Genetic Variability of Craniofacial Dimensions

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Of the various methods employed to determine the influence of heredity on the craniofacial morphology, the twin method has been found to be particularly useful in spite of limitations.[1-4] Some of the twin studies have provided acceptable evidence of the heritability of the craniofacial complex.[5-7] However, the quantitative estimation of the heritability still remains a problem. Attempts have been made to determine if a particular area of the craniofacial complex is more heritable than the complex as a whole[8] and whether one area is more heritable than another area.[6] Similarly, comparative heritability of dimensions oriented in different planes also has been given consideration.[5,7] These questions are of considerable importance to those who wish to alter the morphology of the craniofacial complex by changing environment through therapeutic procedures. It is the object of this study to examine the evidence provided by previous investigations and to test these questions by employing the twin method.

REVIEW OF LITERATURE

In one of the early studies dealing with the application of quantitative cephalometry to the study of heredity, Wylie[9] utilized a sample which included 13 like-sexed twin pairs. To overcome the size differences due to age, he employed angular measurements exclusively. On the basis of a comparison of the twins by similarity rating he concluded that the twins showing a striking resemblance might be quite dissimilar skeletally. However, no attempt was made to determine the zygosity of the twins. Therefore, the interpretation of the conclusion is difficult.

To determine the heritability of the craniofacial complex, Snodgrasse[10] employed a family line approach which included one pair of like-sexed twins of undetermined zygosity. Over-all similarity was observed in measurements of the twin pair. In the absence of the zygosity diagnosis it is difficult to interpret whether the similarity was due to, or in spite of, genetic influences.

Lundstrom[11] used a sample of fifty identical and fifty like-sexed fraternal twins aged 12 to 15 years. A coincidence of zygosity determination by blood group testing and morphologic similarity in 14 pairs was considered sufficient to validate the latter method for the whole sample. He concluded that genetic factors have greater influence than the nongenetic factors for most of the craniofacial measurements. However, a more accurate interpretation could have been obtained if a comparison of differences within identical twins (caused by nongenetic factors) with that within fraternal twins (caused by genetic and nongenetic factors) was carried out after subtracting nongenetic effects from the latter.

Leech[12] reported that skeletal morphology is genetically determined on the basis of a sample of one pair of monozygotic twins. The conclusion was based upon similarity of angle ANB but overlooked differences of 3 and 4 degrees in angles SNA and SNB, respectively.

Krause, Wise and Frei[8] provided an excellent review of literature on herit-

ability of the craniofacial complex and methods of zygosity determination. Using a sample of six like-sexed triplets and the technique of superimposition of lateral cephalograms, they concluded that the traditional types of cephalometric concepts and techniques are not applicable to study of heritability and that heredity plays a predominant role in formation of the skeletal units of the craniofacial complex. The former conclusion was based upon superimposition of craniofacial, cranial, and facial complexes and facial quadrilateral constructs. The latter conclusion was based on superimposition of parts of individual bones. Since the technique of superimposition is purely subjective, the conclusions based upon the technique must remain as acceptable as the technique itself.

To study the role of heredity in variability of the craniofacial complex, Osborne and DeGeorge[5] used anthropometry on a sample of 59 pairs of MZ and 37 pairs of like-sexed DZ twins over 18 years of age. Applying an analysis of variance to measurements of head and face, they observed that in this region, unlike the rest of the body, the genetic component of variability is more marked for measurements other than those taken parallel with the long axis of the body and that measurements which appear to provide the best measurable genetic component of variability are head breadth, upper face height, nose height, bigonial width, and head circumference.

Horowitz, Osborne and DeGeorge[6] carried out a cephalometric study of genetic variation in the craniofacial complex by using a sample of thirty-five MZ and twenty-one like-sexed DZ twins of 18 to 55 years of age. They applied an analysis of variance to 6 linear measurements. Highly significant hereditary components of variation were observed to occur in anterior cranial base, mandibular body length, total face height and lower face height. On the basis of comparison of F ratios they concluded that the lower face height demonstrated a larger degree of genetic variability than the upper face height. As F ratios indicate only whether two variances are significantly different, their use to quantify the magnitude of heritability is questionable.

Hunter[7] used a sample of seventy-two like-sexed twins in a cephalometric study of inheritance of craniofacial characteristics. The sample had an age range of 11 years 10 months to 21 years 1 month. Analysis of variance was applied to 26 linear measurements of depth and height. On the basis of comparison of averaged F ratios, it was concluded that measurements of facial skeletal height, on the whole, show a significantly higher component of genetic variability than do measurements of facial skeletal depth dimensions. However, measurement error was greater than 50% of MZ variance for 13 of the dimensions measured and, in a comparison of the remaining 8 depth dimensions with 5 height dimensions, no significant difference was observed.

In a study of genetic and environmental contributions to variability using sixty-three MZ and thirty-nine like-sexed DZ twin pairs, Shapiro[13] applied analysis of variance to palatal height, width and length dimensions. He determined the measurement error for the whole sample and found a significant difference between measurement error variance and mean MZ intrapair variance, demonstrating environmental contribution to the variability of palatal dimensions. However, genetic contribution to the variability of palatal dimensions was not readily detectable.

Material

The sample for this study consisted of 26 pairs of monozygotic and 16 like-sexed pairs of dizygotic twins of Cau-

casian origin, enrolled at the Child Study Clinic, University of Oregon Dental School. Out of 26 pairs of monozygotic twins, 14 pairs were male and 12 pairs were female. In like-sexed dizygotic twins, 10 pairs were male and 6 pairs were female. The ages of the monozygotic twins ranged from 9.92 to 10.58 years with a mean of 10.09 years. The mean age for the dizygotic twins was 8.86 years with a range of 6.5 to 10.5 years.

Methods

Determination of zygosity

The zygosity was determined on the basis of blood group systems. Blood samples were collected from the subjects and both parents. The serological study was carried out by the University of Oregon Medical School. The blood groupings tested and the antisera used were as follows.

Blood group system	Serum antibodies used
ABO	A, Ai, B
MNS	M, N, S
Rh	C, D, E, c, e, C^W
P	P
Kell	K, k, Kp^b
Duffy	Fy^a
Kidd	jk^a, jk^b

Discordance for any one of these antisera was regarded as sufficient evidence for dizygosity. In this study the probability of dizygosity for concordant twins was established at less than 5% according to the method described by Smith and Penrose.[14] In addition to blood groupings the diagnosis of zygosity was supplemented by dermatoglyphics, phenylthiocarbamide testing and concordance of physical characteristics such as sex, color of eyes and hair, form of ear, and facial configuration.

Mensurational technique

The lateral and frontal cephalograms were taken with the child's head oriented by the Frankfort horizontal plane in a Broadbent-Bolton cephalometer. The following landmarks were traced from both cephalograms: condylion, gonion, gnathion, infradentale, nasion, and sella. Details of the landmarks condylion and gonion and their reliability have been described by Tracy and Savara[15] and Savara, Tracy, and Miller.[16] The landmarks gnathion, infradentale, nasion, and sella were determined according to Krogman and Sassouni.[17] The landmarks were measured to 0.1 mm accuracy in two coordinates on the lateral tracing and one coordinate on the frontal tracing using an analog reader and a decimal converter. The coordinates were then corrected for distortion and enlargement. The distances between the landmarks for each dimension were computed using the corrected coordinates according to the method described by Savara.[18] The following measurements were taken:

1. Left condylion—left gonion
2. Right condylion—right gonion
3. Left condylion—gnathion
4. Right condylion—gnathion
5. Left gonion—gnathion
6. Right gonion—gnathion
7. Left condylion—right condylion
8. Left gonion—right gonion
9. Infradentale—gnathion
10. Sella—gonion
11. Nasion—gonion
12. Sella—nasion

The means of right and left sides for the first six measurements were used in the analysis. For determination of measurement errors, two tracings were made from each set of cephalograms, and two measurements were made on each tracing.

Analyses

The data consisted of 42 pairs of twins (26 MZ pairs and 16 DZ pairs), with two sets of tracings made for each member of each pair and two measurements from each tracing. Pairs of twins, tracings, and measurements were considered random effects while the differences between individuals within a pair were considered fixed, making no contribution to the variability between pairs. A mixed model hierarchic analysis of variance was chosen as the most appropriate design for data analysis. The analysis was performed for the DZ and MZ groups separately, but the measurement and tracing error mean squares were pooled. The "average squared intrapair differences," also called the Var(MZ) and Var(DZ), (which strictly speaking is not an intrapair variance but is rather a "treatment effect" due to the within twin pair differences being fixed) for MZ and DZ twins can be calculated as follows:

$$\text{Var(intrapair)} = \frac{\text{MS(intrapair)} - \text{MS(tracings)}}{4}.$$

Detailed expositions of the anova design and formulae used in calculating the mean squares and also the expected mean squares can be found in Sokal and Rohlf.[19] A comparison of genetic variability of mandibular dimensions with that of craniofacial dimensions was performed according to the Mann-Whitney nonparametric test.[19]

Results

Observed, squared averages for pooled measurement error, pooled tracing error, monozygotic and dizygotic intra- and interpair differences and the F ratios for monozygotic intrapair and pooled tracing error for nine variables are presented in Table I. The variances for monozygotic and dizygotic intrapair differences and their F ratios are shown in Table II. The environmental and genetic components of variability and genetic variability expressed as a percentage of total variability are included in Table III. A comparison of genetic variability in mandibular dimensions with that of craniofacial dimensions is made in Table IV. Table V presents a comparison of genetic variability of height, length and width dimensions of the mandible.

Discussion

The factors which might affect the monozygotic and dizygotic variances differentially should be given careful consideration in twin studies. Age is such a factor, and a diversity in ages of monozygotic and dizygotic twins leads to an incorrect assessment of genetic influences. If the dizygotic group belongs to an older age group than that of the monozygotic group, an overestimate of the genetic influence is obtained as differences due to environmental factors will tend to increase with time. Therefore, a uniformity in age is essential in the two groups, though a younger dizygotic than monozygotic group is permissible as it would result in an underestimation which is preferable to an overestimation of the genetic influence. The second factor is sex. Ideally, monozygotic and like-sexed dizygotic twins should be analyzed sexwise. However, since it has been reported that no significant sex difference is observed in most of the craniofacial dimensions,[11-13] like-sexed male and female groups may be combined without any loss of useful information. Another important factor is experimental error, and its determination is essential in order to test if the method is accurate enough to detect the influence of environment in monozygotic twins and subsequently to detect the influence of heredity in dizygotic twins. The final problem is that of quantification of the environmental and

Squared averages for pooled measurement error, pooled tracing error, monozygotic and dizygotic intra- and inter-pair differences and F ratio for MZ intra-pair and pooled tracing error differences.

Source of Variation	df	MS_1 Co-Go	MS_2 Co-Gn	MS_3 Go-Gn	MS_4 Id-Gn	MS_5 L.Co-R.Co	MS_6 L.Go-R.Go	MS_7 S-Go	MS_8 Na-Gn	MS_9 S-Na
DZ inter-pair	15	.94475	3.1541	1.7810	.23803	2.7495	.65718	1.6628	1.9636	.88435
MZ inter-pair	25	.40294	.65820	.43752	.29280	1.2679	1.4685	.85746	1.1203	.42358
DZ intra-pair	16	.15667	.19759	.11364	.05173	.30221	.15542	.19259	.43052	.06526
MZ intra-pair	26	.07230	.06655	.03269	.02458	.07950	.09762	.06773	.14676	.02635
Tracing error (pooled)	42	.02616	.01623	.01426	.01231	.03046	.00268	.000843	.00714	.00300
Meas. error (pooled)	42	.00078	.00398	.00668	.00069	.00079	.00099	.00071	.00154	.00039
$F=\frac{\text{MZ intra-pair MS}}{\text{tracing error MS (pooled)}}$		2.76**	4.10**	2.29**	2.00*	2.61**	36.43**	8.03**	20.55**	8.78**

* Significant at 95% confidence level
** Significant at 99% confidence level

TABLE I

Variances for monozygotic and dizygotic intra-pair differences and F ratio for monozygotic and dizygotic intra-pair differences.

Source of Variation	df	MS_1 Co-Go	MS_2 Co-Gn	MS_3 Go-Gn	MS_4 Id-Gn	MS_5 L.Co-R.Co	MS_6 L.Go-R.Go	MS_7 S-Go	MS_8 Na-Gn	MS_9 S-Na
V DZ intra-pair	16	.03262	.04534	.02484	.00985	.06793	.03818	.04604	.10584	.01556
V MZ intra-pair	26	.01153	.01258	.00460	.00306	.01226	.02373	.01482	.03490	.00583
$F=\frac{\text{DZ intra-pair}}{\text{MZ intra-pair}}$		2.83**	3.60**	5.40**	3.22**	5.54**	1.60	3.11**	3.03**	2.67*

* Significant at 95% level of confidence
** Significant at 99% level of confidence

TABLE II

The differences due to environmental and genetic effects and genetic variability expressed as percentage of total variability.

	Co-Go	Co-Gn	Go-Gn	Id-Gn	L. Co-R. Co	L. Go-R. Go	S-Go	Na-Gn	S-Na
Venv=VMZ (intra-pair)	.01153	.01258	.00460	.00306	.01226	.02373	.01482	.03490	.00583
$V_{gen}=V_{DZ}-V_{MZ}$ (intra-pair)	.02109	.03276	.02024	.00679	.05567	.01445	.03122	.07094	.00973
$\frac{V_{gen}}{V_{DZ}}$ X 100 (intra-pair)	64.6%	72.2%	81.5%	68.9%	81.9%	37.8%	67.8%	67.0%	62.5%

TABLE III

TABLE IV

Comparison of genetic variability in mandibular and craniofacial dimensions

Mandibular Dimensions	
Co - Go	64.6%
Co - Gn	72.2%
Go - Gn	81.5%
Id - Gn	68.9%
L. Co - R. Co	81.9%
Mean	73.8%
Craniofacial Dimensions	
S - Go	67.8%
Na - Gn	67.0%
S - Na	62.5%
Mean	65.8%

TABLE V

Comparison of genetic variability of height, length and width dimension of the mandible.

Height	
Co - Go	64.6%
Id - Gn	68.9%
Mean	66.7%
Length	
Go - Gn	82.0%
Width	
L. Co - R. Co	81.9%

genetic influences for comparison. The F ratio has been used in the past for this purpose. The F ratio is a valuable test of significance for differences between two variances, but it is not an appropriate measure of the magnitude of environmental and genetic influences. Kempthorn[20] has very rightly pointed out misuse of the F ratio as a quantification of environmental or genetic influence. We have attempted to quantify and standardize the environmental and genetic influences by expressing them as percentages of the total variability. The percentwise quantification is more suitable for comparison and further testing as differences in size will not affect the comparisons between dimensions.

Since there is no reason to expect experimental error to be any different in one kind of twins than the other, these errors were pooled to obtain better estimates. The experimental error was partitioned into measurement error and tracing error, but since the latter included the former it was used to test the accuracy of the method. The F ratios for all measurements except the measurement infradentale-gnathion in monozygotic twins are significant at the 99% level, and the latter measurement is significant at the 95% level (Table I). The significant F ratios show that the method is accurate enough to determine the influence of environment in the monozygotic twins and hence can be used to evaluate the genetic influence in the dizygotic twins. The actual variances were obtained from the observed variances after elimination of the experimental errors. All the F ratios of the actual variances of monozygotic and dizygotic twins are significant at 99% confidence level except the ratio for measurements left gonion—right gonion and sella—nasion of which the latter was significant at 95% level while the former was not significant (Table II). The significance of these ratios indicates that the variability of the craniofacial measurement is indeed influenced by heredity in all dimensions except possibly left gonion—right gonion.

The mean squares of differences due to genetic effects are larger than those due to environmental effects for all dimensions except left gonion—right gonion (Table III). The genetic variability is expressed as a percentage of the total variability in order to standardize and quantify the genetic effect on variability of the craniofacial dimensions. The genetic effect seems to be predominant in influencing the variability in all craniofacial dimensions except in the dimension left gonion—right gonion. It appears that in this dimension variability is predominantly influenced by environment. The influence of the masseter and internal

pterygoid muscles on the shape and size of the gonion is considerable.[21,22]

A comparison of genetic variability of the mandibular and craniofacial dimensions (Table IV) shows that, on the average, mandibular dimensions demonstrate a greater component of genetic variability than that demonstrated by craniofacial dimensions. The difference was significant at 90% level according to the Mann-Whitney test.[19] As the genetic influence was not significant in the dimension left gonion—right gonion, this dimension is not included in this and the following comparison. A comparison of height, length, and width dimensions of the mandible indicates that height dimensions show less genetic variability than the length and width dimensions. The dimension condylion—gnathion was not included in this comparison because it is neither a height nor a length dimension exclusively. From this comparison the height dimensions seem to be more responsive to environmental influences such as therapeutic forces than the length or width dimensions.

Summary and Conclusions

The genetic variability of six mandibular dimensions and three craniofacial dimensions was studied by analyzing the cephalograms of twenty-six monozygotic and sixteen like-sexed pairs of dizygotic twins by a hierarchial analysis of variance. Questions were tested as to whether an individual bone, the mandible in this instance, shows a larger component of genetic variability than is shown by the craniofacial complex and whether the dimensions oriented in different planes show different components of genetic variability. The following conclusions were substantiated:

1. The method was accurate enough to determine the environmental influence on the variability of the dimensions within the monozygotic twins and subsequently the genetic influence on the total variability of the dimensions under consideration.
2. The genetic component was predominant in the variability of all the dimensions measured except the dimension left gonion—right gonion in which the environmental component of the variability was predominant.
3. On the average the mandibular dimensions demonstrated a greater component of genetic variability than that shown by the craniofacial dimensions.
4. The length and the width dimensions of the mandible appeared to have a greater component of genetic variability than did the height dimensions indicating that the latter dimensions are more susceptible to such environmental influences as therapeutic procedures.

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