REVIEW ARTICLE

Twin Studies: Revealing the Genetic Basis of Malocclusion

Dolly P Patel, Bhaskar Gupta, Tanmay Sharma

ABSTRACT

The relative contribution of genes and the environment to the etiology of malocclusion has been a matter of controversy throughout the twentieth century and the first decace of twenty-first century. Twin studies provide important insights into how genetic and environmental factors contribute to variation in dental and craniofacial morphology. This review describes research models involving twins, apart from the traditional comparison of similarities in monozygotic (identical) and dizygotic (nonidentical) pairs, throws some light on zygosity determination, summarizes some landmark twin studies in orthodontics and future directions in dental research involving twins are outlined.

Keywords: Twins, Twin studies, Heredity, Zygosity determination, Monozygotic and Dizygotic.

How to cite this article: Patel DP, Gupta B, Sharma T. Twin Studies: Revealing the Genetic Basis of Malocclusion. J Orofac Res 2012;2(1):48-51.

Source of support: Nil

Conflict of interest: None declared

INTRODUCTION

The classical twin research design, involving comparisons of similarities in monozygotic (MZ) or identical pairs and dizygotic (DZ) or fraternal pairs, has enabled researchers to quantify the relative contributions of genetic (nature) and environmental (nurture) factors to variation in many human physical and behavioral features and disorders. Indeed, there have been several recent reviews emphasizing the value of twin studies in clarifying how genetic factors affect common dental problems, such as dental caries, periodontal diseases and malocclusion.[1] However, with recent advances in molecular biology and the outcome of the Human Genome Project, some may feel that twin studies have become less important or have lost their relevance altogether. This paper highlights research designs involving twins, other than the classical approach, that have the potential to further our understanding of the role of genes in malocclusion. The complex problem of malocclusion is still the most common reasons for people seeking dental treatment but their genetic bases remain unclear.

Why to Study Twins?

Twin studies are one of a family of designs in population genetics which aid the study of individual differences by highlighting the role of environmental and genetic causes on different traits. Twins are invaluable for studying these important questions because they disentangle the sharing of genes and environments.[2] If we observe that children in a family are more similar than might be expected by chance, this may reflect shared environmental influences common to members of family class, parenting styles, education, etc. but they will also reflect shared genes, inherited from parents.[2]

The twin design compares the similarity of monozygotic or identical twins, who share nearly 100% of their genetic polymorphisms, to that of dizygotic or fraternal twins, who share only 50% of their polymorphisms. By studying twins, researchers can then understand more about the role of genetic effects and the effects of shared and unique environment effects. In any trait, both gene and environment are involved and both of them collectively contribute to the ultimate phenotype and it is very difficult to make out their respective contribution, however twin studies can do so by comparing monozygotic with the dizygotic twins. This gives us the information about the relative contribution of genes and environment and how the two interact. Studying monozygotic (identical twins) alone does not solve our purpose as they have not only a similar genetic makeup but also a similar environment. On the other hand dizygotic (nonidentical twins) acts as a control, as they too share the same early environmental factors, but are not genetically alike. The researchers look for traits that show a greater similarity in identical twins than in nonidentical twins—this greater similarity must indicate a shared genetic basis for the trait. This is expressed as a percentage known as 'heritability'.

Zygosity Determination

Zygosity determination[3] mainly aims toward investigating, if the twins are dizygotic (arising from two zygotes) or monozygotic (arising from a single zygote), comparisons of physical features, for example body build, facial appearance, eye color and ear form can provide a reasonably accurate means of distinguishing between MZ and DZ twin pairs, mistakes can still be made, another way is by the use of a questionnaire method which yields an accuracy of about 94%, but this method also has its limitations.[3] Following the discovery of blood groups and enzyme polymorphisms, it became possible to determine whether twins were monozygotic or not with relatively high probability. More recently with advances in DNA technology, a small number of highly polymorphic DNA markers can be used to establish zygosity with very high probability.[3] Rather than obtaining blood samples to extract DNA, it is now possible to isolate DNA from cheek cells obtained using buccal swabs.

Different Types of Twin Designs

The MZ Co-twin Design[2]

A powerful approach to clarify the roles of genetic and environmental influences on normal features, or susceptibility to diseases, involves studying MZ twin pairs who show different phenotypic expressions for a particular trait or disease under investigation.[2]

Alternatively, researchers can manipulate the environment, so that each member of a twin pair is exposed to different environmental conditions. Monozygotic twin pairs are matched perfectly for age and sex and, as they share the same genes except in very rare circumstances, any differences between them will normally reflect environmental effects.

Twins Reared Apart[2]

The ongoing studies of Tom Bouchard et al in Minnesota involve examination of MZ twin pairs who were separated at birth and then reared apart in different surroundings. This model overcomes one of the often mentioned limitations of traditional twin studies – that MZ twin pairs may be more similar than DZ pairs for particular features, not because they share more genes, but because they share more of the environmental factors that influence the trait in question.[2]

Opposite-sexed DZ Twins[2]

If zygosity and sex are considered, there are five main groups of twin pairs that may be studied: MZ female pairs, MZ male pairs, DZ female pairs, DZ male pairs and DZ male-female pairs. Comparison of correlations between same-sex DZ pairs and opposite-sexed DZ pairs provide an opportunity to investigate whether primary or secondary sexual characteristics are affected by diffusion of hormones *in utero*.[2]

The Twin Half-sib Model[2]

This model involves making comparisons between the offspring of MZ pairs and their partners. The advantage of this model is that the children of MZ pairs who are born to different mothers are themselves genetically half-siblings.[2]

Because MZ twin pairs have identical genotypes, their children will share, on average, half their genes whether they have the same twin as a parent or not. Monozygotic pairs, their spouses and their offspring share different levels of genetic relationship, ranging from zero for the spouses of twins in the absence of assortative mating, to unity for the twins themselves.[2]

Some Landmark Studies in Orthodontics

The Pioneer

Galton in 1889[4] was the pioneer and first to discuss the merits of twin investigations. Comparisons of the between twin pair differences yielded relative assessments of the influence of heredity and environment, if the twin pairs were raised in relatively identical environments.

Growth and Development

Garn, Lewis and Poleacheek[5]studied dental developmental stages for mandibular 1st and 2nd molars in two sets of triplets and suggested that dental development is for the most part genetically determined. Picacintini[6] applied the co-twin study method on six sets of same sex triplets in whom the zygosity had previously been determined to a high degree of probability. He concluded that combined increment growth of maxilla and mandible of MZ co-twin show significantly smaller intrapair differences as compared to that of dizygotic co-twins. This proves the role of heredity in governing the growth of these individual bones.

Craniofacial Complex

Kraus et al[7] in a twin study found out almost perfect concordance was found in the craniofacial complex in the MZ triples whereas only a low degree of concordance was found in DZ triplets. They concluded that the morphology of all the bones of the craniofacial complex was under rigid control of the hereditary factors. Horowitz, Osborne and De George[8] did a cephalometric study of craniofacial variation in 56 twin pairs and concluded that there is a highly significant genetic variation in anterior cranial base, mandibular body length and lower face height. They also stated that the upper face height is the more stable element in the facial profiles as it does not contribute greatly to the genetic variability of the face as a whole. Lower face height demonstrates a large degree of hereditary variability.

Tooth Size/Occlusal Variations

Detlefsen[9] stated that tooth shape and size and arch shape and size, were largely determined by hereditary constitutional factors. Lundstrom[10] studied tooth size and occlusion in twins. He concluded that heredity is an important factor in malocclusion. In class I cases, he found 87.3% of MZ twins and 84.6% of DZ twins and in class II, 67.7% of MZ twins and 10% of DZ twins having concordance. Horowitz et al[11] carried out a study on 54 pairs of like sexed adult twins. They studied the tooth dimension of maxillary and mandibular permanent anterior teeth and found strong genetic component of variability of the four maxillary and four mandibular incisor teeth. The canine teeth demonstrated relatively low hereditary component of variability. The differences between the monozygotic and dizygotic twin pairs were statistically highly significant for all the teeth. Corruccini and Potter[12] studied occlusal variation in sample of 32 MZ and 28 DZ twins pairs. Teeth displacement and crossbite were the most significantly heritable criteria of occlusion. Significant heritability of overjet, buccal segment relation, overbite, tooth rotation/ displacement could not be documented. These results demonstrated a considerably increased environmental component of variance in occlusion.

Arch Shape and Palatal Morphology

Goldberg[13] stated for the arch form, that with a few exceptions, unilateral difference between twins were less than bilateral differences between the arch sides of the same twin. Shapiro et al[14] in his study on 102 pairs of twins found that there is greatest influence of genetic factors on palatal height. For palatal length, greatest contributions from environmental factors determined its variability. Riquelme and Green [15]studied palatal width, length and height in 32 pairs of like- sexed Caucasian twins. The palatal width and height and length dimensions revealed a significant component of hereditary variability. Thus, heredity is suggested as strong etiological factor in malocclusions where palatal dimensions are involved. No significant sex differences were found to exist between any of the mean intrapair variances of the MZ and DZ twins.

DISCUSSION

Skeletal jaw discrepancies and malocclusion of genetic origin can be successfully treated orthodontically, except in extreme cases where surgical intervention is required. This is because it is possible to modify the direction of dentofacial growth using orthodontic appliances and therefore change or forestall morphogenetic abnormalities. Orthodontic correction of a malocclusion is in effect altering the phenotypic expression of a particular morphogenetic pattern. The degree to which this can be successfully achieved depends on: (1) The relative contribution of each factor to the existing problem. (2) The extent to which skeletal pattern can be influenced by orthodontic and orthopedic appliances.

In clinical orthodontics it must be appreciated that each malocclusion occupies its own distinctive slot in the genetic /environmental spectrum and therefore, the diagnostic goal is to determine the relative contribution of genetics and the environment. The greater the genetic component, the worse the prognosis for a successful outcome by means of orthodontic intervention. The difficulty, of course, is that it is seldom possible to determine the precise contribution from hereditary and environmental factors in a particular case.

In dentofacial structure and malocclusion are primarily genetic, e.g. severe mandibular prognathism or endogenous tongue thrust, the treatment will either be palliative or surgical. The search for a solution would ultimately focus on delineating the responsible genes. Conversely, if components of dentofacial structure and malocclusion have trivial heritabilities, then the search needs to be directed at environmental factors including malocclusion during growth and development. The dentition in particular provides a very useful model system to investigate developmental mechanisms, given that teeth begin to develop soon after conception and then form in an orderly sequence over an extended period of time. Once formed, teeth are not re-modelled, so they can be used to make retrospective assessment of how developmental disturbances affect morphogenetic processes both pre- and postnatally. Multi-disciplinary studies of twins, with input from orthodontists, molecular geneticists and twin researchers, hold great promise for the future, not only in clarifying how genetic factors contribute to oral diseases and disorders, but also in unraveling the mysteries of how our facial symmetry is determined.

CONCLUSION

With the advances that have occurred in both human quantitative genetics and molecular biology over the past decade, we are now in a position to build a more complete understanding of how our genes and the environment contribute to a range of dental diseases and malocclusions that display multifactorial etiology.[1] Far from being out-dated, well-designed twin studies have a central role to play in this new era. They can throw new light on how genes influence developmental mechanisms.

Our challenge as dental researchers and orthodontists will be to translate the knowledge we will soon have about the genetic basis of disorders affecting the oral hard and soft tissues into improved preventive and treatment strategies for the community at large.

Observations by orthodontists of twin pairs presenting at private or public dental clinics can also provide valuable insights into how genes and the environment interact during development. Finally, we can say that twin studies are here to stay and they will keep throwing light on the relative influence of genetics and environmental factors in the etiology of malocclusion.

REFERENCES

1. Mossey PA. The heritability of malocclusion part II; British Journal of Orthodontics 1999;26:195-203.
2. Townsend GC, Richards L, Hughes T. The value of twins in dental research. Aust Dent J 2003;48(2):82-88.
3. The genetic contribution to orthodontic root resorption: A retrospective twin study, Ngan, Daniel; Master Thesis. University of Sydney.
4. Galton Francis; Natural Inheritance, London (1st ed) 1889.
5. Garn S Lewis, Polecheck D. Sibling similarities in dental development. J Dent Res 1960;39:170-75.
6. Piacentini FD. An investigation of the genetic control of the bones of the human craniofacial complex. Am J Orthod 1962; 40:67-75.
7. Kraus, Wise, Trai RM. Heredity and the craniofacial complex. Am J Orthod 1959;453(173):217-22.
8. Horowitz SL, Osborne RN, Degeorge FV. A cephalometric study of craniofacial variation in adult twins. Angle orthod 1960;30(1): 23-36.
9. Detlefsen JA. Intrinsic hereditary factors vs extrinsic environment factors in determination of tools and oral peculiarities. J Dent Res 1928;8:419-20.
10. Lundstrom A. Tooth size and occlusion in twins, 1948. S Kargen Besle NY cited from Krogmon and Sassouni. A syllabus in roentgenographic cophalometry 1957.
11. Horowitz, Osborne, Degeorge. Hereditary factors in tooth dimensions: A study of anterior teeth of twins. Angle Orthod 1958;28(2):87-92.
12. Corruccini S Potter. Genetic analysis of occlusal variation in twins. Am J Orthod 1980;8:140-45.
13. Goldberg S. Biometrics of identical twins from dental point of view. J Dent Res 1929;9:363-69.
14. Shapiro BL. A twin study of palatal dimensions. Angle Orthod 1969;3:39-45.
15. Riquelme, Green: Palatal width, height and length in human twins. Angle Orthod 1970;39:71-79.

ABOUT THE AUTHORS

Dolly P Patel

Professor and Head, Department of Orthodontics and Dentofacial Orthopedics, Government Dental College and Hospital, Ahmedabad Gujarat, India

Bhaskar Gupta (Corresponding Author)

Senior Lecturer, Department of Orthodontics and Dentofacial Orthopedics, Mahatma Gandhi Dental College and Hospital, Jaipur, Rajasthan, India, Phone: +91-99291-66610
e-mail: bg_bhaskargupta@yahoo.co.in

Tanmay Sharma

Senior Lecturer, Department of Orthodontics and Dentofacial Orthopedics, Mahatma Gandhi Dental College and Hospital, Jaipur Rajasthan, India