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RESEARCH ARTICLE

# Age- and gender-related changes in cerebral ventricle parameters during the pediatric period

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## ABSTRACT

**Aim:** This study focused on investigating age- and gender-related changes in the brain ventricles of healthy pediatric individuals.

**Methods:** Brain MR images of 200 healthy children aged 0-18 years were included in the study. The variables measured were as follows: axis of the third ventricle (ATV), anterior width of the frontal horn (ACF), posterior width of the frontal horn (PCF), width of the frontal horn (WCF), oblique diameter of the frontal horn (OCF), maximum transverse diameter of the skull (MTDS), vertical diameter of the skull (VDS), anteroposterior width of the right temporal horn (ARCT), anteroposterior width of the left temporal horn (ALCT), anteroposterior width of the fourth ventricle (AFV), transverse width of the fourth ventricle (TFV). In addition, the Evans index (EI) has been calculated.

**Results:** Statistically significant results were found between the individuals of the first, second and fourth groups for the ACF and PCF variables; the fourth group for the WCF, VDS, and TFV variables; the first and fourth groups for ARCT; the first group for ALCT; and the third and fourth groups for MTDS. In the pediatric period, while there was no significant difference between the genders until a certain age, it was observed that the difference between the genders increased especially after a certain age (between 7-18 years).

**Conclusion:** It is thought that the study will provide basic data for clinical sciences in the stages of diagnosis and treatment planning.

**Keywords:** Pediatric period, brain ventricles, MRI brain, brain, central nervous system

## INTRODUCTION

The nervous system begins to develop rapidly at a very early embryonic stage and continues to build up at a slower rate after birth. It regulates the control mechanisms of the body, including vital functions such as reflexes, in relation to the endocrine system. As the central nervous system (CNS) develops, the central canal expands in several regions to form the brain's ventricles. The ventricular system of the brain, which is

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hollow and filled with cerebrospinal fluid (CSF), consists of four components: the lateral right and left ventricles, and the third and fourth ventricles. The production and circulation of CSF take place in these structures (1-3). CSF acts both as a protector of the CNS and plays an important role in brain metabolism. Various pathologies in these structures are observed in several neurodegenerative conditions (4,5), resulting in brain atrophy. Ventricular enlargement is the most essential indicator in determining the prognosis of Alzheimer's disease. Therefore, a detailed understanding of the anatomical associations between the ventricular system and the neighboring brain tissue is vital in defining intraventricular pathology and the potential safety risks associated with surgical treatment (6,7). The morphologic development of these structures in the prenatal and postnatal periods is valuable for neurosurgeons, neurologists, and radiologists (8-10). With this in mind, this study conducted in Bolu Abant Izzet Baysal University (BAIBU), Training and Research Hospital (TRH) has focused on examining age- and gender-related changes in the parameters of the brain ventricles during the pediatric period. The results of the study will contribute to the basic data in the relevant literature and clinical sciences.

## MATERIAL AND METHOD

This study was conducted using brain MRI images of 200 children (100 girls, 100 boys) aged 0-18 years who were admitted to BAIBU TRH, with no pathological conditions in the brain or brain ventricles. The ethics committee permission, obtained from BAIBU Clinical Research Ethics Committee with decision number 2022/99, was strictly followed at every stage of the study.

Brain MR images of the subjects who fulfilled the criteria for admission were selected from the PACS of BAIBU TRH in T2 acquisition protocol. MR images were obtained with a 1.5 T Signa Explorer MRI Scanner (GE Medical Systems, Milwaukee, Wisconsin, USA). Images in the PACS system were downloaded in DICOM format. They then were imported into the Radiant DICOM Viewer (RDV) program, which was used as a personal workstation. The parameters of the measurements performed on axial T2 prop MR images were determined as slice thickness 3.5 mm, repetition time 7143 ms, and echo time 115.136 ms.

In the study, the following measurements were acquired; axis of the third ventricle (ATV), anterior width of the frontal horn (ACF), posterior width of the frontal horn (PCF), width of the frontal horn (WCF), oblique diameter of the frontal horn (OCF), maximum transverse diameter of the skull (MTDS), vertical diameter of the skull (VDS), anteroposterior width of the right temporal horn (ARCT), anteroposterior width of the left temporal horn (ALCT), anteroposterior width of the fourth ventricle (AFV), transverse width of the fourth ventricle (TFV), the Evans index (EI). Demonstrations of the measured variables are shown in Figure 1.

To reduce inter-observer error, three measurements were taken by an expert and their averages were recorded. Images of the brain ventricles were examined by dividing the subjects into four groups of 50 individuals (25 boys, 25 girls) in each group according

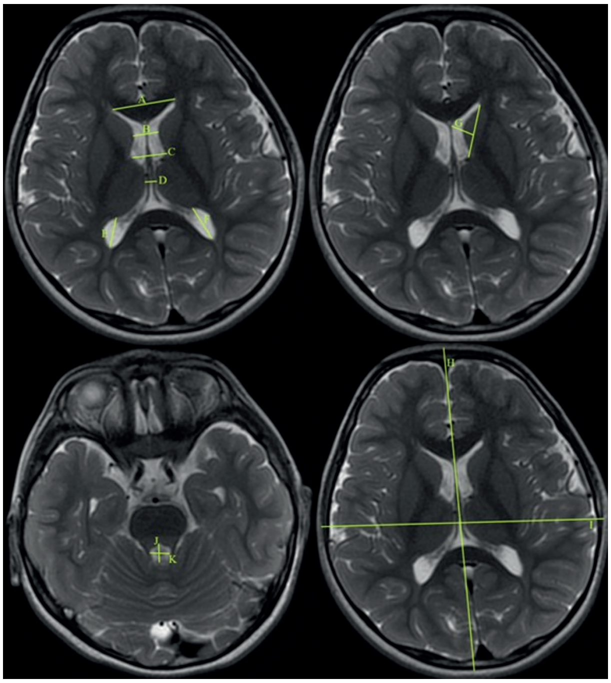

**Figure 1.** Variable demonstrations

A: ACF [anterior width of the frontal horn], B: WCF [width of the frontal horn], C: PCF [posterior width of the frontal horn], D: ATV [axis of the third ventricle], E: ALCT [anteroposterior width of the left temporal].

to age. The groups were as follows: group 1 – healthy children aged 0-2 years; group 2 – healthy children aged 3-6 years; group 3 – healthy children aged 7-11 years; group 4 – healthy children aged 12-18 years.

## Statistical analysis

Statistical analyses were performed with the Minitab® 21.2 program. The appropriateness of the residuals to normal distribution was tested with the Anderson-Darling test. Logarithmic and square root transformations were applied to nonparametric variables. As a result of the transformation, it was determined that the transformations had no effect. The difference between the genders forming each group was tested with independent t test for parametric variables and Mann-Whitney U test for nonparametric variables. For parametric variables, two-factor analysis of variance was applied, and for nonparametric variables, the Kruskal-Wallis test was used. Tukey analysis was performed as a post-hoc test for variables for which the difference between groups was found to be significant as a result of variance analysis. The inter-group test of the variables that were significant as a result of the Kruskal-Wallis test was performed using the Mann-Whitney U test. BoxPlot graphs showing the change of variables according to age and gender were drawn.

# RESULTS

The mean and standard deviation (SD) values of the parametric variables, and the min, max, and median values of the nonparametric variables were calculated. The p values from the two-way ANOVA for age and group interactions of the parametric variables, and the p values from the Kruskal-Wallis test for the nonparametric distributed variables were acquired. Table 1 presents the results of the descriptive statistics for the variables.

**Table 1.** Descriptive statistics results of the variables

| Variables | Gender | n | Group 1 | Group 2 | Group 3 | Group 4 | p value |
|---|---|---|---|---|---|---|---|
| Age | M | 25 | 1.0 (0.0-2.0)$^{a}$ | 5.0 (3.0-6.0)$^{b}$ | 9.0 (7.0-11.0)$^{c}$ | 15.0 (12,0-18.0)$^{d}$ | <0.001$^{k}$ |
| | F | 25 | 1.0 (0.0-2.0)$^{a}$ | 6.0 (3.0-6.0)$^{b}$ | 9.0 (7.0-11.0)$^{c}$ | 13.0 (12.0-18.0)$^{d}$ | <0.001$^{k}$ |
| | p value | | 0.561$^{x}$ | 0.559$^{x}$ | 0.985$^{x}$ | 0.042$^{x}$ | |
| ATV | M | 25 | 4.0 (3.3-4.5)$^{b}$ | 3.5 (3.0-4.0)$^{a}$ | 3.8 (3.0-4.8)$^{b}$ | 3.8 (3.3-5.1)$^{b}$ | 0.002$^{k}$ |
| | F | 25 | 3.9 (2.5-4.5) | 3.4 (3.0-4.3) | 3.5 (3.0-4.8) | 3.6 (3.0-5.1) | 0.065$^{k}$ |
| | p value | | 0.816$^{x}$ | 0.376$^{x}$ | 0.103$^{x}$ | 0.048$^{x}$ | |
| ACF | M | 25 | 29.3±3.2$^{b}$ | 32.0±3.2$^{a}$ | 31.8±2.5$^{a}$ | 33.2±3.0$^{a}$ | <0.001$^{m}$ |
| | F | 25 | 26.8±3.8$^{b}$ | 29.9±2.9$^{a}$ | 31.4±2.5$^{a}$ | 31.4±2.9$^{a}$ | <0.001$^{m}$ |
| | p value | | 0.018$^{y}$ | 0.017$^{y}$ | 0.412$^{y}$ | 0.042$^{y}$ | 0.380$^{m}$ |
| PCF | M | 25 | 15.7±2.4$^{a}$ | 15.0±2.8$^{ab}$ | 13.8±2.0$^{ab}$ | 14.8±2.0$^{b}$ | 0.039$^{m}$ |
| | F | 25 | 13.9±2.4 | 13.1±2.5 | 13.6±2.5 | 12.8±2.0 | 0.410$^{m}$ |
| | p value | | 0.013$^{y}$ | 0.012$^{y}$ | 0.587$^{y}$ | 0.001$^{y}$ | 0.180$^{m}$ |
| WCF | M | 25 | 12.3 (8.4-17.8) | 10.7 (6.3-18.6) | 11.2 (6.6-17.1) | 11.5 (8.4- 15.9) | 0.065$^{k}$ |
| | F | 25 | 11.7 (5.6-17.1) | 10.2 (6.6-15.3) | 9.6 (6.6-17.1) | 9.5 (6.3-17.3) | 0.466$^{k}$ |
| | p value | | 0.130$^{x}$ | 0.101$^{x}$ | 0.132$^{x}$ | 0.003$^{x}$ | |
| OCF | M | 25 | 11.1 (7.2-13.1) | 10.8 (7.2-18.3) | 10.6 (7.6-16.3) | 11.1 (7.7-15.3) | 0.723$^{k}$ |
| | F | 25 | 9.4 (5.8-16.0) | 10.1 (7.8-13.9) | 10.9 (8.7-16.0) | 10.5 (7.3-13.5) | 0.131$^{k}$ |
| | p value | | 0.165$^{x}$ | 0.258$^{x}$ | 0.578$^{x}$ | 0.180$^{x}$ | |
| ARCT | M | 25 | 13.6±2.1 | 14.3±2.7 | 14.7±2.7 | 15.1±2.6 | 0.215$^{m}$ |
| | F | 25 | 12.2±2.0 | 13.1±2.5 | 13.9±2.2 | 13.1±2.7 | 0.095$^{m}$ |
| | p value | | 0.019$^{y}$ | 0.103$^{y}$ | 0.288$^{y}$ | 0.010$^{y}$ | 0.610$^{m}$ |

k: The p value of the Kruskal-Wallis test result, m: The p value of the two-way ANOVA result, x: The p value of the Mann-Whitney U test result, y: The p value of the two-sample t test result.

| **Table 1.** Continued | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Variables** | **Gender** | **n** | **Group 1** | **Group 2** | **Group 3** | **Group 4** | **p value** |
| VDS | M | 25 | 150.5±14.4[c] | 167.8±8.8[b] | 170.2±10.0[ab] | 176.2±6.5[a] | <0.001[m] |
| | F | 25 | 144.2±15.3[c] | 163.9±8.9[b] | 166.5±6.2[ab] | 172.1±6.5[a] | <0.001[m] |
| | p value | | 0.139[y] | 0.132[y] | 0.101[y] | 0.034[y] | 0.909[m] |
| MTDS | M | 25 | 125.1±11.3[c] | 139.2±7,2[b] | 142.7±4,9[b] | 153.2±8.8[a] | <0.001[m] |
| | F | 25 | 118.6±14.5[c] | 136.2±5.0[b] | 139.1±7.0[b] | 144.9±9.3[a] | <0.001[m] |
| | p value | | 0.085[y] | 0.089[y] | 0.033[y] | 0.002[y] | 0.402[m] |
| AFV | M | 25 | 7.8±1.8[b] | 8.7±1.2[ab] | 9.6±1.5[ab] | 9.5±1.5[a] | 0.001[m] |
| | F | 25 | 8.0±1.7[b] | 8.6±1.7[ab] | 8.8±1.2[a] | 9.6±1.7[a] | 0.009[m] |
| | p value | | 0.670[y] | 0.710[y] | 0.041[y] | 0.878[y] | 0.374[m] |
| TFV | M | 25 | 10.2±1.8[b] | 11.3±1.3[b] | 12.6±2.0[a] | 12.9±1.5[a] | 0.001[m] |
| | F | 25 | 10.7±1.7 | 11.4±1.8 | 11.7±1.3 | 11.9±1.6 | 0.078[m] |
| | p value | | 0.341[y] | 0.990[y] | 0.070[y] | 0.034[y] | 0.072[m] |
| EI | M | 25 | 0.2±0.02[a] | 0.2±0.02[ab] | 0.2±0.02[ab] | 0.2±0.02[b] | 0.037[m] |
| | F | 25 | 0.2±0.02 | 0.2±0.01 | 0.2±0.01 | 0.2±0.02 | 0.321[m] |
| | p value | | 0.263[y] | 0.067[y] | 0.776[y] | 0.988[y] | 0.389[m] |

k: The p value of the Kruskal-Wallis test result, m: The p value of the two-way ANOVA result, x: The p value of the Mann-Whitney U test result, y: The p value of the two-sample t test result.

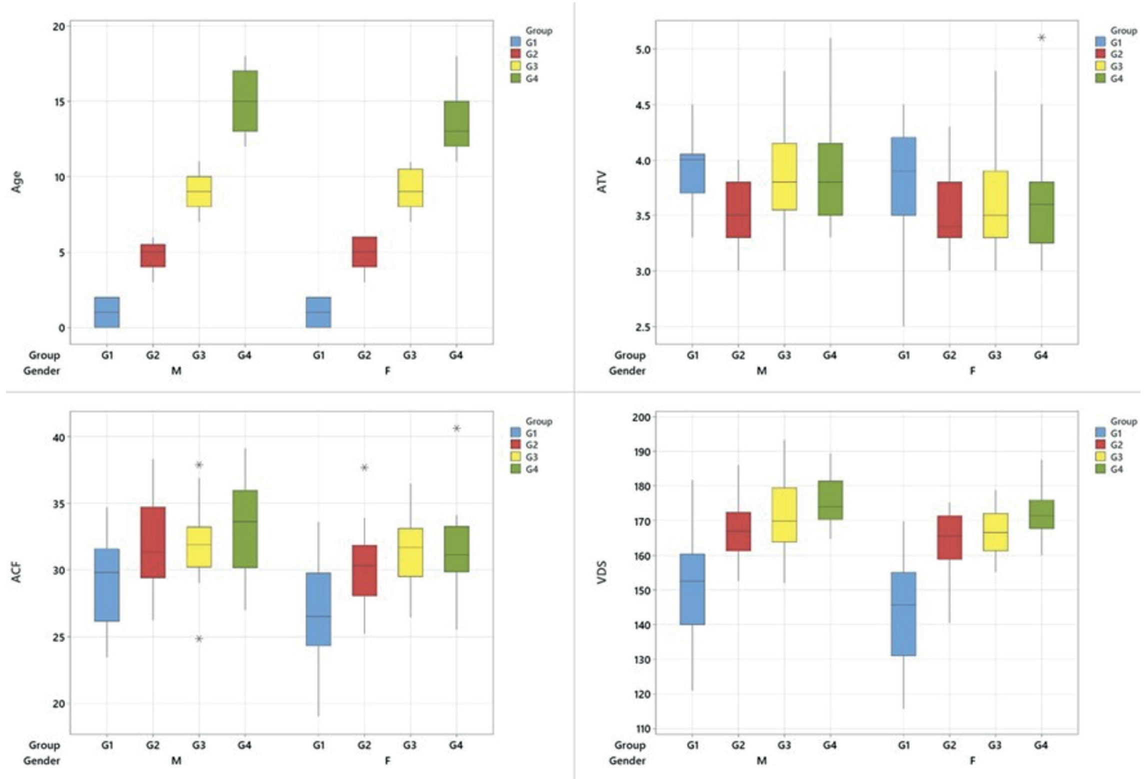


**Figure 2.** Boxplot for the Age, ATV (axis of the third ventricle), ACF (anterior width of the frontal horn), VDS (vertical diameter of the skull).

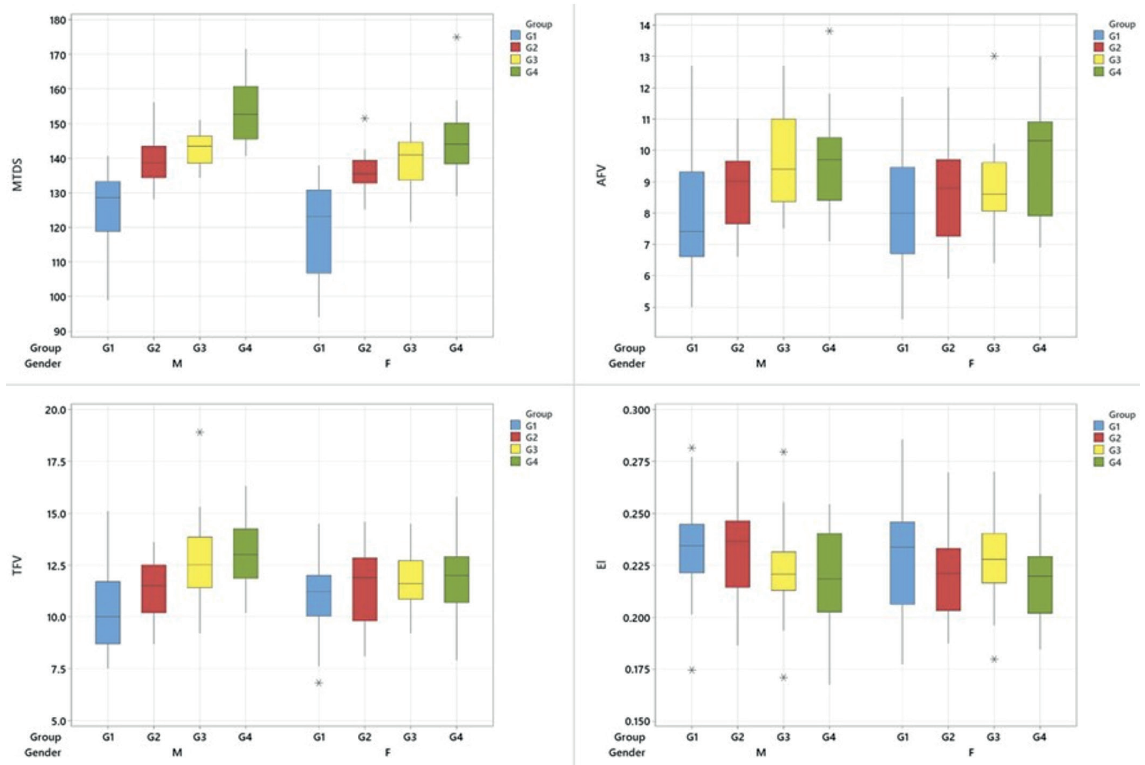


**Figure 3.** Boxplot for the MTDS (maximum transverse diameter of the skull), AFV (anteroposterior width of the fourth ventricle), TFV (transverse width of the fourth ventricle), EI (Evans index).

BoxPlots for Age, ATV, ACF, VDS, MTDS, AFV, TFV, EI variables are presented in Figure 2 and Figure 3.

## DISCUSSION

This research has focused on revealing the changes in the ventricular system of the brain in relation to age and gender in the pediatric period, using brain MR images of 200 children aged 0-18 years, admitted to BAIBU TRH without any pathological condition affecting the brain or brain ventricles. The images of the brain ventricles have been evaluated in four groups based on age. The following parameters have been measured, and the following results have been interpreted: ATV, ACF, PCF, WCF, OCF, MTDS, VDS, ARCT, ALCT, AFV, TFV, and EI. The results have indicated that after a certain age in the pediatric period, the morphometry of the brain ventricles and other variables of the skull differ significantly in relation with gender. The development of brain ventricles in the pediatric period is critical for the early diagnosis of many diseases. It can be seen from the accumulating literature that the number of studies conducted on the ventricular system of the brain and the number of individuals examined in the pediatric period are limited (11-13). Yet, to our knowledge, there is no study using MR images of healthy individuals in this period to evaluate the development of the ventricular system of the brain in particular. Hence, in this study, we have focused on the age- and gender-related changes of the brain ventricles in individuals aged 0-18 years.

It has been shown in the literature that neurodegenerative diseases play an aggregative role in the disruption of the morphometric structure of the brain ventricles (11). Hydrocephalus, an example of a neurodegenerative disease, is a disorder characterized by dilatation of the ventricular system and obstruction of CSF flow. In a study investigating the differences among the brain ventricles of individuals diagnosed with hydrocephalus in relation to gender, a total of 50 patients (27 boys, 23 girls) diagnosed with either myelomeningocele-related hydrocephalus (MHC) or non-myelomeningocele-related hydrocephalus (HC) in the pediatric period have been put under research. ATV and EI variables have been analyzed on CT brain and MR brain images of the individuals. While no statistically significant result has been seen between the genders, the results have differed significantly with age. Statistically significant changes have been found between HC and MHC groups in terms of EI and ATV. While our research has focused on the cerebral ventricle development in healthy individuals, the study indicated above has examined individuals diagnosed with hydrocephalus, expressing greater differences in the median values. This is surely due to hydrocephalus having a very high impact on the morphometry of the brain and brain ventricles. One study has investigated the importance of EI and ventricular indexes in revealing the prognosis of hydrocephalus in 137 patients from birth to six years of age out of the Nigerian population (14). This research has documented that the ventricular index and the EI variable reflect the prognosis of the disease. Another research has examined the structure of the brain ventricles of individuals with multiple sclerosis (MS), another example of a neurodegenerative disease, and the structures of the brain ventricles of healthy people (15). The study has focused on a group of patients with two stages of MS (RR-Relapsing Remitting and SPMS-Secondary Progressive). MR images of 40 MS patients (20 RR and 20 SPMS), and 10 control subjects were used to analyze ATV, AFV, CFAG, ARCT, ALCT, and VDS variables. As a result of the analysis, the ATV variable has been found to be lower in the control group, and the differences among all groups have been found statistically significant. The EI variable has not demonstrated a level of statistical significance, while the AFV, ACF, ARCT, and ALCT variables have differed significantly among the groups. The individuals with MS have shown higher values compared to the control group. Upon analyzing the results, it is well understood that neurodegenerative diseases affect the size and volume of brain ventricles. Therefore, it is vital to know the morphometric dimensions of brain ventricles in healthy individuals, as this can facilitate both the prognosis and the diagnosis of the disease.

Similarly, a study has measured ACF, ATV, TFV, AFV, MTDS, and EI variables in adults, and has found that ACF, ATV, and MTDS variables have shown a statistically significant difference between genders, while no difference has been seen in AFV, TFV, and EI variables (16). Likewise, in a study conducted on MR images of adolescents (17), ATV, OCF and ACF variables have been analyzed, reporting no statistically significant difference in ATV and OCF variables, while a statistically significant difference in ACF in terms of gender was reported. ACF, EI, and MTDS variables have been evaluated in another study conducted on 100 individuals from the Indian population with an average age between 5-90 years, including seven pediatric patients, and the differences among the genders and groups have not been statistically significant in the EI variable (12). Moreover, the differences in the variables ACF and MTDS have been significant, in terms of gender, while no difference has been found between the groups. In a study in which the same variables have been examined in the adult Nigerian population, a statistically significant result has been found for ACF and MTDS variables in terms of gender, and no statistically significant result has been detected in the EI variable (18). In the current study, the EI variable among these variables has not been found to be statistically different in terms of gender, whereas it has been found to be significantly different between individuals in the first and fourth groups. The EI of the individuals in the first group has been found to be lower than that of individuals in the other group. This result shows that the EI variable progresses with age but remains constant after a certain age, ultimately indicating no difference between the genders. As far as the ACF and MTDS variables are concerned, no statistically significant difference has been observed between the second and third groups, while a statistically significant difference has been observed between the first group and the fourth group. It has been determined that these variables have not differed in the period from the age of three to the age of 11. Statistically significant results have been found between the individuals in the first, second, and fourth groups for the ACF variable, and between the individuals in the third and fourth groups for the MTDS variable. After a certain age (seven years), the difference between the genders has increased in the transverse diameter of the skull, indicating that pediatric individuals start to differentiate between genders after the age of seven.

A study conducted on the temporal lobe development of pediatric individuals has examined MR images of individuals aged from three weeks to 14 years (13). The study found that the temporal lobe grows sharply until the age of two, but the growth rate slows down right after this age. The difference in growth rates between the right and left temporal lobes has been found to be statistically significant. Moreover, while temporal lobe volume has been found to be inversely proportional to age, the right temporal lobe has been found to be larger than the left temporal lobe, except for the individuals between the ages of one and two. Similar results have also been acquired in our research. While the ARCT variable has had a higher value in all groups compared to the ALCT variable, no statistically significant difference has been detected between the groups. However, a statistically significant difference has been found among individuals in the first and fourth groups for the ARCT variable, and among individuals in the first group for the ALCT variable, in terms of gender. Having evaluated these results, it is obvious that the growth in the temporal lobe, brain, and skull affects the growth of the left and right temporal horn at a similar rate.

Consequently, this study was conducted to examine changes in the brain ventricles of pediatric individuals in relation to age and gender, has determined that the ACF, PCF, ARCT, and ALCT variables for the first group; the ACF and PCF variables for the second group; the VDS, MTDS, and AFV variables for the third group; and the ATV, ACF, PCF, WCF, ARCT, VDS, MTDS, and TFV variables for the fourth group have differed significantly with respect to gender. Analysis has revealed a significant difference among the age groups for all variables except WCF, OCF, ARCT, and ALCT. It has been observed that in the pediatric period, the differences in the brain ventricles increased between the ages of 12 and 18, and both the vertical and transversal dimensions of the skull notably changed between the ages of seven and 18.

## Ethical approval

This study has been approved by the Bolu Abant İzzet Baysal University Clinical Research Ethics Committee (approval date 10.05.2022, number 2022/99).

## Author contribution

Concept: AR, İK; Design: AR, İK; Data Collection or Processing: AR; Analysis or Interpretation: AR; Literature Search: AR; Writing: AR, İK. All authors reviewed the results and approved the final version of the article.

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The authors declare the study received no funding.

## Conflict of interest

The authors declare that there is no conflict of interest.

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