Eur Spine J (2008) 17:502–508
DOI 10.1007/s00586-008-0605-1

ORIGINAL ARTICLE

Genetic and environmental influences on non-specific low back pain in children: a twin study

Ashraf El-Metwally · Marja Mikkelsson · Minna Ståhl · Gary J. Macfarlane · Gareth T. Jones · Lea Pulkkinen · Richard J. Rose · Jaakko Kaprio

Received: 22 October 2007 / Revised: 25 December 2007 / Accepted: 29 December 2007 / Published online: 18 January 2008

Abstract Aggregation of low back symptoms in families of children with low back pain (LBP) has been described. However, this may be due to genetic factors or common exposure to environmental factors. The aim of this study was to evaluate the relative contribution of genetic and environmental factors to childhood LBP by comparing the pairwise similarity of LBP in pairs of monozygotic (MZ) and dizygotic (DZ) twin children. Data was collected from 1995 to 1998 from a national sample of Finnish 11-year-old twins born between 1984 and 1987. This study sample constituted of 1,790 twin pairs: 610 MZ pairs, 598 same-sex DZ pairs, 582 opposite-sex DZ pairs. LBP pain was determined by using a validated pain questionnaire designed to assess musculoskeletal pains during the preceding 3 months. The outcome measure, LBP, was considered in three categories: none, once a month and at least once a week. Twin similarity in the report of LBP was quantified by correlations. Variance components for genetic and environmental factors were estimated by using biometric structural equation modelling techniques. The prevalence of LBP at least once a month was 15.7%, and at least once a week was 6.6%. The prevalence of frequent LBP in boys was significantly higher than that in girls ($P = 0.04$). In both genders, there were no differences in LBP reporting by zygosity ($P > 0.2$). There were no statistically significant differences between polychoric correlations in male MZ and DZ pairs and between polychoric correlations in female MZ and DZ pairs, suggesting little genetic influence. Results obtained from the best-fitting genetic model suggests that, of the total variance in LBP, 41% (95% CI 34–48) could be attributed to shared environmental factors within families; and 59% (52–66) to unique (unshared) environmental factors. Our results suggest that genetic factors play, at most, a minor role in LBP in children; instead, symptoms seem to be related to a mixture of shared and unshared environmental factors. This study underscore the need for further high-quality research, preferably prospective studies, to identify important modifiable risk factors in order to guide interventions that may prevent LBP in childhood.

Keywords Low back pain · Children · Heritability · Genetics

A. El-Metwally (✉) · G. J. Macfarlane · G. T. Jones
Aberdeen Pain Research Collaboration (Epidemiology Group), Department of Public Health, University of Aberdeen, School of Medicine, Polwarth Building, Foresterhill Aberdeen AB25 2ZD, UK
e-mail: a.el-metwally@abdn.ac.uk

M. Mikkelsson
Rehabilitation Centre, Päijät-Häme Central Hospital, Keskussairaalank 7, 15850 Lahti, Finland

M. Ståhl
Department of Physical and Rehabilitation medicine, Turku University Hospital, Kiinamyllynk 7, 20520 Turku, Finland

L. Pulkkinen
Department of Psychology, University of Jyväskylä, P.O. Box 35, 40014 Jyväskylä, Finland

R. J. Rose
Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN 47405, USA

J. Kaprio
Department of Public Health, University of Helsinki, PO Box 41, Mannerheimintie 172, 00014 Helsinki, Finland

J. Kaprio
Department of Mental Health and Alcohol Research, National Public Health Institute, 00300 Helsinki, Finland

Introduction

In school surveys, the prevalence of self-reported low back pain (LBP), using a 3-month to 1-year recall period, ranges from 6 to 16% in 10–12 olds [27, 30] and from 12 to 67% in older adolescents [1, 33]. A significant proportion of these children will eventually experience pain consequences in the form of activity limitations, health care consultations and school absenteeism [27, 37]. Previous long-term follow-up studies have found that children with LBP are at an increased risk of having back pain in adult life compared to their peers with no back pain [7, 14, 17]. This has shifted the focus of research in the direction of studying determinants of these symptoms in children and young adolescents, which will ultimately improve our knowledge of the aetiology of adulthood LBP.

A number of studies have examined the role of familial factors in the aetiology of LBP in children. Aggregation of low back symptoms in families of children with LBP has been described [2, 34]. However, this may be due to genetic factors, shared exposure to environmental factors or possibly due to the role of parents as "models" for their children's reporting or expression of pain. There is also growing evidence that psychological and psychosocial factors play an important role in the aetiology of childhood LBP [2, 19]. Hence, other possible explanations for this familial correlation might be related to the psychosocial distress and disturbance to the family function secondary to parental LBP.

Most previous studies focusing on the genetic contribution in development of LBP have been conducted in adult populations. Some studies have primarily investigated the genetic role in the pathophysiology of intervertebral disc degeneration [4, 35]. Degenerative disc pathology is believed to be an intermediate finding in the causal pathway of LBP in some, but not all, cases of LBP. Other studies have examined the genetic contribution on non-specific LBP by comparing concordance rates for LBP in twins with different zygosity. Bengtsson and Thorson [6] studied twins, aged 15–47, and found a strong relationship between genetic factors and LBP with functional limitations. Genetic predisposition of LBP in adults has also been demonstrated by other studies [5, 15, 26]. Studying younger twins, Hestbaek et al. [16] documented a considerable genetic contribution on lifetime prevalence LBP in those aged 15–41 years, but a similar genetic influence was not evident in twins aged 12–15 years. This finding suggests that genetic factors start to play a role in LBP only after middle adolescence, but age of onset of LBP was not evaluated in this large Danish study. Thus, a classical twin study of LBP in preadolescents is needed to formally evaluate the role of genetic factors at a younger age than previously studied.

The aim of this study is to evaluate the contribution of genetic factors to childhood LBP, by comparing the pairwise similarity of LBP in pairs of monozygotic (MZ) and dizygotic (DZ) twin children aged 11 years.

Methods

The study population

FinnTwin12 is a population-based sample of twins born in Finland during 1983–1987. All twins were identified through Finland's Central Population Registry, yielding comprehensive and unbiased sample [21, 22]. Data on pain items were collected from four of the five nationwide birth cohorts because the relevant items were not included in the first year of data collection. From 1995 to 1998, a total of 2,487 Finnish families with twins born between 1984 and 1987 were sent an initial questionnaire on the twins' zygosity, childhood development and medical history. Approximately 85% of these families responded, and their children were mailed another personal questionnaire during the late autumn of each year. Each twin received a separate questionnaire with a return envelope with prepaid postage. The response rate among twins was 96% (4,034 individual responses). Eighty-eight individuals had to be dropped from analyses because their co-twins had not replied or the questionnaire response of at least one co-twin was not usable, thus leaving 3,946 responses from 1,973 pairs. The twins' median age when completing the baseline questionnaire was 11.4 years, with 95% of the twins' age at response falling between ages 10.9 and 11.9 years.

Evaluation of zygosity

Zygosity was determined using a well-validated questionnaire completed by both co-twins [13, 36]. Because these twins were younger than in previous studies of the Finnish Twin Cohort, classification was supplemented by parental response to items developed for zygosity classification. In addition, confirmation of zygosity in some pairs was assessed by comparisons of school photographs and additional information obtained from twins' mothers. Definitive zygosity diagnosis of a small group (5%) of same-sex twins awaits genotyping, and these twins were excluded from analyses reported here.

Assessment of LBP

The questions on musculoskeletal pain were taken from a questionnaire developed by Mikkelsson et al. [27]. The

brief test-retest reliability of the questions in detecting those who have pain at least once a week has been found to be satisfactory [Cohen's Kappa (k) = 0.9]. The concurrent validity of the questionnaire compared with interviews has also been studied; the observed agreement of results with the pain questionnaire with the interview technique was 86% and k was 0.67 [27].

This questionnaire evaluated musculoskeletal pain symptoms (including LBP) during the previous 3 months. LBP was classified according to pain frequency (seldom or never, once a month, once a week, more than once a week, almost daily). The body area concerned was indicated on a figure placed next to the question to help the child recognize the named area. The lower back area shown in the picture included the lumbar and sacral regions of the back.

Definition of LBP

Children were categorised as having LBP if they have self-reported pain in their lower back, according to the frequency with which they have reported their pain: (a) once per month (monthly LBP), (b) once per week to almost daily (weekly LBP).

Statistical methods

Comparisons of twin similarity were limited to pairs with confirmed zygosity, with complete data from both co-twins in each pair (n = 1,790 pairs). Sample sizes for these comparisons were 610 MZ pairs, 598 same-sex DZ pairs, and 582 opposite-sex DZ twin pairs.

To estimate genetic and environmental contributions to LBP, biometric modelling was used. The basic model is one in which the individual's deviation from the population mean is assumed to result from both genetic and environmental effects. Genetic effects may be due to additive genetic effects (i.e. the allele-specific average effects at a locus, summed over all relevant loci) or non-additive effects (due to interactions within a locus or between loci). Environmental effects can be further divided into shared and non-shared effects. In terms of variability, the corresponding phenotypic variance is assumed to result from genetic and environmental variances. Data from twins can be used to model and estimate these variance components.

Under the current study design of twins reared together, it is possible to model four separate parameters: an additive genetic (A) component, non-additive effects (D), and shared (C) and non-shared (E) environmental components. The influence of these components on the phenotype is given by parameters (h, d, c and e) that are equivalent to the standardized regression coefficients of the phenotype on the corresponding variance component (A, D, C and E, respectively). The square of these parameters is an estimate of the proportion of variance due to each component. One can fit models based on the different combinations of these parameters: AE, ACE, ADE, and CE, but effects due to dominance and shared environmental effects cannot be simultaneously modelled with data limited to that from twins reared together [28] Because we had data on twins of both sexes and opposite-sex twin pairs, additional hypotheses regarding gender-specific effects could be tested.

For trichotomous variables (No, monthly and weekly LBP), polychoric correlations among twin pairs were computed. In computing polychoric correlations, it is assumed that the distribution of the underlying liability to the trait was continuous and normal, with two thresholds depicting the categorization of subjects. The underlying liability model for bivariate normality in all pairs could not be rejected (P = 0.09), suggesting that a single, continuous measure of liability to back pain frequency accounts adequately for the data.

Some central assumptions of twin analyses were tested. These tests provide evidence of the assumption that first and second twins, twins of both zygosities, and male and female twins all represent the same population. In this analysis, the distributions of back pain frequency were studied using the method of maximum likelihood estimation for raw data observations. An initial fully saturated model, in which all the distributions for the first and second twins in all zygosity-sex groups were free to vary was compared to successively more constrained models by likelihood ratio tests. The distributions were first set equal for first- and second-born co-twins and then set equal for MZ and DZ pairs, and finally equal to be the same in males and females. If significant differences are not found, it can be concluded that birth order, zygosity and sex differences, respectively, are not of major importance. We also tested whether the correlations differed for male and female MZ twin pairs, and, similarly, whether correlations differed among male DZ, female DZ and opposite-sex DZ pairs.

To evaluate the role of genetic and environmental factors, model fitting based on the observed three by three contingency tables was conducted, using scripts available at the Genomeutwin-project Mx-library (http://www.psy.vu.nl/mxbib/). Chi-square goodness-of-fit statistics were used to assess how well a model fit the data. The superiority of alternative, hierarchically nested models was assessed by the difference in chi-square values of the models, which value is distributed as chi-square with degrees of freedom equal to the difference in degrees of freedom of the models to be compared. This was done to compare models where different components of variance have been specified. Based on the best model, variance

components were computed and 95% confidence intervals estimated. Three by three contingency tables were used rather than raw data fitting in order to obtain the confidence intervals.

Results

Out of 3,580 individual twins, 1,717 girls and 1,863 boys, who had responded to the question about LBP, 563 children (15.7%, 95% CI 14.5–16.9) reported LBP in a "once a month" frequency during the previous 3 months, while 240 children (6.7%, 95% CI 5.9–7.5) reported LBP in a frequency of "at least once a week" during the same recall duration. The prevalence of weekly LBP in boys was significantly higher than that in girls ($P = 0.04$). However, there were no differences in LBP reporting within genders by zygosity or order within pairs (Table 1), with P values >0.2 in both genders.

Table 2 shows pairwise distribution of LBP polychoric correlations of liability to LBP according to sex and zygosity. The polychoric correlations were almost identical in male MZ and DZ pairs. On the other hand, the polychoric correlation in female MZ pairs was higher than that in female DZ pairs. This might indicate that the genetic influence on LBP in females may be different than that in males. However, we found no statistically significant difference between correlations for male DZ, female DZ and opposite sex-pairs ($P = 0.37$) indicating that there is probably no sex-specific genetic variation.

Table 3 shows steps of our genetic analysis. Model fitting began by estimating parameters that indicate the relative strength of genetic and environmental influences. The first model was a full-sex differences model (ACE) in which estimates for h, c and e are allowed to differ in magnitude between boys and girls, and the possibility of sex-specific genetic variance was allowed for. However, there was no evidence for sex-specific genetic variance (which would be observed as a significantly lower correlation in opposite-sex twin pairs compared with like-sex DZ pairs). Moreover, the parameter estimates for males and females could be set equal without a significant loss in fit [Chi-square change was 2.93 (2 *df*), and $P = 0.40$]. This was the model against which we tested other models with fewer components of variance. The AE model fitted significantly ($P = 0.01$) worse than a CE model when compared to the ACE model with equal effects in boys and girls. The estimate for the genetic component, A (point estimate in the ACE models for a^2 was less than 10%) was also minor and non-significant. The CE model that is equally large in boys and girls fits the data well (i.e. the model that included only shared and unshared environmental effects). Using the simplest model of no familial effects (i.e. E only) led to a significant deterioration of model fit, and therefore the CE model was chosen as the best fitting model. Results obtained from the final model showed that 59% (95% CI 52–66) of the variance in liability to LBP could be attributed to non-shared environmental factors, while 41% (34–48) of that variance could be attributed to shared environmental effects.

Table 1 Frequency of low back pain (LBP) among twin individuals by sex and zygosity

Sex/zygosity	Frequency of LBP, *N* (%)			
	No.	Monthly	Weekly	Total
Monozygotic females	472 (79.5)	83 (14.0)	39 (6.6)	594
Monozygotic males	463 (74.0)	107 (17.1)	56 (9.0)	626
Dizygotic females	442 (81.6)	72 (13.3)	28 (5.2)	542
Dizygotic males	484 (74.0)	117 (17.9)	53 (8.1)	654
Opposite sex dizygotic	916 (78.7)	184 (15.8)	64 (5.5)	1,164
Total	2,777 (77.6)	563 (15.7)	240 (6.7)	3,580

Discussion

We conducted a classical twin study and found that 59% of the risk to LBP in children at age 11 could be attributed to unshared environmental factors, while 41% of that risk could be attributed to shared environmental effects, emphasising that genetic factors are not of importance at this young age. The estimates had quite tight confidence intervals suggesting that the estimation is accurate.

There are three main assumptions underlying twin studies that require consideration. The first one, which is the equal environments assumption, states that the environmental factors which contribute to risk for a disorder are equally correlated between MZ and DZ twin pairs. This assumption has at times received criticism [20, 32], on the basis of the suggestion that many environmental factors are more often shared by MZ twins than DZ twins [23, 25]. However, many of these supposed environmental factors are also influenced by genetic factors, which would make MZ twins more similar a priori. Moreover, violation of this assumption leads to inflation of heritability estimates rather than underestimation of genetic influences [24]. In our study, the genetic contribution was not significant, so such violation, if it exists, did not comprise an important threat to the validity of the inferences we have drawn. The second assumption underlying twin studies is that twins are representative of the general population, which is predominately composed of non-twins (singletons). Twins experience a more adverse intrauterine environment, and the experience of being brought up as a twin may be unusual in some respects. This might limit extrapolation of

Table 2 Pairwise distribution of Low back pain (LBP) frequency by sex and zygosity

LBP twin 1	LBP in twin 2, *N* (% of total FMZ twins)			
	No.	Monthly	Weekly	Total
Monozygotic females (FMZ)				
No	206 (69.4)	20 (6.7)	8 (2.7)	234
Monthly	22 (7.4)	16 (5.4)	2 (0.7)	40
Weekly	10 (3.7)	7 (2.4)	6 (2.0)	23
Total	238	43	16	297
Polychoric correlation = 0.58 (95% CI 0.43–0.73)				
LBP in twin 2, N (% of total MMZ twins)				
Monozygotic males (MMZ)				
No	188 (60.1)	29 (9.3)	18 (5.8)	235
Monthly	28 (9.0)	19 (6.1)	5 (1.6)	52
Weekly	12 (3.8)	7 (2.2)	7 (2.2)	26
Total	228	55	30	313
Polychoric correlation = 0.41 (95% CI 0.25–0.57)				
LBP in twin 2, N (% of total FDZ twins)				
Dizygotic females (FDZ)				
No	189 (9.7)	28 (10.3)	5 (1.8)	222
Monthly	20 (7.4)	10 (3.7)	3 (1.1)	33
Weekly	11 (4.1)	1 (0.4)	4 (1.5)	16
Total	220	39	12	271
Polychoric correlation = 0.40 (95% CI 0.19–0.61)				
LBP in twin 2, N (% of total MDZ twins)				
Dizygotic males (MDZ)				
No	194 (59.3)	37 (11.3)	11 (3.4)	242
Monthly	35 (10.7)	16 (4.9)	9 (2.8)	60
Weekly	13 (4.0)	4 (1.2)	8 (2.4)	25
Total	242	57	28	327
Polychoric correlation = 0.40 (95% CI 0.24–0.56)				
LBP in female twins, N (% of total OSDZ twins)				
Dizygotic Opposite sex (OSDZ)				
No	375 (64.4)	65 (11.2)	18 (3.1)	458
Monthly	68 (11.7)	18 (3.1)	6 (1.0)	92
Weekly	15 (2.6)	9 (1.5)	8 (1.4)	32
Total	458	92	32	582
Polychoric correlation = 0.32 (95% CI 0.18–0.46)				

results of twin studies. However, twins do not appear to differ markedly from singletons for most types of characteristics [10, 31]. In addition, the prevalence of weekly LBP in this 11-year-old twin population (6.6%) is very similar to that found in a representative sample of Finnish schoolchildren aged 10–12 (6.4%) [27]. Accordingly, we have no reason to believe that our results would not generalise to singletons. The third essential assumption for analysing twin data states that both MZ and DZ twins come from the same base population; hence, the prevalence of the trait being studied should not vary by twin type. This assumption is well satisfied by our data, as there were no significant differences in LBP prevalence by zygosity in either gender.

This study has a number of strengths. It is based on a large and representative sample of Finnish twins aged 11 years. Zygosity was ascertained by the twins and their parents' reporting of physical similarity. Both twin and parental ratings of zygosity have been previously validated against DNA markers [9, 11, 12]. We have also used a questionnaire with acceptable validity and reliability to evaluate LBP. Recall difficulties with respect to pain experience was kept to a minimum by limiting recall period to the previous three months only with an easily memorized starting point "since the summer". The main limitation of the study is that it relied on self-report of frequency LBP, and the intensity of pain and its impact on the children's daily activities were not evaluated.

Table 3 Genetic modelling analysis for low back pain (LBP)

	Model	χ^2	*df*	AIC	χ^2	*df*	*P*-value
I	ACEm, ACEf, sex diff	39.98	31	−22.02	–	–	–
II	ACEm, ACEf, no sex diff	39.98	32	−24.02	0.00	2	1.00
III	ACE equal in boys and girls	42.91	34	−25.09	2.93	3	0.40
IV	AE[a]	49.53	35	−20.47	6.61	1	0.01
V	CE[a]	44.52	33	−25.48	1.57	1	0.21
VI	E[a]	152.88	36	80.88	89.97	2	<0.001

Prevalences were allowed to be different in boys and girls

Model (I) specifies A, C and E effects in boys that are allowed to differ in size from the A, C and E effects in girls, with sex-specific genetic effects

Model (II) is Model I without any sex-specific genetic effects

Model (III) specified A, C, and E effects of equal size for girls and boys,

Models IV, V and VI are compared to model III: ACE model equal in boys and girls

Best fitting model in bold—fewest components without causing significant deterioration in χ^2 goodness-of-fit statistic

A additive genetic, *C* common environmental, *E* unique environmental, *AIC* akaike information criterion = $\chi^2 \times df$

[a] Compared to ACE model equal in boys and girls

Therefore, our survey most likely has detected symptoms that are, on average, milder than those seen in clinical settings. For that reason, our results should be interpreted with caution as the relative contributory role of genetic and environmental factors might be different in children with severe LBP and seeking health care. Our study does not exclude the possibility that for a minor fraction of LBP cases, genetic mutations and variants may account for familial transmission of LBP.

In the current study, boys reported experiencing more LBP than did girls. These results, although reported by others [8, 29], are not in accordance with the majority of previous studies, which document a higher prevalence of subjectively experienced LBP among females [3, 18]. Differences in case-definitions used might be a possible explanation for such inconsistency, but also subtle differences in age and nature of the study samples.

Our study demonstrated that genetic factors seem to play, at most, a very minor role in LBP in children at age 11 years. To our knowledge, there are no directly comparable studies in the literature on the role of heredity on LBP in such young age. Nevertheless, our results concur with results of Hestbaek et al. [16] who demonstrated a minor genetic influence on the aetiology of LBP in adolescents aged 12–15. The genetic predisposition to health problems might vary considerably with age. This might be the case with LBP, as almost all twin studies conducted on adults have shown an important genetic influence on adulthood LBP [5, 6, 15, 16, 26], and that such influence shows a linear trend, especially in males, from age 16–18 till age 33–41 with an overall age-adjusted heritability estimate of 40% in females and 44% in males [16].

The contribution of non-shared environmental factors was slightly more than that of shared environmental factors. The shared environment consists of the family environment and shared influences of school, neighbourhood, social class, etc., whereas the non-shared environment includes factors that are unique for each member of a twin pair (i.e. not shared by family members, such as an injury suffered by a twin). Our results suggest that both types of environmental exposures contribute to the risk of LBP. A variety of potential environmental risk factors for childhood LBP have been investigated in previous studies. These include anthropometric, mechanical, lifestyle, behavioural, psychological and psychosocial factors. In their review article on that topic, Jones and Macfarlane pointed out that current evidence favours a possible link with psychological and psychosocial factors, while inconsistent results have been reported with respect to the predictive role of other factors [18], so the evidence is still limited and not conclusive.

In summary, our data from a large number of male and female twin children suggests that genetic factors play, at most, a minor role in LBP in children; instead, these symptoms can be explained by a mixture of shared and unique environmental factors. Results of the current study underscore the need for further high-quality research, preferably prospective studies, to identify important modifiable risk factors to guide interventions that may prevent LBP in childhood.

Acknowledgments This research analysis was funded by the Spine Society of Europe. Data collection in *FinnTwin12* has been supported by the National Institute of Alcoholism and Alcohol Abuse (grants AA-12502, AA-00145, and AA-09203 to RJR), the Academy of Finland (grants # 100499, 205585, 118555 to JK) and the Finnish

Centre of Excellence Programme (to Lea Pulkkinen and Jaakko Kaprio). We would also like to thank the children and parents who participated in the study.

References

1. Balague F, Dutoit G, Waldburger M (1988) Low-back pain in school children. An epidemiological study. Scand J Rehabil Med 20:175–179
2. Balagué F, Skovron ML, Nordin M, Dutoit G, Waldburger M (1995) Low back pain in schoolchildren. A study of familial and psychological factors. Spine 20:1265–1270
3. Balague F, Troussier B, Salminen JJ (1999) Non-specific low back pain in children and adolescents: risk factors. Eur Spine J 8:429–438
4. Battié MC, Videman T, Gibbons LE, Fisher LD, Manninen H, Gill K (1995) Determinants of lumbar disc degeneration. A study relating lifetime exposures and magnetic imaging findings in identical twins. Spine 20:2601–2612
5. Battie MC, Videman T, Levalahti E, Gill K, Kaprio J (2007) Heritability of low back pain and the role of disc degeneration. Pain 131:272–280
6. Bengtsson B, Thorson J (1991) Back pain: a study of twins. Acta Genet Med Gemellol (Roma) 40:83–90
7. Brattberg G (2004) Do pain problems in young school children persist into early adulthood? A 13-year follow-up. Eur J Pain 8:187–199
8. Burton AK, Clarke RD, McClune TD, Tillotson KM (1996) The natural history of low-back pain in adolescents. Spine 20:2323–2328
9. Bønnelykke B, Hauge M, Holm N, Kristoffersen K, Gurtler H (1989) Evaluation of zygosity diagnosis in twin pairs below age seven by means of a mailed questionnaire. Acta Genet Med Gemellol (Roma) 38:305–313
10. Christensen K, Petersen I, Skytthe A, Herskind A M, McGue M, Bingley P (2006) Comparison of academic performance of twins and singletons in adolescence: follow-up study. BMJ 333:1095–1097
11. Christiansen L, Frederiksen H, Schousboe K, Skytthe A, Wurmb-Schwark N, Christensen K (2003) Age- and sex-differences in the validity of questionnaire-based zygosity in twins. Twin Res 6:275–278
12. Gao W, Li L, Cao W, Zhan S, Lv J, Qin Y, Pang Z, Wang S, Chen W, Chen R, Hu Y (2006) Determination of zygosity by questionnaire and physical features comparison in Chinese adult twins. Twin Res Hum Genet 9:266–271
13. Goldsmith HH (1991) A zygosity questionnaire for young twins: a research note. Behav Genet 21:257–269
14. Harreby M, Neergaard K, Hesselsoe G, Kjer J (1995) Are radiologic changes in the thoracic and lumbar spine of adolescents risk factors for low back pain in adults? A 25-year prospective cohort study of 640 school children. Spine 20:2298–2302
15. Heikkila JK, Koskenvuo M, Heliovaara M, Kurppa K, Riihimaki H, Heikkila K, Rita H, Videman T (1989) Genetic and environmental factors in sciatica. Evidence from a nationwide panel of 9365 adult twin pairs. Ann Med 21:393–398
16. Hestbaek L, Iachine IA, Leboeuf-Yde C, Kyvik KO, Manniche C (2004) Heredity of low back pain in a young population: a classical twin study. Twin Res 7:16–26
17. Hestbaek L, Leboeuf-Yde C, Kyvik KO, Manniche C (2006) The course of low back pain from adolescence to adulthood: eight-year follow-up of 9600 twins. Spine 31:468–472
18. Jones GT, Macfarlane GJ (2005) Epidemiology of low back pain in children and adolescents. Arch Dis Child 90:312–316
19. Jones GT, Watson KD, Silman AJ, Symmons DPM, Macfarlane GJ (2003) Predictors of low back pain in British schoolchildren: a population-based prospective cohort study. Pediatrics 111:822–828
20. Joseph J (2002) Twin studies in psychiatry, psychology science or pseudoscience? Psychiatr Q 73:71–82
21. Kaprio J, Koskenvuo M, Rose RJ (1990) Population-based twin registries: illustrative applications in genetic epidemiology and behavioural genetics from the Finnish Twin Cohort Study. Acta Genet Med Gemellol (Roma) 39:427–439
22. Kaprio J, Pulkkinen L, Rose RJ (2002) Genetic and environmental factors in health-related behaviors: Studies on Finnish twins and twin families. Twin Res 5:366–371
23. Kringlen E (1967) Heredity and environment in the functional psychoses: an epidemiological-clinical study. Universitetsforlaget, Oslo
24. Kyvik KO (2000) Generalisability and assumptions of twin studies. In: Spector TD, Snieder H, MacGregor AJ (eds) Advances in twin and sib-pair analysis. Greenwich Medical Media Ltd, London, pp 67–77
25. Loehlin JC, Nichols RC (1976) Heredity, environment and personality: a study of 850 sets of twin pairs. University of Texas Press, Austin
26. MacGregor AJ, Andrew T, Sambrook PN, Spector TD (2004) Structural, psychological, and genetic influences on low back and neck pain: a study of adult female twins. Arthritis Rheum 51:160–167
27. Mikkelsson M, Salminen JJ, Kautiainen H (1997) Non-specific musculoskeletal pain in preadolescents. Prevalence and 1-year persistence. Pain 73:29–35
28. Neale MC, Cardon LR (1992) Methodology for genetic studies of twins and families. Kluwer, Dordrecht
29. Newcomer K, Sinaki M (1994) Occurrence of low-back pain in children and its relationships to back strength and level of physical activity. Arch Phys Med Rehabil 75:1048–1049
30. Olsen TL, Anderson RL, Dearwater SR, Kriska AM, Cauley JA, Aaron DJ, La Porte RE (1992) The epidemiology of low back pain in an adolescent population. Am J Public Health 82:606–608
31. Pulkkinen L, Vaalamo I, Hietala R, Kaprio J, Rose RJ (2003) Peer reports of adaptive behaviour in twins and singletons: is twinship a risk or an advantage? Twin Res 6:106–118
32. Richardson K, Norgate S (2005) The equal environments assumption of classical twin studies may not hold. Br J Educ Psychol 75:339–350
33. Salminen JJ, Pentti J, Terho P (1992) Low back pain and disability in 14-year-old schoolchildren. Acta Paediatr 81:1035–1039
34. Salminen JJ (1984) The adolescent back: a field survey of 370 Finnish school children. Acta Paediatr Scand 315(Suppl):8–122
35. Sambrook PN, MacGregor AJ, Spector TD (1999) Genetic influences on cervical and lumbar disc degeneration: a magnetic resonance imaging study in twins. Arthritis Rheum 42:366–372
36. Sarna S, Kaprio J, Sistonen P, Koskenvuo M (1978) Diagnosis of twin zygosity by mailed questionnaire. Hum Hered 28:241–254
37. Watson KD, Papageorgiou AC, Jones GT, Taylor S, Symmons DPM, Silman AJ, Macfarlane GJ (2002) Low back pain in schoolchildren: occurrence and characteristics. Pain 97:87–92