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Araştırma

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An Examination of the 2D:4D Ratio, Handedness and Footedness in Attention Deficit Hyperactivity Disorder

Dikkat Eksikliği Hiperaktivite Bozukluğunda 2D:4D Oranı, El ve Ayak Dominansının İncelenmesi

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ABSTRACT

Aim: The purpose of this study was to examine hand 2D:4D ratios and their association with ADHD. The study was intended to compare hand 2D:4D ratios according to hand and foot dominance in individuals with ADHD.

Methods: 168 children were included in the study, 91 diagnosed with ADHD and 77 healthy volunteers. All participants were evaluated via DSM-5 based psychiatric examinations, and their sociodemographic data were collected using forms prepared by the authors. The participants' ADHD symptoms were assessed using the Conners' Parent Rating Scale-Revised Short Form (CPRS-RS). 2D:4D ratios were determined by measuring the lengths of the bilateral second and fourth fingers using a digital compass. Hand and foot dominances were determined by evaluation in a clinical setting. The scores obtained were then compared.

Results: Lower right and left hand 2D:4D ratios were determined in the individuals with ADHD than in the healthy controls (p=0.001 for both). No correlation was found between ADHD subscales and right or left hand 2D:4D ratios in the case group (p>0.05). No differences in 2D:4D ratios were also observed according to hand and foot dominances in the case group (p>0.05).

Conclusion: This study produced important findings concerning whether hand 2D:4D ratios can be used as a marker of ADHD. We think that the data obtained may be of assistance to other studies assessing the phenotype characteristics of individuals with ADHD.

Key Words: Attention deficit hyperactivity disorder, 2D:4D ratio, handedness, footedness

ÖZ

Amaç: Bu çalışmada fetal testosteron maruziyetinin göstergesi olan el 2D:4D oranları ile DEHB arasındaki ilişkinin incelenmesi amaçlanmıştır. Ayrıca DEHB olanlarda el ve ayak tercihlerine göre el 2D:4D oranlarının karşılaştırılması amaçlanmıştır.

Yöntem: Çalışmaya 91 DEHB tanılı ve 77 sağlıklı gönüllü olmak üzere 168 katılımcı ergen alındı. Tüm katılımcılar DSM-5 temelli psikiyatrik muayene ile değerlendirildi ve sosyodemografik verileri araştırmacılar tarafında hazırlanan formlar ile elde edildi. Katılımcıların DEHB belirtileri Conners Anababa Dereceleme Ölçeği-Yenilenmiş Kısa Form (CADÖ-YK) ile değerlendirildi. 2D:4D oranları, her iki elin 2. ve 4. parmak uzunlukları dijital kumpas ile ölçülerek belirlendi. El ve ayak tercihleri klinik ortamda değerlendirilerek belirlendi. Elde edilen skorlar istatistiksel olarak karşılaştırıldı.

Bulgular: DEHB olan bireylerde sağlıklı kontrollere göre sağ ve sol elde daha düşük 2D:4D oranları saptandı (sırasıyla p=0,001, p=0,001). Olgu grubunda DEHB alt ölçekleri ile sağ ve sol el 2D:4D oranları arasında ilişki bulunmadı (p>0.05). Olgu grubunda 2D:4D oranları ile el ve ayak tercihleri arasında fark saptanmadı (p>0.05.

Sonuç: Çalışmamızda 2D:4D oranlarının DEHB de bir belirteç olarak kullanılabileceğine dair önemli sonuçlar elde edilmiştir. Elde ettiğimiz veriler gelecekte DEHB li bireylerin fenotipik özelliklerini değerlendiren diğer çalışmalara katkıda bulunabileceği kanaatindeyiz.

Anahtar Kelimeler: Dikkat eksikliği hiperaktivite bozukluğu, 2D:4D Oranı, el tercihi, ayak tercihi

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Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by hyperactivity, inattention, and impulsivity.[1] The global prevalence of ADHD in children and adolescents is 5-7.1.[2] The condition is 2-4 times more common in male gender.[3] Despite this greater prevalence in boys, this gender variation has not yet been explained, although the focus is on genetics and hormones.[4] Sex hormones in the prenatal period are known to affect fetal brain development.[5]

The evaluation of fetal testosterone levels in the intrauterine period is invasive and costly. Two finger ratios have therefore been employed instead of fetal testosterone levels in research.[6] Fetal testosterone levels in the prenatal period are known to affect the second and fourth finger ratio (2D:4D) and the length of those fingers. The 2D:4D ratio is inversely correlated with fetal testosterone levels in both sexes, the ratio decreasing as fetal testosterone rises.[7] Few studies have investigated the relationship between the 2D:4D ratio and clinically diagnosed ADHD, and their results are inconsistent. One such study reported a significantly lower 2D:4D ratio in boys diagnosed with ADHD compared to healthy controls, together with a significant negative correlation between the severity of ADHD subtypes and 2D:4D.[8] However, another study reported no difference in 2D:4D ratios between ADHD and control groups.[9]

Cerebral lateralization refers to one hemisphere of the brain being responsible for specific functions. While the right hemisphere is responsible for some cerebral functions, the left hemisphere is dominant in others, and both hemispheres are currently regarded as being specialized to perform certain functions and process information in a specific manner. Several behavioral asymmetries emerge as a result of hemispheric asymmetry, the most marked of which being hand dominance. Handedness is directly linked to hemisphere dominance.[10] Studies have reported atypical cerebral lateralization in individuals with ADHD.[11] Only limited numbers of studies have directly examined the association between ADHD and handedness. While some have observed more frequent left hand and mixed use in individuals with ADHD[12,13], others have determined no atypical handedness.[14] Research has suggested that individuals exposed to excessive testosterone during the fetal period exhibit greater left handedness.[15] However, no research has evaluated the relationship between fetal testosterone exposure and hand and foot dominance in individuals with ADHD.

There has been little research into the relationship between the 2D:4D ratio and ADHD in children with the condition, and the reported findings are inconsistent. To the best of our knowledge, no previous research has compared 2D:4D ratios, an indicator of fetal testosterone exposure, in terms of handedness and footedness in individuals diagnosed with ADHD. This research compared the 2D:4D ratios of children diagnosed with ADHD with those of healthy controls, and examined the relationship between ADHD symptoms and the 2D:4D ratio. The unique aspect of this study is that it compared 2D:4D ratio according to handedness and footedness in children diagnosed with ADHD.

Method

Sampling and Application: The study was performed with 168 children and adolescents aged 6-18 years, 91 diagnosed with and under follow-up for ADHD, and 77 healthy volunteers. All participants underwent psychiatric evaluations based on the Turkish version of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5 TR). These evaluations were conducted by experienced child and adolescent mental health and diseases specialists. The study was completed in October and November 2023. Written and verbal consent was obtained from the families of all particıpating adolescents. Children wıth additional psychiatric diagnoses or with known physical diseases were excluded from the study. The participating families' sociodemographic data were collected using forms prepared by the authors and face-to-face interviews. Participants with difficulties in reading and understanding the forms or who were unable to complete the evaluation process were excluded. The parents completed the Conners' Parent Rating Scale-Revised Short form (CPRS-RS) in order to scan the ADHD symptoms of the children in the study group. The bilateral index and ring fingers of the children and adolescents enrolled in the study were measured using a digital caliper sensitive to 0.01 mm from the proximal fold on the volar surface of the metacarpophalangeal joint to the tip of the finger, and the ratio of the length of the index finger to the length of the ring finger was determined from these values. The children's hand and foot dominances were determined by the authors by means of evaluations in a clinical setting. Ethical approval for the study was granted by the Alanya Alaaddin Keykubat University clinical research ethical committee, Türkiye, under decision no. 14-03.

Tools

Sociodemographic Information Form: This was used to elicit sociodemographic characteristics, including name and surname, age, sex, education status, the ages of the mother and father, and the parents' education levels, occupations, and incomes. Psychiatric and physical problems experienced during pregnancy, alcohol and sub-

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stance use, treatments received, modes of delivery and gestational complications were also investigated.

Conners' Parent Rating Scale-Revised Short Form (CPRS-RS): This scale was developed by Conners for the purpose of evaluating behaviors in childhood.[16] The CPRS-RS consists of 27 items in three subscales - (Oppositional -O, Cognitive Problems/ Inattention- CP-I, and Hyperactivity-H) and one assistant scale (ADHD Index -ADHD-I). Each item is scored between 0 and 3; never (at no time, very rarely) 0; sometimes true (sometimes) 1; often true (frequently) 2; and very true (very frequently) 3. The higher the score, the greater the possession of problems described in the CPRS-RS. Reliability and validity were investigated by Kaner.[17]

Statistical Analysis: Frequency and percentage values were calculated for categorical data and mean and standard deviation values for continuous data. Normality of distribution of the data collected through the scales was evaluated using skewness-kurtosis values, histograms, and Q-Q plot graphics. For kurtosis and skewness, values in a range of ±1.5 were evaluated in favor of normal distribution. Levene's test was applied to examine whether the measured variable variances in the groups were equal. The applicability of the scales used for the study group was examined using the Cronbach-alpha method. The independent samples t test was applied for differences between the groups. Relationships between parameters were evaluated using Pearson correlation coefficient results. Statistical analyses were conducted on SPSS version 22 software, and p values <0.05 were regarded as significant.

Results

One hundred sixty-eight individuals voluntarily agreeing to take part and providing informed consent were enrolled in the study. Ninety-one (54.2%) individuals diagnosed with ADHD constituted the case group and 77 (45.8%) individuals similar to that group in terms of age and sex were included as the control group. Girls constituted 101 (60.1%) of the participants. The mean age of the participants was 9.45±2.28 years. Right hand dominance was present in 150 (89.3%) participants and right foot dominance in 136 (81%).

No difference was determined between the case and control groups in terms of age (p = 0.094) or sex (p = 0.315). No difference was also determined between the groups in terms of hand dominance (p = 0.104) or foot dominance (p = 0.66). Right hand 2D/4D values were lower in the case group than in the control group (t (166) = -3.403, p = 0.001). Similarly, left hand 2D/4D values were significantly lower in the case group (t (166) = -3.364, p = 0.001) (Table 1).

The skewness and kurtosis values used as evaluation tools were within the ±1.5 range and possessed a good level of internal consistency. No associations were found between finger ratios and O (right hand; $p = 0.995$, left hand; $p = 0.764$), BP/D (right hand; $p = 0.487$, left hand; $p = 0.475$), H (right hand; $p = 0.669$, left hand; $p = 0.263$), or ADHD-1 (right hand; $p = 0.823$, left hand; $p = 0.589$) in the case group (Table 2).

No significant difference was determined between individuals with right and left hand dominance in terms of right 2D:4D results ($t_{(89)} = -0.957$, $p = 0.341$). No significant difference in hand dominance was also found in left hand 2D:4D ratios (t (89) = -1.957, $p = 0.127$). In terms of footedness, no significant differences were found between the right and left foot dominance groups for either right foot 2D:4D results ($t_{(89)} = -0.884$, $p = 0.379$) or left foot 2D:4D results ($t_{(89)} = -0.877$, $p = 0.384$) (Table 3).

Discussion

The 2D:4D ratio was significantly lower in the children diagnosed with ADHD in this study compared to the healthy controls, but no association was determined between the severity of ADHD symptoms and 2D:4D ratios. In addition, 2D:4D ratios were investigated in terms of hand and foot dominances in the children with ADHD, but no significant differences were found.

Table 1. A comparison of the case and control group measurements

	Case	Control	χ2. *t*	*P*
Gender (F)	60 (65.9%)	41 (53.2%)	2.800	0.094
Age (years)	9.60 ± 2.60	9.26 ±1.83	1.007	0.315
Tight hand ratio (2D/4D)	0.98 ± 0.046	1.01 ± 0.043	-3.403	**0.001**
Left hand ratio (2D/4D)	0.97 ± 0.043	0.99 ± 0.044	-3.364	**0.001**
Hand dominance (right)	78 (87.7%)	72 (93.5%)	2.647	0.104
Foot dominance (left)	69 (75.8%)	67 (87%)	3.386	0.066

Chi-square test, Independent Samples t Test, p<0.05 results shown in bold

Table 2. Relationships between ADHD subdimension characteristics and finger ratios

	Mean±SD (Min-Max)	RIGHT 2D/4D *P* (Pearson's r)	LEFT 2D/4D *P* (Pearson's r)	Skew	Kurt	α
O	9.45±5.11(0-18)	0.995 (0.001)	0.764 (-0.032)	-0.02	-1.17	0.876
CP/I	11.41±4.42(0-18)	0.487 (-0.074)	0.475 (-0.076)	-0.43	-0.60	0.838
H	8.58±5.05(0-18)	0.669 (-0.045)	0.263 (-0.119)	0.16	-0.92	0.873
ADHD-I	21.90±7.23(2-35)	0.823 (-0.024)	0.589 (-0.057)	-0.45	-0.13	0.859

O: Opposition, CP/I: Cognitive Problems/Inattention, H: Hyperactivity. ADHD-I: ADHD-Index, α: Cronbach Alpha. Skew: Skewness. Kurt: Kurtosis. Min: minimum, Mac: Maximum, SD: Standard Deviation, p<0.05 results shown in bold

Table 3. A comparison of hand 2D:4D ratios in terms of handedness and footedness

	Hand Dominance	Mean± SD	*t*	*p*	Foot Dominance	Mean± SD	*t*	*p*
Right hand ratio (2D/4D)	Right	0.98±0.05	-0.957	0.341	Right	0.98±0.04	-0.884	0.379
	Left	0.99±0.03			Left	0.99±0.05		
Left hand ratio (2D/4D)	Right	0.97±0.04	-1.539	0.127	Right	0.97±0.04	-0.877	0.384
	Left	0.99±0.03			Left	0.98±0.04		

Independent Samples t Test, p<0.05 results shown in bold

Martel et al. observed a significant lower 2D:4D ratio in children diagnosed with ADHD than in healthy controls.[8] Another study reported significantly lower 2D:4D ratios in both boys and girls with ADHD.[18] However, Lemiere et al. compared children with ADHD and healthy controls and determined no significant difference.[9] Similarly in the present study, 2D:4D ratios for both hands were significantly lower in the children with ADHD than in the healthy controls. In the light of the association between a low 2D:4D ratio and fetal testosterone exposure, it may be suggested that children diagnosed with ADHD were exposed to high levels of testosterone in the intrauterine period.

Various studies have examined the relationship between the severity of ADHD symptoms and the 2D:4D ratio, although the results are inconsistent.[8,9,19,20] Lemier et al. found no association between ADHD symptoms and the 2D:4D ratio.[9] Similarly, Wang et al. determined no relationship between ADHD symptoms and 2D:4D ratios.[21] However, other studies have reported a negative correlation between ADHD and the 2D:4D ratio.[8,22] The present research investigated correlations between ADHD symptoms in children with the condition and the 2D:4D ratios for both hands, and observed no significant association. Hand 2D:4D ratios vary depending on age, sex, and hand.[23] The inconsistencies among research findings may be attributable to different gender distributions and age groups in previous studies and the sample group in some consisting only of males.

Although several studies have investigated atypical cerebral lateralization in ADHD, the means by which this lateralization occurs is still unclear.[24] One meta-analysis concerning ADHD and hand preference reported that the condition does not affect the individual's preference but does result in limitations in extremity function.[11] No significant differences were determined between 2D:4D ratios for both hands in the present study and the hand and foot dominances of the children with ADHD. Societal norms encouraging or obliging the use of the right hand may be present in some societies. This results in hand preference not representing an unbiased indicator in showing cerebral lateralization.[25] The fact that the present research was conducted in a society with norms encouraging right hand and foot use may account for this findings.

Limitations: This study will make an important contribution to the existing literature by examining 2D:4D ratios and hand and foot dominances in children diagnosed with ADHD. However, there are also a number of limitations to this study. One is the use of a self-report scale completed only by mothers for the determination of the severity of ADHD. Another limitation is that no structured scale was employed for hand and foot dominance.

Conclusions: 2D:4D ratios were lower in the children with ADHD than in the healthy controls. No relationship was determined between the severity of ADHD symptoms and 2D:4D ratios. No significant variation was determined between the bilateral hand 2D:4D ratios according to hand

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and foot dominance in the children with ADHD. This study elicited important results concerning whether or not 2D:4D ratios can be used as an indicator of ADHD in the future. We think that the data emerging from this study may also be useful to future studies evaluating the phenotypic characteristics of individuals with ADHD.

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