Dental development and craniofacial morphology in school-age children

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Introduction: The growth of the craniofacial complex is important for establishing a balanced relationship among the teeth, jaws, and other facial structures. However, there is still a lack of information about craniofacial parameters that are affected by the rate of dental development. The aim of this study was to investigate the association between dental development and craniofacial morphology in school-age children. **Methods:** This study was embedded in the Generation R Study, Rotterdam, The Netherlands. In 3,896 children aged 8 to 11 years, dental development was assessed from panoramic radiographs and craniofacial morphology was assessed by combining cephalometric parameters into 9 uncorrelated principal components, each representing a distinct skeletal or dental craniofacial pattern. The statistical analysis was performed using linear and nonlinear regression model. **Results:** Dental development was positively associated with the bimaxillary growth ($\beta = 0.04$; 95% CI 0.01 to 0.08). Children with above-average dental development had a tendency toward Class II jaw relationship ($\beta = -0.08$; 95% CI -0.13 to -0.04). Regarding dental parameters, the proclination increased for incisors and lips with advanced dental development ($\beta = 0.15$ [95% CI 0.10 to 0.19] and $\beta = 0.13$ [95% CI 0.09 to 0.17], respectively), but the incisor proclination remained more pronounced in children that had above-average dental development. **Conclusions:** The findings of this large population-based study show that dental development is associated with specific dental and skeletal cephalometric characteristics in school-age children. Further longitudinal studies are necessary to confirm the observed effects over time. (Am J Orthod Dentofacial Orthop 2019;156:229-37)

The growth of the craniofacial complex is important for establishing a balanced relationship among the teeth, jaws and other facial structures that participate in the formation of occlusion. Disturbances in the development of craniofacial structures may lead to malocclusions that require orthodontic treatment or sometimes even orthognathic surgery. Therefore, understanding genetic, epigenetic, and environmental factors that affect the occurrence of these disturbances has significant clinical value.[1]

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Genes that regulate the migration of ectomesenchymal cells and the cells of the neural crest are responsible for the beginning of facial development at around 28 days of gestation.[2] Strong genetic influence is also evident in studies that investigated the variability of craniofacial parameters in populations with different ethnic background,[3] and in studies that examined craniofacial characteristics in patients with specific congenital syndromes.[4] On the other hand, the epigenetic and environmental components of craniofacial development are still largely unknown. Biologic indicators of craniofacial morphology that have been previously investigated are nutrition,[5] growth and other hormones,[6] height,[7,8] and skeletal maturation.[9-12]

Dentition and the rate of its development play a role in the development of surrounding tissues of the face. For example, children with a vertical growth pattern or a long face have advanced dental development compared with children with horizontal growth patterns or short faces.[13] Also, the change of vertical dimensions of occlusion and the occurrence of malocclusions occur most often during the eruption of deciduous and permanent teeth.[14] During the process of eruption and simultaneously to the development of teeth, important changes in the growth patterns may occur in the adjacent hard and soft tissues. Ultimately, this process facilitates the movement of the teeth until reaching the plane of occlusion. Furthermore, local or general disturbances in the dental development are associated with structural, morphologic, and positional abnormalities of the teeth,[14-17] which also affect the facial morphology as represented by cephalometric parameters.

Although previous studies acknowledge the importance of considering dental eruption and type of dentition when examining dental, skeletal, and soft tissue relationships in the facial region,[18,19] studies that have investigated the impact of the rate of dental development on craniofacial morphology are scarce.[13,20] Furthermore, studies on this topic in a large population-based cohort are lacking.

Therefore, the aim of the present population-based prospective cohort study was to investigate whether the rate of dental development is associated with specific dental and skeletal characteristics in the craniofacial region of school-age children.

MATERIAL AND METHODS

This study was embedded in the Generation R Study, a multiethnic population-based prospective cohort study from fetal life onward, which was initiated to identify early environmental and genetic determinants of growth, development, and health.[21] The study was approved by the Medical Ethics Committee of the Erasmus Medical Center (MEC-2012-165) in Rotterdam, The Netherlands. At the start of each phase, mothers and their partners were asked for their written informed consents. This study conformed to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for human observational studies.

Out of 8548 children invited to participate in the Generation R Study at the age of 9 years, 2501 were not available for the study and 185 twins were excluded. The remaining 5862 children visited the research center (Fig 1). Of those children, 1301 had no dental panoramic radiograph (DPR), 114 had a DPR of poor quality, and in 75 dental development could not be assessed owing to symmetric hypodontia in the lower jaw. Finally, 476 children without proper cephalometric assessment were excluded. The remaining 3896 singleton children (1950 boys and 1946 girls) aged 9.8 ± 0.3 years were eligible for the study.

DPRs and cephalograms of children were exposed in a standardized manner by trained personnel with the use of a digital dental imaging unit (OP/OC 200D; Tuusula, Finland). Tooth development was quantified on DPRs by means of the method described by Demirjian.[22] Following this approach, 7 teeth excluding third molars located on the left side of the mandible were scored with 1 of the 8 developmental stages (A-H) depending on the calcification of the crown and root. Each child's overall dental development was established by calculating the mean value of the standard deviation (SD) scores for the 7 teeth. Because of nonnormal distribution, the overall dental development score was normalized by means of rank-based transformation. So, for example, children whose dental development was more advanced were referred to as having an above-average SD score and children whose dental development was more delayed were referred to as having a below-average SD score. The interobserver agreement between 2 raters was determined on a random subsample of 100 subjects for each of the 7 teeth with the use of the intraclass correlation statistic, and coefficients ranged from 0.653 to 0.797 which is considered to indicate substantial agreement according to the conventional criteria.[23] Central incisors were not taken into account owing to the absence of variation in the stage of tooth development.

In total, 22 cephalometric landmarks were used in this study and from these points, 35 cephalometric parameters were derived: 16 angular, 15 linear, and 4 indexes (Supplementary Tables I and II, available at www.ajodo.org). A cephalometric analysis including measures adapted from the analyses by Down, Steiner, Ricketts, and Pancherz was performed on each tracing.[24-27] Cephalometric points were digitized by a trained investigator using Viewbox software, version 4.0 (dHAL Software, Kifissia, Greece). Interobserver agreement was calculated based on the subsample of 93 subjects, and the intraclass correlation statistic ranged from 0.710 from 0.931, which is considered to indicate substantial agreement according to the conventional criteria.[23] To efficiently reduce the number of cephalometric parameters, we combined highly correlated parameters by means of principal component (PC) analysis.[28,29] The use of this method in our study sample has been described previously.[30] Briefly, 47 cephalometric parameters were combined into 9 PCs, each representing a distinct skeletal or dental craniofacial pattern (Fig 2; Supplementary Table III, available at www.ajodo.org). In total, we identified 6 skeletal craniofacial patterns: facial divergence, bimaxillary growth, sagittal jaw relationship, ramus height, and lower anterior facial height, and cranial base angle. Lip position, incisor angulation, and overjet were identified as dental craniofacial patterns.

Information on each child's sex and date of birth were available from medical records and hospital registries. The age of a child was calculated as the interval between the date when the DPR was taken and the date of birth. Height and weight of the children were measured

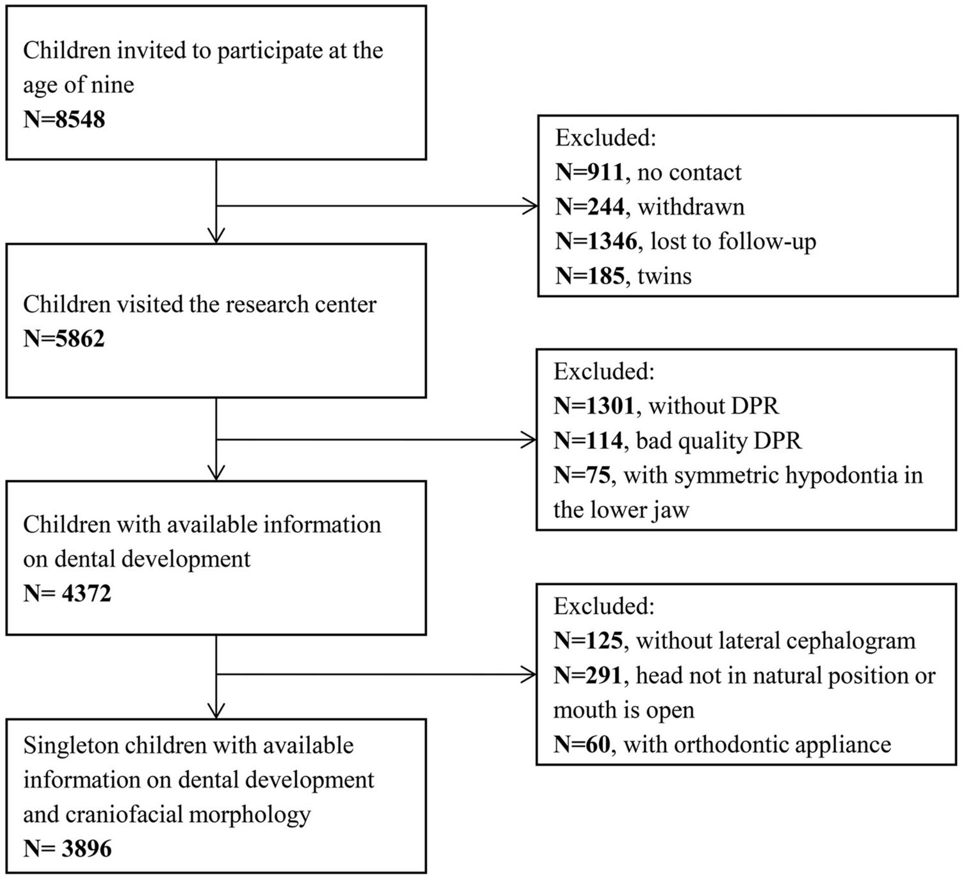

Fig 1. Flowchart of the participants included in the study. *DPR*, dental panoramic radiograph.

by trained personnel at the research center following a previously described protocol and subsequently body mass index (BMI) was calculated. We obtained information on ethnicity and maternal educational level by means of questionnaires. Ethnicity and educational attainment were defined according to the classification of Statistics Netherlands. One experienced examiner ascertained hypodontia from the DPRs. Children with hypodontia had 1 or more congenitally missing teeth (no sign of formation or calcification in DPR). Covariates were included in the regression models based on previous literature or a change of >10% in effect estimates.

Statistical analysis

The associations between dental development with each of the 9 PCs of craniofacial morphology were analyzed with the use of linear regression models. Regression models were adjusted for age, sex, BMI, height, ethnicity, maternal education, and hypodontia. The nonlinearity of exposure variables was tested by means of restricted cubic splines with 3-5 knots. Values of variables dental development score and craniofacial PCs were considered to be outliers and excluded if they were outside the range of −3 and +3 SD. Statistical interaction between dental development and child's sex was investigated by adding a product term of these 2 variables in the linear regression analysis. Missing data were handled by generating 5 imputed datasets by means of the Markov Chain Monte Carlo method, from which the pooled effect estimates are presented in this study (effect size [β], 95% confidence intervals [CIs], and *P* value). Results were considered to be statistically significant for a *P* value of ≤0.05. Statistical analyses in this study were performed with the use of statistical software SPSS version 21.0 (IBM, Armonk, NY) and R statistical package version.3.3.2 (R, Vienna, Austria).

RESULTS

The characteristics of the study population are provided in Table 1. Among all children included in this study, 2305 (59.2%) were Dutch and 1502 (38.6%) were of other ethnicity. One-sided hypodontia was found in 144 cases (3.7%). The largest group of mothers

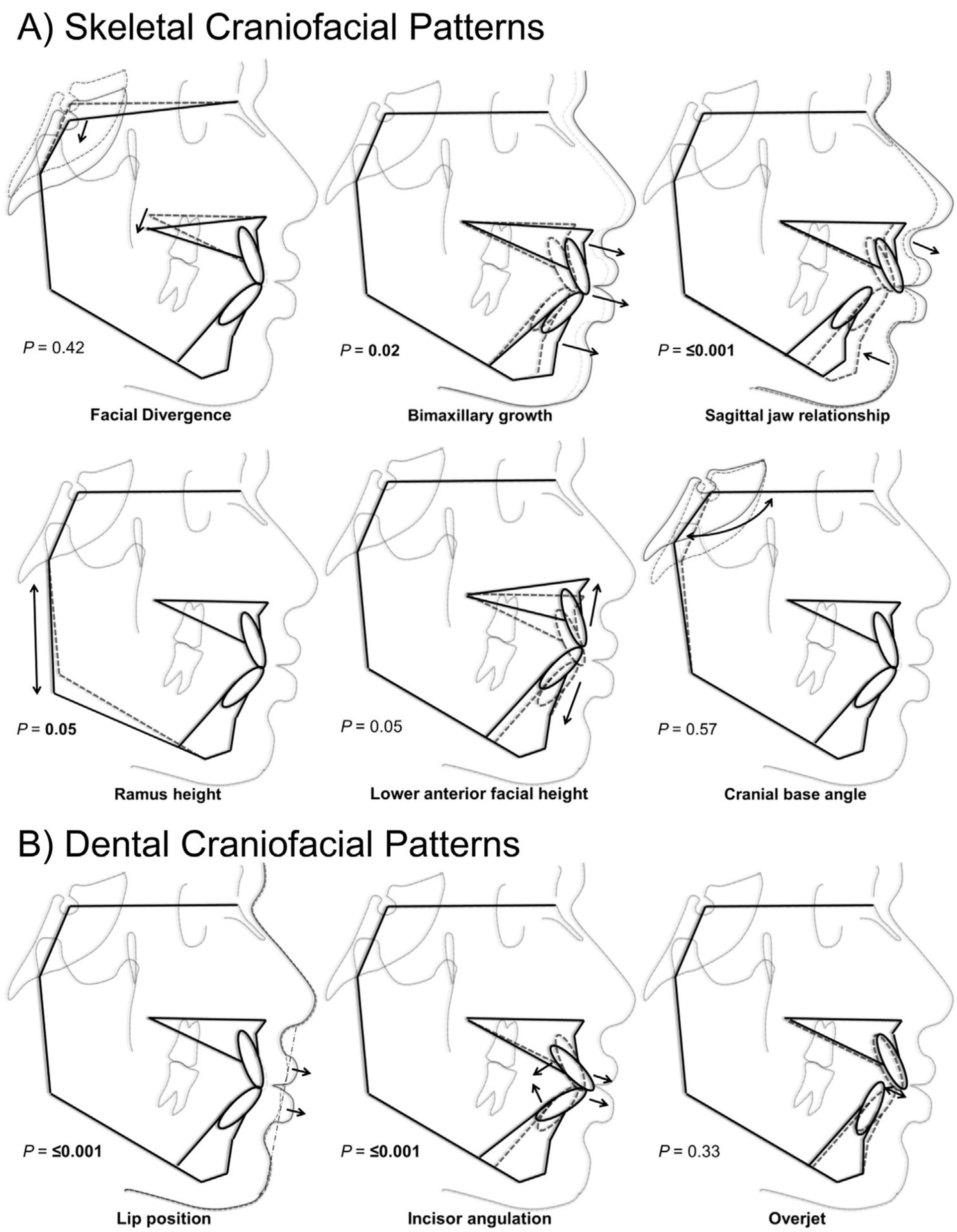

Fig 2. Changes in cephalometric parameters with increasing dental development score. Craniofacial parameters are represented by principal components (PCs), each representing a specific **A,** skeletal or **B,** dental craniofacial pattern. *P* values denote significance levels of the association between dental development and the craniofacial PCs.

attained higher education (n = 1845; 47.4%), followed by those with secondary education (n = 1450; 37.2%), and 273 mothers (7.0%) attained only primary education. The median stage of development for mandibular canines, first premolars, second premolars, and second molars was 6 (out of 8), whereas mandibular central incisors, second incisors, and first molars almost reached full development, presenting a median stage of 8. The mean value of the children's BMIs was 17.62 ± 2.79 kg/m^2 and they were on average 141.70 ± 6.72 cm tall. Craniofacial PCs and dental development scores were converted to SD scores with mean value = 0 and SD = 1 (not presented in Table I).

The results of the association between dental development and 9 cephalometric patterns are presented in Table II and illustrated in Figure 2. Advancement in

Table I. Characteristics of subjects included in the study (n = 3896)

Characteristic	*Value*
Girls	1946 (49.9%)
Chronologic age, y	9.81 ± 0.33
Ethnicity	
Dutch	2305 (59.2%)
Non-Dutch	1502 (38.6%)
Missing	89 (2.3%)
Maternal education	
Primary	273 (7.0%)
Secondary	1450 (37.2%)
Higher	1845 (47.4%)
Missing	328 (8.4%)
Body mass index, kg/m^2	16.96 (14.4-23.1)
Height, cm	141.73 ± 6.6
Dental characteristics	
Stage of tooth development	
Central incisor	8 (8-8)
Lateral incisor	8 (8-8)
Canine	6 (5-7)
First premolar	6 (5-7)
Second premolar	6 (5-7)
First molar	8 (7-8)
Second molar	6 (4-7)
Hypodontia cases	144 (3.7%)

Values for categoric variables and continuous variables with a skewed distribution are represented as n (%) or median (interquartile range). Values for continuous variables with a normal distribution are represented as mean ± SD.

dental development was associated with a decrease in the sagittal jaw relationship PC (β = −0.08; 95% CI −0.13 to −0.04), indicating a tendency toward skeletal Class II relationship. However, by applying a nonlinear transformation to the dental development, we observed that tendency toward Class II relationship was mainly present in children with above-average dental development (dental development score >0 SD; Fig 3, *A*). Also, dental development was positively associated with the bimaxillary growth PC (β = 0.04; 95% CI 0.01 to 0.08). The results of the linear regression analysis showed that with increasing dental development score, the ramus height PC (β = 0.04; 95% CI 0.00 to 0.09), and the lower anterior facial height PC increased (β = 0.04; 95% CI 0.00 to 0.09) with borderline significance (P = 0.05). No significant association was observed for between dental development and the facial divergence PC or the cranial base angle PC.

Regarding dental parameters, the lip position PC and incisor angulation PC were increasing along with dental development (β = 0.15 [95% CI 0.10 to 0.19] and β = 0.13 [95% CI 0.09 to 0.17], respectively), indicating an increased proclination for both incisors and lips. Still, the incisor proclination was more pronounced in children that had above-average dental development (dental development >0 SD; Fig 3, *B*), based on the nonlinear transformation of dental development. We did not observe a significant association between dental development and the overjet PC.

We did not observe a significant statistical interaction between dental development and child's sex.

DISCUSSION

The results of this study indicate that the rate of dental development is associated with the bimaxillary growth of the craniofacial complex and to some extent changes in vertical facial parameters, as represented by the increased ramus height and the lower anterior facial height. Furthermore, children with advanced dental development showed a tendency toward Class II jaw relationship. This tendency was more pronounced in children with above-average dental development than in children with normal and below-average dental development. The strongest effect of advanced dental development was shown for dental parameters involving incisors proclination and lip protrusion.

Our findings indicate that dental development is positively associated with vertical and sagittal jaw growth. A common genetic background is the most probable explanation why the development of these 2 traits is closely related. *BARX1*, *PITX2*, *MSX*, and *DLX* are genes that are involved in the development of the first pharyngeal arch from which facial bones, maxilla, and mandible are derived. *BARX1* regulates jaw, muscle, and tongue development,[31] *PITX2*, regulates the development of oral ectoderm,[32] *MSX* is involved in the migration of neural crest and mesenchymal cells,[33] and *DLX* is involved in the development of the maxillary and mandibular arch.[34] The same genes are involved in the process of odontogenesis. *BARX1* takes part in the early stage of odontogenesis,[2,35] *PITX2* is expressed in all cells of the tooth bud,[32] *MSX* shows regulatory capabilities specific to root formation,[36] and *DLX* regulates amelogenesis.[37] Therefore, we postulate that *BARX1*, *PITX2*, *MSX*, and *DLX* genes have a biologically pleiotropic effect on both craniofacial and dental development. This could also explain why similar craniofacial changes are also present in subjects with tooth agenesis.[30] Further genetic studies are necessary to investigate the genetic background of the complex dentofacial growth.

In addition to the known conventional genetic components that control craniofacial skeletal growth, the literature raises the importance of the growth of craniofacial bones as a mechanical response to the development of functional matrices, such as teeth, muscles,

Table II. The association between dental development and craniofacial morphology

Dental development (SDS)	*Craniofacial pattern*								
	Skeletal						*Dental*		
	Facial divergence	*Bimaxillary growth*	*Sagittal jaw relationship*	*Ramus height*	*Lower anterior facial height*	*Cranial base angle*	*Lip position*	*Incisor angulation*	*Overjet*
β	−0.02	0.04	−0.08	0.04	0.04	0.01	0.13	0.15	0.02
95% CI	−0.06 to 0.03	0.01 to 0.08	−0.12 to −0.03	0.00 to 0.09	0.00 to 0.09	−0.03 to 0.06	0.09 to 0.17	0.10 to 0.19	−0.02 to 0.06
P value	0.42	0.02*	≤0.001*,†	0.05	0.05	0.57	≤0.001*	≤0.001*,†	0.33
n	3878	3875	3876	3883	3872	3878	3871	3875	3851

β, regression coefficient; *CI*, confidence interval; *SDS*, standard deviation score; n, number of subjects in the imputed dataset after exclusion of outliers (±3 SD).
Models were adjusted for age, sex, body mass index, height, ethnicity, maternal education, and hypodontia.
*Statistically significant ($P \leq 0.05$); †Significant nonlinear effect.

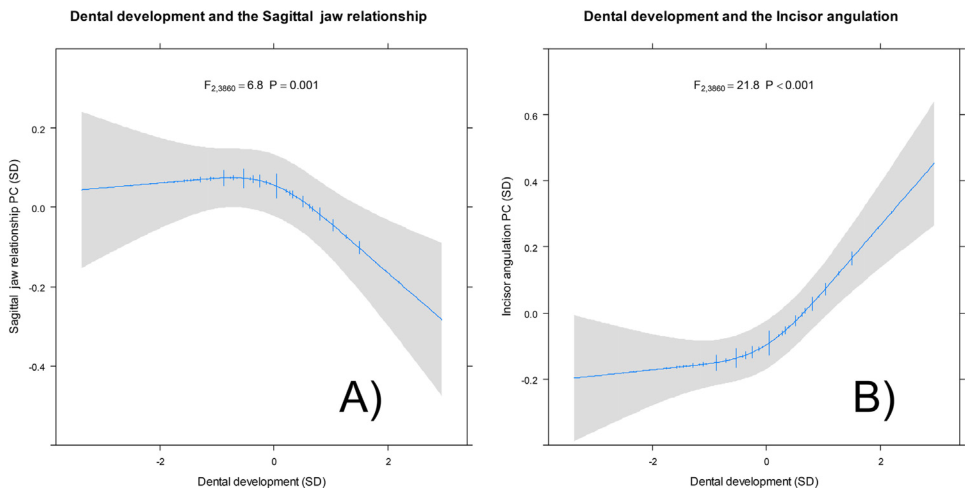

Fig 3. Nonlinear association between dental development and craniofacial principal components (PCs). The *x*-axis indicates a change in standard deviation (SD) score of dental development. Lower values indicate delayed dental development and higher values indicate advanced dental development. The *y*-axis indicates a change in SD score of: **A,** sagittal jaw relationship PC, with lower values indicating a tendency toward skeletal Class II relationship and higher values a tendency toward skeletal Class III relationship; and **B,** incisor angulation PC, with lower values indicating incisor retroclination and increased interincisal angle and higher values incisor proclination and decreased interincisal angle. The model was adjusted for age, sex, body mass index, height, ethnicity, maternal education, and hypodontia.

salivary glands, sinuses, and other tissues.[38] Acting as a functional matrix, dental development contributes to the sagittal and vertical growth of the maxilla and mandible, which undergo a rapid remodeling process in the period from 3 to 18 years of age.[38,39] In the present study, development of the teeth contributes to the increase of vertical facial parameters, as a result of the increased ramus height and the lower anterior facial height. A possible mechanism to explain our findings is that the eruption and development of the maxillary and mandibular teeth, as well as the growth of the maxillary bone in the vertical direction, triggers the compensatory vertical growth of the mandible. Thus, the plane of occlusion is maintained in a straight line.[2] However, if the dental development and eruption are accelerated, the lowered maxillary arch comes in earlier contact with the mandibular teeth in the posterior region which leads to downward and backward rotation of the mandible.[40] This is why we also observed a tendency toward Class II occlusion in children with advanced dental development, which was also reported in previous studies.[20,41] Another explanation for the tendency toward Class II might be a difference in the response between the maxilla and the mandible to the teeth that grow inside them. Because the maxilla is a fixed bone with a spongy structure, the effect of the forces generated by the developing teeth would also be increased growth of the upper jaw. In contrast, the mechanical forces created by the growing teeth inside the mandible are reduced by the compact structure of the bone. Therefore, it seems that the growth of the teeth favors the growth of the upper jaw. However, by looking into the nonlinear relationship between dental development and sagittal jaw relationships (Fig 3, *A*), we demonstrated that the tendency toward Class II was present only in the children with above-average dental development. In contrast, normal and delayed dental development did not have an effect on the sagittal jaw relationship.

We also demonstrated incisor proclination and lip protrusion in relation to the nose-chin line in children with advanced dental development. Furthermore, lip protrusion was independent from the effect of incisor proclination, and vice versa, as indicated by the weak correlation between the PCs. We can postulate that with earlier development of the upper teeth, incisors erupt in a more labial direction to increase the length of the arch. Again, by looking at the nonlinear relationship between dental development and incisor angulation PC (Fig 3, *B*), we observed that incisor proclination is present only in children with above-average dental development. In contrast, we did not observe any association between dental development and incisor angulation in children with normal or delayed dental development, probably because of compensatory growth of maxilla, which comes into balance with developing maxillary teeth. Other studies reported an increased incisor proclination during the mixed dentition, which later stabilizes in the permanent dentition.[18,19] Therefore, careful interpretation of our findings is necessary as a consequence of catch-up growth of maxilla late mixed and permanent dentition period. Regarding the soft tissue parameters, we assume that the nose and chin are located more backward in children with advanced dental development, from which lips seem more protruded.

The differences in facial growth patterns between boys and girls have been studied in the past. Studies have reported sex-specific changes in hard and soft tissue parameters.[42] Some studies showed that malocclusions of II or III are more prevalent in male subjects. On the other hand, it is reported that facial growth patterns do not differ until around 12 years of age.[2,43] In line with previous studies, we adjusted for child's sex in the regression analysis. However, we did not analyze boys and girls separately as some previous studies did, owing to the nonsignificant interaction term between child's sex and dental development score.

The findings of this study could be used as a clinical guide to early diagnosis, treatment planning, and prognosis of orthodontic treatment. Early assessment of the rate of dental development in a child could help the orthodontist to estimate the facial type or jaw relationship in the later stage of life. For example, identifying advanced dental development or eruption might indicate a tendency toward bimaxillary Class II relationship and lip protrusion or incisor proclination. Furthermore, assessing the rate of dental development could serve as a favoring or impeding prognostic factor for orthodontic treatment. Therefore, the next step would be to develop a predictive model that could estimate craniofacial development at a later stage of life or even predict the occurrence of craniofacial-related anomalies, based on the dental maturity score calculated and filled in by the clinicians. Further studies are necessary that will take into account clinical parameters to develop and validate a predictive model of craniofacial development. Ultimately, the final decision for the adequate treatment would remain primarily based on individual patient characteristics, clinical parameters, and the expertise of a clinician.

Strengths and limitations

The main strength of the present study is the inclusion of a large number of subjects from a multiethnic population-based prospective cohort, with exclusive measurements of dental development and craniofacial characteristics.

In studies that analyze the human face, large inter- and intrapopulation variations occur owing to numerous genetic, epigenetic, and environmental factors that regulate the process of human craniofacial growth and development.[3] Despite adjusting analysis for multiple confounders, residual confounding may still be an issue in our study. For example, environmental factors, such as general living conditions, nutrition, health status, and stressors, have been strongly associated with growth and development status.[15,44,45] Because of practical limitations of the study, some confounders were addressed by adding similar variables to the confounders (proxy confounders). For example, we adjusted for the education of mothers, which resembles a socioeconomic class of the family, but it does not take into account household income and living conditions, although they are highly correlated. BMI is a measurement of food intake, but it does not express eating behaviors qualitatively.

Because previous studies showed that skeletal maturation correlates significantly with craniofacial growth,[10,46] we attempted to minimize the influence of skeletal maturation on the association between dental maturation and craniofacial characteristics by adding the height of a child in the analysis, which served as a proxy for general growth and skeletal maturation.[47-49] Furthermore, we quantified dental development as SD score. The disadvantage of applying SD scores is that the unit of measurement is expressed as SD instead of dental age. We also used a rank-based normalization method to correct for the nonnormal distribution. By applying this procedure, we were able to include, for example, children with extreme values for dental development. As a result, the initial distribution of dental development scores is narrowed, implicating that the actual dental development differences might be greater than the observed differences. Also, PC analysis is a good method to group correlated cephalometric parameters into a single trait. However, determining the number of craniofacial patterns, choosing the method of factor rotation, and interpretation are subjective questions for the investigator. Therefore, we opted to minimize subjectivity by using analysis protocols reported in previous studies.[28,30]

CONCLUSIONS

The findings of this large population-based study show that dental development is associated with specific dental and skeletal cephalometric characteristics in school-age children. We observed an increased sagittal and vertical growth of the dentofacial structures in children with advanced dental development. Furthermore, children with above-average dental development showed a tendency toward Class II occlusion and increased incisor and lip protrusion. Further longitudinal studies are necessary to explore the stability of observed effects over time.

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APPENDIX

Supplementary Table I. Description of the cephalometric landmarks

Abbreviation	*Name*	*Definition*
S	Sella	Center of sella turcica
N	Nasion	The most anterior limit of the frontonasal suture
Ar	Articulare	Point where the posterior outline of the condyle passes over the posterior and lower margin of the cranial base
Go	Gonion	Midpoint of the angle of the mandible
Me	Menton	Most inferior point on the symphysis of the mandible
Pg	Pogonion	Most anterior point on the symphysis of the mandible
B	B-point	Deepest point on the contour of the mandible
A	A-point	Deepest point on the contour of the premaxilla
ANS	Anterior nasal spine	Tip of the anterior nasal spine
PNS	Posterior nasal spine	Most posterior point in the sagittal plane on the bony hard palate
Is	Incision superius	Incisal tip of the most anterior maxillary central incisor
Rs	Upper incisor apex	Root apex of the most prominent upper incisor
Msc	Molar superius cusp	The mesiobuccal cusp tip of the maxillary first molar; when double projection gives rise to 2 points, the midpoint is used
Ii	Incision inferius	Incisal tip of the most anterior medial mandibular central incisor
Ri	Lower incisor apex	Root apex of the most prominent lower incisor
G′	Glabella	The most prominent anterior point in the midsagittal plane of the forehead
NT' (P)	Pronasale	Most prominent point of the nose
MP'	Steiner S-point	The middle of the 'S' formed by the lower border of the nose
RN'	Retro-nasale	Point at which the columella (nasal septum) merges with the upper lip in the midsagittal plane
Ls'	Labrale superius	Most prominent point of the vermilion border of the upper lip
Li'	Labrale inferius	Most prominent point of the vermilion border of the lower lip
PG'	Soft-tissue pogonion	Most anterior point on the chin

Supplementary Table II. Definition of cephalometric parameters by facial region and descriptive statistics

Facial region	*Abbreviation (units)*	*Definition*	*n*	*Mean*	*SD*
Cranial base	SArGo (°)	Articular angle formed by points S, Ar, and Go	3896	141.8	6.1
	NSAr (°)	Saddle angle formed by points N, S, and Ar	3896	124.1	5.2
	ArGoMe (°)	Gonial angle formed by points Ar, Go, and Me	3896	127.9	5.3
Jaw relationship	SNA(°)	Angle formed by points S, N, and A according to Steiner analysis	3896	81.1	3.8
	SNB (°)	Angle formed by points S, N, and B according to Steiner analysis	3896	77.3	3.5
	ANB (°)	Angle formed by points A, N, and B according to Steiner analysis	3896	3.8	2.2
	SNPg (°)	Angle indicating chin prominence formed by points S, N, and Pg	3896	77.6	3.5
	MxSN (ANSPNS-SN) (°)	Angle formed by plane connecting points S and N and palatal plane (plane formed by points ANS and PNS)	3896	6.7	3.2
	MnSN (GoMe-SN) (°)	Angle formed by plane connecting points S and N and mandibular plane (plane formed by points Go and Me)	3896	33.9	5.1
	MxMn (ANSPNS-GoMe) (°)	Angle formed by palatal (plane formed by points ANS and PNS) and mandibular (plane formed by points Go and Me) planes	3896	27.3	5.1
	N-A-Pg (°)	Angle of convexity formed by points N, A, and Pg according to Downs analysis	3896	172.8	5.4
	A⊥NPg (mm)	Convexity of point A: distance between point A and facial plane (plane formed by points N and Pg) according to Ricketts analysis	3896	3.1	2.3
Dental parameters	Interincisal angle (°)	Angle formed by the lines going through axes of maxillary and mandibular incisors according to Steiner analysis	3896	126.2	10.0
	LI-Mn (°)	Incisor–mandibular plane angle: formed by the intersection of the mandibular plane (plane formed by points Go and Mn) with a line passing through the incisal edge and the apex of the root of the mandibular central incisor according to Downs analysis	3896	97.2	6.7
	UI-Mx (°)	Incisor–palatal plane angle: formed by the intersection of the mandibular plane (plane formed by points ANS and PNS) with a line passing through the incisal edge and the apex of the root of the maxillary central incisor	3896	109.4	6.7
Vertical indices	LAFH (ANSMe/NMe)	Percentage of lower anterior facial height (distance between points ANS and Me) as a fraction of total anterior face height (distance between points N and Me)	3896	57.4	2.3
	LPFH (ArGo/SGo)	Percentage of lower posterior facial height (distance between points Ar and Go) as a fraction of total posterior face height (distance between points S and Go)	3896	58.9	3.5
	Jarabak ratio (SGo/NMe)	Percentage of total posterior face height (distance between points S and Go) as a fraction of total anterior face height (distance between points N and Me)	3896	64.2	4.3
	NPNS/PNSMe	Ratio between distance connecting points N and PNS and distance connecting points PNS and Me	3896	1.0	0.1
Soft tissue	G′-RN’-PG′(°)	Angle of facial convexity for soft tissue is formed by points G′, RN’, and Pg’	3896	165.9	5.3
	Ls’-Sl (mm)	Distance between point Ls’ and Steiner line (line connecting points Pg’ and MP’)	3896	0.6	2.4
	Ls’-El (mm)	Distance between point Ls’ and Ricketts esthetic line (line connecting points Pg’ and NT’)	3896	1.3	2.7
	Li’-Sl (mm)	Distance between point Li’ and Steiner line (line connecting points Pg’ and MP’)	3896	−0.3	2.6
	Li’-El (mm)	Distance between point Li’ and Ricketts esthetic line (line connecting points Pg’ and NT’)	3896	0.7	2.8

Supplementary Table II. Continued

Facial region	*Abbreviation (units)*	*Definition*	*n*	*Mean*	*SD*
Sagittal analysis by Pancerz	A┴OLp (mm)	Distance between point A and line going through point S perpendicularly on occlusal plane*	3896	70.4	4.5
	Pg┴OLp (mm)	Distance between point Pg and line going through point S perpendicularly on occlusal plane*	3896	74.2	5.9
	Is┴OLp (mm)	Distance between point Is and line going through point S perpendicularly on occlusal plane*	3896	78.1	5.4
	Ii┴OLp (mm)	Distance between point Ii and line going through point S perpendicularly on occlusal plane*	3896	73.9	5.4
	IsOLp-IiOLp (overjet) (mm)	Distance Is┴OLp minus distance Ii┴OLp	3896	4.3	1.9
	AOLp-PgOLp (mm)	Distance A┴OLp minus distance Pg┴OLp	3896	-3.8	3.5
	IsOLp-AOLp (mm)	Distance Is┴OLp minus distance A┴OLp	3896	78.1	5.4
	IiOLp-PgOLp (mm)	Distance Ii┴OLp minus distance Pg┴OLp	3896	73.9	5.4
Vertical analysis by Pancerz	ANS-Me (mm)	Distance between points ANS and Me	3896	58.7	4.7
	Is┴Mx (mm)	Distance between point Is and palatal plane (plane formed by points ANS and PNS)	3896	25.5	2.5
	Ii┴Mn (mm)	Distance between point Ii and mandibular plane (plane formed by points Go and Mn)	3896	35.5	2.9

*Occlusal plane is plane that goes through points Is and Msc.

Supplementary Table III. Description of craniofacial patterns explained through principal component (PC) analysis

		Interpretation			*PC analysis**	
Facial region	*PC*	*Craniofacial pattern*	*Positive value of PC*	*Negative value of PC*	*Cephalometric parameters*[†]	*Explained variability (%)*
Skeletal	PC2	Facial divergence	Hypodivergent/ low-angle face	Hyperdivergent/ high-angle face	+SNB; +SNPg; +SNA; –NPNS/PNSMe	16
	PC3	Bimaxillary growth	Toward bimaxillary protrusion	Toward bimaxillary retrusion	+Pg$^{\perp}$OLp; +A$^{\perp}$OLp; +Is$^{\perp}$OLp; + Ii$^{\perp}$OLp	12
	PC4	Sagittal jaw relationship	Toward Class III relationship	Toward Class II relationship	–ANB; +N-A-Pg; + A$^{\perp}$ NPg; +G′-RN'-PG′; –AOLp-PgOLp	9
	PC6	Ramus height	Increased ramus height	Decreased ramus height	–ArGoMe; +LI-Mn; –GoMe- SN; +Jarabak ratio	5
	PC7	Lower anterior facial height	Increased lower anterior facial height	Decreased lower anterior facial height	+LAFH; +ANS-Me; –MxSN; +Is$^{\perp}$Mx; +Ii$^{\perp}$Mn; +ANSPNS-GoMn	5
	PC8	Cranial base relationship	Increased cranial base angle	Decreased cranial base angle	–SArGo; +NSAr; +LPFH;	4
Dental	PC1	Lip position	Protruded lips	Retruded lips	+Ls'-SL; +Li'-SI; +Ls'-El; +Li'-El	25
	PC5	Incisor angulation	Incisor proclination and decreased interincisal angle	Incisor retroclination and increased interincisal angle	+UI-Mx; –interincisal angle; +IiOLp-PgOLp; +IsOLp-AOLp	8
	PC9	Overjet	Increased overjet	Decreased overjet	+Overjet	4

*Cephalometric parameters describe a PC based on the primary (strongest) loading of a cephalometric parameter from the pattern matrix of the principal component analysis with the use of a direct oblimin rotation procedure. Secondary and subsequent factor loadings of cephalometric parameters were not higher than 0.56 and therefore not taken into account; [†]+denotes positive and – negative correlation of a cephalometric parameter with the PC; descriptions of cephalometric parameters are provided in Supplementary Tables I and II.