1970

THE APPLICATION OF AN INDEX TO DETERMINE GENETIC AND ENVIRONHENTAL CONTRIBUTIONS TO DENTOFACIAL GROWTH IN TWINS AND SIBLINGS

Richard Charles Hayes

THE APPLICATION OF AN INDEX TO DETERMINE GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO DENTOFACIAL GROWTH IN TWINS AND SIBLINGS

BY

Richard Charles Hayes

B.S., University of South Carolina, 1964
D.D.S., Medical College of Virginia, 1968

Thesis

submitted in partial fulfillment of the requirements for the

Degree of Master of Science in the Department of

Genetics at the Medical College of Virginia

Health Sciences Division

Virginia Commonwealth University

Richmond, Virginia

October, 1970

This thesis by Richard Charles Hayes

is accepted in its present form as satisfying the thesis requirement for the degree of Master of Science

Date:

October 9, 1970

October 9, 1970

10 - 9 - 1970

10 - 9 - 70

10 - 9 - 70

October 9, 1970

Approved:

[redacted]

Advisor, Chairman of Graduate Committee

[redacted]

APPROVED: [redacted]

Dean of the School of Graduate Studies

CURRICULUM VITAE

ACKNOWLEDGEMENT

Deepest gratitude is expressed to my advisor, Dr. J. Ives Townsend for his guidance and suggestions throughout the courses of this investigation. I should like to thank my preliminary advisor, Dr. Roscoe D. Hughes for suggesting that I study facial growth and for his generosity in making available the data for this study.

My appreciation is expressed to Dr. James E. McIver for initially encouraging my interest in a graduate degree program, and for his continued interest and patience.

My sincere thanks are extended to Drs. Walter H. Carter, Jr. and Roger E. Flora for their unselfish guidance, advice, and technical assistance. Without their help this work would not have been possible.

Support for my course of study was received from the National Institute of Dental Research Training Grant Number DE00008-13. This support was made possible through the efforts of Dr. Holmes T. Knighton who holds this grant.

Acknowledgement is made of the invaluable technical assistance of Mr. A.A. Slaymaker. I also wish to thank Dr. Francis M. Bush for his advice in the preparation of this thesis.

CONTENTS

INTRODUCTION 1

MATERIAL AND METHODS 9

RESULTS 19

DISCUSSION AND CONCLUSION 27

SUMMARY 33

LITERATURE CITED 35

INTRODUCTION

The problems of growth changes and development in the dentofacial region are of great interest in the fields of Orthodontics, Genetics, and Anthropology. Investigations have produced some interesting generalizations, for example, that genetic factors have a strong influence on skull form (Johnson, 1940). Developmental processes involve a myriad of complex interactions between genes and environment, that determine rate, magnitude, and direction of growth. Much still remains to be done to resolve and understand these complexities.

The clinician is faced with a strange paradox; for while it is certain that heredity plays an important role in structuring the facial region, there is at present no genetic information that can be used by practitioners to effectively treat dental disorders, such as malocclusions, that are known to have genetic components. It is hoped that developments in genetics may soon rectify this, and perhaps in the not too distant future knowledge of developmental genetics may even be used to prevent the development of such anomalies.

Elaborate appliances have been devised to correct malocclusions, but orthodontists have often questioned whether improvement achieved by mechanical methods might not in some instances have appeared without assistance in the normal course of growth. Knowledge of the direction and rate of normal facial growth is, therefore, required to determine the nature and extent of mechanical therapy, as well as the duration of therapy in such questionable cases.

Much is known about the anatomical growth of the face. The bones of the face and the areas to which they contribute exhibit considerable

variability in their rate, time, and sequence of growth, as well as in their final size. According to Hellman (1935), increases in size of the face are continuous but not uniform. Annual increments in many facial dimensions at early ages may be so small as to be statistically imperceptible (Goldstein, 1936). Growth in three dimensions leads to alteration of the shape of the face (Brodie, 1953; Meredith, 1962; Merow, 1962). Postnatal changes in facial proportion consist of relatively greater increases in height and depth than in width. Growth of different parts in the same plane, or of the same part in different planes, alternates in velocity (Hellman, 1935). The most rapid growth in facial dimensions takes place in the first four or five years of life (Goldstein, 1936; Graber, 1966), then the rate of growth gradually diminishes up to the age of 10 to 11 years, but during puberty, it increases again (Nanda, 1955; Bambha, 1961; Meredith, 1961; Miklashevskaya, 1969).

It is convenient for the orthodontist to classify the stage of maturation on the basis of the onset of the pubertal growth spurt. This spurt occurs in girls earlier than in boys (Tanner, 1962; Bambha and Natta, 1963), and this differential does not appear to vary to a considerable extent between populations (Hiernaux, 1968). Typically, the differential between the sexes with respect to the onset of the pubertal growth spurt is about two years (Burstone, 1963). Nevertheless, at all ages, the head dimensions in boys appear to be greater than those in girls (Goldstein, 1936; Woods, 1950; Meredith, 1959; Tanner, 1962; Wei, 1970). Growth spurts in facial dimensions do not begin for almost a year after the initiation of the generalized height spurt (Krogman, 1958, Bambha, 1961).

Post-adolescent growth decreases rapidly, and the age at which growth is completed is closely correlated with the age at which the pubertal growth spurt is completed (Hiernaux, 1968). From age 14 to 18 years the rate of growth in girls is minimal while it reaches its peak in boys (Miklashevskaya, 1969). At the end of adolescence, boys average 10% greater than girls in most body dimensions including those of the lower face, whereas sex differences in the upper face and the calvaria average 3-5% (Tanner, 1962).

There are several ways in which sex differences in size may arise (Tanner, 1962). They can develop during a particular period of fetal life, or continuously throughout the entire period of growth; they may develop as a result of differential hormone secretion at puberty or as a result of the later occurrence of the male pubertal growth spurt.

In addition to sexual differences in growth rates, there may be racial differences. Matsuda (1963) finds that Negro girls grow more slowly than Caucasian girls in bicristal width, prior to eight years of age. However, the differential in bicristal width growth is not maintained after this age. Studies of racial growth differences are few (Garn, 1961). Although some investigators (Hiernaux, 1968; Miklashevskaya, 1969) suggest that any racial growth differences are probably the result of environmental differences between populations, the relative contributions of the environment and the genes to such differences remains undetermined.

The orthodontist is particularly interested in determining the developmental level of the orthodontic patient and in predicting how much growth will occur during and subsequent to treatment. One statement

that can be made with certainty is that the face of the normal pre-adolescent will change in dimension. Important to the orthodontist are the direction, magnitude, and timing of these changes. Burstone (1963) states that there are two advantages of treating the patient during the pubertal growth spurt. Firstly, growth increments are at their maximum; therefore, the amount of tooth movement required for correction of both a distoclusion and deep overbite is minimized, if the direction of growth is favorable. Secondly, tooth movement may be facilitated by the endocrine interrelationships associated with this period. A reliable pre-treatment prediction of the amount and timing of growth is not presently available to the dental profession (Horowitz and Hixon, 1966; Ackerman and Proffit, 1970).

According to Graber (1966) the concept that craniofacial skeletal growth is dependent upon musculature development has recently come into vogue, particularly with reference to the functional matrix theory of Moss (Moss, 1960; Moss and Salentijn, 1969). This theory views craniofacial skeletal growth as a process primarily controlled by soft tissues, with hard tissues making adjustive responses, serving protective functions, and providing form. Other researchers, however, contend that hard tissues are the source of the primary growth initiatives (Weinmann and Sicher, 1955). Thus, the intricacies of this most basic mechanism of the growth process are still uncertain.

The genetic aspects of growth and development have received considerable attention in recent years. In genetic studies of man, the closest and most efficient approach to evaluating the heredity-environment problem, particularly with respect to multifactorial traits, can theoretically

be made by the study of twins (Waardenburg, 1957; Osborne and DeGeorge, 1959; Kempthorne and Osborne, 1961; Shapiro, 1969; Riquelme and Green, 1970). The twin method, as originally conceived by Galton, and as presently applied, is based on the existence of two types of twins: monovular or monozygotic twins (MZ) resulting from the division of a single fertilized ovum, and diovular or dizygotic twins (DZ) resulting from the independent fertilization of two distinct ova.

Twin studies provide an analytic method particularly well suited to the investigation of a variety of dental problems, provided that the following criteria are met: acceptable diagnostic methods for zygosity; adequate sample classification with respect to existing dental pathology, methods of selection, sex, race and socioeconomic background; adequate sample size; and precise measurements or descriptions of the traits under consideration (Osborne, 1962). Other sources of potential bias inherent in twin studies (Osborne and DeGeorge, 1959; Scarr, 1968; Shapiro, 1969) include: The possibility of a third type of twinning, derived from either fertilization by different sperm cells after division of the ovum or from fertilization of the second polar body; the assumption that the magnitude of environmental differences between MZ and DZ twins are equivalent; and the possibility of constitutional inferiority of MZ twins. Nevertheless, the twin method is the only method available in human genetics for attempting to answer questions concerning the relative role of genetic and environmental factors in contributing to the development of complex traits (Allen, 1965).

Growth of the human face is studied by several methods. Most studies of facial growth in humans utilize superimposition of lateral

cephalometric roentgenograms. Different reference points are sometimes used in the various studies, partly because there is no truly stable landmark in the human head (Nanda, 1955; Coben, 1961). The implant method, as described by Björk (1955), is an attempt to establish stable radiographic landmarks for cephalometry. Facial growth may also be studied by the experimental method on non-human primates and mammals, or by measurements on human skulls or the human head, so-called anthropometric measurement (Krogman, 1958).

Several studies utilizing both anthropometric and cephalometric methods suggest the probability of genetic influences upon craniofacial morphology, although the mechanism and extent of this influence is inconclusive. Hughes (1942) uses anthropometric measurements in comparing craniofacial similarities in families. He concludes that hereditary factors can be divided into two groups; those that display familial patterns throughout the growth process and those that fail to give any hereditary evidence until puberty.

Wylie (1944) uses lateral cephalometric roentgenograms to study similarities of angular relationships of cranial and facial points, between family members. His study includes 13 pairs of twins, with no attempt at zygosity determination. Wylie concludes that although twins may show considerable external facial similarity, they may show considerable dissimilarity in craniofacial pattern. Lundstrom (1955), applying the same technique, calculates a number of craniofacial diameters and angles on a group of 100 pairs of twins, 50 MZ and 50 DZ (like sex), mostly between 12 and 15 years of age. He concludes that "genetic factors have a greater influence than non-genetic factors for most of the

characteristics studied." His method of zygosity determination is largely based on external appearance, a method which is open to question.

Horowitz, Osborne, and DeGeorge (1960) report a study of genetic influences on variation in several cranioracial dimensions in 56 pairs of like-sexed adult twins (35 MZ and 21 DZ pairs). The anterior nasal spine is considered to separate the face into upper and lower components. These investigators use linear cephalometric measurements to conclude that, whereas the upper face exhibits little genetic variation, the lower face exhibits a significant degree of genetic variation, particularly in mandibular body length.

In an attempt to improve upon the technique utilizing traditional cephalometric measurements, Kraus, Wise, and Frei (1959) use lateral and antero-posterior roentgenographic cephalograms of six sets of triplets to determine heritability in the craniofacial complex. Among these six sets there are monozygotic triplets, as well as some mixed sets that include a pair of monozygotic twins, and other mixed sets that are trizygotic. The complex is divided into 17 continuous osseous contours, and tested for zygosity by superimposition of these 17 "traits". Within the monozygotic triplet set and monozygotic pairs, sibs exhibit a much higher degree of similarity of contours than do sibs within the dizygotic triplet sets. Kraus et al. (1959) contend "that the simplest type of trait, morphologic aspects of a single bone, is the best indicator of the control of hereditary factors in the craniofacial complex." Their data are not analyzed statistically because their method of superimposition is dependent upon the observer's interpretation of the degree of conformity and, therefore, subjective. Furthermore, they assume that

entire bones are concordant because a single contour conforms.

More rigorous analytical techniques have recently been applied to the study of facial growth. These include factor analyses (Landauer, 1962; Brown, Barrett, and Darroch, 1965), multiple regression analyses (Singh, Savara, and Miller, 1967; Hunter, Balbach, and Lamphiear, 1970), harmonic analyses (Lu, 1965), and principal component analyses (Heflin, 1970). Principal component analysis (Anderson, 1958) appears to be particularly suitable to the data of the present study, and is therefore used and modified by the formulation of a single composite index of growth, based on a variety of measurements of the individual, for purposes of genetic analysis and comparison amongst individuals.

The purposes of the present study are multifold: to determine the relative contributions of eight selected facial variables to the overall facial variation between individuals during a five year period of growth; to devise a method of reducing a large volume of data for an individual into a single component (growth index) indicative of overall facial growth for that individual; to evaluate the need for multiple classification systems (age, race, and sex) in the study of facial growth by means of this growth index; to evaluate the relative influence of genetic and environmental factors on the growth rates of the selected group of facial dimensions.

MATERIAL AND METHODS

The data available for analysis were collected during the interval of 1957-1963 in the Department of Biology and Genetics, Medical College of Virginia. These data consisted of measurements made from tracings of lateral cephalometric roentgenograms and from plaster dental casts, and directly from the subjects.

Families for the study were selected as follows: the family must have had at least one pair of like-sexed twins between the ages of five and nine, the twins must not have exhibited any visible anatomic defects, and the siblings of the twins must have been available for study. Enrollment in the study was also based on willingness of the families to participate, residence in or near Richmond, Virginia, and probable continued residence in the area.

Ninety-five children were studied, each for four consecutive years. They consisted of male and female MZ and like-sexed DZ twins and their siblings of both sexes. Caucasians and American Negroes were approximately equally represented among the subjects. The Caucasian children were largely of western European lineage. The distribution of the subjects by race, sex, and zygosity are presented in Table 1, and by age in Table 2.

The technique for determination of zygosity was that described by Smith and Penrose (1955). In the present study a diagnosis of monozygosity was based on a monovular probability of 0.90 or higher, because of the limited number of twins available. Any twin pair differing in any of the blood group systems tested (ABO, MN, Rhesus, Kell, Lewis, Duffy) was automatically classified as dizygotic.

Table 1

Distribution of 95 subjects by race, sex, and zygosity.

Race	Sex	Twin pairs		Singles	Total individuals
		MZ	DZ		
Caucasian	Male	2	7	3	21
	Female	5	4	8	26
Negro	Male	3	4	10	24
	Female	1	7	8	24
Total individuals		22	44	29	95

Table 2

Age (in Months) of 95 Children at Entrance to Study

Zygosity	Race	Sex	Age at entrance	
			Mean	Range
MZ twins	Caucasian	Males	79.0	66 - 92
		Females	82.6	62 - 114
	Negro	Males	81.6	70 - 96
		Females	95.0	95
DZ twins	Caucasian	Males	74.6	57 - 96
		Females	90.5	83 - 97
	Negro	Males	90.0	75 - 106
		Females	89.4	77 - 105
Singles	Caucasian	Males	105.0	91 - 113
		Females	111.3	62 - 147
	Negro	Males	105.3	66 - 135
		Females	117.5	85 - 145
All types			92.2	57 - 147

Lateral cephalometric roentgenograms, impressions for dental casts, and direct facial measurements, were made at approximately yearly intervals for each subject. Roentgenograms of the head in norma lateralis were obtained with each subject fixed in a Margolis cephalostat (Margolis, 1940). Tracings of the cephalometric roentgenograms were made on tracolene paper with the aid of an illuminated tracing table. Measurements of casts and of cephalometric tracings were made to the nearest 0.1 mm with the use of vernier calipers. Direct facial measurements were made to the nearest millimeter with anthropometric calipers. All measurements were made by two separate observers, working independently, and each repeated his measurements a second time. The mean of the four measurements was used.

The present study was restricted to six cephalometric variables, Sella-Nasion, Nasion-A Point, Sella-A Point, B Point-Gnathion, B Point-Gonion, and Gnathion-Gonion; and two anthropometric variables, bizygomatic width and bigonial width. The cephalometric landmarks are shown in Figure 1. The remaining variables, available but not used in this analysis were less objective for the following reasons. For the cephalograms, consistancy of vertical dimension was difficult to ascertain, and positioning of the ear rods varied for the variables that included Porion. Landmarks were not standardized for measurements of the dental casts. The remaining direct facial variables were difficult to obtain with accuracy.

Definitions for the cephalometric landmarks used in this study followed those of Graber (1966).

A Point: The deepest midline point on the premaxilla between anterior nasal spine and prosthion.

B Point: The most posterior point in the concavity between

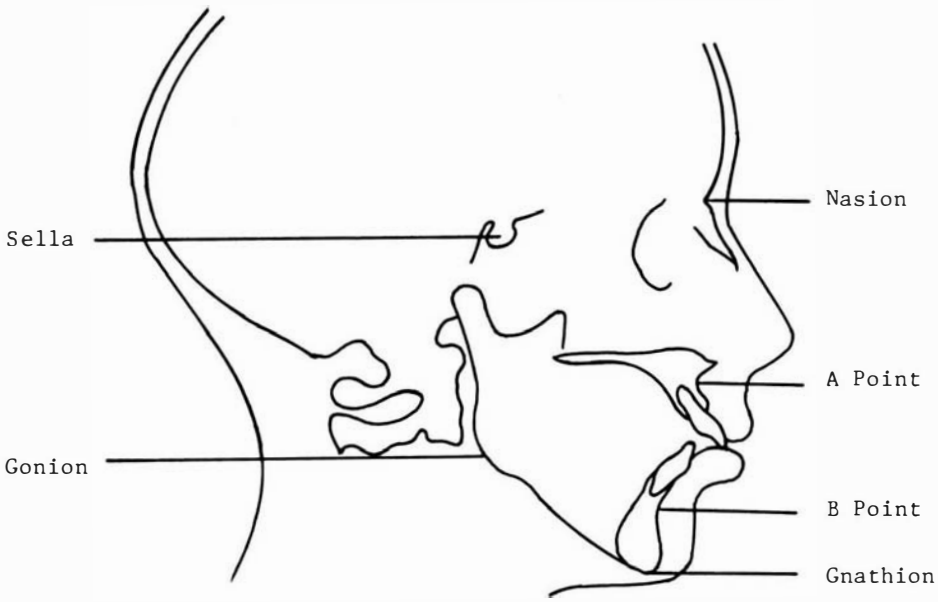

Figure 1: Cephalometric landmarks used in study

infradentale and pogonion.

Gnathion: The most inferior point in the contour of the chin.

Gonion: The point that on the jaw angle was the most inferiorly, posteriorly, and outwardly directed.

Nasion: The intersection of the internasal suture with the nasofrontal suture in the midsagittal plane.

Sella: The midpoint of sella turcica, determined by inspection.

Only two anthropometric measurements were used. Bizygomatic width was defined as the distance between the most lateral aspects of the right and left zygomatic arches, and bigonial width was defined as the widest distance between the right and left gonions.

In the analyses, measurements of the eight variables for each individual, in each of five consecutive years, were transformed to natural logarithms, in order to conform to the allometric law (Huxley, 1932; Laird, Barton, and Tyler, 1968). A linear model, $E \ln y = \alpha + \beta t$, was fit to the transformed data, where $E \ln y$ represents the expected value of the natural logarithm of the observed value y, and:

$\alpha = E \ln y$ when $t=0$,

$\beta = \frac{dE \ln y}{dt}$ = growth rate, and

t = age in months.

Both α and β were estimated by the least squares method (Dixon and Massey, 1957). Since eight variables were used, eight estimated growth rates were obtained for each individual. The method of principal

components was then applied to obtain a single growth index for each individual. The 8 X 8 correlation matrix for these estimated growth rates was determined and its largest eigenvalue and associated eigenvector were obtained. The eigenvector contained eight elements which were the weights assigned to the eight variables. The elements, γ_i, of this eigenvector for twins were used to form a growth index for each individual (twins and siblings) as follows:

$$\text{Growth Index} = \gamma_1\hat{\beta}_1 + \gamma_2\hat{\beta}_2 + \ldots\ldots\gamma_8\hat{\beta}_8$$

The growth index represented that linear combination of growth rates having maximum variation among individuals in the study.

Means and variances of the growth index were calculated for, and tested between, races, sexes and different age groups, within twin types. F-tests were used to test equality of variances prior to testing equality of means. Where variances were found to be equal, equality of means was tested using Student's t-test. Where variances were found to be unequal, equality of means was tested using approximate t-tests, as described by Dixon and Massey (1957).

Genetic analyses were based on the methods of Osborne and DeGeorge (1959), as modified by Shapiro (1969). Since MZ twins were genotypically identical, variation between the two members of a twin pair was considered as the result of variation due to environmental differences [$V(E_T)$] and variation due to measurement error [$V(ME)$] . Variation between the two members of a dizygotic twin pair was regarded as the result of $V(E_T)$ and $V(ME)$, as well as variation due to genetic differences [$V(G)$]. It was assumed that the average environmental differences between cotwins were

the same for DZ twins and for MZ twins. Variability between siblings within the same family [V(Sib)] was the result of V(G) and V(ME), as well as variation due to environmental differences within families [$V(E_S)$]. The sources of variability between individuals were summarized as follows:

$$V(MZ) = V(E_T) + V(ME)$$

$$V(DZ) = V(E_T) + V(ME) + V(G)$$

$$V(Sib) = V(E_S) + V(ME) + V(G)$$

Thus, it was possible to find the relative contributions of genetic and environmental factors to the growth index by estimating V(MZ), V(DZ), V(Sib), and V(ME), and solving for $V(E_T)$, V(G), and $V(E_S)$, respectively.

The average variability of the growth index between MZ twins [V(MZ)] and that between DZ twins [V(DZ)] was obtained by the method of Osborne and DeGeorge (1959).

Average variability of the growth index between sibships was estimated by obtaining variability within sibships of two or more siblings, and pooling this variability for all sibships of two or more siblings such that:

$$V(Sib) = \frac{\underset{\text{families}}{\overset{\text{over}}{\Sigma}} \left(\underset{\text{families}}{\overset{\text{within}}{\Sigma}} x^2 - \frac{(\Sigma x)^2}{n} \right)}{\text{degrees of freedom within families}}$$

where X = the growth index for an individual, n = the number of individuals in a family, and d.f. = $(n_1-1) + (n_2-1) + \ldots . (n_k-1)$, where k = the number of families.

Ten individuals, for whom four replicate measurements were available for each variable, were used to estimate the variance associated with measurement error, V(ME). A growth index was calculated four times for

each individual and a within variance was obtained. The within variances were pooled for the 10 individuals, resulting in an estimated value of the variance associated with measurement error.

The population of interfamilial variance for the growth index (VIF) was estimated by obtaining the average variability between sibships of two or more siblings such that:

$$V(IF) = \frac{\sum_{\text{between families}} \left(\frac{T_i.^2}{n_i} \right) - \frac{T..^2}{N}}{\text{degrees of freedom between families}}$$

where $T_i.$ = growth index total for the ith family, n_i = number of siblings in the ith family, $T..$ = overall growth index total, N = total number of individuals, and d.f. = number of families minus 1.

Intrafamilial environmental factors were represented by the difference between V(MZ) and V(ME). If the difference between V(MZ) and V(ME) was statistically significant, then environmental factors were considered detectable.

The difference in average variability between DZ twins, V(DZ), and between MZ twins, V(MZ), was used as an estimate of the intrafamilial genetic portion of the total variation. If V(DZ) was significantly greater than V(MZ), then a genetic source of variation was considered detectable.

The difference between total population variability, V(IF), and that between siblings, V(Sib), served as an estimate of extrafamilial (genetic and environmental) variability since,

$$V(Sib) = V(E_S) + V(G) + V(ME), \text{ and}$$

$$V(IF) = V(E_S) + V(G) + V(ME) + V(P), \text{ where}$$

V(P) = extrafamilial variability.

If the population or interpair variance, V(IF), was significantly greater than V(Sib), then extrafamilial factors were considered detectable.

It was possible to test each of the above variance comparisons by the use of F ratios.

RESULTS

The relative weights of the eight variables used for computation of the growth index, and the contribution of the eight variables to the variation between individuals, are shown in Table 3. The major part of the total variation between individuals is accounted for by four variables; Sella-Nasion, Sella-A Point, B Point-Gonion, and Gnathion-Gonion, contributing 21.85%, 21.80%, 20.56%, and 18.14%, respectively. Two variables, Nasion-A Point and B Point-Gnathion, contribute somewhat less (9.42% and 7.46%, respectively), and approximately equally to the variation between individuals. The remaining variation between individuals (less than 1.0%) is the result of both bigonial width, contributing 0.68%, and bizygomatic width, contributing 0.08%. The negative weight obtained for bigonial width can essentially be considered as zero.

Means and variances of the growth index, grouped according to twin type, sex, and age at entrance into the study, are summarized in Table 4. Tests of the growth index means, within twin types (Table 5), reveal no significant differences ($P > 0.05$) between males and females entering the study during the same age interval (lines 1 and 2), or between members of the same sex entering the study during the two age intervals noted (lines 3 and 4). Thus, no pubertal growth spurt or sexual difference is detectable for the variables represented by the growth index.

Table 6 summarizes means and variances of the growth index grouped according to twin type, race, and sex. Tests of the growth index means, within twin types (Table 7), reveal no significant differences ($P > 0.05$) between males of both races, between females of both races, or between

Table 3

Relative weights of the eight variables used for computation of the growth index, and their contribution to the variation between individuals.

Variable	Relative weight	Contribution to the variation between individuals
Cephalometric		
Sella-Nasion	0.467420	21.85%
Sella-A Point	0.466900	21.80%
Nasion-A Point	0.306860	9.42%
B Point-Gnathion	0.273190	7.46%
B Point-Gonion	0.453470	20.56%
Gnathion-Gonion	0.425920	18.14%
Anthropometric		
Bigonial width	-0.082685	0.68%
Bizygomatic width	0.028748	0.08%

Table 4

Means and variances of the growth index according to twin type, sex, and age at entrance into study

Twin type	Sex	Age at entrance					
		57 - 84 months			85 - 114 months		
		number of individuals	mean	variance	number of individuals	mean	variance
MZ	Male	6	0.65876	0.021302	4	0.59099	0.087050
	Female	6	0.55238	0.003640	6	0.59572	0.249010
DZ	Male	14	0.57484	0.017930	8	0.59874	0.029490
	Female	8	0.57077	0.024540	14	0.57260	0.005750

Table 5

Comparisons of mean growth indices from Table 4.*

Sex	Age in months	Twin type			
		MZ		DZ	
		d.f.	t-value	d.f.	t-value
males vs. females	57 - 84	7	1.64945	20	0.06380
males vs. females	85 - 114	8	-0.00535	9	0.40527
males	57 - 84 vs. 85 - 114	8	0.49098	20	-0.36455
females	57 - 84 vs. 85 - 114	5	-0.21146	8	-0.03102

* All tests not significant ($P > 0.05$)

Table 6

Means and variances of the growth index according to twin type, race, and sex.

Twin type	Race	Sex	Number of individuals	Mean	Variance
MZ	Caucasian	Male	4	0.64689	0.01629
		Female	10	0.58606	0.00958
	Negro	Male	6	0.62149	0.01568
		Female	2	0.51397	0.00060
DZ	Caucasian	Male	14	0.54139	0.01763
		Female	8	0.59203	0.23061
	Negro	Male	8	0.65727	0.02069
		Female	14	0.56045	0.01668

Table 7

Comparisons of mean growth indices from Table 6.*

Twin type		Caucasian males		Negro females	
		d.f.	t-value	d.f.	t-value
MZ	Negro males	8	0.30292	6	1.15142
	Caucasian females	12	0.93412	10	0.07254
DZ	Negro males	20	-1.90937	20	1.62494
	Caucasian females	8	-0.29202	8	-0.37494

* All tests not significant ($P > 0.05$).

males and females of the same race. This suggests that there is no racial difference in growth rate detectable for the variables represented by the growth index and confirms that there are none between the sexes even when race is considered.

Because no significant differences in the growth index are apparent between age groups, sexes, or races, individuals in these categories are pooled within each zygotic class for genetic analysis. The results of the genetic analysis are summarized in Table 8, wherein estimates of the contributions of five sources (ME, MZ, DZ, IF, and Sib) to variation in the growth index are given.

The very highly significant difference (a) between V(MZ) and V(ME) ($P < 0.0005$) indicates that the growth index is sufficiently sensitive to detect environmentally caused differences between MZ twins; (b) between V(DZ) and V(MZ) ($P < 0.005$) indicates a relatively large genetic component of variability in a population for the traits represented by the growth index; and (c) between V(IF) and V(Sib) ($P << 0.0005$) indicates that extrafamilial factors are detectable.

Table 8

Variances of mean growth indices.

Source of variation	Variance	d.f.	F-value
Measurement error	0.0002809	30	
MZ/ME			6.88857***
MZ twins	0.0019350	11	
DZ/MZ			5.23720***
DZ twins	0.0101340	22	
Interfamilial	0.8748540	4	
IF/Sib			34.84185***
Siblings	0.0251090	8	

*** ($P < 0.005$)

DISCUSSION AND CONCLUSIONS

The finding in the present study that the eight different facial variables make different contributions to the variation between individuals (Table 3) is in conformity with the findings of Krogman (1958). The relative contribution of each variable to the variation between individuals may be arranged in order of decreasing magnitude as follows: (Sella-Nasion, Sella-A Point, B Point-Gonion, Gnathion-Gonion) > (Nasion-A Point, B Point-Gnathion) > (bigonial width, bizygomatic width). Although two of these variables, Sella-A Point and Gnathion-Gonion, have height components, they are primarily depth variables. Thus, the relative magnitudes of contribution are: depth variables > height variables > width variables. Since Krogman (1958) finds that the amount of facial growth achieved postnatally is 65-70% depth, 55-60% height, and 40-45% width, it, therefore, appears that the greater the amount of growth to be achieved postnatally, the greater the chance for variation. It is no accident that most "growth failures" in the face during the childhood years are manifested in depth dimensions, for example, mandible to maxilla (Krogman, 1958).

The lack of any evidence of a pubertal growth spurt in the present study may at first appear surprising; however, there is a wide assortment of factors that may tend to conceal any underlying pubertal growth spurts in the analysis. The experimental design shows no particular sensitivity for detecting a pubertal growth spurt because the groups compared are made up of individuals entering or leaving the study at different ages. Pooling of measurements for individuals of such disparate ages may well

conceal any age-dependent growth spurts. Variation in the pubertal growth spurt itself may make it difficult to detect in a composite index. Even though pubertal growth spurts are known to occur for some variables, such as bizygomatic width (Henriques, 1953; Miklashevskaya, 1969), pubertal growth spurts sometimes do not occur for other variables, such as bigonial width (Newman and Meredith, 1956). Traits that are known to undergo a pubertal growth spurt in some individuals, for example, mandibular depth, do not undergo a spurt in other individuals (Meredith, 1961). Earlier childhood growth spurts (ages six to nine) may also take place in some variables, such as Sella-Nasion and Sella-A Point, although not as regularly as the pubertal growth spurt (Bambha, 1961). Should such an early childhood growth spurt occur in a trait, it would tend to mask any later (pubertal) growth spurt in the same trait.

The lack of any detectable differences in growth rates between the sexes may be the result of several factors. The same factors that may obscure differences in growth between different age groups may also obscure growth differences between sexes, particularly individuals entering or leaving the study at different ages. Since sex differences in size of head and face appear during fetal development and boys are larger than girls at birth (Tanner, 1962; Miklashevakaya, 1969), the growth rates of the two sexes may be quite similar, with the exception of a temporary readjustment at puberty.

The lack of any detectable differences in the two races in this study is not surprising in view of several factors in addition to those that tend to obscure any differences between groups of different age or different sex. One reason that no differences between races are found

is that growth rates may not differ between racial groups with similar environments (Hiernaux, 1968; Miklashevskaya, 1969), for example, Greulich (1957) finds that American-born children of Japanese origin are similar to American Caucasians in rates of ossification, rather than to native Japanese children. Another reason is that genetic differences between American Caucasians and American Negroes are reduced because American Negro populations are known to include quite a large infusion of Caucasian genes, as much as 30.56% (see review in Glass, 1954).

Because of these various factors that may obscure differences between groups, particularly because of the different ages of the individuals when entering or leaving the study, the usefulness of multiple classification systems (age, sex, and race) in the study of facial growth by means of the growth index cannot be determined from the present study. However, the application of the growth index in the present study does permit the estimation of the relative contributions of the genotype, environment, and measurement error to differences in facial growth rates between cotwins, their sibs, and unrelated individuals.

The very highly significant V(MZ)/V(ME) ratio (Table 8) shows that the growth index is sufficiently sensitive to detect environmentally caused differences between MZ twin pairs. Since V(ME) is quite small, it is probable that extragenic factors of even smaller magnitude would still be detectable. This finding suggests that an investigation of specific environmental agents affecting the growth rates of the variables represented by the growth index might be fruitful.

The very highly significant V(DZ)/V(MZ) ratio (Table 8) indicates a

relatively large genetic component of variability in a population for the growth rates of the variables represented by the growth index. It would be highly desirable to resolve what genetic factors are involved and how they act to determine facial growth, but any one of the eight variables in the present study is likely to be determined by a number of genes interacting with the environment. While considerable advances have been made in genetic analyses of quantitative traits in humans (see Falconer, 1960), the genetics of human facial growth is more complicated than anything yet understood.

It is expected that the variance for the growth index among unrelated individuals would be greater than the variance between siblings. The very highly significant V(IF)/V(Sib) ratio (Table 8) indicates that both genetic and environmental factors in different families account for the variation in growth among families to a much greater extent than comparable factors within families. Unfortunately, factors accounting for variability among families cannot, at present, be resolved (Shapiro, 1969).

The sources of variability (Table 9) for the growth index for twins, have the following relative magnitudes: extrafamilial > genetic > environmental > error. For siblings the relative magnitudes of the sources of variability are: extrafamilial > environmental > genetic > error. Thus, environmental factors are relatively more important between siblings than between twins. This is to be expected since a number of environmental factors including maternal pre-natal nutrition, post-natal nutrition, maternal illnesses, childhood illnesses, and socio-economic conditions, are expected to vary more between children born at different times than between children born at the same time to a couple.

Table 9

Relative magnitude of components of variance in the growth index.

Source of variation	Estimated	Estimate
Extrafamilial	V(IF) - V(Sib)	0.84975
Genetic	V(DZ) - V(MZ)	0.00819
Environmental (twins)	V(MZ) - V(ME)	0.00137
Environmental (sibs)	V(Sib) - V(G) - V(ME)	0.01663
Error	V(ME)	0.00028

Heredity is a strong contributor to variability among individuals in so far as growth is concerned. Thus, members of a family who, of course, share a common genetic background, are more likely to grow at quite similar rates. Important to the orthodontist is the even larger environmental component of variability in sibs. If growth were totally dependent on genotype, then mechanical attempts to re-direct facial growth (see review in Graber, 1969) would have little or no success. But it is the existence of the large environmental component of variability that leads to success in the use of mechanical devices by the orthodontist to re-direct facial growth.

Since the results obtained with the growth index depend on the variables chosen for study, different conclusions would doubtlessly be obtained from similar analyses employing partially or totally different variables. The number of variables that could be studied in this type of approach would be limited only by time and economics. In any future studies of this type particular care should be given to the variables chosen, as Hanna, Turner, and Hughes (1963) have cautioned, in order to insure that they are relatively independent, because two or more variables that are highly correlated with each other provide little more information than any one alone.

SUMMARY

The method of principal components may be used to reduce a large quantity of data for an individual into a single statistic, a growth index, indicative of overall facial growth, and to make a determination of the relative contribution of each variable, as well as the genotype and the environment, to the variation between individuals. When this method is applied to four consecutive years of cephalometric and anthropometric data from each of 95 children, consisting of Caucasian and Negro monozygotic twins, like-sexed dizygotic twins, and their siblings of both sexes, it discloses that:

1. The relative contributions of the variables studied to the variation among individuals are as follows: facial depth variables > facial height variables > facial width variables.
2. No differences in growth rates, as represented by the growth index, are apparent between males and females entering the study during the same age interval, between members of the same sex entering the study during two age intervals, between sexes including all age intervals, and between races. Failure of the investigation to disclose any such differences may result from the design of the experiments.
3. A very highly significant environmental component of variability for the growth index is found in the population studied, which suggests the need for further studies of specific environmental agents affecting the

growth rates of the variables involved.

4. A very highly significant genetic component of variability for the growth index also is found, however, the complicated polygenic nature of facial inheritance renders analysis of the specific genetic factors involved quite difficult, because of the present limited knowledge of the inheritance of quantitative traits.

5. A very highly significant extrafamilial (genetic and environmental) component of variability for the growth index also is found.

6. The sources of variability for the growth index for twins, have the following relative magnitudes: extrafamilial > genetic > environmental > error. For siblings the relative magnitudes of the sources of variability are: extrafamilial > environmental > genetic > error. Thus, as expected, environmental factors are relatively more important between siblings than between twins.

LITERATURE CITED

Ackerman, J.L., and W.R. Proffit. 1970. Treatment response as an aid in diagnosis and treatment planning. Amer. J. Orthodont. 57: 490-496.

Allen, G. 1965. Twin research: problems and prospects. Prog. Med. Genet. 4: 242-269.

Anderson, T.W. 1958. Introduction to multivariate statistical analysis. John Wiley and Sons, Inc., New York. 374 p.

Bambha, J.K. 1961. Longitudinal cephalometric roentgenographic study of face and cranium in relation to body height. J. Amer. Dent. Assoc. 63: 776-799.

Bambha, J.K. and Pearl Van Natta. 1963. Longitudinal study of facial growth in relation to skeletal maturation during adolescence. Amer. J. Orthodont. 49: 481-493.

Björk, A. 1955. Facial growth in man, studied with the aid of metallic implants. Acta odont. scand. 13: 9-34.

Brodie, A.G. 1953. Late growth changes in the human face. Angle Orthodont. 23: 146-157.

Brown, T., M.J. Barrett, and J.N. Darroch. 1965. Craniofacial factors in two ethnic groups. Growth 29: 109-123.

Burstone, C.J. 1963. Process of maturation and growth prediction. Amer. J. Orthodont. 49: 907-919.

Coben, S.E. 1961. Growth concepts. Angle Orthodont. 31: 194-201.

Dixon, W.L., and F.J. Massey. 1957. Introduction to statistical analysis. 2nd Ed. McGraw-Hill Book Co., Inc. New York. 488 p.

Falconer, D.S. 1960. Introduction to quantitative genetics. The Ronald Press Co., New York. 365 p.

Garn, S.M. 1961. Human races. Charles C. Thomas, Springfield, Illinois. 137 p.

Glass, B. 1954. Genetic changes in human populations, especially those due to gene flow and genetic drift. Advances Genet. 6: 95-139.

Goldstein, M.S. 1936. Changes in dimensions and form of the face and head with age. Amer. J. Phys. Anthrop. 22: 37-89.

Graber, T.M. 1966. Orthodontic principles and practice. 2nd Ed. W.B. Saunders Co., Philadelphia. 922 p.

Graber, T.M. 1969. Dentofacial orthopedics. p. 919-988. In T.M. Graber, Current orthodontic concepts and techniques, W.B. Saunders Co., Philadelphia.

Greulich, W.W. 1957. A comparison of the physical growth and development of American-born and native Japanese children. Amer. J. Phys. Anthrop. 15: 489-515.

Hanna, B.L., M.E. Turner, and R.D. Hughes. 1963. Family studies of the facial complex. J. Dent. Research. 42: 1322-1329.

Heflin, B.M. 1970. A three-dimensional cephalometric study of the influence of the midpalatal suture on the bones of the face. (Abstr.) Amer. J. Orthodont. 57: 194-195.

Hellman, M. 1935. The face in its developmental career. Dent. Cosmos 77: 685-699, 777-787.

Henriques, A.C. 1953. The growth of the palate and the growth of the face during the period of the changing dentition. Amer. J. Orthodont. 39: 836-858.

Hiernaux, J. 1968. Ethnic differences in growth and development. Eugen. Quart. 15: 12-21.

Horowitz, S.L., and E.H. Hixon. 1966. The nature of orthodontic diagnosis. The C.V. Mosby Co., St. Louis. 393 p.

Horowitz, S.L., R.H. Osborne, and F.V. DeGeorge. 1960. A cephalometric study of craniofacial variations in adult twins. Angle Orthodont. 30: 1-5.

Hughes, B.O. 1942. Heredity as a factor in cranial and facial development. Am. J. Orthodont. Oral Surg. 28: 357-360.

Hunter, W.S., D.R. Balbach, and D.E. Lamphiear. 1970. The heritability of attained growth in the human face. Amer. J. Orthodont. 58: 128-134.

Huxley, J.S. 1932. Problems of relative growth. The Dial Press, New York. 276 p.

Johnson, A.L. 1940. The constitutional factor in skull form and dental occlusion. Am. J. Orthodont, Oral Surg. 26: 627-663.

Kempthorne, O., and R.H. Osborne. 1961. The interpretation of twin data. Amer. J. Hum. Genet. 13: 320-339.

Kraus, B.S., W.J. Wise, and R.H. Frei. 1959. Heredity and the craniofacial complex. Amer. J. Orthodont. 45: 172-217.

Krogman, W.M. 1958. Problems in growth and development of interest to the dentist. Dent. Clin. N. Amer. 2: 497-514.

Laird, Anna Kane, A.D. Barton, and Sylvanus A. Tyler. 1968. Growth and time: an interpretation of allometry. Growth 32: 347-354.

Landauer, Cynthia A. 1962. A factor analysis of the facial skeleton. Hum. Biol. 34: 239-253.

Lu, K.H. 1965. Harmonic analysis of the human face. Biometrics 21: 491-505.

Lundström. A. 1955. The significance of genetic and nongenetic factors in the profile of the facial skeleton. Amer. J. Orthodont. 41: 910-916.

Margolis, H.I. 1940. Standardized x-ray cephalometrics. Am. J. Orthod. Oral Surg. 26: 725-740.

Matsuda, R. 1963. Relative growth of Negro and white children in Philadelphia. Growth 27: 271-284.

Meredith, H.V. 1959. A longitudinal study of growth in face depth during childhood. Amer. J. Phys. Anthrop. 17: 125-135.

Meredith, H.V. 1961. Study of change in a mandibular dimension during childhood and adolescence. Growth 25: 229-242.

Meredith, H.V. 1962. Childhood interrelations of anatomic growth rates. Growth 26: 23-40.

Merow, W.W. 1962. A cephalometrical statistical appraisal of dentofacial growth. Angle Orthodont. 32: 205-213.

Miklashevskaya, N.N. 1969. Sex differences in growth of the head and face in children and adolescence. Hum. Biol. 41: 250-262.

Moss, M.L. 1960. A functional analysis of human mandibular growth. J. Prosth. Dent. 10: 1149-1160.

Moss, M.L. and L. Salentijn. 1969. The primary role of functional matrices in facial growth. Amer. J. Orthodont. 55: 568-577.

Nanda, R.S. 1955. The rates of growth of several facial components measured from serial cephalometric roentgenograms. Amer. J.Orthodont. 41: 658-673.

Newman, K.J., and H.V. Meredith. 1956. Individual growth in skeletal bigonial diameter during the childhood period from 5 to 11 years of age. Amer. J. Anat. 99: 157-187.

Osborne, R.H. 1962. Application of twin studies to dental research, p. 79-91. In C.J. Witkop, Genetics and dental health, McGraw-Hill Book Co., Inc., New York.

Osborne, R.H., and F.V. DeGeorge. 1959. Genetic basis of morphological variation. Harvard Univ. Press, Cambridge, Massachusetts. 204 p.

Riquelme, A., and L.J. Green. 1970. Palatal width, height, and length in human twins. Angle Orthodont. 40: 71-79.

Scarr, Sandra. 1968. Environmental bias in twin studies. Eugen. Quart. 15: 34-40.

Shapiro, B.L. 1969. A twin study of palatal dimensions partitioning genetic and environmental contributions to variability. Angle Orthodont. 39: 139-151.

Singh, I.J., B.S. Savara, and Patricia A. Miller. 1967. Interrelations of selected measurements of the face and body in pre-adolescent and adolescent girls. Growth 31: 119-131.

Smith, Sheila M., and L.S. Penrose. 1955. Monozygotic and dizygotic twin diagnosis. Ann. Hum. Genet. 19: 273-289.

Tanner, J.M. 1962. Growth at adolescence, 2nd Ed. Blackwell Scientific Publ., Oxford. 325 p.

Waardenburg, P.J. 1957. The twin study method in wider perspective. Acta Genet. 7: 10-20.

Wei , S.H.Y. 1970. Craniofacial width dimensions. Angle Orthodont. 40: 141-147.

Weinmann, J.P., and H. Sicher. 1955. Bone and bones. C.V. Mosby Co., St. Louis. 508 p.

Woods, G.A. 1950. Changes in width dimensions between certain teeth and facial points during human growth. Amer. J. Orthodont. 36: 676-700.

Wylie, W.L. 1944. A quantitative method for the comparison of craniofacial patterns in different individuals: its application to a study of parents and offspring. Amer. J.Anat. 74: 39-60.