Genetic Factors in the Shape of the Craniofacial Complex

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In the skull, as in other parts of the skeleton, there are two major sources of variability, genetic and environmental. The respective importance of the roles of these factors in determining the normal adult size and shape of the craniofacial complex is one of the most controversial and important problems in orthodontics. Evidence has been accumulating in favor of Brodie's[1] contention that the development of the skull, face and dentition is based on an inheritable growth pattern, the genetic factors involved acting separately on different components of the craniofacial complex, but the identity of these components and their specific mode of genetic control remains largely unknown.

One of the major problems which has delayed progress in the investigation of the influence of heredity is the complex nature of multifactorial inheritance. It is generally accepted that virtually all of the dentofacial characteristics that are of interest to the orthodontist are polygenic and continuously variable. However, traditional types of cephalometric analyses, utilizing line and angle constructs and dimensions, offer information of limited value to heritability studies. Since these constructs are generally defined in terms of widely separated landmarks which often span several anatomic structures and growth sites, and since each dimension may be influenced by changes in any or all of the structures, the conclusions obtained from this approach must be accepted with some caution. As stated by Margolis, Hodge and Tanner,[2] "A small area of the skull surface may be under pure genetic control or pure environmental control or a combination of both, but unless a small area is considered, multiple, and possibly independent mechanisms may be operating, which may nullify each other and therefore make recognition or study impossible."

In agreement with this line of reasoning, several investigators have suggested that the morphological aspects of single bones or bone segments, as expressed by their contours traced from cephalograms, may be the best indicator of the genetic control in the craniofacial complex. Stein, Kelly and Wood[3] noted that if different genes do affect different parts of the skull, then measurements involving relationships between localized areas might show hereditary resemblances more consistently than those involving larger and more widely separated areas. Kraus, Wise and Frei[4] suggested that the contour of a bone segment is an expression of what they called the "total morphologic configuration" of that bone, and thus, may reflect the genetic control of the bone. Building on these ideas, and using an experimental design suggested by Margolis, Hodge and Tanner,[2] the present paper reports the results of a study designed to compare the frequency of concordance of small bony contours between related and nonrelated individuals.

METHODS AND MATERIALS

The present study is concerned with the comparison of the similarity of nine

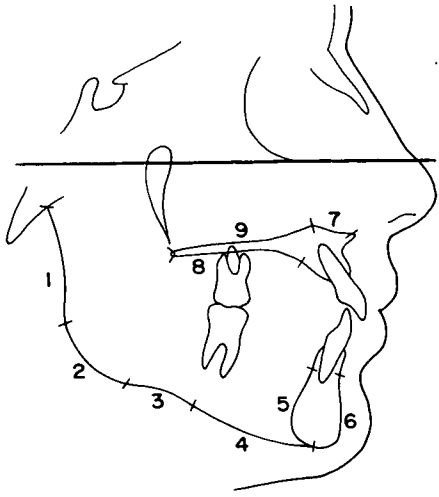

Fig. 1 Definition and location of the nine contours studied for familial similarities.

small bony contours, six in the mandible and three in the maxilla, in groups of related and nonrelated individuals. The nine contours are: (1) posterior border of the ramus, (2) gonial angle, (3) antegonial notch, (4) subsymphyseal contour, (5) lingual symphysis, (6) chin button, (7) anterior nasal floor, (8) palate and (9) posterior nasal floor. The locations of these contours are illustrated in Figure 1.

Each of these contours has been examined for similarity among various pairings of related and nonrelated individuals. The measurement procedure involved placing a pair of tracings on an x-ray view box and then comparing each of the contours separately, i.e., one at a time. The two acetate sheets were adjusted until as nearly perfect superimposition as possible was obtained. Our method deviated here from that of Margolis, Hodge and Tanner in that an attempt was made to remove size differences. Thus, shape alone was the determinant of the similarity or dissimilarity of each contour. For example, if two contours perfectly superimposed, they were called *concordant* (following Margolis, Hodge and Tanner) but we also counted contours having the same shapes as *concordant,* irrespective of differences in size (Fig. 2). If perfect superimposition could not be achieved, even after the removal of size differences, the contour pair was counted as being *discordant.* All the comparisons reported here were made by one of the authors (S.S.W.) and at the time of comparison he did not know whether the pair of tracings was from the related or nonrelated groups of individuals. If the two individuals of a pair showed concordance for a contour, then it was assumed that the individuals shared more common genes for the bony area than if the contours were not superimposable.

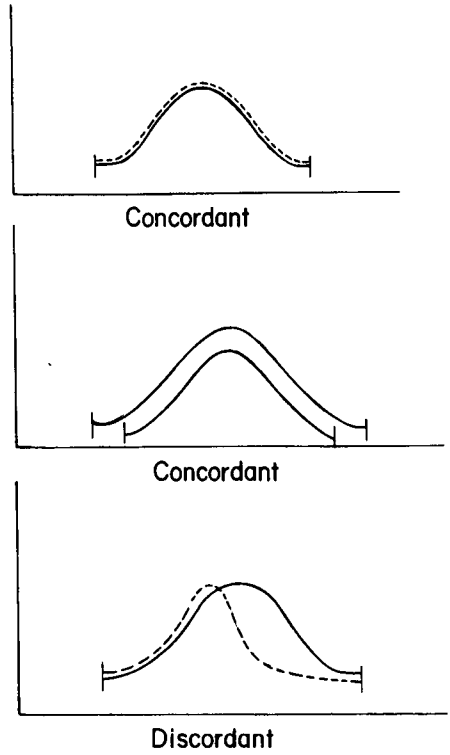

Fig. 2 Examples of concordant and discordant contours. A contour pair is concordant if the contours have the same shape, irrespective of size.

The basic data consisted of 268

TABLE I

Observed proportions of concordant measurements in related and nonrelated (control) groups.

Relationship	Contour Number 1	2	3	4	5	6	7	8	9
Brother/Brother	.633	.700	.566	.766	.533	.700	.700	.533	.666
(Control)	(.500)	(.350)	(.250)	(.200)	(.100)	(.400)	(.400)	(.350)	(.300)
Sister/Sister	.500	.777	.777	.555	.611	.777	.611	.277	.500
(Control)	(.266)	(.333)	(.266)	(.533)	(.133)	(.466)	(.266)	(.200)	(.066)
Brother/Sister	.548	.806	.645	.483	.483	.645	.548	.387	.451
(Control)	(.300)	(.300)	(.500)	(.200)	(.250)	(.500)	(.250)	(.200)	(.150)
Total Sib Group	.569	.759	.645	.607	.531	.696	.620	.417	.544
(Control)	(.363)	(.327)	(.345)	(.290)	(.163)	(.454)	(.309)	(.254)	(.181)

tracings of lateral cephalograms of children attending the University of Michigan Elementary School. The pairs of related individuals included 30 brother/brother pairings, 18 sister/sister pairings and 31 brother/sister pairings for a total of 79 sib pairs. Each related group was controlled by a nonrelated group matched for age and sex with the corresponding group of related individuals. The control group contained 55 pairs of nonrelated individuals, including 20 male/male pairs, 15 female/female pairs and 20 male/female pairs. All cephalograms used in this study were taken with the aid of a rotating anode x-ray source and a Thurow cephalostat. The source-midsagittal plane distance was 5 feet and the midsagittal plane to film distance was 7.5 inches.

Results

The proportions of concordant pairings for each of the contours in each of the groups studied and in the combined related and combined control groups is given in Table I. The proportions in parentheses refer to the control group in each instance. A glance at this table is perhaps sufficient to indicate that concordance is much more common among sibs than among nonrelated individuals.

The significance of the observed differences in the proportions of concordant measurements may be tested by means of the chi-squared test for 2x2 contingency tables[5] and the chi-squared values for the combined sib and combined control groups are given in Table II. Individual chi-squared tests for each of the related and nonrelated subgroups were also carried out but these are not independent components of the test for the combined groups (methodological problems of this type were discussed by Kowalski[6]). They are based on relatively small sample sizes and are not considered in any detail in this report. The critical values for the chi-squared statistic (with one degree of freedom) are 2.71 for the 10% level of significance, 3.84 for the 5% level of significance, and 6.63 for the 1% level of significance. In the comparison of the proportions of concordant measurements in the combined sib and combined nonrelated groups, then, it is seen that contours No. 2 through No. 7, and No. 9 are significant

TABLE II

Chi-square values and associated P-values for the observed differences in the proportions of concordant measurements between the combined sib and combined control groups.

1. Posterior border ramus	4.71	$.01<P<.05$
2. Gonial angle	23.16	$P<.01$
3. Antegonial notch	10.53	$P<.01$
4. Sub-symphysis contour	11.80	$P<.01$
5. Lingual symphysis	17.10	$P<.01$
6. Chin button	6.93	$P<.01$
7. Anterior nasal floor	11.35	$P<.01$
8. Palate	3.11	$.05<P<.10$
9. Posterior nasal floor	16.34	$P<.01$

at the 1% level; contour No. 1 is significant at the 5% level; and contour No. 8 reaches the 10% level of significance.

Discussion

A consideration of the results summarized in Tables I and II provides some insight into the heritability of each of the contours both in the combined groups and within each of the sib pair groupings. It may be noted from Table I that in *every* subgroup considered the proportion of concordant measurements is *always* higher for sibs than for the nonrelated controls for each of the contours considered. Table II provides the results of formal tests comparing the proportions of concordance for the combined sib and combined control groups. But, while all the contours show *some* familial aggregation, the strength of this aggregation is not the same for all of the contours studied. Contour No. 8, for example, exhibits relatively weak familial aggregation ($0.05 < P < 0.10$); this tends to indicate that functional mechanisms exert more control on the shape of the palate than do purely genetic factors. However, it should be noted that these functional mechanisms may themselves be the result of other inherited factors such as tooth size, eruption timing, tongue size and shape, etc.[7] Contour No. 1, the posterior border of the ramus, also shows a relatively weak familial pattern. According to Margolis, Hodge and Tanner, this can be explained on the basis of the functional adaptation of this sector to three environmental influences: musculature, since both the internal pterygoid and masseter attach here; bone remodelling and appositional growth; and to vertical growth changes in response to condylar growth. So while there is an indication of some familial influence on the shape of the posterior border of the ramus, there are also strong functional mechanisms present which tend to contribute to large normal development a variation. In the combined sib and combined nonrelated groups the remaining contours show a definite tendency toward familial aggregation, though this tendency is not always statistically significant in each of the subgroups considered.

It should be noted that while the data do provide evidence of strong familial patterns for most of the contours considered, they do not provide much insight into specific modes of inheritance. Further, it would be of considerable interest to extend the present study to include comparisons of the shape of these morphologic units between parents and siblings. Nevertheless, this type of approach is sufficient to indicate the *existence* of familial similarities in certain components of the craniofacial complex and hence provides a firm foundation for not only more extensive studies of the heritability of dentofacial form, but also for direct clinical application. Extensive craniofacial variation in American society has placed the clinician at a severe disadvantage in the prediction of his patients' growth potential which is fundamental to a meaningful diagnosis and treatment plan. Population norms have severe limitations, even when age and sex are taken into account, if used as the only parameter to ascertain the patient's *individual* growth potential. In this heterogeneous population, then, the utilization of familial data becomes more than academic interest, and studies such as this indicate that the family taken together with the patient provide a potentially important opportunity for increasing the accuracy of the prediction of the size and shape of the craniofacial complex. Many orthodontists already study the patient's family in order to gather an over-all impression of the genetic po-

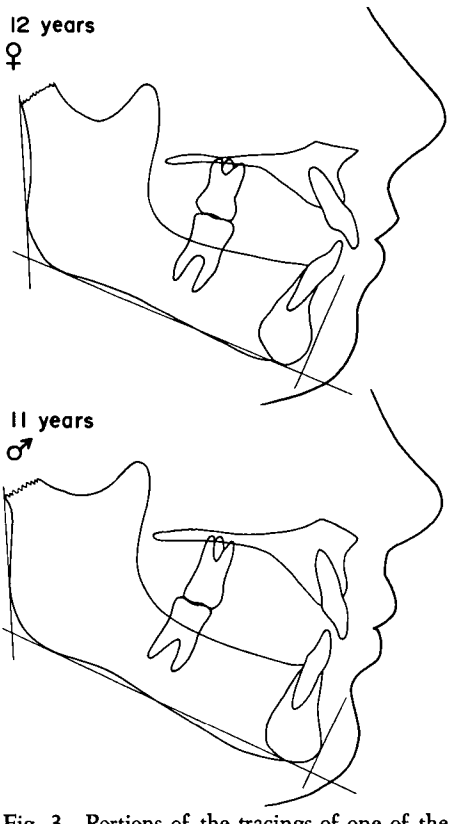

Fig. 3 Portions of the tracings of one of the sib pairs used in the study illustrating shape similarities despite differences in size and emphasizing the need to measure degree of concordance.

tential of the patient, and the method of comparison of bony profiles used in this study is simply an attempt to quantify certain aspects of this procedure (Fig. 3).

Finally, it might also be noted that by simply counting the numbers of concordant contour pairs observed in the various groups a considerable amount of information may be lost concerning the *degree* of concordance. From Figure 3, where portions of the tracings of one of the sib pairs used in this study are illustrated, it is apparent that the quantification of shape information would allow much more subtle comparisons to be made and we are pursuing such studies in the context of the model of craniofacial morphology developed by Walker[8] and described in detail by Walker and Kowalski.[9] These studies, based on the degree of concordance, promise to exhibit even more striking familial patterns than those indicated here.

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The design of the study reported here was a slight modification of that suggested by Margolis, Hodge and Tanner.[2]

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