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The Genetic Contribution to Dental Maturation

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Abstract. It has been established in the literature that there is a major genetic impact on tooth size (Potter *et al.*, 1976; Corruccini and Sharma, 1985; Sharma *et al.*, 1985), tooth morphology (Kraus and Furr, 1952; Biggerstaff, 1970), and root formation (Garn *et al.*, 1960; Green and Aszkler, 1970). None of the studies concerning root formation, however, used the more advanced method of path analysis and model fitting to estimate genetic influence. The aim of the present study was to determine the genetic and environmental influence on dental maturation. Dental age scores were determined on panoramic radiographs of 58 pairs of twins—26 monozygotic (MZ) and 32 dizygotic (DZ)—with the method of Demirjian *et al.* (1973). No mirror-image effect was found between the sides of the same individual or between twin members, so dental maturation seems to be symmetrical for both left and right sides of the mandible. Correlation coefficients were significantly higher in MZ than in DZ twins, which suggests a genetic influence. Model fitting showed that the variation in dental age was best explained by additive genetic influences (A-component) (43%) and by environmental factors common to both twins (C-component) (50%). The specific environment (E-component) added only 8% to the model. The importance of the common environmental factor can be explained by the fact that twins, being raised together, share the same pre-natal, natal, and immediate post-natal conditions that are of importance for the formation of the teeth.

Key words: dental maturation, heritability, twins, model fitting.

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Introduction

Twin studies are an ideal way to evaluate the interactions between genetic ("nature") and environmental ("nurture") influences on a particular phenotype. Since twins result from the same fertilized ovum, monozygotic (MZ) twins are genetically identical. Therefore, any difference between MZ twins cannot be due to genetic factors but rather only to environmental ones. Dizygotic (DZ) twins, on the other hand, originate from two ova that are separately fertilized, and are therefore no more genetically alike than are full siblings. They are also called fraternal or non-identical twins.

By comparison of identical and fraternal twins raised together, and thus subjected to the same common environmental factors, the genetic contribution to a specific phenotypic characteristic can be assessed. Several studies have been conducted on the heritability estimates of dental and dentofacial characteristics in identical and fraternal twins (Lauweryns *et al.*, 1993). However, few have been published on the genetic contribution to dental maturation in twins. Most of the early studies report a hereditary influence on the dental eruption status of permanent (Bachrach and Young, 1927) and deciduous (Hatton, 1955) teeth in twins. Studies of dental development of mandibular canines, premolars, and first and second molars measured on radiographs also suggest a genetic determination of dental maturation on the basis of correlation coefficients, intra-pair differences, or variances between MZ and DZ twins or triplets (Garn *et al.*, 1960; Green and Aszkler, 1970).

The aim of the present study was to determine the genetic influence on dental age by means of a comparison between MZ and DZ twins, using the more advanced method of path analysis and model fitting (Neale and Cardon, 1992).

Materials and methods

Subjects

The twins used in this study were selected from the East Flanders Prospective Twin Survey (EFPTS) (Derom *et al.*, 1985). This register covers all twins and multiple births born in East Flanders since 1964. Their zygosity was accurately determined at birth by placental examination (fetal membranes), blood group (ABO, rhesus- and subgroups, MNSs), and five DNA VNTR markers (monozygosity with a certainty of 95%)

Table 1. Exclusion of 26 twin pairs from the original sample of 84 twins.

	Monozygote	Dizygote	Total
Included	**36**	**48**	**84**
Excluded	**10**	**16**	**26**
- maximal dental age score	8	7	15
- extraction of a permanent mandibular tooth	1	4	5
- agenesis of a permanent mandibular tooth (exception of third molar)	-	3	3
- unclear radiograph	1	2	3
Remaining	**26**	**32**	**58**
- Male+Male	15	9	24
- Female+Female	11	10	21
- Male+Female	-	13	13

(Vlietinck, 1986). All of the twins between eight and 15 years of age who were willing to participate in the study were included. Pairs of whom at least one member had had any orthodontic treatment were excluded. All the parents were informed of the protocol of the study, which had been approved by the Ethical Committee of the Faculty of Medicine of the KU Leuven.

Panoramic x-rays of 84 twins were taken. After examination of the radiographs, twin pairs of whom at least one member had a maximum dental age score (full maturation of all seven teeth), or extraction or agenesis of at least one tooth of the lower jaw (wisdom teeth not included), or where the radiograph was unclear due to moving of the child during exposure, were excluded (Table 1). The final sample consisted of 58 twin pairs: 26 pairs of monozygotic (MZ) twins, 15 male and 11 female, and 32 pairs of dizygotic (DZ) twins, nine male, ten female, and 13 opposite-sexed (Table 1). Their mean age was 11.3 years, with a range between 8.11 and 14.11 years.

Method and measures

The dental age was determined on panoramic radiographs by the method of Demirjian (Demirjian *et al.*, 1973; Demirjian and Goldstein, 1976). We used the Demirjian dental development computer program (SilverPlatter Multimedia Database, SilverPlatter Information Inc., Norwood, MA, USA) to train and evaluate the examiner to score the different stages of development correctly and consistently. The individual scores of a radiograph can easily be inserted into the clinical evaluation program, which converts them into a maturation and a dental age score.

To assess the reliability of the method, the same examiner measured the scores of 20 children twice with an interval of one month.

The maturation and dental age scores of the 58 twin-pairs were then determined for the left and right sides of the mandible so that lateralization and mirror imaging of dental maturation could be detected.

Statistical analysis

The SAS 6.04 computer package was used for the descriptive statistical analysis (SAS, 1988). The means were compared by unpaired *t* tests, and the differences between repeated measurements were tested by paired *t* tests. The package was also used to test whether twins have to be considered each other's mirror image. If this is the case, the teeth on the left side of one twin would have to be compared with those on the right side of the other twin, and *vice versa* for the teeth on the right side of the first twin and the teeth on the left side of the second twin. Dental maturation in twins was considered to be a mirror image when the differences in maturation scores between the left side of the one twin and the right side of the other twin (L_1-R_2) were less than the same-side difference between them (L_1-L_2)(R_1-R_2) and *vice versa*. The similarity of dental maturation was measured by intra-pair correlations. The Gaussian distribution of the data was assessed by the Kolmogorov Smirnoff test statistic.

Analysis of genetic and environmental factors

The contribution of genetic and environmental influences to the individual differences in the observed variables was estimated by genetic model fitting (Neale and Cardon, 1992), which decomposes the variation in the observed phenotype into genetic and environmental variance. The genetic variance may be due to additive (A) or dominant (D) genetic influences, and the environmental variance may be due to common environmental factors shared by both twins reared in the same family (C) and to unshared environmental factors (E). Hypotheses were translated into mathematical models according to the rules set out in Neale and Cardon (1992). The AE model assumes that variance is explained by only two factors: an additive genetic factor and a unique environmental factor. If dominance or shared environment is included, the models are referred to as ADE or ACE, respectively. The CE and E models assume no genetic influence at all. For each model, the path coefficients and the expected values are estimated by the maximum likelihood method.

The goodness-of-fit of the models was evaluated by comparison of the observed values with those predicted by the model and was evaluated based on the chi-square value (χ^2), with a smaller chi-square giving a better fit. When the probability of the χ^2 was > 0.05, the fit of the model was considered acceptable. The Akaike (1987) Information Criterion (AIC), which combines the χ^2 with the degrees of freedom (df), gives a good idea of the parsimony of the model (Williams and Holahan, 1994). Between alternative hypotheses, the most parsimonious (lowest AIC) is preferred. The statistical modeling package Mx (Neale, 1994) was used to evaluate the fitting of the models.

The amount of variance explained by the main sources—additive (a^2) or dominant (d^2) genes and common (c^2) and unique (e^2) environment—is expressed as a proportion of the total phenotypic variance. [For a detailed description of univariate fitting, see Neale and Cardon (1992).]

Results

Measurement error

There was no significant difference between the means of the first and second sets of measurements (960.2 and 962.9). The absolute intra-observer error was 2.65, and the relative intra-observer error was 0.002, both of which were acceptable and not statistically significant.

Comparison of dental age and chronological age

A comparison between the dental and the chronological ages of the twins was made. The mean dental age was 11.8 years, which is five months older than the mean chronological age of 11.3 years. This is in conformity with the results of other studies, which found an overestimation of six to seven and ten months with Demirjian's method (Hägg and Matsson, 1985; Staaf *et al.*, 1991).

Descriptive

No mirror-image effect was observed, *i.e.*, there was no significant evidence that one side of the one twin was more concordant with the other side of the other twin. For further analysis, only the teeth of same sides were compared with each other.

Correlation coefficients

The intra-pair correlation coefficients were calculated for the maturation scores of the left and right sides of the mandible. The correlation between both members was significantly higher in the MZ than in same-sexed DZ (p value < 0.01) and in all DZ twins (p value < 0.001) (Table 2), which suggests genetic influences.

Table 2. Correlation coefficients of the maturation scores on each or both sides between twin members

Type	Number	Left Side	Right Side	Both Sides		
Monozygote	26	0.93	0.93	0.93	_a	_b
Dizygote same sex	19	0.72	0.74	0.73		
Dizygote	32	0.67	0.69	0.68		

Significance of comparison of correlation coefficients of MZ compared with DZ twins:
[a] p value < 0.01
[b] p value < 0.001.

Genetic and environmental

The goodness-of-fit statistics and parameter estimates of the most parsimonious models are summarized in Table 3. For both sides, the ACE model, which incorporates additive genes and common and specific environmental factors, provided the best explanation of the variations in dental age. This model fitted the data very well, as indicated by the probability levels (p) of the χ^2.

The contributions of each factor (genetic and environmental) were similar for both sides: Additive genes explained 45% and 41% on the left and right sides, respectively, and the common environment explained from 46% to 53% of the variation on left and right sides, respectively. The specific environmental factor was less than 8% on either side.

Discussion

No mirror-image effect was observed for the formation of the mandibular teeth. Correlation coefficients for the mean maturation score for both the left and right sides of the mandible between the MZ and DZ same-sexed twins as well as between the MZ and DZ twins in general were significantly different. For both sides, the ACE model—additive genes (43%) and common (50%) and specific (8%) environmental factors—gave the best fit to the data.

Comparing the results of this study with previous findings is difficult, since we know of only two studies (Garn *et al.*, 1960; Green and Aszkler, 1970) that used tooth formation on radiographs to assess the dental age of the twins. One of them (Garn *et al.*, 1960) compared the correlation coefficients of only two sets of triplets and found that the correlation coefficient of the MZ triplet (r = 0.91) exceeded the correlation coefficient of the DZ triplet (r = 0.33). The other study (Green and Aszkler, 1970) compared the intra-pair differences and variances of 38 MZ and 31 DZ twins and found that the mean intra-pair differences and variances for the dental development were significantly less in MZ twins than in DZ twins, which suggests a genetic component.

The study of correlation coefficients between twin members reveals the linear relation of a variable between two twin members of a pair, but this method is unable to distinguish the common from the specific environmental effects or the additive from the non-additive genetic variance. However, the high correlation coefficients in MZ twins and a significant difference between MZ and DZ twins indicate that the trait is genetically influenced, which makes further model fitting relevant.

In the present study, the variation in dental age was best

Table 3. Goodness-of-fit statistics and standardized parameter estimates of best-fitting univariate model for dental age

	Left Side	Right Side	Both Sides
Chi^2	13.82	17.17	15.50
DF	12	12	12
p	0.312	0.144	0.228
AIC	-10.174	-6.835	-8.505
a^2	0.45	0.41	0.43
c^2	0.46	0.53	0.50
e^2	0.08	0.07	0.08

a^2, c^2, e^2 give the proportion of the total phenotypic variance explained by the main sources: additive genes and common and unique environment.

explained by an ACE model and was similar for both the left and the right sides. Although the sample size was not very large, the contribution of a common environmental factor was significant and responsible for 50% of the total variance. This somewhat unexpected importance of the common environment in dental maturation can be explained by the fact that twins, being raised together, are apparently subjected to the same pre-natal, natal, and post-natal conditions that are of importance for tooth formation. They share the same intra-uterine feeding (calcium and fluoride intake, as well as medication), the same birth time—often premature—with the accompanying high degree of stress, and the same post-natal nutrition and oral hygiene habits that may influence dental maturation. To see which part is played by the post-natal common environmental factor (C component), investigators should compare twins not reared together with twins reared together. A large degree of impact of the common environment is expected in the formation of the first molars and incisors, since they are formed largely pre-natally, as opposed to, for example, the premolars and canines. Therefore, separate heritability estimates for each tooth should also be calculated.

However, the contribution of the specific environmental factor was less than 10% for both sides, which indicates a low error of measurement.

Although typical examples of mirror imaging exist, such as agenesis of second lower premolars (Lauweryns *et al.*, 1992), no mirror-image effect was found in this study for the formation of the lower teeth. Dental maturation seems to be symmetrical for the left and the right sides of the mandible. This confirms the findings of Demirjian *et al.* (1973) and was the reason only the seven teeth of the lower left mandible were used in their method of dental age assessment. This also concurs with the findings of Green and Aszkler (1970), who concluded that dental development is almost bilaterally symmetrical in MZ and DZ twins.

In conclusion, the present study confirmed the genetic determination of dental maturation. Because of the high accuracy of the zygosity determination by DNA and the sensitivity of the analytical tools used, a common environmental influence on dental maturation due to shared pre-natal, natal, and immediate post-natal conditions was detected. Further investigation, including the comparison of twins reared together with those not reared together, and the calculation of heritability estimates of the maturation scores of each individual tooth are necessary for these common environmental factors to be identified.

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