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Relation of Face Shape to Susceptibility to Congenital Cleft Lip*

A Preliminary Report

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It is becoming increasingly clear that the genetic basis for the predisposition to congenital cleft lip is a multifactorially determined threshold character (Fraser, 1963; Carter, 1964, 1969; Fraser, 1970). That is, a number of genetic and environmental factors, individually indistinguishable, interact to determine whether a given developmental event reaches a certain threshold necessary for normal development. If it does, the resulting baby is born without the defect; if it does not, the baby is born with a malformation. For cleft of the secondary palate the nature of the developmental event and threshold are beginning to be understood. The palate shelves must move from either side of the tongue to above the tongue and meet in the midline before growth of the head has carried them too far apart to reach each other (Fraser, Walker, and Trasler, 1957; Fraser, 1968, 1969). For cleft of the primary palate and lip (hereafter referred to as cleft lip), virtually nothing is known about the nature of the developmental threshold. Observations on the relevant susceptibility of two inbred mouse strains to cleft lip induced by maternal treatment with aspirin (Trasler, 1965) have suggested that the relevant developmental threshold may be related to the shape of the embryonic primordial face (Trasler, 1968).

If the shape of the embryonic face is related to the shape of the postnatal face, and if face shape is at least in part genetically determined, and if face shape is indeed related to the predisposition to cleft lip, it follows that the parents of children with congenital cleft lip should have faces that are, on the average, of a different shape than those of the general population. The following study was done to test this hypothesis.

Material and Methods

The experimental subjects were 50 parents (25 males, 25 females) of children with congenital cleft lip (with or without cleft of the secondary palate) ascertained from the files of the Department of Medical Genetics and the Orthodontic Clinic of The Montreal Children's Hospital. The control group consisted of 20 male and 30 female subjects who were parents of children referred to the Department of Medical Genetics for reasons other than cleft lip or other abnormalities of the head, and members of the hospital staff. This control group was not an ideal one, but was considered adequate for this preliminary study. Its average age was younger (31·0 years) than that of the experimental group (40·7 years), but none of the relevant variables appears to be age-dependent within the age range being considered. Neither are there significant differences between the sexes in these variables.

Eleven measurements of the superficial dimensions of the face were made on each subject (Fig. 1), and photographs were taken under standardized conditions. In order to record the superficial topography of the face, the 'physioprint' technique of Sassouni (1962; Sassouni and Nanda, 1964) was used, in which a grid is projected onto the subject's face and photographed at right angles to the plane of projection. In the assessment of differences in face shape, several methods, both objective and subjective, were tried out.

(1) **Direct measurements.** Measurements were made on the subject's face, using an ordinary draftsman's compass. Each measurement was taken twice; if the two measurements did not coincide further measurements were taken until two identical readings were obtained.

(2) **Photography.** Photographs were taken with a single-lens reflex 35 mm. camera with a 100 mm. lens,

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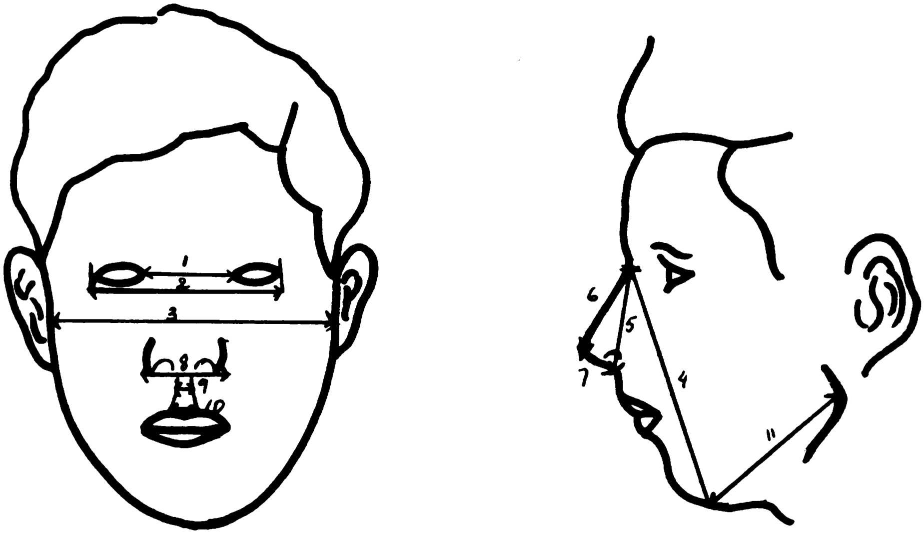

FIG. 1. Measurements taken on the faces and on the prints.

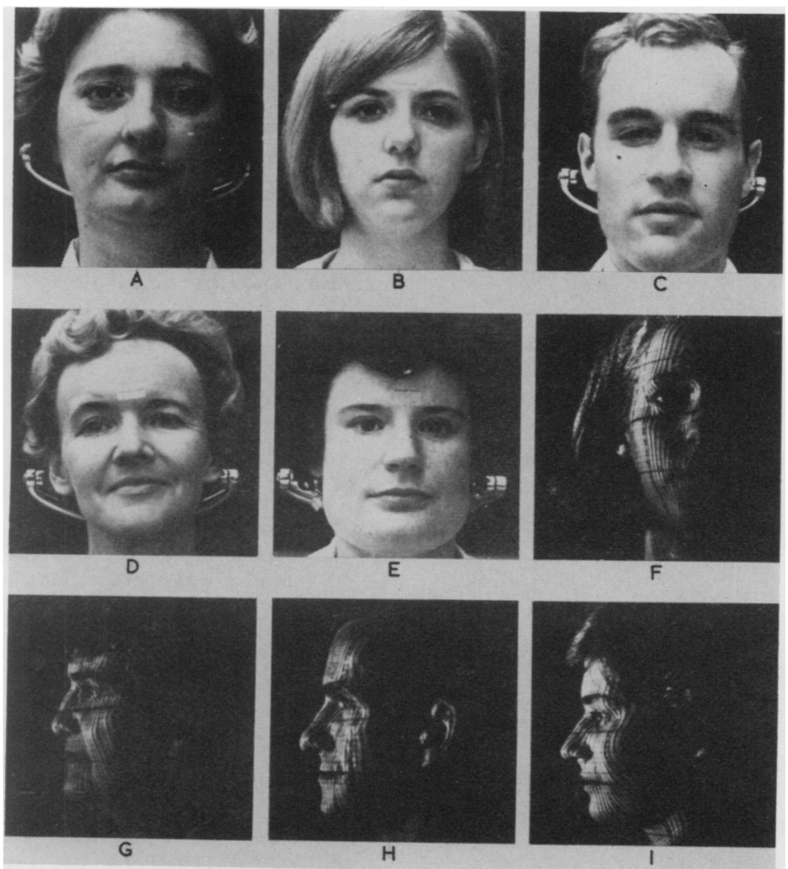

FIG. 2. Classification of face shapes into the five categories (A–E). Full face with subject facing camera and grid projected on right side of face (F). Physioprints showing the three types of contour patterns: G = receding; H = vertical; I = convex pattern.

and the projector had a 90 mm. lens. The subjects were seated 114 cm. away from the projector and 137 cm. away from the camera. The measurements were taken from the zygomatic bone to the rim of the lens of the camera and the lens of the projector. The physioprint profiles were taken with the subject facing the projector and the grid projected on the face. The head was in the vertical position with the transverse line horizontal at the level of the infraorbital margin (felt by palpation) and the upper border of the external auditory meatus (Fig. 2G–I). The full-face physioprints were taken with the subject facing the camera and the grid projected on the right side of the face (Fig. 2F).

(3) **Measurements from photographs.** In general measurements made on the full-face and profile prints correlated well with the direct measurements, but were somewhat more variable; the print measurements were therefore used only for the study of linear dimensions not obtained by direct measurement.

(4) **Measurements from physioprints.** (Fig. 2G–I, and Fig. 3). In an attempt to quantify roughly the

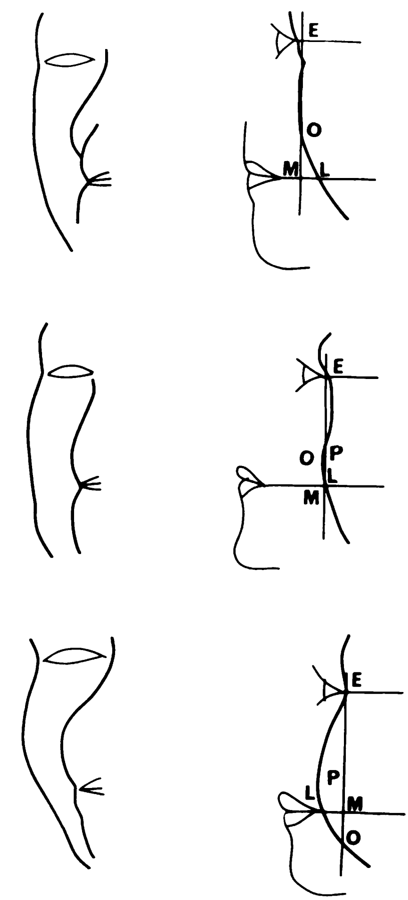

FIG. 3. The different patterns of contour lines as they appear when traced from the physioprints.

variations in facial topography recorded by the physioprints, the following procedure was adopted.

(a) *LM distance.* On the profile physioprint the vertical contour line closest to the outer angle of the eye (hereafter referred to as the *contour line*) was traced on a card. A *vertical line* was also drawn from the outer angle of the eye, and a horizontal line was drawn from the angle of the mouth. The intersection of these two lines is the reference point M; the point at which the contour line crosses the horizontal line is point L; the distance LM was measured on the card. A positive value was assigned to the distance LM when L was anterior to M, and a negative value when L was posterior to M. Thus LM provided a rough quantitative measure of the relation of the contour line to the vertical line.

(b) *P distance.* The distance P was measured as the greatest horizontal distance between the contour line and the vertical line between the points E and M.

(c) *Contour line pattern* (Fig. 3). On subjective review the physioprints could be classified into three major categories:

(i) *The receding type*, in which the contour line swept back, posterior to the vertical, thus giving a negative value to LM.
(ii) *The vertical type*, in which the contour line was approximately vertical, and the LM value was 0.
(iii) *The convex type*, in which the contour line swept anteriorly to the vertical, giving a positive value to LM.

Thus positive values of LM represent a more prominent maxilla than negative values.

(d) *Full-face shape category.* The full-face photographs could be classified subjectively into five categories of shape (Fig. 2A, B, C, D, E). These are:

the round (A)
the oval (B)
the rectangular—dizygomatic and mandibular regions of approximate equal width (C)
the trapezoid—dizygomatic wider than mandibular region (D)
the square (E).

Classification was done by three independent observers, without knowing which groups the individuals were from. In only 5 cases did one observer differ from the other two, and in these the majority view was accepted.

(e) *Relation of upper to lower lip* (Fig. 2G–I). The profile view photographs were classified according to whether the upper lip protruded beyond, was level with, or receded behind the lower lip.

Results

(A) **Face measurements.** Table I presents the mean values for the face measurements and contour values, the standard errors, and the p values for the differences between the experimental and control group.

Of the 11 facial measurements, 2 were found to show a significant difference. These were the dizygomatic and the intraocular chin measurements.

TABLE I

SUMMARY OF MEASUREMENTS

Face Measurements	Control (50) Mean Values ± SE	Experimental (50) Mean Values ± SE	p
Intraocular	3·08 ± 0·037	3·12 ± 0·052	0·90 – 0·80
Biocular	9·55 ± 0·03	9·58 ± 0·078	0·80 – 0·70
Dizygomatic	12·02 ± 0·08	12·42 ± 0·12	0·01 – 0·001
Intraocular—chin	11·4 ± 0·09	11·8 ± 0·13	0·02 – 0·01
Filtrum—upper	0·75 ± 0·026	0·74 ± 0·024	0·80 – 0·70
Filtrum—lower	1·3 ± 0·041	1·35 ± 0·037	0·30 – 0·20
Nose—length	4·93 ± 0·051	5·06 ± 0·038	0·80 – 0·70
Nose—oblique length	4·92 ± 0·068	5·06 ± 0·068	0·20 – 0·10
Nose tip—ala	3·53 ± 0·069	3·59 ± 0·053	0·50 – 0·40
Nose—inter alae	3·15 ± 0·05	3·25 ± 0·046	0·20 – 0·10
Length of mandible	10·1 ± 0·21	10·1 ± 0·36	0·9
E—M	2·73 ± 0·048	2·76 ± 0·071	0·80 – 0·70
E—O	3·18 ± 0·02	2·89 ± 0·014	0·20 – 0·10
P	0·49 ± 0·03	0·38 ± 0·03	0·01 – 0·001
L—M	0·24 ± 0·04	0·022 ± 0·024	0·01 – 0·001

Fig. 4 is a histogram of the intraocular chin face measurements. The experimental mean was 11·8 ± 0·13, and the control mean was 11·4 ± 0·09.

The difference in the means was significant at the 2% level. The experimental group appears skewed to the right—that is, it contains a comparatively large number of individuals with a large intraocular chin measurement.

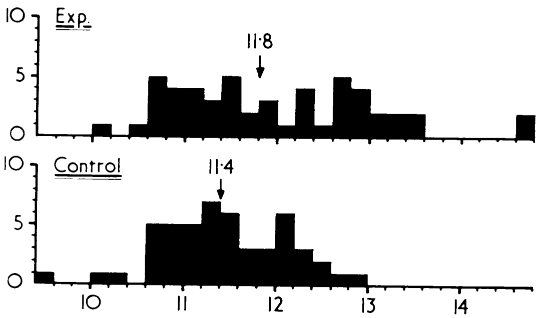

FIG. 4. Distribution of the intraocular chin on face measurements, 50 experimentals and 50 controls.

The mean dizygomatic measurement was 12·42 ± 0·12 for the experimental group and 12·02 ± 0·08 for the control group. The difference was significant at the 1% level. Thus the experimental group tended to have a wider dizygomatic diameter than the control group.

Fig. 5 shows a histogram of the intraocular face measurements. The experimental mean was 3·12 ± 0·05, and the control mean 3·08 ± 0·03 (0·9 > p > 0·8).

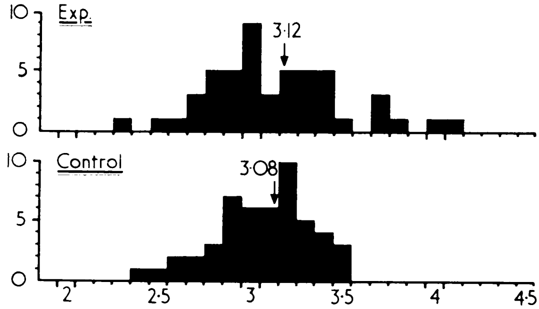

FIG. 5. Distribution of the intraocular face measurements on 50 experimentals and 50 controls.

The difference between the means was not significant, but inspection of the histograms shows that the distribution is skewed to the right. There is a higher proportion of individuals with a wider intraocular measurement in the experimental group.

(B) **Contour measurements.** Of the 4 contour measurements, 2 were found to show a significant difference.

Fig. 6 shows a histogram of the LM values.

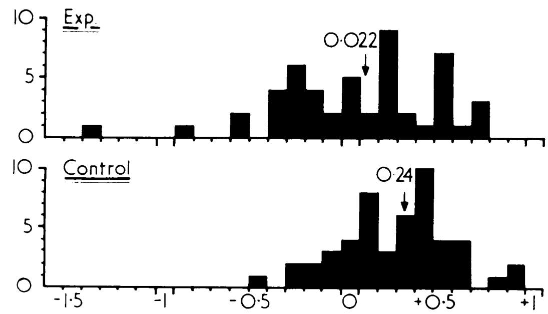

FIG. 6. Distribution of the LM values in 50 experimentals and 50 controls.

The mean for the LM value was 0·022 ± 0·024 for the experimental and 0·24 ± 0·04 for the control. The difference is significant at the 1% level. Thus in the experimental group the maxillae tended to be relatively underdeveloped.

The other contour measurement to show a significant difference between the two groups was P (significant at the 1% level). This measure also indicates a relative degree of underdevelopment of the maxilla in the experimental group.

(C) **Face shapes.** Table II presents the distribution of face shapes in the experimental and control groups.

The experimental group contained a relatively high proportion of rectangular and trapezoid face shapes, and the two groups are significantly different by the heterogeneity χ^2 test ($p < 0{\cdot}001$).

TABLE II

DISTRIBUTION OF FACE SHAPES (%) IN 50 PARENTS OF CHILDREN WITH CLEFT LIP, WITH OR WITHOUT CLEFT PALATE, AND 50 CONTROL INDIVIDUALS

	Control	Experimental
Round	6	6
Oval	63	42
Rectangular	25	40
Trapezoid	2	12
Square	4	0

In summary, so far the experimental group tend to have wider and longer faces, flat maxillae, and a significantly high proportion of rectangular and trapezoid-shaped faces.

(D) **Relationship of lips.** The classification of the position of the upper lip in relation to the lower lip showed that the inferior margin of the upper lip was behind the superior margin of the lower lip in 41·0% of the cases compared to 18·0% of cases in the controls (Table III, $\chi^2 = p < 0{\cdot}001$). These results are consistent with the findings in the mouse (D. G. Trasler, unpublished) where the A/J (susceptible to cleft lip) newborn animals had thinner lips than C57BL/6J (resistant) animals.

TABLE III

RELATION OF UPPER TO LOWER LIP IN 50 PARENTS OF CHILDREN WITH CLEFT LIP, WITH OR WITHOUT CLEFT PALATE, AND 50 CONTROL INDIVIDUALS

	Upper Lip Ahead of Lower	Even	Upper Lip Behind Lower
Experimental	46	12	42
Control	50	32	18

Discussion

The results support the hypothesis that parents of children with cleft lip, with or without cleft palate, tend to differ from the general population in certain dimensions of facial topography. Specifically they appear to have, on the average, longer intraocular chin dimensions, narrower dizygomatic diameters, underdeveloped maxillae, fewer ovoid and more rectangular and trapezoid face shapes, and thin upper lips. According to the hypothesis, parents who have had two children with cleft lip should show more extreme deviations than those with only one. Our data show some suggestion of such a trend, but numbers are inadequate to permit tests of significance.

These findings should be corroborated by more extensive studies, not only on the near relatives of children with cleft lip, but on populations differing greatly in the frequency of cleft lip. The Japanese, for instance, have a relatively high frequency of cleft lip (Neel, 1958), and by the above hypothesis should show differences in face shape similar to those of the near relatives of children with cleft lip. In a series of 20 Japanese individuals provided through the kindness of Dr. M. Yasuda of the Department of Anatomy, University of Kyoto, and Dr. J. R. Miller, Department of Paediatrics, University of British Columbia Medical School, the face shapes were classified as 5% round, 20% oval, 35% rectangular, and 40% trapezoid, a distribution which supports the hypothesis. 75% were found to have a negative value for LM, i.e. a receding type of contour pattern.

Though the genetic basis for the quantitative differences demonstrated in this study are likely to be complex, it is possible that specific traits showing simple Mendelian inheritance can be distinguished. Their identification would help to clarify the biological basis for the genetically determined susceptibility to cleft lip. Even if this is not possible, the quantitative differences may help to identify 'high risk' families and thus improve recurrence risk estimates for genetic counselling.

Summary

The present study was done to test the hypothesis, based on teratological studies in mice, that face shape is causally related to the genetic predisposition to congenital cleft lip in man. Eleven surface dimensions were measured, and facial topography was recorded by the 'physioprint' method of Sassouni, in a series of Caucasian parents of children with cleft lip, with or without cleft palate (the experimental group) and in a control series.

There was a significant tendency for the anterior surface of the maxilla to be flatter, i.e. less prominent, in the experimental group than in the controls. The mean dizygomatic and intraocular chin measurements were larger, the frequency of rectangular and trapezoid shapes was higher, and the

upper lip was less protuberant relative to the lower lip in the experimental group than in the controls.

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