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A Study of Fluctuating Dermatoglyphic Asymmetry in the Sibs and Parents of Cleft Lip Propositi

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Fluctuating asymmetry can be described as random deviation from symmetry in a bilateral organism. It was first shown by Adams and Niswander [1] that propositi with cleft lip with or without cleft palate (CL[P]) who have a family history of this congenital malformation demonstrate increased fluctuating asymmetry of their dermatoglyphics and molar teeth, but CL(P) propositi without a positive family history do not. This observation was confirmed for palmar dermatoglyphics using the *atd* angle as the measurement [2]. Based upon models developed by others [3–5], Adams and Niswander [1] proposed that polygenic systems buffer the development of an organism against environmental influences; the substitution of genes in one of these systems lowers developmental stability and thereby increases the probability of the occurrence of CL(P) and, concomitantly, increased fluctuating asymmetry. This proposal implies that polygenes tend to account for the familial cases of CL(P), while the sporadic cases tend to have different etiologies, including unknown exogenous factors acting during development.

Recently, we looked for fluctuating asymmetry in the normal sibs and parents of CL(P) propositi with and without a family history of this congenital malformation by studying the *atd* angle [2]. Although these relatives could not be distinguished from the controls by comparing intrapair variances, the array of differences for the first-degree relatives of familial cases, which was intermediate to the controls and propositi, suggested the presence of the responsible polygenes in these individuals.

We have now decided to study fluctuating asymmetry in the relatives of CL(P) propositi by using other dermatoglyphic traits. The present study examines the *a-b* ridge count and fingerprint patterns of normal sibs and normal parents of CL(P) propositi with and without a family history of this congenital malformation.

MATERIAL AND METHODS

The ascertainment of propositi with CL(P) and the controls has been described previously [2]. A propositus was categorized as a familial case if CL(P) occurred in a relative with a coefficient of relationship greater than $r = 1/32$. Permanent dermal prints were obtained using the technique of Aase and Lyons [6]. The *a-b* ridge count is the number of ridges occurring in the second interdigital area between the *a* and *b* digital triradii [7]. In determining this count, all ridges which cut or touch a straight line between the triradii are counted, except for nascent ridges and

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triradial points. A ridge termination which meets the line is included in the count; when the line cuts through a point of bifurcation, two ridges are counted. If triradius *a* is duplicated because of a pattern in the interdigital area, the triradius nearer to the radial border of the palm is used. To measure the degree of fluctuating asymmetry, the difference in *a-b* count was determined for the right and left hands. Absolute values were used in calculating the variance (intrapair variance) of these differences. *F* values were obtained by dividing the intrapair variance for the propositi, normal sibs, and normal parents by the intrapair variance for the controls.

Since the purpose of the previous study was to measure the *atd* angle, palm prints were the primary interest, and the fingerprints appeared only as an extension of the palm prints; hence, the fingerprints represent plain prints as compared with rolled prints. Individuals were excluded from the study when the fingerprints were technically incomplete. Each print was classified into one of three groups: arch, loop, or whorl. The paired structures (i.e., right thumb and left thumb, right index finger and left index finger, etc.) were then compared for presence or absence of symmetry. Individuals were given a score from zero to five, indicating the number of dissimilar paired digits. For example, whorls on both thumbs, arches on both index fingers, and loops on the remaining digits gives a score of zero; loops on all digits except for a whorl on the left index finger and a whorl on the right fourth finger gives a score of two. The mean values for the propositi, normal sibs, and normal parents were then compared with the mean value for the controls by using the Mann-Whitney U test. When only plain prints are used, certain errors of classification may result; for example, a whorl may be classified as an arch [7]. The effect in this study, which should be small, would be to increase the degree of asymmetry; however, all groups would be subjected to the same error.

Spearman rank correlation coefficients were calculated to determine if relationships exist among the variables measuring fluctuating asymmetry obtained in the previous [2] and present study. Positive relationships would be expected if a genetic mechanism can account for generalized increased fluctuating asymmetry.

RESULTS AND DISCUSSION

The summary data for the *a-b* ridge counts are given in table 1. The three *F* values for familial cases of CL(P) and their normal sibs and parents are all highly significant; the *F* values for the sporadic cases of CL(P) and their normal sibs and parents are not significant. Similar results occurred in the paired fingerprint study (table 2). For the controls, the mean number of dissimilar paired digits was 0.9. This mean was increased significantly in the familial cases of CL(P) and their normal parents and sibs but not in the sporadic cases of CL(P) and their normal parents and sibs.

Grouping all individuals ($n = 449$) gave a weak but highly significant Spearman rank correlation coefficient ($r_S = .13$; $P<.01$) when the variables measuring the asymmetry of the *atd* angles were compared with those measuring the asymmetry of the *a-b* ridge counts. The other two correlation coefficients (*atd* angles vs. fingerprint patterns and *a-b* ridge counts vs. fingerprint patterns) were not significant, probably because of the weak relationships and the nature of the variables measuring asymmetry of the fingerprint patterns. These variables showed limited variation.

The overall results of this study support the findings of Adams and Niswander [1] and Woolf and Gianas [2] that familial and sporadic cases of CL(P) are different entities and give evidence for a genetic mechanism in the parents and sibs of the familial cases that may account for this congenital disorder and, concomitantly, increased fluctuating asymmetry.

The etiologic heterogeneity of CL(P) complicates genetic studies. CL(P) may occur as one expression of different syndromes resulting from a mutant gene [8] or

TABLE 1

ANALYSIS OF *a-b* RIDGE COUNTS IN RIGHT AND LEFT HANDS

Individuals	No.	Intrapair Variance	*F* Value
Family History of CL(P):			
Propositi	68	7.6	2.30*
Normal sibs	90	5.6	1.70*
Normal parents	74	6.9	2.09*
No Family History of CL(P):			
Propositi	55	3.5	1.06
Normal sibs	103	4.2	1.27
Normal parents	83	3.8	1.15
Controls	166	3.3	. . .

* Significant at the .01 level.

chromosomal imbalance [9], but these syndromes account for only a small proportion of CL(P) cases. A prominent example of the action of a single dominant gene is the van der Woude (lip pit) syndrome [10]. After excluding cases of this syndrome and related syndromes, no evidence was found [11] for the importance of dominant inheritance for CL(P) in a study of individuals who had a parent and a sib with this congenital malformation. Carter [12] and Fraser [13] have proposed a polygenic threshold model for the majority of CL(P) cases. This model has been supported by Woolf [14], Czeizel and Tusnady [15], and Bear [16]. Chung et al. [17] were unable to distinguish between polygene and single gene models based upon data collected in Hawaii. Melnick and Shields [18] argue against the polygene model for CL(P) and propose that CL(P) occurs in some individuals because of the action of a single mutant gene operating in an "allelic restriction" system and in others because of the action of environmental factors.

TABLE 2

COMPARISON OF RIGHT AND LEFT HANDS FOR FINGERPRINT PATTERNS

Individuals	No.	Mean ($\bar{x}$) No. of Dissimilar Paired Digits	*z* Value*
Family History of CL(P):			
Propositi	63	1.29	2.63†
Normal sibs	91	1.29	2.73†
Normal parents	100	1.16	2.59†
No Family History of CL(P):			
Propositi	61	0.85	0.02
Normal sibs	98	1.06	1.58
Normal parents	104	1.04	1.22
Controls	166	0.90	. . .

* *z* value determined from Mann-Whitney U test.
† Significant at the .01 level.

If some cases of CL(P) have a polygenic basis and others result from unknown exogenous factors acting during development, the parents and sibs of familial cases would be expected to have a higher concentration of the responsible genes than the sibs and parents of sporadic cases. If these same genes are also responsible for increased fluctuating asymmetry, differences should exist between the close relatives of the familial and sporadic cases for this dermatoglyphic trait. Hence, the results of the present study are compatible with the hypothesis of etiologic heterogeneity for CL(P) where polygenes play a major role. However, they are also compatible with the hypothesis that the genetic mechanism for CL(P) is a single gene with low penetrance, where the presence of the gene also leads to increased fluctuating asymmetry. Further studies are needed to distinguish between these two genetic models.

Only three dermatoglyphic traits have been studied by the present authors in CL(P) propositi and their relatives. The trend for the *atd* angles and the significant results for the *a-b* ridge counts and the paired fingerprint patterns in the first-degree relatives of familial cases of CL(P) indicate the etiologic value of data on fluctuating asymmetry. Similar studies with other types of congenital malformations purported to have a polygenic basis should also be interesting.

SUMMARY

Fluctuating asymmetry was studied in cleft lip propositi and their normal sibs and parents. The traits examined were *a-b* ridge counts and fingerprint patterns. Propositi with a family history of this congenital malformation and their normal sibs and parents were significantly different from the controls for this type of asymmetry. Propositi without a family history and their normal sibs and parents were similar to the controls. These results support the hypothesis that familial and sporadic cases of congenital cleft lip are different entities and give evidence for a genetic mechanism in the parents and sibs of the familial cases that may account for this congenital disorder and, concomitantly, increased fluctuating asymmetry.

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