Relative roles of heredity and physical activity in adolescence and adulthood on blood pressure

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Hernelahti, Miika, Esko Levälahti, Riitta L. Simonen, Jaakko Kaprio, Urho M. Kujala, Arja L. T. Uusitalo-Koskinen, Michele C. Battie, and Tapio Videman. Relative roles of heredity and physical activity in adolescence and adulthood on blood pressure. J Appl Physiol 97: 1046–1052, 2004.—Part of the association between physical activity and low blood pressure (BP) may be a consequence of genetic selection. We investigated the association of genetic factors and physical activity in adolescence and adulthood with BP. BP was measured with a Finapres device in 71 monozygotic and 104 dizygotic male twin pairs using no antihypertensive medication. Subjects’ mean age was 50.4 yr (range 40–72 yr). Subjects were interviewed about their lifetime exercise and other health habits. Exercise was classified as aerobic, power, or other, and these were further divided into adolescence (12–20 yr of age), the previous year, and lifetime. Genetic modeling was conducted to estimate genetic and environmental components of variance of systolic and diastolic BP. Aerobic exercise in adolescence and high-intensity aerobic exercise throughout the lifetime were associated with low diastolic BP in adulthood. Of the variance in diastolic BP, genetic factors accounted for 35% and aerobic exercise in adolescence for 5%. For systolic BP, genetic factors accounted for 39% of the variance. In turn, genetic factors accounted for 44% of the variance in aerobic exercise in adolescence. The genetic factors in part accounting for the variance in diastolic BP and those in part accounting for variance in aerobic exercise in adolescence were correlated. The association between aerobic exercise in adolescence and low diastolic BP in adulthood is a new finding, as is the observation that the factors partly share the same genes.

LEISURE-TIME PHYSICAL ACTIVITY is associated with low blood pressure (BP) levels and a reduced risk for hypertension (30, 31). The role of genetic selection in this association is, however, difficult or impossible to assess in traditional population-based studies. BP levels and leisure-time physical activity are both significantly heritable. Estimates of heritability (the proportion of variance accounted for by genetic factors) of BP levels and hypertension vary from 15 to 73% (8, 14, 15, 20). Participation in leisure-time physical activity has also been shown to have a genetic component, which was higher for high-intensity exercise than for moderate activity (5, 21, 22, 27). Reports of the heritability of sports participation vary between 35 and 83%, and those of daily physical activity vary between 16 and 62% (5, 22, 38). The genetic components affecting BP on one hand and leisure-time physical activity levels on the other hand may be correlated. A common genetic background would partly explain the known association between high physical activity levels and low BP.

The aim of the present study was to estimate the effects of inherited characteristics and leisure-time physical activity on BP levels among healthy men. We investigated the effects of different types of leisure-time physical activity, including physical activity in adolescence, and of genetic and nongenetic familial factors on interindividual variation of BP levels in adulthood using a sample of male twin pairs from the Finnish Twin Cohort.

MATERIALS AND METHODS

Subjects. The subjects were male twins selected from the Finnish Twin Cohort, which comprised all same-sex twin pairs born in Finland before 1958 and with both twins alive in 1967 (19). The cohort members were mailed a questionnaire in 1975 and in 1981. The response rates were 89 and 84%, respectively. From this cohort, 117 monozygotic (MZ) and 120 dizygotic (DZ) twin pairs were selected on the basis of consistent discords in occupational physical loading, exercise and sports activity, vehicular driving, or smoking, assessed by these two questionnaires. The exposures were originally selected to study the main suspected risk factors for spinal disorders in the Twin Spine Study (3). Added to the sample were 30 MZ and 33 DZ pairs chosen at random from the pool of remaining pairs.

Of the entire original sample, 105 MZ and 153 DZ twin pairs were examined in 1997–1999 when BP measurements were included. The remaining MZ pairs were examined before inclusion of BP measurements and were therefore excluded from analyses. The BP measurements of 20 subjects (from 6 MZ pairs and 13 DZ pairs) were not registered due to technical problems, such as cold fingers, amputated fingers, or arrhythmias.

Thus BP was available in 99 MZ pairs and 140 DZ pairs. We excluded those twin pairs in which at least one of the twins had diabetes (3 concordant and 3 discordant MZ pairs, and 11 discordant DZ pairs) or used medication for hypertension or other cardiovascular medication influencing BP (14 concordant and 14 discordant MZ pairs, and 11 discordant and 18 discordant DZ pairs). Some of these subjects had both aforementioned conditions. Thus there were 71 MZ pairs and 104 DZ pairs in our final study group. The mean age of the subjects was 52.0 yr (range 40–72 yr) for the MZ pairs and 49.3 yr (range 40–70 yr) for the DZ pairs (Table 1).

Zygosity was defined by the questionnaire method described by Sarna et al. (36). The validity of zygosity has been studied in a
Aerobic exercise intensity, %
No aerobic exercise 6 ± 4 16 ± 8
Mean intensity: 0.1–0.5 45 ± 32 62 ± 30
Mean intensity: 0.6–1 46 ± 32 78 ± 37
Mean intensity: 1.1–1.5 26 ± 18 40 ± 19
Mean intensity: 1.6–3 19 ± 14 12 ± 6

Aerobic exercise intensity, past year, %
No aerobic exercise 35 ± 25 52 ± 25
Mean intensity: 0.1–1 51 ± 36 106 ± 51
Mean intensity: 1.1–3 56 ± 39 50 ± 24

Power exercise, ≥1 yr
≥2 times/wk, % 18 ± 13 23 ± 11
≥1 yr 3 ± 4 8 ± 4
≥2 times/wk, ≥1 yr 3 ± 15 8 ± 11
≥2 times/wk, ≥1 yr 27 ± 19 45 ± 22
≥2 times/wk, ≥1 yr 10 ± 7 11 ± 5
≥2 times/wk, ≥1 yr 19 ± 13 29 ± 14
Systolic blood pressure (95% CI), mmHg 128 (124–132) 128 (125–131)
Diastolic blood pressure (95% CI), mmHg 76 (73–78) 76 (78–80)

Values are means ± SD. 95% CI, 95% confidence interval; MZ, monozygotic; DZ, dizygotic. Aerobic intensity: 1, light; 2, medium; 3, heavy.
*Different MZ and DZ proportions (P < 0.05).
significant variables. *P* values of <0.05 were regarded as significant. All significance tests were two tailed. No correction was applied for multiple statistical tests.

To estimate genetic and environmental components of variance for BP and for statistically significant leisure-time physical activity variables, standard univariate twin analyses were carried out (34, 44). Tests of homogeneity of means and variances across twin type (MZ vs. DZ) were carried out by STATA SVY procedures (StataCorp, 1999). We estimated genetic and environmental components of variance for BP and for leisure-time physical activity variables using maximum likelihood based on sample covariance matrices and means, as described in detail elsewhere (29, 34). Univariate twin models with regressors and bivariate twin models were estimated based on matrices of Pearsonian, polyserial, and bisurel correlations, depending on the nature (continuous, categorized, dichotomous) of the variables (29, 34). The correlations between twin A and twin A, and twin B and twin B, respectively, are cross-trait correlations, i.e., the phenotype correlations between BP and exercise variables. The correlations between twin A and twin B are cross-trait-crossover correlations. Larger cross-trait-crossover correlations for MZ twins than for DZ twins would indicate that a genetic correlation explains part of the phenotype correlation. The univariate models are based on ICCs for MZ pairs and DZ pairs, and the bivariate models are based on the ICCs and cross-trait correlations. Twins were ordered at random with respect to birth order in the data set, and the twin A and B notation is only used to distinguish between the first and second twin in pair, respectively.

Under the present study design of twins reared together, it is possible to model four separate parameters: an additive genetic (A) component, effects due to genetic dominance (D), and shared (C) and nonshared (E) environmental components. One can fit models based on the different combinations of these parameters (e.g., AE, ACE, ADE, and E), but effects due to dominance and shared environmental effects cannot be simultaneously modeled with data limited to that from twins reared together, because the models are not identified (29, 34). We used the principle of parsimony to support accepting a simple model (e.g., ACE) requires us to abandon it. The $\chi^2$ goodness-of-fit statistics were used to assess how well the models fit the data. The superiority of alternative, hierarchically nested models was assessed by Akaike information criterion (AIC; $\chi^2 \times 2 \times$ degrees of freedom). This was done to compare models where different components of variance have been specified. Lower AIC indicates better fit.

After the basic univariate models, specific independent variables and age were added as regressors to the BP models to evaluate how much variance each specific variable accounted for and how much of the remaining variance was then accounted for by age, genetic, and environmental components.

We also carried out a bivariate twin analysis with age correction to examine whether the genetic and environmental effects on leisure-time physical activity are correlated with the genetic and environmental effects on BP. This analysis was made for leisure-time physical-activity variables that were significant regressors in BP models. The selection of which variance components to include is based on the results of the univariate models. The analysis explores to what extent the observed correlation between a leisure-time physical-activity variable and BP (as seen in the individual-based regression models) can be accounted for by a correlation between additive genetic effects on the physical activity variable and on BP, and a correlation between the unique environmental effects of physical activity and of BP, respectively. The significance of the genetic and environmental correlations can be further tested by examining the change in fit of the bivariate model when that specific correlation is and is not included. In other words, is a genetic or environmental correlation needed to account for the observed phenotypic correlation. The analysis was carried out using a bivariate Cholesky decomposition parametrization (29, 34) and the genetic and environmental correlations computed from path coefficients as described by Neale and Cardon (29). The genetic models were estimated by using the Mx program (28).

**RESULTS**

High occupational physical loading during the previous year was associated with low levels of systolic BP, whereas regular participation in aerobic exercise during the previous year was surprisingly associated with high levels of systolic BP. Aerobic exercise in adolescence and intensity of aerobic exercise during the whole lifetime were associated with low levels of diastolic BP. All of these associations were also statistically significant when adjusted for age (Tables 2 and 3). Power-type exercise, other exercise, use of alcohol, and body mass index were not associated with BP levels.

The ICCs for systolic BP were 0.38 for MZ and 0.21 for DZ pairs, and 0.36 (MZ) and 0.20 (DZ) for diastolic BP. ICCs for aerobic exercise in adolescence were 0.41 for MZ and 0.30 for DZ pairs, and for lifetime aerobic exercise intensity were 0.49 for MZ and 0.15 for DZ pairs. The cross-trait matrices for BP and exercise variables are shown in Tables 4 and 5.

In the univariate twin analyses for both systolic BP and diastolic BP, all models except the E model fit the data satisfactorily and were not statistically significantly different from each other; however, the models with additive genetic effects and unique environment only (AE) models fit the data best (for details about the variance components A, C, and E, refer to MATERIALS AND METHODS). In the AE model for systolic BP, unique environment accounted for 61% [95% confidence interval (CI): 0.45, 0.80] and additive genetic effects 39% (95% CI: 0.20, 0.55) of the variance [AIC = −10.02; $P = 0.78$ (which indicates that the model fits the data well)]. Variability of diastolic BP in the AE model was mostly accounted for by unique environmental effects [64% of the variation (95% CI: 0.48, 0.82)], whereas genetic effects accounted for 36% (95% CI: 0.18, 0.52) [AIC = −9.13; $P = 0.68$]. When the environmental effects shared by both twins were added to the model (an ACE model), the importance of unique environmental

**Table 2. Systolic and diastolic blood pressure in different exercise categories for aerobic exercise during adolescence and aerobic exercise intensity during the whole lifetime in individuals**

<table>
<thead>
<tr>
<th>Lifetime Aerobic Exercise Intensity (average score)</th>
<th>Adolescence Aerobic Exercise (at least 2 times/wk)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>129 (122, 136)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>77.7 (72.4, 83.0)</td>
</tr>
<tr>
<td>No. of subjects</td>
<td>22 (6%)</td>
</tr>
</tbody>
</table>

Values are means (95% CI); n = 350 subjects. Significantly different means: *P < 0.05, †P < 0.01.

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Aerobic exercise in adolescence was associated with low diastolic BP in adulthood. Genetic factors accounted for more than one-third and aerobic exercise in adolescence alone accounted for 5% of the variance in diastolic BP in adulthood. In turn, interindividual genetic differences accounted for about one-half of the variance in aerobic exercise in adolescence. The genetic and environmental factors accounting for variance in diastolic BP in adulthood and those accounting for aerobic exercise in adolescence seem to be correlated.

High-intensity aerobic exercise throughout life was also associated with low diastolic BP in adulthood. When the effect of this variable on diastolic BP was assessed together with genetic and environmental effects, it did, however, not remain significant. Power-type exercise and other exercise were not associated with diastolic BP. For systolic BP, high occupational loading was associated with low pressure, and aerobic exercise during the whole past year was surprisingly associated with high pressure. No other physical activity variables were associated with systolic BP, 39% of which was accounted for by genetic effects.

### DISCUSSION

Aerobic exercise in adolescence was associated with low diastolic BP in adulthood. Genetic factors accounted for more than one-third and aerobic exercise in adolescence alone accounted for 5% of the variance in diastolic BP in adulthood. In turn, interindividual genetic differences accounted for about one-half of the variance in aerobic exercise in adolescence. The genetic and environmental factors accounting for variance in diastolic BP in adulthood and those accounting for aerobic exercise in adolescence seem to be correlated.

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Several studies have demonstrated that BP is partly determined genetically (9, 25). Our present results are concordant with those of earlier studies, where the proportion of variance in BP accounted for by interindividual genetic differences ranges from 15 to 73% (8, 9, 14, 15, 16, 20, 24, 37, 39, 42).

Our result that aerobic exercise in adolescence is associated with low diastolic BP in adulthood is a new finding. Four European cohort studies have assessed subjects’ physical activity at 12–19 yr of age and subjects’ BPs at 20–40 yr of age and have not found an association between physical activity in youth and low BP in adulthood (6, 11, 23, 41). Several factors may have contributed to the seemingly conflicting findings. The subjects in the studies that did not find associations between physical activity in youth and BP in adulthood were younger at follow-up than the subjects in our present study (20–40 vs. 35–70 yr) (6, 11, 23, 41). Another factor that may contribute to the findings of no association can be inaccuracy in measuring physical activity and the type of exercise, especially the intensity of the activities, which is often used in calculation of total physical activity (35, 40) and perhaps may be more inaccurate in our study because the data were collected retrospectively. Also, importantly, in the aforementioned studies, physical activity in adolescence included all kinds of physical activity, aerobic exercise as well as strength- and endurance-demanding activities (6, 11, 23, 41), whereas our present study examined aerobic exercise separately. One study (1) found a relationship between a positive attitude to aerobic exercise in adolescence and decreased risk for high systolic BP (diastolic BP was not reported). In that study, as in our present study, leisure-time sports activity in adolescence was not associated with low systolic BP.

Interestingly, the same genetic factors that are associated with participation in aerobic exercise in adolescence seemed to be associated with low diastolic BP in adulthood. Three different bivariate models fit the data about equally well. The ability to distinguish between different well-fitting models depends on the number of subjects in the study. Because this number is not very large in our present study, it cannot be concluded which one of the three models is the best one, and thus the general conclusion is that both genetic effects and unique environmental effects accounting for aerobic exercise in adolescence on one hand and diastolic BP on the other hand seem to be correlated.

Our finding that regular aerobic exercise during the past year was associated with high systolic BP is contradictory to earlier studies. An association between physical activity and low risk for hypertension has been found (10, 12, 30, 31, 33), as well as between physical activity and low BP (26, 43). There are no clear explanations for our present findings. One possibility is that those who have had elevated BP readings may have been advised to exercise by their physician. The negative results may also reflect the difficulties in assessing lifetime physical activity. In earlier studies (12, 13), we used questionnaires from which present metabolic equivalent hours per week were calculated and used in analyses. For all studies of the topic, obtaining a valid lifetime exercise history is a problem for which there is almost never a good practical solution. However, an in-depth interview eliciting regularly performed activities, using significant life events and stages to assist with recall, would appear to be a reasonable approach, which is supported by good response reliability of some measures as investigated with a 5-yr test-retest interval (35). Another source of concern in our study are those subjects belonging to the original cohort who were examined before BP measurements were included in the examinations and thus were excluded from the study. However, this drop out was random and thus unlikely to affect the results. Also, the history of aerobic exercise did not differ between those of the original cohort, who were included in the study, and those who were excluded (results not shown). Furthermore, in those who were excluded due to missing BP measurements, the prevalence of medication for hypertension was 14% (13 of 91 subjects), whereas it was 17% (85 of 509 subjects) in those in whom BP measurements were made.

We did find an association between high-intensity aerobic exercise and low diastolic BP. Some controversy concerning high-intensity exercise and risk for hypertension exists (10, 26, 30, 31, 33). This probably reflects difficulties in measuring intensity of exercise (35, 40).

In conclusion, aerobic exercise in adolescence and high-intensity exercise throughout life were associated with low

### Table 6. Univariate twin models with regressors (determinant, age) for diastolic blood pressure with genetic environmental models, which include the additive genetic effects and environmental effects unique to each subject

<table>
<thead>
<tr>
<th>Proportions Accounted for by</th>
<th>Unique environment</th>
<th>Additive genetic effects</th>
<th>Age</th>
<th>Determinant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome Variable</td>
<td>Determinant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>Adolescent aerobic exercise</td>
<td>0.66 (0.51, 0.81)</td>
<td>0.29 (0.15, 0.43)</td>
<td>0.00 (0.00, 0.01)</td>
</tr>
<tr>
<td></td>
<td>Lifetime aerobic exercise intensity</td>
<td>0.66 (0.51, 0.82)</td>
<td>0.33 (0.18, 0.48)</td>
<td>0.00 (0.00, 0.01)</td>
</tr>
</tbody>
</table>

Values are means (95% CI); n = 71 MZ pairs and 104 DZ pairs. Aerobic exercise during adolescence (12–20 yr) and intensity of aerobic exercise during the whole lifetime are included as determinants. Age is also included in the models. Variance component estimates (proportions of the variability of the outcome variable accounted for by the different components) and their 95% CI are presented.

### Table 7. Bivariate twin models for the correlations between genetic effects and unique environmental effects accounting for interindividual variability of diastolic blood pressure on one hand and aerobic exercise in adolescence on the other hand

<table>
<thead>
<tr>
<th>Model</th>
<th>rs</th>
<th>re</th>
<th>AIC</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>rS + rE</td>
<td>-0.27 (-0.57, 0.08)</td>
<td>-0.18 (-0.40, 0.05)</td>
<td>-12.93 0.37</td>
<td></td>
</tr>
<tr>
<td>rs</td>
<td>-0.40 (-0.65, -0.19)</td>
<td>-12.52 0.29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>re</td>
<td>-0.27 (-0.46, -0.12)</td>
<td>-12.40 0.28</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are means (95% CI). Correlation coefficients with 95% CI. Akaike information criterion (AIC) values, and P values (P > 0.05 indicates good fit) for the models are presented. rs Correlation between genetic effects; re Correlation between unique environmental effects.
diastolic BP in adulthood. Genetic effects partly accounted for both diastolic BP levels and aerobic exercise in adolescence, and these genetic effects seemed to be correlated.

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