dot{V}O_{2\max}$ and a significant decrease in body fat content. Significant changes were observed in fasting plasma insulin and in the insulin response to an oral glucose tolerance test.

Plasma triglycerides, total cholesterol, LDL-cholesterol and apo B as well as the HDL-cholesterol to total cholesterol ratio were also modified. However, again, significant within MZ pair resemblance was observed for the response of fasting plasma insulin, and LDL-cholesterol ratio were also modified. However, again, significant within MZ pair resemblance was observed for the response of fasting plasma insulin, and LDL-cholesterol, HDL-cholesterol, the HDL-cholesterol to total cholesterol ratio and for the improvement in body fat content and in fat topography. Thus being genetically different translates into heterogeneity in the adaptation to exercise programs.

CONCLUSIONS

Genetic individuality is important because it has an impact on the physical activity, fitness and health paradigm. The results summarized here reveal that there is highly suggestive evidence that genetic variation accounts for most of the individual differences in the response to regular exercise of health-related fitness components and of various risk factors for cardiovascular disease and diabetes. Not only is it important to recognize that there are individual differences in the response to regular physical activity but research also indicated that there are nonresponders in the population. Typically, there is a 3 to 10 fold difference between how responders and high responders, depending upon the phenotype considered, as a result of exposure to the same standardized physical activity regimen for a period of 15 to 20 weeks.

An appreciation of the critical role of DNA sequence variation in human responses to a variety of challenges and environmental conditions has become essential to those interested in the physical activity, fitness and health paradigm. It can only augment our understanding of human individuality and make us more cautious when defining fitness and health benefits that may be anticipated from a physically active lifestyle. Incorporating biological individuality into our thinking will increase the relevance of our observations to the true human situation.

Physical Activity and Fitness Quote

"Not only is it important to recognize that there are individual differences in the response to regular physical activity, but research indicates that there are non-responders in the population. Heredity may account for fitness differences as large as 3 to 10 fold when comparing low and high responders who have performed the same physical activity program."

Claude Bouchard

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