

Morphometric characteristics of craniofacial features in patients with schizophrenia

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Abstract

Background: High incidence of craniofacial dysmorphology in patients with schizophrenia confirms the developmental disruptions during embryonic period. Anthropometry of head and face can give us several clues regarding the maldevelopment of brain. The aim of this study was to assess various dimensions of skull in Schizophrenics. **Methods:** One hundred and one (101) male and female patients that have been diagnosed with chronic schizophrenia were selected from a psychiatric hospital and 101 healthy controls, which were mostly the paramedical staff of another hospital, were included in the study. The age for both the groups was between 20 to 60 years. The head length, width and height and coronal, axial and sagittal arc lengths, and also body height and weight and BMI of participants were measured. **Results:** Mean anthropometric measurements of head length, width and height were 18.92, 14.08 and 12.69 in patients and 18.90, 13.89 and 13.38 centimeter in control, also axial, coronal and sagittal arc lengths were 55.85, 35.21 and 33.00 in patients and 55.70, 34.54 and 32.19 centimeter in control group, respectively. Compared to controls the patients had significantly increased coronal ($P < 0.022$) and Sagittal ($P < 0.001$) arc lengths. The patients also showed significantly lesser head height ($P < 0.001$) as compared with controls. **Conclusion:** The linear measurements of skull in patients with Schizophrenia do not significantly differ from normal populations and/or have slightly differences. Future studies may investigate whether head can be an anatomical marker for patients with schizophrenia.

Keywords: Anthropometry; Craniofacial; Morphogenesis; Schizophrenia

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Introduction

Schizophrenia is a mental disorder that is seen in acute and chronic form which can lead to social problems and long-term disability. Despite differences in geographic, social and cultural backgrounds, about one ten thousandth of young population (15-35 years) in the world is affected by this disorder each year. Thereby, one percent of the populations (15-60 years) in the world are suffering from schizophrenia¹⁻⁵.

So far, the etiology of schizophrenia is not known clearly yet, but the interplay of genetic, environmental and social factors are believed to be involved. There is much evidence indicated that disturbed prenatal development significantly increases the risk of schizophrenia^{6,7}. These observations have been confirmed by many studies. According to current literature, the adults suffering from schizophrenia have several physical malformations, especially in the craniofacial region. Most fetal disorders occur in the first and second trimester of embryonic development⁸⁻¹². In initial stages of embryogenesis, there is a very close relationship between

the craniofacial development and ventral portion of brain; therefore, maldevelopment in one predisposes the other for malformation^{11,13}. Also, there is scientific evidence to show the important relationship between cleft lip and palate and brain development^{14,15}. Anthropometric analysis also shows the presence of maldevelopment of the middle portion of skull in patients with schizophrenia^{6,11,16}.

Nonetheless, the biology of brain development is not properly understood, but as biology of facial development is completely clear, it can be used to understand the morphogenesis of brain¹¹. Facial deformity can be used as a valuable index to trace the abnormalities of brain development¹⁷. It has also reported that, the craniofacial dysmorphogenesis and schizophrenia are associated with Velocardiofacial syndrome^{18,19}. The morphological relationship between the face and brain should not only be studied over anatomical or embryonic basis, but should be also done at the level of brain function¹⁷.

Schizophrenia is a complex and unique disease²⁰, therefore many hypotheses have been postulated regarding the factors and causes that are responsible for schizophrenia. These hypotheses have different assumptions, some based on environment, genetics, social or biological backgrounds²¹. Among all, neurodegeneration and neurodevelopmental hypotheses are more accepted. In the past two decades neurodevelopmental hypothesis has been paid more attention²⁰. According to this hypothesis, the schizophrenia may be as a result of some primary damages to the brain during prenatal or postnatal period which leads

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to maldevelopment in its maturity. These damages can have different backgrounds like genetic, embryonic and even during delivery²¹. Neurodevelopmental hypothesis is also based on the studies of cerebral cortex. Neuropathologic studies in patients with schizophrenia show changes in the structure of the brain, which may result in miss size, misplace and disorganize of cortical neurons in second trimester of fetal development²²⁻²⁶. The lack of gliosis in the brain shows that schizophrenia is not a result of neurodegeneration, but as a result of the damage of neurons caused before the 20th week of embryogenesis²⁷. Reduced grey matter volume has also been reported in patients with schizophrenia undergoing MR²⁸.

The neurodevelopmental hypothesis is further confirmed by the presence of neural cell adhesion molecules and growth-associated protein-43 in the brains of patients suffering from schizophrenia^{29,30}. Abnormal sulci and gyri which present in the brain of postmortem patients with schizophrenia confirm the possibility of maldevelopment of brain, because the sulci and gyri are developed during 16-29th weeks of fetal life³¹⁻³³. High incidence of craniofacial malformation in patients with Schizophrenia also confirms neurodevelopmental hypothesis, in particular dysmorphology which present in the structures with ectodermal origin³⁴. The thalamus of the rhesus monkeys exposed to radiations, were later found to present with dysmorphogenesis of face³⁵. Craniofacial anthropometry can be very useful indexes to further support the neurodevelopmental hypothesis of craniofacial dysmorphology in patients with schizophrenia³⁶. The aim of this study was to assess various dimensions of skull in the patients with schizophrenia and compare them with general population.

Methods

Subjects

Participants in this study, 101 male and female in patients with chronic schizophrenia (based on DSM-IV criteria) were selected from a psychiatric hospital and 101 healthy male and female volunteers, mainly the staff of teaching hospitals of Shiraz Medical School were recruited as a control group. All of the participants were between 20-60 years of age. The participants were excluded if they had any history of skull fractures or any other diseases that could had influenced their skull size.

Techniques

According to the study of Peter F Buckley et al (2002),³⁵ the following cranial dimensions were measured in each individual:

a- Head length: Projective distance from glabella to

opsithocranion (the point in the occipital region most distant to glabella).

b- Head width: Projective distance between the both trignons.

c- Head height: Perpendicular distance from the Frankfurt horizontal plane to the vertex (in addition to the study of Buckley).

d- Axial arc length: Head circumference.

e- Coronal arc length: Arc length between the both trignons, through the vertex.

f- Sagittal arc length: Arc length between glabella and opsithocranion, through the vertex (in addition to the study of Buckley).

Head length and head width were measured using a head and neck stainless steel 45cm caliper. To further enhance the accuracy, the reading from the head and neck stainless steel caliper was again measured by a digital sliding caliper (Mutitoya 193 digital calipers, Japan). Head height was measured using a centimeter/millimeter scale. Axial, coronal and sagittal arc lengths were measured by an anatomical tape measure (Seca S201 anatomical tape measure-ses007). To ensure further accuracy the measurements were done by two individuals, one of which was unaware of the diagnosis. We spent as much as necessary time for each individual to make the accuracy measurement.

Body height and weight and BMI of patients and normal subjects were also measured by a digital scale (Seca professional digital column scale). This study was approved by the ethical committee of SUMS (Shiraz University of Medical Sciences). The statistical analysis for this study was conducted using SPSS Inc. USA, 15 Software.

Results

Out of 101 patients with schizophrenia, 68 were males and 33 were females. The mean (\pm SD) age in the patient group was 44.02(\pm 9.50) years. Among the control population, there were 51 females and 50 males. The mean (\pm SD) age in this group was 30.86 (\pm 6.68) years. The parameters of age, weight, height and body mass index of both the groups with their respective mean, maximum, minimum and standard deviation are shown in Table 1.

The statistical analysis of sex ratio and the age between the two groups were significantly differences, with $P < .001$ for sex ratio using chi-square and $P < .010$ for age using t-test. Since this statistical significance probably had influenced our results, the six cranial measurements were compared and calculated using univariate analysis of variance taking

Table 1: Age, weight, height and body mass index in individual whit schizophrenia and normal population

	Group	Minimum	Maximum	Mean	Std. deviation
Age (years)	1	24	60	44.02*	9.50
	2	22	48	30.86	6.68
Weight (kilograms)	1	40	96.4	66.46	13.22
	2	41.5	100.3	65.87	14.45
Height (centimeters)	1	103	185	162.79	11.58
	2	139.5	187	164.45	9.60
Body mass index	1	13.6	38.2	24.64	4.67
	2	16.2	36.3	24.24	4.17

Group 1: Patients (n=101) and Group 2: Control (n=101).

*Significant differences with control group. $P < .010$

age and sex as covariate, therefore, omitting their influence, if any, over the results. Compared to controls the patients with schizophrenia had significantly increased coronal and sagittal arc lengths with $P<0.022$ & $P<0.001$ respectively (Tables 2). In the patient group, the mean of coronal arc length was 35.22 cm and the mean of sagittal arc length was 33.01 cm, and their respective standard deviations were 2.58 & 1.81. The patients also showed significantly lesser head height as compared to control group ($P<0.001$) (Table 2). The mean head height in patient group was 12.70 cm with a standard deviation of 0.73. For all participants, there were no statistical significant differences for the other three cranial measurements which include head length ($P<0.790$), head width ($P<0.650$) and axial arc length ($P<0.719$). The mean and the standard deviation of all the six cranial measurements in both groups (patients & controls) are depicted in Table 2.

Discussion

Two hypotheses have been proposed for the etiology of schizophrenia, one is based on the factors affecting primary and secondary brain development "early and late neurodevelopment" and the second is based on brain regression "neurodegeneration". In the past two decades the neurodevelopmental hypothesis has come to more focus^{20,21,36,37}. The presence of minor physical anomalies in craniofacial region of patients with schizophrenia^{10,38,39} points toward the common origin of craniofacial region from ectoderm and their simultaneous development in the first trimester of gestation^{38,40-42}. Since different factors like environmental, genetic, climatic or even race may be responsible for the malformation of craniofacial features in patients with schizophrenia^{21,42,43}, therefore it is necessary to study the relationship between these factors and their influence on the craniofacial features in patients with schizophrenia⁴⁴. Our study is also based on the grounds of previous hypotheses where we try to evaluate the preliminary morphometric differences between craniofacial features in patients with schizophrenia and compare them with healthy individuals in Shiraz city.

According to our knowledge, only one study has evaluated the craniofacial features in patients with schizophrenia has been done in Iran and this will be the first to be done in Shiraz city (a city with rich cultural background and internationally acclaimed Shiraz University of Medical Sciences).

The strengths of this study include that it's the first study of

this kind in Iran which could pave the way for future research in this particular field and several interesting findings will be revealed. Compared to other studies, our sample in both the groups was more which was in accordance to the suggestions made by several authors in their studies^{11,43,45}. Schizophrenia, being a complicated disorder, the more the number of patients more will be validity of results, for example the patient sample should be more than 100³⁵.

Unlike the studies of Buckley et al (2002) and Kelly et al (2005),^{35,46} and like the study done by Robin et al (2007),¹¹ our study included the participants from both sexes, because the development of craniofacial region after 6-9 week of gestation is dependent on sex hormones and several other factors that are specific for a particular sex¹⁷. To ensure a high credibility and accuracy two assessors were employed to take the measurements, one of who was blind to diagnosis. Unlike the study of Robin et al (2007),¹¹ in this study height, weight and BMI were also measured in all the participants. Because the increase in weight can itself be a predisposing factor for the development of schizophrenia, or even increased BMI could also predispose a patient with schizophrenia to several other co morbidities like cardiovascular or respiratory diseases. However, studies have shown that obesity in patients with schizophrenia may be due to administration of drugs, but in contrast to this, it also could be the result of negligence to diet, patients with schizophrenia suffer from malnutrition and low body weight^{41,46-49}. In this study, in addition to the study of Buckley et al (2002),³⁵ we measured head height and sagittal arc length of participants.

The principle limitation of this study was the lack of more samples in both the groups that might have enhanced the accuracy of the results. The lack of previous studies of this kind in Iran that could have helped to understand the relationship between craniofacial dysmorphology and its incidence in Iran. Another limitation of this study was the linear measurements that we performed, as the development of the skull and brain is a three dimensional process^{41,50-55}, so, it cannot be evaluated or measured well using a linear method of measurement¹⁷. Another limitation of this study was the non-uniform age among the patients and controls which can be attributed to the fact that patients with chronic schizophrenia are usually old and secondly the control group was generally the paramedical staff of a teaching hospital that was comparatively younger. Therefore the mean age of the patient group was more than that of control group and

Table 2: Cranial dimensions in individual whit schizophrenia and normal population

Measurements	Groups	Mean (centimeters)	Std. deviation (centimeters)
Head length	1	18.92	0.91
	2	18.91	4.40
Head width	1	14.08	0.72
	2	13.90	1.45
Head height	1	12.70*	0.73
	2	13.40	0.75
Axial arc length	1	55.85	2.04
	2	55.71	1.77
Coronal arc length	1	35.22*	2.58
	2	34.55	1.58
Sagittal arc length	1	33.01*	1.81
	2	32.20	1.41

Group 1: Patients (n=101) and Group 2: Control (n=101).

*Significant differences with control group. ($P<0.001$), ($P<0.022$) and ($P<0.001$) respectively

in order to omit its influence over the results, univariate analysis variance test was used.

In this study the patients with schizophrenia showed increased weight and BMI, while the height was less than the normal group. However, these findings were not statistically significant. The findings of Ainsah et al (2008) showed increased BMI and waist in patients with schizophrenia and suggested a tight control over the diet and monitoring sugar and lipid levels in patients with schizophrenia⁴⁹. In this study, short stature of patients with schizophrenia was similar to the findings of Fanin et al (2006) who concluded that children of short stature are more prone to schizophrenia in youth, particularly if this short stature was present since birth⁵⁶⁻⁵⁸. The findings of Nopoulus et al (1998) also confirm the short stature of patients with schizophrenia⁵⁹.

Increase in the length of coronal arc and decrease in the height of the skull in individual whit schizophrenia in our study, represent a somewhat widen in the base of skull, which may be as a result of alteration in the ossification sequences of chondrocranium and associated with expansion of middle cranial fossa, and consequently the volume of cerebral temporal lobe^{11,60,61}. Despite, increase in the sagittal arc length can be as a result of early closure of sagittal suture, it is insufficient to create the troubles for development of the brain. Overall, in this study, the head circumference, head length and head width have no significant differences in individual whit schizophrenia compared to control group, and the coronal and sagittal arc lengths and cranial height are not considerably differences in the skull of patients to make changes in the cranium obviously. These results are according to the findings of Buckley et al (2002) and Kelly et al (2005); they have demonstrated that dysmorphogenesis of the cranium and brain in schizophrenia are two separated proceedings^{35,42}. Also, the findings of William et al (1991) confirm the lack of association between schizophrenia and abnormalities of head and face⁶². But Lane et al (1997) has been believed that, head and face abnormalities are associated with individual whit schizophrenia and maldevelopment of the brain⁶. Robin et al (2007) has been supposed that, there are much cellular and molecular relationships between head and face evolution, therefore, morphogenesis of face and head can be irrefutable evidence to show the existence of schizophrenia, even more than the brain evaluation¹¹. In view of the fact that, the face and head morphogenesis is influenced by different factors such as age, sex, race, weight, etc.; a large number of participants are needed to find involved factors in the brain development and schizophrenia⁶⁰.

On the other hand, partial or lack of differences in the skull dimensions in individual whit schizophrenia in our study, may be due to apply linear measurement technique, which, it cannot shows definite size of cranium, although, classical anthropometric techniques were used by McGrath et al (2004) and Lane et al (1997) to demonstrate morphogenesis of head and face^{3,6}. Robin et al (2002, 2005) has been suggested that, this issue could be resolved by using other methods such as Laser scanning and geometric morphometric analysis, which can show all aspects and three-dimensional view of the head and face^{16,17}. Buckley et al (2005) have demonstrated some differences of face and head morphogenesis in individual whit schizophrenia by using Laser scanning,⁶³ unlike his previous findings, which had used the linear measurements³⁵. In addition, absolute measuring, which are used in the most morphological

studies of head and face, cannot achieve useful information compare to the proportional measuring⁶⁴. Also, the outer linear measurements, due to presence of soft tissue around the skull and its thickness, can not indicate the exact volume of intracranial space and it is not extensible to the brain volume changes. But MRI shows the accurate size and definite volume of the skull and even the brain size^{35,65,66} and can determine the relationship between face and head and brain dysmorphogenesis¹¹.

The findings of this study indicate that linear measurements of cranial dimensions in individual whit schizophrenia do not significantly differ from normal populations and/or there are slightly differences in some dimensions. Therefore, we suggest that; a- The MRI, Laser scanning, geometric morphometric analysis and photogrammetric,^{67,68} technique can be used to measure and confirm the accurate and authentic morphology of head and face and volume of interior of the cranium and pathobiological alterations of the brain in the individual whit schizophrenia. b- Considering to the diverse geographic regions and climatic conditions and various people in our vast country, it is recommend to measure the morphology of head and face of individual whit schizophrenia in different regions.

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