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Fluctuating asymmetry of the normal facial skeleton

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Abstract

The purpose of this study was to produce reliable estimations of fluctuating facial asymmetry in a normal population. Fifty-four computed tomography (CT) facial models of average-looking and symmetrical Chinese subjects with a class I occlusion were used in this study. Eleven midline landmarks and 12 pairs of bilateral landmarks were digitized. The repeatability of the landmark digitization was first evaluated. A Procrustes analysis was then used to measure the fluctuating asymmetry of each CT model, after all of the models had been scaled to the average face size of

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Ethical approval

Exempted study, determined by Houston Methodist Research Institute IRB.

Patient consent

Not required.

Competing interests

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the study sample. A principal component analysis was finally used to establish the direction of the fluctuating asymmetries. The results showed that there was excellent absolute agreement among the three repeated measurements. The mean fluctuating asymmetry of the average-size face varied at each anthropometric landmark site, ranging from 1.0 mm to 2.8 mm. At the 95% upper limit, the asymmetries ranged from 2.2 mm to 5.7 mm. Most of the asymmetry of the midline structures was mediolateral, while the asymmetry of the bilateral landmarks was more equally distributed. These values are for the average face. People with larger faces will have higher values, while subjects with smaller faces will have lower values.

Keywords

fluctuating asymmetry; normal facial skeleton; computed tomography; Procrustes analysis; principal component analysis

Introduction

The human face has bilateral symmetry, i.e. it can be divided in two, each part being the mirror image of the other^{1,2}. Like in other biological forms, this symmetry is approximate³⁻⁵. Normal populations have small random variations in symmetry, called fluctuating asymmetry^{2,6}. Certain individuals, however, have an asymmetric deformity, a condition where the asymmetry is so large that it is no longer considered normal⁷.

There is at present no reliable cephalometric method to quantify asymmetric deformity. A logical way of measuring facial asymmetry is to compare the right and left facial halves after the halves have been superimposed. This superimposition requires four steps. In the first step, the face is split along the boundary outlined by all midline features. In the second step, one of the facial halves is flipped to create a mirror-image. In the third step, the mirror-image is moved until it is situated in the middle of the opposite half. In the fourth step, the moved image is rotated (about its center) until the difference between the two facial halves is minimal⁸.

The above method works very well when the face has minor asymmetries, but it is inaccurate when the asymmetries are large. The problem is that the asymmetric regions of the face can skew the superimposition⁹. This problem can be avoided by assigning different weights to the different facial regions during the superimposition. For example, a facial region that is very asymmetric can be given low importance, while other more symmetric regions can be valued higher. To calculate these weights, however, one needs to know the fluctuating asymmetries of the normal population. Unfortunately, current available data are unreliable^{1,10-19}.

Prior studies of fluctuating facial asymmetry can be divided into two groups: old studies done on cephalograms and newer studies done on computed tomography (CT) scans. Old studies measured the skeletal asymmetries on cephalograms – radiographs that are taken with the head lined up in a cephalostat^{10,11,13,15,17,19}. Unfortunately, the cephalostat places both external auditory canals in the same vertical and horizontal position causing an artificial alignment. This alignment minimizes any asymmetry that may be present near the ear, while

maximizing the asymmetry of distal structures. Perhaps because of this phenomenon, some studies have shown that the cranial base is more symmetric than the rest of the face^{13,14}. However, most conditions that produce facial asymmetry affect the mandibular condyles, the cranial base, or both (e.g., hemifacial macrosomia, unilateral condylar hyperplasia, and plagiocephaly).

Newer studies done on CT scans have avoided a cephalostat and have provided three-dimensional (3D) information; however the data are skewed for another reason: they measure the asymmetry using Cartesian coordinate systems^{16,18}. Cartesian systems can be used to measure asymmetry, but only if they contain the subjects' real planes of symmetry. Finding these planes, however, is difficult. In the prior CT studies, the investigators erected their Cartesian frames using a few cephalometric landmarks^{13,15–18}. This approach is flawed, because criss-crossing a frame of reference through some landmarks makes these landmarks symmetric, even if they are not. Also because, in any face, one can build hundreds of different frames depending on what cephalometric points are picked. Furthermore, each different frame of reference will yield a different study result⁹.

It is clinically important in the treatment of patients with asymmetry to establish a threshold separating the normal subjects with fluctuating asymmetry (i.e., clinical symmetry) from the abnormal subjects with obvious asymmetry. However, in order to accomplish this, reliable estimations of fluctuating facial asymmetry in a normal population need to be established first. Such new estimations will provide important information to any investigator trying to develop a diagnostic test for facial asymmetry and convey to any clinician the size, distribution, and direction of normal facial asymmetry in future studies.

Materials and methods

Subjects

A collection of 54 CT facial models of normal-looking and symmetrical Chinese subjects was obtained from the digital archive at the Department of Oral and Craniomaxillofacial Surgery of Shanghai 9th People's Hospital, Shanghai, China. The models had been obtained for an unrelated study²⁰, and were de-identified in accordance with the Health Insurance Portability and Accountability Act (HIPAA), including the removal of the soft tissues of the face. Prior to initiating this study, the Institutional Review Board (IRB) was contacted and it was determined that no IRB approval was necessary.

In the original prospective study, the selection criteria for the normal subjects were as follows: (1) subjects with normal-looking, symmetrical and harmonic facial features; (2) subjects with no noticeable craniofacial asymmetry; (3) subjects with no history of orthodontic treatment, orthognathic surgery, cosmetic surgery, facial trauma, or temporomandibular disorder; (4) subjects with a normal overbite, overjet, class I occlusion, and complete dentition (except the third molars); and (5) subjects with no noticeable crowding, spacing, or upper and lower dental midline deviations²⁰. The subjects were evaluated and selected together by three experienced oral and maxillofacial surgeons and three orthodontists. The full-head CT models of these normal subjects were obtained using a GE CT scanner (General Electric, Little Chalfont, UK), with a 25-cm of field of view, 512 ×

512 matrix, and slice thickness of 1.25 mm. The CT data were segmented and a 3D bone model was reconstructed using Mimics software (Materialise NV, Leuven, Belgium). Each 3D model was divided into two pieces: a combined cranium and midface, and a mandible.

Landmarks

At the beginning of the study, the 3D models were imported into the software 3ds Max (Autodesk, San Rafael, CA, USA). In 3ds Max, a single investigator (T.L.J.) digitized 35 landmarks on each 3D model. Eleven midline landmarks and 12 pairs of bilateral landmarks were located (Table 1). Each landmark was situated on the surface of the hard tissue model, except for sella. Sella was located by first constructing the largest sphere that fitted the confines of sella turcica, and then by selecting the center of the sphere as sella. The three-dimensional Cartesian coordinates (x , y , z) of each landmark were transferred from 3ds Max into an Excel 2010 spreadsheet (Microsoft Corporation, Redmond, WA, USA) following the right-hand rule (positive x , y , and z coordinates indicating left, posterior, and superior). A second investigator (K.C.C.) verified the transfer of data.

Error analysis

The repeatability of the landmark digitization was evaluated. For this, 10 models were selected using a random number table. The original investigator (T.L.J.) digitized all of the landmarks a second and a third time at intervals of more than 1 month. During the digitization, the previously digitized landmarks were hidden.

Three sets of coordinates were generated for each landmark. The overall intra-class correlation (ICC) with absolute agreement definition was initially used to determine whether the three measurements were absolutely agreed upon. In addition, the digitization error was quantified using the overall mean absolute deviation (MAD) in each (x , y , z) direction. The following equation was used to calculate the MAD for each patient, landmark, and coordinate direction:

$$MAD = \frac{1}{3} \sum_{n=1}^3 |x_i - m(X)|,$$

where x_i was the repeated coordinate of each landmark in the x , y , and z directions for a given patient, and $m(X)$ was the mean of the coordinates in a given direction for a given patient. Overall means of MAD were subsequently calculated by averaging the MAD in each direction.

Fluctuating asymmetry

The fluctuating asymmetry of each CT model was measured using a Procrustes analysis. The analysis was done in a custom MATLAB program (MathWorks, Natick, MA, USA). In the first step, the 54 faces were scaled to the average size of the study sample. This was necessary because the size of the face affects the measurement of asymmetry, as measured by the Procrustes method²¹.

The sizes of the faces were determined in the following manner. First, the centroid of each face was computed. Then, the root mean squared distances between the centroid and each facial landmark were measured. Finally, all of the distances were added. The centroid of each face was calculated by averaging the x , the y , and the z coordinates of its facial landmarks.

In the second step of the analysis, all of the faces were superimposed over each other using a generalized Procrustes approach. Face 1 was used as the template over which all other faces were superimposed. Before superimposing the faces on each other, face 1 was aligned on a 3D Cartesian coordinate system. The face was translated to locate its centroid at the origin of the coordinate system. Then, it was rotated, around the origin, until its sagittal plane and Frankfort planes were aligned to the ZY and XY planes, correspondingly.

Each face was superimposed on face 1 by first translating it until its centroid was laid on the origin of the coordinate system, and then by rotating it (about the origin) until the sum of squared distances between its landmarks and the corresponding landmarks of face 1 was minimal. After all faces were superimposed, the average face of the study sample was generated (Fig. 1).

In the third step of the analysis, the asymmetry of each face was measured. First, each face was divided into two half-forms: right and left. To divide the faces, the landmarks of each face were separated into two groups: the right set contained the coordinates of all right landmarks as well as all of the midline landmarks; the left set contained the coordinates of all left landmarks and again the midline landmarks.

Next, the centroids of the right and left half forms were calculated and the two half-forms superimposed using a series of transformations. The first transformation reflected (flipped) the left half-form around its sagittal plane, creating a mirror image – this operation made the half-forms comparable. The second transformation translated the left half-form until its centroid was laid on the centroid of the right form. The third transformation rotated the left half-form around its centroid, until the form was best aligned to the right. Alignment was reached when the sum of all the distances between corresponding landmarks – of the right and the left half-forms – was minimal.

Afterwards, the asymmetry at each landmark site was measured by calculating the vector that connected the left landmark (tail) to its corresponding right landmark (head). Finally, each asymmetry vector was mapped to the average face of the study sample. The mapping was done by translating each vector until its tail was located on the corresponding landmark of the average face (Fig. 1).

To estimate the size of the fluctuating asymmetry of the study sample, the mean Procrustes distance of each landmark was calculated. In addition, the upper Bland–Altman limit [sample mean + (2 × SD)] was also calculated²².

After calculating the size of the fluctuating asymmetry of each landmark, its direction was also measured. The directions were established using a principal component analysis (PCA), which puts the vectors into a new coordinate that best de-correlates them. The first principal

component (PC) has the largest possible variance. The succeeding components have in turn the highest variance possible under the constraint that it is orthogonal to the preceding components. The first principal component (PC1) represents the direction in which the vectors have the largest variation. The second principal component (PC2) represents the direction with the second largest variation, and so on.

Results

Error analysis

There was excellent absolute agreement among the three repeated measurements: the ICC ranged from 0.95 to 1.00. In addition, the size of the digitization error was small. The MAD result was 0.22 mm for the x direction, 0.24 mm for the y direction, and 0.18 mm for the z direction.

Fluctuating asymmetry

The sizes of the faces were normally distributed, ranging from 322.1 mm to 386.3 mm, with an average of 354.3 mm. The mean fluctuating asymmetry of the average-size face varied at each anthropometric landmark site, ranging from 1.0 mm to 2.8 mm. At the 95% upper limit, the asymmetries ranged from 2.2 mm to 5.7 mm (Table 2).

The direction of the asymmetry also varied at each landmark site (Figs. 2 and 3). For the whole study sample, PC1 explained 68% of the variation, PC2 explained 22%, and PC3 explained 10%. PC1 should be interpreted as the direction in which the landmark is more likely to fluctuate. For example, in the case of the frontozygomatic suture (Table 2 and Fig. 2), 67% of the fluctuating asymmetry was found to occur along a vector that was directed superiorly, anteriorly, and medially. In general, the majority of the asymmetry of the midline structures was mediolateral, while the asymmetry of the bilateral landmarks was more equally distributed.

Discussion

This study determined the fluctuating asymmetry of the facial skeleton in a sample of normal Chinese subjects. The mean fluctuating asymmetry was found to be between 1.0 mm and 2.8 mm, with an upper limit of 2.2 mm to 5.7 mm. These values are for the average face. People with larger faces will have higher values, while subjects with smaller faces will have lower values.

Clinically, facial asymmetry is considered a pathological condition, yet asymmetry is a continuum. All individuals have some degree of facial asymmetry. Because of this, a threshold must be established to separate normal from abnormal. The normative data assembled in this study gives us an idea of where the limit between normal and abnormal may be. However, they are not sufficient on their own to determine the threshold that separates clinical symmetry for asymmetry. For this, it will be necessary to compare the asymmetries of individuals with clinical symmetry to those of individuals with obvious asymmetry. Before this study can be completed, the investigators must first develop a

reliable method to measure facial asymmetry. The results of this study are the first step towards this goal.

As the present study only included Chinese people, one may ask how applicable the results of this study are to other ethnicities. It is well known that facial form varies from one ethnic group to another and that one should not apply cephalometric norms obtained in one ethnic group to another^{23,24}. However, this study was conducted in such a way that the results may apply to other populations, as is explained below.

A morphometric analysis of symmetry does not measure the shape of the whole face; it compares the size and shape of one of its sides with the other. Thus, overall facial shape does not influence the results. Based on this, one can deduce that the results may apply to all ethnicities. However, a counter-argument can be made that fluctuating asymmetries may vary from one population to another²⁵. Our genes are programmed to produce perfect facial symmetry, yet this never occurs. As mentioned before, all individuals have some degree of asymmetry. The resultant asymmetry is the result of stressors that derail the master plan of the genes^{26–28}. Stressors can modify the genes, the epigenetic mechanisms, or the environment. Different populations of individuals may be exposed to different stressors and may end up having varying degrees of asymmetry.

This study included only individuals who looked symmetrical. Thus, what was determined was the degree of asymmetry individuals might have despite having imperceptible asymmetry. These particular data may therefore apply to other populations, because there is no reason to believe that a different whole-face shape would influence this value. User beware, because this statement is conjecture.

A strength of this study is that it used a Procrustes analysis, a method that can measure asymmetry without a frame of reference. Previous studies have used a frame of reference to quantify the asymmetry. The problem with this approach is that accurate frames of reference are almost impossible to define, using any method. For example, the natural head posture method is unreliable because it changes with time. The landmark method is also unreliable because the fluctuating asymmetries one is trying to measure influence the frame of reference.

This study only measured fluctuating asymmetry at specific landmarks. It will be important, in the future, to analyze the fluctuating asymmetry using a surface-based approach (generic facial mesh)^{29–31}.

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Fig. 1.

Mean face of the study sample. Blue lines show the mean midface and red lines show the mean mandible.

Fig. 2.

Fluctuating asymmetry of the midface. Interconnecting lines show the average midface. The clouds of points surrounding each landmark show the fluctuating asymmetry. The red, green, and blue arrows show the first, second, and third principal components.

Fig. 3. Fluctuating asymmetry of the mandible. Interconnecting lines show the average mandible. The clouds of points surrounding each landmark show the fluctuating asymmetry. The red, green, and blue arrows show the first, second, and third principal components.

Table 1

Cephalometric landmarks.

Abbreviation	Long name	Definition
A	Point A	Point located on the labial surface of the intermaxillary suture, where the alveolar ridge joins the basal maxilla
ANS	Anterior nasal spine	Tip of the anterior nasal spine
AntiGo	Antigoniion	The deepest point of the left antegonial notch
B	Point B	Point located on the labial surface of the mandibular symphysis, where the alveolar ridge joins the basal mandible
Ba	Basion	The most anterior point of foramen magnum
Co	Condylion	Point located in the middle of the posterior articulating surface of the left mandibular condyle
Cor	Coronion	Tip of the coronoid process
Fz	Frontozygomatic suture	The most medial point of the frontozygomatic suture
Go	Gonion	The most posterior and inferior point of the angle of the mandible
J	Jugale	Point where the temporal and frontal processes of the zygomatic bone meet
L0	Lower incisal midpoint	The point at the intersection of the lower dental midline and the imaginary arc formed by the edges of the lower incisors
LM	Lower molar	The tip of the mesiobuccal cusp of the mandibular first molar
Me	Menton	The most inferior point of the symphysis menti
Na	Nasion	The point of intersection of frontonasal suture with the intranasal suture
Or	Orbitale	The point where the zygomatic maxillary suture crosses the infraorbital rim
Pg	Pogonion	The most protuberant point of the symphysis menti
PNS	Posterior nasal spine	The tip of the posterior nasal spine
Po	Porion	The most superior and anterior point of the external auditory meatus
Sella	Sella	The center of sella turcica
Sig	Sigmoidale	The deepest point of the sigmoid notch
U0	Upper incisal midpoint	The point at the intersection of the upper dental midline and the imaginary arc formed by the edges of the upper incisors
UM	Upper molar	The tip of the mesiobuccal cusp of the maxillary first molar
Zy	Zygion	The most lateral point of the temporozygomatic suture

Table 2

Fluctuating facial asymmetries of the average-size face.

Landmarks	Mean asymmetry, MRSD (mm)	Bland–Altman upper limit (95%) (mm)	PCA: percentage of variance explained by each principal component (PC)		
			PC1	PC2	PC3
B	1.0	2.2	72	23	4
PNS	1.1	2.2	69	20	12
ANS	1.2	2.8	87	10	2
A	1.2	2.7	87	10	3
U0	1.2	2.7	84	12	4
L0	1.3	2.7	85	12	3
Na	1.4	3.2	79	18	3
Pg	1.4	3.1	82	16	3
LM	1.5	3.2	57	25	18
Sella	1.6	3.2	73	19	8
Me	1.6	3.3	79	18	3
UM	1.9	3.5	49	34	17
Ba	2.0	3.9	85	12	3
Co	2.0	4.0	45	37	18
J	2.1	3.6	62	27	10
Sig	2.1	4.0	58	31	11
Or	2.1	4.5	69	22	10
Fz	2.2	4.1	67	21	12
Po	2.2	4.4	53	24	23
Ctip	2.2	4.4	52	25	23
Go	2.7	5.3	46	36	18
AntiGo	2.7	5.5	58	27	14
Zy	2.8	5.7	60	32	9
			68	22	10

MRSD, mean relative squared difference; PCA, principal component analysis.