Acta Genet Med Gemellol 47: 31-41 (1998)

Sex Differences in Genetic Determinants of Craniofacial Variations - A Study Based on Twin Kinships

K. Sharma

Department of Anthropology, Panjab University, Chandigarh, India

Abstract. Race, sex, nutritional status and cultural factors affect craniofacial morphogenesis. Out of these, sex is a major factor in craniofacial differentiation, because it can be stronger in one ethnic group and weaker in another. In this study, sex differences in genetic variance and heritability of 13 craniofacial traits are investigated. The study is based on a sample of 45 MZ and 101 DZ twin pairs and their 125 singleton siblings, 104 fathers and 103 mothers in 146 families drawn from an urban population of Chandigarh. Results of t'-tests for equality of the means reveal association of zygosity with the mean value of bigonial diameter in female twins and for none in males. Heterogeneity of variance is observed in about 50% traits in females as compared to 15% in males. This invalidates conventional within-pair genetic variance estimates for these traits. The revised genetic variance ratios are higher on an average in males than in females. However, there is greater MZ environmental covariance in male twins than their female counterparts. Family data indicate higher maternal effect for ear height, nasal height and frontal breadth, while greater paternal effect is seen in cranial traits. Sex-wise midparent-child regression coefficients show greater heritability in daughters for nasal traits and bigonial breadth, while sons show higher genetic component for head size measures.

Key words: Sex differences, Genetic determinants, Craniofacial traits, Twins, Family data, India

INTRODUCTION

The polygenic inheritance model gives a good account of individual variation in craniofacial traits. The gene pools of mendelian human populations are hypothesized to differ in the frequencies of genes involved in determining craniofacial morphology. This partly accounts for the considerable variation among human populations for craniofacial traits. Beside genetic factors, these variations are also attributed to environmental factors and their interaction. Traditional twin studies [13 17, 19, 29] have concluded that heredity

play a far greater role than environment in the development of craniofacial morphology. During late 1970s, several researchers have questioned this conventional wisdom. Perhaps foremost reason for this has been the methodologic strides in clarification of the several implicit sources of error in the classic twin studies. Failure to account for unequal means and variances in mono- and dizygotic twin samples introduce serious biases in the most of the earlier works. The later refinements in twin methodologies take these assumptions into account [3, 4]. These improved methods have demonstrated significant environmental determination of several craniofacial dental and occlusal traits [9, 10, 24-26, 28].

A review of literature on family and twin studies on morphological traits [23, 26, 27] does indicate sex differences in heritability of these traits. In an ontogenic process, a phenotype is subjected to a wide variety of stresses, stimulants and environmental constraints. Environmentally induced modification of a trait is called phenotypic plasticity, regardless of the fact that environmentally induced variation is adaptive or not.

Sex and nutritional status have been shown to be more variable factors in craniofacial determination in a study conducted on experimental rats by Pucciarrelli [22]. Sex factors may be stronger in one ethnic group or population and weaker in another. So there is need to report sex-based heritability estimates for various traits and hence the present study was undertaken to explore this issue in detail.

MATERIALS AND METHODS

Thirteen head and facial measurements were taken on a sample of 45 monozygotic (MZ) and 101 dizygotic (DZ) twin pairs, their 125 singleton siblings, 104 fathers and 103 mothers in 146 families. These families belonged to an urban Punjabi population of predominantly middle socio-economic levels and enjoyed satisfactory nutritional status and medical care according to Indian standards.

A subsample of same-sexed, postadolescent and young adult twin pairs from the above sample was selected and included 28 male (14 MZ and 14 DZ) and 29 female (14 MZ and 15 DZ) pairs. Twin zygosity of the same-sexed twin pair was determined by concordance for genetic traits at seven different loci: A_1, A_2, BO, Rh, MN, Kell and Duffy serologic traits, P.T.C. tasting ability and ABH secretor status.

The anthropometric techniques followed in the present study were after Martin and Saller (1957). Both members of the twin pair were measured on the same day while the other family members were measured in subsequent visits to their households.

The approach for the genetic analysis of the twins data has been detailed previously [24, 26]. Several hidden assumptions are implicit in traditional twin model and these have been documented by Christian [3, 4].

Twin zygosity should not be associated with the mean of the trait under discussion. A modified t-test based on nested structure of twin data has been recommended in which intra pair mean squares are used as an error term and degrees of freedom are approximated [3]. Significant differences in mean values between MZ and DZ twins would reflect inherent biological differences associated with the twinning process.

Christian et al. [4] argue that total variance within zygosities must be equal for the standard twin model to hold. If there is evidence of heterogeneity of total variance, the

environmental factors are postulated to be unequal between zygosities. These environmental factors may result from competitive or convergent influences that differ for the two twin types [15]. Christian et al. [4] suggest 0.2 probability level to be used for testing variance heterogeneity by F test to control type 2 error as the test is relatively insensitive to common variance in the zygosities. Christian et al. [4] also provide an unbiased genetic variance estimate if there is evidence of variance heterogeneity.

Genetic variance estimates will also be biased by inequality of environmental covariances of MZ and DZ twins [3]. If environmental covariance is relatively greater for MZ than for DZ twins ($C_{MZ} > C_{DZ}$), heritability will be exaggerated. In that event, it is unlikely that any substantial proportion of the total variance is genetic [3, 5].

From the twins data three different types of heritability estimates were calculated to quantify the proportion of total variance attributable to genetic influences. The within-pair heritability estimate h^2_{WP} was computed as $h^2_{WP} = 4$ (WDZ-WMZ) / (TDZ + TMZ), following Kang et al. [14]. The Holzinger heritability coefficient $h^2_{holz} = (r_{MZ} - r_{DZ}) / (1 - r_{DZ})$ was also calculated for allowing comparison with traditional studies. In addition, the third estimate as suggested by Cavalli-Sforza and Bodmer [1], $h^2_{CS} = 2 (r_{MZ} - r_{DZ}) / (1 + r_{MZ} - 2r_{DZ})$ was also computed. Estimates derived from the twin studies are referred to as broad heritabilities since the genetic influences may include additive, dominance and epistatic effects. Lundstrom [17, 18] used an estimate of cultural inheritance, $C^2 = (2r_{DZ} - r_{MZ})$, to indicate the importance of familial similarity due to common familial environment rather than genetic effect. This estimate of cultural inheritance was also calculated.

In the family data analysis, the first step was to take into account age and sex differences among the family members. The anthropometric measures were normalized for these differences by converting them into standard scores, thereby eliminating both linear and non linear differences [23]. The resultant scores were then further utilized to compute regression of offspring on parent for different sex combinations.

RESULTS

Twin study

Results of mean and variance equality between zygosities and the F test to check against environmental covariance between the two sexes are contrasted in Table 1. The t'-test yields only one significant result, i.e. for bigonial breadth in females, which can be attributed to Type-I error. The F' test shows that MZ and DZ twins differ more in variances than in means. Fundamentally different patterns are observed between the two sexes. In males, heterogeneity of variance is observed in only two of the 13 traits (head length and nasal height), and in both cases MZ twins are significantly more variable than DZ twins. In contrast to males, the null hypothesis between zygosities is rejected for seven of 13 instances in females. The results thus clearly show that variability between zygosities in females is much higher than that in males. ADZ/WDZ ratio also exhibit sex differences. The F-test is not significant for six of the 26 traits (23%). This may be attributed to higher environmental covariance of MZ than DZ twins in males than in females. These results are contrary to the pattern emerging from F' tests.

https://doi.org/10.1017/S0001566000000350 Published online by Cambridge University Press

Table 1 - Tests of equality of mean, total variance and the test to exclude $C_{MZ} > C_{DZ}$

Measurement	Males (Probability)			Females (Probability)		
	t'	F'	$C_{MZ} > C_{Dz}$	t'	F'	$C_{MZ} > C_{DZ}$
Head length (HL)	0.30	0.15	0.04	0.28	0.82	0.00
Head breadth (HB)	0.15	0.26	0.02	0.80	0.15	0.03
Frontal breadth (FB)	0.66	0.55	0.00	0.75	0.08	0.23
Bizygomatic breadth (BZB)	0.33	0.70	0.00	0.15	0.05	0.04
Bigonial breadth (BGB)	0.89	0.36	0.13	0.00	0.08	0.01
Physiognomic facial height (PFH)	0.59	0.37	0.23	0.78	0.19	0.04
Morphological facial height (MFH)	0.86	0.84	0.18	0.16	0.44	0.00
Nasion-stomion length (NSL)	0.82	0.86	0.02	0.78	0.74	0.01
Nasal height (NH)	0.93	0.12	0.04	0.37	0.11	0.06
Nasal breadth (NB)	0.55	0.81	0.69	0.33	0.31	0.07
Mouth breadth (MB)	0.24	0.98	0.01	0.35	0.69	0.03
Ear height (EH)	0.65	0.76	0.06	0.52	0.16	0.57
Ear breadth (EB)	0.38	0.53	0.07	0.94	0.42	0.00

Table 2 presents various estimates of genetic variance (GV) and heritability. By employing Christian's notation, i.e. substituting among component for within pair estimates wherever required under the model, GV estimates are significant for all the traits in male twins. In females, however, all except three traits (frontal breadth, bizygomatic breadth and bigonial breadth) manifest significant genetic component of variation.

The various heritability estimates that are presented in Table 2 highlight the need for caution in interpreting these results. The within pair heritability estimates (h^2_{WP}) are generally lower than the other two types (h^2_{holz} and h^2_{CS}). The heritability estimates based on correlation coefficients between twins are generally inflated. Because the twin method would usually assume that environmental effects are similar for both MZ and DZ twins, and that greater similarity within MZ pairs compared with DZ pairs reflects genetic component. These assumptions may not be valid in all situations [21]. The table 2 also shows that some estimates of cultural inheritance (C^2) are of high magnitude, e.g., bizygomatic breadth, frontal breadth, head breadth etc. in males. Sex differences are observed in the pattern of cultural inheritance. The females show higher cultural inheritance for head length, bigonial breadth, morphological facial helght, etc. Interestingly, for all these traits, cultural inheritance estimates in the males show negative values. The traits showing higher cultural component manifest lower within pair estimates of heritability.

Figure 1 gives comparative within-pair GVRs between the two sexes. In Figure 2 the GVRs, by employing Christian's notation, are contrasted between male and female twins. The general trend, as projected in Figure 2, shows that males manifest higher GVRs than females. At times, the traits behave exceedingly opposite in males and

https://doi.org/10.1017/S0001566000000350 Published online by Cambridge University Press

Table 2 - Estimates of Genetic Variance (GV), heritability (h^2) and cultural inheritance (C^2)

Measurement	Males						Females					
	GV_{WP}	GV_{AC} (if valid)	h^2_{WP}	h^2_{holz}	h^2_{CS}	C^2	GV_{WP}	GV_{AC} (if valid)	h^2_{WP}	h^2_{holz}	h^2_{CS}	C^2
Head length	0.22*	0.68*	0.32	0.94	0.97	-0.05	0.07*	–	0.19	0.65	0.79	0.57
Head breadth	0.12*	–	0.39	0.45	0.62	0.35	0.01	0.11*	0.05	0.52	0.69	0.13
Frontal breadth	0.05*	–	0.34	0.88	0.93	0.40	0.08*	0.02	0.95	0.65	0.79	-0.37
Bizygomatic breadth	0.06*	–	0.18	0.91	0.95	0.58	0.12*	-0.01	0.76	0.72	0.82	-0.03
Bigonial breadth	0.18*	–	0.51	0.95	0.97	-0.34	0.06*	-0.04	0.43	0.27	0.41	0.41
Physiognomic facial height	0.69*	–	0.80	0.73	0.84	-0.38	0.15*	0.44*	0.26	0.76	0.87	-0.06
Morphological facial height	0.33*	–	0.62	0.87	0.93	-0.40	0.05*	–	0.18	0.71	0.84	0.38
Nasion-stomion length	0.10*	–	0.40	0.86	0.92	0.09	0.05*	–	0.32	0.76	0.87	0.15
Nasal height	0.05*	0.19*	0.26	0.89	0.94	0.00	0.05*	0.14 *	0.34	0.89	0.94	-0.21
Nasal breadth	0.03*	–	0.90	0.85	0.91	-1.10	0.02*	–	0.41	0.86	0.92	-0.24
Mouth breadth	0.05*		0.27	0.70	0.84	0.33	0.04*	–	0.51	0.7i	0.87	0.07
Ear height	0.12*	–	0.57	0.93	0.98	-0.06	0.05*	0.09 *	0.67	0.94	0.96	-0.85
Ear breadth	0.03*	–	0.42	0.89	0.91	-0.10	0.02*	–	0.37	0.82	0.91	0.36

* $P < 0.05$

females. For example, the GVRs in males for bigonial breadth, frontal breadth, bizygomatic breadth vary from about 10 to 13. While those for females are nearing one and statistically not significant. The revised average GVR in males is 7.29 (S.D. = 4.17), while in females 3.21 (S.D. = 2.07).

Family study

The results of the analyses of regression coefficients between children of either sex to their mid-parent value are presented in Figure 3. Daughters manifest higher coefficients than the sons especially for nasal traits and bigonial breadth. While sons show greater semblance with the midparental values for measures of head size. Midparent-son regression coefficients are all statistically significant at 1% level of probability. Midparent-daughter regression coefficients are also statistically significant for all the traits except head breadth.

Figure 4 shows that the resemblance of children with their parents of either sex is not equal as revealed by regression coefficients. The hypothesis of higher maternal effect is observed in traits like ear height, nasal height and frontal breadth. Conversely, higher paternal effect is noticed in cranial traits. However, frontal breadth behaves more like a facial trait.

DISCUSSION

The results do not confirm the commonly advanced hypothesis that girls are genetically more buffered than boys against environmental determinants of growth. Because males, on an average, manifest higher genetic component of variation than females. A similar, but of lesser magnitude, trend has been noticed in the Belgian twin data [26, 28]. Such a situation may partly arise if environmental factors do not operate randomly between the two sexes for the different traits. Sex differences in the variance heterogeneity clearly indicate greater environmental stress on females than males. The environmental factors which can be listed in the case of Indian twins are that despite modernization, parental care, including materialistic and psychological cares, still favours males. Consequently the females receive less nourished food, inferior schooling, they have to render help in the household chores and are subjected to greater restrictions. These correlates may in turn affect the determinants of craniofacial morphology.

The above observations are further strengthened by studies, conducted on experimental animals, that have shown the effects of sex and nutritional status on craniofacial morphology [22]. Subtle neurological sex differences in the neuroanatomical structures and behaviour patterning are well appreciated by anthropologists and psychologists. For example, sex differences in spatial ability are known both in humans and laboratory rodents, and these studies have been reviewed in detail by Gaulin [12]. Here, a question that can strike any investigating mind is that how such sexual dimorphism originates. Sex hormones influence the ontogeny of many adaptive sex differences [11]. From evolutionary biologist's perspective, Lancaster [16] emphasizes that a species does not evolve as a single entity but rather that the adaptations of the two sexes must be understood independently of each other. These observations strengthen the hypothesis that sex

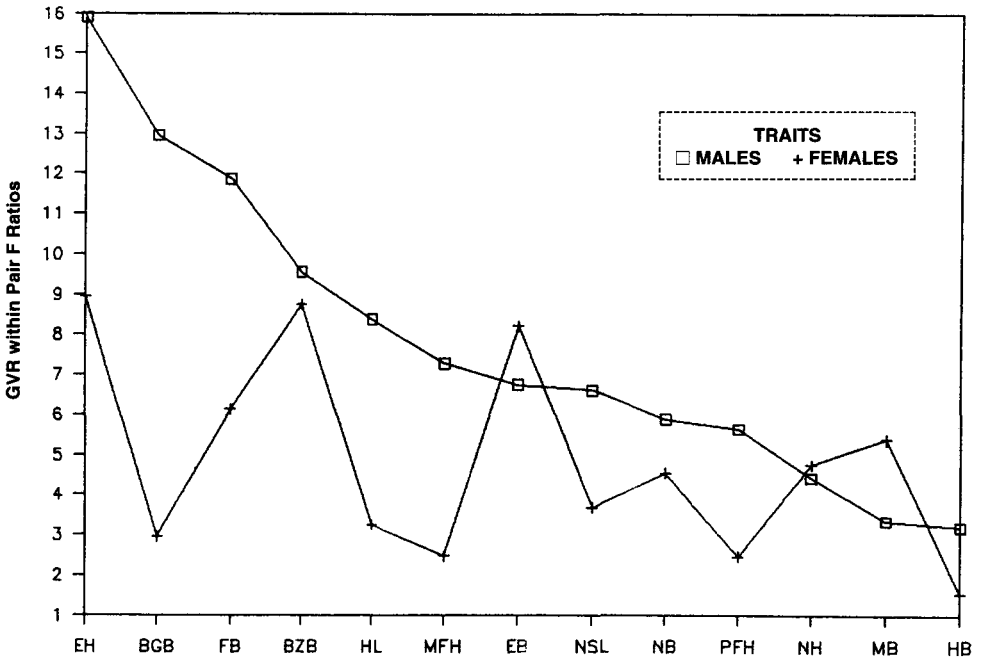

Fig. 1 - Comparative within pair genetic variance ratios between male and female twins.

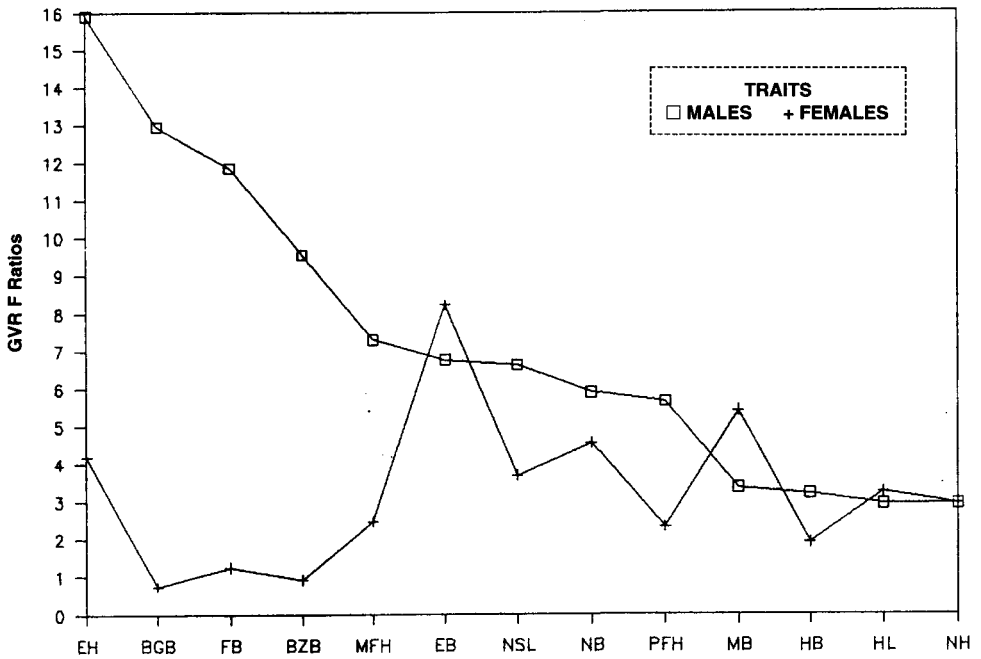

Fig. 2 - Comparative genetic variance ratios between male and female twins.

https://doi.org/10.1017/S0001566000000350 Published online by Cambridge University Press

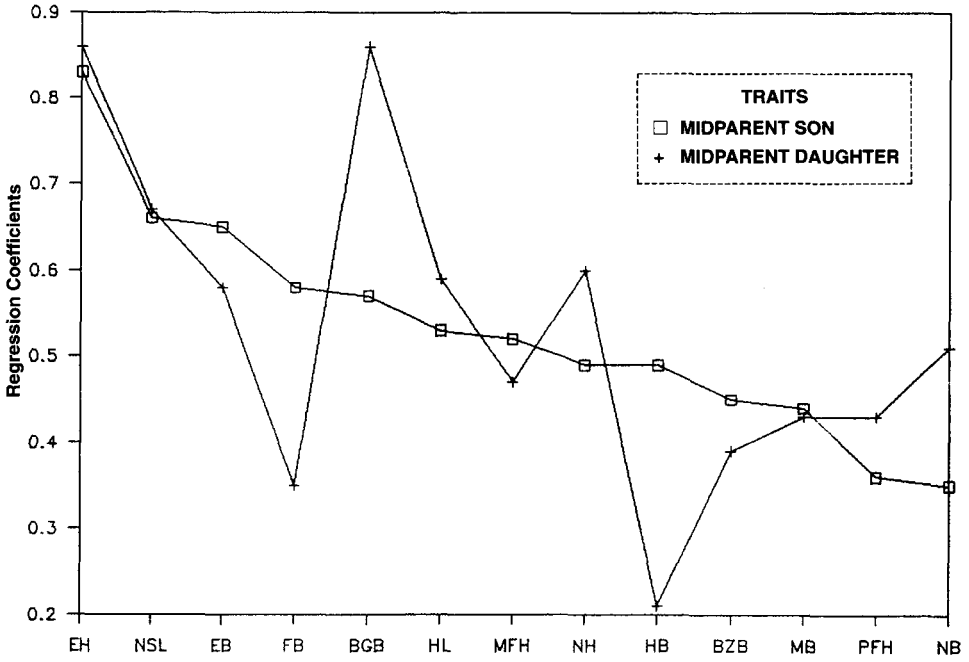

Fig. 3 - Comparative heritability estimates (b) between sons and daughters.

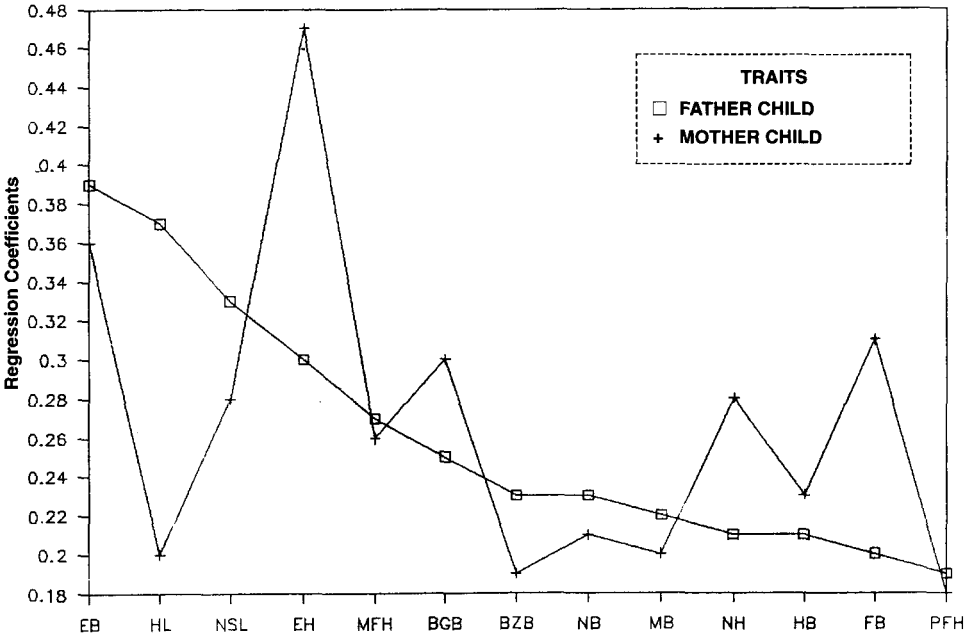

Fig. 4 - Comparison of regression coefficients between father-child and mother-child.

https://doi.org/10.1017/S0001566000000350 Published online by Cambridge University Press

may act as a variable factor in the heritability of craniofacial traits. Osborne and DeGeorge [20] have also shown strong environmental and sex influences affecting the covariation of head length and head breadth. They have further added that there are sex differences in health and disease and morphological variances would appear to follow similar patterns that tend to run in opposite or compensatory directions.

The results of the present study confirm and extend the observations of previous workers concerning the occurrence of phenomenon of higher maternal or paternal effects in some traits. Of these, the hypothesis of higher maternal effect in determination of some traits is often advanced in studies analyzing familial resemblance for anthropometric and other quantitative traits. Because the geneticists know that a higher maternal effect occurs when the genotype of the mother influences the phenotype of the progeny either through substances present in the egg that affect early development or through the effects of culture. Cytoplasmic or maternal inheritance in determining craniofacial morphology is ruled out. Higher midparent-child regression coefficients than single parent-child coefficients are consistent with almost perfect additive heredity model. But the phenotypes seem to be modified by factors associated with sex. However, there is no evidence of X-linked inheritance for any of the head and facial trait [23].

The data presented by previous studies including the present study indicate higher paternal effect. To the best of my knowledge, no previous study ever attempted to explain these curious results. The usual explanation given would attribute it to some statistical artifact or measurement error. However, the role of the environment including cultural practices in influencing a phenotype can be manifold. In some instances, specific environmental changes may modify the development of an organism so that its phenotype simulates the effect of a genotype. Such environmental factors can depress or inflate the value of the parent-child regression coefficient for some craniofacial-traits. This may erroneously cause higher maternal or paternal component. Such an explanation seems justified and explainable on the basis of existing anthropological literature.

Many human groups are known to practice artificial reshaping of the cranial vault by various constraining appliances. These practices provide a natural experiment for investigating relationship between cranial vault growth and facial growth in humans.

Chevrud et al. [2] have reviewed such earlier studies and analyzed two skeletal series including both normal and artificially modified crania of a prehistoric Peruvian Ancon sample and a Songish Indian sample from British Columbia. Their study clearly shows that artificially reshaping of the cranial vault leads to a cascade of developmental effects on the growing cranial base and face. These results have wider implications in understanding human craniofacial growth and evolution. These results indicate that the growing craniofacial parts are not largely functionally independent.

To conclude, the changes brought by any environmental factor to the growth of cranial vault will also have some effect on the growth of other parts of craniofacial complex. There is need to analyze and document such environmental factors and also the exact influence of these factors on the magnitude of reported parent-child correlation or regression coefficients.

Acnknowledgements: I am grateful to Professor Charles Susanne for considerable analytical assistance and advice.

REFERENCES

1. Cavalli-Sforza LL, Bodmer WF (1971): The Genetics of Human Populations. San Francisco: Freeman.
2. Cheverud JM, Kohn LAP, Konigsberg LW, Leigh SR (1992): Effects of fronto-occipital artificial cranial vault modification on the cranial base and face. Am J Phys Anthropol 88: 323-345.
3. Christian JC (1979): Testing twin means and estimating genetic variance. Basic methodology for the analysis of quantitative twin data. Acta Genet Med Gemellol 28: 35-40.
4. Christian JC, Kang KW, Norton JA (1974): Choice of an estimate of genetic variance from twin data. Am J Hum Genet 26: 154-161.
5. Christian JC, Feinleib M, Norton JA (1975): Statistical analysis of genetic variance in twins. Am J Hum Genet 27: 807.
6. Christian JC, Kang KW, Norton JA (1977): Comparison of within-pair and among component estimates of genetic variance from twin data. Am J Hum Genet 29: 208-210.
7. Christian JC, Norton JA (1977): A proposed test of the difference between the means of monozygotic and dizygotic twins. Acta Genet Med Gemellol 26: 49-53.
8. Corruccini RS, Potter RH (1980): Genetic analysis of occlusal variation in twins. Am J Orthod 78: 140-154.
9. Corruccini RS, Sharma K, Potter RHY (1986): Comparative genetic variance and heritability of dental occlusal variables in US and Northwest Indian twins. Am J Phys Anthrop 70: 293-299.
10. Corruccini RS, Townsend GC, Richards LC, Brown T (1990): Genetic and environmental determinants of dental occlusal variation in twins of different nationalities. Human Biology 62: 353-367.
11. Daly M, Wilson M (1983): Sex, Evolution and Behaviour. 2nd ed. Belmont, CA Wordsworth.
12. Gaulin SJC (1992): Evolution of sex differences in spatial ability. Yearbook of Physical Anthropology 35: 125-151.
13. Horowitz SD, Osborne RH, DeGeorge FVA (1960): A cephalometric study of cranio-facial variation in adult twins. Angle Orthod 30: 1-5.
14. Kang KW, Christian JC, Norton JA (1978): Heritability estimates from twin studies. 1. Formulae of heretability estimates. Acta Genet Med Gemellol 27: 39-44.
15. Kempthorne O, Osborne RH (1961): The interpretation of twin data. Am J Hum Genet 13: 320-339.
16. Lancaster JB (1991): A feminist and evolutionary biologist looks at women. Yearbook Phys Anthropol 34: 1-11.
17. Lundstrom A (1984): Nature versus nurture in dento-facial variation. Eur J Orthod 6: 77-91.
18. Lundstrom A, McWilliam JS (1987): A comparison of vertical and horizontal cephalometric variables with regard to heretability. Eur J Orthod 9: 104-108.
19. Nakata M, Yu P, Davis B, Nance WE (1974): Genetic determinants of cranio-facial morphology: A twin study. Ann Hum Genet 37: 431-443.
20. Osborne RH, DeGeorge FV (1959): Genetic Basis of Morphological Variation. Cambridge: Harvard University Press.
21. Potter RHY, Yu P, Christian JC (1979): Association of twin zygosity with the mean and variance of tooth size. Acta Genet Med Gemellol 28: 211-223.
22. Pucciarrelli HM (1980): The effects of race, sex and nutrition on craniofacial differentiation in rats; A multivariate analysis. Am J Phys Anthropol 53: 359-368.
23. Sharma K (1987): Familial resemblance for craniofacial traits in a Punjabi population. Z Morph Anthrop 77: 157-165.

24. Sharma K, Corruccini RS (1986): Genetic basis of dental occlusal variations in northwest Indian twins. Europ J Orthod 8: 91-97.
25. Sharma K, Corruccini RS, Henderson AM (1985): Genetic variance in dental dimensions of Punjabi twins. J Dent Res 64: 1389-91.
26. Sharma K, Susanne C (1991): Comparative genetic variance and heritability of head and facial traits in Northwest Indian and Belgian twins. Am J Hum Biol 3: 315-324.
27. Susanne C (1975): Genetic and environmental influences on morphological characteristics. Ann Hum Biol 2: 279-287.
28. Susanne S, Defrise-Gussenhoven E, Wanseele PV, Tassin A (1983): Genetic and environmental factors in head and face measurements of Belgium twins. Acta Genet Med Gemellol 32: 229-238.
29. Watnick SS (1972): Inheritance of cranio-facial morphology. Angle Orthod 42: 339-351.

Correspondence: Dr Krishan Sharma, T-II-44, Sector 25, P.U. Campus, Chandigarh - 160014, India.