Original Article

Analysis of Major Lobe Volume and Asymmetry of the Brain by Gender: A vol2Brain Study

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Abstract

Objective: In recent years, with the use of three-dimensional (3D) software tools, volumetric measurements of brain morphometry have gained importance. In this study, we aim to investigate the ratio of the volumes of the major structures of the brain (frontal, parietal, temporal, and occipital lobes) to the volume of the intracranial cavity (ICC) and the change of asymmetry according to gender, using web-based vol2Brain, which is one of the current and automatic software tools. **Materials and Methods:** 3D-T1-weighted magnetic resonance images of 80 healthy individuals (43 females and 37 males) of both genders were included in our study. The volumes of major brain lobes were calculated with the vol2Brain pipeline software tool and their ratio to ICC was compared by gender. **Results:** Males ICC volume, frontal, parietal, temporal, and occipital lobe total volume values were statistically higher than females ($P < 0.05$). Similarly, the right and left volume values of male were higher than those of female in all measurements. However, when the frontal, parietal, temporal, and occipital lobe volumes of male and female were proportion to the ICC volume, there was no statistically significant difference ($P > 0.05$). There was no statistically significant difference in the asymmetry results of these cortical structures examined in both genders ($P > 0.05$). **Conclusions:** Although the male brain is known to be large, no difference was found between the male and female brains as a result of the ratio. Considering the asymmetry values, frontal, parietal, occipital, and temporal lobe volume asymmetry values did not differ statistically in both genders.

Keywords: *Asymmetry, cortical, proportion, three-dimensional imaging, volume*

Introduction

Many studies investigate the relationship between gender and volume or morphometric measurements of neuroanatomical structures.[1-3] Some studies have reported that it does not differ according to gender.[4,5] The prognosis of many neurodegenerative and neuropsychiatric diseases related to the brain shows sexual dimorphism.[6,7] Many studies in the literature state that male brain components are greater than females.[8,9] In a large-scale meta-analysis study, it was reported that total brain volume (11%) and intracranial volume (12%) were greater in males.[10] This situation reveals the differences in structures such as cortical volume, surface area, and thickness.[11]

Many techniques have been used to measure cerebral structures.[3,12,13] First, autopsy studies are included because the actual volume and weight are measured. However, in autopsy studies, it was thought that the type of disease and the duration of removal of the brain would affect the results.[9] With the development of non-invasive imaging methods, objective information about the brain structures of living people can be obtained.[14] The human brain is examined using different methods with developing and advancing technology. Magnetic resonance imaging (MRI) is especially important in the detailed investigation of brain structure and function.[15]

In recent years, traditional data processing has been replaced by automatic/semi-automatic volume and segmentation techniques.[16-19] One of these software tools, volBrain, provides web-based, reliable, online, and time-saving volumetric analysis of three-dimensional (3D) structural MRI. Thus, MRI volumetric measurements of brain structures are important in the early diagnosis and follow-up of various diseases.[20]

Our aim in this study is to investigate the effects of the brain's major lobes on the

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intracranial cavity (ICC) volume ratio and asymmetry change according to gender using the vol2Brain software program, which is one of the volBrain segmentation tools.

Materials and Methods

Participants

MRI of eighty healthy individuals (43 females and 37 males) between the ages of 18 and 75 years was included in the study. Healthy individuals of both sexes, who did not undergo neurosurgery and did not have neurological or psychiatric diseases, were included in the study.

This study was approved by the human subjects ethics board of Kirsehir Ahi Evran University Faculty of Medicine Clinical Research Ethics Committee (Date: June 21, 2022, Approval Decision No: 2022-12/119).

Neuroimaging

MRI data were taken using a standard head coil on a 1.5 Tesla (GE SIGNA Explorer, 2020, United States) device. High-resolution, sagittal plane, T1-weighted 3D BRAVO sequence was taken. Repetition time: 7, echo time: 2.99 ms, field of view: 250 mm × 250 mm, matrix: 256 × 256, section thickness was taken as 1 mm.

The participants' 3D T1-weighted brain MRI data were exported with Picture Archiving and Communication Systems. These transferred data are uploaded to the personal computer. These data in Digital Imaging and Communications in Medicine format were anonymized with the free software MRIcron (https://www.nitrc.org/projects/mricron) and converted into the Neuroimaging Informatics Technology Initiative (NIfTI) format. In NIfTI format, these MRI data were uploaded to the vol2Brain pipeline system, volBrain's segmentation tool (v. 1.0, http://volbrain.upves). When the data processing process was finished, two reports were automatically created by the program, in the form of Portable Document Format and Comma-separated Values files, containing patient information, brain volumes, and their results in the Montreal Neurological Institute space.

The vol2Brain is a free, online, web-based data processing program that automatically segments MRI data. It provides automatic segmentation by dividing the human brain into 135 structures. The vol2Brain pipeline segments tissues, macrostructures, and lobes and provides information about cortical thickness.[15] Calculated tissue volumes are measured in absolute value (cm^3) and presented as a ratio (covering 100%) to ICC volume. It is expressed as the sum of ICC tissue, namely, white matter (WM), gray matter (GM), and cerebrospinal fluid (CSF).[20] In our study, cortical volumes will be examined using this program. The vol2Brain data were displayed in 3D with ITK-SNAP and MRIcroGL (https://www.itksnap.org and https://www.nitrc.org/projects/mricrogl) [Figures 1 and 2].

The asymmetry index (AI) provides information about the differences in the bilateral cortical structures of the brain. In our study, the AI value of the volumes of cortical structures (frontal, parietal, occipital, and temporal lobe) was calculated in the gender category. The AI value was obtained by dividing the right and left volume differences by their mean (as a percentage).[20,21] Hence, AI = (right volume-left volume)/2 (right volume + left volume) ×100. Positive values of the calculated AI results represent a right-oriented asymmetry, and negative values represent a left-oriented asymmetry. It was thought that the area showed lateralization as the AI value calculated with the volume values of the left and right regions of the cortical structures moved away from zero.

Statistical method

The data were evaluated in the Statistical Package Program of IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA). Descriptive statistics were given as number of units (*n*), percentage (%), mean, standard deviation (SD), standard error (sh), median (M), minimum (min), maximum (max), and interquartile range values. The normal distribution of the data of numerical variables was evaluated with the Shapiro–Wilk normality test. The ages of the participants by gender were compared with the *t*-test in independent samples. The relations between age and asymmetry variables were evaluated with the Spearman correlation coefficient, and the relations between age and other variables were evaluated with the Pearson correlation coefficient. Asymmetry data by gender were compared with the Mann–Whitney *U*-test. One-way analysis of covariance was used to compare age-related variables by

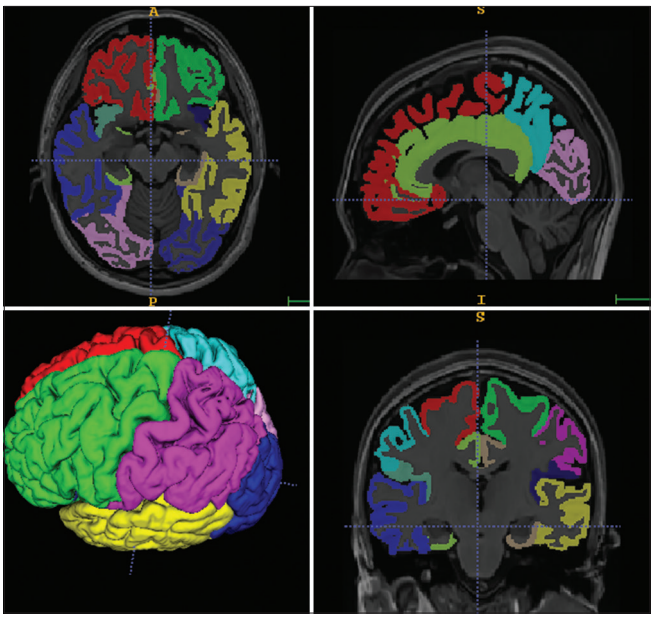

Figure 1: ITK-SNAP rendering and three-dimensional modeling of cortical structures in different planes

gender. A value of $P < 0.05$ was considered statistically significant.

Results

A total of 80 participants, 37 (46.3%) males and 43 (53.7%) females participated in the study. The participants were between 18 and 75 years old, and the mean age (±SD) was 41.5 ± 15.6. The mean age of males (±SD) was 40.9 ± 17.3 years, and the mean age of females (±SD) was 42.1 ± 14.1 years. There was no statistical difference between the ages of males and females ($t = 0.332$; $P = 0.741$).

Pearson correlation analysis revealed a negative correlation between ICC volume, total frontal volume, total temporal volume, total parietal volume, and occipital total volume variables and age values ($P < 0.05$; $r_1 = -0.291$, $r_2 = -0.593$, $r_3 = -0.544$, $r_4 = -0.637$, and $r_5 = -0.469$, respectively).

According to the results of Pearson correlation analysis, a negative correlation was found between the proportion of frontal lobe, temporal lobe, occipital lobe, and parietal lobe volumes to ICC volume separately and age values ($P < 0.001$; $r_1 = -0.684$, $r_2 = -0.599$, $r_3 = -0.447$, and $r_4 = -0.716$, respectively).

According to the results of Spearman's correlation analysis, there was no statistically significant relationship between the age of the participants and the frontal lobe, temporal lobe, parietal lobe, and occipital lobe asymmetry values ($P > 0.05$; $rho_1 = 0.122$, $rho_2 = -0.165$, $rho_3 = 0.012$, and $rho_4 = 0.029$, respectively).

In the comparisons made according to gender, the variables other than the asymmetries were adjusted for age.

Table 1 shows that male's ICC, frontal, temporal, parietal, and occipital total volume values were statistically higher than female's ($P < 0.05$).

Right and left frontal, temporal, parietal, and occipital lobe volume values of males are statistically higher than females ($P < 0.05$) [Table 2].

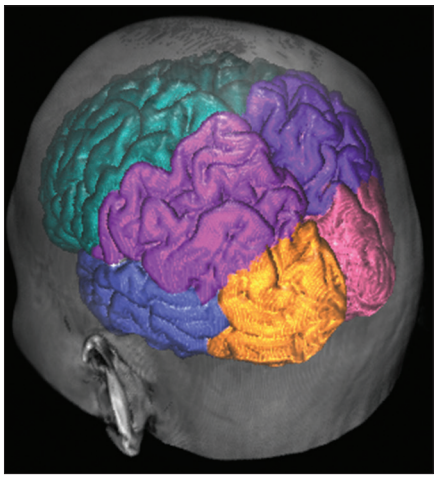

Figure 2: Three-dimensional imaging of vol2Brain data with MRIcroGL

Table 3 shows no statistically significant difference between male's and female's frontal lobe volume/ICC volume, temporal lobe volume/ICC volume, occipital lobe volume/ICC volume, and parietal lobe volume/ICC volume values ($P > 0.05$).

There was no statistically significant difference between the frontal lobe, temporal lobe, parietal lobe, and occipital lobe volume asymmetry values of males and females ($P > 0.05$) [Table 4].

Discussion

Brain morphometry has gained momentum with the development of neuroimaging methods.[9] In the past, manual segmentation was used with MRI volume analysis of brain structures. However, this method was limited in terms of application in neuroanatomical structures. Because it took much time, it was replaced by software tools that perform automatic brain volume analysis. Among these software tools, volBrain, which provides modern, web-based, up-to-date, unbiased, and automatic segmentation, can be used as a neuroimaging study in MRI.[20] In the current study, we aimed to investigate the ratio of the volumes of the major structures of the brain to the ICC volume and the variation of the asymmetry according to the genders using vol2Brain in a homogeneous and healthy population. This study may be one of the first studies, as we know, to analyze gender differences in healthy individuals using both the

Table 1: Comparison of volumes by gender

Region volume (cm^3)	Gender		Test statistics*	
	Male	Female	*F*	*P*
ICC volume	1408.2±20.5	1302.4±19.1	14.208	<0.001
Frontal total volume	182.9±2.9	171.8±2.7	7.634	0.007
Temporal total volume	120.9±1.7	110.4±1.6	18.997	<0.001
Parietal total volume	106.8±1.5	98.9±1.3	14.964	<0.001
Occipital total volume	77.1±1.2	69.5±1.1	21.789	<0.001

*One-way analysis of covariance. The parts determined in bold are statistically significant ($P<0.05$). Numerical data corrected for age are given as mean±SE. SE: Standard error, ICC: Intracranial cavity

Table 2: Comparison of right and left volumes by gender

Region volume (cm^3)	Gender		Test statistics*	
	Male	Female	*F*	*P*
Frontal right volume	92.22±1.49	86.38±1.38	8.337	**0.005**
Frontal left volume	90.65±1.46	85.48±1.36	6.738	**0.011**
Temporal right volume	60.80±0.92	55.33±0.86	18.709	**<0.001**
Temporal left volume	60.14±0.86	55.14±0.79	18.041	**<0.001**
Parietal right volume	53.88±0.81	49.71±0.74	14.434	**<0.001**
Parietal left volume	53.01±0.73	49.24±0.68	14.049	**<0.001**
Occipital right volume	38.67±0.60	34.97±0.55	20.207	**<0.001**
Occipital left volume	38.42±0.66	34.57±0.61	18.525	**<0.001**

*One-way analysis of covariance. The parts determined in bold are statistically significant ($P<0.05$). Numerical data corrected for age are given as mean±SE. SE: Standard error

Table 3: Comparison of lobe volume values/intracranial cavity volume proportion by gender

Parameters	Gender		Test statistics*	
	Male	Female	*F*	*P*
Frontal lobe volume/ICC volume	0.130±0.001	0.132±0.001	1.966	0.165
Temporal lobe volume/ICC volume	0.086±0.001	0.085±0.001	1.149	0.287
Occipital lobe volume/ICC volume	0.055±0.001	0.053±0.001	3.152	0.080
Parietal lobe volume/ICC volume	0.076±0.001	0.076±0.002	0.034	0.854

*One-way analysis of covariance. Numerical data corrected for age are given as mean±SE. SE: Standard error, ICC: Intracranial cavity

Table 4: Comparison of volume asymmetry values by gender

Parameters	Gender		Test statistics*	
	Male	Female	*Z*	*P*
Frontal volume asymmetry	1.44 (3.96)	0.79 (3.09)	1.134	0.257
Temporal volume asymmetry	1.13 (4.21)	0.61 (4.69)	0.767	0.443
Parietal volume asymmetry	1.61 (6.72)	0.81 (5.25)	0.883	0.377
Occipital volume asymmetry	2.04 (8.19)	1.41 (9.87)	0.005	0.996

*Mann–Whitney *U*-test. Numerical data are given as median (IQR) values. IQR: Interquartile range

vol2Brain method and the ratio of major brain structures to ICC.

The size of the human brain has been investigated for many years.[22] Many studies stated that the female brain is generally smaller than the male brain.[10,23] Filipek *et al*.[24] reported in their study that the difference between the sexes in total brain volume was 8%. It has been stated that the effect of gender on the volume difference is small, and most of the difference may be related to the ICC volume.[25] It has been reported that the ICC volume increases during childhood and adolescence and decreases after age 40.[26] Similarly, in our study, the mean age of the participants was 41.5 ± 15.6, and it was determined that the ICC volume differed according to the age variable.

Whether the brain exhibits sexual dimorphism is still debated.[27] Many studies have determined that the ICC volume measured in healthy individuals is greater in males.[9,25,28,29] Similarly, in our study, ICC volume was higher in males ($P < 0.05$). However, it was stated that the difference was almost gender independent when the brain volume was proportional to the ICC volume.[9]

Murphy *et al*. reported that males' whole brain volume was greater. In addition, it has been reported that whole brain volume and frontal and temporal lobe volumes decrease with age in males, whereas parietal lobe volume decreases more in females.[30] Similarly, in our study, all measured volumes were higher in males, and there was a negative correlation with age in both sexes.

Garcia-Falgueras *et al*.'s study, GM, WM, and CSF volumes were higher in males. However, it has been reported that there is no difference between genders when each of these structures is proportioned to the total brain volume separately and when the GM volume is proportioned to the WM volume in the same way.[31] In another study, the proportion of GM, WM, and CSF volume to ICC volume was reported to be higher in males.[9,28] Although there were methodological differences in our study, Garcia-Falgueras *et al*.[31] as in the results, there was no statistically significant difference between the genders ($P > 0.05$). It is thought that the reason for the differences in the results may be due to the sample size, differences in the measurement methods, and ethnic origin.

Carne *et al*.[32] examined the right–left volumes of the frontal, parietal, occipital, and temporal lobes in 97 healthy individuals (49 females and 48 males) aged between 15 and 69 years, according to gender. Other lobe volumes were statistically higher in males except for the left parietal lobe ($P < 0.066$). Allen *et al*.[8] the major brain lobe volumes of 46 healthy individuals aged between 22 and 49 years (23 females and 23 males) were found to be statistically higher in males in all cases. However, the occipital lobe volume is less dimorphic, and the left occipital lobe volume was not statistically significant. In our study, males' right and left lobe volumes were statistically higher than females. We think the differences in the right or left lobe volumes are due to the number of participants, age factor, and differences in measurement methods.

Cowell *et al*.[1] analyzed the frontal and temporal lobe volumes of the 18–40 (young) and 41–80 (old) age groups according to gender. It has been reported that the total frontal volume of males in the young group is 16% larger than in the elderly group, whereas there is no difference in volume between the two groups in females. Temporal lobe volume was similarly larger in males, and the right volume has been reported to be larger than the left.[1] In our study, although there were no age groups, bilateral frontal and temporal lobe volumes were statistically higher in males according to gender. Therefore, it is mentioned in the literature that dimorphisms in human neuroanatomy vary in conditions such as the person's lifestyle, sexual hormone levels, smoking, and alcohol use. However, since our study was retrospective, no comment could be made on these parameters.

Allen *et al*.[8] reported that the temporal and occipital lobe asymmetry was not statistically significant in both genders, and the frontal and parietal lobe AI was not statistically

significant only in males. In addition, only female's frontal and parietal lobe asymmetry was right oriented. Kovalev *et al*.[33] reported that the male brain is more asymmetrical than the female brain. Gurlek Celik and Tiryaki[34] examined the asymmetry differences between gender and age, in which subcortical structures were examined in detail. In this study, it was reported that SR-SL-SM asymmetry values were high only in males. In the same study, it was determined that there were no asymmetry differences in the age category.[34] Lehtola *et al*.[35] study, 68 healthy infants aged 2-5 weeks showed asymmetry towards the right in the temporal lobe and towards the left in the parietal and occipital lobes in both genders. In the same study, frontal lobe asymmetry results were not statistically significant. Cowell *et al*.[1] reported that right frontal lobe asymmetry values were higher in females aged 41–80 and right temporal lobe asymmetry values in males in the same age group. In our study, frontal, parietal, occipital, and temporal lobe asymmetry values were high in the right region in both genders. However, although the asymmetry results were high, there was no statistically significant difference between the asymmetry values of males and females ($P > 0.05$). The differences between studies are related to the anatomical structure and physiology of the human brain. Although it is thought that this structural and morphometric variability may be affected by factors related to gender, age, and dominant hand use, it is thought to be an area open to extensive research.[36]

Many studies are in the literature on the proportion of total brain volume to ICC. However, as far as we know, no studies evaluate the proportion of bilateral major brain lobes to ICC and their asymmetry according to gender. We think that such studies will be meaningful in neurodegenerative diseases.

Conclusions

In our study, the proportion and asymmetry of major brain lobes to ICC in healthy individuals between the ages of 18–75 were investigated. Our results showed that, as in many studies, the brain volume of males was larger than that of females. However, when we proportion each of the frontal, parietal, occipital, and temporal lobe volumes to ICC, it was found that there was no statistically significant difference in both genders. Therefore, although the male brain is known to be large, as a result of the proportion, no difference was found between the male and female brains. Furthermore, considering the asymmetry values, frontal, parietal, occipital, and temporal lobe volume asymmetry values did not differ statistically in both genders. Therefore, we think that the volume ratio and asymmetry measurements between the major brain structures will be important in evaluating the diseased structures from a clinical point of view and whether there is a difference between the sexes.

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Conflicts of interest

There are no conflicts of interest.

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