Stability and change in genetic and environmental influences on hand-grip strength in older male twins

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Carmelli, Dorit, and Terry Reed. Stability and change in genetic and environmental influences on hand-grip strength in older male twins. J Appl Physiol 89: 1879–1883, 2000.—The aim of this study was to investigate aging-related changes in the contribution of genetic and environmental influences to hand-grip strength in late adulthood. Subjects in this study are 152 intact twin pairs (77 monozygotic and 75 dizygotic pairs) from the National Heart, Lung, and Blood Institute Twin Study assessed repeatedly for hand-grip strength at mean ages of 63 and 73 yr. Structural equation genetic modeling was used to investigate stability and change in the genetic and environmental components of variance of hand-grip strength in late adulthood. Average decline in strength over the 10 yr of follow-up was \(-1.05 \pm 6.8\) (SD) kg and was highly significant \((P = 0.003)\). The test-retest correlation between baseline and follow-up grip strength was 0.62 \((P < 0.001)\). Bivariate genetic modeling found significant genetic and shared environmental stability in hand-grip strength over the 10 yr of follow-up, with genetic and shared environmental influences accounting for 35 and 48%, respectively, of the test-retest phenotypic correlation. We conclude from these results that stability in hand-grip strength in late adulthood is due primarily to continuity of genetic and familial influences.

Hand-grip strength has long been used as a measure of total body strength, and poor muscle strength in middle adulthood has been shown to predict functional limitations and disability in old age (6, 15, 19). Conversely, when strength is well above the minimum required level, a reserve capacity may exist that could prevent functional limitations that may result from inactivity, acute illness, or aging (1, 5). A rapid decline in hand-grip strength after 60 yr of age, by as much as 20% from peak levels, has been observed in cross-sectional and longitudinal studies, although great interindividual differences have also been noticed, with a substantial percentage of elderly showing no decline in strength (7, 20). For example, Kallman et al. (10) found that, over an average 9-yr follow-up period, 15% of subjects ≥60 yr of age showed no decline in strength.

The contributions of genetic and environmental influences to hand-grip strength in late adulthood have not been widely studied. We first reported a heritability of 48% for absolute grip strength in 127 monozygotic (MZ) and 130 dizygotic (DZ) male twins from the National Heart, Lung, and Blood Institute (NHLBI) Twin Study who were 59–70 yr of age when first tested as part of the third examination cycle of this cohort (21). Also, the largest estimate of heritability of hand-grip strength in that study (65%) was found after adjustment for age, weight, height, and anthropometric variables. We concluded from these data that grip strength in late adulthood is a genetically determined trait independent of body size. We were unable, however, with these cross-sectional data to test hypotheses concerning the age dependency of genetic influences. Nor could we estimate the extent to which genetic and environmental influences on hand-grip strength remain stable over a period of adult life when rapid decline is expected.

More recently, a 10-yr follow-up was conducted in the NHLBI Twin Study, and repeat measurements of hand-grip strength were obtained on a large subset of twins with third-examination data. Thus, for the first time, a two-wave twin data set was available to examine the heritability of hand-grip strength at two time points 10 yr apart. In this study we used these data to investigate the extent to which genetic and environmental influences across different ages were the same or different.

METHODS

Participants in this study are from the NHLBI Twin Study, which began in 1969 (4, 9). Briefly, 514 twin pairs volunteered to participate in a study of cardiovascular risk factors conducted at five regional centers in the United States. Subjects are members of a larger twin registry of World War II veterans born between 1917 and 1927 and followed for 23–28 yr, with subsequent examinations conducted in 1981–82, 1986–87, and 1995–97. At the third and fourth examination cycles, hand-grip strength was determined as part of a 3-h protocol. As previously described, medical interviews and physical examinations on each member of a twin pair were performed independently by two trained physicians who were blind to zygosity. Subjects’ self-reports of cardiovascular events and medical procedures were consequently blinded.

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were confirmed with medical and hospital records (22). The final diagnosis of stroke or cerebrovascular accidents was determined by medical staff who reviewed the medical records and the physical examination data. Subjects in this study are 152 intact twin pairs (77 MZ and 75 DZ pairs) with baseline and follow-up measurements of hand strength. Subjects with clinical evidence of stroke were removed from the present analysis. Mean age of twins at the 1995–97 follow-up was 73 yr (range 69–80 yr).

Grip strength was measured with an adjustable mechanical hand dynamometer (Lafayette Instrument, Lafayette, IN). Subjects were seated, and the outer stirrup on the dynamometer was set at 4 cm. For subjects with smaller hands, the setting was shortened so that when the subject held the dynamometer, the second phalanx was against the inner stirrup. Three trials, with brief pauses, were allowed for each hand alternately. Subjects were encouraged to exert their maximal grip. The best result was chosen for analysis.

Statistical analysis. The objective of a genetic analysis is to decompose the observed phenotypic variance of a measured trait (e.g., hand-grip strength) into genetic and environmental components. Sources of phenotypic variance could be additive genetic (A; i.e., the sum of the average effects of the individual genes), shared environmental (C; i.e., experiences that twins have in common such as the prenatal and early shared familial influences), and unique environmental (E) effects. Additive genetic influences are correlated 100% between members of an MZ twin pair and 50% between members of a DZ twin pair. Shared environmental influences, if present, are assumed to contribute equally to similarity in MZ and DZ twin pairs, whereas unique environmental influences are uncorrelated between twin pairs and include measurement error. A greater within-pair resemblance in MZ than in DZ twins is considered evidence for the presence of genetic effects.

When data on twins have been collected on two separate occasions, a triangular or Cholesky decomposition is used to analyze the combined longitudinal data. Using a bivariate longitudinal genetic analysis, we can separate new genetic and environmental effects specific to the second measurement from effects that are common to both time points. The computer program Mx (16) was used to fit a bivariate Cholesky model to the 4×4 variance-covariance matrices of the combined time 1 and time 2 hand-grip data. Models were fitted separately for each twin zygosity. In the bivariate model, we assumed that common genetic and environmental effects are influencing the observed measurements at times 1 and 2, whereas time-specific genetic and environmental effects are influencing only time 2 measurements. Figure 1 depicts the structural equation model for one member of a twin pair. A1, C1, and E1 are the additive genetic and shared and nonshared environmental influences common to times 1 and 2; A2, C2, and E2 are the genetic, shared environmental, and nonshared environmental influences specific to time 2. The effects of A1, C1, and E1 are represented by parameters h, c, and e, respectively; specific A2, C2, and E2 effects are represented by parameters h’, c’, and e’ respectively.

RESULTS

For the sample as a whole, mean absolute strength was 40.8 ± 8.8 (SD) kg at baseline in 1985–86 and 39.8 ± 8.8 kg at follow-up in 1995–97. Average decline in strength over the 10 yr of follow-up was −1.05 ± 6.8 kg and was highly significant (P = 0.003). Annualized and expressed as percent change from baseline, average decline in strength was 0.26%/yr. The test-retest correlation between baseline and follow-up measurements was 0.62 and was highly significant (P < 0.001). Hand-grip strength was significantly associated with subjects’ age, height, and waist circumference. Older twins had lower strength; taller and more obese twins had greater strength. Together with baseline grip strength, subjects’ age, height, and waist circumference predicted 52% of the variance of grip strength at follow-up (F = 108.9, P = 0.0001).

Longitudinal genetic analyses. To determine possible bias due to loss to follow-up, we compared nonparticipants twins with participants in the 1995–97 follow-up on age and baseline grip strength. We found that participants were younger than nonparticipants but did not differ significantly on mean hand-grip strength in 1985–86. We also compared participant twin pairs with nonparticipant pairs on the ratio of MZ to DZ intraclass correlation and found no significant difference. Thus bias from loss to follow-up of twin pairs or singletons should be minimal in the longitudinal analyses of twin-pair similarities.

The first step in the longitudinal genetic analyses was to examine the pattern of MZ-DZ correlations at
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Table 1. Longitudinal genetic model and submodels fit to 1985–1986 and 1995–1997 hand-grip data

<table>
<thead>
<tr>
<th>Model</th>
<th>df</th>
<th>$\chi^2$</th>
<th>$P$</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: Full ACE model</td>
<td>11</td>
<td>18.39</td>
<td>0.07</td>
<td>−3.61</td>
</tr>
<tr>
<td>2: No effect of common genetic</td>
<td>12</td>
<td>22.81</td>
<td>0.03</td>
<td>−1.19</td>
</tr>
<tr>
<td>3: No effect of common shared environment</td>
<td>12</td>
<td>23.57</td>
<td>0.02</td>
<td>−0.43</td>
</tr>
<tr>
<td>4: No effect of common individual environment</td>
<td>12</td>
<td>38.16</td>
<td>&lt;0.01</td>
<td>14.16</td>
</tr>
<tr>
<td>5: Model 1 with no occasion-specific genetic effect</td>
<td>12</td>
<td>18.39</td>
<td>0.10</td>
<td>−5.61</td>
</tr>
<tr>
<td>6: Model 1 with no occasion-specific shared and/or individual environmental effects</td>
<td>13</td>
<td>23.94</td>
<td>0.03</td>
<td>−2.06</td>
</tr>
</tbody>
</table>

A, additive genetic; C, shared environmental; E, nonshared environmental; AIC, Akaike’s information criterion; df, degrees of freedom.

Longitudinal genetic, shared environmental, and nonshared environmental correlation can also be calculated from Fig. 2 by dividing the cross product (i.e., covariance) of genetic, shared environmental, and nonshared environmental path coefficients by the square root of the genetic and shared and nonshared environmental variances at times 1 and 2. We found that the genetic, shared, and nonshared environmental correlations over the 10 yr of follow-up were 0.66, 0.88, and 0.44, respectively. From these values we then derived the proportions of stable phenotypic variance attributable to genetic, shared, and nonshared environmental effects. We found that genetic and shared environmental influences accounted for 35 and 48%, respectively, of the stable variation, whereas only 17% of the stable variation was due to nonshared environmental influences. Thus the observed stability in hand-grip strength in this cohort of twins is due primarily to stability of genetic and shared familial influences.

DISCUSSION

This study is the first to investigate the contributions of genetic and environmental influences to individual differences in hand-grip strength in late adulthood. Using a two-wave data set collected on a relatively large sample of healthy male twins, we found that 83% of the stable variation in hand-grip strength was due to persistence of genetic and shared familial influences from middle age to old age. We also observed a decrease in genetic variance from 35% at baseline to 22% at follow-up and a slight increase in shared environmental influences from 39 to 45%. We found no evidence for newly expressed genes at follow-up; however, new shared and nonshared environmental influences not expressed at baseline contributed significantly to hand-grip variability at follow-up.
What might be the cause for the observed longitudinal stability of genetic influences on hand-grip strength? In part, the genetic stability in hand-grip strength can be explained by the genetic stability of correlated physiological traits such as height, weight, and muscle mass (3, 8). Strength relates to the total number of muscle fibers, the area of fibers, fiber tension, and the percentage of fibers activated (11, 24). These, in turn, can be strongly influenced by early shared environmental influences, including early training and learned behaviors associated with muscle use (e.g., leisure time activity, diet). The results from our analyses indicate strong stability of shared environmental influences and even suggest an increase over time in the contribution of these effects.

The average annualized grip-strength decline in this sample of elderly twins was 0.26%/yr. Earlier longitudinal studies have reported greater declines in average grip strength of 0.7–3%/yr (10, 19). Older people are also more likely to show steeper decline than younger people (14). Decline in muscle mass has been suggested as the direct cause of age-related strength decline (23). With age there is a replacement of muscle fibers by fat and connective tissue and a shift to a lower percentage of fast-twitch fibers (18). Thus the observed decline in heritability over the 10-yr period may be due to genetic differences in aging of musculoskeletal capacity. Previous investigations, however, found that the relationship between age and grip strength remained after adjustment for the replacement of muscle fibers by fat, so other unidentified factors also may be involved (12).

Others have suggested that lower strength is most likely to result from a decline in excitation-contraction coupling, a decline in the activation of high-threshold motor units, or a decrease in the number of fibers (2). In stroke victims, the injury in the central nervous system will affect the descending neural pathways and result in poor motor unit activation (13). Muscle weakness is one of the manifestations of impaired neurological function after stroke (13). Therefore, a probable explanation for the decline in the heritability of grip strength could be alterations in cerebrovascular auto-regulation mechanisms occurring as a result of aging. This, in turn, may be influenced largely by the persistence of shared cultural and environmental factors, including sedentary habits, smoking, and alcohol consumption, all known risk factors for a steeper loss in grip strength. Indeed, shared environmental factors contributed significantly in the present study to stability of hand-grip strength.

Twins included in this study have participated in two physical examinations 10 yr apart and can be characterized as cooperative and in good health. Recruitment and response biases are potential problems in twin research but are less threatening when participation in the study is uncorrelated with the trait being analyzed. In this study, participants at both examinations were younger than nonparticipants, but no difference was found between the two groups on baseline grip strength. We therefore believe that recruitment bias was not a confounding factor in the present analysis. The present sample was also restricted to one ethnic and gender group: Caucasian men. Our findings, however, can probably be generalized to other populations. The physiological processes investigated in the present study are unlikely to differ materially by race or gender, although in principle the environmental or genetic factors predisposing women or people of other racial groups to accelerated strength loss may be different.

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