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Araştırma/ Research Article

INVESTIGATION OF THE RELATIVE CONTRIBUTION OF GENETICS AND ENVIRONMENT ON MANDIBULAR MORPHOLOGY WITH THE CLASSICAL TWIN METHOD

GENETİK VE ÇEVRENİN MANDİBULAR MORFOLOJİYE KATKISININ KLASİK İKİZ YÖNTEMİ İLE ARAŞTIRILMASI

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ABSTRACT
Aim: The purpose of this study was to explore the contribution of the genetics and the environment on the mandibular morphology of the Turkish twins.
Materials and Methods: This retrospective study conducted with the archival records of the twins who have applied between 2012 and 2018.-Condylar height, ramus height, gonial angle, intercondylar distance and intergonial distance were measured on the panoramic radiographs with computer software. The correlations between the monozygotic (MZ) and dizygotic (DZ) twins, and heritability estimates were evaluated.
Results: Moderate to high heritability observed in condylar height, ramus height, intercondylar distance and left gonial angle. Low heritability observed in intergonial distance and right gonial angle. Similar intra-pair correlations were found within the MZ and DZ male and female twin pairs for the measured parameters. However, no significant correlations observed within the DZ opposite sex twins. No significant difference also observed within the MZ male and female twin pairs in terms of the measured parameters except the significant difference in right ramus height of male MZ twins.
Conclusion: Horizontal parameters were found to be more susceptible to environmental factors than vertical ones. Gender was found to be caused similar variability in the measured parameters. Beside the results of the present study, it should be considered that the heritability is a concept that related with population rather than an individual, it would not be correct to reach definitive conclusions regarding the prevention of the disruptions, and prognosis of the treatments. Thus, the results should be interpreted cautiously when they are transformed into the clinical applications.
Keywords: Heritability, twin study, mandible

ÖZ
Amaç: Bu çalışmanın amacı, genetik ve çevrenin, Türk ikizlerinin mandibular morfolojisine katkısını araştırmaktır.
Gereç ve Yöntem: Bu retrospektif çalışma 2012 ve 2018 yılları arasında başvuruda bulunan ikizlerin arşiv kayıtları ile yapılmıştır. Panoramik radyografilerde bilgisayar yazılımı ile kondiler yükseklik, ramus yüksekliği, gonial açı, interkondiler mesafe ve intergonial mesafe ölçülmüştür. Monozigotik (MZ) ve dizigotik (DZ) ikizler arasındaki ilişki ve kalıtım derecesi tahminleri değerlendirilmiştir.
Bulgular: Orta ila yüksek derecede kalıtım etkisi kondiler yükseklik, ramus yüksekliği, interkondiler mesafe ve sol gonial açı parametrelerinde gözlendi. İntergonial mesafe ve sağ gonial açıda ise düşük kalıtım etkisi tespit edildi. Ölçülen parametreler için MZ ve DZ erkek ve kadın ikiz çiftlerinde benzer korelasyonlar bulunmakla birlikte, DZ farklı cinsiyetteki ikizler arasında anlamlı bir ilişki gözlenmedi. MZ erkek ve kadın ikiz çiftlerinde, ölçülen parametreler açısından, erkek MZ ikizlerinin sağ ramus yüksekliğindeki anlamlı fark dışında, anlamlı bir fark gözlenmedi.
Sonuçlar: Yatay parametrelerin dikey olanlara göre çevresel faktörlere daha duyarlı olduğu bulunmuştur. Cinsiyetin ölçülen parametrelerde benzer değişkenliğe neden olduğu görülmüştür. Bu çalışmanın sonuçlarının yanı sıra, kalıtımın bir bireyden çok popülasyonla ilgili bir kavram olduğu, tedavi aksamalarının önlenmesi ve prognozu konusunda kesin sonuçlara varmanın doğru olmayacağı dikkate alınmalıdır. Bu nedenle sonuçlar klinik uygulamalara dönüştürülürken dikkatli yorumlanmalıdır.
Anahtar Sözcükler: Kalıtım derecesi, ikiz çalışması, mandibula

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INTRODUCTION

The growth of mandible is a complex biological event which is known to occur in response to genetic and environmental effects.[1,2,3] The contribution of the genetics to the morphology of the growing mandible pose clinical importance in terms of the growth modification, therapeutic interventions and estimation of the prognosis.[4] Twin studies regarded as a powerful tool in the evaluation of the contribution of genetics and the environment on various traits or disorders in humans. Classical twin model based on the assumption that monozygotic (MZ) twins share all of their genes, while dizygotic (DZ) twins, share on half average of their genes. By comparing the differences within pairs of MZ and DZ twins, in the classical method genetic contribution on the variation of a trait or anomaly can be determined.[2,5-9] The differences between MZ twin pairs are considered to be originated from the environmental differences, while those in DZ twin pairs considered to be originated from both genetic and environmental factors.[10]

Modification of the development of mandible is based on that the heritability and environment are both responsible for its ultimate morphology. Nevertheless, the exact genetic contribution to mandibular morphology not completely clarified.[1,11] Therefore, the aim of this study was to explore the contribution of environment and genetics on mandibular morphology of Turkish twins.

MATERIALS AND METHODS

Patients

This retrospective study was conducted with the panoramic radiographs of the twins who have applied to the Oral and Maxillofacial Surgery Department of Ordu University, between 2012 and 2018. The study protocol was approved by the Ethics Committee of the Ordu University (No: 2019-28) and conducted in accordance with the ethical standards in the Helsinki Declaration of 1964 and its subsequent amendments.

Inclusion Criteria:

- Twins with complete demographic, and radiological data
- Twin pairs who were taken the panoramic film at the same day
- Twin pairs with high-quality radiographic images

Exclusion Criteria:

- Twin pairs who have low-quality radiographic images that prevent the measurements

Zygosity of the twin pairs was determined based on responses to a standard zygosity questionnaire [12], sex and blood groups.

Radiography

The archive was scanned through the Turcasoft software (Turcasoft Dent, Samsun, Turkey) and the patients' panoramic films were reached. All panoramic radiographs had obtained by means of the Kodak 8000C Digital Panoramic System (Kodak Dental Systems, Rochester, NY). All measurements were performed by the same researcher using Turcasoft software. Radiographic measurements made separately from both sides in all patients by the same researcher. The researcher reviewed the radiographs on two separate sessions, one week apart. Intra-observer reliability was determined by comparing the first and second measurements. The average of the calculations was accepted as the value of the parameter. The horizontal, vertical and angular measurements on panoramic radiograph were shown in Figure 1.

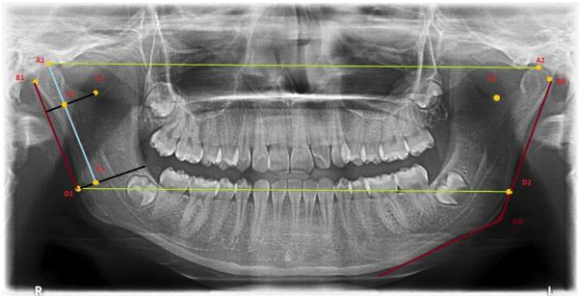

Figure 1. Panoramic film showing mandibular measurements.
A_1, A_2: Most superior point of the condylar head
B_1, B_2: Most outer point on the posterior border of condylar head
C_1, C_2: Most inferior part of the sigmoid incisura
D_1, D_2: A point on the bony contour determined by bisecting the gonial angle
A_1-E_1 line: Condylar height
A_1-f_1 line: Ramus height
A_1-A_2 line: Intercondylar distance
D_1-D_2 line: Intergonial distance
GA (Gonial angle): The angle between the tangential line of the posterior border of the mandibular ramus and the lower border of the mandibular body

Statistical analysis

Statistical analyses were performed by using the IBM SPSS Statistics for Windows software (version 23.0, IBM Corp, Chicago, USA). Data were represented as mean (SD) and median (Min-Max). Normality of the data assess by the Kolmogorov Smirnov test. Pearson or Spearman correlations

performed to explore the correlation in the vertical, horizontal and angular measurements within the twin pairs. Paired t test or Wilcoxon test was used to compare the difference within the MZ male and female twins. To estimate the heritability of the measured parameters, Falconer's formula of heritability was applied. Narrow-sense heritability-additive genetic (h^2), shared environmental (c^2) and non-shared environmental (e^2) variance calculated with the formulas as follows; $h^2 = 2(r_{MZ} - r_{DZ})$, $c^2 = 2r_{DZ}-r_{MZ}$, $e^2 = 1-r_{MZ}$. The intra-observer reliability was evaluated by comparing the measurements of the researcher at the first and the second sessions with the intraclass correlation coefficient (ICC). All tests were two-tailed and were based on a 0.05 were significance level.

RESULTS

This study consists of 70 pairs of Turkish twins. 20 of the twins were MZ while 50 of them DZ. The demographic data of the twins showed in Table 1. Statistically significant correlations were found between MZ twin-pairs in terms of measurements except for intergonial distance. Significant correlations were also found between DZ twin-pairs in terms of measurements except for left condylar height and intercondylar distance. Descriptive of the measurements and heritability estimates among MZ and DZ twin pairs were shown in Table 2 and 3. Regarding gender significant correlations were observed in terms of left condyle and ramus height, gonial angles and intercondylar distance in female MZ twin pairs while significant correlations found in terms of left condylar height, right-left ramus heights, gonial angles and intergonial distance in male MZ twin pairs (Figure 2). Female DZ twin pairs were showed significant correlations in right condylar height, gonial angles, intercondylar and intergonial distances. Male DZ twin pairs were showed significant correlations in left ramus height, gonial angles, intercondylar and intergonial distances. However, opposite-sex twin pairs did not show significant correlations in any of the measure-

Table 1. Demographic characteristics of the sample

	MZ	DZ
Age		
(Mean±SD)/(Min-Max)	19.55 (12.89)/ (9-54)	12.28 (3.65)/ (6-24)
Gender (%)		
Female	8 (40 %)	19 (26 %)
Male	12 (60 %)	13 (38 %)
Opposite Sex	-	18 (36 %)

Table 2. Descriptive of the measured parameters

			MZ_1		MZ_2		r_{MZ}	*p*
			Mean±SD	*Median (Min-Max)*	*Mean±SD*	*Median (Min-Max)*		
MONOZYGOTIC (MZ)	Condylar height	R	1.88±0.32	1.80 (1.50-2.88)	1.81±0.19	1.85 (1.15-2.18)	0.568	0.009*
		L	1.81±0.25	1.85 (1.15-2.18)	1.79±0.25	1.76 (1.18-2.27)	0.797	<0.001*
	Ramus height	R	2.75±0.44	2.73 (2.26-3.72)	2.84±0.41	2.74 (2.18-4.04)	0.808	<0.001*
		L	2.74±0.48	2.73 (1.95-4.14)	2.84±0.39	2.80 (2.18-3.72)	0.858	<0.001*
	Gonial angle	R	127.66±22.72	122.44 (107.69-220.51)	122.62±7.41	122.58 (108.53-137.66)	0.528	0.017*
		L	124.44±6.78	124.75 (112.44-139.71)	124.57±7.73	125.19 (105.78-135.66)	0.747	<0.001*
	Intercondylar distance		17.77±1.9	17.55 (14.86-22.26)	17.98±1.75	18.48 (14.58-20.62)	0.511	0.021*
	Intergonial distance		16.06±1.37	15.91 (14.41-19.53)	16.41±1.5	16.46 (13.61-19.56)	0.402	0.079
			DZ_1		DZ_2		r_{DZ}	*p*
			Mean±SD	*Median (Min-Max)*	*Mean±SD*	*Median (Min-Max)*		
DZYGOTIC (DZ)	Condylar height	R	1.81±0.20	1.81 (1.37-2.40)	1.80±0.21	1.84 (1.20-2.31)	0.299	0.035*
		L	1.85±0.33	1.80 (1.34-3.32)	1.84±0.30	1.84 (1.17-2.84)	0.114	0.433
	Ramus height	R	2.51±0.39	2.49 (1.31-3.82)	1.80±0.21	1.84 (1.20-2.31)	0.295	0.038*
		L	2.57±0.35	2.53 (1.85-3.87)	2.53±0.34	2.45 (1.87-3.43)	0.585	<0.001*
	Gonial angle	R	124.56±7.46	124.84 (105.76-137.35)	125.46±10.66	126.64 (67.55-143.25)	0.459	0.001*
		L	126.67±6.91	128.64 (110.85-139.20)	127.54±6.36	126.75 (114.38-147.64)	0.420	0.002*
	Intercondylar distance		17.47±1.75	17.18 (13.36-21.87)	18.97±11.44	17.24 (13.83-97.42)	0.272	0.056
	Intergonial distance		15.67±1.91	15.36 (10.13-21.11)	15.56±1.60	15.39 (10.62-18.67)	0.575	<0.001*

R: Right, **L:** Left, **SD:** Standard deviation, **r:** correlation coefficient, *****: significant (Pearson or Spearman correlation)

ments (Figure 3). No significant difference observed within the MZ male and female twin pairs in terms of the measured parameters except the significant difference in right ramus height of male MZ twins ($p<0.001$). The ICC for the first and second measurements were between 0.976-0.998 (IC 0.958–0.999) for the measurements of DZ twins and 0.978-0.999 (IC 0.944–1) for the measurements of MZ twins.

Table 3. Heritability estimates for variables

Phenotype	h^2	c^2	e^2
Condylar height_R	0.53	0.03	0.43
Condylar height_L	1.36	-0.56	0.20
Ramus height_R	1.02	-0.21	0.19
Ramus height_L	0.54	0.31	0.14
Gonial angle_R	0.13	0,39	0.47
Gonial angle_L	0.65	0.09	0.25
Intercondylar distance	0.47	0.03	0.48
Intergonial distance	-0.34	0.74	0.59

R: Right, **L:** Left

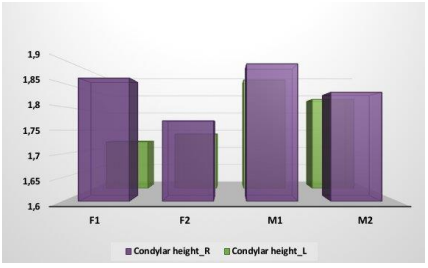

Fig 2A

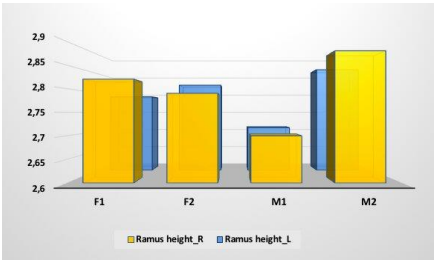

Fig 2B

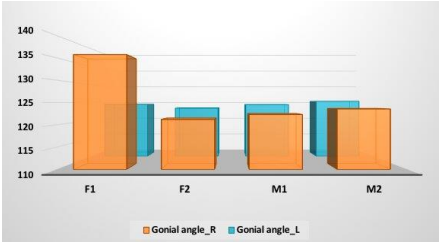

Fig 2C

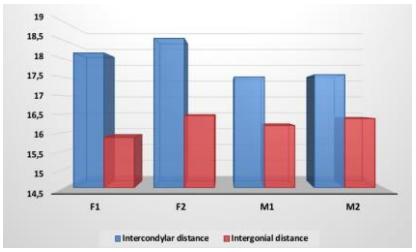

Fig 2D

Figure 2: A. Condylar height (mm), **B.** Ramus height (mm), **C.** Gonial angles, **D.** Intercondylar and intergonial distances-(mm) among gender of MZ twins

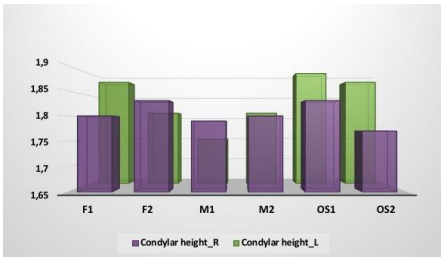

Fig 3A

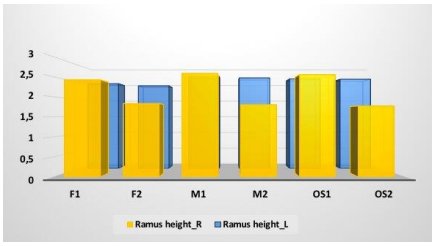

Fig 3B

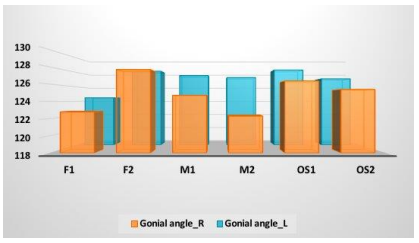

Fig 3C

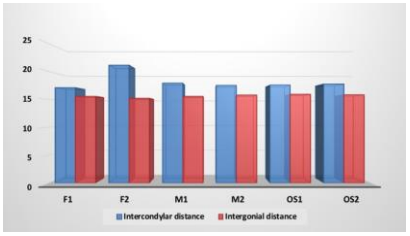

Fig 3D

Figure 3:A. Condylar height (mm), **B.** Ramus height (mm), **C.** Gonial angles, **D.** Intercondylar and intergonial distances-(mm) among gender of DZ twins

DISCUSSION

The final phenotype of the craniofacial morphology, represents complex interaction between genetics and environmental factors.[1,10] Studies that explore the exact role of the genetics and environmental components of this interaction on mandibular morphology reported different results regarding morphological parts responsible for the size and form of the mandible. In the study of Sıdlauskaset al.[1] that conducted on 141 same-gender adult twin pairs high heritability values reported for the gonial and mandibular arc angles. In the cross-sectional twin study of Amini et al.[10] gonial angle values showed high heritability. Similarly, Manfredi et al.[12] found high heritability for the gonial angle. However, a moderate heritability was also reported by Carels et al.[9] for the gonial angle. In this study we found high heritability for the left gonial angle while low heritability values observed for the right gonial angle. This result may be originated from the different amount of the contribution of the genetic, environmental, and epigenetic factors on these parameters or may be due to the skewness of the data regarding zygosity.

Regarding linear variables, it is reported that the horizontal parameters are majorly determined by genetic factors rather than the vertical ones.[1, 2] Some researchers however were insisted on the opposite.[9, 10,14] Sıdlauskas et al.[3] reported in their cephalometric study on 90 MZ twin pairs that total mandibular and corpus lengths showed the highest intra-pair correlation. In another study of the same authors it is reported that mandibular length, ramus width and height showed low genetic determination.[1] High heritability values for mandibular length were found in the studies of Dudas and Sassouni.[15] and Carels et al.[9] However, Nakataet al.[8] and Amini et al.[10] observed low and moderate heritability for mandibular length, and ramus height, respectively. We found that ramus height and condyle height were showed higher heritability, than the intercondylar and intergonial distances. Regarding the effect of gender on mandibular morphology Šidlauskas et al.[4] found that females showed significant differences in terms of mandibular length within MZ twin pairs. They suggested that this may indicate the role of hormonal influence on mandibular development. But, in our study similar correlations were found within the MZ twin pairs for the measured parameters between males and females. These differences among the results of the studies may be originated from the differences in the determination of zygosity, size of the sample, maturity stage of the patient, radiological evaluation methods and statistical methods used. Thus, the results of twin studies should be interpreted with caution. Also, further prospective studies should be conducted with larger samples and more clinical/radiological parameters to the exact reason behind the contribution of the genetic, epigenetic and environmental factors on mandibular morphology.

The radiologic method used is an important factor that determines the accuracy of the evaluations. Panoramic radiography is usually the first imaging modality of choice to overview the teeth and jaws with low radiation exposure. It is a practical, fast and safe method when studying with large number of samples and has favorable cost-benefit relationship.[16-19] Also, the repetition of the measurements is acceptable when the position of the patient's head positioned correctly. Thus, linear measurements have been performed, such as alveolar height, and condylar dimensions by this technique.[17,20] Although in the majority of the studies cephalometric radiographs utilized for the evaluation of the mandibular morphology, because of the retrospective design of our study and usability of the panoramic radiography for performing linear measurements we used digital panoramic radiographs of the twins that had obtained at the same time.

There are potential limitations. It is reported that the contribution of the genetic and environment changes with the age.[6, 21] Also, the precise evaluation of the genetic contribution is difficult with narrow samples.[10] Thus, the design of the present study did not assess the genetic contribution with high precision. As in other twin studies difficulty in establishing zygosity is another limitation.[6] In that the exact genetic contribution on mandibular morphology can be determined when the growth is completed, the maturity of the sample is also another problem.[1]

CONCLUSIONS

Despite the limitations, it can be concluded that moderate to high heritability observed in condylar and ramus height, intercondylar distance and left gonial angle. Low heritability observed in the intergonial distance and right gonial angle. The female MZ twin pairs showed similar variability in the measurements when compared to the male MZ twin pairs. Therefore, no hormonal influence seems to be present. Beside the results of the present study, it should be considered that the heritability is a concept that

related with population rather than an individual, it would not be correct to reach definitive conclusions regarding the prevention of the disruptions, and prognosis of the treatments. Thus, the results should be interpreted cautiously when they are transformed into the clinical applications.

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Conflict of Interest:
The authors declare that they have no conflict of interest.

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