Genetic analysis of physical activity in twins

Genetic analysis of physical activity in twins[1,2]

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ABSTRACT

Background: The reduced contribution of physical activity (PA) to daily energy expenditure contributes to the increased prevalence of obesity. A genetic control of activity-induced energy expenditure (AEE) may contribute to a genetic susceptibility to obesity.

Objective: Our aim was to investigate the relative contribution of genetic and environmental factors to the variation and covariation in AEE and PA.

Design: Twelve monozygotic and 8 same-sex dizygotic (including 2 same-sex sibling pairs; age differences: 2 and 2.5 y) twin pairs aged between 18 and 39 y participated. AEE was measured in a respiration chamber for 24 h and with doubly labeled water in daily life for 2 wk. PA was recorded simultaneously with a triaxial accelerometer. Structural equation modeling was used to separate and quantify the observed variance into sex-adjusted additive genetic and common and unique environmental contributions.

Results: In the respiration chamber, common and unique environmental factors explained the variance in AEE and PA, and no genetic contribution was found. In daily life, genetic factors explained 72% of the variance in AEE and 78% of the variance in PA. Unique environmental factors explained the remaining variance. The same additive genetic factors explained 67% of the covariance in AEE and PA in daily life.

Conclusions: In the present exploratory study that used gold standard measurements for AEE and PA but a limited sample size, genetic influence explained a large part of the variation in AEE and PA in daily life, whereas both AEE and PA were influenced by environment only within the confined area of the respiration chamber. *Am J Clin Nutr* 2005;82:1253–9.

KEY WORDS Genetic influence, heritability, physical activity, activity-induced energy expenditure, accelerometry, doubly labeled water, twins

INTRODUCTION

Epidemiologic data show that a sedentary lifestyle is associated with several diseases, such as cardiovascular diseases, type 2 diabetes, and obesity (1). The link between physical inactivity and obesity is likely to be causal, because overweight and obesity are determined by the long-term imbalance between energy intake and energy expenditure (2). Both environmental and genetic factors can influence energy balance. Thus, a genetic control of activity-induced energy expenditure (AEE) may contribute to a genetic susceptibility to obesity and can have important implications in the prevention and treatment of obesity.

Total energy expenditure (TEE) consists of the following 4 components: sleeping metabolic rate (SMR), energy cost of arousal, diet-induced thermogenesis, and AEE. Of these components, AEE is the most variable between persons (3). AEE is measured by the amount of physical activity (PA), the intensity of the activities, body characteristics (size and composition), and indirectly by physical fitness (4, 5).

In daily life, the contribution of AEE to TEE can range from 25% in sedentary persons to 75% in extreme situations during heavy, sustained exercise (6). PA includes a spontaneous component, such as fidgeting, sitting, standing, and walking; an obligatory component, such as occupation, household, and daily living activities; and a voluntary component, such as participation in sports (7). In a respiration chamber, without an exercise protocol, PA is limited to the spontaneous component because of the limited space available. Even within this confined environment, PA and AEE are highly variable between subjects and contribute substantially to energy expenditure, emphasizing the important contribution of low-to-medium intensity activities to total daily activity levels (7, 8). In addition, high levels of PA and AEE in the respiration chamber predict high levels of PA and AEE in daily life, with correlation coefficients of 0.30–0.57 and 0.50–0.53 for PA and AEE, respectively (8, 9), which could be based on genetics. To test for a genetic contribution, we used a twin design, which allowed us to separate the genetic and environmental variance components of AEE and PA when measured in the respiration chamber and in daily life. The classic twin design is based on the comparison of monozygotic twins, who are genetically identical, with dizygotic twins, who share (on average) 50% of their genes, similar to siblings. Intrapair differences in monozygotic twins are due to environmental factors and measurement errors, whereas intrapair differences in dizygotic twins are additionally affected by genetic factors. We hypothesized that genetic factors would contribute to a predisposition to PA and a high AEE and that these genetic factors are shared for PA and AEE.

SUBJECTS AND METHODS

Subjects

Twin pairs were recruited through advertisements at the university, at the university hospital, and in the local press and

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Received March 15, 2005.

Accepted for publication September 9, 2005.

through the City Council of Maastricht and the Dutch Twin Register (10). Selection criteria included being a same-sex twin or a sibling pair, aged between 18 and 40 y (the age difference between sibling pairs had to be <3 y), white, either nonsmoking or occasional smoking, and not following a weight-loss or -gain dietary regimen. The subjects were medically screened by a detailed health questionnaire; only twins in good health without physical limitations were included. The study was approved by the Ethics Committee of Maastricht University. All subjects received verbal and written information and signed a written consent form. Twelve monozygotic (5 male and 7 female), 6 dizygotic (1 male and 5 female) same-sex twin pairs, and 2 female same-sex sibling pairs (with age differences of 2 and 2.5 y) participated in the study. Because dizygotic twins are similar to siblings, except for an age difference in siblings, the siblings were included in the dizygotic group, making a total of 8 dizygotic twin pairs. The zygosity of the twins was established with the use of 9 polymorphic DNA markers. Both monozygotic and dizygotic twin pairs were studied in equal distributions over the seasons.

Experimental design

Individual study periods covered 17 consecutive days. Both members of a twin pair were measured on the same days. In the evening of day 1, each member of a twin pair entered 1 of 2 respiration chambers for a period of 36 h. No exercise protocol was imposed. Meals were served at fixed hours. Energy intake was calculated as SMR during the first night multiplied with a 1.4 activity level to reach energy balance (8). The macronutrient composition of the diets reflected that of the average Dutch diet (15% of energy from protein, 50% from carbohydrates, and 35% from fat). Body weight and composition were measured after the subjects left the respiration chamber on the morning of day 3. A fasting blood sample was drawn for analysis of zygosity. Consecutively, the twins went home where total free-living energy expenditure was measured with the doubly labeled water (DLW) method for 15 d. Measurements were not available for 2 monozygotic twin pairs because of the lack of availability of DLW. The subjects wore an accelerometer for the entire study period to measure PA.

Procedures

Anthropometry and body composition

Measurements were carried out in the morning after voiding and before breakfast. Body weight and height were measured to the nearest 0.01 kg and 0.1 cm, respectively. Body mass index was calculated as body weight (in kg) divided by height^2 (in m). Body density was measured by underwater weighing with simultaneous measurement of residual lung volume with the helium dilution technique. Total body water was measured with deuterium dilution as described in the Maastricht protocol (11). Body composition was calculated from body density and total body water with the 3-compartment model of Siri (12).

Respiration chamber

TEE was measured over the last 24 h (0730–0730) of a 36-h stay (1930–0730) in a respiration chamber from oxygen consumption and carbon dioxide production according to the Weir formula (13). The respiration chamber measures 14 m^3 and is furnished with a bed, chair, table, television, radio, telephone, computer, washbowl, and toilet facilities (14). During the daytime, the subjects were allowed to move freely, sit, lie down, study, telephone, listen to the radio, watch television, and use the computer; only sleeping and strenuous exercise were not allowed. The SMR was defined as the lowest observed energy expenditure for 3 consecutive hours during the night, generally between 0300 and 0600. The SMR of the second night was used for additional calculations. AEE was calculated as (0.9 × TEE) –SMR, with an assumed diet-induced thermogenesis of 10% (3).

Daily life

The average daily metabolic rate (ADMR) was measured with the DLW technique as described in the Maastricht protocol (11). Briefly, isotopes were administered as a mixture of 5 atom% ^2H_2O and 10 atom% $H_2{}^{18}O$, which results in an initial excess body water enrichment of 150 ppm for deuterium and 300 ppm for oxygen-18 and leaves a sufficient excess enrichment at the end of the observation period. The volume of the isotope mixture consumed was 80–160 mL. The subjects collected a background urine sample immediately before isotope consumption to correct for isotopic backgrounds; subsequent urine samples were collected at the second and the last voiding on the first, middle, and last days of the 15-d observation period. Isotope enrichments of the urine samples were analyzed with isotope ratio mass spectrometry (Optima; VG Isogas, Middlewich, United Kingdom). Theoretical considerations and calculations of energy expenditure by the DLW method are described in detail elsewhere (11). AEE was calculated as (0.9 × ADMR) –SMR, with an assumed diet-induced thermogenesis of 10% (3).

Physical activity

PA was registered with a triaxial accelerometer for movement registration (Tracmor; Philips Research, Eindhoven, Netherlands), which measures body accelerations in anterioposterior, mediolateral, and vertical directions. PA was expressed in kcounts/d by summing the minute values of all axes per day. The triaxial accelerometer has been validated against DLW (15) and has been used before in our department (16, 17). The subjects wore the accelerometer on a belt at the lower back during waking hours, except during water activities.

Statistical analysis

Descriptive analysis

Twins were considered as individuals for this analysis. Results are presented as means ± SEs. An F test followed by a Student's unpaired t test (2-sided) were used to compare 2 groups. A P value < 0.05 was considered statistically significant.

Intrapair correlations for monozygotic and dizygotic twins were calculated with Pearson's correlation coefficients (r). From these correlations, the heritability (h^2) was calculated as $h^2 = 2 \times (r\text{monozygotic} - r\text{dizygotic})$. The comparison of r_{aee} (AEE in twin 1 correlated with AEE in twin 2) or r_{pa} (PA in twin 1 correlated with PA in twin 2), ie, the intrapair correlation, between monozygotic and dizygotic twins indicates an additive genetic (a^2), common environmental (c^2), and unique environmental (e^2) influence in AEE and PA, respectively (18).

Univariate analysis

Structural equation modeling was used to separate and quantify the observed phenotypic variance (V_{tot}) in AEE and PA into

TABLE 1
Characteristics of the 40 subjects by zygosity and sex[1]

		MZ		DZ	
	Mean total ($n = 40$)	Men ($n = 10$)	Women ($n = 14$)	Men ($n = 2$)	Women[2] ($n = 14$)
Physical characteristics					
Age (y)	25	25 ± 2.5[3]	28.3 ± 2.1	20[4]	21.6 ± 0.5[5]
Height (m)	1.72	1.81 ± 0.04	1.67 ± 0.02[6]	1.83[4]	1.69 ± 0.01[7]
BMI (kg/m^2)	23.4	22.9 ± 0.8	24.2 ± 1.6	21.0 ± 0.3	23.1 ± 1.3
BW (kg)	68.9	75.2 ± 3.4	67.2 ± 4.3	70.2 ± 0.4	65.9 ± 3.4
FFM (kg)	49.9	60.6 ± 2.3	44.3 ± 1.1[6]	60.7 ± 1.1	46.3 ± 1.6[7]
FM (kg)	19.0	14.6 ± 1.9	22.8 ± 3.8	9.5 ± 1.5	19.6 ± 2.3
SMR (MJ/d)	6.3	7.1 ± 0.3	6.1 ± 0.2[6]	6.9 ± 0.1	6.0 ± 0.2[7]
Respiration chamber					
TEE (MJ/d)	8.9	10.1 ± 0.4	8.5 ± 0.2[6]	9.5[4]	8.4 ± 0.3
AEE (MJ/d)	1.7	2.0 ± 0.2	1.6 ± 0.1[8]	1.6 ± 0.1	1.5 ± 0.1
AEE/BW (MJ · kg^{-1} · d^{-1})	0.024	0.027 ± 0.002	0.024 ± 0.002	0.023 ± 0.002	0.024 ± 0.001
PA (megacounts/d)	149	170 ± 11	143 ± 10	136 ± 7	140 ± 7
Daily life					
ADMR (MJ/d)	11.5	14.0 ± 0.8	9.9 ± 0.3[6]	12.6 ± 0.1	10.7 ± 0.6
AEE (MJ/d)	4.1	5.5 ± 0.5	3.1 ± 0.3[6]	4.4 ± 0.2	3.7 ± 0.4
AEE/BW (MJ · kg^{-1} · d^{-1})	0.060	0.073 ± 0.005	0.052 ± 0.006[6]	0.063 ± 0.003	0.055 ± 0.005
PA (Mcounts/d)	368	419 ± 19	318 ± 37[8]	387 ± 105	381 ± 36

[1] Twins were considered as individuals for comparison of characteristics with an F test followed by Student's t test (unpaired, two-sided). MZ, monozygotic; DZ, dizygotic; BW, body weight; FFM, fat-free mass; FM, fat mass; SMR, sleeping metabolic rate; TEE, total energy expenditure; AEE, activity-induced energy expenditure; PA, physical activity (measured with accelerometry); ADMR, average daily metabolic rate.
[2] DZ female group included 2 same-sex sibling pairs (age difference ≤2.5 y).
[3] $\bar{x}$ ± SE (all such values).
[4] No variation was observed for the 2 individuals of the 1 DZ male twin pair.
[5] Significantly different from MZ females, $P < 0.01$.
[6,8] Significantly different from MZ males: [6] $P < 0.01$, [8] $P < 0.05$.
[7] Significantly different from DZ males, $P < 0.05$.

its different components: additive genetic contribution ($a^2 = V_a/V_{tot}$; heritability) and common (or shared, equal to both members of the twin pair) environmental ($c^2 = V_c/V_{tot}$) and unique (or specific, different for each member of the twin pair) environmental ($e^2 = V_e/V_{tot}$) contributions. This additive model assumes no dominant genetic effects, no interaction between genes, no interaction between genes and environment, and that monozygotic and dizygotic twins share common environmental factors to the same extent.

On the basis of the results from the descriptive analysis, the correlation matrix, and the sex differences in absolute measurement levels, alternative univariate models (ACE, CE, AE, and E, where A = a^2, C = c^2, and E = e^2) with sex as an explanatory variable were fitted to the raw data with the use of a maximum likelihood approach with accompanying Akaike's information criterion (AIC) (18). The ACE model and submodels were compared with one another with the AIC. The model with the lowest AIC reflects the best model in which the pattern of variances and covariance is explained by as few measurements as possible. The goodness-of-fit of the submodels was also evaluated by hierarchical chi-squared tests. Note that only nested models can be compared with this test; therefore, the AE and CE models were not compared.

Bivariate analysis

On the basis of the univariate structural equation models, we tested whether a genetic, common environmental, or unique environmental correlation was present between AEE and PA in a bivariate model. The bivariate heritability (the part of the phenotypic correlation that is due to shared genes) is calculated as $\sqrt{(a^2_{aee})} \times r_a \times \sqrt{(a^2_{pa})}$, the bivariate c^2 as $\sqrt{(c^2_{aee})} \times r_c \times \sqrt{(c^2_{pa})}$, and the bivariate e^2 as $\sqrt{(e^2_{aee})} \times r_e \times \sqrt{(e^2_{pa})}$. SPSS 11 for Macintosh (2002; SPSS Inc, Chicago, IL) was used for the descriptive analysis; Mx (19) was used for correlations and structural equation modeling.

RESULTS

Descriptive analysis

The characteristics of the 40 subjects are shown in **Table 1**. Data were normally distributed. Overall, monozygotic twins were slightly older than dizygotic twins ($P < 0.05$); other physical characteristics were not significantly different between monozygotic and dizygotic twins. As can be expected from the general population, the men were significantly taller ($P < 0.0001$) and had a higher fat-free mass ($P < 0.0001$) and a lower fat mass ($P = 0.01$) than did the women.

No significant differences were seen for AEE and PA between monozygotic and dizygotic twins, both in the respiration chamber and in daily life. Except for PA in daily life, AEE and PA were significantly higher in the men than in the women ($P < 0.05$). AEE and PA in daily life were significantly higher than in the confined area of the respiration chamber ($P < 0.001$).

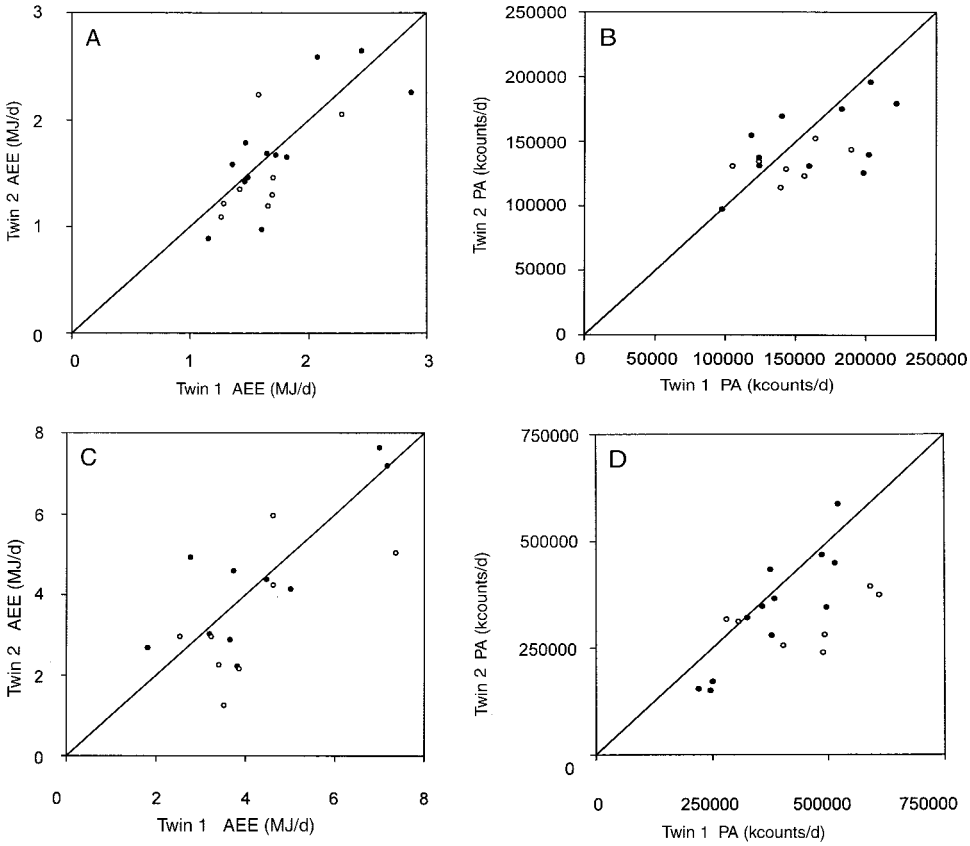

FIGURE 1. Twin 1 × twin 2 plots of monozygotic (●) and dizygotic (○) twins for activity-induced energy expenditure (AEE) in the respiration chamber (A), physical activity (PA) in the respiration chamber (B), AEE in daily life (C), and PA in daily life (D). Members of a twin pair were randomly assigned to be twin 1 or twin 2.

Intrapair correlations

The twin 1 × twin 2 plots for AEE and PA are shown in **Figure 1**; the accompanying intrapair correlations and heritabilities are shown in **Table 2**. In the confined area of the respiration chamber, the ratio of monozygotic to dizygotic correlations was <2 for both AEE and PA, which suggest not only genetic but also common and unique environmental influences on AEE and PA, separately. In daily life, the ratio of r_{aee} monozygotic to r_{aee} dizygotic was <2 as well. In contrast with the respiration chamber, the r_{pa} monozygotic was twice the r_{pa} dizygotic in daily life, which suggests that PA in daily life is determined by additive genetic and unique environmental influences without common environmental influences. The overall correlation between PA and AEE, which was calculated from one randomly selected member of each twin pair, was 0.46 ($P < 0.05$) in the respiration chamber and 0.65 ($P < 0.001$) in daily life.

TABLE 2
Intrapair Pearson's correlation coefficients (r) and heritabilities (h^2) in monozygotic (MZ) and dizygotic (DZ) twins[1]

	*r*MZ	*r*DZ	h^2[2]
Respiration chamber			
AEE	0.78[3]	0.60[4]	0.36
PA	0.56[4]	0.43	0.26
Daily life			
AEE	0.82[3]	0.64[4]	0.36
PA	0.88[3]	0.42	0.92

[1] AEE, activity-induced energy expenditure; PA, physical activity (measured with accelerometry).

[2] Calculated as $h^2 = 2 \times (r\text{MZ} - r\text{DZ})$. Differences between *r*MZ and *r*DZ were not statistically significant for all variables.

[3,4] Significantly different intrapair values: [3] $P < 0.001$, [4] $P < 0.05$.

Univariate analysis

Because absolute levels of AEE and PA (except for PA in daily life) were significantly higher for males than females, sex was added as an explanatory variable into the analyses. Variance estimates of additive genetic, common environmental, and unique environmental influences were derived from the best-fitting and most parsimonious (ie, lowest AIC) univariate structural equation model, although the difference between the models was not always large (**Table 3**). In the confined area of the respiration chamber, the common environment accounted for 68% of the total variance in AEE, whereas in daily life, genetic factors were the main contributors (72%). Unique (59%) and common (41%) environmental factors explained the variance in PA in the respiration chamber, whereas in daily life, genetic factors (78%) mainly accounted for the total variance in PA, as measured by accelerometry.

Bivariate analysis

Because univariate structural equation modeling showed that genetic factors played a role only in daily life and not in the respiration chamber, we focused on the correlation between PA

TABLE 3
Univariate variance estimates (95% CIs) of additive genetic (a^2), common environmental (c^2), and unique environmental (e^2) contributions to activity-induced energy expenditure (AEE) and physical activity (PA)[1]

				Model fit			Compared with ACE model	
	a^2	c^2	e^2	−2LL	df	AIC	$-2\Delta LL^2$	*P*
Respiration chamber								
AEE								
ACE	0.08 (0, 0.85)	0.62 (0, 0.86)	0.30 (0.13, 0.63)	32.48	35	42.48		
CE[3]	—	0.68 (0.37, 0.86)	0.32 (0.14, 0.63)	32.52	36	40.52	0.04	0.85
AE	0.70 (0.37, 0.87)	—	0.30 (0.13, 0.63)	33.67	36	41.67	1.19	0.28
E	—	—	1	45.00	37	51.00	12.52	0
PA								
ACE	0 (0, 0)	0.41 (0, 0.72)	0.59 (0.28, 1)	841.17	31	851.17		
CE[3]	—	0.41 (0, 0.72)	0.59 (0.28, 1)	841.17	32	849.17	0	1
AE	0.40 (0, 0.71)	—	0.60 (0.29, 1)	841.61	32	849.61	0.44	0.51
E			1	844.57	33	850.57	3.40	0.18
AEE/BW								
ACE	0.02 (0, 0.87)	0.77 (0, 0.91)	0.21 (0.09, 0.46)	231.23	35	241.23		
CE[3]	—	0.78 (0.54, 0.91)	0.22 (0.1, 0.46)	231.23	36	239.23	0	0.95
AE	0.78 (0.52, 0.90)	—	0.22 (0.1, 0.48)	233.66	36	241.66	2.43	0.12
E	—	—	1	250.28	37	256.28	19.05	0
Daily life								
AEE								
ACE	0.44 (0, 0.89)	0.26 (0, 0.80)	0.29 (0.11, 0.76)	115.69	31	125.69		
CE	—	0.58 (0.20, 0.81)	0.42 (0.19, 0.81)	124.00	32	132.00	8.31	0
AE[3]	0.72 (0.29, 0.89)	—	0.28 (0.11, 0.71)	115.96	32	123.96	0.27	0.60
E	—	—	1	123.97	33	129.97	8.28	0.02
PA								
ACE	0.78 (0.57, 0.87)	0 (0, 0)	0.22 (0.13, 0.44)	983.93	33	993.93		
CE	—	0 (0, 0)	1 (1, 1)	993.06	34	1001.06	9.13	0
AE[3]	0.78 (0.57, 0.87)	—	0.22 (0.13, 0.44)	983.93	34	991.93	0	1
E	—	—	1	993.06	35	999.06	9.13	0.01
AEE/BW								
ACE	0.29 (0, 0.85)	0.33 (0, 0.79)	0.38 (0.14, 0.85)	299.41	31	309.41		
CE[3]	—	0.54 (0.14, 0.79)	0.46 (0.21, 0.86)	299.67	32	306.67	0.26	0.61
AE	0.65 (0.17, 0.86)	—	0.35 (0.14, 0.83)	299.80	32	306.80	0.39	0.54
E	—	—	1	305.95	33	311.95	6.54	0.04

[1] Estimates included sex as an explanatory variable. BW, body weight; LL, log likelihood; AIC, Akaike's information criterion (18). Models ACE, CE, AE, and E are defined in the text.
[2] $-2\Delta LL$ follows a χ^2_{df} distribution.
[3] The best-fitting and most parsimonious model (lowest AIC).

and AEE in daily life. From the correlations and the variance estimates of the individual variables, we calculated the percentage of the variance in both phenotypes that was explained by the same genes or the same environment. A bivariate model with only additive genetic factors provided the most appropriate fit for the data, as measured by the goodness-of-fit and the parsimonity of the model (**Figure 2**). The correlation between additive genetic effects on AEE and PA in daily life was 0.90 (95% CI: 0.56, 1). In this model, 67% of the phenotypic covariance was accounted for by shared genetic factors.

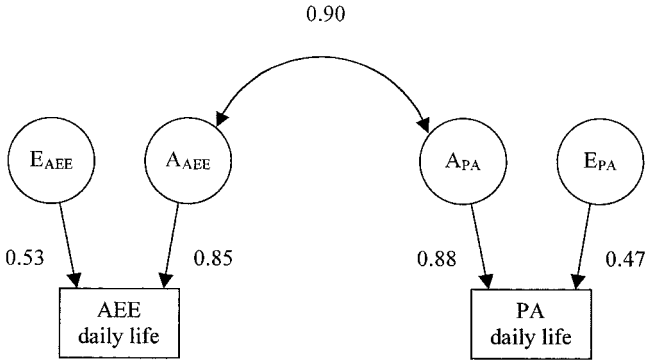

FIGURE 2. Correlation and path coefficients for the best-fitting bivariate model for activity-induced energy expenditure (AEE) and physical activity (PA) in daily life. The square of the path coefficients reflects the amount of the total variance accounted for by additive genetic or unique environmental factors in AEE and PA. A, additive genetic influence on AEE (A_{AEE}) or PA (A_{PA}); E, unique environmental influence on AEE (E_{AEE}) or PA (E_{PA}). The presented model had the lowest Akaike's information criterion and was therefore the best-fitting and most parsimonious one.

DISCUSSION

The aim of the present study was to determine the relative contribution of genetic and environmental factors to AEE and PA and to the covariance of these measurements. AEE is not only highly correlated with the amount of PA, but also with body characteristics (size and composition), physical fitness, and intensity of the activities—factors that can influence AEE directly

and indirectly through PA. We hypothesized that genetic factors contributed to a predisposition to PA and to a high AEE. High levels of PA and AEE in the respiration chamber predicted high levels of PA and AEE in daily life (8, 9), which indicates a major contribution of low-intensity activities to total PA and suggests a genetic basis. Therefore, we compared measurements in the confined area of the respiration chamber and measurements in daily life in twins. We did not find genetic influences on the variation in AEE and PA in the respiration chamber. The restrictions of the small environment in the respiration chamber, which limited activities to the spontaneous component of PA (essentially non-weight-bearing and low-intensity activities), seemed to influence a person stronger than did genotype. However, in daily life, when PA not only includes a spontaneous component but also obligatory and voluntary components (both weight-bearing and non-weight-bearing activities and a wide range of intensities), we found a high genetic contribution to the variation in AEE and PA. As hypothesized, the correlation between AEE and PA in daily life was largely due to shared genetic factors that affect both AEE and PA. This suggests that genes determine whether a person is prone to engage in activities and how much energy is expended for these activities. The combination of results from the confined, controlled area of the respiration chamber and the self-selected environment in daily life suggests that the genetic influence is more pronounced on the obligatory and voluntary components of PA than on the spontaneous component. Therefore, we also analyzed AEE normalized for body weight. In the respiration chamber, results for AEE and AEE/BW were the same. In daily life, however, the AE model was favorable for the uncorrected AEE, whereas almost no difference was observed between the CE and AE models for AEE/BW, with CE as the best-fitting model for AEE/BW. This suggests that body weight contributes to the genetic influence on AEE but that additional genetic factors are involved. Additional analyses of genetic and environmental influences on body composition, SMR, TEE, and ADMR showed a large contribution of genetic factors (a^2 between 0.79 and 0.87, data not shown). As previously reported (20), SMR and fat-free mass were highly heritable, and the genetic contribution found in the components of TEE was reflected in TEE and ADMR, which confirms the findings for AEE and PA.

In the present study, we used gold standard techniques for the measurements of energy expenditure (respiration chamber and DLW) and PA (accelerometry). The triaxial accelerometer used (Tracmor) measures frequencies of activities of daily living, which are mainly between 0.3 and 3.5 Hz (21). When placed on a belt at the lower back, the accelerometer can clearly distinguish small body movements; the output of an accelerometer positioned on a belt at the lower back of a subject performing low-intensity activities, such as computer work, writing, or reading (eg, static work), is significantly higher than the output of an accelerometer lying still on a table (22). To our knowledge, the only other study that investigated genetic influence on AEE with objective measurements was performed by Goran (23). After adjustment of the ADMR, which was measured with DLW in 37 young (aged 5−9 y) sibling pairs, for resting metabolic rate, Goran still found a significant sibling-pair correlation, which suggested separate genetic influences on the resting metabolic rate and nonresting energy expenditure (23). However, this family study did not include monozygotic twin pairs and could therefore not quantify genetic contributions. Epidemiologic twin studies have investigated PA with activity questionnaires. The findings of these studies, including those from a review on genetic determinants of PA, showed that PA is genetically influenced, with heritability coefficients between 0.29 and 0.68 (24–27), which still leaves a considerable influence of shared environmental factors (28). However, questionnaires rely on subjective interpretations of PA, which depends on how the question is asked and the type of responses offered as options (27).

The classic twin design used in the present study requires some remarks. First, a major assumption of the twin design is that monozygotic twins share a common environment to the same extent as dizygotic twins. If monozygotic twin pairs have a more similar environment than do dizygotic twin pairs, either as adults or as children, then heritability estimates are overestimated and common environmental influence is underestimated. The more obvious common environments of the present study, ie, living in the same house (with parents) and the amount of contact within pairs, were similar for monozygotic and dizygotic twins. Second, the twin design assumes that the twins studied represent the general young adult population. In our subjects, the mean value for the PA level (calculated as ADMR/SMR) was 1.81 (range: 1.39–2.29), which is comparable with the value of 1.75 (range: 1.2–2.5; lower because the PA level was calculated by dividing ADMR by BMR instead of SMR) that was reported for the general population (29). Third, the strict measurement protocol and the high costs of the measurement techniques, but mainly the difficulty of recruiting twins who are both willing to participate, limited the number of twins studied and thus the power of the present study. Therefore, it can be difficult to distinguish between additive genetic and common environmental factors. We cannot rule out the possibility of a small common environmental factor in the other coefficients. In addition, not enough power is available with this sample size to test for sex differences in path coefficients, especially because of the low number of male twins. However, statistical analyses that included only the female twins yielded the same results.

Although the numbers of twins in our study was limited, we were able to detect a significant genetic contribution to PA and AEE, and these results were confirmed with other measurements of energy expenditure and body composition. The use of a longitudinal study design and of objective measurements (DLW and accelerometers) in larger and more diverse populations will provide more information about the genetic determinants of AEE and PA. Quantification of genetic factors that contribute to AEE and PA provides a direction for the identification of genes involved. Finding those genes may identify persons at risk for obesity, because PA contributes to energy balance regulation. Furthermore, this allows for personalized prevention and treatment strategies for obesity based on a person's genetic background.

In conclusion, in the present exploratory study, which used gold standard techniques to measure AEE and PA but had a limited sample size, genetic influence explained a large part of the variation in AEE and PA in daily life, whereas both AEE and PA were influenced by environment only within the confined area of a respiration chamber.

We thank Loek Wouters for the analysis of the doubly labeled water samples, Paul Schoffelen for technical assistance with the respiration chambers, Rob Janssen for zygosity determination, and Patrick Lindsey for statistical advice. We thank the City Council of Maastricht and the Dutch Twin Register for their help with recruiting the twins.

AMCPJ contributed to the experimental design, data collection and analysis, and writing of the manuscript. MG contributed to data analysis and provided constructive, critical review of the manuscript. RV and KRW contributed to the experimental design and provided constructive, critical review of the data analysis and of the manuscript. None of the authors had any conflicts of interest.

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