Genetic Modeling of Primary Tooth Emergence: A Study of Australian Twins

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The aim of this study was to quantify contributions of genetic and environmental factors to variation in timing of emergence of the primary teeth in a sample of monozygotic and dizygotic twins, using univariate model-fitting approaches. The sample comprised 94 pairs of monozygotic twins and 125 pairs of dizygous twins, all of European ancestry, aged from 2–6 years. Tooth emergence timing was based on parental report, with a subset of data validated by clinical assessment. Heritability estimates for tooth emergence timing were generally high, around 90%, however estimates for the lower right lateral incisor and the lower canines were around 50%. These findings confirm a strong genetic influence on observed variation in the timing of emergence of the human primary teeth.

Keywords: teeth, development, humans, genetics

The Craniofacial Biology Research Group in the School of Dentistry at the University of Adelaide has been involved in studies of the teeth and faces of Australian twins and their families for over 25 years. Investigations have involved three main cohorts of twins (Townsend et al., 2006). Our studies of twins have quantified the contributions of genetic and environmental influences to observed variation in dental crown components (Townsend and Martin, 1992; Townsend et al., 2003), whole dental crowns (Dempsey and Townsend, 2001; Hughes et al., 2000), the size and shape of the dental arches (Eguchi et al., 2004) and the contacts between opposing teeth (Hughes et al., 2001).

The collection of longitudinal data provides an opportunity to assess whether genetic and environmental factors contribute to changes in phenotypic variation in dental and facial structures over time. This study focuses on our third cohort of twins and other family members who are currently being examined at regular intervals, and for whom data on tooth emergence and oral health have been collected.

Emergence times of the human teeth have been a focus of several studies in the past (Hughes et al., 2007; Mihailidis et al., 2009; Parner et al., 2002). However, despite extensive research in humans and animals, understanding of the biological processes that cause teeth to erupt through the jaws and into the oral cavity remains incomplete (Craddock & Youngson, 2004; Wise et al., 2002). One aspect of the continual process of tooth eruption is the event of tooth emergence; that is, the time at which a tooth appears in the oral cavity. Apart from one early study of twins by Hatton (1955) that showed a relatively strong genetic contribution to variation in primary tooth emergence timing, and a more recent paper on genetic factors influencing dental maturation (Pelsmaekers et al., 1997), there have been very few published studies on the genetic basis of human tooth eruption and emergence. Recently, we used a model-fitting approach to analyze emergence data for primary incisor teeth in Australian twins, confirming that there was a strong genetic contribution to observed variation, with narrow-sense heritability estimates ranging from 82–94% for these teeth (Hughes et al., 2007).

The use of twins to study emergence times of the primary dentition enables estimates to be made of the contributions of genetic influences, both additive genetic (A) and non-additive (D), to the observed phenotypic variation, as well as the contributions of shared environment (C) and non-shared environment (E). The use of data based on parental reports, validated by clinical examination, has also enabled the timing of tooth emergence to be recorded to the day of the event, thus providing a distinct advantage over previous clinical cross-sectional studies.

To our knowledge, there have been no other previous studies aimed at modeling specific genetic and environmental factors that influence emergence of all the human primary teeth. The aim of the present study was, therefore, to extend our previous studies on the emergence of the primary incisors to include all of the primary teeth. Specifically, we sought to compare descriptive statistics summarizing the timing of primary tooth emergence in our sample of twins; to fit genetic models to data for each primary tooth; and to

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calculate narrow-sense heritability estimates. Based on our previous findings (Hughes et al., 2007), it was hypothesized that there would be evidence of a strong genetic contribution to variation in timing of emergence of all the primary teeth. Better understanding of the genetic control of human tooth emergence has implications for both research into the basic biological processes involved in tooth eruption, and also in the clinical management of children displaying anomalies in dental development.

Methods

Study Cohort

The study sample comprised 217 pairs of twins aged between 2 and 6 years who are enrolled in an ongoing study of dental development and oral health. Parents provided informed consent for their children. All of the twins were of European ancestry, and their zygosities were confirmed by analysis of 16 polymorphic genetic loci on 10 chromosomes. The probability of dizygosity, given concordance for all of the loci, has been calculated to be less than 0.1%.

The present study included 41 pairs of monozygotic (MZ) males, 51 pairs of MZ females, 43 pairs of dizygous (DZ) males, 24 pairs of DZ females, and 58 pairs of opposite-sexed DZ twins. The study was approved by the University of Adelaide, Human Research Ethics Committee (H-78-2003).

Recording Methods

Emergence timing was based on parental report with each tooth emergence date recorded on a specially designed tooth emergence chart. Parents were given a diagram of the primary dentition showing the crown morphology of all the teeth to facilitate identification of each emerged tooth (Figure 1). The parents were instructed that if any part of the crown was visible through the oral soft tissues, a tooth was to be recorded as emerged and they were also instructed on how to palpate the tooth if uncertain about its emergence. The validity of the parental recordings was confirmed in a subset of the study sample via clinical examination of a random selection of twins aged 3 months to 2 years (Hughes et al., 2007). In assessing the validity of parental reports, clinical records were compared against those records observed by the parent and then assessed for concordance. Internal consistency was also examined by looking for any significant divergence in emergence timing and sequence between the clinical and parental reports.

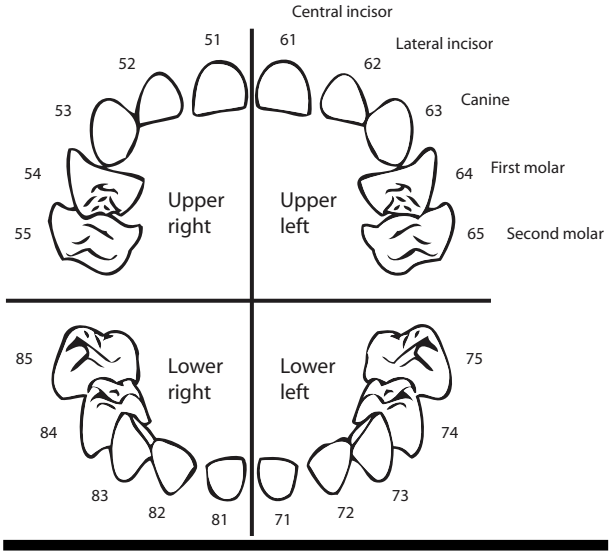

Figure 1

The Fédération Dentaire Internationale (FDI) two-digit notation system is used to identify each primary tooth. The first digit denotes the quadrant (e.g., 5 = upper right, 6 = upper left, 7 = lower left, 8 = lower right) and the second digit denotes the tooth position relative to the midline.

Descriptive Statistics

Analyses were performed on tooth emergence data calculated by subtracting date of birth from date of tooth emergence (reported in days). No allowance was made for variation in gestation length, which will be addressed in later studies. Data were assessed for departures from normality within tooth type and checked for conspicuous errors by calculating z-scores. Means and standard deviations (SD) were calculated for each tooth using one randomly selected twin from each twin pair.

Basic Inferential Statistics

Statistical significance was set at $p < 0.05$ for all tests. Student's unpaired t-tests and variance ratio (F) tests were used to compare central tendency and dispersion between sexes and zygosity groups. The coefficient of variation (CV = SD/Mean) was used to compare variation in timing of emergence between teeth. Directional asymmetry in emergence timing was assessed using paired *t* tests between bilateral tooth pairs (antimeres). Pearson's correlation coefficient was calculated between pairs of individual teeth and between twins for each of their teeth. To explore the influence of gestation length, Pearson's correlation coefficent was also calculated between gestation length and tooth emergence time from birth for all 20 teeth.

Genetic Modeling

Before proceeding with modeling of covariance structure, we explored the data to test for any genotype-by-environment (G × E) interaction and to determine the likelihood of detecting any non-additive genetic variation that may have existed. The presence of GxE interactions is indicated by significant regression of MZ pair variances on MZ pair means (Jinks & Fulker, 1970). In the absence of G × E interaction, directional dominance is indicated by significant regression of DZ pair variances on DZ pair sums, or by significant coefficients of skewness evident in DZ twins only (Martin et al., 1978). The probability of detecting dominance by fitting models to twin data is generally low, even when there is complete dominance and high heritability, unless there is a strong directional component (Martin et al., 1982). As a test for GxE interactions and directional dominance in our data, the absolute pair difference, which is proportional to the

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square root of the intra-pair variance, was regressed onto pair sum, and onto the square of the pair sum. In case the relationship was not linear, square and logarithmic (log) transformations of the data were also tested for significant regression. Coefficients of skewness were calculated and compared between MZ and DZ twin pairs. Although underpowered and sensitive to trait normality (Purcell, 2002), these approaches were considered appropriate for this phase of our study.

The approach adopted for the subsequent genetic analyses followed that of our previous studies of dental variation (Dempsey et al., 1995; Hughes et al., 2000; Hughes et al., 2001). Genetic and environmental covariance of individual teeth were analyzed in the twin data using the general structural equation modeling program Mx (Neale et al., 2006). Implicit in the model-fitting approach were the normal assumptions of the twin method — that mating was random, that trait-related shared environmental influences on MZ and DZ twins were equal, and that there was no GxE interaction or gene–environment covariation (Jinks & Fulker, 1970).

Four influences on phenotypic variation can be modeled for a pair of twins, namely:

A the additive effect of an individual's genome

D the non-additive effect of an individual's genome

C the influence of the shared, or common, twin environment

E the influence of the non-shared, or unique, individual environment (in the classical twin model, E also subsumes experimental error variance).

Since fitting models with four parameters to data from a classical twin study (MZ and DZ twins reared together) results in an under-identified model, subsets of three or fewer parameters were chosen. The choice was made simpler by the negative confounding of genetic dominance with common environmental influences (Grayson, 1989; Hewitt, 1989), so that a twin model may not contain both D and C.

Variable length files of raw data were prepared as described in Neale et al. (2006) and utilized directly for the univariate analyses. Initially, a path coefficient model with unique environmental influences only (E model) was fitted. Where this failed, the model was extended to include additive genetic variation (AE model), shared environmental variation (CE model) or both (ACE model). A model incorporating both additive and non-additive genetic effects (ADE) was also fitted to the data. Path coefficients (a, d, c, e) were estimated and the -2*log likelihood values for goodness-of-fit of the models were calculated. Chi-square (χ^2) tests were used to compare model fit between more saturated models and any nested submodels (e.g. ACE vs AE). Akaike's Information Criterion (AIC = -2*log likelihood – 2* degrees of freedom) was used to compare model fit between non-nested models (e.g., ACE vs. ADE). The smaller or more negative the AIC, the more parsimonious the model. The general approach was that of accepting a more complex model only when a simpler one had a significantly worse model-fit. Various hypotheses were tested by setting different combinations of the paths to zero, and examining the difference between the resulting goodness-of-fit and AIC values. For those models incorporating an additive genetic component, heritability (h^2) was calculated from the ratio of genetic variation to total phenotypic variation.

Sources of heterogeneity in mean values and variances between males and females were evaluated by fitting models in which individual parameter estimates were allowed to vary freely between sexes, and by comparing model fit with models in which the same parameter estimates were constrained to be equal between the sexes. In the case of additive or dominance genetic variance effects, heterogeneity was evaluated in both quantitative and qualitative contexts. Although less versatile than the continuous moderator model outlined by Martin et al. (1987), which was comprehensively elaborated by Purcell (2002), the approach used was considered to be a reasonable approximation at this stage of the study prior to future planned multivariate analyses.

Results

Tooth emergence times were approximately normally distributed within tooth type and analytical approaches used were robust to deviations from normality. No distinct outliers were observed within tooth type.

Summary statistics are presented in Figure 2. Emergence sequence was as expected from the literature but mean timing of individual tooth emergence was generally later than published estimates in singletons (Woodroffe et al., 2010). The first teeth to emerge were the lower central incisors (71, 81) at approximately 9 months post-natally. The last teeth to emerge were the upper second molars (55, 65) at approximately 28 months post-natally. Relative variation in emergence timing showed a trend to decrease antero-posteriorly.

There were no significant sex or zygosity differences in mean values or variances except for the lower second molars, which were more variable in emergence timing in females than in males. This is most likely to be the result of sample size as there were fewer females than males in our sample. Paired *t* tests yielded no compelling evidence of directional asymmetry in tooth emergence timing, either tooth-by-tooth or for the dentition overall.

Correlation analyses performed between all possible tooth pairs for the full cohort yielded coefficients that were universally positive, ranging in value from 0.02 to 0.96. Adjacent and opposing teeth were more highly correlated than teeth that were anatomically more separate (Table 1).

Table 2 presents correlations between twin pairs on a tooth-by-tooth basis. Correlations between MZ co-twins ranged from 0.85 to 0.98. Correlations between DZ co-

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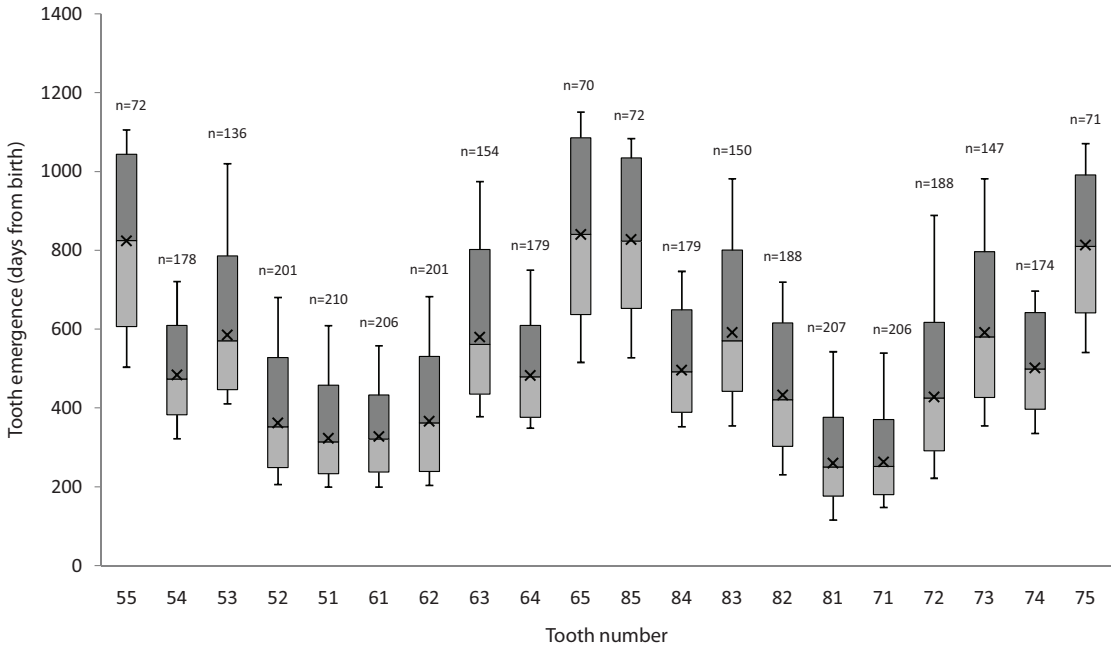

Figure 2

Box and whisker plot illustrating emergence of the primary dentition in days from birth.

Table 1

Inter-Tooth Correlation Matrix for Timing of Primary Tooth Emergence

	55	54	53	52	51	61	62	63	64	65	85	84	83	82	81	71	72	73	74	75
55		51	50	29	59	56	39	54	58	96	84	58	60	27	50	37	36	63	61	83
54	63		60	47	53	56	46	58	87	54	41	84	51	46	56	47	44	54	82	44
53	52	47		65	73	73	67	99	64	59	44	65	87	67	69	72	67	88	66	54
52	18	41	64		76	76	87	64	49	37	27	55	63	66	63	60	68	58	54	31
51	20	51	68	81		96	75	72	56	67	48	61	72	66	80	77	69	71	63	53
61	16	53	66	77	97		77	73	59	68	49	61	70	67	80	78	69	70	63	58
62	04	40	64	91	78	76		68	49	49	29	55	63	65	70	67	71	61	56	37
63	52	51	98	62	71	70	65		63	63	47	65	85	66	71	71	66	87	66	57
64	71	89	47	45	52	56	46	54		67	56	80	49	40	55	53	44	53	83	61
65	97	52	48	18	22	19	09	53	68		84	64	64	38	56	48	48	69	67	87
85	73	48	58	27	43	47	28	57	55	75		51	53	20	51	42	27	57	55	97
84	26	75	48	44	51	55	49	50	72	28	48		69	54	63	52	53	70	95	59
83	45	49	89	56	61	65	57	87	50	54	62	58		71	72	72	73	98	66	60
82	28	49	64	61	65	68	59	66	44	34	61	59	66		66	67	93	68	54	28
81	22	42	76	71	80	79	69	79	39	23	60	43	68	69		90	72	72	61	60
71	25	45	74	69	79	80	70	77	42	24	61	51	67	69	96		72	71	57	49
72	30	42	65	67	70	73	65	68	49	37	59	50	70	90	74	70		70	54	36
73	38	49	86	61	64	68	62	85	52	46	58	57	98	72	77	77	72		69	64
74	18	70	46	43	50	55	51	53	77	26	48	91	56	56	43	49	51	55		63
75	70	47	46	17	36	41	19	47	58	74	96	46	58	59	62	61	55	53	47	

Note: Data for girls below the diagonal and data for boys above the diagonal
Value = r × 100
Black boxes = High positive correlation > 0.75
Grey boxes = Correlation not significantly different from zero.

twins ranged from 0.24 to 0.72. Three out of four of the same-sex DZ correlations for first molars were not significantly different from zero. Opposite-sex DZ correlations were similar in value to their same-sex DZ counterparts, with the exception of the lower lateral incisors, which were not significantly different from zero in opposite-sex twins.

Phenotypic correlations between gestation length and tooth emergence time from birth were generally small and negative, ranging from -0.21 to 0.01. Approximately 50% were not significantly different from zero.

There was no evidence of G × E interaction for any of the 20 teeth. For all univariate models of tooth emergence, a model incorporating, at a minimum, both

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Table 2

Co-Twin Correlations for Timing of Emergence by Tooth

	MZSS		DZSS		DZOS	
	n	r	*n*	r	*n*	r
Upper						
55	33	0.96	14	0.81	17	0.52
54	80	0.91	44	0.38	45	0.63
53	64	0.97	30	0.67	35	0.61
52	86	0.91	54	0.55	52	0.40
51	88	0.96	63	0.48	53	0.43
61	89	0.94	60	0.50	53	0.48
62	87	0.90	56	0.39	52	0.49
63	66	0.97	32	0.57	36	0.55
64	76	0.94	48	0.19*	45	0.70
65	33	0.94	12	0.83	17	0.63
Lower						
85	34	0.85	13	0.65	15	0.53
84	76	0.88	43	0.28*	44	0.52
83	62	0.96	34	0.78	32	0.64
82	82	0.88	53	0.42	47	0.02*
81	87	0.95	62	0.52	53	0.37
71	87	0.94	64	0.49	54	0.41
72	79	0.89	51	0.41	46	0.02*
73	62	0.98	33	0.70	34	0.55
74	77	0.91	42	0.28*	44	0.50
75	34	0.85	16	0.69	15	0.54

Note: * Not significantly different from zero ($p > 0.05$)

an additive genetic effect and a non-shared environmental effect was most parsimonious. Including a shared environment component (ACE) provided a significant improvement in model fit for the lower right and lower left canines. The addition of a non-additive genetic component (ADE) provided a significant improvement in model fit for the lower right lateral incisor. There was evidence of significant sexual heterogeneity in individual variance components for a number of teeth. Patterns of heterogeneity were evident in the lateral incisors, the second molars, and the lower canines. Table 3 presents standardized parameter estimates derived from the most parsimonious model for each tooth. Heritability estimates were generally moderate for the lower canines and lower lateral incisors, and high for all other teeth.

Discussion

Although parental reports of tooth emergence timing provide researchers with challenges in relation to accuracy and reliability, these can be managed with careful experimental design. Parental reports offer advantages over clinical examinations for large cohort studies, as they provide better resolution (days rather than months) and are easier to manage logistically. For genetic studies, errors in reporting are most likely to reduce the additive genetic variance, thereby leading to conservative heritability estimates. The results of our previous error study (Hughes et al., 2007) showed that parental report of incisor tooth emergence provided accurate data for subsequent analysis.

It has been shown that dental development, dental eruption and tooth size may be delayed or reduced in low birthweight, prematurely born children (Fearne & Brook, 1993; Harris et al., 1993; Seow et al., 1988; Seow & Wan, 2000), features that are common to many twin births. Mean emergence times in our twin cohort were two months later, on average, than those reported by Hitchcock et al. (1984) for healthy Australian singletons, but the order of mean emergence times for the different teeth was as expected.

The observed phenotypic correlations between gestation length and tooth emergence times from birth were negative, but small, suggesting that the event of birth may play a significant role in mediating tooth emergence timing, possibly as a consequence of a change in nutrition. In an effort to develop simple univariate models of tooth emergence in the current study, emergence times were calculated from birth, and no correction for gestation length was made in subsequent analyses. We intend to examine this relationship more fully once further data become available by modeling tooth emergence time from conception, using time from birth as a covariate.

In interpreting the findings of this analysis, it is important to acknowledge that the timing of tooth emergence is not an isolated event with each tooth emerging independently of the others. Rather, it is a sequential progression stimulated by a cascade of molecular and cellular events where there is a significant degree of association both within and between tooth fields and arches.

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Table 3

Standardized Variance Components (A, C, D and E) and 95% Confidence Intervals For Primary Tooth Emergence Timing

Tooth	Sex	A	C	D	E
Upper					
55	M	0.98 (0.96,0.99)	—	—	0.02 (0.01,0.04)
	F	0.95 (0.88,0.97)	—	—	0.05 (0.03,0.12)
54	P	0.91 (0.87,0.94)	—	—	0.09 (0.06,0.13)
53	P	0.96 (0.95,0.97)	—	—	0.04 (0.03,0.05)
52	P	0.90 (0.85,0.92)	—	—	0.10 (0.08,0.15)
51	P	0.95 (0.94,0.97)	—	—	0.05 (0.03,0.06)
61	P	0.93 (0.91,0.95)	—	—	0.07 (0.05,0.09)
62	M	0.94 (0.91,0.96)	—	—	0.06 (0.04,0.09)
	F	0.86 (0.79,0.90)	—	—	0.14 (0.10,0.21)
63	P	0.96 (0.94,0.97)	—	—	0.04 (0.03,0.06)
64	P	0.94 (0.91,0.96)	—	—	0.06 (0.04,0.09)
65	P	0.96 (0.93,0.98)	—	—	0.04 (0.02,0.07)
Lower					
85	M	0.80 (0.66,0.89)	—	—	0.20 (0.11,0.34)
	F	0.95 (0.90,0.98)	—	—	0.05 (0.02,0.10)
84	P	0.90 (0.85,0.93)	—	—	0.10 (0.07,0.15)
83	M	0.48 (0.30,0.75)	—	0.49 (0.22,0.67)	0.03 (0.02,0.06)
	F	0.46 (0.29,0.72)	—	0.47 (0.21,0.64)	0.07 (0.04,0.12)
82	M	0.48 (0.30,0.75)	0.49 (0.22,0.67)	—	0.03 (0.02,0.06)
	F	0.46 (0.29,0.72)	0.47 (0.21,0.64)	—	0.07 (0.04,0.12)
81	P	0.96 (0.94,0.97)	—	—	0.04 (0.03,0.06)
71	M	0.94 (0.92,0.96)	—	—	0.06 (0.04,0.08)
	F	0.94 (0.91,0.96)	—	—	0.06 (0.04,0.09)
72	M	0.84 (0.77,0.89)	—	—	0.16 (0.11,0.23)
	F	0.83 (0.75,0.88)	—	—	0.17 (0.12,0.25)
73	M	0.34 (0.18,0.72)	—	0.64 (0.27,0.81)	0.02 (0.01,0.03)
	F	0.72 (0.47,0.98)	—	0.25 (0.00,0.50)	0.02 (0.01,0.04)
74	P	0.92 (0.89,0.94)	—	—	0.08 (0.06,0.11)
75	M	0.79 (0.58,0.89)	—	—	0.21 (0.11,0.42)
	F	0.95 (0.89,0.98)	—	—	0.05 (0.02,0.11)

Note: M = male, F = female, P = pooled across sexes

Phenotypic correlations between antimeric, isomeric and adjacent teeth, especially the central incisors and canines, were reasonably high. Correlations between the more spatially distant teeth were low to moderate. Tooth group emergence times for the incisors and the canines were also reasonably highly correlated. Emergence timing demonstrated a distinct antero-posterior temporal gradient (Figure 2). Given the distinct differences in morphology between primary incisors, canines and molars as a consequence of fundamental differences in embryogenesis of developing tooth primordia, it is perhaps unsurprising to observe such a correlation pattern. Contributing factors may include:

- qualitative and quantitative differences in gene expression mediating tooth development (for example, enamel knot formation associated with cusp number, enamel deposition, overall length and volume)
- a significant gradient in the total length of time for individual tooth development and subsequent eruption antero-posteriorly, which would allow for significantly greater environmental variation, both shared pre-natally and non-shared post-natally.

The field model of dental development (Butler, 1939; Dahlberg, 1945), postulates that mammalian tooth primordia grow and differentiate within 'fields' of diffusing morphogenetic substances, with one field for each tooth type. The earliest developing tooth in each field is considered to be a 'polar' tooth relative to the diffusion pattern, and consequently should display less morphogenetic variability than later teeth in the field. The field model of the human dentition, which has been applied primarily to the permanent teeth, suggests the most mesial tooth in each tooth class (incisor, canine, premolar, molar), apart from the mandibular incisors, tends to be the most stable in terms of size, morphology and timing of emergence. The pattern of variation in timing of primary tooth emergence that we observed in the maxillary incisors and molars, and in the mandibular incisors, was similar to that which has been observed previously in the permanent dentition. However, the observed pattern in the mandibular primary molars was reversed relative to observations in the permanent dentition — timing of emergence showed greater relative variability in the first molar than in the second molar. This was despite concerns that data for the second molars could be more variable due to parental reporting error, as a consequence of their significantly later emergence times and position within the dental arch. Previous researchers have suggested that the second primary molars may more

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appropriately be considered to be the key teeth within the molar tooth class, including the permanent molars, and their relative stability in the current study supports this hypothesis (Farmer and Townsend, 1993).

More recently, a number of researchers (Chávez-Lomelí et al., 1996; Kjær, 1998) have suggested that differential innervation may also play a role in the relative variability of individual teeth within a tooth class. Embryologically, the tooth primordia tend to arise in a sequence paralleled by, and associated with, the development of the distinct branched structure of the trigeminal nerve. The innervation theory suggests that the further a tooth is from its original nerve source, the more likely it is to be missing or morphologically atypical, possibly as a consequence of a greater susceptibility to the influence of the pre-natal environment, including factors such as pre-natal stress. The innervation of the primary dentition identifies similar 'fields' to those proposed by Butler (1939) and, based on the pattern of innervations, identifies the same key or polar teeth within each field.

Although we agree with Feldman and Lewontin (1975) that estimates of heritability for human quantitative traits are of limited value on their own, they can provide useful insights into the contribution of additive genetic effects to observed variation if interpreted cautiously. Estimates of heritabilities are specific to the population studied and so comparisons between studies need to be made with caution. Variation in timing of emergence of the primary teeth was found to be under strong genetic control, with a small but significant contribution from the external environment (Table 3). Other studies of tooth structure and dental features have also yielded similar results, suggesting odontogenesis is a fundamental biological process with a strong link to inherited genes (Townsend at el., 2009).

The notable exceptions in the current study were emergence timing of the lower lateral incisors and canines, which are located adjacent to each other in the dental arch. There was modest evidence of a non-additive genetic influence on one of the lower lateral incisors and a relatively small heritability estimate for its antimere. Whilst the confidence intervals for these estimates were relatively broad, we think that they are worthy of consideration, as our group has previously reported evidence of non-additive effects on the morphology of the permanent lateral incisors (Dempsey & Townsend, 2001). Genes that are related to selective fitness tend to display non-additive genetic variation (Dean et al., 1988; Fisher, 1958; Kacser & Burns, 1981), so the presence of this type of variation may indicate selective pressures acting on these teeth either currently or sometime in the past. This may be a consequence of the association between the emergence timing of the lower anterior teeth and the mean age at weaning in Western populations. A non-additive effect may also provide further empirical evidence that the lower lateral incisors are the polar teeth in the lower incisor morphogenetic field.

Emergence timing of the lower canines showed evidence of shared environmental effects, and a degree of sexual heterogeneity, with the shared environmental influence being larger in males. The shared environment effect may reflect the significantly greater length of time that the primary lower canine teeth spend developing prenatally, relative to other teeth (Kraus & Jordan, 1965). These teeth tend to emerge when their roots are approximately two-thirds formed, so environmental influences during this time could affect their timing of emergence. The development of the canine teeth starts around 4–6 weeks post-conception with morpho-differentiation, occurring between 12–16 weeks post-conception, coinciding with a surge in testosterone in male fetuses (Knickmeyer and Baron-Cohen, 2006; Reyes et al., 1974), possibly explaining the observed sexual dimorphism in emergence timing.

The findings of our genetic modeling approach for tooth emergence timing are consistent with previous results for other dental phenotypes (Hughes et al. 2000; Dempsey & Townsend 2001). In these earlier investigations, models incorporating additive genetic and unique environmental variance (AE model) or common environmental and unique environmental variance (CE model) accounted for observed morphological variation in all primary teeth, with narrow-sense heritability estimates ranging from around 60 to 90%. We acknowledge that many of the limitations of the univariate approaches used in this study could be overcome with a full multivariate analysis and this is planned for the future. Nevertheless, the present study provides new estimates of genetic and environmental contributions to variation in the timing of emergence of each of the primary teeth. In addition, the present study has provided evidence substantiating the existence of distinct developmental fields within the primary dentition.

Over the past decade, there have been major advances in our understanding of the molecular basis of dental development, with over 200 genes thought to be involved (Sperber, 2004). Our application of model-fitting approaches to primary incisor emergence data in twins has provided the first estimates of narrow-sense heritability for this important developmental event. Having confirmed strong genetic influence on variation in the timing of the human primary teeth, our next challenge is to identify the genes involved, building on the recent genome-wide association study of tooth emergence by Pillas et al. (2010).

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