Chapter 24

Genetics of Exercise Behavior

Janine H. Stubbe and Eco J.C. de Geus

Introduction

A sedentary lifestyle has been cited as one of the main causes of the explosive rise in obesity that starts at an increasingly younger age (Martinez-Gonzalez, Martinez, Hu, Gibney, & Kearney, 1999). Furthermore, regular exercisers have lower risks for cardiovascular disease (CVD) and type 2 diabetes than non-exercisers (Albright et al., 2000; Kaplan, Strawbridge, Cohen, & Hungerford, 1996; Kesaniemi et al., 2001) and the percentage of people at risk because of inactivity is higher than for hypertension, smoking, and cholesterol (Caspersen, 1987; Stephens & Craig, 1990). Despite these well-documented benefits of exercise, a large proportion of adults in the Western world do not exercise on a regular basis (Crespo, Keteyian, Heath, & Sempos, 1996; Haase, Steptoe, Sallis, & Wardle, 2004; Stephens & Craig, 1990). As a consequence, a sedentary lifestyle – and the accompanying risk for obesity – remains a major threat to health in today's society. This is reflected in public health recommendations which unanimously include an encouragement to a more active lifestyle (WHO/FIMS Committee on Physical Activity for Health, 1995; U.S. Department of Health and Human Services, 2005).

To increase the success of intervention on this important health behavior, much research has been devoted to the determinants of exercise behavior. The bulk of these studies have attempted to explain low exercise prevalence in terms of social and environmental barriers. These include, amongst others, poor access to facilities (Matson-Koffman, Brownstein, Neiner, & Greaney, 2005; Varo et al., 2003), low socioeconomic status (Haase et al., 2004; Varo et al., 2003), non-Caucasian race (Kaplan, Lazarus, Cohen, & Leu, 1991), high job strain (Payne, Jones, & Harris, 2005; Van Loon, Tijhuis, Surtees, & Ormel, 2000), subjective "lack of time" (Shephard, 1985; Sherwood & Jeffery, 2000), inadequate health beliefs (Haase et al., 2004), and low social support by family, peers, or colleagues (King et al., 1992; Orleans, Kraft, Marx, & McGinnis, 2003; Sherwood & Jeffery, 2000). Despite their face validity, none of these factors has emerged as a strong causal determinant of exercise behavior (Dishman, Sallis, & Orenstein, 1985; Seefeldt, Malina, & Clark, 2002). Increasingly, therefore, biological factors have been invoked to explain why exercisers exercise and why non-exercisers do not (Rowland, 1998; Thorburn & Proietto, 2000; Tou & Wade, 2002). As will become evident in this chapter, these factors should prominently include a genetic disposition to exercise.

Before examining in detail the existing behavior genetics work on this topic, we will briefly go into the definition of exercise behavior and review a number of large-scale studies that give insight into the current prevalence of exercise behavior.

Definition of Exercise Behavior

Operational definitions of exercise behavior have differed strongly across studies. First, a distinction can be made between studies querying "pure" exercise activities (jogging, gymnasia, and all individual or team sports) versus studies including all physical activities which may improve cardiorespiratory health but are not primarily intended that way (gardening, walking the dog, or bicycling to school/work) (Caspersen, Powell, & Christenson, 1985). Even when we restrict ourselves to pure exercise activities in leisure time, exercise definitions differ across studies (Table 24.1). Only two very specific phenotypes have been defined in a highly comparable way. *Sedentary* subjects simply do not engage in any type of leisure time physical activity, whereas *vigorous exercisers* perform activities above the intensity and frequency thresholds required to maintain a continued increase in aerobic fitness above their sedentary level. To achieve such an increase, subjects need to engage in large muscle dynamic

E.J.C. de Geus (✉)
Department of Biological Psychology, Vrije Universiteit, Amsterdam
1081 BT, The Netherlands
e-mail: JCN.de.Geus@psy.vu.nl

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Table 24.1 Three exercise levels used across studies to categorize exercise behavior

Exercise level	Definition
Sedentary	Does not engage in any type of leisure time exercise behavior
Vigorous exercise	Performs leisure time exercise activities above the intensity and frequency thresholds required to maintain a continued increase in aerobic fitness above their sedentary level, i.e., engage in large muscle dynamic exercise activities requiring more than 50% of their maximal oxygen consumption for at least three times a week for 20 min or more per occasion
Light-to-moderate exercise	All exercise behavior in between sedentary and vigorous exercise. A further distinction can be made between light exercise (less than 60 min a week or intensity below 4 METs) and moderate exercise (at least 60 min weekly with a minimum intensity of 4 METs), but note that not all studies collect data on intensity and frequency

exercise activities requiring more than 50% of their maximal oxygen consumption for at least three times a week for 20 min or more per occasion (Blair et al., 1996; Pate et al., 1995).

Measures of *light-to-moderate exercise*, i.e., all activity levels in between sedentary and vigorous exercise, are much harder to compare across studies. Studies use different criteria for the minimum frequency and the minimum intensity that is required to classify participants as "regular exercisers". Criteria for frequency have varied from once per 2 weeks (Haase et al., 2004; Steptoe et al., 1997, 2002) to five or more times a week (Caspersen, Pereira, & Curran, 2000). In some studies the reported specific exercise activities were coded for intensity and had to meet a certain minimal intensity (De Geus, Boomsma, & Snieder, 2003; Perusse, Tremblay, Leblanc, & Bouchard, 1989; Stubbe, Boomsma, & De Geus, 2005), whereas in others no specific exercise activities were reported or no minimum intensity was specified (Haase et al., 2004; Steptoe et al., 1997).

The differences in the operational definition of regular exercise are compounded by the varying methods of assessment of regular exercise. Some studies use surveys with only a single YES/NO question (Boomsma, Vandenbree, Orlebeke, & Molenaar, 1989; Koopmans, Van Doornen, & Boomsma, 1994) whereas others query the type, duration, frequency, and intensity in great detail (Martinez-Gonzalez et al., 2001). Some studies use an interview strategy (Caspersen et al., 2000) rather than a survey-based approach, or even direct measurements of energy expenditure with accelerometry or physiological recording (Pate et al., 2002; Sirard & Pate, 2001). This makes it difficult to either pool or compare the prevalence of exercise behavior across studies. Fortunately, there are five very large studies that, together, provide a reasonable insight into the prevalence of exercise in industrialized societies (Caspersen et al., 2000; Haase et al., 2004; Martinez-Gonzalez et al., 2001; Steptoe et al., 1997, 2002). We will describe their assessment strategies and outcomes in more detail in the next paragraph.

Prevalence of Exercise Behavior

The European Health and Behavior Study (EHBS) (Steptoe et al., 1997) and the International Health and Behavior Study (IHBS1/IHBS2) (Haase et al., 2004; Steptoe et al., 2002) are two large survey studies assessing the prevalence of leisure time physical activity in 18- to 30-year-old university students. The EHBS survey was carried out in 16,483 students from 21 European countries in 1990 (Steptoe et al., 1997). The 2000 IHBS1 and IHBS2 studies used the same measures as the EHBS study and partly the same sample. The IHBS1 study (Steptoe et al., 2002) included 10,336 participants from 13 of the 21 European countries included by the EHBS. The IHBS2 study (Haase et al., 2004) extended the sample by using more countries worldwide resulting in a final sample of 19,298 university students from 23 countries.

In all three studies, leisure time exercise participation was assessed by responses to three items. The first item asked whether an individual had participated in any exercise (e.g., sports activities, physically active pastime) over the past 2 weeks. Those who responded positively were asked what kind of activity they carried out. The most reported forms of activity were jogging/running, swimming, football (soccer), and aerobics. Furthermore, participants were asked how many times they had exercised in the past 2 weeks. Data were analyzed by dividing the sample into three groups. Inactive subjects (i.e., sedentary subjects) did not engage in any exercise at all; subjects who engaged one to four times per 2 weeks in exercise were considered regular exercisers at "low-frequent activity" (corresponding to light to moderate as defined in the previous paragraph); subjects who exercised more than five times per 2 weeks were considered "frequent" exercisers (this corresponds roughly to vigorous exercise in Table 24.1, but note that no intensity was coded). Regular exercise was defined as exercising at least once over the past 2 weeks.

In the 1990 study, 73% of the men and 68% of the women exercised regularly, suggesting that 27% of the male and 32% of the female students are sedentary. A total of 36% of men and 30% of women were vigorous exercisers, i.e., had exercised on five or more occasions during the previous 2 weeks (Steptoe et al., 1997). In the EHBS study (Steptoe et al., 2002), the survey was repeated 10 years later for 13 of the 21 countries (IHBS1). Figure 24.1 shows that the

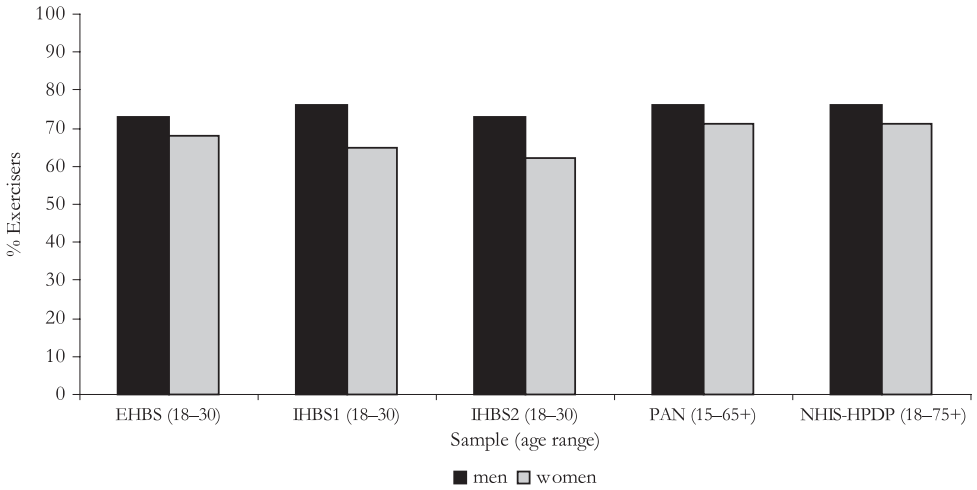

Fig. 24.1 Prevalence of regular exercise in five different studies, the Health and Behavior Study (EHBS, IHBS1, and IHBS2), the pan-European study of adults from 15 member states of the European Union (PAN), and the National Health Interview Survey-Health Promotion/Disease Prevention (NHIS-HPDP)

prevalence of regular exercise remained fairly stable over a 10-year time period. Extending the sample with students from countries worldwide (IHBS2) again resulted in comparable prevalences (Haase et al., 2004).

All three studies showed that men were more likely than women to have exercised in the previous 2 weeks. In the third and largest study, for instance, more women than men reported to be sedentary (38% versus 27%), whereas the proportion engaged in vigorous exercise was larger in men (28%) than that in women (19%). There was no overall difference in the proportion of men (45%) and women (43%) active at light to moderate levels (active one to four times per 2 weeks).

The samples used in the EHBS and IHBS studies may not be representative for the whole population, because it was conducted in students 18–30 year old. A pan-European study (PAN) of adult exercise participation by Martinez-Gonzalez and colleagues (2001) used a population-based sample of more than 15,000 adults from 15 member states of the European Union. Subjects were divided in age bins of 10 years, starting at age 15 and leading up to a final category of subjects aged 65 and over. To assess activity levels, subjects were asked to select the activities in which they participated from a list of 17 activities (i.e., athletics, cycling, dancing, equestrian sports, fishing, football, gardening, golf, hill walking, climbing, keep fit, aerobic, jogging, martial arts, racquet sports, rowing, canoeing, skiing, skating, swimming, team sports, walking, and water sports). Metabolic equivalents (METs) assigned to each activity were used to quantify the amount of leisure time physical activity, with one MET representing the rate of energy expenditure of an individual at rest which is approximately 1 kcal/kg/h (Ainsworth et al., 1993, 2000). Participants also indicated the number of hours a week they participated in each activity. Regular exercise was defined as engaging in any of the queried exercise activities, with constraints on intensity and frequency.

Across the entire age range studied, an average of 76% of the male and 71% of the female EU population participated in some kind of exercise activity. With increasing age, exercise participation decreased, ranging from 83% in 15–24 year old to 65% in people aged 65 years and over. A wide variability was found in the prevalence of exercise activities among European countries. Northern European countries showed higher exercise prevalences than southern ones. Figure 24.1 shows that, across all countries, the overall percentage of regular exercisers is in close agreement with the estimates of prevalence by the EHBS and IHBS studies (Haase et al., 2004; Steptoe et al., 1997; Steptoe et al., 2002). As in the EHBS and IHBS studies, a higher percentage of men engaged in any leisure time exercise activities, and the average intensity of their activities (in METs) was higher than in women.

In the 1991 National Health Interview Survey-Health Promotion/Disease Prevention (NHIS-HPDP) study, physical activity levels were assessed in 43,732 men and women from the USA, aged 18 years and over (Caspersen et al., 2000). Frequency and duration were assessed of gardening and exercise activities (i.e., walking for exercise, stretching exercises, weightlifting, jogging, aerobics, bicycling, stair climbing for exercise, swimming for exercise, play tennis, golf, baseball, basketball, volleyball, handball, soccer, football, racquetball or squash, bowling, and skiing (downhill, cross-country, and water). To get information about the intensity level, questions were asked about increases in breathing or heart rate. According to the Healthy people 2000 objectives (U.S. Department of Health and Human Services, 2005) exercise

behavior of the participants was categorized into three activity patterns: physically inactive (i.e., no participation in any leisure time physical activity), engaging in regular, sustained light to moderate activities (five or more times a week and 30 min or more per occasion of any activity), and engaging in regular, vigorous activities (three or more times per week and 20 min or more per occasion of any activity performed at ≥50% of maximal oxygen consumption). These activity patterns correspond closely to the three exercise levels listed in Table 24.1.

The average prevalence across adulthood for any form of exercise behavior (i.e., light to moderate or vigorous) varied between 73% for women and 79% for men. Women not only had a significantly higher prevalence of being sedentary than men; they also reported less engagement in light to moderate exercise (27% versus 21%). For vigorous activity the difference between men and women was small at 18–29 years (4% more males), moderate at 65–74 years (9% more males), but very large at ≥75 years (16% more males).

A clear picture arises from these five studies. Despite the well-documented benefits of exercise, a large group of young adolescents and adults do not engage in exercise on a regular basis. Worldwide, the prevalence for sedentary behavior varies between 21 and 27% for males and between 27 and 38% for females. Prevalence for light to moderate exercise ranges between 27 and 45% for males and between 21 and 43% for females. Finally, between 28 and 36% of males are engaged in vigorous activities and this percentage varies between 19 and 30% for females.

What factors cause exercisers to exercise and, more importantly, what keeps non-exercisers from doing the same? The remainder of this chapter will review evidence from behavioral genetics for a significant genetic contribution to voluntary exercise.

Family Studies on Exercise Behavior

As with many other traits, exercise behavior appears to run in the family. Familial resemblance in exercise behavior has been tested by the correlation of exercise behavior in parent–child, sister–sister, brother–brother, and sister–brother pairings. Significant familial resemblance in exercise behavior between parents and their offspring has been reported in various studies. Parent–offspring correlations have ranged from low ($r = 0.09$–0.13) for participation defined as activities requiring at least five times the resting metabolic rate (Perusse et al., 1989) or weekly time spent on the main exercise activity during the previous year (Simonen et al., 2002) to moderate ($r = 0.29$–0.37) for exercise participation coded as a dichotomous variable using the single question "Do you participate in sports?" (Koopmans et al., 1994).

In the Canadian Fitness Survey (Perusse, Leblanc, & Bouchard, 1988), the degree of familial resemblance for leisure time energy expenditure, total time spent on leisure time activities and the activity level (derived from total time spent on leisure time activities and total number of months for the reported activities) was assessed in 16,477 subjects, aged 10 years and older. Siblings and parent–offspring pairs were formed to compute familial correlations in energy expenditure, time spent on activities and activity level. These familial correlations ranged between 0.12 and 0.62 for the three variables, suggesting evidence for familial resemblance. However, familial correlations were higher within generations (siblings) than across generations (parent–offspring). Also a significant correlation between spouses was found and, within the same generation, correlations for spouses and siblings were of the same magnitude. This suggested to the authors that familial resemblance resulted primarily from environmental factors common to members of the same generation (i.e., family, neighborhood, facilities, and general cultural attitudes on exercise). However, parent–offspring studies underestimate heritability if different genes are expressed at different ages, and spousal correlations may also partly represent assortative mating.

Twin Studies on Exercise Behavior

Twin studies can directly decompose familial resemblance into shared genetic and shared environmental influences by comparing the resemblance in exercise behavior between monozygotic (MZ) and dizygotic (DZ) twins. As opposed to parent–offspring family designs they do so within members of the same generation. A variety of twin studies have shown that genetic factors contribute to individual differences in exercise participation and measures of exercise frequency, duration, and/or intensity (Aarnio, Winter, Kujala, & Kaprio, 1997; Beunen & Thomis, 1999; Boomsma et al., 1989; De Geus et al., 2003; Frederiksen & Christensen, 2003; Heller et al., 1988; Koopmans et al., 1994; Kujala et al., 2002; Lauderdale et al., 1997; Maia, Thomis, & Beunen, 2002; Perusse et al., 1989; Stubbe et al., 2005, 2006). The main results of these studies are summarized in Table 24.2. Studies were included only if estimates of genetic (a^2 or d^2) or shared environmental (c^2) contribution to total variance were given in the paper or if the correlations of MZ and DZ twins were supplied. The latter makes it possible to calculate the contribution of additive ($a^2 = 2(r_{MZ}–r_{DZ})$ or non-additive ($d^2 = 4r_{DZ}–r_{MZ}$) genetic factors or of shared environmental ($c^2 = 2r_{DZ}–r_{MZ}$) factors (Plomin, DeFries, McClearn, & McGuffin, 2000). Table 24.2 shows these various estimates to range widely across studies. The large range in these estimates may be caused in part

by the use of various definitions of exercise, but as we will argue in detail below, also by the vastly different age ranges studied.

Five twin samples have been used to address the heritability of exercise participation in adolescents. In a large family cohort based on the Quebec family study, a three-day activity record was used to determine the activity level of young adolescent twins (mean age 14.6) (Perusse et al., 1989). Each day was divided into 96 periods of 15 min, and for each 15-min period subjects were asked to note, on a scale from one to nine, the energy expenditure of the dominant physical activity of that period. Regular vigorous exercise behavior was assessed from the number of periods in which exercise activities or moderate to intense manual work (i.e., tree cutting, snow shoveling, etc.) were reported that were rated 6 or higher on the nine-point scale (i.e., activities requiring 4.8 times the resting oxygen consumption). The average value of the ratings across these periods was used as the measure of regular exercise. Monozygotic and dizygotic twin correlations did not differ significantly from each other, indicating that genetic factors explained 0% of the variation in regular exercise behavior. Individual differences in regular exercise were attributed to common environmental (74%) and unique environmental factors (26%).

In a Dutch twin study, exercise participation was assessed in 2,628 young complete twin pairs aged between 13 and 20 (Stubbe et al., 2005). Ainsworth's Compendium of physical activity was used to recode the reported exercise activities into METs. Subjects were classified as regular exercisers if they engaged in competitive or non-competitive leisure time exercise activities with a minimal intensity of four METs for at least 60 min per week. In the classification scheme of Table 24.1 this would include both light to moderate and vigorous exercisers. Genetic and common environmental contributions to exercise participation were computed separately within age groups 13–14 years, 15–16 years, 17–18 years, and 19–20 years. Very large familial resemblance was found at all ages. In agreement with the study by Perusse and colleagues (1989), genes were of no importance to exercise participation in 13- to 16-year-old children, whereas environmental factors shared by children from the same family largely accounted for 78% (15–16 years) to 84% (13–14 years) of the individual differences in participation. Genetic influences started to appear (36%) at the age of 17–18 years with the role of common environment rapidly decreasing (47%). After the age of 18 years, genes almost entirely explain individual differences in exercise participation (85%) and common environmental factors do not contribute at all.

The large shift from common environmental to genetic influences on exercise habits in adolescence implies that studies collapsing twin data across this age range will arrive at "mixture" estimates. That this indeed happens is illustrated by two other studies on the Dutch twins that had previously estimated the genetic and environmental influences on individual differences in exercise participation in Dutch adolescents using smaller samples with larger age ranges (Boomsma et al., 1989; Koopmans et al., 1994). Both studies defined exercise participation by the response to the single question "Have you been involved in exercise activities during the last 3 months?". In 90 adolescent Dutch twin pairs aged 14–20 years (average age = 17 years old) heritability was estimated at 64% for both males and females but evidence for common environment was also suggested (Boomsma et al., 1989). In 1,587 13- to 22-year-old Dutch twins (mean age of 18 years), Koopmans et al. (1994) estimated heritability and common environmental influences to be 48 and 38%, respectively.

A combination of common environmental and genetic influences in adolescence has also been reported by other studies, which additionally suggest a sex difference such that the common environment loses its importance earlier in boys than in girls. In the Leuven Longitudinal Twin Study (Beunen & Thomis, 1999), 92 Flemish male twins and 91 female twins aged 15 years reported the number of hours they exercised each week. For girls, 44% of the variation in exercise participation was explained by genetic factors and 54% by common environmental factors. For boys, genetic factors already explained about 83% of the total variance at age 15. In a study based on 411 Portuguese twins aged 12–25 years (mean age was approximately 17 years) an exercise participation index was computed as a composite score of items that takes into account the expected energy expenditure for a given exercise activity, number of hours practiced per week, and number of months per year (Maia et al., 2002). In agreement with Beunen and Thomis (1999), larger heritability estimates were found for males (68%) compared to females (40%). Finally, Aarnio and colleagues (1997) found substantially lower opposite-sex twin pair correlations than dizygotic same-sex twin pair correlations in 16-year-old Finnish twins, which is again in keeping with a different genetic architecture for males and females in this age range.

To our knowledge, five studies have investigated the influences of genes and environment on exercise behavior in adults (Frederiksen & Christensen, 2003; Heller et al., 1988; Kujala et al., 2002; Lauderdale et al., 1997; Stubbe et al., 2006). An Australian study of 200 twin pairs assessed genetic influences on several lifestyle risk factors, including a single exercise question, "vigorous exercise in the past 2 weeks" (Heller et al., 1988). Ages ranged from 17 to 66 years with the mean ages of MZ and DZ twins being 36.9 (SD = 13.2) and 35.6 (SD = 11.5) years, respectively. Heritability was estimated at 39% for this question. In 3,344 male twin pairs aged 33–51 years from the Vietnam Era Twin Registry (Lauderdale et al., 1997), regular exercise was assessed with five questions about vigorous forms of exercise (>4.5 METs) performed in the last 3 months: (1) jog

Table 24.2 Twin studies on exercise participation

Study	Sample	Phenotype	Categorization	Results
Stubbe et al. (2006)[1]	13,676 MZ and 23,375 DZ pairs from seven different countries participating in the GenomEUtwin project (aged 19–40)[2]	Engage in leisure time exercise activities with a minimal intensity of 4 METs for at least 60 min per week (yes/no)	Light to moderate plus vigorous exercise	a^2 = 27–67%; c^2 = 0–37% for males a^2 = 48–71%; c^2 = 0% for females
Stubbe et al. (2005)[1]	2,628 Complete Dutch twin pairs (aged 13–14, 15–16, 17–18, 19–20)	Engage in leisure time exercise activities with a minimal intensity of 4 METs for at least 60 min per week (yes/no)	Light to moderate plus vigorous exercise	a^2 = 0%; c^2 = 84% for 13- to 14-year-old twins a^2 = 0%; c^2 = 78% for 15- to 16-year-old twins a^2 = 36%; c^2 = 47% for 17- to 18-year-old twins a^2 = 85%; c^2 = 0% for 19- to 20-year-old twins
Beunen et al. (2003)[1]	92 Male and 91 female Belgium twin pairs (aged 15)	Number of hours spent on sports each week	Moderate plus vigorous exercise	a^2 = 83%; c^2 = 0% for males a^2 = 44%; c^2 = 54% for females
De Geus et al. (2003)[1]	157 Adolescent (aged 13–22) and 208 middle-aged Dutch twin pairs (aged 35–62)[2]	Average weekly METs spent on sports or other vigorous activities in leisure time in the last 3 months (≥4 METS)	Moderate plus vigorous exercise	a^2 = 79%; c^2 = 0% for adolescent twins a^2 = 41%; c^2 = 0% for middle-aged twins
Frederiksen et al. (2003)[1]	616 MZ and 642 same-sex DZ twin pairs (aged 45–68)	Engage in leisure time in any of the 11 different exercise activities (yes/no)	Moderate plus vigorous exercise (jogging, gym, swim, tennis, badminton, football, handball, aerobics, rowing, table tennis, volleyball	a^2 = 49%; c^2 = 0% for males and females
Kujala et al. (2002)[3]	Data on both members of 1,772 MZ and 3,551 dizygotic same-sex twin pairs (aged 24–60)	Participation in vigorous physical activity based on the question: "is your physical activity during leisure time about as strenuous, on average, as (1) walking, (2) alternatively walking and jogging, (3) jogging (light running), or (4) running?". Those who chose alternative 2, 3, or 4 were classified as participating in vigorous activity	Vigorous exercise	a^2 = 56%; c^2 = 4% for vigorous activity
Maia et al. (2002)[1]	411 Portuguese twin pairs (aged 12–25)	A composite sports participation index (SPI), that takes into account the energy expenditure for a given sport, number of hours practiced per week, and number of months per year	Moderate plus vigorous exercise	a^2 = 68%; c^2 = 20% for males a^2 = 40%; c^2 = 26% for females

Table 24.2 (continued)

Aarnio et al. (1997)[3]	3,254 Twins at age 16, their parents, and grandparents	The categorical phenotype consisted of five physical activity categories ranging from very active to hardly active based on two questions about the – frequency of leisure time PA – intensity of leisure time PA	Light to moderate plus vigorous exercise	$a^2 = 54\%$; $c^2 = 18\%$ for males $a^2 = 46\%$; $c^2 = 18\%$ for females
Lauderdale et al. (1996)[3]	3,344 Male twin pairs of the Vietnam Era Twin Registry (aged 33–51)	Five questions assessed regular participation in specific, intense athletic activities (running, bicycling, swimming, racquet, and other sports) (yes/no)	Vigorous exercise	$a^2 = 0\%$; $d^2 = 53\%$ for jogging $a^2 = 48\%$; $c^2 = 4\%$ for racquet sports $a^2 = 30\%$; $c^2 = 17\%$ for strenuous sports $a^2 = 0\%$; $d^2 = 58\%$ for bicycling $a^2 = 8\%$; $c^2 = 31\%$ for swimming
Koopmans et al. (1994)[1]	1,587 Adolescent Dutch twin pairs (aged 13–22)	Do you participate in leisure time exercise? (yes/no)	Light to moderate plus vigorous exercise	$a^2 = 48\%$; $c^2 = 38\%$ for males and females
Boomsma et al. (1989)[1]	44 MZ and 46 DZ Dutch adolescent twin pairs (aged 14–20)	Do you participate in leisure time exercise? (yes/no)	Light to moderate plus vigorous exercise	$a^2 = 64\%$
Heller et al. (1988)[3]	200 Twin pairs (aged 17–66)	Engaged in vigorous exercise in the past 2 weeks (yes/no)	Vigorous exercise	$a^2 = 39\%$
Perusse et al. (1989)[3]	55 Monozygotic and 56 dizygotic Canadian twin pairs (aged 15)[2]	A 3-day activity record was used to determine the activity level of the subjects. The number of periods corresponding to activities with an intensity of $\geq$4.8 METs was counted each day and the average value was used as an indicator of exercise participation	Moderate plus vigorous exercise	$a^2 = 0\%$; $c^2 = 78\%$ for males and females

[1]Heritability was estimated using variance component methods.
[2]The variable age is used as a regressor.
[3]Heritability was estimated using formulas to calculate the percentage by hand.

or run at least 10 miles per week, (2) play strenuous racquet sports at least 5 h per week, (3) play other strenuous sports (basketball, soccer, etc.), (4) ride a bicycle at least 50 miles per week, (5) swim at least 2 miles per week. For all of the measures, MZ correlations were higher than DZ correlations, suggesting that genes play a role in explaining individual differences in regular exercise. For running or jogging, racquet sports, and bicycling, broad-sense heritability was estimated between 48 and 58%. For bicycling and jogging, MZ correlations exceeded the DZ correlations by more than a factor of 2, making this the only study to report significant non-additive effects. In a Finnish twin study, heritability was estimated in 3,551 dizygotic same-sex twin pairs and 1,772 monozygotic same-sex twin pairs aged 24–60 years (Kujala et al., 2002). Participation in vigorous physical activity was based on the question: "is your physical activity during leisure time about as strenuous, on average, as (1) walking, (2) alternatively walking and jogging, (3) jogging (light running), or (4) running?". Those who chose alternative 2, 3, or 4 were classified as participating in vigorous activity. Heritability was estimated at 56%.

Recently we conducted the largest twin study on exercise behavior ever (Stubbe et al., 2006). The GenomEUtwin project ("Genome-wide analyses of European twin and population cohorts to identify genes predisposing to common diseases") entails one of the largest research consortia in genetic epidemiology in the world with a collection of over 0.8 million twins. Self-reported data on frequency, duration, and intensity of exercise behavior from Australia, Denmark, Finland, Norway, the Netherlands, Sweden, and the UK were used to create an index of exercise participation in each country. Participants had to be engaged in exercise activities for at least 60 min per week with a minimum intensity of about four METs to be classified as regular exercisers. Results obtained in 85,198 twins aged 19–40 years showed an average percentage of male and female exercisers of 44 and 35%, respectively.

Per country, the estimates of the heritability of regular exercise participation are depicted in Table 24.3. The median heritability of exercise participation was 62% across the seven countries and ranged, in males, from 27% in Norway to 67% in the Netherlands and, in females, from 48% in Australia to 71% in the UK. Shared environmental effects played a role only in exercise participation of the Norwegian males (37%), but were of no importance in the other countries.

Frederiksen and Christensen (2003) were the only ones to report the influence of genetic factors on exercise participation in a group of middle-aged to elderly twins. Information on leisure time exercise participation of people aged 45–68 years was assessed through the questions: "Do you in your leisure time participate in any of the following sports: jogging, gymnastics, swimming, tennis, badminton, football, handball, aerobics, rowing, table tennis, or volleyball?" The exercisers were defined as those indicating participation in any of these activities, whereas the sedentary participants did not report any participation. Genes explained 49% of the variance in exercise participation.

Twin Studies on Physical Activity

Since the innate drive to exercise will be most obvious in leisure time we have focused above on voluntary leisure time exercise behavior. A number of twin studies have quantified regular total physical activity rather than exercise activities limited to leisure time only. Since a large part of regular physical activity in these studies could effectively be attributed to voluntary exercise activities in leisure time, we briefly review these studies here. Slightly more caution is needed in the interpretation of these studies, because the heterogeneity in the definition of regular physical activity will be larger than that in the definition of regular leisure time exercise.

Table 24.4 summarizes the relevant twin studies, again including only those where heritability and "environmentability" estimates or correlations of MZ and DZ twins were given in this chapter. Common environmental influences were again almost completely restricted to children and young adolescents. In adults, reported heritability estimates vary between 46 and 56%. In spite of the larger heterogeneity in the phenotype, Table 24.4 confirms the overall finding that genetic factors contribute significantly to individual differences in physical activity of adults.

Table 24.3 Heritability of exercise participation in subjects aged 21–40 in seven countries participating in the collaborative GenomEUtwin project

Country	No. of complete twin pairs	Percentage exercisers		Heritability estimates	
		Male (%)	Female (%)	Male (%)	Female (%)
Australia	2, 728	64	56	48	48
Denmark	9, 456	43	33	52	52
Finland	8, 842	37	29	62	62
The Netherlands	2, 681	58	55	67	67
Norway	3, 995	55	51	27	56
Sweden	8, 927	37	23	62	62
United Kingdom	422	–	53	–	70

Table 24.4 Twin studies on physical activity level (PA)

Study	Sample	Phenotype	Results
Franks et al. (2005)[1]	100 Same-sex dizygotic ($n = 38$) and monozygotic ($n = 62$) twin pairs (aged 4–10)	(1) Physical activity energy expenditure (PAEE) (2) Total energy expenditure (TEE) labeled water	$a^2 = 0\%$; $c^2 = 69\%$ $a^2 = 19\%$; $c^2 = 59\%$
Maia et al. (2002)[1]	411 Portuguese twin pairs (aged 12–25)	The continuous variable leisure time PA is a composite score based on the following four items: – hours watching TV – frequency of walking in leisure time – minutes spent walking per day – frequency of cycling	$a^2 = 63\%$; $c^2 = 0\%$ for males $a^2 = 32\%$; $c^2 = 38\%$ for females
Kujala et al. (2002)[2]	Data on both members of 1,772 MZ and 3,551 dizygotic same-sex twin pairs (aged 24–60)	Assessment of leisure time physical activity was based on a series of structured questions on leisure PA (frequency, duration, and intensity of PA sessions) and PA during journey to and from work. The activity MET index was expressed as the summary score of leisure MET-hours per day. Subjects whose volume of activity was ≥2 MET-hours per day were classified as physically active at leisure	$a^2 = 46\%$; $c^2 = 0\%$
Perusse et al. (1989)[1]	55 Monozygotic and 56 dizygotic Canadian twin pairs (aged 15)	A 3-day activity record was used to determine physical activity of the subjects. Each day was divided into 96 periods of 15 min, and for each 15-min period the subjects were asked to note on a scale from 1 to 9 the energy expenditure of the dominant activity of that period. The categorical scores were summed over the 96 15-min periods of each day and the mean sum of the 3 days was used as an indicator of the level of habitual PA	$a^2 = 20\%$; $c^2 = 52\%$
Perusse et al. (1989)[1]	55 Monozygotic and 56 dizygotic Canadian twin pairs (aged 15)	A 3-day activity record was used to determine physical activity of the subjects. Each day was divided into 96 periods of 15 min, and for each 15-min period the subjects were asked to note on a scale from 1 to 9 the energy expenditure of the dominant activity of that period. The categorical scores were summed over the 96 15-min periods of each day and the mean sum of the 3 days was used as an indicator of the level of habitual PA	$a^2 = 20\%$; $c^2 = 52\%$
Kaprio et al. (1981)[2]	1,537 MZ and 3,507 DZ male twin pairs (aged ≥18 years)	Leisure time PA was based on the amount of physical activity currently engaged in, its intensity and duration, and number of years of physical activity engaged in the adult life. The intensity and duration scores were multiplied together to obtain an activity score	$a^2 = 46\%$; $d^2 = 11\%$ (age adjusted)

[1]Heritability was estimated using variance component methods.
[2]Heritability was estimated using formulas to calculate the percentage by hand.

Differences in Genetic Architecture of Exercise Behavior Across the Life Span

When we summarize the studies reviewed in Tables 24.2, 24.3 and 24.4, two striking findings stand out: (1) the genetic architecture of exercise behavior is vastly different across the life span with the largest differences seen between the ages 15 and 20 and (2) all studies in *adult* twins consistently suggest a significant genetic contribution to adult exercise participation. Figure 24.2 plots the heritability estimates from the twin studies in Tables 24.2 and 24.3 as a function of the mean age of the sample. Up till age 13–14, genes are of no importance in explaining individual differences in exercise participation, whereas a huge familial resemblance is found through common environmental effects. In late adolescence (from approximately age 17–18 onward), genetic factors start to appear and the role of common environment decreases. Genetic factors peak in their contribution to exercise behavior around age 19–20 to decrease again from young adulthood onward to reach a stable value of about 50% in middle-aged subjects.

The tentative curve drawn through this plot clearly shows that the genetic architecture is different at various points in the life span. These differences have direct bearing on studies assessing heritability using parent–offspring correlations or younger–older sibling correlations. Such studies have systematically yielded lower heritability estimates than twin studies. This may be due to a violation of the assumption that the genetic architecture is the same in younger and older members of the family. If this is not the case, e.g., when different genes are expressed in parents and offspring, the parent–offspring correlation does not estimate the heritability in either parental or offspring generations correctly. We suggest, therefore, that the lower heritability estimates from these family studies may partly reflect the comparison of "apples and oranges".

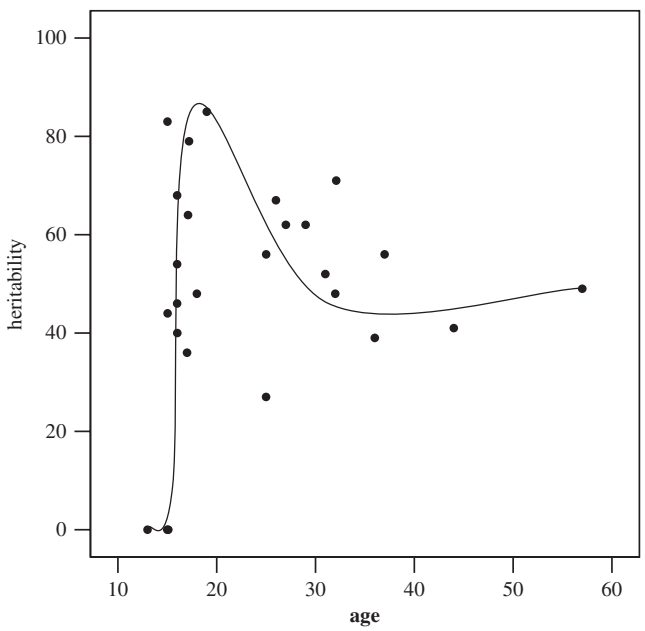

Fig. 24.2 Heritability estimates for exercise participation as a function of the mean age of the twin sample

The Lack of Common Environmental Influences on Adult Exercise Behavior

A number of studies show low to moderate tracking from childhood exercise behavior to adult exercise behavior (Beunen et al., 2004; Fortier, Katzmarzyk, Malina, & Bouchard, 2001; Malina, 1996; Simonen, Levalahti, Kaprio, Videman, & Battie, 2004; Twisk, Kemper, & van Mechelen, 2000). Tracking, or stability, refers to the maintenance of relative rank or position over time. Inter-age correlations between repeated measures of the trait are generally used to estimate stability. It has been suggested that correlations <0.30 are considered to be indicative of low stability, whereas those ranging from 0.30 to 0.60 are moderate, and those >0.60 are high (Malina, 1996). A review by Malina (1996) shows that, although different indicators of physical activity and different methods of analysis are used, it appears that physical activity tracks low to moderately from adolescence to adulthood. This is consistent with results from the longitudinal Amsterdam Growth and Health Study (Twisk et al., 2000). In subjects with a mean age of 13.1 ($\pm$0.8) years, total time spent on all habitual physical activities in relation to school, work, sports, and other leisure time activities was measured with an interviewer-administered activity questionnaire. During the first 4 years of the study, yearly measurements were carried out. Later on, two follow-up measurements took place after 8 and 14 years, respectively. The stability coefficient, summarizing tracking across all intervals, was 0.34 (95% CI = 0.19–0.49) for daily activity, indicating that there was low to moderate tracking.

Using data from the Netherlands Twin Registry (NTR), we essentially replicated this finding. Table 24.5 shows 7-year tracking of exercise participation from ages 13–16 to ages 20–23. Again low to moderate tracking coefficients were found ranging from 0.22 to 0.44. Model-fitting results showed that these correlations did not significantly differ from each other ($p = 0.56$), resulting in an overall tracking coefficient of 0.37 from ages 13–20 to 16–23, which is in keeping with the stability coefficient of 0.34 found in the Amsterdam Growth and Health Study, even though our cohort was born more than 10 years later.

In view of the striking shift in genetic architecture during adolescence, this tracking is puzzling. If common environmental factors influence exercise behavior among children and their exercise behavior tracks into adulthood,

Table 24.5 Seven-year tracking of exercise participation from adolescence into young adulthood in the Dutch Twin Survey

Initial age and age at follow-up	Number of subjects participating in two surveys	Tetrachoric correlation
From age 13 to 20	169	0.41
From age 14 to 21	184	0.22
From age 15 to 22	181	0.44
From age 16 to 23	214	0.36

one would expect to find enduring effects of the environment they shared as youngsters even after they reach adulthood. In spite of this expectation, most of the studies in adults do not find evidence for common environment at all, including six of the seven samples in the GenomEUtwin study. A first potential explanation for the failure to detect C in adult samples is a lack of power to detect common environment in smaller-sized twin studies. Most studies measured exercise behavior as a dichotomy, and at heritabilities between 30 and 70%, large samples are needed to detect additional common environmental influences of modest size as is shown in Table 24.6 (Neale, Eaves, & Kendler, 1994). However, at least three samples of the GenomEUtwin study (with heritability at 50%) easily exceed this sample size number and yet did not detect common environment.

A second potential explanation is that in adulthood common environmental factors interact with genetic make-up. Since twin studies cannot discriminate between main effects of genes and their interaction with common environmental influences (C × G), in the classical twin model any C × G interaction would end up as a main effect of genetic factors (Purcell, 2001). There is, in fact, a straightforward theoretical account for a C × G interaction on exercise behavior that would be compatible with such a scenario. It has been suggested that genetic influences on exercise ability, which are very strong both for strength and endurance phenotypes (Arden & Spector, 1997; Bouchard et al., 1998; Thomis et al., 1997), may explain part of the heritability of exercise behavior (Stubbe et al., 2006).

The basic idea is that people will seek out the activities that they excel in. This is particularly true in adolescence. Being "good in sports" is an important source of self-esteem for teenagers and the athletic role model is continuously reinforced by the media (Field et al., 1999; Pope, Olivardia, Borowiecki, & Cohane, 2001). Hence, genes coding for exercise ability may well become genes for adolescent exercise behavior. The parents and older siblings may be helpful to make sure the youngsters regularly get to the playing field in the first place, and to provide positive feedback on their performance. The extent of positive feedback, however, may depend on their (exercise ability) genotypes. This is even truer for feedback by peers and colleagues, who will base their judgment entirely on performance rather than family ties. The family environment, in short, determines exposure and encouragement in early adolescence, but actual ability will determine whether they like exercising enough (by excelling in it) to maintain the behavior when the perception of peers and colleagues increases in importance in late adolescence.

A final possibility is that the estimates of common environmental influences in early adolescence include genetic effects that are correlated with the family environment. Such a correlation would come about if the parents that most encourage their children to become engaged in exercise were themselves of above-average athletic ability. If they pass on these genes and create a family environment that encourages sports, a positive correlation between common environmental and genetic influences would arise and in the twin samples genes for exercise ability would then become correlated to an encouraging environment shared by the twins. It has been shown that a correlation of genes and shared environment inflates the estimates of common environmental effects in twin studies (Purcell, 2001).

Different Genes at Different Ages?

The above C × G scenario would still leave unexplained why there is a peak in heritability around age 18–25. This peak was most clearly demonstrated in a study that assessed exercise behavior as weekly energy expenditure in an identical way in a cohort of 17-year-old and a cohort of 45-year-old twins (De Geus et al., 2003). Heritability was found to be much higher in adolescents (79%) than in adults (41%). Does the impact of the unique environment on exercise habits increase after young adulthood, for instance, due to factors like work stress and child care load? That is entirely possible, and would fit with data indicating that the most often reported barrier to exercise is "lack of time" (King et al., 1992; Sallis & Hovell, 1990). However, total variance in leisure time energy expenditure was also seen to go down in the same study (De Geus et al., 2003). This does not rule out an

Table 24.6 Sample size in subjects (N) needed to detect common environmental influences (V_C) in full ACE models under varying levels of variation due to additive genetic sources (V_A)

	$V_A = 30\%$		$V_A = 40\%$		$V_A = 50\%$		$V_A = 60\%$		$V_A = 70\%$	
V_C (%)	10	20	10	20	10	20	10	20	10	20
N	13,681	3,152	12,908	2,918	12,007	2,661	11,000	2,387	9,919	2,108

Note: MZ/DZ ratio = 1/1; significance level $\alpha = 0.05$; power $(1–\beta) = 0.80$.

increase in environmental variance, but it does mean that a decrease in genetic variance must have occurred. Another possibility, therefore, is that different genes play a role in exercise behavior in adolescence than in adulthood.

As stated above, core components of exercise ability like aerobic endurance and muscular strength show large heritability, and the genes influencing exercise ability may play an important role in the choices of adolescents. Exercise ability, however, may start to loose significance in adulthood when recreational exercise start to become more prominent than competitive exercise. In this phase, genes that determine personality may increasingly start to influence exercise behavior. In adult samples a modest but highly significant association between neuroticism and extraversion and exercise participation is found (De Moor, Beem, Stubbe, Boomsma, & De Geus, 2005), for instance, whereas this link is absent in adolescence (Allison et al., 2005). Physical and mental health benefits of exercise may also become increasingly important motives in adulthood. If there are differences in the genetic sensitivity to these health benefits of exercise, genes coding for this differential sensitivity may well become genes for adult exercise behavior.

In favor of this hypothesis, standardized training programs have already shown some persons to be more responsive to the same exercise regime than others in terms of increased aerobic fitness (Bouchard et al., 1999), increased muscular strength (Thomis et al., 1998), reduced body fat (Perusse et al., 2000), increased HDL/LDL cholesterol ratio (Rice et al., 2002), decreased C-reactive protein (Lakka et al., 2005), increased insulin sensitivity and glucose effectiveness (Boule et al., 2005; Teran-Garcia, Rankinen, Koza, Rao, & Bouchard, 2005), and decreased heart rate and blood pressure (An et al., 2003; Rice et al., 2002). By studying the response of family members to an identical exercise program, these differential health effects were shown to largely reflect differences in genetic make-up (An et al., 2003; Bouchard et al., 1999; Boule et al., 2005; Lakka et al., 2005; Perusse et al., 2000; Rice et al., 2002; Teran-Garcia et al., 2005; Thomis et al., 1997). Although currently unknown, psychological benefits may well show a similar dependency on genotype.

As it stands, the idea that different genes influence exercise behavior across the lifespan remains hypothetical. This hypothesis can be fully tested, however, in longitudinal twin data. Ideally these should span the crucial period between age 18 and 30.

Assortative Mating

So far, we have suggested that twin studies of exercise behavior in adolescence may be complicated by the presence of C $\times$ G interaction and by adolescence-specific genetic effects. Additional complexity may derive from assortative mating. In a three-generation Finnish study (Aarnio et al., 1997), intra- and inter-generational associations of leisure time physical activity among family members were examined. The sample consisted of 3,254 twins at the age of 16, their parents and grandparents. The correlation was 0.19 between parents, 0.33 between paternal grandparents and 0.43 between maternal grandparents, suggesting that assortative mating is present. In the Quebec family study, familial aggregation of physical activity phenotypes was investigated in 696 subjects from 200 families (Simonen et al., 2002). For moderate to strenuous physical activity, the parental correlation was 0.22. Similar assortment was found in our own sample (Willemsen, Vink, & Boomsma, 2003). Tetrachoric correlations between exercise participation of spouses as a function of the duration of the relationship were 0.45, 0.42, and 0.49 for relations lasting <5 years, ≥ 5 years, and >15 years, respectively.

How will assortment for exercise participation affect the estimates in twin studies? If the environment causes assortment no effects on genetic variance will be seen. If the assortment is phenotypic, as we expect, it will act to both increase total genetic variance and heritability (Falconer & Mackay, 1996). In the classical twin design, however, phenotypic assortment will look like common environmental influences when fitting an ACE model because it also increases the average amount of shared genes of DZ pairs above the theoretical 50%. Thus, the heritability in the population increases as a consequence of phenotypic assortment but use of the classical twin design will increase the estimate of common environmental influences. Does the common environmental influence on exercise found in studies on adolescent twins in part reflect assortative mating?

At first sight, the finding that common environmental effects disappear in later adulthood seems to argue against assortative mating since the higher than 50% genetic resemblance should stay in effect throughout the lifespan. However, in the above we argued that genes that are expressed in early adulthood may partly differ from the genes that influence exercise later in life. If the assortment is phenotypic, it will exclusively operate on the genes that are in effect during the main mating period, e.g., in late adolescence and young adulthood. In this case, the genes that affect exercise in later stages of life may still be under random mating. Future modeling of exercise data obtained in twins as well as their parents and their spouses may shed more light on these issues. As it stands, early conclusions based on the resemblance of young sibling–sibling and spousal correlations that "familial resemblance is the result of environmental factors shared by members of the same generation rather than inherited factors" (Perusse et al., 1988) seem premature in retrospect.

Future Directions

The prevailing theoretical perspective in preventive medicine now holds that social and environmental factors largely account for voluntary lifestyle choices. Here, in contrast, it is shown that in adulthood some of the choices for a healthy lifestyle reflect differences in genetic make-up, although potentially in interaction with shared environment. This requires a change in our perspective, such that we change from "population-based" intervention strategies to "personalized" intervention strategies. Currently, this concept of "personalized medicine" is increasingly being applied to curative medicine and pharmacotherapeutic intervention. We suggest extending this concept to preventive medicine.

Crucial to such personalized preventive medicine is a mechanistic understanding of the genetic pathways that underlie the genetic contribution to individual variation in this behavior. Such understanding may not only help to improve intervention strategies but may impact on research on health in general. Randomized controlled training trials have clearly shown that regular exercise has a causal effect on mental (Babyak et al., 2000; Moore & Blumenthal, 1998; Steptoe, Edwards, Moses, & Mathews, 1989) and physical health (Berlin & Colditz, 1990). It is possible, therefore, that the well-known heritability of many health parameters like depression (Kendler & Aggen, 2001), obesity (Schousboe et al., 2003), thrombosis (Dunn et al., 2004), hypertension (Kupper et al., 2005), diabetes (De Lange et al., 2003), and even cardiovascular mortality (Zdravkovic et al., 2004) may partly reflect the genetic factors causing the adoption and maintenance of regular exercise behavior. In that case, finding the "genes for exercise behavior" immediately translates to finding genes that contribute to the heritability of mental and physical health.

So which genes could explain the heritability of exercise behavior? Unfortunately, this is a vastly under-explored question. For exercise, *ability* coordinated efforts exist worldwide and successful association has been reported for a number of genes influencing endurance or strength phenotypes, some of which have been replicated in independent samples. Specifically, a systematic and yearly update of the Human Gene Map for Performance and Health-Related Fitness Phenotypes is published in *Medicine and Science in Sports and Exercise* (Perusse et al., 2003; Rankinen et al., 2001, 2002, 2004; Wolfarth et al., 2005). For exercise *behavior* no such coordinated effort exists, although the most recent version of this *MSSE* Gene Map included for the first time a new section on this topic (Wolfarth et al., 2005). Fortunately, as we have argued above, genetic variation in exercise ability may partly overlap with genetic variation in exercise behavior, which means that many of the genes on the Human Gene Map for Performance and Health-Related Fitness Phenotypes can be considered promising candidate genes.

One example that illustrates this is the insertion/deletion (I/D) polymorphism in the angiotensin-converting enzyme (ACE) gene. Montgomery and colleagues (Williams et al., 2000; Woods, Humphries, & Montgomery, 2000) determined the ACE I/D genotype in British army recruits who were tested for a number of fitness traits before and after a 10-week training program. Efficiency of the muscles, or delta efficiency, computed as the increase in power output for a given increase in oxygen consumption, was found to increase almost ninefold more in subjects homozygous for the I allele. Almost no training effect was found in those homozygous for the D allele. As previously noted people generally like doing what they are good at, and will pursue those activities in leisure time as much as possible. Taking this one step further, we may reasonably assume that people feel specifically competent when they notice themselves to gain more in performance compared to others who nonetheless follow the same exercise regime. In support of this "competence hypothesis" a multicenter study in Italian borderline hypertensives (Winnicki et al., 2004) showed that the ACE polymorphism accounted for 21% of the variance in exercise participation. The most sedentary group had a clear excess of the genotype (DD) that caused the lowest increase in muscle efficiency after training in the British recruits. Here, at least, a genetic effect on exercise ability indeed coincided with reduced amounts of exercise behavior.

Apart from the link between the ACE polymorphism and exercise behavior, association for other candidate genes has been reported. In women but not in men, physical activity levels were associated with polymorphisms in the dopamine D2 receptor gene, which is proposed to play a role in rewarding mechanisms (Simonen, Rankinen, Perusse, Leon, et al., 2003). In 331 early postmenopausal women, physical activity was associated with a polymorphism in the CYP19 (aromatase) gene (Salmen et al., 2003). In the Quebec Family study, the Melanocortin-4 receptor gene (MC4R-C-2745T variant) showed significant associations with moderate-to-strenuous activity scores and with inactivity scores (Loos et al., 2005). Finally, in 97 healthy girls, physical activity was associated with polymorphisms in a calcium-sensing receptor gene (Lorentzon, Lorentzon, Lerner, & Nordstrom, 2001). To our knowledge, only one whole genome scan based on linkage analysis exists for physical exercise (Simonen, Rankinen, Perusse, Rice, et al., 2003). A few putative genomic regions were identified that might harbor genes influencing participation in regular exercise, but the evidence was only suggestive, as the power for linkage in this relatively small and unselected sample was small.

Combining the importance of exercise for health to the strong evidence for its heritability makes it paramount that

large-scale gene finding studies start targeting this crucial behavior.

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