Schmorl’s Nodes: Common, Highly Heritable, and Related to Lumbar Disc Disease

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Objective. Schmorl’s nodes (SN) are common, but little is known of their relationship with degenerative change and back pain or genetic and environmental factors influencing their expression. We studied healthy female twin volunteers to determine the prevalence and clinical features associated with SN.

Methods. Serial sagittal T1- and T2-weighted magnetic resonance images of the lower thoracic and lumbar spine were analyzed in 516 healthy female twins (150 monozygotic and 366 dizygotic). The images were scored for lumbar degenerative change. Presence of SN was noted at cranial and caudal vertebral levels T9 to L5. Data on physical activity and back pain were collected by questionnaire. Heritability of SN was calculated using variance components modeling.

Results. SN were found in 30% of subjects. Of the 374 SN, 153 (41%) were in the lumbar spine and 221 (59%) were in the thoracic spine. SN heritability was >70%. There was a positive association between SN and lumbar disc disease (LDD). SN were more frequent in subjects with back pain (for ≥2 SN: odds ratio [OR] 2.68, 95% confidence interval [95% CI] 1.11–6.47, P = 0.03), but this was largely accounted for by the association of SN with LDD (OR 1.97, 95% CI 0.78–5.0, P = 0.15 adjusted for LDD). No independent association of SN with back pain was identified.

Conclusion. SN are common in middle-aged women and are strongly genetically determined. They are associated with lumbar degenerative change, which is a risk factor for back pain, but are not themselves an independent risk factor for back pain.

KEY WORDS. Schmorl’s nodes; Lumbar disc disease; Heritable; Osteoarthritis; Spine.

INTRODUCTION

Schmorl’s nodes (SN) are commonly observed in the human spine, both on routine radiographs and at autopsy (1). They represent herniation of the nucleus pulposus of the intervertebral disc into the adjacent cartilaginous end plate of the vertebra (2). The herniated tissue forms a defect in the upper or lower surface of the involved vertebra and the lesions tend to occur near the central or posterior axis of the vertebrae (Figure 1). SN are also a common radiographic feature of Scheuermann’s disease (3–5) and chondrodysplasias such as multiple epiphyseal dysplasia. Previous studies have reported an association between lumbar Scheuermann’s disease and degeneration of the spine (3,6,7).

One study of 98 individuals without back pain detected SN in 19% using magnetic resonance imaging (MRI) (8), and SN are generally considered to be asymptomatic. In contrast, lumbar disc disease (LDD) is a major cause of work disability and a costly health care problem. Although it has been reported that SN may give rise to disc degeneration (3,9), the relationship of SN with disc disease in the spine and their clinical significance as a source of low back pain in the general population remain unknown.

Environmental factors such as occupational physical loading, trauma, and smoking have been widely investigated as possible risk factors for both back pain and structural changes in the spine. These factors have been shown to have only modest effects (10) and much variability remains unexplained. Genetic factors make an important contribution to LDD (11–13), and although one radiographic study of identical twins suggested familial clustering (14), the relative genetic and environmental contribution to SN has yet to be formally evaluated.

The dearth of data on SN in the population led us to undertake this investigation to determine the prevalence, distribution, and clinical features associated with SN in a
SUBJECTS AND METHODS

Subjects. Healthy adult female twins were recruited from the St. Thomas’ Hospital Twin Registry (16). Zygosity was determined by a standardized questionnaire and, where ambiguous, by genotyping. Twins were neither selected nor excluded by history of back pain or disc disease. None of the twins had a history of spinal fractures or spine surgery. Ethics committee approval had been obtained, and the twins gave informed consent to participate but were unaware of the precise hypothesis being tested. MRI was performed in the subjects using a Siemens (Munich, Germany) 1.0T superconducting magnet. Serial sagittal images of the thoracolumbar junction and lumbar spine (T9–L5) were obtained using a fast spin-echo sequence of time to recovery (TR)/time to echo (TE) 5,000–4,500/112 msec, with a slice thickness of 4 mm. To minimize diurnal variation in disc height, all MRI scans were performed >1 hour after subjects awoke from sleep in the morning, with no exercise or supine rest allowed between awakening and the scan. Members of each twin pair were scanned at the same appointment and on the same machine.

Definition of SN phenotype and MRI scoring for LDD. T2-weighted MRI images were graded by a single reader (NJM) blinded to the subjects’ zygosity and clinical history. The observer evaluated each intervertebral disc on all available sagittal images with respect to SN. SN were characterized by a localized defect in a vertebral end plate with a well-defined herniation pit in the vertebral body with or without a surrounding sclerotic rim (low signal on all sequences) (Figure 1). SN were noted to be either absent (score 0) or present (score 1) at cranial and caudal vertebral levels T9 to L5. Multiple nodes at a particular vertebral level were recorded as present and received a score of 1. Small erosive defects of the end plate in degenerate segments were not considered SN (also visible in Figure 1). Intraobserver reproducibility was tested on a subgroup of 60 MRIs with kappa scores >0.70. The MRI films had been previously scored for features of LDD at the 5 lumbar discs (L1/L2 to L5/S1) by means of a standardized atlas using a 4-point grading scale for disc height, disc bulge, signal change, and anterior osteophytes (13). An LDD severity score was constructed from the sum of scores of degenerative changes, as was done previously.

Assessment of low back pain. Participating twins also underwent a nurse-led interview. Without conferring, twins completed a standardized questionnaire relating to lifetime history of low back symptoms, either at their visit or within 2 weeks of attending. The low back questionnaire followed the format of questions used in the Medical Research Council Nurses Study (17). The questionnaire 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 as being located between the twelfth ribs and the gluteal folds (illustrated on the diagram). Pain associated with fever, menstruation, or pregnancy was excluded. Our analyses focused on pain with a total duration >1 month and that was associated with disability in activities of daily living, defined as any one of the following 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 the car, going up and down stairs, putting on socks or stockings, and cutting toenails. Details of potential confounding variables were recorded at the initial interview: height, weight, history of smoking, and history of manual work including occupations in which some or part of the time was spent performing physical activities such as cleaning or lifting.

The repeatability of the back pain questionnaire was assessed using the kappa statistic in a sample of 51 subjects (selected to have a prevalence of back pain reporting of 50%) who were interviewed between 1 and 5 years after completing the questionnaire. Agreement was found for back pain >1 month (κ = 0.54) and for severe pain associated with disability (κ = 0.54).
**Statistical analysis and genetic modeling of twin data.** The association of SN with LDD was explored through multiple linear regression, with covariates including age and other potential confounding factors. The data were further analyzed by variance components modeling. This approach considers the phenotypic variation among twins to have potential contribution from additive (A) and dominant (D) genetic variance, from the shared family environmental variance (C), and individual-specific component E that includes random environmental variation and measurement error. Additive genetic factors have a correlation of 1 in monozygotic (MZ) twins and 0.5 in dizygotic (DZ) twins, shared environmental factors have a correlation of 1 in both MZ and DZ twins, and individual specific environmental factors are uncorrelated. By contrasting the pattern of observed correlations in MZ and DZ twins, it is possible to measure how well the distribution of data fits to a set of models containing the variance component combinations ADE, ACE, AE, and CE. The model that represents the best balance between fit and parsimony is selected as the most appropriate explanation of the data. Heritability is estimated as the ratio of genetic variance components to overall variation in the most appropriate model (18).

For each individual, the number of SN was recorded as a discrete count, and this variable had a positively skewed distribution. In the regression analyses, the SN count in the thoracic and lumbar spine was dichotomized into variables including subjects with no SN, those with ≥1 SN, and those with ≥2 SN. LDD severity score was normally distributed and was also examined in quartiles. Analyses took into account the pairing of twin data. Variance components analysis also took into account full pairwise distribution of counts in the twins using a threshold model that assumed that the number of SN was determined by a continuous underlying liability (19). The effect of age and body mass index (BMI) on heritability was taken into account in the modeling by regression.

**RESULTS**

Characteristics of the female twin pairs are shown in Table 1. The mean age of the MZ twins was greater than that of the DZ twins (54.8 years versus 51.9 years; *P* < 0.001), and MZ twins had significantly lower mean weight (63.3 kg versus 66.4 kg; *P* = 0.006) and BMI (Table 1). Height did not differ significantly between the 2 groups, and they were matched in terms of lifestyle variables. Age and BMI were taken into account in subsequent analyses.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>MZ (n = 150)</th>
<th>DZ (n = 366)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>54.8 ± 7.1</td>
<td>51.9 ± 7.5</td>
</tr>
<tr>
<td>Height, cm</td>
<td>162.4 ± 5.3</td>
<td>163.0 ± 5.8</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>63.3 ± 9.4</td>
<td>66.4 ± 12.1</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.0 ± 3.4</td>
<td>25.0 ± 4.6</td>
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</tbody>
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* Values are the mean ± SD. MZ = monozygotic; DZ = dizygotic; BMI = body mass index.

**Figure 2.** Frequency of Schmorl’s nodes (SN) on magnetic resonance imaging by vertebral level. CA = caudal; CR = cranial surface of disc on which SN lie.

SN were found in 30% of subjects at any vertebral level, and multiple SN (≥2 nodes) were found in 14%. In 9,288 vertebral end plates examined, 374 SN were found: 153 (41%) in the lumbar spine (L-SN) and 221 (59%) in the thoracic spine (T-SN). Caudal SN occurred more frequently than cranial nodes at all levels except L3 (Figure 2). The most common site for SN was at the T11 vertebral level. There was a positive association between SN and age but not SN and BMI, smoking, menopausal status, or history of manual work.

**Relationship of SN with lumbar disc degeneration and back pain.** After adjusting for age and BMI, there was a strong association of both ≥1 and ≥2 L-SN with features of LDD: in both cases this association was significant for both the third and fourth quartiles of LDD (Table 2). There was no such relationship with either single or multiple T-SN. Low back pain occurring and lasting for at least a month was reported by 45% of the women, with 19% reporting severe pain associated with some disability. Severe low back pain was associated with LDD (odds ratio 1.13, 95% confidence interval 1.07–1.18, *P* < 0.001, adjusted for age and BMI). Examining various categories of SN (≥1 SN, ≥2 SN, multiple thoracic, multiple lumbar) demonstrated that there was no association between ≥1 SN and severe low back pain, but there was an association with ≥2 SN (Table
However, this association was largely due to the association of SN with LDD (Table 3) and no consistent independent effect of SN on severe back pain could be detected in this data set.

Heritability. Heritability estimates are shown in Table 4. Both lumbar and thoracic SN were shown to have large genetic contributions to heritability (80% and 72%, respectively). The estimates of heritability did not change significantly after age and BMI were included in the analysis.

DISCUSSION

This is the first study investigating both the prevalence of SN and their association with LDD using MRI. We found that the presence of multiple SN is closely related to degenerative disease. In this cohort of healthy twins not selected for back pain, SN were also shown to be highly heritable with little influence of the environment.

This study has several advantages. Studies conducted before the availability of MRI used plain radiographs, which are incapable of direct visualization of the disc. In some surveys, only one-third of SN could be identified radiographically, with a much higher prevalence noted on MRI of the same subjects (20). In cadaver studies, the prevalence of SN has varied from 38% (2) to 58% (21) to 79% (9). MRI is the most sensitive imaging modality, and the frequency of SN (30%) in the present study is consistent with a previous MRI study involving 372 subjects of similar age (22). Furthermore, despite the large number of investigations devoted to degenerative disc disease, to our knowledge the relationship with SN has not been addressed previously.

The results must be interpreted in the context of potential limitations. One limitation is the representativeness of twin subjects. Comparisons of disease and lifestyle characteristics between this twin cohort and population-based singleton women drawn from a UK population demonstrate a remarkable degree of similarity in prevalence of osteoarthritis and a range of age-related diseases and traits (23). Any investigation of pain reporting inevitably depends on recall. Although the possibility of recall bias in our data cannot be discounted, the prevalence of severe pain was similar to that of other cross-sectional studies. Underreporting of symptoms is likely to bias our findings towards the null. Pain reporting is not likely to have differed between MZ and DZ twins, therefore we believe heritability estimates to be accurate. Although MRI is considered the most sensitive method for assessing the spine, there is no accepted or standard definition of SN, nor did we assess their size. An underestimation of the prevalence of SN is likely because the study focused on the presence of definite herniations into the vertebral body, and at higher thoracic levels it is difficult to grade the smaller vertebral end plate.

This is the first article to report the heritability of SN and to demonstrate that genetic factors are major determinants in the pathogenesis of SN. Although evidence from family and twin studies has shown that disc degeneration is highly heritable (10,13), it is not known whether a specific gene effect of relatively large magnitude exists or if the genetic contribution is due to the small effects of many genes. A number of genes have been implicated in disc degeneration including an aggrecan gene polymorphism (24,25), a vitamin D receptor (26), and matrix metalloproteinase 3 gene alleles (27). Several mechanisms may be proposed to account for genetic factors influencing SN. Synthesis and breakdown of disc anatomic and biochemical structures could be genetically determined and lead to accelerated degenerative changes in some persons; for example, SN are more common in Scheuermann’s disease and the chondrodysplasias, both of which are associated with premature disc degeneration. Disc disease may therefore be a constellation of several related phenotypes, and SN may be at the more severe end of the spectrum. Some researchers contend that because SN are present during skeletal maturation they are unlikely to be the result of disc degeneration (9). In subjects under 50 years of age disc degeneration in the T10–L1 region is more frequent in discs with SN than in those without SN; in subjects over 50 years of age this difference becomes even more marked (9). It is plausible, therefore, that in the T10–L1 region of the spine, SN originating in childhood or adolescence
to earlier-onset disc degeneration. Only longitudinal studies will determine this relationship, and these studies are currently underway.

The distribution of SN is of interest. The occurrence of more nodes in the lower thoracic spine, compared with the upper lumbar spine, and the higher incidence of nodes on caudal (inferior) surfaces of vertebrae T10 and T11 are consistent with studies of cadavers (9). Predominance in the T10–L1 region suggests that this region is particularly susceptible to stress (28) and is similar to the sites of occurrence of acute SN, supporting the view that trauma weakens the cartilaginous end plates, resulting in disc herniation and formation of chronic SN (29). However, such weakening of the end plate (30) may not be a prerequisite for disc extrusion. Cadaveric human lumbar spines developed SN under conditions of dynamic axial compression simulating physiologic rigorous activity (31). Acute disc herniation from axial trauma preferentially extrudes through the vertebral end plate rather than through an intact and normal annulus fibrosus (32). In addition, alterations of the subchondral bone of the vertebral body, due to either developmental defects or systemic processes such as osteopenia, may underlie formation of SN (33).

An interesting result of this large study is the finding that the presence of SN is not itself a risk factor for back pain, but is an indicator of LDD. There is little agreement on the most appropriate definition of low back pain for population studies (34). Analyses of population data from the Saskatchewan Health and Back Pain Survey indicate that definitions not taking account of pain intensity or duration associated with disability. We have shown previously using the twin cohort that the strongest predictor of severe low back pain is disc degeneration (35). In the present study, single or multiple SN in either the thoracic or lumbar spine were not independently associated with low back pain.

In conclusion, our data highlight the frequent occurrence of SN in adult women. SN are more common in persons with LDD, which has been shown by us and by others to be a cause of back pain, but in this analysis there was no evidence for an independent association of SN with severe low back pain. A clinician treating a patient with back pain can reasonably say that SN do not cause low back pain but that they do form part of the degenerative disease phenotype, which does cause low back pain. Our data also indicate that SN are under considerable genetic influence. These results shed new light on the pathogenesis of SN and confirm their association with degenerative change.

AUTHOR CONTRIBUTIONS

Dr. Williams had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study design. Spector, MacGregor.

Acquisition of data. Manek, Sambrook, MacGregor.

Analysis and interpretation of data. Williams, MacGregor.

Manuscript preparation. Williams, Manek, MacGregor.

Statistical analysis. Williams, MacGregor.

REFERENCES