

# Structural, Psychological, and Genetic Influences on Low Back and Neck Pain: A Study of Adult Female Twins

ALEXANDER J. MACGREGOR,<sup>1</sup> TOBY ANDREW,<sup>1</sup> PHILIP N. SAMBROOK,<sup>2</sup> AND TIM D. SPECTOR<sup>1</sup>

**Objective.** To assess genetic and environmental influences on low back and neck pain in a classic twin design and to examine the extent to which these are explained by structural changes seen on magnetic resonance imaging (MRI) and psychological and lifestyle variables.

**Methods.** The subjects comprised 1,064 unselected women (181 monozygotic [MZ] and 351 dizygotic [DZ] twin pairs) recruited from a national registry of twin volunteers. Outcome measures included lifetime history of low back and neck pain (using a range of increasingly stringent definitions), MRI scores of disc degeneration in the lumbar and cervical spine, psychological distress as assessed by the General Health Questionnaire (GHQ), and lifestyle variables assessed by questionnaire.

**Results.** For all definitions of pain, there was a consistent excess concordance in MZ when compared with DZ twins, equating to a heritability for low back pain in the range of 52–68% and for neck pain in the range of 35–58%. The strongest associations were between low back pain and MRI change (odds ratio [OR] 3.6, 95% confidence interval [95% CI] 1.8–7.3) and between neck pain and response on the GHQ (OR 3.3, 95% CI 2.1–5.0). These associations were mediated genetically.

**Conclusions.** Genetic factors have an important influence on back and neck pain reporting in women. These factors include the genetic determinants of structural disc degeneration and an individual's inherited tendency toward psychological distress. MRI changes are the strongest predictor of low back pain.

**KEY WORDS.** Monozygotic twins; Dizygotic twins; Magnetic resonance imaging; Back pain; Neck pain; Heritability.

## INTRODUCTION

The high prevalence, associated morbidity, and socioeconomic cost of low back and neck pain are well documented (1). However, epidemiologic studies to date have implicated few risk factors of only small or moderate effect (2). The causes of pain are manifestly complex, and one explanation for this may be that an individual's susceptibility to back pain is genetically determined.

A genetic basis for back pain might be suspected for a number of reasons. Twin and family studies have shown

that genetic factors contribute to the development of degenerative changes in the spine, accounting for up to 80% of the variance in changes observed on magnetic resonance imaging (MRI) (3,4). Psychological distress—one of the only consistent associations seen in population studies of back pain (5)—has a substantial genetic component (6,7). Animal models of pain suggest there is a genetic basis to variation in responsiveness to specific nociceptive and neuropathic stimuli (8).

In this study, we use a classic twin design conducted among female twin pairs to assess the extent of the genetic contribution to the reporting of low back and neck pain in the adult population. Magnetic resonance images were examined, together with measures relating to constitutional, psychological, and environmental risk factors. The data allow us to develop a new model for the genetic determinants of back pain that extends the current clinical perception of the disease.

The role of MRI as a diagnostic tool in mild to moderate back pain is still unclear, with large variations in practice. Previous studies have shown that many normal asymptomatic subjects have minor MRI changes (9,10). In the current study, we also explore for the first time the predic-

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<sup>1</sup>Alexander J. MacGregor, MD, Toby Andrew, MSc, Tim D. Spector, MD: St. Thomas Hospital, London, UK; <sup>2</sup>Philip N. Sambrook, MD: University of Sydney, Sydney, Australia. Address correspondence to A. J. MacGregor, MD, Twin Research Unit, St. Thomas Hospital, London SE1, UK. E-mail: alex.macgregor@kcl.ac.uk.

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tive value of an MRI scan for low back and neck pain in a large unselected group of women.

## SUBJECTS AND METHODS

**Subjects.** The study subjects were female participants in the St. Thomas Hospital UK Adult Twin Registry (11). This is a volunteer-based group of adult twins drawn from the UK population, which has been assembled through successive media campaigns. Since the register was founded in 1994, monozygotic (MZ) and dizygotic (DZ) twins have been invited at random to attend a clinical assessment of a range of age-related traits and diseases. None of the twins who volunteered to take part was aware of the specific hypotheses under test. All twins attended assessment as pairs. The twins were neither selected for, nor excluded if there was a history of low back pain, neck pain, or disc disease. Zygosity was established by a standardized questionnaire and confirmed by DNA fingerprinting in doubtful cases.

**Assessment of low back and neck pain.** Participating twins attended an assessment that included a nurse-led interview and a number of clinical and laboratory tests. As part of the study, the twins completed a standardized questionnaire relating to their lifetime history of low back and neck symptoms. The questionnaires were completed by each twin separately either at their visit or within 2 weeks of attending.

The low back pain questionnaire followed the format of questions used in the Medical Research Council Nurses Study (12), which in turn has many features in common with questionnaires used in several other contemporary population studies of back pain (13–17). It included both written questions and a pain diagram allowing an assessment of the timing, distribution, radiation, severity, and duration of pain together with information relating to functional disability. Low back pain was defined on a mannequin as being located between the 12th rib and the gluteal folds. The neck pain questionnaire followed the same format, with neck pain defined on a mannequin as being located between the occiput and the third thoracic vertebra.

There is no agreement on the most appropriate definition of low back and neck pain for use in population studies. Recent analysis of population data from the Saskatchewan Health and Back Pain Survey (13,18) indicates that definitions that do not take into account pain intensity or disability overestimate trivial pain that is of little or no public health importance. For this reason, while information was included that allowed pain to be classified according to a range of definitions, our analysis focused on pain with a total duration of >1 month and associated with disability. For the low back, disability was defined as having resulted in any one of the following activities being impossible: walking around the house, standing for 15 minutes, getting up from a low chair, getting out of the bath, getting in and out of a car, going up and down the stairs, putting on socks and tights, and cutting toenails. For the neck, the activities determining

disability were looking over the shoulder, reaching up, driving, reading for 15 minutes, turning over in bed, washing or brushing hair, working at a desk for 15 minutes, and carrying heavy bags. Our definition of pain related to the lifetime prevalence of pain (that is report of pain ever) rather than the 1-year period prevalence in common use in case-control studies. This definition was used because of the importance of correctly classifying both cases and non-cases in studies of familial recurrence risk (19).

The repeatability of the back pain questionnaire has been assessed in an independent study in which respondents were asked to complete the questionnaire on 2 occasions, 12 months apart (20). Kappa statistics for a range of characteristics associated with the pain, including radiation and disability, were >0.6. This was confirmed in a sample of 51 subjects from the present study (selected to have a prevalence of back pain reporting of 50%) who were interviewed between 1 and 5 years after they completed the questionnaire. This showed comparable agreement ( $\kappa = 0.54$  for back pain >1 month,  $\kappa = 0.52$  for report of radiation to the legs,  $\kappa = 0.54$  for severe pain associated with disability), the slightly lower values most probably reflecting the longer interval for recall. Evaluation of the neck pain questionnaire in our own subjects showed moderate agreement for neck pain >1 month ( $\kappa = 0.34$ ) and for radiating pain ( $\kappa = 0.34$ ), and reasonable agreement for severe pain >1 month associated with disability ( $\kappa = 0.53$ ).

**Magnetic resonance imaging.** Magnetic resonance imaging was performed on a sample of subjects who participated (between 1995 and 1998) in a study of the heritability of features of disc degeneration (4). MRI was performed using a Siemens 1.0 T superconducting magnet (Munich, Germany). Sagittal images were obtained using a fast spin-echo sequence of repetition time/echo time 5,000–4,500/112 msec with a slice thickness of 4 mm. Grading was performed by a single reader blinded to zygosity and clinical history of the twin using a standardized atlas (21) that employed a 4-point grading system for disc height, signal change, disc bulge, and anterior osteophytes. These variables were graded at 6 cervical (C1/2 to C6/7) and 5 lumbar (L1/2 to L5/S1) discs. All MRI scans were performed more than 1 hour after rising and all twin pairs were scanned at the same appointment and on the same machine. A disease severity score was constructed from the sum of scores for disc bulge, height, signal change, and narrowing in the lumbar and in the cervical spine, as previously described (4).

**Psychological and lifestyle variables.** The General Health Questionnaire (GHQ) is a self-report screening instrument, used extensively in epidemiologic and clinical studies in a variety of formats ranging from 12 to 60 items, to detect cases of psychological distress (22). In the present study, we used a 28-item version. Physical exercise was assessed using a modification of the Allied Dunbar Fitness Survey (23) and for the purposes of analysis, classified as current and past weightbearing activity. Socioeconomic status was classified using the occupation-based UK Gen-

eral Registrar Classification scheme (A/B = senior management and professionals; C1 = skilled nonmanual worker; C2 = skilled manual worker; and D/E = semiskilled or unskilled worker).

**Analytic approach.** The similarity in the twins' report of low back and neck pain was measured by estimating casewise concordance (Cc) (24). This is a measure of risk to a twin if their co-twin is classified as a case. Familial aggregation is suggested if Cc among either MZ or DZ twins exceeds the prevalence of the trait or disease in the population. Excess Cc in MZ compared with DZ twins suggests a genetic contribution.

Inferring the size of a genetic influence from concordance data alone is not straightforward. A more readily interpretable measure is obtained through estimating heritability. For a continuous trait, heritability can be defined as the extent to which the population-level variance in the trait can be attributed to genetic variation (25). For discrete traits with a multifactorial etiology (such as the presence or absence of a history of pain), heritability can be inferred by assuming that the trait is determined by a continuously distributed underlying liability and that the trait is expressed when the liability exceeds a certain threshold value (26). Concordance figures and heritability cannot be equated simply, particularly in circumstances in which the prevalence and concordance of a trait are dependent on age, when heritability is most appropriately estimated by statistical modeling.

Heritability for low back and neck pain was estimated through standard variance components analysis (27). The approach considers low back and neck pain reporting in the twins to have a potential contribution from additive (A) and dominance (D) genetic variance components, and from environmental factors shared by twin pairs (C) and unique to individual twins (E). These variance components are estimated by contrasting the correlation in liability in MZ and DZ twins derived from their respective concordance estimates. The most appropriate model for the data was selected by comparing a set of models containing different combinations of the variance components A, C, and D, together with E. All 4 variance components cannot be specified in a single model because of collinearity, and the approach initially examined the fit of the ACE and ADE models. Variance components were dropped sequentially, and retained only if they showed a significant contribution as assessed by the change chi-square goodness-of-fit statistic with a threshold significance set at  $P < 0.05$  (26). The final choice of model represented the best balance between goodness of fit and parsimony. In standard model fitting, the biologically implausible DE model is not examined and the E variance component (representing unique environmental effects) is always retained. A variance component representing age effects was also retained in all the models examined.

The analysis was extended to examine the influence of specific risk factors on the occurrence of pain. The risk factors analyzed included the MRI score in the lumbar and cervical spine and lifestyle and environmental variables. The association with individual risk factors was first as-

essed by univariate logistic and linear regression methods. In all these analyses, the generalized estimating equation was used to account for the underlying correlation between twin pairs.

Covariates found to have a significant association with pain reporting were entered into a multivariate extension of the variance components model. The relationship between neck and back pain and each covariate was considered in separate pairwise analyses. The multivariate model accounted for the influences of A, D, C, and E that are unique to each variable and shared between pairs of variables by constructing specific and shared regression paths. As in the univariate analysis, the starting point was to consider ACE and ADE models. Variance components were eliminated sequentially if they did not contribute significantly to the fit of the model. Age and unique environmental effects were retained in all models. In the final model, the product of the regression paths shared between variables provided a measure of genetic and environmental covariance, from which genetic and environmental correlation could then be derived.

Twin concordances, odds ratios, and their respective confidence intervals were estimated using Stata (28). The variance components analysis was conducted using the statistical software Mx (29).

## RESULTS

**Study sample.** Low back pain and neck pain questionnaires were completed by 1,064 women: 181 MZ and 351 DZ twin pairs. Their characteristics are shown in Table 1. The mean age of the MZ twins was approximately 3 years older than the DZ twins. The MZ and DZ groups were matched in terms of their physical characteristics and lifestyle variables. Data from MRI examinations were available for 510 subjects (81 MZ and 174 DZ twin pairs). The characteristics of the twins who underwent MRI examinations did not differ from those of the MZ and DZ groups from which they were sampled. The mean MRI scores were slightly higher in MZ when compared with DZ twins, as expected from their older mean age.

**Concordance and heritability of low back and neck pain.** The prevalence of low back pain ranged from 70% for pain ever to 14% for severe pain associated with radiation and disability (Table 2). For equivalent definitions, the prevalence of neck pain varied from 52% to 8%. For all definitions of pain severity, there was an excess concordance in MZ when compared with DZ twins, indicating a genetic contribution. Variance components modeling rejected a contribution from the shared twin environment and resulted in significant estimates of heritability ranging from 52% to 68% for low back pain and 35% to 58% for neck pain. In general, more severe definitions of pain were associated with a higher heritability.

**Influence of covariates.** The influence of measured covariates on the risk of severe low back pain (of total duration >1 month with disability) and severe neck pain (for

Table 1. Characteristics of the twins\*

	MZ (n = 362 individuals)	R/Cc	DZ (n = 702 individuals)	R/Cc
Age, mean (range) years	57.6 (45–72)	1	54.7 (45–79)	1
Height, mean (SD) cm	162.0 (5.8)	0.83	162.0 (5.9)	0.59
Weight, mean (SD) kg	63.8 (9.6)	0.69	65.5 (11.4)	0.41
Smoking ever, %	46	0.65	46	0.59
Alcohol ever, >10 units per week, %	15	0.47	13	0.23
Postmenopausal, %	90	0.98	76	0.89
Current weightbearing activity, %	8.5	0.35	11	0.31
Past weightbearing activity, %	39	0.78	25	0.41
GHQ, $\geq 6$ , %	16	0.51	18	0.38
Socioeconomic class				
A/B	23	0.46	32	0.61
C1	60	0.70	42	0.59
C2/D/E	17	0.45	26	0.44
MRI score back, mean (SD)	16.4 (7.2)	0.73	13.3 (7.0)	0.51
MRI score neck, mean (SD)	19.4 (5.19)	0.66	17.6 (6.3)	0.43

\* MRI scores were available in 81 MZ and 174 DZ pairs. Socioeconomic class as defined by UK General Registrar Classification scheme (see text). MZ = monozygotic; DZ = dizygotic; R = intraclass correlation; Cc = casewise concordance; GHQ = General Health Questionnaire; MRI = magnetic resonance imaging.

an equivalent definition) is shown in Table 3. The strongest predictor of low back pain in this group was the MRI score: those with scores in the upper quartile were at 3.6-fold increased risk of reporting pain compared with those with scores in the lowest quartile. Body mass index, score on the GHQ, and smoking were all associated significantly with the report of low back pain. By contrast for neck pain, MRI scores were not associated; the strongest association was with GHQ score. The contrast between the MRI-low back and MRI-neck pain associations is illustrated in Figure 1. Smoking history also showed significant associations with neck pain. Pregnancy history was not found to influence back or neck pain.

**Multivariate analysis.** Table 4 lists the phenotypic correlation between severe back and neck pain (as defined above) and the covariates shown to be associated with them. The phenotypic correlation with MRI score and low back pain is predominantly explained by genetic factors in common between these 2 variables. Likewise, the associ-

ation between GHQ and both neck and back pain and between weight and back pain is explained mostly by shared genetic factors rather than environmental factors. In contrast, the associations observed between pain reporting and smoking is explained by factors in the shared family environment of the twins. The association between back pain and height is also explained by environmental as opposed to genetic factors. In the models, the majority of variation in neck and back pain remains unexplained by measured covariates. For the variables showing the strongest association, MRI accounted for only 5% of the genetic variation in susceptibility to back pain and GHQ score accounted for only 1% of the genetic variation in neck pain.

## DISCUSSION

It is well recognized that there are large interindividual differences in the experience of pain associated with a

Table 2. Prevalence, concordance, and heritability of back pain\*

	Prevalence	MZ (n = 181 pairs) Cc	DZ (n = 351 pairs) Cc	Model	h <sup>2</sup>	95% CI
Back pain						
Ever	0.70	0.82	0.72	A, E, age	0.52	0.33–0.72
Ever radiated	0.38	0.60	0.46	A, E, age	0.53	0.33–0.72
Severe disabling pain	0.18	0.49	0.26	A, E, age	0.57	0.35–0.78
Severe disabling pain with radiation	0.14	0.54	0.21	A, E, age	0.68	0.44–0.91
Neck pain						
Ever	0.52	0.67	0.59	A, E, age	0.48	0.29–0.67
Ever radiated	0.23	0.37	0.33	A, E, age	0.38	0.16–0.61
Severe disabling pain	0.12	0.30	0.18	A, E, age	0.35	0.09–0.61
Severe disabling pain with radiation	0.08	0.28	0.17	A, E, age	0.58	0.27–0.89

\* Model indicates the final choice of model established through sequential elimination of variance components. The parameters included in the models are shown in the column: A represents additive genetic variance, E represents unique environmental variance, and age represents variance attributable to age effects. MZ = monozygotic; DZ = dizygotic; Cc = casewise concordance; h<sup>2</sup> = heritability; 95% CI = 95% confidence interval.

**Table 3. Risk factors associated with severe back and neck pain\***

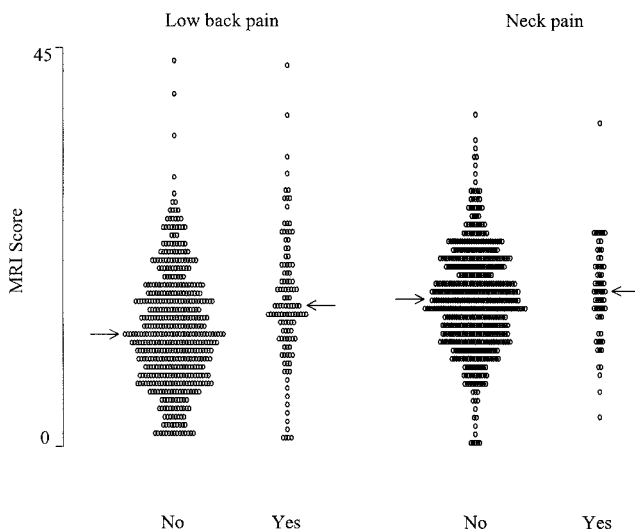
	Back pain (n = 1,064 individuals)			Neck pain (n = 1,064 individuals)		
	OR	95% CI	P	OR	95% CI	P
Age, years						
<50	1.00	—	—	1.00	—	—
≥ 50	1.20	0.77–1.85		1.95	1.04–3.67	0.04
Height, cm						
141–157	1.00	—	—	1.00	—	—
158–162	1.48	0.94–2.31	0.09	0.79	0.46–1.38	
162–166	1.59	1.02–2.48	0.04	1.02	0.61–1.73	
166–188	2.03	1.30–3.18	0.00	0.86	0.48–1.51	
Weight, kg						
40–56	1.00	—	—	1.00	—	—
57–62	1.94	1.22–3.09	0.01	0.93	0.52–1.66	
63–69	2.25	1.42–3.56	0.00	1.22	0.70–2.10	
70–139	2.36	1.47–3.76	0.00	1.36	0.78–2.36	
Smoking ever	1.60	1.15–2.23	0.01	1.58	1.04–2.39	0.03
Alcohol ever, >10 upw	1.03	0.63–1.67		1.08	0.59–1.96	
Postmenopausal	1.35	0.86–2.13		1.06	0.62–1.81	
Current weightbearing activity, Y/N	0.77	0.44–1.37		0.40	0.16–1.01	0.05
Past weightbearing activity, Y/N	1.25	0.76–2.05		1.03	0.56–1.92	
GHQ, ≥6, %	2.03	1.36–3.02	<0.01	3.84	2.46–6.01	<0.01
Social class						
A/B	1.00	—	—	1.00	—	—
C1	1.17	0.67–2.04		0.95	0.49–1.82	
C2/D/E	1.27	0.66–2.43		0.84	0.38–1.88	
MRI score						
Lower quartile	1.00	—	—	1.00	—	—
Second quartile	1.25	0.58–2.70		1.41	0.61–3.27	
Third quartile	3.45	1.74–6.85	<0.01	1.66	0.70–3.96	
Upper quartile	3.63	1.81–7.25	<0.01	1.52	0.62–3.74	

\* Socioeconomic class as defined by UK General Registrar Classification Scheme (see text). MRI was available in 634 individuals. OR = odds ratio; 95% CI = 95% confidence interval; upw = units per week; GHQ = General Health Questionnaire; MRI = magnetic resonance imaging.

variety of pathologic conditions. The role of genetic factors in explaining such variability is starting to be revealed (8,30). Using the twin model in a large unselected population sample of women, this study has suggested a signif-

icant genetic effect on severe low back and neck pain in the community. We also find the sources of this variation to be complex, with major contributions from structural (MRI) changes for low back pain and from psychological factors for neck pain.

The emphasis of studies of the epidemiology of back pain to date has been on occupational and environmental factors. In general, these have confirmed modest effects of weight, height, smoking, and occupation, and psychological factors similar to those seen in this study (31). Psychological factors and previous pain experience also emerge as the most important in longitudinal studies that have examined risk factors for new episodes of pain (2). By contrast, data on genetic risk factors for pain are limited. Race and nationality have been considered potential risk factors in a number of surveys with no effect demonstrated (32). Two questionnaire-based surveys conducted in the Nordic twin registries using nonstandard case definitions have had conflicting results. A relatively small genetic influence was observed in a Finnish survey for sciatica diagnosed by a physician (where heritability was estimated as 21%) (33). A larger genetic contribution (heritability 50%) was observed in a survey conducted in Finland for a single question relating to back pain resulting in absence from work (34). Neither study included objective measures of disc degeneration or covariates.



**Figure 1.** Association between magnetic resonance imaging (MRI) score and lifetime history of severe pain in the low back and neck. **Arrows** indicate the median value.

**Table 4. Bivariate analyses of the genetic and environmental contribution to the correlation between severe back and neck pain and measured covariates\***

	Back pain					Neck pain				
	Rp	Model	Ra	Rc	Re	Rp	Model	Ra	Rc	Re
MRI	0.27	A,E, age	0.22		0.04					
GHQ	0.17	A,E, age	0.11		0.04	0.34	A,E, age	0.25		0.07
Height	0.18	A,C,E, age	0.00	0.10	0.07					
Weight	0.19	A,C,E, age	0.16	0.00	0.02					
Smoking ever	0.13	A,C,E, age	0.00	0.11	0.02	0.14	A,C,E, age	0.00	0.13	0.01

\* Only covariates showing significant association with back and neck pain were examined. Rp = measured phenotypic correlation; Ra = estimated additive genetic correlation; Rc = estimated correlation attributable to the shared family environment of the twins; Re = estimated correlation attributable to unique environmental effects. In the model, the residual phenotypic correlation (i.e., unexplained by the correlation with additive genetic variance [A], environmental factors shared by twin pairs [C], and environmental factors unique to individual twins [E]) is attributable to age. MRI = magnetic resonance imaging; GHQ = General Health Questionnaire.

The strongest predictor of severe low back pain in our study was MRI score. The use of radiographic and MRI measures of degenerative spinal disease have hitherto been regarded of little importance in predicting back pain in population samples. Indeed, several studies have noted an apparent poor correlation between MRI findings, such as disc prolapse or bulging, and clinical symptoms. For example, Jensen et al (9) performed MRI scans in 98 asymptomatic subjects and found 52% had a bulge at 1 level, 27% had a protrusion, and 1% had an extrusion. Similarly, Boden et al (35) examined 67 subjects who had never had low back pain or sciatica and found 20% had MRI evidence of a herniated disc. To date, however, no study has addressed the association in a population sample including subjects both with and without pain. Our data are the first to show a clear relationship between disc degeneration in the lumbar spine and the propensity to report pain in the lumbar spine, although interestingly no clear relationship exists for neck pain. MRI of the lumbar spine thus provides an objective measure against which to assess the influence of risk factors for the development of back pain.

We have previously shown that degenerative changes in the lumbar spine are substantially influenced by genetic factors (4). It is not surprising, therefore, that our analysis shows that the association between MRI changes and the reporting of pain is mainly attributable to genetic factors in common with both of these traits. Data emerging from candidate gene studies tend to support the involvement of specific genes in determining clinical pain. Recent data show an association between lumbar disc disease and 2 mutations (Trp2 and Trp3) of genes encoding the alpha 2 and alpha 3 subunits of collagen IX. In these studies, cases of disease were defined as having unilateral discogenic sciatica and the diagnosis was supplemented by MRI, electroneuromyography, and periradicular infiltration of the nerve root (36,37). These results are consistent with there being a genetically mediated association between clinical low back pain and degree of MRI change.

In addition to showing a structural basis for low back pain reporting, our data also confirm its multifactorial nature. In the low back, associations were found with physical characteristics such as weight, height, and smoking exposure and with measures of psychological distress

as assessed by the GHQ. The strongest association with pain reporting in the neck was with GHQ score. This risk factor profile is consistent with a number of other cross-sectional population-based studies that also demonstrate a contrast between risk factors that determine pain in the low back and neck (38,39).

The nature of this relationship between psychological factors and back pain—in particular, whether distress is a cause or consequence of pain—is frequently debated (40). Our data show for the first time that the psychological component of both low back and neck pain reporting has a genetic basis. While this observation itself does not resolve the question of cause and effect, it provides a different perspective on the origin of an individual's propensity for pain. A genetic basis for psychological distress has been shown previously in twin studies (7). Our data suggest that the progress in identifying genes associated with anxiety and depression may be of direct relevance in understanding the development of clinically important back pain.

The majority of the genetic component to neck and back pain reporting remains unexplained by measured covariates, and additional mechanisms must therefore be operating. Of interest are recent reports of genetic correlations of pain-related phenotypes in both mouse and human models. For example, among different mouse strains, a negative genetic correlation is exhibited between initial nociceptive sensitivity and subsequent responses to morphine analgesia (41). In humans, linkage to a 5-cM region of chromosome 9 has recently been established for hereditary sensory neuropathy type 1 (42), a condition characterized by loss of sensation to pain and temperature. Congenital insensitivity to pain with anhidrosis has been associated with mutations of the *TRKA* gene encoding a receptor for nerve growth factor (43). Familial hemiplegic migraine has been linked to mutations in a P/Q calcium channel 1 subunit gene (44).

The relative contribution of different biopsychosocial factors in the reporting of pain in human populations remains unclear. The only reported study of physiological pain responses was conducted in our own twin sample and was limited to 1 pain modality: acute pain threshold as assessed by pressure dolorimetry (45). Our results also showed the importance of the shared environment with only a relatively small genetic contribution to acute pain

reporting. However, this simple model of acute pain is unlikely to be relevant to the severe, more chronic pain experience examined in the present study. Additional studies on the genetic epidemiology of human nociceptive and neuropathic responses are clearly needed.

The assumptions inherent in our interpretation of these data merit discussion. Inferring a genetic etiology by contrasting MZ and DZ twins rests on the assumption that these 2 groups of twins share a common family environment to the same extent. This assumption clearly does not hold for a number of environmental variables recorded here: exercise history, for example, shows a greater similarity in MZ than DZ twins. However, these effects are modest and a substantial genetic effect persists when covariates are taken into account in the analysis. Although the influence of unmeasured covariates cannot be excluded in any data set, it is unlikely that an unmeasured variable exists with sufficiently strong association with back pain to introduce important bias (46). Twin studies also rely on the assumption that twins (with their unique gestational history) are representative of the singleton population with respect to the expression of adult disease. This assumption has been the source of debate, in particular for traits and diseases, such as cardiovascular disease, where the fetal environment is postulated as having an etiologic contribution (47). A comparison of characteristics between this twin sample with nontwin females drawn from a UK population shows a remarkable degree of similarity in the prevalence of osteoarthritis and a range of age-related diseases and traits (48). Furthermore, the strength of the association of reported pain with weight, height, smoking, and measures of psychological distress shown in these twins also shows a remarkable degree of similarity with those reported in population cross-sectional studies, strongly supporting the generalizability of our findings. Finally, any investigation of pain reporting inevitably depends on recall. Although the possibility of recall bias in our data cannot be discounted, we note the prevalence of severe pain reporting for the range of definitions used is similar to those reported in other cross-sectional studies. Furthermore, there is no reason to suspect a differential recall bias between MZ and DZ twins.

In conclusion, this study shows a substantial genetic contribution to the occurrence of severe back pain in the community. Our results also suggest that low back pain has a complex genetic etiology that is only partly accounted for by the genetic determinants of disc degeneration. The search for specific genes for back pain should therefore extend to include a broad range of pathologic, physiologic, and behavioral mechanisms. The strong predictive value of MRI in low back pain and psychological assessments in neck pain should help clinicians and researchers to progress the understanding and treatment of these common and complex complaints.

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