Heritability of lumbar flexibility and the role of disc degeneration and body weight

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Battie MC, Levalahti E, Videman T, Burton K, Kaprio J. Heritability of lumbar flexibility and the role of disc degeneration and body weight. J Appl Physiol 104: 379–385, 2008. First published November 29, 2007; doi:10.1152/japplphysiol.01009.2007.—Spinal range of motion is evaluated in assessing patients with back problems and monitoring outcomes, as well as in general fitness assessments. Yet, determinants of the substantial interindividual variation in spinal range of motion are not well understood. Substantial genetic effects on global measures of range of motion and hypermobility have been suggested from earlier studies, but genetic influences specifically on spinal range of motion have not been previously studied. The objectives of the present study were to investigate the relative role of genetic and environmental influences on lumbar range of motion in adult men and the pathways through which genes may influence range of motion. Thus we conducted a classic twin study of 300 monozygotic and dizygotic male twin pairs with consideration of covariates, using standard statistical methods. All subjects underwent a clinical examination, including general anthropometrics, lumbar range of motion, and lumbar MRI to assess disc degeneration, as well as an extensive interview on environmental and behavioral exposures and back pain history. We found the proportion of variance in lumbar range of motion attributable to genetic influences (heritability estimate) to be 47%. The extent of lumbar range of motion in flexion was predominantly determined by genetic influences (64%), while extension was influenced to a somewhat greater degree by environmental and behavioral factors. Statistically significant age-adjusted genetic correlations were found between lumbar extension and disc degeneration variables ($r_a = -0.38$ to $-0.43$) and between flexion and body weight ($r_a = -0.33$), suggesting two pathways through which genes influence lumbar range of motion.

lumbar spine; range of motion

SPINAL RANGE OF MOTION measures continue to be in common use in assessing patients with back problems and monitoring outcomes, as well as in general fitness assessments. Yet, determinants of the substantial interindividual variation in spinal range of motion are not well understood.

Subject’s age and sex have been associated with lumbar spine flexibility in adulthood, as have body weight or BMI, intervertebral disc degeneration, and low back pain history to more modest degrees (2, 8, 31). Effects of physical activity and sports participation have been less clear (8, 9). Genetic influences specifically on spinal range of motion have not been previously studied. However, moderate to high genetic influences on global flexibility, as judged from the sit-and-reach test, have been suggested from the results of several family and twin studies (11, 16, 17, 23), but not all (10). Furthermore, Mikkelson et al. (20) found flexibility as measured with the sit-and-reach test to be highly stable from adolescence to middle age, whereas other fitness components were much less stable. Although their sample was relatively small, the result was clear and would be congruent with a substantial genetic component that is maintained throughout life. A large genetic influence also was found for hyperflexibility, as defined through a self-report questionnaire, in a recent classic twin study of adult women (13). Yet, despite evidence suggesting a substantial familial influence, there has been little insight into the mechanisms through which genetic factors influence range of motion or flexibility (12).

The objectives of the present study were to investigate the relative role of genetic and environmental influences on lumbar spine range of motion in adult men, as well as the pathways through which genes may influence range of motion. To meet these objectives, we conducted a classic twin study with consideration of covariates. The overall genetic contribution or heritability of a phenotype, in this case range of motion, refers to the proportion of population variance in the trait attributable to interindividual genetic variation. Extending the analyses to include multivariate analyses and correlations between the genetic components of range of motion and a second phenotype, such as intervertebral disc degeneration, expresses the extent to which the same genes account for the genetic influences on the two phenotypes. This can provide clues as to the mechanisms or pathways through which genes influence range of motion. Similar correlations can be examined for environmental components of range of motion to gain insights on mechanisms of influence. In particular, on the basis of an earlier association observed between greater disc degeneration and lesser lumbar range of motion (8), as well as the substantial influence of genetics on disc degeneration (3, 26), we were interested in examining the hypothesis that disc degeneration may be one pathway through which genes influence lumbar range of motion. Lumbar flexibility has also been associated with body weight (8), which also has a substantial genetic component (18, 28) and may represent another genetic pathway influencing lumbar flexibility (19).

SUBJECTS AND METHODS

Subjects

Monozygotic (MZ) and dizygotic (DZ) twin pairs were selected in an analogous way from the population-based Finnish Twin Cohort based on cotwin discordance in common environmental and behavioral exposures (exercise, smoking, occupational materials handling, etc.) and body weight. Further details are presented in Battie et al. (2006). The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
sitting, and driving) (3). The sample size was then increased by adding randomly selected MZ and DZ pairs for a total of 147 MZ and 153 DZ male twin pairs (age 35–70 yr). The sample of MZ twins was compared with the larger twin cohort on a multitude of factors, including history of low back pain, and found to be representative. The only exceptions were a slightly greater likelihood of being employed and having higher physical job demands, as these were initial selection criteria (29).

The validity of the questionnaire-based diagnosis of zygosity was studied previously, and 100% agreement in classification between the questionnaire data and 11 blood markers was found, with an estimated probability of misclassification of 1.7% at the population level (27). The accuracy of the method has been further confirmed by genetic analyses in the present sample.

Study protocols were reviewed and approved by the Ethical Committee of the Department of Public Health at the University of Helsinki and the Faculty of Rehabilitation Medicine of the University of Alberta. All subjects received written information about the study procedures and provided informed consent before participating.

Data Acquisition

All study subjects were transported to a central location in Finland where an extensive, structured interview was conducted, which included data on health histories, as well as routine occupational and leisure time physical activities. Clinical examinations of each subject also were conducted.

Environmental and behavioral exposures. Subjects were asked to discuss each job in which they had been employed since entering “work life” through the present time. This included the job title and a description of the associated tasks, as has been described in detail previously (3). On the basis of this detailed history, a job code was created using a four-point scale of 1 (= sedentary work), 2–3 (= progressive degrees of materials handling and postural loading), and 4 (= very heavy physical loading). The job code for the longest job held was used in analyses to represent occupational loading history.

The subjects were asked to describe the tasks performed in their current job(s), including the number of hours per day spent working in twisted or bent postures. To assist in defining these postures, the subjects were asked to select, from pictures representing work positions of various degrees of flexion and extension, the one(s) that best depicted their actual work postures. Subjects estimated the approximate number of hours spent each day working in postures with the trunk flexed to 40 degrees or more, as well as the time spent working overhead. For purposes of analyses, subjects were categorized as either working in bent postures or not, as was also the case for overhead work in an extended position.

A limited evaluation of interview reliability was conducted of occupational exposures. The intraclasse correlation coefficients (ICC) using a 1-yr test-retest interval were 0.75 for sitting time and 0.60 for mean total lifting per day (3).

Subjects were also questioned about regularly performed exercise and other leisure time physical activities during adolescence and adulthood. Information included the type of exercise or activity, time span of participation in years, months per year of participation, and mean frequency, duration, and intensity, and whether or not participation was at a competitive level, if sports related. A summary variable was calculated by summing the weekly hours separately for exercise category and other physical leisure time activities. Test-retest reliability, using a 5-yr test-retest interval, of the summary variable of mean hours of exercise per week yielded acceptable reliability (ICC, 0.73) (24).

Low back pain history. Recent low back pain history was determined from several questions, including the following: 1) Are you having back problems today? 2) Over the past 12 mo, how often have you experienced low back aches/pains? A seven-point scale was used (1 = daily; 2 = not daily, but at least once per week; 3 = not weekly, but at least once per month; 4 = several times per year; 5 = 2–3 times per year; 6 = once per year; and 7 = none at all). 3) How would you rate your worst low back pain/ache over the past 12 mo using a scale from 0 to 100, with 0 being no pain and 100 being the worst pain imaginable?

Disc degeneration. Lumbar MR images were obtained, including T1, T2, and proton-weighted images using a 1.5-T imager with a surface coil (Magnetom, Siemens AG Erlangen, Germany) (3). Spin-echo techniques were used to obtain sagittal and axial images of the lumbar spine. Field of view was 260 mm, and the slice thickness and interslice gap were 4 mm and 0.4 mm, respectively, for axial slices. The cotwins were imaged after one another, and each spent at least 30 min lying supine immediately before MRI to control for diurnal and activity effects on the disc (5, 6).

Disc height narrowing was assessed qualitatively using an ordinal scale from 0 to 3, with 0 being normal and 3 representing severe narrowing with end plates almost in contact. Similarly, an ordinal scale from 0 to 3 was used for disc bulging and vertebral rim osteophyisis. All assessments were completed by one experienced spine surgeon blinded to twinship and subject background. The weighted kappa value for the intrarater reliability was 0.80 for disc height narrowing, 0.53 for disc bulging, and 0.50 for osteophyisis.

Lumbar range of motion. Lumbar range of motion in the sagittal plane was measured using the flexicurve method (7, 32). Briefly, a flexible curve is applied to the lumbar spine in standardized postures of maximal flexion and extension, and the locations of S1, L4, and T12 are marked. A paper trace of the curve is made, and a digitizer is used to record the curve and calculate angles for flexion and extension in upper and lower lumbar regions. This methodology has been shown to be valid and suitably reliable for group comparisons (32). All measures were obtained by one of three research clinicians and digitized by an operator blinded to the source of the curves. Anthropometric measures included standing height and weight.

Data Analysis

Quantitative genetic modeling was done to estimate common and specific genetic or environmental variance components for back pain variables and identified covariates. 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 dominance (D), and shared (C) and nonshared (E) environmental components. One can fit models based on the different combinations of these parameters: AE, ACE, ADE, and E, but effects due to dominance, additive genetic effects, and shared environmental effects cannot be simultaneously modeled with data limited to that from twins reared together (22). Thus it is not possible to distinguish a purely additive genetic effect from the combined influence of additive genetic, genetic effects due to dominance, and shared environmental effects. However, parsimony would support accepting a simple model until evidence in support of a more complex model requires us to abandon it. Chi-square 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’s information criterion (AIC = $\chi^2 + 2 \times \text{free parameters}$) (1). This was done to compare models, where different components of variance have been specified. Lower AIC indicates a better fit.

First we fitted univariate genetic factor models for range of motion phenotypes. In the next step, bivariate factor modeling was performed assuming a variance component structure for range of motion phenotypes suggested by univariate modeling.

The bivariate genetic factor model with Cholesky decomposition parameterization was used to estimate to what degree the genetic (or environmental) effects on one phenotype are correlated with the genetic (or environmental) effects on another phenotype. Only significant predictors for range of motion phenotypes in regression models were considered if at least one of two MZ cross-twin cross-trait
correlations were also significant. The contribution of genes or environmental factors to the observed phenotypic variables is measured by genetic or environmental correlation. A higher proportion of total genetic/environmental variation in range of motion phenotypes explained by common genetic/environmental variation indicates that the same genes or environmental factors influence more than one trait at a time while a lower proportion of variance indicates an influence of different genes or environmental effects.

Univariate genetic factor models and bivariate genetic factor models for continuous determinants were fitted using maximum likelihood estimation. Bivariate models for range of motion phenotypes and categorical or binary variables were fitted using mean and variance weighted least squares estimation. All genetic factor models were age-adjusted.

Tests comparing means, variances, and proportions and regression models were computed using survey estimation methods because observations on twin individuals can be correlated with twin pairs. Survey statistics and other descriptive statistics were estimated in STATA (version 9) (30). Genetic modeling was done in Mplus using raw data estimation methods (21).

RESULTS

Overall, the sample on which analyses are based consisted of 134 MZ twin pairs and 150 DZ pairs with complete lumbar range of motion data for both twin brothers. One MZ pair was excluded from analyses because of an outlier extension value (71.8°). Subjects ranged in age from 35 to 70 yr. The characteristics of the MZ and DZ twins were similar on most factors studied, but MZ twins had slightly greater lumbar extension (mean 40° vs. 36°) and therefore total range of motion (64° vs. 60°) compared with DZ twins. MZ twins also were somewhat less likely to have lumbar osteophytes apparent on MRI than were DZ twins (Table 1).

Intraclass correlation coefficients demonstrated clearly greater degrees of similarities within MZ twin pairs than in DZ pairs for lumbar flexion, extension, and total range of motion, implying a genetic influence (Table 2). The models with additive genetic and unique environmental components (AE)
provided the best fit for lumbar flexion and extension. Using these models, 64% of the variance [95% confidence interval (CI), 0.55–0.73] in flexion was explained by additive genetic factors and the remainder by unique environmental factors (not shared between cotwins). The heritability estimate for lumbar extension was somewhat smaller (39%, 95% CI, 0.27–0.52), with total range of motion being intermediate. All analyses were adjusted for age (Table 2).

Statistically significant age-adjusted genetic correlations were found between lumbar extension and disc degeneration as indicated through disc height narrowing \(r_a = -0.43\) and bulging \(r_a = -0.38\). In other words, the same genes were influencing, in part, both disc degeneration and lumbar extension. Up to 18% of the variance in extension explained by genetic effects was due to genetic influences shared by the disc degeneration variables. Greater disc degeneration was associated with less range of motion (Table 3). In contrast, none of the unique environmental influences were in common with both the variability in extension and disc degeneration variables.

The age-adjusted bivariate model for lumbar flexion revealed shared genetic influences with body weight. Eleven percent of the genetic variance in flexion was explained by the same genes affecting weight. Greater weight was associated with less flexion (Table 3). There were no unique environmental influences shared by both flexion and another covariate examined, with the exception of a modest correlation of flexion and bulging \((r = 0.20, 95\% CI, 0.02–0.39)\), explaining 4% of total unshared environmental influences on flexion.

The most parsimonious bivariate factor model for total range of motion yielded a genetic correlation of \(-0.32\) (95% CI, \(-0.55, -0.09\)) with disc height narrowing (Table 4, Fig. 1). The bivariate model examining the genetic correlation of flexion and extension revealed a genetic correlation of \(-0.22\) (95% CI, \(-0.41, -0.01\)). The proportion of genetic variance in flexion accounted for by the same genes affecting extension was only 0.03. There were no unique environmental correlations of total range of motion with the covariates studied.

**DISCUSSION**

Heritability is the proportion of total phenotypic variance attributed to genetic variation between individuals, with values ranging from 0% (no genetic influence) to 100% (entirely determined by genes). Among adult Finnish men, we found a heritability estimate of 47% for total lumbar range of motion in the sagittal plane. The extent of lumbar range of motion in flexion appears to be predominantly influenced by interindi-

### Table 2. Univariate models for range of motion: MZ twin correlations, DZ twin correlations, and estimated heritabilities

<table>
<thead>
<tr>
<th>Variable</th>
<th>rMZ (95% CI)</th>
<th>rDZ (95% CI)</th>
<th>Heritability Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extension</td>
<td>0.45 (0.32–0.59)</td>
<td>0.08 (–0.08–0.24)</td>
<td>0.39 (0.27–0.52)</td>
</tr>
<tr>
<td>Flexion</td>
<td>0.66 (0.56–0.75)</td>
<td>0.26 (0.11–0.41)</td>
<td>0.64 (0.55–0.73)</td>
</tr>
<tr>
<td>Total range of motion</td>
<td>0.44 (0.31–0.58)</td>
<td>0.30 (0.15–0.44)</td>
<td>0.47 (0.35–0.58)</td>
</tr>
</tbody>
</table>

Values in parentheses are 95% CIs. rMZ, MZ twin correlations; rDZ, DZ twin correlations. The estimate (from AE model) of heritability is simply \(h^2 = \frac{a^2}{a^2 + c^2}\), i.e., proportion of total variance due to genetic effects.

### Table 3. Most parsimonious age-adjusted bivariate factor models for lumbar extension and flexion: cross-twin cross-trait correlations, genetic correlations, and estimates of the proportions of genetic variance

<table>
<thead>
<tr>
<th>Phenotype 1</th>
<th>Phenotype 2</th>
<th>Extension</th>
<th>Flexion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MZ Twins: Cross-Twin, Cross-Trait Correlation</td>
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<tr>
<td></td>
<td>Genetic Correlation</td>
<td>DZ Twins: Cross-Twin, Cross-Trait Correlation</td>
<td>Genetic Correlation</td>
</tr>
<tr>
<td></td>
<td>PG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disc height</td>
<td>(-0.21 (0.38, -0.03))</td>
<td>(-0.43 (0.24, -0.12))</td>
<td>(-0.05 (0.20, 0.10))</td>
</tr>
<tr>
<td>Disc bulging</td>
<td>(-0.17 (0.30, -0.03))</td>
<td>(-0.38 (0.70, -0.05))</td>
<td>(-0.01 (0.10, 0.13))</td>
</tr>
<tr>
<td>Weight (logarithm of)</td>
<td>(0.07 (0.04, 0.17))</td>
<td>(0.14)</td>
<td>(-0.12 (0.05, 0.32))</td>
</tr>
</tbody>
</table>

Values in parentheses are 95% CIs. PG is proportion of genetic variance in phenotype 1 (range of motion) accounted for by genetic correlation with phenotype 2 (covariate)
individual genetic differences (64%), while extension was influenced to a somewhat greater degree by environmental and behavioral factors. However, a larger number of subjects would have been beneficial in providing more precise estimates through narrower 95% CIs.

Although there are no other studies specifically examining genetic influences on spinal range of motion, the heritability estimates we found fall within the range of previously reported heritability estimates calculated for measures of global range of motion and flexibility. Previous studies of familial transmissibility estimates for sit-and-reach test performance and overall hypermobility have been moderate to high (11, 23) as have been heritability estimates (38–70%) (13, 16, 17), with the exception of one twin study of small sample size that suggested a modest genetic influence (10). Similar to our study results, Hakim et al. (13) found additive genetic and unique environmental components (an AE model) provided the best explanation of their data on hyperflexibility. However, in studies of sit-and-reach test performance, models including additive genetic influences and unique and shared environmental influences provided the best fit (16, 17). It must be kept in mind that heritability estimates are dependent on genotype and exposure to influential environmental factors, which may vary between populations and cultures with different environmental exposures or behavioral norms, as well as within populations over time. Heritability of a trait is not a fixed characteristic with a single value. Hypothetically, if range of motion were very dependent on childhood and school physical activity and training, for example, there may be differences in the heritability of range of motion between men born during a period when physical activity in school and leisure were emphasized and those born during a period when this was not the case. Our findings relate to adult men engaging in activities and lifestyles typical of a current developed country.

One assumption of the twin method is that the trait means do not differ by zygosity, implying that the MZ and DZ twins are representative of the same base population. However, for total range of motion, related to extension, the MZ twins had a higher mean value by about one-half of a standard deviation, which could indicate that the MZ and DZ twins do not represent the same base population, or that there are factors specific to MZ twins increasing range of motion. Another explanation is that despite statistical significance, the difference arose by chance. The fact that only extension but not flexion differed by zygosity suggests that it is most likely to be a chance result; nonetheless, it could conceivably be related to the developmental aspects in utero that are specific to MZ twins (14). For other traits investigated using the same study sample, we have not found differences in means of MZ and DZ pairs for a wide range of traits (4, 25), suggesting that the difference is not due to a selection bias for healthier MZ individuals, although the MZ twins did demonstrate somewhat greater back muscle performance in strength and static isometric endurance (25). If MZ and DZ twin differences in lumbar flexibility are found in other studies, the reason for these differences would need to be investigated more thoroughly.

Suboptimal precision and reliability of measurements of the phenotype, lumbar range of motion, and the covariates of disc degeneration and activity exposures pose some degree of limitations for all studies that include such variables, as is the case in the present study. The measurement error involved in assessing the phenotype can be expected to contribute to and inflate the unique environmental component of the phenotype’s determinants, diluting estimates of genetic influences. Error in the measurement of covariates will diminish associations.

A strong feature of this study was the representativeness of the sample of the population of Finnish men from which it was drawn. Thus one can expect the findings to generalize to the Finnish adult male population and quite likely to adult men in developed countries overall. Another study strength was the availability of clinical examination data, including height, weight, and lumbar range of motion, as well lumbar MRI and extensive interview data on possible covariates of interest. The availability of these data allowed the testing of hypotheses related to disc degeneration and body weight as possible
pathways through which genes may exert influence on lumbar range of motion.

In a review of genetic influences on physical functioning, including range of motion (12), it was noted that there has been very little insight into the mechanisms through which genetic factors influence related phenotypes. The present study provides some insight. The genetic component of lumbar extension was moderately correlated with those of disc degeneration measures, indicating a pathway through which genetic influences may affect extension. Similarly, genetic determinants of lumbar flexion were correlated with the genetic component of body weight, suggesting body weight as one pathway through which genes influence the extent of range of motion of lumbar flexion. After taking both disc degeneration and body weight measures into account, the proportion of genetic variance in total range of motion left unaccounted for was 90%, indicating the existence of substantial “direct” genetic influences or the effects of covariates other than those assessed in the present study. Notably, the proportion of genetic variance in flexion accounted for by the same genetic influences on extension was only 3%. This suggested that different genetic influences are operating in limiting maximal flexion vs. extension relative to the standing position.

Once a substantial genetic influence is established, it is natural to turn to the identification of associated genes in hopes of revealing the biochemical basis of the variations observed in structure or function. Yet, there has been a noted absence of specific genetic variants consistently associated with physical functioning phenotypes (12). This is also the case for the other relevant phenotypes identified in this study, lumbar disc degeneration and body weight or obesity. There remains a large discrepancy in the ability to detect overall genetic effects at population levels using quantitative methods and success in identifying individual causal genes. It has been suggested, however, that there are numerous candidate genes of interest with respect to flexibility, including those related to collagen genes, elastin, fibrin, and tenacins (13). Supporting an interest in collagen genes, a study of the COL9A2 tryptophan allele among patients with sciatica revealed that subjects with the Trp allele had significantly more lumbar flexibility as indicated through the modified Schober test (15). Other candidate genes for disc degeneration would also be of interest related to lumbar range of motion. However, the gene forms identified to date appear to explain little of the variance in associated disc degeneration phenotypes and, therefore, may be unlikely to explain substantial degrees of the variation seen in lumbar range of motion. New genes or their combinations would likely explain substantial degrees of the variation seen in lumbar degeneration phenotypes and, therefore, may be unlikely to account for by the same genetic influences on extension was 90% indicating the existence of substantial “direct” genetic influences or the effects of covariates other than those assessed in the present study. Notably, the proportion of genetic variance in flexion accounted for by the same genetic influences on extension was only 3%. This suggested that different genetic influences are operating in limiting maximal flexion vs. extension relative to the standing position.

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In conclusion, lumbar range of motion in the sagittal plane in adult men appears to be in large part genetically influenced, with higher estimates for genetic influences on range into flexion than extension relative to the standing position. One pathway through which genetic influences appear to affect lumbar extension is through degenerative changes of the spinal motion segment, as seen through disc height narrowing, which explained approximately one-fifth of the genetic influence on lumbar extension. One pathway of genetic effects on lumbar flexion appears to be through genetic influences on body weight. Other pathways comprising the majority of genetic influences on lumbar range of motion remain unexplained.

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REFERENCES