International Journal Of Multidisciplinary Research In Science, Engineering and Technology (IJMRSET)

| ISSN: 2582-7219 | www.ijmrset.com | Impact Factor: 4.988

| Volume 4, Issue 5, May 2021 |

Phenotypic Variations in Few Facial Traits of Human Beings

Dr. Sadhana Kesharwani

Professor, Department of Zoology and Biotechnology, Govt. MH College of Home Science and Science, Jabalpur, MP, India

ABSTRACT: Generally speaking, phenotypic variation in shape (or size) tends to be less studied as compared to less integrated traits (eg, pigmentation intensity and patterns). One-third of the mutations listed by Martin and Orgogozo concern morphological evolution (384 of 1008, including 281 in metazoans). Yet, we counted only 27 mutations (for a total of 18 genes) involved in body or organ shape changes and 25 mutations (for a total of 23 genes) involved in body or organ size changes. Only four case studies have pointed genes associated with changes in size and shape in epithelial tissues directly: three of them deal with insect wings. Epigenetic modifications can cause phenotypic variation within a single generation. This timeframe means that, in response to a changing environment, the epigenetic inheritance system has the potential to be much more flexible than traditional genetic mutations, and also that epigenetic inheritance systems may have far greater consequences for adaptive evolution than has previously been recognized. Given this potential, it is important to consider epigenetics' role in speciation. It is thought that epigenetics may contribute considerably in the initial stages of population divergence, enabling speciation by facilitating phenotypic adaptation through epigenetic modifications, after which genetic changes reinforce the divergence. This concept, largely inspired by Jablonka and Lamb, as well as others, has led to widespread acknowledgement regarding the evolutionary significance of epigenetic inheritance. Accordingly, population-epigenetic models have recently been formulated, incorporating parameters considered central to epigenetic inheritance systems.

The human face is extraordinarily variable, and the extreme similarity of the faces of identical twins indicates that most of this variability is genetically determined. We have devised an approach to increase the chance of identifying specific large genetic effects on particular facial features, by choosing features with high heritability and selecting individuals with relatively extreme facial phenotypes for comparison with a control population. This has yielded three specific and replicated genetic variants, two for features of facial profiles, and one for the region around the eyes. Further application of these methods should enable the understanding, eventually at the molecular level, of the nature of this extraordinary genetic variability, which is such an important feature of our everyday human interactions.

I. INTRODUCTION

To discover specific variants with relatively large effects on the human face, we have devised an approach to identifying facial features with high heritability. This is based on using twin data to estimate the additive genetic value of each point on a face, as provided by a 3D camera system. In addition, we have used the ethnic difference between East Asian and European faces as a further source of face genetic variation. We use principal components (PCs) analysis to provide a fine definition of the surface features of human faces around the eyes and of the profile, and chose upper and lower 10% extremes of the most heritable PCs for looking for genetic associations. Using this strategy for the analysis of 3D images of 1,832 unique volunteers from the well-characterized People of the British Isles study and 1,567 unique twin images from the TwinsUK cohort, together with genetic data for 500,000 SNPs, we have identified three specific genetic variants with notable effects on facial profiles and eyes.[1]

The human face is an important interface of social interaction; communication, sensory input and expression in humans are to a large extent based on facial characteristics and traits1. Normal facial variation is associated with emotional expression2, attractiveness3 and even lifetime reproductive success4. Recent evidence suggest that evolution has contributed to increased diversity and complexity in human facial morphology, presumably due to the role of the face as a primary medium of individual identification and recognition5. The influence that facial features have in our life has spurred a long and ongoing interest in unraveling the roles that genes and environment play in the morphological characteristics of the human face.Heritability studies were carried out to quantify the extent of phenotypic variation that can be explained by genetic variability using, for instance, facial features extracted from cranial measurements. Moderate heritability, varying approximately between 0.35 and 0.65, was found for traits such as nasion-basion and nasion-sella distances.. More recent studies used facial photographs instead, due to the simplicity in which the images

| ISSN: 2582-7219 | www.ijmrset.com | Impact Factor: 4.988

| Volume 4, Issue 5, May 2021 |

can be obtained. However, common traits such as the upper lip height, as well as nasal breadth and vertical eye distance, extracted from standard photographs, were only found to be moderately heritable. Given the almost perfect resemblance of identical twins, such heritability values appear surprising low. Attempts to replicate these findings across independent studies generated inconsistent evidence. A comparison of eight heritability studies reported low correlation (<0.4) between heritability estimates for commonly examined traits such as head circumference, facial height and nose width.[2,3]

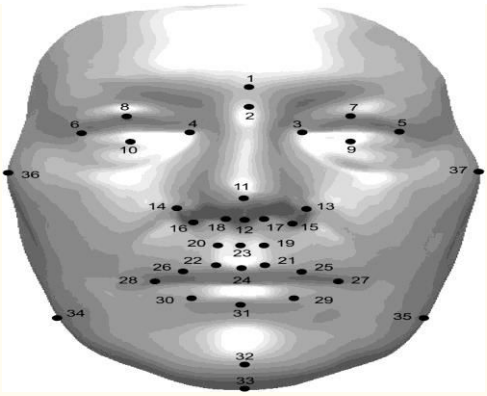

Fig 1-Thirty-seven anthropometric landmarks (14 bilateral and 9 mid-sagittal) used in the study.

Over the last decade, a few studies have investigated 3D facial characteristics of twins . Using facial colour maps of twins (depicting the deviation between faces), Naini and Moss found that the triangular area encompassing the orbital rims, intercanthal area, and the nose is genetically driven in British twins; MZ twins showed similarities in the shape of the eyebrows, bridge of the nose and infraorbital ridges, whereas other parts of the face such as cheeks, chin, and lips showed significant variation . Similar findings were reported in the preliminary study performed on American twins .These 3D studies dealt with small, convenient samples that were not representative of the respective populations. In addition, there was no robust estimation of heritability. Therefore, our current knowledge on heritability of craniofacial traits mainly stems from two-dimensional studies with some conflicting results on heritability estimates of horizontal and vertical skeletal parameters.[4,5]

II. DISCUSSIONS

Phenotypic variation in humans is produced through a complex interplay between genotype and environment, but the characterization of phenotype lags behind the characterization of the genotype . In facial research, there is no uniform approach to the analysis of facial phenotype due to: 1) variable facial data acquisition (two-dimensional or three-dimensional techniques); 2) lack of a standardized way to quantify spurious expressions (relying on subjective opinion of the examiner); 3) variable selection and/or definition of phenotypic traits; 4) the amount of information analysed (sparse or spatially-dense points across the facial surface that can be identified manually or automatically) and 5) statistical analyses (univariate/multivariate).In this study, facial phenotype was characterized by principal components and linear distances based on 37 anthropometric landmarks manually identified on the 3D facial images. Most of the landmarks could be reliably identified (within 2 mm), except for soft tissue ‘zygion’ (difficult to describe in anatomical terms and traditionally identified by trial measurement), ‘gonion’ (normally identified by palpation), ‘pogonion’ and ‘gnathion’ (these were difficult to identify in vertical plane if a chin had a flat surface) . However, as the sample was quite large (1380 twin faces), it was decided to include these landmarks in the subsequent analyses.[6,7,8]

| ISSN: 2582-7219 | www.ijmrset.com | Impact Factor: 4.988

| Volume 4, Issue 5, May 2021 |

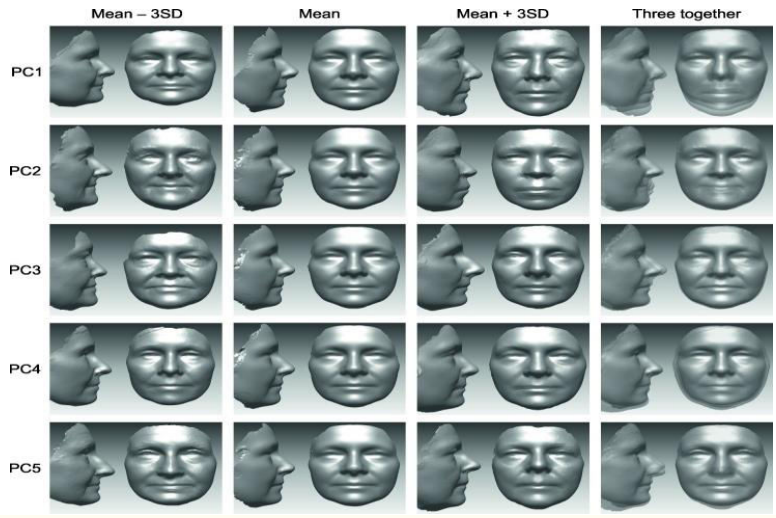

Fig 2-The effects of the first five unscaled principal components on the face.

We found that soft tissue facial traits in adult British female twins have moderate to high heritability, which is in general agreement with previous family and twin studies. In Koreans the heritability values ranged from 0.25 (lower facial height, sn-gn) to 0.61 (intercanthal width; en-en) for linear measurements derived from digital photographs of family members; the authors also identified three factors with heritability estimates from 0.45 (total face height, upper face height and nose height) to 0.55 (lower face height and width of the mandible, mouth and nose). High correlations between parents and offspring and siblings were also found in Indian families for mandibular position, chin prominence, nasal prominence, nasal width, lip length at philtrum, lip prominence and facial height. However, heritability was not calculated. In Belgian families heritability estimates for soft tissue facial parameters ranged from 0.46 (nose height) to 0.72 (external biocular breadth). Cephalometric analysis of soft tissue parameters in Turkish siblings revealed high heritability (0.72 to 1.0) for soft tissue chin thickness, soft tissue facial angle, Merrifield angle (formed by the Frankfort plane and profile line joining the chin and the more prominent lip, usually the upper) and Holdaway angle (formed by a line tangent to the chin and upper lip with the cephalometric NB line). Differences in estimates can be explained by different methodology: photos or lateral cephalograms measurement errors; small samples and different ethnicities. In addition, the components of genetic variance for a given trait vary from population to population .The first 3D twin study focusing on soft tissues was performed on British twins (10 pairs of MZ and 8 pairs of same-sex DZ twins aged 9 to 17 years) using stereophotogrammetry. Significant differences between faces of MZ and DZ twins were found for intercanthal width, right eye width, nose width, nose height, mouth width, and upper lip height. This coincides with our results, despite the obvious differences in the sample size and age. In faces of British twins (10 pairs of MZ and 10 pairs of same-sex DZ twins) were also analysed using laser scanning. It was apparently the first time that facial surfaces were suggested for analysis apart from analyzing linear distances. Significant genetic determination was revealed for midfacial parameters, especially left eye width, intercanthal width, nose height, and nose width. However, the study by Naini and Moss did not show any significant differences in mouth width and upper lip height, which contradicts the study done by Burke as well as our findings, which show a strong genetic contribution above 60% for these traits. The differences can be explained by the small sample used in wide age range of participants (6–42 years) and their mixed ethnicity, as well as no formal heritability calculation.In a well-known British population study (ALSPAC) was the source of 37 twin pairs, whose faces were captured using laser scanning. Configurations of 21 facial landmarks as well as facial surfaces were compared between 19 MZ and 18 DZ twin pairs aged 15 years. Procrustes analysis did not reveal any significant difference in facial landmark configurations. On the other hand, average female MZ and DZ twin faces coincided in the eyes, supraorbital and infraorbital ridges, philtrum and lower part of the cheeks. In the absences of heritability estimates, the findings of that study indirectly show that central facial structures are the most heritable ones.[9,10,11]

A preliminary study performed on American twins 10 MZ and 11 same-sex DZ twins 5–12 years of age, found that only three out of nine extracted principal components showed statistically significant genetic contribution. These were related to the horizontal separation between the eyes, the length, breadth and projection of the nose, and the height and projection of the upper lip. Heritability estimates approached 1.0 and the authors explained this over-estimation by the small sample size, small number of landmarks and a very crude calculation of heritability. In our study, a significantly greater number of landmarks were used and therefore more principal components were extracted. Most of these components showed an evidence of statistically significant genetic contribution.

| ISSN: 2582-7219 | www.ijmrset.com | Impact Factor: 4.988

| Volume 4, Issue 5, May 2021 |

Various landmark-based traits (e.g.,distances, angles, ratios and principal components) as well as surface-based traits (e.g., geodesic distances and curvatures) can be used to seek genes responsible for normal facial morphological variation. Only a few genome-wide association studies have been conducted so far, which have revealed a relatively small number of associations between certain facial traits and single-nucleotide polymorphisms (SNPs). The findings are in agreement with our results on highly heritable traits, especially those associated with the morphology of the nose and lips. The SNPs found in the *PAX3* gene are associated with the nasal root morphology in Europeans and Latin Americans. In addition, multiple intronic SNPs in the *PRDM16* gene are associated with nose width and nose height [53]. A SNP close to the *C5orf50* gene is associated with the position of the landmark 'nasion'[53]. An intronic SNP in *TP63* gene is associated with the inter-ocular distance and a missense SNP in *COL17A1* is associated with the distance between the eyes and 'nasion' . Significant associations were recently found for three more nose-related traits: columella inclination (4q31), nose bridge breadth (6p21) and nose wing breadth (7p13 and 20p11) [54]. The rs642961 SNP in the *IRF6* gene (a known risk factor of non-syndromic cleft lip/palate) was found to strongly predict normal lip shape variation in Han Chinese females but not males .The finding that facial asymmetry is not genetically driven complies with the results of two studies, and In the first one, the amount of three-dimensional asymmetry was calculated after superimposing (registering) the original face with its mirror reflection and measuring the average distances between the two facial surfaces. There was no statistically significant difference in the amount of facial asymmetry between MZ and DZ twins . In the other study, the relationship between facial asymmetry (evaluated from nine mid-facial landmarks) and genetic variation at 102 SNP loci (recently associated with facial shape variation) was investigated. The authors failed to identify any SNP relating to either fluctuating or total asymmetry .[12]

Our finding on the mandibular ramus height is in agreement with a recent cephalometric study conducted on 141 adult Lithuanian twin pairs with completed mandibular growth and DNA confirmed zygosity . The authors estimated the significance of additive (A) and non-additive (D) genetic factors as well as shared (C) and unique environment (E) using a maximum likelihood genetic structural equation. Their results indicate that the shape and sagittal position of the mandible is under stronger genetic control than is its size and vertical relationship to cranial base. For linear measurements, such as mandibular body length, ramus width and ramus height, the best-fitting model was found to be ACE, indicating low genetic determination.The present study has certain advantages and limitations, which will be discussed below. One of the merits is a large sample size, which enabled us to use additional landmarks (in comparison to previous studies on facial morphology) and contributed to the validity of heritability estimates (without compromising statistical power). In addition, the sample was homogenous in terms of ethnicity and came from a well-designed population-based study. Finally, zygosity was confirmed by genetic testing, hence avoiding the misclassification of twins.

On the other hand, the limitations of the study were due to: 1) limitations of the classical twin design, 2) complexity of facial morphology and 3) inclusion of only female individuals in the sample. The observed facial morphological variation is a combination of: 1) genetic contribution (encompassing additive and non-additive genetic effects as well as gene interactions), 2) environmental contribution (consisting of common and unique environment), 3) gene-environment interaction and 4) measurement errors (due to scanning and landmarking).

The trait correlation between twins is the result of their genetic similarity and sharing common environment. However, the classical twin design does not allow for the determination of any gene-environment interactions. In addition, the scanning and landmarking errors (usually included in the unique environment component) may have some effect (generally negligible) on the heritability values of some traits, especially those that just reach statistical significance (*p*-values less than but close to 0.05). Genetic contributions calculated here are likely to be slightly overestimated because the model disregards gene-environment interactions. Furthermore, the imperfections of the classical twin model can lead to heritability values (h^2) over 1, which are demonstrated by the following results: the heritability (h^2) of sPC1 was evaluated as 1.015 (95%CI: 0.755 to 1.279), h^2 of the linear distance 'prn-men' was 1.002 (95%CI: 0.798 to 1.217) and h^2 of the 'prn-mex' distance was 1.048 (95%CI: 0.832 to 1.271). However, these do not diminish the importance of our findings. Instead of focusing on the actual value of an estimate, it is more important to reveal which facial traits demonstrate the most compelling evidence of heritability and use that knowledge for future genome-wide association studies of normal facial morphology.The second limitation is related to the complexity of studying facial morphology (as explained in the introductory paragraph of the discussion). The third limitation is due to inclusion of only females in the sample. This reflects the prevalence of females in the TwinsUK register [34]. In the data available to us, there were 15 males, which were excluded intentionally as they were too few for a separate statistical analysis; the inclusion of male individuals in a predominantly female sample could have affected the findings. This issue needs to be addressed in future studies. It would be interesting to look at a sufficiently large male twin sample and compare the results with

| ISSN: 2582-7219 | www.ijmrset.com | Impact Factor: 4.988

| Volume 4, Issue 5, May 2021 |

those for female twins. In addition, the sample we dealt with was ethnic specific and further research is needed on other populations, since environmental effects and gene alleles frequencies may differ between populations[13]

III. CONCLUSIONS

The study provides the estimates of genetic and environmental contributions to three groups of landmark-based facial traits in adult female twins. Based on the analysis of principal components, statistically significant genetic influence on the facial form was found to range from 38.8% to 78.5%, whereas that on the facial shape accounts for 30.5% to 84.8% of the total phenotypic variance. Genetic factors can explain more than 70% of the phenotypic variance in 7 principal components related to facial form, 5 principal components related to facial shape and 474 linear distances. These facial parameters represent: facial size (height), nose (width, prominence and height), lips prominence and inter-ocular distance. A few traits show potential dominant genetic influence, namely the prominence and height of the nose, the prominence of the lower lip in relation to the chin and length of the upper lip philtrum. The highly heritable traits are likely candidates for genome-wide association studies. Environmental contribution to facial variation is the greatest in the mandibular ramus height and horizontal facial asymmetry. This heritability study may inform future genetic studies which facial traits should be focused on.

REFERENCES

1. Prescott SL, Srinivasan R, Marchetto MC, Grishina I, Narvaiza I, Selleri L, et al. Enhancer divergence and cis-regulatory evolution in the human and chimp neural crest. *Cell*. 2015;163(1): 68–83. 10.1016/j.cell.2015.08.036 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
2. Claes P, Shriver MD. Establishing a multidisciplinary context for modeling 3D facial shape from DNA. *PLoS Genet*. 2014;10(11): e1004725 10.1371/journal.pgen.1004725 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
3. Smeets D, Claes P, Vandermeulen D, Clement JG. Objective 3D face recognition: Evolution, approaches and challenges. *Forensic Sci Int*. 2010;201(1–3): 125–132. 10.1016/j.forsciint.2010.03.023 [PubMed] [CrossRef] [Google Scholar]
4. Gunn DA, Rexbye H, Griffiths CE, Murray PG, Fereday A, Catt SD, et al. Why some women look young for their age. *PLoS One*. 2009;4(12): e8021 10.1371/journal.pone.0008021 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
5. Germine L, Russell R, Bronstad PM, Blokland GA, Smoller JW, Kwok H, et al. Individual aesthetic preferences for faces are shaped mostly by environments, not genes. *Curr Biol*. 2015;25(20): 2684–2689. 10.1016/j.cub.2015.08.048 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
6. Kim HJ, Im SW, Jargal G, Lee S, Yi JH, Park JY, et al. Heritabilities of facial measurements and their latent factors in Korean families. *Genomics Inform*. 2013;11(2): 83–92. 10.5808/GI.2013.11.2.83 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
7. Byers D. Components of phenotypic variance. *Nature Education*. 2008;1(1): 161. [Google Scholar]
8. Hallgrimsson B, Mio W, Marcucio RS, Spritz R. Let's face it–complex traits are just not that simple. *PLoS Genet*. 2014;10(11): e1004724 10.1371/journal.pgen.1004724 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
9. Lopes MS, Bastiaansen JW, Janss L, Knol EF, Bovenhuis H. Estimation of additive, dominance, and imprinting genetic variance using genomic data. *G3 (Bethesda)*. 2015;5(12): 2629–2637. [PMC free article] [PubMed] [Google Scholar]
10. Da Y, Wang C, Wang S, Hu G. Mixed model methods for genomic prediction and variance component estimation of additive and dominance effects using SNP markers. *PLoS One*. 2014;9(1): e87666 10.1371/journal.pone.0087666 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
11. Vinkhuyzen AA, Wray NR, Yang J, Goddard ME, Visscher PM. Estimation and partition of heritability in human populations using whole-genome analysis methods. *Annu Rev Genet*. 2013;47: 75–95. 10.1146/annurev-genet-111212-133258 [PMC free article] [PubMed] [CrossRef] [Google Scholar]
12. Miko I. Epistasis: Gene interaction and phenotype effects. *Nature Education*. 2008;1(1): 197. [Google Scholar]
13. Proffit WR, Fields HW, Sarver DM. Contemporary Orthodontics 5th ed. St. Louis, Missouri: Mosby Elsevier; 2012. [Google Scholar]