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Otizm Spektrum Bozukluğunda El 2D:4D Parmak Oranı ve Yüz Simetrisi

Araştırma Makalesi / Research Article

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Öz

Otizmin etiyolojisi ile ilgili birçok teori vardır ve en çarpıcı olanı anne karnında testosterona maruz kalma teorisidir. Bu çalışmada, otizm spektrum bozukluğu (OSB) tanılı erkek çocuklar ve normal gelişimi olan çocuklarda ikinci ile dördüncü parmak ve yüz ölçümlerinin simetrik olup olmadığı araştırılmıştır. Çalışma için, OSB tanısı konan 30 erkek çocuk, normal gelişim gösteren 30 erkek çocukla karşılaştırılmıştır. Her bireyin yüz fotoğrafları dijital ortamda çekilmiş ve yüz yarılarında sekiz farklı referans uzunluğunda ölçüm yapılmıştır. Otizm tanısı alan çocuklarda yüz yarısı ölçümleri kendi aralarında ve normal sağlıklı gelişimi olan kontrol grubu ile karşılaştırılmıştır. Ek olarak simetri tespiti için sağ ve sol eller fotoğraflanarak ikinci (2D) ve dördüncü (4D) parmakların uzunlukları ölçülerek simetri düzeyi analiz edildi. Yüz ve parmak analizi sonucunda OSB'li bireylerin yüzlerinin normal gelişim gösteren bireylere göre daha simetrik olduğu ve 2B-4B parmak uzunluklarının normal gelişim gösteren çocuklara göre birbirine daha yakın uzunlukta olduğu belirlendi. Ayrıca otizmin şiddeti arttıkça hem yüzde hem de parmaklarda simetri eğiliminin arttığı tespit edildi. Yüzde ve elde tespit edilen simetriye eğilim, otizmli bireylerin anne karnında maruz kalınan yüksek testosteron seviyesi ve buna bağlı olarak aşırı erkek beyni teorisi ile uyumludur.

Anahtar Kelimeler

Otizm spektrum bozukluğu,
otizm,
simetri,
yüz simetrisi,
2D:4D parmak oranı

Makale Hakkında

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Symmetry of Hand 2D:4D Digit Ratio and Face in Autism Spectrum Disorder

Abstract

There are many theories about the etiology of autism, and the most striking is the theory of testosterone exposure in the womb. In this study, it was investigated whether the second and fourth finger and face measurements were symmetrical in boys with autism spectrum disorder (ASD) and children with normal development. For the study, 30 boys diagnosed with ASD were compared with 30 normally developing boys. Photographs of each individual's face were taken digitally and measurements were made at eight different reference lengths on the face halves. Half-face measurements in children diagnosed with autism were compared among themselves and with the control group with normal healthy development. In addition, the symmetry level was analyzed by photographing the right and left hands and measuring the lengths of the second (2D) and fourth (4D) fingers for symmetry detection. As a result of the face and finger analysis, it was determined that the faces of the individuals with ASD were more symmetrical than the individuals with normal development, and the 2D-4B finger lengths were closer to each other than the children with normal development. In addition, it was determined that as the severity of autism increased, the tendency for symmetry increased in both the face and fingers. The tendency to symmetry detected in the face and hand is compatible with the high testosterone level exposed in the womb of individuals with autism and, accordingly, the excessive male brain theory.

Keywords

Autism spectrum disorder,
autism,
symmetry,
facial symmetry,
2D:4D ratio

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Introduction

Symmetry means position between two or more things, shape and size suitability for a specific axis, structure and shape similarity of the two regions of an axis, as a term of biology, the similarity of the organ, section and joints of the body with respect to a line or a plane. Symmetry is in constant and tight cooperation with the laws of nature. When we come to human, there are certain symmetry features as part of nature. While we earn some of these in life, we have the vast majority of them, like other living things, by birth. For example, two ears, two eyes and our other internal and external double organs are our own examples of balance-symmetry. The feeling of symmetry in humans is so sensitive and powerful that it immediately recognizes the distortion of symmetry in every living thing or inanimate, and this worries (Stewart, 2007).

In studies conducted on humans, symmetrical facial appearance and beautiful perception were associated (Penton-Voak, 2001). It shows that the attractiveness of the face (indirectly hidden symmetry) has strong biological basis.. From this point of view, the symmetrical face, which is attractive in men, has been suggested to have information about being stronger and healthier and testosterone level (Borraz-Leon, 2017). Testosterone is a steroid hormone produced in the testicles and adrenal glands, regulating the development and expression of primary and secondary sex characteristics. Since the male and female bone structure is affected by the hormones that dominate their bodies, namely testosterone and estrogen, the features that are perceived as masculine on the male face are reported as the dislocation of the cheekbones, the hard and strong-wide jaw structure, the thick eyebrows and the width of the face, the lower part of the nose and are attractive. Excessive masculine traits are associated with some negative traits such as aggression (Archer, 2006), controlling, coercive (Sanchez-Pages, 2009). The effect of testosterone starts from the embryonic period and continues for life. Many previous studies have shown that the male fetus in the uterus is exposed to approximately ten times more testosterone hormones than the female fetus (Borráz-León, 2014; Auyeung et al., 2009; Baron-Cohen et al., 2011; Beking et al., 2018).

It is suggested that the level of testosterone to which the fetus is exposed prenatally (in-utero) is important in the development of masculine or feminine features of the face. In a finding that supports this view, 2D:4D ratio is lower in men than in women. As the prenatal testosterone level increases, this ratio decreases, that is, finger lengths converge and symmetry tendency occurs (Hodges-Siemon, 2016). Women attach importance to handsome personality, which expresses healthy genes, and long height, wide shoulder and muscular body, which express power. Handsomeness and beauty are about the golden ratio and also symmetry (Grammer, 1994; Little, 2014; Fink, 2014).

Autism spectrum disorders (ASD) occurs 3-5 times more often in boys than girls. The fact that ASD is approximately 4 times higher in men suggested that it may be associated with prenatal androgen exposure. It is known that testosterone has an important and powerful effect on the development of the central nervous system outside the genital area in the prenatal period. Theories have been proposed that exposure of the developing brain to high testosterone levels in prenatal period may play a role in the etiopathogenesis of autism. According to Baron-Cohen, the assumption that explains the development of autism is the

'extreme male brain' theory. Based on the behavioral criteria of this theory, Baron-Cohen has shown that both boys and girls with autism are based on a large set of data showing that they have masculine brains and in other studies, it is the high level of testosterone exposed in the womb due to the high risk in children with autism (Baron-Cohen, 2002).

ASD is a neurodevelopmental disorder in which there are insufficient social functions, abnormalities in verbal and nonverbal communication, limited and stereotyped interests and behaviors, and repetitive behaviors occur in the first years of life, it was thought to be based on psychological factors and was explained by the 'cold mother' model. The typical gender differences Empatizing - Systemizing (ES) theory shows that individuals can be classified based on empathy and systematization. The Extreme Male Brain (EMB) theory, which is an extension of the ES theory, shows that autistic people shift towards a more masculine brain on average. Regarding empathy and systematization, they suggest that autistic individuals have an average "masculine" brain type on average. EMB theory is supported by brain imaging studies that detect autistic women are masculine in both brain structure and function (Baron-Cohen, 2002).

Face symmetry and 2D:4D ratios appear very early in human development. Small physical anomalies appear to be the result of developmental instabilities during early embryonic development. These physical anomalies occur in the first trimester of pregnancy and persist throughout life (Mackus, 2017). The extreme male brain theory proposed in 1997 is an extension of the typical theory of gender differences. In the first major update since 2005, the possible biological mechanism that takes into account male bias is the effect of fetal testosterone in the womb (Baron-Cohen, 2011). A decrease in cognitive, emotional and sociability occurs in the relationship between ASD and testosterone. Many studies suggest that the symmetry in the facial structure, 2D:4D ratio in men is caused by the effect of testosterone. In line with this view, it has been suggested that the 2D:4D ratio may be a biomarker for the risk of developing autism (Manning, 2000; Baron-Cohen, 2003).

Because the 2D:4D ratio is linked to various physical and mental properties, finger length ratios have attracted great interest among researchers. Different methods such as direct caliper measurement, photocopy measurement, photographic measurement, and self-measurement are used to measure the ratio of the fingers (Caswell, 2006; Sandnes, 2014; Kemper, 2009; Bundred, 2004; Olapido, 2009; Jaim, 2012; Kanchan, 2010).

In this study, an extreme male brain theory based on excessive testosterone exposure was researched for ASD. This theory suggests that ASD is an extreme example of male behavioral characteristics associated with excessive testosterone exposure in the womb. On the other hand, there is a lot of research that the symmetrical facial/limb appearance in men is related to testosterone. If the extreme male brain theory is correct in autistic patients due to high testosterone levels exposed in the womb, the exposed testosterone is also expected to have an effect on increasing symmetry tendency on anatomical structure such as fingers and faces.

Methodology

Study Groups

In this study, 30 boys between the ages of 3-10 years old who were diagnosed with ASD and received education at the Yeni Erenkoy Special Education and Rehabilitation Center, and 30 healthy boys between the ages 3-10 years old were selected. In order to reduce the variability of age in the study, the number of children of the same age was taken from the same group. Permission was obtained from the parents of 60 boys for the study. Permission for the study was obtained and approved by the Üsküdar University ethics committee (61351342/2019-41).

The average age of 30 autistic children who participated in the study was 7.03±1.732. There was no statistically significant difference compared normal controls (mean age 7.00±1.681). All children were selected as boys to free from possible gender influence. When those with ASD are grouped according to their health reports, there are 3 children with autism, 13 mild, 4 moderate, 4 severity and 6 common developmental disorders.

Facial Measurements

In order to carry out this study, measurements from two different groups were obtained through anthropomorphic measurement. For face measurements, dual 12 MegaPixel, f/1.5-2.4, 26 mm, f/2.4, 2X optical zoom interchangeable aperture camera were used. The camera distance was kept constant at 50 cm. The participants were asked to sit in a chair and pose with a neutral expression and look directly at the camera. The hair on the face was attached to the head during the imaging process. Biometric photographs were obtained by taking shots from the scalp and chin to the full face in order to get a full face image. Codes determining the measuring points were made on the face photographs. The photos of the children with autism were obtained by fixing their heads with the assistant in front of the camera as much as possible. In some cases, repeated shots were taken. Despite all efforts, due to adaptation problems of children with autism, side/curve/angled/oblique stop and posture differences preventing the correct measurement appeared and optimal facial photographs could not be obtained. In this case, the values that could not be measured were recorded as "missing" data for statistical analysis and did not participate in the calculations. However, the number of "missing" data in this way was only 2.1% and these data were processed as "missing data" in statistical analysis.

On the other hand, standard photographs were made at a distance of approximately 40-50 cm for each child to make ideal facial measurements. Since the distant kids' face area is smaller in the photo, the closer one is larger, the photos are not in inches or millimeters in units, but the pixels in D1-D8 measurements on face photos, standard photo on the right face half and left face half, also in Microsoft Paint with pixels measured in units (Figure 1). For this, the face was divided into two in the middle with the vertical line drawn from the end of the scalp to the middle of the chin, and D1-D8 measurements were made separately on the right and left face halves to understand symmetry. Since the pixel measurements differed significantly in the individual according to whether the photograph was far or near, the raw pixel values

of each person were not compared. Instead, right-to-left face distance measurements were compared on the person's own face, and these ratios were compared with normal healthy faces that were transformed in the same way. Measurements were made by another independent person (O.A.) who was not involved in the study and did not know the cases as normal or autistic.

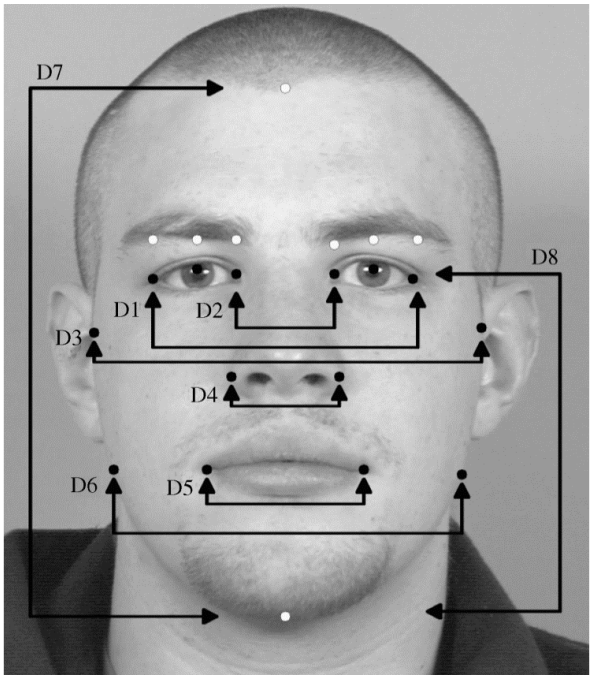

Figure 1. Standardization of percentage measurements in individuals with normal and autism. D1, distance between the outer edges of the eyes; D2, distance between the inner edges of the eyes; D3, the outermost part of the face in front of the ear; D4, nose wing outer length; D5, lip edge length; D6, outer length of the chin; D7, face length, between scalp and under chin; D8, length between the outer part of the eye and under the chin. These values were measured in pixel on standard photographs taken. At the same time, the middle line, the face was separated from each other with the perpendicular line between the scalp and the tip of the chin, and the measurements on both sides were measured as the right face and the left face half (Penton-Voak, 2001).

In this study, the logic of searching for symmetry is approaching lengthens and approaching 1 to length ratios. For example, when the D1-Right/D1-Left pixel length measurement is proportional to 0.98, the ratio value to be obtained was considered as symmetry between the two halves of the face, and a value such as 1.5 is the deviation from the symmetry. In this way, eight different length (D1-D2-D3-D4-D5-D6-D7-D8) measurements standardized in the right-left face approached the ratio of 1:1 ratio to the ideal symmetry direction, while the deviations from this value were considered as deviation, drift or divergence from the symmetry. At the same time, the high standard deviation (*SD*) of length measurements was thought to be related to symmetry or divergence, while it's low was considered to be symmetrical. For comparison of symmetry on the faces, these values were compared between the right and left faces of autistic and normal children, as well as children of the normal age group.

Second (2D) and Fourth (4D) Finger Length Measurements in Hand

In the shots for 2D:4D finger ratio in both hands, the hands of the subjects were placed on the flat ground with the palms facing up, and a full color photograph was taken in the appropriate light. The image was taken with multiple shots by the individual independent of each participant and the best was

chosen. Finger lengths were measured in calipers in millimeters over the photographs obtained, and also data were obtained in pixels on digital photographs.

Results

Comparison Results of Faces

The raw data obtained from the photographs were subjected to the right-left half-face correlation relationship in children with autism, the distances measured in D1-D8 directly on the faces without any data conversion. It was predicted that if two hundred half symmetry increase or ideal symmetry was reached, the correlation coefficient would approach 1 or vice versa, the correlation coefficient would decrease or move away from 1 in case of symmetry decrease (increase of symmetry) (Table 1).

Table 1. Mean and ±Standard Deviation (SD) values of lengths in right-left half of face D1-D8 measurements in autistic and normal children

	Normal Children, n=30				Children with Autism Spectrum Disorder, n=30			
	Right Face mean±SD	**Left Face mean±SD**	**Correlation r Coefficient**	**p**	**Right Face mean±SD**	**Left Face mean±SD**	**Correlation r Coefficient**	**p**
D1	332,00 ±136,050	329,66 ±135,625	0,987	**0,01**	271,97 ±179,886	261,40 ±174,717	0,982	**0,01**
D2	127,17 ±51,428	122,50 ±50,404	0,943	**0,01**	103,77 ±65,566	96,03 ±62,917	0,943	**0,01**
D3	491,38 ±210,030	466,67 ±198,321	0,966	**0,01**	401,70 ±262,724	369,25 ±253,431	0,985	**0,01**
D4	136,40 ±59,481	134,73 ±55,743	0,943	**0,01**	112,67 ±76,468	104,27 ±71,020	0,987	**0,01**
D5	174,72 ±82,419	173,32 ±71,920	0,992	**0,01**	141,37 ±93,717	129,10 ±92,425	0,985	**0,01**
D6	385,23 ±171,561	377,93 ±170,424	0,979	**0,01**	324,14 ±211,792	286,81 ±194,655	0,991	**0,01**
D7*	1313,14 ±554,827		**-**		1088,63 ±728,046		**-**	
D8	747,14 ±301,178	734,27 ±302,932	0,997	**0,01**	586,53 ±404,983	567,75 ±407,459	1,000	**0,01**

*Since D7 is the only measurement from the midline, there is no right-left half measurement. Figure-1 can be seen for D1-D8 face reference points.

According the Table 1, at the same time, the correlation relationship between the right face measurements in autistic children and the right face measurements in normal children, and the left face measurements in autistic children and the left face measurements in normal children investigated based on raw data. The aim of this comparison is to compare the right-left faces of normal children with autism, to decrease the correlation coefficient, in other words, to search for the increase of symmetry (decrease of symmetry) between autistic and healthy face. The expected correlation between children with autism and normal children is lower in their faces (right-left) compared to the correlation coeffients.

Comparison Results of Faces

In total, the average pixel of 30 subjects with ASD is 144.30 for the right 2D and 159.63 for 4D; left hand for 2D 140.73; 156.43 was found for 4D. When analyzed according to diagnostic degrees in autism, p value is 0.005 for right 2D and 0.016 for 4D. The p value is 0.004 for left 2D and 0.009 for 4D. The

severity of autism, that is, the right 2D size was shortened when going from autism to mild, moderate and heavy. It was the shortest with an average of 83 pixels in heavy autistic and statistically significant (F=4.8 and p<0.005).

As the severity of autism increased, the left 2D length became shorter. While children with severe autism were the shortest with an average of 80.25 pixels, 165.46 pixels were detected in mildly autistic children. The difference was statistically significant (F=4.8 and p<0.005). And also, as autism severity increased, the left 4D length was shortened. It was the shortest with an average of 88.25 pixels in children with severe autism and statistically significant (F=5.3 and p<0.003). As the severity of autism increased, the right 4D length beacme shorter. It was the shortest with an average of 90.50 pixels in children with severe autism, 178.54 in mild autism, and the difference was statistically significant (F=4.7 and p<0.005).

There was no statistical length difference between the fingers in the measurements between right and left 2D pixels in boys with ASD and who showed normal development (for right 2D F=0.026, p=0.873 and for left 2D F=0.005, p=0.945). however, 2D length was found shorter in normal developing boys (for right hand 133 against pixel 144 and for left hand 129 against pixel 140). There was no significant difference in left and right hand between 4D in boys with ASD and who showed normal development (for right hand 4D; F=0.001, p=0.982 and for left hand 4D; F=0.013, p=0.910).

Besides the length of the fingers, the finger ratios were also compared. When looking at 2D:4D ratios in the right-left hand, there was no statistical difference in boys with ASD and showed normal development. While the average 2D:4D ratio was 0.92 with normal boys in the right hand, 0.91 was found in those with ASD (F=0.781, p=0.381). the rate was 0.89 in boys with normal development in the left hand, and 0.90 in boys with ASD. There waas no significant difference between 2D:4D finger ratios in autism and normal group (F=3.11 and *p*=0.083). However, 2D:4D ratio was lower in the right hand of boys with ASD (for right hand 0.91, for left hand 0.92). In the left hand, 2D:4D ratio is lower than 0.89 in boys with normal development, while 0.90 is moderate in boys with ASD.

Considering the correlation relationship between the lengths of the fingers, the correlation coefficient of 2D and 4D lengths in the left hand of boys with normal development was r=0.959 (p=0.001), while this correlation coefficient was higher with 0.973 in boys with ASD (p=0.001). In those with ASD, they were considered as the indicator of symmetry or the similarity or proximity to 2D and 4D fingers. Considering the correlation of the length between 2D and right-handed pixels of boys with normal development and ASD, Pearson was r=0.980 in boys with normal development (p=0.001) and r=0.995 in the boys with ASD (p=0.001). According to these results, the higher correlation coefficient in the right and left hands (boys with ASD in terms of 2D, r=0.980 vs 0.995) shows higher symmetry and sameness in the second finger in the right-left hands.

When the correlation between 4D fingers in the right and left hands of the normal development and the ASD of the boys with their own hands, based on the length measurements in pixels, the Pearson r value was 0.961 in boys with normal development (p=0.001), while the r value was 0.994 in boys with ASD detected (p=0.001). According to these results, the higher correlation coefficient (r=0.994 vs 0.961) in boys with ASD in terms of 4D in their right and left hands indicates higher symmetry and sameness in right-left hands.

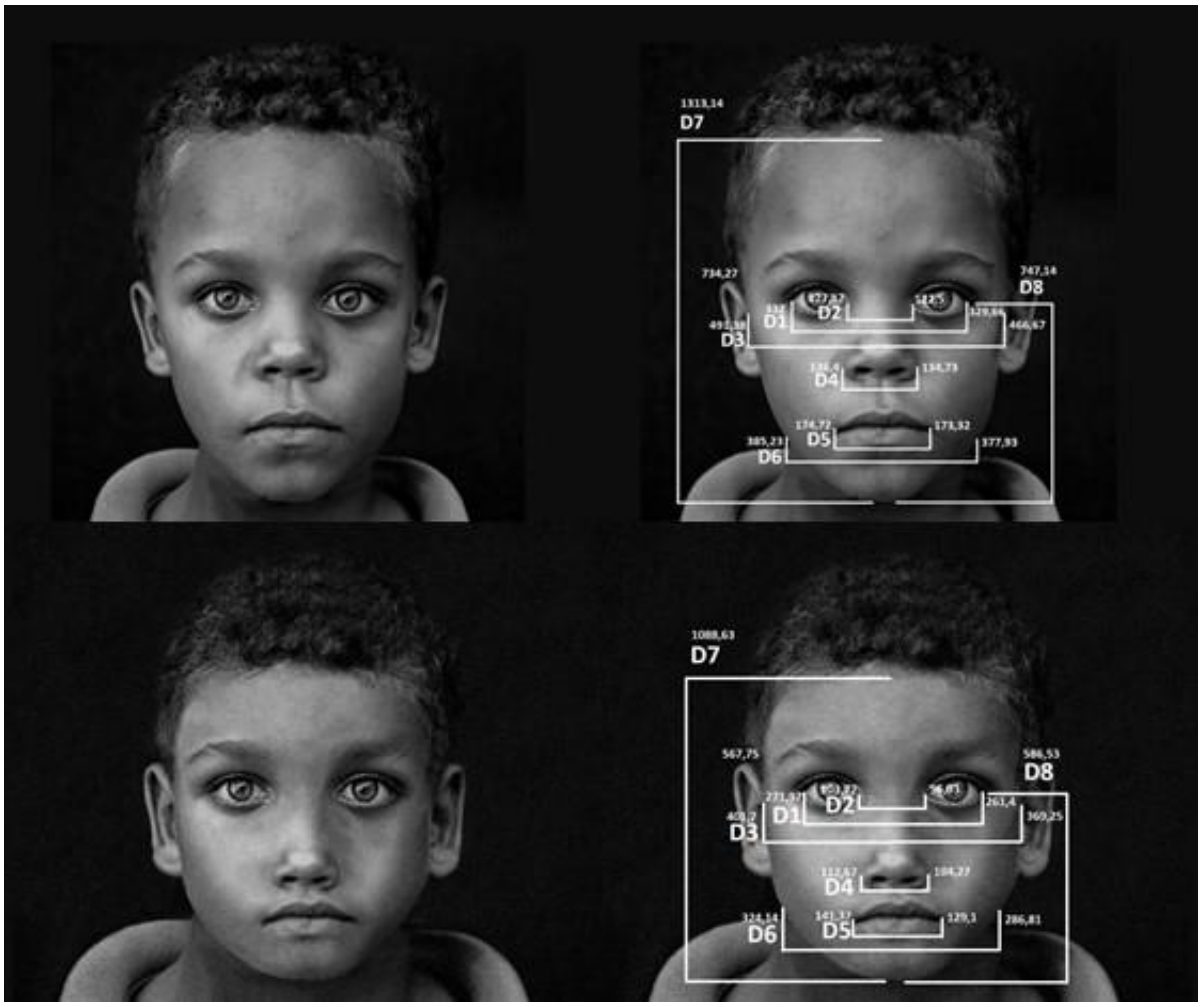

Figure 2. Sketch photos created from the average values obtained from the face averages of the boys with ASD (above) and the face measurements of boys with normal development (below). (Measurements were made on pixels)

According the Figure 2, there is a significant difference in measuring the margins of the eyes and chin ends (D8) only in the right half of the face when comparing each other, namely boys with ASD and developing normally. When face measurements of those with normal development are proportionally compared, there is a significant difference between D1 to D2, D3, D5, D6; D2 to D1, D3, D4, D5, D6; D3 to D1, D2, D5, D6; D4 to D2, D5, D6; D5 to D1, D2, D3, D4, D6; D6 to D1, D2, D3, D4, D5. When face measurements of those with ASD are compared proportionally, there is a similarity between D1 to D2, D3, D6; D2 to D1, D3, D6; D3 to D1, D2, D6; D6 to D1, D2, D3. When the face measurements of the two groups are compared as pixes, there is a significant difference in D1 and D2. There is a significant difference between the second and fourth fingers of the left and right hands of the ASD and normal developing group. As a result of their data, it is seen that the faces of individuals with ASD are more symmetrical than the individuals with normal development (above).

Discussion

Many studies have reported that autism spectrum disorder may be a result of high testosterone exposure in the womb. The ratio of the second and fourth fingers is used for prenatal testosterone exposure as an

indicator. In a study conducted in Slovakia, 2D:4D ratio was compared in two male groups with and without ASD, and the 2D:4D ratio of the group with ASD was found to be lower than the control group. With this finding, reference was made to the 'extreme male brain' theory (Krajmer, 2011). In the UK, a large study was carried out by the National Autistic Community, which also included families of individuals with ASD. As a result of the research, 2D:4D ratios were obtained below the normal level in the society, including family members, and they suggested that prenatal testosterone may be a biomarker (Baron-Cohen, 2001). In a study that compared the group with and without autism in Thailand, electronic caliper measurement method, which is similar to our study, was used to investigate the status of 2D:4D ratio as a risk factor for autism. Children with autism had a lower 2D:4D ratio than children without autism. This has been associated with an increased risk of autism (Noipayak, 2014). In a study conducted in Saudi Arabia, a significant relationship was found between high fetal testosterone and 2D:4D finger ratio. It is concluded that this is a risk factor for autism (Al-Ayadhi, 2015). In a study conducted jointly in the USA and the UK, the connection between the face width/height ratio and testosterone was investigated and a positive relationship was found (Lefevre, 2012). Exposure to increased prenatal testosterone levels has been found to be associated with ASD and evidence is provided that a more masculine facial structere may be associated with the ASD phenotype (Gilani, 2015).

In the study, face halves of children with ASD and normal development were compared among themselves similar results was found. When boys with ASD and normal development are compared with each other, there is a significant difference only in the measurement of the margins and chin end (D8) in the right half of the face. As a result, it was concluded that the faces of individuals with ASD are more symmetrical than the individuals with normal development and their 2D and 4D finger lengths are close to each other. In addition, similarity among ASD diagnostic groups worsens as the level of disease weight increases.

Suggetions

This study is based on the theory of the over-masculine male brain due to exposure to excessive testosterone for ASD. This theory proposes that ASD is an extreme example of male behavioral traits with symmetry. The tendency for symmetry in our results is consistent with this theory. ASD is a relatively common disease, and investigating the relationship of the tendency to symmetry with autistic child blood testosterone levels, maternal testosterone or derivatives levels, or maternal amniotic fluid levels will also yield more illuminating results etiologically. At the same time, researching the tendency to symmetry with 3-dimensional face scanning systems will yield more remarkable results.

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