Statistical Shape Analysis and Usage in Medical Sciences: Review

İstatistiksel Şekil Analizi ve Tıp Bilim Dallarında Kullanımı

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ABSTRACT Most of the studies in medicine are releated with the examination of geometrical properties of an organ or organism. Commonly, quantitative or qualitative data sets in the statistical analysis consisted of measuring values, today's an organ or organism's appearance or shape began to be used as input data by the development of imaging techniques. In recent years, it is observed that there has been considerable interest in the statistical analysis of shape. Statistical shape analysis is a geometrical analysis of the statistics measured from sets of shapes that determines the features of similar shapes or of different groups comprising similar shapes. Distance between shapes, mean shape and shape variation can be predicted and obtained using statistical shape analysis. Two groups comparison, asymmetry, growth and allometry studies can be given as example for the most used statistical shape analysis applications. Thin Plate Spline analysis, Procrustes analysis and Euclidean Distance Matrix Analysis can be given as examples of frequently used methods in statistical shape analysis. Examining shape differences between groups, shape deformation, examining asymmetry, classification, growth and allometry studies can be given as examples of statistical shape analysis applications in medicine. The last two decades, a growing interest in the use of statistical shape analysis has been observed in the field of medicine. The main reasons for statistical shape analysis is used widely in medicine are advances in imaging technology, and tendency to investigate the effects of diseases and the environmental factors effects on the structure of the organ or organism.

Key Words: Statistical shape analysis; landmark; TPS; EDMA; procrustes analysis; asymmetry; classification; growth; allometry

ÖZET Tıp alanında yapılan pek çok çalışmada, bir organın ya da organizmanın geometrik özellikleri üzerinde çalışılmaktadır. Yaygın olarak istatistiksel analizlerde veri setleri kantitatif veya kalitatif ölçüm değerlerinden oluşurken, günümüzde görüntüleme tekniklerindeki gelişmeyle bir organın veya organizmanın görüntüsü veya şekli de veri girdisi olarak kullanılmaya başlamıştır. Son yıllarda, şeklin istatistiksel analizine olan ilginin daha da fazla artmış olduğu gözlenmektedir. İstatistiksel şekil analizi, benzer şekillerin ya da benzer şekillerden oluşan farklı grupların özelliklerini tanımlamak amacıyla ölçülen istatistiklere ait şekiller kümesinin geometrik analizidir. İstatistiksel şekil analizi kullanılarak şekiller arasındaki uzaklığın ölçüsü elde edilebilmekte, ortalama şekil ve şekil değişkenliği tahmin edilebilmektedir. Şekil verilerinin kullanıldığı çalışmalara; iki örneklemin karşılaştırılması, asimetri, büyüme ve allometri çalışmaları örnek olarak verilebilir. İstatistiksel şekil analizinde sıklıkla kullanılan yöntemler ince levha eğrileri analizi, Procrustes analizi ve Öklit uzaklık matrisi analizi olarak sayılabilir. Tıp alanında yapılan istatistiksel şekil analizi uygulamalarına gruplar arasında şekil farklılıklarının incelenmesi, şekil deformasyonunun incelenmesi, asimetrinin incelenmesi, şekillerin sınıflandırılma çalışmaları, büyüme çalışmaları ve allometri çalışmaları örnek olarak verilebilir. Son yirmi yılda istatistiksel şekil analizinin tıp alanında kullanımında artan bir ilginin olduğu gözlenmektedir. İstatistiksel şekil analizinin tıp alanında yaygın olarak kullanılmaya başlanmasının başlıca sebepleri olarak görüntüleme teknolojisindeki ilerlemeler, hastalıkların ve çevresel faktörlerin organ veya organizma yapılarına olan etkilerin araştırılması eğilimi sayılabilir.

Anahtar Kelimeler: İstatistiksel şekil analizi; landmark; ince levha eğrileri; öklit uzaklık matrisi analizi; procrustes analizi; asimetri; sınıflandırma; büyüme; allometri

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The statistical shape analysis has recently become more important in the medical and biological sciences. Most of the studies in medicine are releated with the examination of geometrical properties of an organ or organism. Commonly, quantitative or qualitative data sets in the statistical analysis consisted of measuring values, today's an organ or organism's appearance or shape began to be used as input data by the development of imaging techniques.

Shape analysis is of great interest in a wide variety of disiplines. Some specific applications are seen in biology, medicine, image analysis, archaeology, geography, geology, agriculture and genetics.[1] Statistical shape analysis is a relatively new method for biological and medical research. Therefore, in this review it is aimed to give information about the development of shape analysis, mostly used methods and some examples for application in medical research.

In recent years, it is observed that there has been considerable interest in the statistical analysis of shape.[2] Statistical shape analysis is a geometrical analysis of the statistics measured from sets of shapes that determines the features of similar shapes or of different groups comprising similar shapes. Distance between shapes, mean shape and shape variation can be predicted and obtained using statistical shape analysis.[1] Two groups comparison, asymmetry, growth and allometry studies can be given as example for the most used statistical shape analysis applications.[3-5]

In the traditional methods which are used in shape analysis, linear distance, angles and ratios of these measurements are used in multivariate statistical analyses.[6] In 1926, Pearson studied on a "coefficient of racial likeness" which is a measure of similarity between skulls based on length measurements between the landmarks.[7] In the 1960's and 1970's, biometricians began using all of the multivariate statistical methods to describe patterns of shape variation within and among groups.[8]

After the 1980's, developments in the field of statistical shape analysis allowed us to work on two or more dimensional landmark coordinates of individuals. Including these coordinates directly as variables to the analysis, can be possible by removing the effects of position, direction and scaling.[1] So it has been possible to work on directly the geometric object itself, instead of the quantities which are obtained from the organisms.

Morphometrics is a field concerned with studying variation and change in the form (size and shape) of organisms and morphometrics can also be defined as the quantitative analysis of biological form.[9,10] The field has developed rapidly over the last two decades to the extent that we now distinguish between traditional morphometrics and the more recent geometric morphometrics.[10] Traditional morphometrics consisted of applying multivariate statistical analyses to sets of traditional measurements such as angle, distance measured between points which have biological and anatomical meaning and to be used to define a shape called landmarks. Geometric morphometrics is defined as a field that involves statistical shape analysis applications based on landmarks.

The field of geometric morphometrics represents an new paradigm for the statistical study of variation and covariation of the shapes of biological structures.[11,12] Complete retention of geometric information from data collection through analysis and visualization is the reason coordinate-based approaches are generally referred to as geometric morphometrics.[13] Additionally, in the way of determining amount of the difference between shapes, the elucidation of the properties of multidimensional shape space defined by this metric are the fundimental advantages of geometric morphometrics over traditional approaches.[9,11,12]

The fundamental advances of geometric morphometrics over traditional approaches (multivariate morphometric techniques) are in the development of powerful statistical methods based on models that are used for examining the shape variation of all configurations which correspond to morphologic landmark locations. [9,11,12] In many biological or biomedical researches, the most efficient way to analyze the forms of whole biological organs or organisms is by registering landmarks.[13]

LANDMARK

A landmark is a point in two- or three-dimensional space that corresponds to the position of a particular feature on an object of interest[14] (Figure 1). Each landmark has Cartesian coordinates as ordered pairs in two dimensional plane or ordered triplet in three dimensional space.

Landmark coordinate data, for both computational and statistical purposes, are most conveniently represented as a matrix. The set of landmarks on a particular object is named as a configuration. Configuration matrix is the k×m matrix of Cartesian coordinates of the k landmarks in m dimension. The configuration space is the space of all possible landmark coordinates.[1] Configuration corresponds to a single point in this space.

In general case, the landmark approach implies some loss of information about the shape, in such a way that the transformation taking shapes to landmarks becomes degenerated and no longer invertible, consequently defining an approximate representation. As a matter of fact, it is observed that the original shape is always perfectly represented when all its infinite points are taken into account as landmarks.[15]

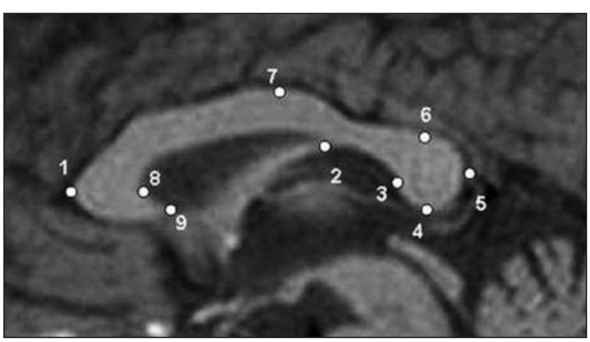

FIGURE 1: Landmarks that were used in statistical shape analysis.[3] (Ozdemir et al. marked landmarks for comparing shape of corpus callosum according to gender)

LANDMARK TYPES

Dryden ve Mardia has classified landmarks into three groups as anatomical, mathematical and pseudo landmarks:[1]

a. Anatomical Landmark: It is a point assigned by an expert that corresponds between organisms in some biologically meaningful way. Anotomical landmarks designate parts of an organism that corrspond in terms of biological derivation and these parts are called homologous. Anatomical landmarks that are found at the joins of tissues/bones are usually the easiest and most reliable to locate. [1]

b. Mathematical landmarks: They are points located on an object according to some mathematical or geometrical property of the figüre. The use of mathematical landmarks is particularly useful in automatic recognition and analysis. [1]

c. Pseudo landmarks: They are constructed points on an organism, located either around the outline or in between anatomical or mathematical landmarks. [1]

Another classification of the landmarks is performed by Lele and Richestmeier.[14] Lele and Richestmeier classified the landmarks collected from biological objects intothre e general groups as traditional landmarks, fuzzy landmarks and constructed landmarks.[14]

a. Traditional landmarks: They are precisely delineated points corresponding to the location of features of some biological significance. There are two classes of traditional landmarks: those whose definition is not dependent upon a coordinate system, and those whose definition is tied to a particular orientation or a coordinate system.[14]

b. Fuzzy landmarks: A fuzzy landmark is a point corresponding to a biological structure that is precisely delineated and that corresponds to a locus of some biological significance, but that occupies an area that is larger than a single point in the observer's reference system. The definition of a fuzzy landmark usually includes a positional reference (e.g., centroid, apex) that corresponds with a place on the feature that best represents it as a point. Fuzzy landmarks become necessary when portions of the form under study are made up of relatively large, smooth surfaces or features and do not include sufficient traditional landmarks. Due to their nature, placement of fuzzy landmarks on an object may require multiple data collection episodes with the average of the coordinates from several data collection episodes being used for analysis.[14]

c. Constructed landmarks: Constructed landmarks are points corresponding to locations that are defined using a combination of traditional landmarks and geometric information. These landmarks are located to the surfaces of interest that are void of traditional landmarks and fuzzy landmarks.[14]

LANDMARK RELIABILITY

To locate landmarks in shape analysis, it is important to understand the various sources of error that can affect what is measured. A lack of precision results in variability among repeated measures of the same specimen and has two components: a) Observer error in locating landmarks. b) Instrument error in identifying landmark coordinates.[14,16] For this reason landmark reliability should be examined.

In certain situations it may be necessary to study using more than one rater and to analyze data obtained in this way. In such situations, the reliability of landmark locations should be examined with a sub-sample and, if the reliability is sufficient, the data collection stage should begin. If the reliability is sufficient, it means that the raters are in agreement on the landmark locations.[17]

In the case of a single rater, which is the ideal situation, if it is possible with all the subjects in the study, or if it is impossible with only one sub-sample, the reliability of the landmark locations using another experienced rater or raters should be examined on the same specimens.[17]

In the case of a single rater, another reliability examination is performed with repeated landmark locations for the same rater, and this will give an indication of consistency for the rater's landmark locations.[17]

If the inter-rater reliability is low, the error sources should be checked. Also related with the raters, their knowlegde, experience and their points of view should be examined.[19] If the landmark locations are being made on the image, as well as the rater examination, image resolution should also be examined.[17-19]

LANDMARK BASED APPROACH

There exist different morphometric algorithms for analysis of landmark data. Two general classes of morphometric methods can be used to analyze landmark coordinate data: Coordinate-based methods and coordinate-free methods. In coordinate-based methods, the choice of coordinate system is arbitrary: Results can be rotated to any coordinate system without change in or loss of information, and a coordinate system is a necessary part of the analytical machinery. Coordinate-based methods measure form difference as a deformation from a reference to a target form, or as the fit resulting from the superimposition of two forms. Coordinate-free methods analyze form difference without reference to a coordinate system.[20]

COMMON METHODS USED IN STATISTICAL SHAPE ANALYSIS

Thin Plate Spline analysis, Procrustes analysis and Euclidean Distance Matrix Analysis can be given as examples of frequently used methods in statistical shape analysis.

THIN PLATE SPLINE ANALYSIS -TPS

Using the adaptation of TPS in morphometric field was offered by Bookstein.[21,22] TPS models the 'biological homology' of landmark pairs. The TPS function, known as the 'bending energy' is visualized as an infinitely thin metal sheet draped over a set of landmarks, extending to infinity in all di-

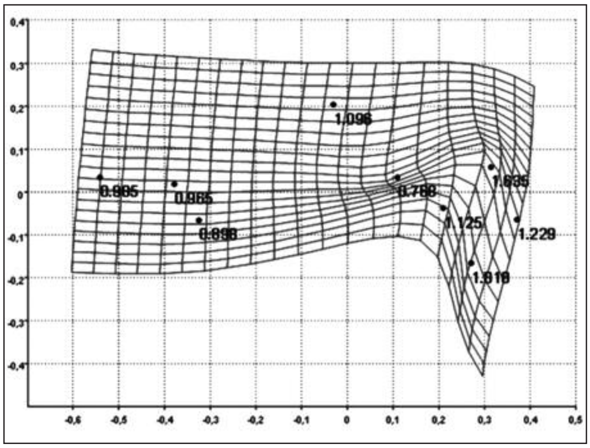

FIGURE 2: Thin-plate spline demonstrating shape deformation from male to female mean shape of corpus callosum. Expansion factors at the landmarks are shown numerically (expansion factors larger than one).[3]

rections. The height over each landmark is equal to the differences between the forms. If the two forms are identical, then the bending energy is zero, and the plate is flat. The magniude and location of bending energy can be identified depending on the size and position of the deformation of the plate[23] (Figure 2).

PROCRUSTES ANALYSIS

Procrustes analysis is known in shape analysis as the approach that obtains the minimum sum of squared differences between the landmarks. Procrustes analysis involves matching configurations with similarity transformations (translation, rotation, scaling) to be as close as possible according to Euclidean distance, using least squares techniques.[1]

Procrustes analysis has two types called Generalized Procrustes Analysis (GPA) and Ordinary Procrustes Analysis (OPA). GPA involves matching of minimum two configurations using the similarity tranformations, where OPA involves matching of two configurations using the similarity tranformations. OPA is not symmetrical in the ordering of the objects, whereas GPA is invariant under re-orderings of the objects.[1]

Procrustes mean shape is obtained by taking arithmetic mean of configurations that are superimposed by using Procrustes method.[1] Additionally, Procrustes mean shape is the primary eigenvector of sum of squares and product matrices of standardized data.[20]

Procrustes analysis was devoloped for factor analysis, afterwards it became a useful tool for shape and image analysis by using in multidimensional scaling.[24] Procrustes analysis is used in shape analysis in order to estimate average shape of dataset and to compare shapes in dataset.[1]

EUCLIDEAN DISTANCE MATRIX ANALYSIS

In Euclidean distance matrix analysis (EDMA), form of an object is defined to be that characteristic which remains invariant under translation, rotation, and reflection of the object. Since the form of an object is invariant under translation, rotation, and reflection, an approach for comparing forms should start with a representation which is invariant under these operations. Such a representation for landmark data is given by the Euclidean distance matrix analysis (EDMA).[25]

STATISTICAL SHAPE ANALYSIS APPLICATION IN MEDICINE

Some of the studies that are performed commonly in medicine and biology are related to how shape of an organ or organism's shape is affected by disease; how shape is related to covariates such as sex, age or environmental conditions; comparision of shapes; how to discriminate and classify using shape; how to describe shape variability; how shape changes during growth; and how shape is related to size.[1] Two-dimensional or three-dimensional shape data are evaluated by statistical shape analysis or image analysis in medicine and biology. Application examples that have been performed with statistical shape analysis in medicine fields are given below with headlines:

STUDIES ABOUT EXAMINING SHAPE DIFFERENCES BETWEEN GROUPS

Ercan et al.[26] study is about shape differences of nose according to gender. Colak et al.'s[5] study is about 2-dimensional images and, Sonat et al.'s[27]

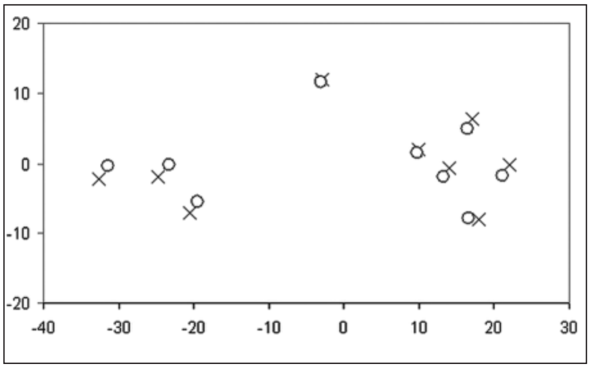

FIGURE 3: Procrustes mean shapes for corpus callosum images of Behcet patients and controls (Cases: X, Controls: O).[5]

study is about rat hipocampal slides. These studies can be given as an example to investigate the difference in organisms created by diseases. Ercan et al.[26] examined nose shape differences according to gender in Turkish population in their study. Colak et al.[5] stated that corpus callosum shape of patient who have Behcet disease was different from healty person in their study (Figure 3). Sonat et al.[27] stated that shape of epileptic rat hipocampal slides was different from non-epileptic rat.

STUDIES ABOUT SHAPE DEFORMATION

These are the studies which the shape deformations from shape of a single subject to another shape or from mean shape to another mean shape could be examined. The studies of Ozdemir et al.[3] and Sonat et al.[27] can be given as examples of shape deformation studies. In their study, Ozdemir et al.[3] have determined shape deformations from men to women of corpus callosum by the TPS method, using average shapes obtained by Procrustes analysis and Sonat et al.[27] have illustrated the hippocampal shape deformation due to epilepsy (Figure 2).

STUDIES ABOUT EXAMINING ASYMMETRY

The studies of Ferrario et al.[28] Ercan et al.[4] and Claes et al.[29] can be given as examples of asymmetry studies. In their study, Ferrario et al.[28] evaluated human facial asymmetry in young healty adults and reported that the mean faces of males and females were significantly asymmetric. Ercan et al.[4] examined facial asymmetry in males and females in Turkish population and showed that asymmetry was greater in females (Figure 4, 5). Claes et al.[29] assessed facial asymmetry in healthy

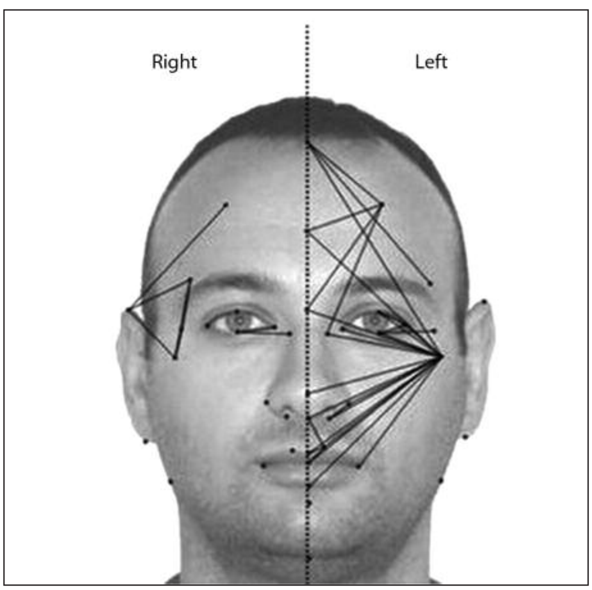

FIGURE 4: Asymmetry in males: the lines show bigger inter-landmark distances than on the other side.[4]

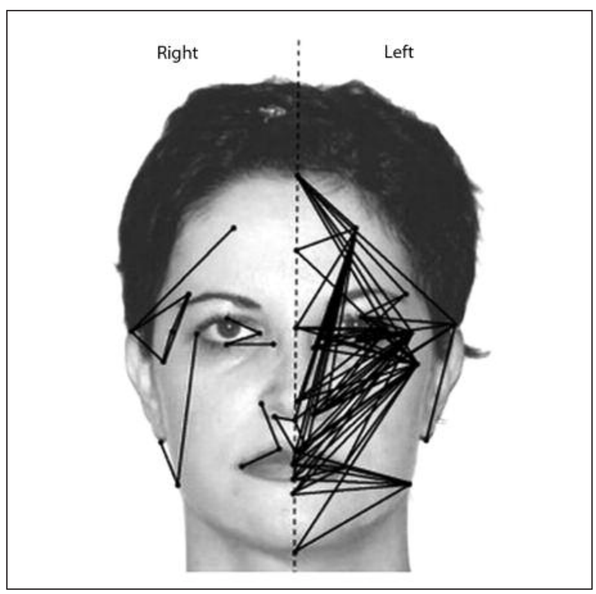

FIGURE 4: Asymmetry in females: the lines show bigger inter-landmark distances than on the other side.[4]

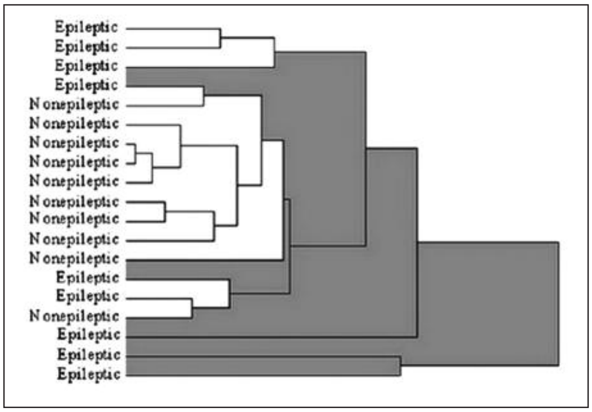

FIGURE 6: Dendogram indicating classification of cases regarding levels of Procrustes dissimilarity.[27]

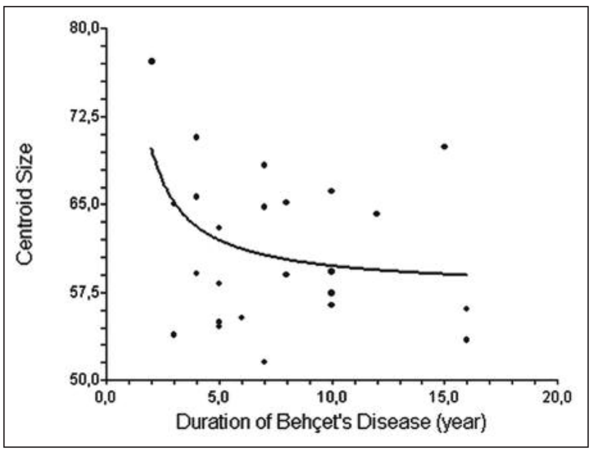

FIGURE 7: The relationship between corpus callosum size and the duration of Behcet's disease in Behcet patients.[5]

GROWTH STUDIES

Growth is the composite of geometric changes in biological structure occurring through ontogenetic time.[14] The relation between time and size is examined usually by nonlinear models.[31] Colak et al.[5] investigated the relationship between size of the corpus callosum shape and the disease duration in Behcet patients and reported that a decrease was occurred in the corpus callosum size of the Behcet patients as the duration of disease was increased (Figure 7).

ALLOMETRY STUDIES

Allometry is an association between shape and size.[32] The studies of Lynch et al.[33] Rosas and Baster,[34] Gonzalez et al.[35] should be given as examples of allometry studies.

Lynch et al.[33] investigated craniofacial allometry in homo in their study which they had evaluated craniofacial variation in homo sapiens and pan troglodytes. They found that there was a significant but minor relationship between craniofacial size and shape, and 14.9% of the variation in shape variation could be explained by centroid size in their data set.[33] Rosas and Baster's[34] investigated the size and shape relationship in the human craniofacial complex and reported that, size had significant influences on shape. They indicated that the influence of centroid size on shape (allometry) revealed a shift in the proportions of the

individuals and individuals with disordered facial growth, and reported that asymmetry in males was more extensive and of a greater magnitude than in females.

CLASSIFICATION STUDIES

Ozdemir et al.[30] and Sonat et al.[27] studies can be given as examples of classification of units according to shape similarities. Ozdemir et al.[30] classified late Byzantine and Modern period human cranium shapes in their study. Sonat et al.[27] classified rat hipocampus shapes with cluster analysis for examining epilepsy effects on hipocampus in their study (Figure 6).

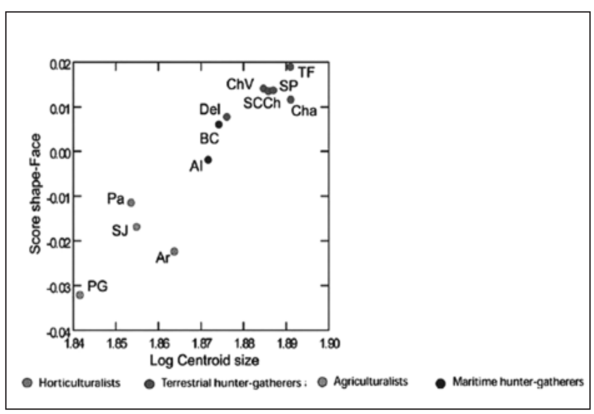

FIGURE 8: Evolutionary allometry of South American human populations. The shape scores, obtained from the multivariate regression of superimposed Procrustes coordinates on log centroid size, as a function of size (for the face).[35]

neurocranium and the viscerocranium, with a marked allometric variation of the lower face.[34] Gonzalez et al.[35] evaluated the influence of size variation on craniofacial shape disparity among human populations from South America and showed that size accounts for a significant amount of shape variation among populations for the vault and face but not for the base, suggesting that the three modules did not exhibit a uniform response to changes in overall growth. (Figure 8).

CONCLUSION

The last two decades, a growing interest in the use of statistical shape analysis has been observed in the field of medicine. The main reasons for usage of statistical shape analysis widely in medicine are advances in imaging technology, and tendency to investigate the effects of diseases and the environmental factors effects on the structure of the organ or organism.

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