Foetal alcohol syndrome: a cephalometric analysis of patients and controls

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SUMMARY Foetal alcohol syndrome (FAS) consists of multi-system abnormalities and is caused by the excessive intake of alcohol during pregnancy. The teratogenic effect of alcohol on the human foetus has now been established beyond reasonable doubt and FAS is the most important human teratogenic condition known today. The purpose of this study was to analyse the craniofacial parameters of children with FAS and compare them with matched controls.

Ninety children diagnosed with FAS (45 males, 45 females) and 90 controls were matched for age, gender, and social class. The mean age of the FAS children was 8.9 years with the controls slightly older at 9.1 years. This age difference was not significant (P = 0.34). A standard lateral cephalometric radiograph of each subject was taken. The radiographs were digitized for 20 linear and 17 angular measurements. These 37 variables were formulated to assess the size, shape, and relative position of three craniofacial complexes: (1) the cranial base, (2) midface, and (3) mandible. In addition, nine variables were computed to compare the soft tissue profiles.

The study showed that measurements related to face height and mandibular size appear to be the most important features when distinguishing FAS children. Overall, the FAS children in the present study presented with vertically and horizontally underdeveloped maxillae, together with features of long face syndrome with large gonial angles and a short ramus in relation to total face height. There was also a tendency for the development of an anterior open bite, which appears to be compensated for by an increase in the vertical dimension of the anterior alveolar process to bring the incisor teeth into occlusion. The latter adaptation occurred mainly in the mandible.

Introduction

Foetal alcohol syndrome (FAS) consists of multi-system abnormalities and is caused by the excessive intake of alcohol during pregnancy. The teratogenic effect of alcohol on the human foetus has now been established beyond reasonable doubt and FAS is one of the most important human teratogenic conditions known today. The syndrome, first described by Lemoine *et al.* (1968) in the French literature and in the English literature by Jones and Smith (1973), has since been corroborated by numerous animal and human studies.

The typical characteristics of FAS are (1) facial abnormalities including microcephaly, a narrow forehead, micrognathia, maxillary hypoplasia, a flat midface, narrow palpebral fissures, a short and small nose, a long upper lip with a narrow vermillion border, diminished or absent philtrum and epicanthal folds; (2) central nervous system dysfunction with mental retardation ranging from mild to severe; (3) growth deficiency as in lower weight and height at birth persisting into the post-natal period; and (4) various cardiovascular and skeletal abnormalities (Jones and Smith, 1973). The purpose of this study was to analyse the craniofacial parameters of children with FAS and to compare them with matched controls.

Methodology

Ethical considerations

The protocol was approved by the Research Ethics Committee of the University of Stellenbosch. Written, informed consent was obtained from the principal of each participating school and the parents or guardians of each child. Access to the participants of the study was made initially by letter to the participating school principals and parents. An introduction by the researcher, the basic aims and objectives of the study, what participating in the study would involve, what examinations were to be carried out, and how long the examination would take were fully explained in their native language. It was emphasized that strict confidentiality would be maintained at all times and that the results of the study would be presented in a manner that ensured anonymity. Once a signed informed consent form was received for each child, arrangements were made for the clinical examinations to be carried out at a time convenient to the participants and schools. Children were collected from the schools and brought to School for Oral Health Sciences, Faculty of Health Sciences at Tygerberg Hospital.

Following the dental assessment, specific interventions for any child (subject or control) found to have medical problems related to the study were carried out at the Avalon Treatment Centre, Foundation for Alcohol-related Research, Department of Genetics, University of Cape Town, where full specialist and psycho-social support were provided. This included, in some cases, the provision of growth hormone therapy.

Children with dental, orthodontic, and other oral-healthrelated problems were treated at the School for Oral Health Sciences at the University of Stellenbosch and its' outreach clinics. In addition, each child received an individual oral health report within 3 months of completion of the survey, with appropriate advice. Written informed consent was obtained from the parents of the children whose photographs were used for reporting purposes.

Diagnosis and screening of FAS cases

The FAS subjects were diagnosed by active case ascertainment in the Wellington community in the Western Cape (Institute of Medicine, 1996). Details have been published previously (Naidoo *et al.*, 2006).

Ninety children diagnosed with FAS (45 males, 45 females) were matched for age, gender, and social class with 90 controls. A standard lateral cephalometric radiograph of each subject was taken using a cephalostat in the Division of Maxillofacial Radiology at the University of Stellenbosch (Cranex TOME Ceph machine, Soredex Orion Corporation, Helsinki, Finland), with an object-to-film distance of 15 cm, 8 mAs exposure (0.8 seconds 10 mA current) and a 66–70 kVp. The cephalometric radiographs were developed using an Agfa CP-GL Medical X-ray film green sensitive, 18 × 24 cm. All radiographs were taken by the same operator.

The lateral cephalometric radiographs were digitized using a computer program Quick Ceph ImageTM (Orthodontic Processing, Chula Vista, California, USA) for 20 linear and 17 angular measurements. These 37 variables allowed assessment of size, shape, and relative position of three craniofacial complexes: (1) the cranial base, (2) midface, and (3) mandible. In addition, nine variables were computed to compare soft tissue profiles.

Figure 1 shows the cephalometric landmarks and Figure 2 the linear measurements taken from each cephalometric radiograph. All the on-screen cephalometric measurements were carried out twice by the same operator and no significant intra-examiner error was found. These data were then exported into a spreadsheet version for statistical analysis. The standard cephalometric radiographs were analysed using Bolton standards of dentofacial development growth data (Bolton, 1962; Broadbent *et al.*, 1975) and the Wits analysis (Jacobson, 1975). The basic units of analysis used were degrees and the linear distances are given in millimetres.

Statistical methods

Descriptive analysis involved computing the mean, standard deviation (SD), minimum, maximum, and range of the



Figure 1 The lateral cephalometric landmarks used in the study (Frias *et al.*, 1982; Gir *et al.*, 1989): Se, sella; Na, nasion; Or, orbitale; A, point A; IX, IU root tip; IU, IU incisal tip; LI, LI incisal tip; IN, LI root tip; B, point B; Pg, pogonion; Gn, gnathion; Me, menton; Go, gonion; Ba, basion; Op, opisthion; Oc, occipitale; Po, anatomic porion; Cd, centre of condylion; Pt, pterygoid point; Sp, sphenoid point; PNS, posterior nasal spine; ANS, anterior nasal spine; Fh, supraorbital prominence of forehead; Na', soft tissue nasion; Sn, subnasale; LS, labrale superius; LI, labrale inferius; Pg', soft tissue pogonion NT, tip of nose.



Figure 2 Linear measurements taken from the cephalometric radiographs. All points are described in Figure 1.

cephalometric parameters. Both univariate and multivariate techniques were used in the analyses. Spearman correlation coefficients were calculated between chronological age and each of the cephalometric measurements to determine which measurements had significant age associations.

To evaluate the discriminative ability of the cephalometric analysis between FAS and controls the following statistical analyses were carried out: (1)For each individual measurement an age-dependent standardization was undertaken using the data from the controls as a reference. The age dependence of the measurement was determined by means of a linear regression on age. The absolute residuals from this model were then used in a second linear regression on age to determine the age dependence of the SD (Altman, 1993). For each child in the study the estimated age, specific mean, and SD from the normal control were then used to standardize a variable. (2) Stepwise logistic regression models were used for variable selection from the age-standardized measurements. (3) A linear discriminant with a common covariance structure for the two groups of children was carried out using the selected subset of standardized variables from the stepwise logistic regression analysis. The 'jackknife' classification of the variables is reported. (4) A canonical variate analysis (CVA) biplot (Gardner, 2002) was used to display the separation between the FAS and control children in the multi-dimensional space of the subset of selected standardized variables. It is a two-dimensional representation of the multi-dimensional scatter plot of the variables.

Results

Demography

The 90 children diagnosed with FAS and the 90 controls were matched for age, gender, and social class. The mean age of the subjects was 8.9 years with the controls slightly older at 9.1 years. This age difference was not significant (P = 0.34) and the age ranges for both the groups were the same. There was an equal gender distribution in both the subjects and controls with 45 males and 45 females in each group, as would be expected as a result of sample matching.

Cephalometric analysis

None of the angular measurements except for the palatal plane to Frankfort Horizontal (FH) angle showed any significant differences between the subjects and controls. However, several linear measurements in the FAS children were found to be significantly different from the controls, especially those related to the cranial base, midface, and mandible (Table 1). Statistical analysis was confined to correlations between the linear measurements, as it was found that they contributed greatly to distinguishing and describing the FAS children.

Individual component analysis

Cranial base. In this study, there were five variables measuring cranial base size and angulation (Table 1). The sella–nasion (S–N) plane serves as a relatively stable base from which to assess changes in the dentofacial complex. It lies parallel to the anterior cranial fossa, the development of which is completed quite early and is a valid and stable reference plane (Graber, 1969). Although the angulation of the cranial base was not statistically significantly different, all of the linear measurements were statistically significantly different. The decreased S–N length represented shortening of the anterior cranial base. The lengths of the basion–nasion, basion–sella, and S–N were also shorter than normal.

Midface. Midface height (N–ANS) was found to be significantly different in the FAS children compared with the controls (Table 1). The palatal plane was rotated downwards posteriorly, which decreased the posterior midface height (Pt–PNS, PNS \perp FH) and increased the angle of the palate with the FH; PNS \perp FH and palatal plane to FH angle being statistically significant. This localized displacement thus appears to affect the sagittal position of the anterior (vertical) limit of the palate as seen with the N–ANS height. The variables used to assess the size and shape of the midface are given in Table 1. All the vertical linear measurements were significant at P < 0.01.

Mandible. Since previous reports have commented on the retrognathia of the mandible in children with FAS, the morphology and relationships of the mandible were examined in detail (Table 1). Several parameters were assessed: antero-posterior and sagittal size and position of the mandible and its components, sagittal heights of the lower third of the face, and tooth positions and angulations. The resulting picture was of a mandible that is in a normal antero-posterior and sagittal position. The FAS mandible appeared to be undersized and indeed the corpus length (Go-Pg) was significantly shorter than that of the controls. The effective mandibular length was measured from condylion to gnathion (Co-Gn). Relative component sizes appeared to differ significantly in the FAS children: the FAS mandible had a shorter corpus (P < 0.01) a shorter ramus (P < 0.01) but a slightly larger gonial angle. The significant decrease in the ANS-Me and S-Go lengths reflects shortened anterior and posterior face heights, respectively.

Incisor relationships. There were no significant differences between tooth positions and angulations (Table 1).

Integumental profile. Soft tissue parameters of the nose, lips, and facial proportions (Table 1) were found to be similar in the two groups, the one exception being the LI–pogonion' length, which was significantly different (P < 0.01). This may be due to the shorter ramus seen in the FAS children.

Age—an important parameter

A subset of standardized variables were selected: BaN, NANS, ANSMe, PNSFH, and SNAPo. The linear regressions on age of the mean and SD for the selected measurements are shown in Table 2. The BaN distance was the only measurement in the subset which showed hetroscedasticity over the age range of the normal children. Tables 3 and 4 provide the means and covariance matrix of the standardized measurements. Tests for normality of the standardized measurements showed that this assumption was valid for all five measurements. The test for the homoscedasticity of the covariance matrices

Table 1	Variables used	to assess t	the size and	l shape of th	e cranial ba	se, midface	, mandible,	, facial ai	nd integumental	profile and	incisor
relationsh	ips in children	with foetal	alcohol sy	ndrome (FAS	S) and contr	ols.					

Variable	Sample mean	Paired t-test	
	FAS $(n = 90)$	Controls $(n = 90)$	
Cranial base			
Basion-sella length (BaS)	40.88 (SD 3.09)	42.59 (SD 3.37)	< 0.01
Basion-nasion length (BaN)	91.37 (SD 5.44)	95.54 (SD 5.50)	< 0.01
Sella-nasion length (SN)	60.16 (SD 3.61)	63.12 (SD 3.82)	< 0.01
Basion-sella-nasion angle	128.74 (SD 5.51)	128.44 (SD 4.62)	0.69
Sella–nasion FH angle	9.75 (SD 3.60)	9.60 (SD 3.38)	0.77
Midface			
Nasion-ANS length	39.84 (SD 3.22)	42.69 (SD 3.76)	< 0.01
Sella-nasion-A angle	94.66 (SD 4.88)	95.06 (SD 4.60)	0.55
Nasion-A to FH angle	95.09 (SD 3.81)	94.54 (SD 3.50)	0.24
Pt-vertical/nasion length	50.06 (SD 3.26)	52.86 (SD 3.34)	< 0.01
Pt-vertical/A length	51.54 (SD 3.77)	54.24 (SD 3.93)	< 0.01
$PNS \perp FH$ length	24.84 (SD 2.61)	25.98 (SD 3.13)	< 0.01
Pterygoid–PNS length	22.84 (SD 2.46)	23.18 (SD 3.01)	0.37
Palatal plane to FH angle	6.08 (SD 3.44)	4.72 (SD 2.64)	< 0.01
Mandible			
Nasion-menton length	98.21 (SD 5.92)	103.22 (SD 6.78)	< 0.01
ANS-menton length	59.67 (SD 4.04)	61.81 (SD 4.55)	< 0.01
Sella-nasion-B point angle	79.92 (SD 4.39)	79.92 (SD 4.13)	1.00
Sella-nasion-pogonion angle	78.36 (SD 4.30)	78.64 (SD 4.08)	0.63
Y axis angle (S–Gn)	93.76 (SD 4.04)	93.07 (SD 4.17)	0.20
Condylion-gnathion length	94.56 (SD 5.72)	99.40 (SD 5.80)	< 0.01
Condylion-gonion length	37.20 (SD 4.33)	40.15 (SD 3.76)	< 0.01
Gonion-pogonion length	65.55 (SD 4.61)	68.61 (SD 5.14)	< 0.01
Sella-gonion length	58.25 (SD 5.13)	62.04 (SD 4.60)	< 0.01
Condylion-gonion-menton angle	125.59 (SD 6.90)	124.53 (SD 5.86)	0.27
Gonion-menton to FH angle	29.47 (SD 5.21)	28.72 (SD 4.83)	0.28
AOBO difference (mm)	3.77 (SD 2.21)	3.86 (SD 2.45)	0.78
Incisor relationships			
Interincisal angle	123.07 (SD 9.02)	122.21 (SD 8.39)	0.51
UI to FH angle	115.07 (SD 6.57)	114.98 (SD 6.39)	0.93
LI to gonion-menton angle	92.38 (SD 6.53)	94.10 (SD 6.73)	0.04
Facial and integumental profile			
Nasion'-subnasale-pogonion angle	155.00 (SD 5.89)	155.87 (SD 6.00)	0.31
Forehead-nasion'-NT angle	141.97 (SD 12.23)	138.64 (SD 13.11)	0.08
NT \perp nasion–pogonion distance	22.29 (SD 2.75)	23.19 (SD 2.99)	0.01
Nasion'-NT-subnasale angle	119.74 (SD 6.94)	118.94 (SD 6.56)	0.43
NT-subnasale-LS angle	46.66 (SD 7.82)	47.60 (SD 10.37)	0.50
Subnasale'-LS length	17.09 (SD 3.07)	17.11 (SD 3.49)	0.97
LI-pogonion' length	22.80 (SD 4.40)	25.45 (SD 4.37)	< 0.01
$LS \perp nasion' - pogonion' distance$	12.34 (SD 2.41)	12.36 (SD 2.78)	0.96
$L1 \perp$ nasion'-pogonion' distance	10.17 (SD 2.25)	10.47 (SD 2.65)	0.38

All lengths in millimetres, all angles in degrees.

of the two groups showed that this assumption was acceptable (P = 0.32). Hotelling's *T*-squared test for differences in means between the two groups was highly significant, P < 0.001. The cross-validation table of the group classification from the linear discriminant analysis is shown in Table 5.

The overall accuracy of this subset of variables from the cephalometric analysis was 78 per cent and the accuracy in the groups was nearly the same. The CVA biplot of the subset is shown in Figure 3. The adequacy (Gardner, 2002) of the representation of the observed data in the biplot was good since none of the adequacy values was close to zero. The

NANSZ variable was nearly perfectly represented since its adequacy was close to one: BNAZ (0.78), NANSZ (0.91), ANSMeZ (0.24), PNSFHZ (0.29), and SNAPoZ (0.46).

The CVA biplot can be used to project the values of a new child onto the graph for classification (Gardner, 2002). The cephalometric analysis undertaken had a misclassification rate of 1 in 4 children for both the FAS and control children. This overlap was present in all dimensions of the facial and dental structures. This overlap resulted from the fact that the FAS group displayed growth retardation in this setting. The cephalometric analysis can be an aid in the identification of FAS children and probability regions of the biplot can be used to plot a suspected case in the multivariate space. However, the diagnosis will have to be supplemented by other markers, for example, history and clinical features.

Discussion

In spite of the considerable interest, few studies have attempted to quantify the craniofacial features of FAS (Frias et al., 1982; Riekman, 1984, Gir et al., 1989; Jackson and Hussain, 1990). Many reports have suggested that FAS children exhibit midface insufficiency (Jones et al., 1973; Hanson et al., 1976; Clarren and Smith, 1978; Spohr and Steinhausen, 1984; Streissguth et al., 1985). In this study, midface height was significantly different in the FAS children compared with the controls (Table 1). This differs from Gir et al. (1989), who reported that midface height (N-ANS) and the antero-posterior position relative to the cranial base (SNA, PtVert-A, N-FH) and the facial angle (N-A to FH) were virtually identical in the FAS and control subjects. However, the deviant cant of the palatal plane in the FAS children noted in this study concurs with the findings of Gir et al. (1989).

Table 2Linear regressions on age: mean and standard deviation(SD) for the selected measurements.

Variable	Intercept (mean)	Slope (mean)	SD	Intercept (SD)	Slope (SD)
NANS (mm) ANSMe (mm) PNSFH (mm) SNAPo (°)	34.636 52.451 17.081 72.441 75.250	0.883 1.027 0.976 0.680 2.225	3.599 4.383 2.882 4.006	-1.265	0.580

 Table 3
 Group means for a subset of selected measurements.

Midface insufficiency (hypoplasia) is a commonly cited feature of FAS. A below-average corpus length of the mandible contributes to this impression of a small midface. In addition, the soft tissue features, such as the short palpebral fissures and thin upper lip with an indistinct philtrum, further exaggerate the perception of a hypoplastic mandible. In this study, facial depth measurements showed that there were deficits in the upper, middle, and lower face, with the midface being most severely affected (Table 1). This finding partially supports clinical reports of a hypoplastic midface (Korányi et al., 1981; Frias et al., 1982; Vitéz et al., 1984; Clarren et al., 1987; Gir et al., 1989; Jackson and Hussain, 1990, Astley et al., 1992, Astley and Clarren, 1995). However, it is noteworthy that no quantitative documentation of midface hypoplasia is available; indeed, previous cephalometric studies of FAS children found midface heights to be unremarkable and true midface hypoplasia could not be demonstrated (Frias et al., 1982; Gir et al., 1989). Instead, Frias et al. (1982) suggested that an abnormal positioning of the maxilla due to restricted forward growth of the face, which in turn was due to abnormal brain growth and shortening of the anterior cranial base, gave the appearance of midface hypoplasia. In addition, Riekman (1984) previously came to the same conclusion that the apparently flat midface in FAS is not of skeletal origin, but rather due to the absence of a well-defined philtrum, a broad nasal base, and short palpebral fissures. Gir et al. (1989) suggested that over-development of the upper third of the face (frontal bossing) and lower third of the face (elongated mandibular corpus) produced the impression of a small midface. The anthropometric data in the present study showed that there was generalized reduction in all facial depths, and the midface measurements tended to be reduced by a greater amount than those of the upper and lower face.

	Group means						
	BaNZ	NANSZ	ANSMeZ	PNSFHZ	SNAPoZ		
Control $(n = 90)$ Foetal alcohol syndrome $(n = 90)$	-0.00168 -0.79758A	-0.00001 -0.74491	-0.00080 -0.44540	-0.00103 -0.34003	0.00062 -0.03756		

Table 4Covariance matrix of a subset of variables.

	BaNZ	NANSZ	ANSMeZ	PNSFHZ	SNAPoZ
BaNZ NANSZ ANSMeZ PNSFHZ SNAPoZ	0.8424425	0.4388890 0.8915475	0.3777153 0.2403867 0.8332598	0.3590273 0.3635290 0.3582994 0.7786948	-0.283921 -0.596433 -0.296562 -0.033194 1.039911

Table 5 Cross-validation of the group classification from the linear discriminant analysis.

	Control	Foetal alcohol syndrome (FAS)	Percentage error
Control FAS Overall	70 19	20 71	22 21 22



Figure 3 Biplot of a subset of variables with 50 per cent alpha bags. The projected multivariate means of the two groups are represented by the square blocks in the graph. The obvious feature of the graph is the fact that the majority of the foetal alcohol syndrome children were in the negative domain of the variables, indicating a growth restriction compared with the controls. The alpha bags depict the regions containing the central 50 per cent of the distribution of each group as projected in two dimensions (Wurz *et al.*, 2003). The projected mean of each group lay outside the bag of the opposite group for the 50 per cent level. The 22 per cent misclassification rate of the discriminant function was evident from the overlap between the groups. The SNAPoZ axis on the graph corresponded closely (as a visual aid) with the linear discriminant function for the variables MANSZ and BNAZ, these measurements had more variability compared with the other variables. SNAPoZ had the least variability in this respect.

All vertical measurements of the face [anterior total face height (N–Me), upper anterior face height (N–ANS), lower anterior face height (ANS–Me), and mandibular ramus height (Cd–Go)] were statistically significantly different (P < 0.01) for the FAS children. This reduction both in midface and lower face height caused a greater deficit in total face height.

None of the angular measurements, except for the palatal plane to FH angle, revealed any significant differences between the subjects and controls. This appears to indicate that the relationships between the various structures of the face (based on angular measurements) are not affected as much as the distances between certain landmarks, concurring with observations of Frias *et al.* (1982) and Moore *et al.* (2002). Several linear measurements in the FAS children were found to be significantly different from the controls, especially those related to the cranial base, midface, and mandible. Thus from the findings of the present study, it seems that growth retardation is most pronounced in the craniofacial components with a high relative and absolute growth potential in childhood, and concurs with a previous study (Buschang *et al.*, 1983).

Linear measurements of the jaws and skulls of the FAS children in this study were significantly affected, as was also described by Hernandez-Guerrero *et al.* (1998). The underlying mechanisms that give rise to these effects cannot be fully explained by the present research. Pre-natal alcohol exposure is complicated by interactions at the membrane levels of developing cells, neurochemical, and biochemical processes needed for normal growth (Rawat, 1975; Druse and Hofteig, 1977; Ellis *et al.*, 1978; Jacobson *et al.*, 1978; Henderson *et al.*, 1979; Stibler *et al.*, 1983).

It has been demonstrated that FAS children have smaller calvaria (Jones et al., 1973; Clarren and Smith, 1978; Clarren et al., 1978; Streissguth et al., 1978) and microcephaly is regarded as one of the cardinal features of children with FAS (Jones and Smith, 1973; Jones et al., 1973). Although in this study, the angulation of the cranial base was not statistically significantly different, all of the linear measurements were reduced and statistically significantly different for the FAS children (Table 1). The decreased SNa length represents shortening of the anterior cranial base. Analysis of the cranial base linear dimensions (Table 1) revealed particular underdevelopment of the posterior cranial base. The posterior cranial base, which is an important centre for cartilaginous growth, comprises the basicciput and the posterior part of the basisphenoid that are united at the speno-occipital synchondrosis. Posterior cranial base growth is mainly due to growth at the sphenooccipital synchondrosis (Ford, 1958), which is the only cranial base synchondrosis to remain active after 7 years of age, usually remaining active until 16 years of age in males and 13 years of age in females (Konie, 1957).

Sella basion (SBa) and nasion basion (NBa) were statistically significantly reduced in FAS children. This could be explained by a primary defect in the cranial base resulting from premature closure of the spheno-occipital and spheno-ethmoidal synchondrosis (Burdi *et al.*, 1986). Growth at this centre displaces the anterior cranial structures to which the upper facial skeleton is related. Korkhaus (1957) reported that the premature fusion of the cranial base synchondrosis is related to underdevelopment of the nasomaxillary complex and this may therefore account for the nasomaxillary hypoplasia in FAS. The incisor relationships determined primarily by angular measurements related to the positioning of the incisors (Table 1) were unremarkable for both the FAS children and the controls.

Conclusions

This study has shown that measurements related to face height and mandibular size appear to be the most important features when distinguishing FAS children. Overall, the FAS children in the present study presented with a vertically and horizontally underdeveloped maxilla, together with features of a long face syndrome with a large gonial angle and a short ramus in relation to total face height. There was also a tendency for the development of an anterior open bite, which appears to be compensated for by an increase in the anterior alveolar process to bring the incisor teeth into occlusion. The latter adaptation occurred mainly in the mandible.

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