Heritability of objectively assessed daily physical activity and sedentary behavior\textsuperscript{1–4}

Marcel den Hoed, Søren Brage, Jing Hua Zhao, Kate Westgate, Ayrun Nessa, Ulf Ekelund, Tim D Spector, Nicholas J Wareham, and Ruth JF Loos

ABSTRACT

Background: Twin and family studies that estimated the heritability of daily physical activity have been limited by poor measurement quality and a small sample size.

Objective: We examined the heritability of daily physical activity and sedentary behavior assessed objectively by using combined heart rate and movement sensing in a large twin study.

Design: Physical activity traits were assessed in daily life for a mean (±SD) 6.7 ± 1.1 d in 1654 twins from 420 monozygotic and 352 dizygotic same-sex twin pairs aged 56.3 ± 10.4 y with body mass index (in kg/m\textsuperscript{2}) of 26.1 ± 4.8. We estimated the average daily movement, physical activity energy expenditure, and time spent in moderate-to-vigorous intensity physical activity and sedentary behavior from heart rate and acceleration data. We used structural equation modeling to examine the contribution of additive genetic, shared environmental, and unique environmental factors to between-individual variation in traits.

Results: Additive genetic factors (ie, heritability) explained 47% of the variance in physical activity energy expenditure (95% CI: 23%, 53%) and time spent in moderate-to-vigorous intensity physical activity (95% CI: 29%, 54%), 35% of the variance in acceleration of the trunk (95% CI: 0%, 44%), and 31% of the variance in the time spent in sedentary behavior (95% CI: 9%, 51%). The remaining variance was predominantly explained by unique environmental factors and random error, whereas shared environmental factors played only a marginal role for all traits with a range of 0–15%.

Conclusions: The between-individual variation in daily physical activity and sedentary behavior is mainly a result of environmental influences. Nevertheless, genetic factors explain up to one-half of the variance, suggesting that innate biological processes may be driving some of our daily physical activity. \textit{Am J Clin Nutr} 2013; 98:1317–25.

INTRODUCTION

Physical activity energy expenditure (PAEE)\textsuperscript{5} is the most variable component of total energy expenditure (1), and both PAEE and body movement are important determinants of cardiometabolic health in adults (2–4) and children (5, 6). In addition, the time spent in moderate-to-vigorous intensity physical activity and sedentary behavior has been associated with metabolic risk (7–9). Although it is clear that environmental factors play a major role in the determination of physical activity levels at the population level (10), the role of intrinsic, biological factors in the regulation of physical activity levels within individuals has not received much attention in humans. Such biological factors consist of the interaction of proteins and peptides with receptors, the function of which is largely determined by their structure that, in turn, is encoded by the sequence of the respective gene. Epigenetic processes that modify the genome without altering the genetic sequence may also play a role by affecting gene expression.

Since the early work of Rundquist (11) on the inheritance of spontaneous activity in rats, a body of literature has provided evidence for a role of genetic factors in spontaneous physical activity in rodent models. In humans, family and twin studies have suggested that genetic factors may contribute to the between-individual variation in daily physical activity and sedentary behavior, but heritability (\(h^2\)) estimates that have been reported vary widely, ranging from 0% to 57% in family studies (12–16) and 0% to 78% in twin studies (17–24). These wide

\footnotesize{1 From the Medical Research Council Epidemiology Unit, University of Cambridge, Institute of Metabolic Science, Addenbrooke’s Hospital, Cambridge, United Kingdom (MdH, SB, JHZ, KW, UE, NJW, and RJFL); the Department of Medical Sciences, Molecular Epidemiology and Science for Life Laboratory, Uppsala University, Uppsala, Sweden (MdH); the Department of Twin Research and Genetic Epidemiology Unit, St Thomas’ Campus, King’s College London, St Thomas’ Hospital, London, United Kingdom (AN and TDS); the Department of Sports Medicine, Norwegian School of Sport Sciences, Oslo, Norway (UE); and The Charles Bronfman Institute for Personalized Medicine (RJFL), The Mindich Child Health and Development Institute (RJFL), and The Genetics of Obesity and Related Metabolic Traits Program (RJFL), The Icahn School of Medicine at Mount Sinai, New York, NY.

2 The British Heart Foundation had no involvement in the collection, analysis, or interpretation of data.

3 Supported by the British Heart Foundation (grant PG/07/108/23369). This is a free access article, distributed under terms (http://www.nutrition.org/publications/guidelines-and-policies/license/) that permit unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

4 Address correspondence to R Loos, The Charles Bronfman Institute for Personalized Medicine, The Icahn School of Medicine at Mount Sinai, One Gustave L Levy Place, Box 1003, New York, NY 10029. E-mail: ruth.loos@mssm.edu.

5 Abbreviations used: A, additive genetic factors; C, common or shared environmental factors; D, nonadditive or dominant genetic factors; E, unique or nonshared environmental factors; ICC, intrapair correlation coefficient; MET, metabolic equivalent of task; PAEE, physical activity energy expenditure.

Received June 30, 2013. Accepted for publication August 27, 2013. First published online September 18, 2013; doi: 10.3945/ajcn.113.069849.
ranges of $h^2$ estimates may partly reflect differences in the way that physical activity was assessed. Most of the reported family and twin studies have relied on a subjective assessment of physical activity [eg, the use of use questionnaires (13–19, 23, 24)]. Such methods are prone to recall bias and measurement error, some of which stems from the difficulty in translating answers to quantitative estimates of overall physical activity and, therefore, may result in an imprecise reflection of daily physical activity (25). Few twin studies have used more-objective methods to estimate the daily physical activity (ie, indirectly, by using a combination of doubly labeled water and indirect calorimetry and/or directly by using accelerometry). Such studies have been limited by small sample sizes ($n < 120$ twin pairs) (20–22). Because of the limitations of previous studies, we performed heritability analyses of daily physical activity and sedentary behavior assessed objectively by using combined heart rate and movement sensing in a large twin study.

**SUBJECTS AND METHODS**

**Participants**

We recruited twins from the TwinsUK registry, which consists of a national twin volunteer population of $>12,000$ adult twins aged 18–103 y of whom 83% are women. Monozygotic twins make up 51% of the cohort and dizygotic twins make up 49% of the cohort (26).

For the current study, we contacted 1842 twins, mainly from the ongoing Healthy Ageing Twin Study, which aims to address how closely changes at several organs or tissues correlate with the overall physiologic decline over time (26). Of those individuals, 1659 twins of 775 complete pairs agreed to participate (90% response rate). On average, twins who agreed to participate were younger (aged 56 compared with 60 y; $P = 3.2 \times 10^{-6}$) and leaner (BMI 26.1 compared with 27.5 kg/m$^2$; $P = 1.2 \times 10^{-3}$) than twins who did not accept our invitation. A total of 1296 twins were fit with a combined heart rate and movement sensor (Actiheart; CamNtech) (27) while visiting the clinic in St Thomas’ Hospital Campus, London (78% of responders). The remaining 363 twins (22% of responders), who had either recently completed or were not part of the Healthy Ageing Twin Study, received the sensor by mail, accompanied by instructions on how to attach the device.

We instructed twins to wear the sensor continuously for 7 d data collection in daily life and derived 1 d of physical activity data for 1551 of 1659 twins (93%), 1233 of whom had the sensor fit in the clinic (74% of participants) and 318 of whom received it by mail (19%). To maximize the quality of our data, we re-invited 107 twins for whom no physical activity data were acquired during the first measurement period and 87 twins with $<4$ d of physical activity data to wear the sensor for a second period of 7 d, to which 159 twins agreed. These twins received the sensor for a second period of physical activity assessment by mail. The second measurement period resulted in the acquisition of good-quality data in all 159 participating twins, which resulted in the acquisition of $81$ d of physical activity data in 1658 of 1659 twins who participated (Figure 1). There was no difference between monozygotic and dizygotic twins in the proportion of twins who received the monitor in the clinic or by mail [$P = 0.27$ (chi-square test)]. Data from one opposite-sex dizygotic pair, one twin of unknown zygosity, and one member of a dizygotic triplet were excluded from the analysis, which resulted in a total study population of 1654 twins. All physical activity measurements were performed between January 2008 and November 2010.

The 1654 twins represented 772 complete, same-sex twin pairs and 110 twins for whom data from the co-twin was not available. The 1654 twins had a mean ($\pm$SD) age of $56 \pm 10$ y (range: 17–82 y) and BMI of $26.1 \pm 4.8$ kg/m$^2$ (range: 15.5–48.2 kg/m$^2$) (Table 1; see Supplementary Table 1 under “Supplemental data” in the online issue). Monozygotic twins were leaner than dizygotic twins (BMI: 25.8 compared with 26.4 kg/m$^2$; $P = 0.03$) and had a higher variance in age (10.8 compared with 10.0 y; $P = 0.03$). The proportion of men was also higher in monozygotic twins [3.3 compared with 0.7%; $P = 1.7 \times 10^{-4}$ (chi-square test)]. Of 1654

![FIGURE 1: Flowchart showing the process of participant recruitment and quality control.](image-url)
resulted in a misclassification of zygosity in reported zygosity compared with the use of genotyping data. Unpublished observations in TwinsUK data suggested that self-zygosity was used in 435 twins from 20 complete pairs. We confirmed zygosity by using genotyping.

The majority of the 772 complete twin pairs lived in separate households at the time of participation (Table 1). The zygosity status did not affect the likelihood of twin pairs living together ($P = 0.50$ (chi-square test)). Seventy-nine twins from 32 complete monozygotic and 36 complete dizygotic pairs reported a disability that restricted their daily physical activity (eg, asthma or arthritis). The prevalence of such disabilities was not dissimilar in complete monozygotic and dizygotic pairs ($P = 0.20$ (chi-square test)).

The study conformed to the standards set by the Declaration of Helsinki of 1975 as revised in 1983, and the local ethics committee approved the study. All participants provided written informed consent before participating in the study.

### Objective methods of physical activity assessment

We initialized the combined heart rate and movement sensor for long-term recording, by summarizing the data into 1-min epochs. We aimed to start the assessment of daily physical activity on the same day for co-twins from the same twin pair, in which we succeeded for 598 of 772 complete pairs (77%). For 49 of the remaining pairs, the difference in the start date was 1–7 d (6%). The remainder could mainly be explained by the re-assessment of physical activity in twin pairs with <4 d data during the first measurement period. The within-pair difference in the start date did not differ by zygosity status [difference (chi-square test): $>0$ d, $P = 0.07$; $>7$ d, $P = 0.08$; $>14$ d, $P = 0.12$; $>31$ d, $P = 0.07$]. Monozygotic twins were monitored more frequently in the summer than were dizygotic twins [25.1% compared with 19.9%, $P = 1.2 \times 10^{-2}$ (chi-square test)] and less frequently in the winter [17.9% compared with 22.3%; $P = 7.4 \times 10^{-3}$ (chi-square test)].

We downloaded data collected during free living to a personal computer and processed the heart rate trace by using a robust Gaussian process regression method to handle potential measurement noise (28). Periods of nonwear time were inferred from a combination of nonphysiologically plausible heart rate and prolonged periods of inactivity as indicated by the sensor’s accelerometer; this classification was verified by inspection of time-series plots for all participants. All 1654 twins from 772 complete pairs had $\geq 1$ d (24 h wear) physical activity data in both twins; 1581 twins had $\geq 4$ d data (95.6%), which was shown previously to achieve a reliability of physical activity levels $>80%$ (29, 30) (see Supplementary Table 2 under “Supplemental data” in the online issue).

The calibration equation of the uniaxial trunk acceleration to whole-body workload was the same for all participants (31). The relation of the heart rate with workload was determined on an individual level according to age, sex, sleeping heart rate, and $\beta$-blocker use modeled in an independent calibration study in which 1941 healthy, middle-aged participants each performed two 8-min ramped-step tests (31, 32). At each time point, we estimated the physical activity intensity (in J · min$^{-1}$ · kg$^{-1}$) by using a branched equation framework (33). We collapsed the acquired physical activity intensity into the average time that participants spent in moderate-to-vigorous intensity physical activity and sedentary behavior (in min/d). Moderate-to-vigorous intensity physical activity has an intensity of $>3$ times resting metabolic.

### Table 1

<table>
<thead>
<tr>
<th>Description</th>
<th>Monozygotic twins</th>
<th>Dizygotic twins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals ($n$)</td>
<td>899</td>
<td>755</td>
</tr>
<tr>
<td>Women ($n$)</td>
<td>869</td>
<td>750</td>
</tr>
<tr>
<td>Complete pairs ($n$)</td>
<td>420</td>
<td>352</td>
</tr>
<tr>
<td>Complete pairs living apart [$n$ ($%$)]</td>
<td>371 (88)</td>
<td>325 (92)</td>
</tr>
<tr>
<td>Complete pairs living together [$n$ ($%$)]</td>
<td>28 (7)</td>
<td>21 (6)</td>
</tr>
<tr>
<td>Complete pairs with unknown residential status [$n$ ($%$)]</td>
<td>21 (5)</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Complete pairs with a self-reported disability [$n$ ($%$)]</td>
<td>32 (8)</td>
<td>36 (10)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>56 ± 11$^2$</td>
<td>57 ± 10</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>25.8 ± 4.6</td>
<td>26.3 ± 4.9</td>
</tr>
<tr>
<td>PAEE (kJ/d)</td>
<td>2517 (1906, 3110)$^5$</td>
<td>2318 (1821, 3022)</td>
</tr>
<tr>
<td>PAEE (kJ · kg$^{-1}$ · d$^{-1}$)</td>
<td>37.5 (29.2, 46.7)</td>
<td>35.1 (27.1, 44.2)</td>
</tr>
<tr>
<td>Acceleration (m/s$^2$)$^4$</td>
<td>0.113 ± 0.050</td>
<td>0.105 ± 0.044</td>
</tr>
<tr>
<td>MVPA (min/d)$^5$</td>
<td>37 (18, 61)</td>
<td>30 (15, 54)</td>
</tr>
<tr>
<td>Sedentary (min/d)$^6$</td>
<td>1039 ± 127</td>
<td>1055 ± 129</td>
</tr>
<tr>
<td>Wearing time (d)</td>
<td>6.7 ± 1.2</td>
<td>6.7 ± 1.1</td>
</tr>
</tbody>
</table>

$^1$MVPA, moderate-to-vigorous intensity physical activity; PAEE, physical activity energy expenditure.

$^2$Mean ± SD (all such values) (for normally distributed traits).

$^3$Median; IQR in parentheses (all such values) (for skewed distributions).

$^4$Average acceleration of the trunk along the vertical axis of the body.

$^5$Time spent in MVPA (>3 metabolic equivalent of task).

$^6$Time spent in sedentary behavior (≤1.5 metabolic equivalent of task).
rate, which is commonly referred to as the metabolic equivalent of task (MET) and sedentary behavior of ≤1.5 METs. We used the standard definition of activity intensity, whereby 1 MET equaled an oxygen uptake of 3.5 mL O$_2$ · min$^{-1}$ · kg body mass$^{-1}$. In addition, we analyzed data by using the Oxford resting metabolic rate equations (34), which yielded similar results. We summarized all individual time series into daily physical activity traits, while minimizing the diurnal information bias caused by potential nonwear. We multiplied body mass–specific PAEE by individual body mass to compute the average daily PAEE (in kJ/d). Finally, information acquired by the sensor’s uniaxial accelerometer was summarized in the average daily acceleration of the trunk along the vertical axis of the body (in m/s$^2$). Acceleration of the trunk provides the purest reflection of whole-body movements but is limited by the types of activity that people partake in because accelerometers are more sensitive to weight bearing than non-weight bearing activities (35, 36).

Anthropometric measurements

In twins who visited the clinic, height and weight were measured by using standard procedures. Body mass was measured with twins dressed in light clothing and without footwear to the nearest 0.1 kg by using a Seca Alpha Weight scale (Seca), and height was measured to the nearest 0.1 cm by using a Leicester Height Measure (Seca). BMI was calculated as body mass divided by height squared. For twins who received the sensor by mail, we used height and body mass as measured during the most recent clinic visit a median of 7.5 mo earlier (IQR: 2.3–14.4 mo).

Statistical analysis

PAEE and time spent in moderate-to-vigorous intensity physical activity were inverse-normally transformed to normalize distributions. We subsequently created residuals of daily physical activity traits adjusted for sex, age, and age-squared. For reasons provided in Heritability Analyses, we created residuals of physical activity traits and sedentary behavior with and without additional adjustment for BMI.

Classical twin studies assume that means and variances of monozygotic and dizygotic twins are the same, which we tested by using 2-tailed, unpaired t tests. Monozygotic twins were more physically active and spent less time in sedentary behavior than did dizygotic twins and showed a higher variance in acceleration of the trunk ($P<0.05$; see Supplementary Table 1 under “Supplemental data” in the online issue). However, these differences were attenuated and no longer reached significance after adjustment for sex, age, BMI, ethnicity, and seasonality after adjustment for multiple testing (see Supplementary Table 1 under “Supplemental data” in the online issue). Differences in the mean and variance of acceleration of the trunk were additionally driven by the 9 monozygotic twins with the largest acceleration and did not reach significance after their exclusion from the analysis ($P$-mean = 0.06, $P$-variance = 0.11 after exclusion). Additional adjustment of heritability analyses for ethnicity and seasonality or exclusion of 9 monozygotic twins with the largest acceleration of the trunk did not affect results. Hence, we performed heritability analyses as planned.

Heritability analyses

Twins raised together share part of their environment and this sharing is assumed to be the same for monozygotic and dizygotic twins (19). Monozygotic twins are genetically identical, whereas dizygotic twins share on average 50% of genotypes. This implies that a higher resemblance in daily physical activity and sedentary behavior in monozygotic compared with dizygotic pairs is indicative of a role for genetic factors.

We first assessed the nature of genetic and environmental contributions to the variance in daily physical activity and sedentary behavior by comparing Pearson’s intrapair correlation coefficients (ICCs) for residuals of the 4 traits after adjustment for covariates in monozygotic and dizygotic pairs by using data from all 1654 available twins. Next, we performed structural equation modeling to estimate the contribution of additive genetic factors (A), shared or common environmental factors (C), and unique or nonshared environmental factors (E) to the observed phenotypic variance by using OpenMx software, version 1.3 (37). We a priori hypothesized that a model in which all phenotypic variance is explained by a combination of A, C, and E (ACE model) is the biologically most plausible model, and we fit this model to the residuals for all traits first. ICCs that are >2-fold higher in monozygotic than dizygotic twins suggest that a nonadditive or dominant genetic factors (D) may also play a role. Hence, we fit ADE models to the data for traits that adhered to this criterion.

Alternative nested models were fit by constraining variance component(s) to zero, which resulted in AE, CE, DE (where appropriate), and E models. Nested models were compared with ACE and ADE models (where appropriate) by using a maximum likelihood approach with the accompanying Akaike’s information criterion (38). The model with the lowest Akaike’s information criterion is generally considered the best compromise between the goodness of fit and parsimony. We applied a bootstrapping approach to obtain 95% CIs of variance component estimates by using the percentile method (39) after resampling the appropriate number of twins 10,000 times from the original data set for all traits and (nested) models.

Compared with lean individuals, obese individuals were shown previously to have a similar absolute PAEE but a lower level of objectively assessed daily body movement (40). The latter was already observed in the early 1960s (41). Because increased levels of adiposity may prevent a physically active lifestyle, and adiposity is highly heritable itself (42), the heritability of unadjusted daily physical activity traits may, at least partly, reflect the heritability of adiposity. Therefore, we estimated the heritability of daily physical activity and sedentary behavior by using BMI-adjusted residuals and subsequently compared $h^2$ estimates for all traits calculated by using residuals with and without adjustment for BMI.

We performed sensitivity analyses to examine if the inclusion of twin pairs with a potentially suboptimal data quality affected results. First, we examined if the exclusion of the 73 twins with <4 d data changed estimates. Second, we examined if a within-pair difference in start date of physical activity assessment influenced results by excluding the 174 twin pairs for whom the measurement period started on a different day in both co-twins, which was followed by an analysis in which the 125 twin pairs for whom the start date differed by ≥1 w were excluded.
Because self-reported information on zygosity may result in underestimates of $h^2$ (42), we next examined whether the exclusion of the 435 twins with self-reported zygosity influenced results. We also repeated the structural equation modeling after the exclusion of the 79 twins with a self-reported disability that seriously restricted daily physical activity because such impairments may override the normal pattern of genetic and environmental factors that influence daily physical activity. Finally, we performed a sensitivity analysis in which the 35 male twins were excluded from the analyses to examine if the combination of data from men and women affected results.

The results are presented as means ± SDs for normally distributed variables and medians (IQRs) for traits with skewed distributions. Statistical analyses were performed with SAS version 9.2 for Windows software (SAS Institute) and OpenMX software, version 1.3 (37).

RESULTS

Pearson’s ICCs were higher in monozygotic than dizygotic pairs for all daily physical activity traits and sedentary behavior, which suggested a role for genetic factors (Table 2). The structural equation modeling in data from all 1654 twins showed that $h^2$ estimates ranged from 31% (95% CI: 9.4%, 50.5%) for the time spent in sedentary behavior to 47.4% (95% CI: 28.9%, 53.8%) for PAEE under the ACE model and reached significance for all traits except for bodily movements as reflected by acceleration of the trunk (95% CI: 0.0%, 44.2%). The variance that remained unexplained by genetic factors (A) was largely explained by environmental factors that were unique to each twin and random (measurement) error (E) (Figure 2, Table 3). The contribution of shared environmental factors (C) was small and nonsignificant for all traits and ranged from 0.0% (95% CI: 0.0%, 16.6%) for the time spent in moderate-to-vigorous intensity physical activity to 14.5% (95% CI: 0.0%, 32.1%) for the time spent in sedentary behavior (Figure 2, Table 3).

ICCs were 2–3 times higher in monozygotic than dizygotic pairs for acceleration of the trunk and time spent in moderate-to-vigorous intensity physical activity, which suggested that dominant genetic factors may play a role for these traits. Structural equation modeling subsequently showed that approximately one-third of the heritability of the time spent in moderate-to-vigorous intensity physical activity consisted of dominant genetic factors, whereas dominant genetic factors did not play a role in acceleration of the trunk. ACE and ADE models fit the data equally well for both traits and resulted in similar $h^2$ estimates (Table 3). Hence, we selected results from the a priori hypothesized ACE model for additional analyses to ensure the comparability of results across traits.

The AE model provided the most parsimonious fit for all traits (Table 3). Heritability estimates of the AE model deviated <2.0% from estimates acquired by using the ACE model for all traits, except for the time spent in sedentary behavior, for which the AE model provided a 16% higher $h^2$ estimate. Because constraining variance components to zero may inflate $h^2$ estimates (42), and the identification of a small contribution of shared environmental factors is still informative, we preferred the conservative $h^2$ estimates acquired by using the ACE model.

Adjustment of the analyses for BMI did not substantially affect $h^2$ estimates, with estimates that were between 3.9% higher for PAEE and 2.4% lower for acceleration of the trunk in unadjusted compared with adjusted analysis (see Supplementary Table 3 under “Supplemental data” in the online issue). The exclusion of twins with <4 d data, a different start date of physical activity assessment, a self-reported disability, or of male pairs did not materially change the results either, although the $h^2$ estimate of acceleration of the trunk did reach significance after the exclusion of twins with self-reported disabilities (95% CI: 0.8%, 45.6%). The inclusion of data from twin pairs with self-reported zygosity may have resulted in an underestimation of the heritability of the time spent in sedentary behavior but did not affect estimates for the other traits (see Supplementary Table 4 under “Supplemental data” in the online issue). Taken together, sensitivity analyses showed that $h^2$ estimates of daily physical activity traits and sedentary behavior were robust and mostly

![FIGURE 2. Variance component estimates of the ACE model for daily physical activity traits and sedentary behavior. Variance component estimates as acquired by using structural equation modeling are shown for A, C, and E for PAEE, average daily acceleration of the trunk along the vertical axis of the body (Acceleration), and time spent in MVPA (≥3 METs) and sedentary behavior (≤1.5 METs). A, additive genetic factors; C, common or shared environmental factors; E, unique or nonshared environmental factors; MET, metabolic equivalent of task; MVPA, moderate-to-vigorous intensity physical activity; PAEE, physical activity energy expenditure.](image-url)
<table>
<thead>
<tr>
<th>Model</th>
<th>Variance components</th>
<th>Model fit</th>
<th>Compared with ACE and ADE models</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>C</td>
<td>D</td>
</tr>
<tr>
<td>Physical activity energy expenditure (kJ/d)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE</td>
<td>0.465 (0.234, 0.534)</td>
<td>0.015 (0.000, 0.211)</td>
<td>—</td>
</tr>
<tr>
<td>AE</td>
<td>0.481 (0.413, 0.545)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>CE</td>
<td>—</td>
<td>0.369 (0.306, 0.428)</td>
<td>—</td>
</tr>
<tr>
<td>D</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>E</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Acceleration of the trunk along the vertical axis of the body (m/s^2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE</td>
<td>0.352 (0.000, 0.442)</td>
<td>0.016 (0.000, 0.320)</td>
<td>—</td>
</tr>
<tr>
<td>ADE</td>
<td>0.370 (0.000, 0.433)</td>
<td>—</td>
<td>0.000 (0.000, 0.416)</td>
</tr>
<tr>
<td>AE</td>
<td>0.370 (0.289, 0.449)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>CE</td>
<td>—</td>
<td>0.311 (0.239, 0.378)</td>
<td>—</td>
</tr>
<tr>
<td>D</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>E</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Time spent in moderate-to-vigorous intensity physical activity (&gt;3 METs) (min/d)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE</td>
<td>0.474 (0.289, 0.538)</td>
<td>0.000 (0.000, 0.166)</td>
<td>—</td>
</tr>
<tr>
<td>ADE</td>
<td>0.312 (0.000, 0.521)</td>
<td>—</td>
<td>0.170 (0.000, 0.515)</td>
</tr>
<tr>
<td>AE</td>
<td>0.474 (0.400, 0.541)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>CE</td>
<td>—</td>
<td>0.361 (0.289, 0.426)</td>
<td>—</td>
</tr>
<tr>
<td>D</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>E</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Time spent in sedentary behavior (≤1.5 METs) (min/d)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE</td>
<td>0.310 (0.094, 0.505)</td>
<td>0.145 (0.000, 0.321)</td>
<td>—</td>
</tr>
<tr>
<td>ADE</td>
<td>0.470 (0.404, 0.532)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>AE</td>
<td>—</td>
<td>0.384 (0.322, 0.437)</td>
<td>—</td>
</tr>
<tr>
<td>CE</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>E</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

1 Variance explained by A, C, D, and E. Estimates (95% CIs) of variance components were acquired by using structural equation modeling and adjusted for sex, age, age-squared, and BMI. Results from the ACE model were preferred for all traits over those of the most parsimonious model. \(\Delta -2LL\) and \(P\) values show comparisons with the ACE model for the AE, CE, and E models and with the ADE model for the DE model. A, additive genetic factors; AIC, Akaike’s information criterion; C, common or shared environmental factors; D, nonadditive or dominant genetic factors; E, unique or nonshared environmental factors; MET, metabolic equivalent of task; \(\Delta -2LL\), \(\Delta df\) and \(P\) values show comparisons with the ACE model for the AE, CE, and E models and with the ADE model for the DE model. A, additive genetic factors; AIC, Akaike’s information criterion; C, common or shared environmental factors; D, nonadditive or dominant genetic factors; E, unique or nonshared environmental factors; MET, metabolic equivalent of task. \(\Delta -2LL\), \(\Delta df\) and \(P\) values show comparisons with the ACE model for the AE, CE, and E models and with the ADE model for the DE model. A, additive genetic factors; AIC, Akaike’s information criterion; C, common or shared environmental factors; D, nonadditive or dominant genetic factors; E, unique or nonshared environmental factors; MET, metabolic equivalent of task.

2 Traits were analyzed after inverse normal transformation.
unaffected by the inclusion of data of potentially suboptimal quality.

DISCUSSION

In the largest twin study with objective measurements of physical activity, we showed that daily physical activity and sedentary behavior were moderately heritable. Our $h^2$ estimates of 35–47% for different physical activity traits and 31% for the time spent in sedentary behavior suggested that biological processes influence daily physical activity levels. $h^2$ estimates were robust and largely unaffected by adjustment for BMI or the inclusion of twins with potentially suboptimal data quality. Besides the moderate contribution of genetic factors, most of the variance in daily physical activity and sedentary behavior was explained by a combination of environmental factors that were unique to each twin and random (measurement) error. Environmental factors that were shared between twins within a pair played a marginal role at most.

PAEE and bodily movements as reflected by acceleration of the trunk have both been used in epidemiologic studies as estimates of the latent and unobservable phenomenon of habitual physical activity. When assessed by combined heart rate and movement sensing, there are intrinsic differences between the 2 traits that should not be dismissed. The sensor’s accelerometer provides a better reflection of some activities, such as walking, compared with activities that involve little movement of the upper body along the vertical axis of the body, such as cycling. The latter activities are recognized more accurately when information from the sensor’s accelerometer is integrated with that of its heart rate sensor. Combined sensing also discriminates better between walking with or without an external load as well as between walking on a flat or sloping surface compared with acceleration alone. Thus, PAEE provides a more comprehensive estimate of daily physical activity than acceleration of the trunk alone. However, PAEE has limitations when acquired by a combined heart rate and movement sensor in large epidemiologic data sets, in which the individual calibration of the association between the heart rate and workload during a graded exercise test is not feasible. We used the results of a calibration study in an independent sample, which leads to slightly less precise estimates of PAEE (31). As such, our $h^2$ estimates for PAEE and bodily movements are likely conservative.

Combined heart rate and movement sensing was also used to objectively assess the time spent in sedentary behavior, which should be interpreted as the absence of physical activity. Although piezoelectric accelerometers such as the one in our sensor have often been used to quantify sedentary behavior objectively, other devices such as inclinometers, piezoresistant accelerometers, or piezocapacitive triaxial accelerometers are able to distinguish between lying, sitting, and standing (43, 44) and, therefore, may be better suited to assess sedentary behavior depending on one’s definition of sedentary behavior.

Our $h^2$ estimates were similar to those reported previously in relatively large twin studies with self-reported physical activity traits (17–19, 23, 24) but differed from estimates obtained in small twin studies with objectively assessed physical activity (20–22). We cannot exclude the possibility of true population differences in the relative contribution of genetic and environmental factors because heritability estimates are, by definition, population and time specific. Nevertheless, the difference between our $h^2$ estimates and those reported previously in twin studies with objectively assessed physical activity may partly reflect the small sample size of previous efforts (22), a potentially higher level of heritability in adults compared with that in children and adolescents (20, 21, 45), a more accurate quantification of some activities by triaxial compared with uniaxial accelerometers (46), and the inclusion of same-sex, non-twin siblings in dizygotic twin pairs by other authors (22).

$h^2$ estimates shown in our twin study were higher than estimates reported previously in family studies with questionnaire-derived physical activity (13–16). Although twin studies typically result in higher $h^2$ estimates of complex traits than family studies (42), the difference in $h^2$ estimates for physical activity likely reflected the use of self-reported relatedness in family studies with self-reported physical activity because our estimates were similar to those of a large family study with objectively assessed physical activity in which relatedness was assessed by using a gene-based method (12). Although a range of factors complicates a straightforward comparison of our results with those of previous studies, to our knowledge, our study is the largest twin study with objective measurements of daily physical activity and confirms a role for genetic factors in physical activity regulation.

Our findings have important consequences for public health initiatives, because adherence to a physical activity intervention program is likely more challenging for individuals who lack a biological drive to be active, and might even experience adverse effects in response to being physically active (47), than for individuals with a strong genetic predisposition to being physically active. Thus, such a predisposition might explain in part why some individuals respond better to physical activity intervention programs than others.

Thus far, 2 genes have been identified as playing a role in physical activity regulation on the basis of evidence from ≥4 independent lines of research, all of which were animal studies (48). DRD1 encodes a dopamine receptor and likely influences physical activity via the reward system (49, 50), whereas NHLH2 encodes nescient helix loop helix 2, which presumably exerts its effect by affecting β-endorphin production and interacting with the melanocortin-4 receptor (MC4R) (51, 52). Equally convincing evidence from human data is lacking. Some candidate-gene studies have provided promising leads (53–57), but few associations have been replicated in subsequent efforts (58). This situation likely reflects a poor choice of candidate genes, resulting from limited insights from biology, poor coverage of genetic variation, the small scale of studies, and the complexity of the trait for which small effect sizes are anticipated. Hypothesis-free approaches (ie, linkage) (12, 59, 60) and genome-wide association studies (61) have not identified loci that are robustly associated with physical activity traits in humans either. Larger efforts with more-detailed phenotypic information will likely clarify biological pathways that are relevant for daily physical activity and sedentary behavior in humans, because large-scale genome-wide association studies have previously identified loci that are associated with other cardiovascular risk factors of comparable heritability (62–64). Besides aerobic capacity and sensitivity to internal and external rewarding cues, such pathways may relate to susceptibility to fatigue, physical discomfort after physical activity,
perception of ability, and triggering of food intake when physical activity is used as a weight-loss strategy.

A limitation of the current study is that our sample consisted almost exclusively of women. However, our heritability estimates were comparable with those of a family study with objectively assessed daily physical activity traits in both sexes, some of which reported higher \( h^2 \) estimates in men than women (17, 18). Another limitation related to the difference in age and BMI between twins who agreed to participate and those who declined. This healthy participant bias, whereby participants in epidemiologic studies present with fewer risk factors than those who decided not to participate, has been described previously and does not necessarily affect the representativeness of results for the general population (65, 66). Importantly for our effort, there was no difference in the response rate between monozygotic and dizygotic twins.

In conclusion, to our knowledge, our study is the first in which heritability estimates are based on results from a large number of twins with objectively assessed physical activity and shows that daily physical activity and sedentary behavior are moderately heritable in adults. This result implies that physical activity regulation is influenced by biological factors.

We appreciate the efforts associated with recruiting twins by TwinsUK as well as the efforts required for processing heart rate and movement sensor (Actiheart; CamNtech) data by the physical activity technical team at the Medical Research Council Epidemiology Unit. We also thank the twins participating in the study for their time and efforts.

The authors’ responsibilities were as follows—MdH, SB, UE, TDS, NJW, and RJFL: designed the research; SB, UE, TDS, NJW, and RJFL: provided essential materials; MdH and KW: analyzed data; MdH and JHZ: performed DjH: had primary responsibility for the final content of the manuscript. None of the authors had a conflict of interest.

REFERENCES


