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Research Article

Investigation of Age- and Gender-Related Changes in Anatomical Variables of the Cerebellum in Healthy Adults Using MR Imaging

Gulcin Ray[1], Abdullah Ray[1], Ibrahim Kurtul[1], Saadet Erdem[2], Basel Malaysheh[1]

[1] Bolu Abant İzzet Baysal Universty, Faculty of Medicine, Department of Anatomy, Bolu, Türkiye
[2]Bolu Abant Izzet Baysal University, Faculty of Health Sciences, Department of Nursing, Bolu, Türkiye

Abstract

Aim: The aging process and gender are thought to cause changes in anatomical regions of the brain. The present study was designed to present age- and gender-related changes in the morphometric characteristics of the cerebellum, which is known to be mainly responsible for the coordination of the skeletal system and balance.
Material and Method: Brain magnetic resonance (MR) images of healthy individuals aged 25-55 years were analyzed. MCRae line (MCL), Klaus index (KI), clivus length (LC), supraocciput length (LSO), diameter of the posterior cranial fossa (PDFC), height of the posterior cranial fossa (PHFC), lateral diameter of the cerebellum (LDC), cerebellum height (HCL), cerebellum width (WCL), cerebrum height (HC), anterior dural angle of the cerebellum (ADAC), angle of the cerebellar clivus (ACC), anteroposterior diameter of the right cerebellar hemisphere (RCHD) and anteroposterior diameter of the left cerebellar hemisphere (LCHD) variables were measured.
Results: It has been determined that the difference between the groups for age, MCL, LSO, PHFC, HCL variables is statistically significant. The difference between genders is statistically significant for KI, LC, PHFC, LDC, WCL, HC, RCHD, LCHD variables in the first group, MCL, KI, LDC, HC, LCHD variables in the second group, LC, LDC, HCL, WCL, HC, ACC, LCHD variables in the third group.
Conclusion: Overall, the results show that aging and gender cause changes in cerebellum morphometry in healthy individuals for the Bolu (Türkiye) population.

Keywords: Cerebellum, magnetic resonance imaging, morphometry, sex differences, brain

INTRODUCTION

The cerebellum, situated in the posterior cranial fossa behind the pons and bulbus, is separated from these structures by the fourth ventricle to the posterior aspect of the cerebral trunk by bundles of the nerve fibers called pedunculus (1,2). Although it occupies only 10% of the brain in total volume, it contains 80% of the neurons of the brain (3). Thanks to these neuromuscular networks, it maintains the coordination of agonist and antagonist muscles, thus movement, and ensures the maintenance of posture and balance (3,4). Furthermore, recent studies have emphasized that the cerebellum has several striking functional spectrums such as perception, language, working memory, cognitive control, and thus contributes to cognitive and social development (4-6). Numerous studies have reported that the morphometric structure of the cerebellum, which is known to be anatomically and functionally extremely complex (7), is affected by neurodegenerative diseases (8,9) and habits such as alcohol (1,10), smoking (11), and sportive activities (12,13). Moreover, studies have presented the effects of the aging process on the cerebellum that provide a clearer understanding of the pathophysiological mechanisms (14,15). Research focusing on the morphometry of structures related to the brain has been employing the MRI device, which allows us to visualize and evaluate soft tissues clearly (13-15). Despite the substantial number of studies reporting how the cerebellum is affected in different populations and in different diseases and conditions (7-15), it is noteworthy to point out that studies concentrating particularly on the age- related anatomical changes in healthy individuals are limited (16-18). In this regard, this study has been designed to observe and evaluate the age and gender related changes in the morphometry of the cerebellum in healthy adults.

CITATION
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Corresponding Author: Gulcin Ray, Bolu Abant İzzet Baysal Universty, Faculty of Medicine, Department of Anatomy, Bolu, Türkiye
E-mail: g.ahmetoglu00@gmail.com

MATERIAL AND METHOD

The retrospective cross-sectional study was designed to present the morphometric changes of angular and linear variables of the cerebellum and cerebrum in a healthy adult Turkish population in relation to age and gender. Approval number 2024/61 was obtained from Clinical Research Ethics Committee, Bolu Abant İzzet Baysal University. Brain MR images taken between March and July 2024 and stored in the Picture Archiving and Communication Systems (PACS) of Bolu Abant Izzet Baysal University Training and Research Hospital, were used. Those diagnosed with cardiovascular, neurodegenerative, psychiatric diseases and those with ischemic attacks were excluded from the study. The sample group consisted of 300 healthy adults (150 women and 150 men) aged 25-55 years, and were divided into three age groups (25-34, 35-44, 45-55) and each group consists of 50 women and 50 men. Brain MR images obtained from the PACS archive were imported into MicroDicom DICOM Viewer 2024.1 (64 bit) for measurement of the identified variables. MR images were taken with 1.5 T Signa Explorer MRI Scanner (GE Medical Systems, Milwaukee, Wisconsin, USA. The measurements were performed by one person only to avoid inter-observer errors. Variables measured were as follow; diameter of the posterior cranial fossa (PDFC), MCRae line (MCL), Klaus index (KI), supraocciput length (LSO), height of the posterior cranial fossa (PHFC), cerebellum width (WCL), cerebrum height (HC), cerebellum height (HCL), anterior dural angle of the cerebellum (ADAC), clivus length (LC), clivus angle of the cerebellum (ACC), lateral diameter of the cerebellum (LDC), anteroposterior diameter of the left cerebellar hemisphere (LCHD), anteroposterior diameter of the right cerebellar hemisphere (RCHD). Demonstration of the variables are given in Figure 1.

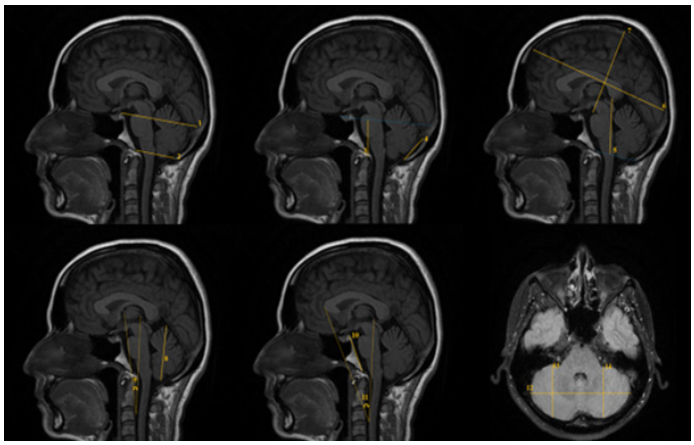

Figure 1. 1-PDFC, 2-MCL, 3-KI, 4-LSO, 5-PHFC, 6-WCL, 7-HC, 8-HCL, 9-ADAC, 10-LC, 11-ACC, 12-LDC, 13-LCHD, 14-RCHD; PDFC: diameter of the posterior cranial fossa, MCL: MCRae line, KI: Klaus index, LSO: supraocciput length, PHFC: height of the posterior cranial fossa, WCL: cerebellum width, HC: cerebrum height, HCL: cerebellum height, ADAC: anterior dural angle of the cerebellum, LC: clivus length, ACC: clivus angle of the cerebellum, LDC: lateral diameter of the cerebellum, LCHD: anteroposterior diameter of the left cerebellar hemisphere, RCHD: anteroposterior diameter of the right cerebellar hemisphere

Statistical Analysis

Analyses were conducted with RStudio (23.12.1) open-source software program. A two-factor analysis of variance was performed for all the variables in relation with age and gender. The normality distribution of the residual values was then tested with the Anderson Darling Test. Logarithmic and square root transformation was applied for the variables that do not fit the normal distribution. It yielded no significant result. Nonparametric variables analyzed the differences with the Kruskal-Wallis Test. For the variables that were significant upon the analysis with this test, Mann Whitney U Test was applied in pairs and the differences were again analyzed. For nonparametric variables, the differences of the individuals forming the groups were analyzed with Mann Whitney U Test in terms of gender, and parametric variables were checked with two-factor analysis of variance. Tukey Test was applied as a post-hoc test for parametric variables for the significant differences among the groups. Additionally, for the significant variables among the individuals of each group in terms of gender, Independent T Test was employed. As descriptive statistics, mean and standard deviation (sd) values for parametric variables, median, minimum (min) and maximum (max) values for nonparametric variables were calculated. $P<0.05$ was considered statistically significant.

RESULTS

The median values for the age variable in males and females respectively were 27.5 and 29 in the first group, 38.5 and 40 in the second group, and both 50 in the third group. The difference between the groups in age, MCL, LSO, PHFC, HCL variables was statistically significant. All groups were statistically different from each other in the age variable ($p<.001$). The difference between the first and third groups for the MCL variable was statistically significant ($p=0.018$). For the LSO variable, the difference between the second and third groups was statistically significant ($p=0.002$). In the HCL variable, the difference between the first and second group was not statistically significant, while the difference between the first and second group and the third group was statistically significant ($p=0.008$). The difference between the first and the third group in the PHFC variable was statistically significant ($p=0.012$).

In analyzing the individuals forming the groups in terms of gender, it was found that the difference in the variables of KI, LC, PHFC, LDC, WCL, HC, RCHD, LCHD was statistically significant for the first group. For the second group, the difference in MCL, KI, LDC, HC, LCHD variables is statistically significant. For the third group, the difference in LC, LDC, HCL, WCL, HC, ACC, LCHD variables was statistically significant.

Descriptive statistics of the variables and the results of the analysis among the groups in terms of gender were given in Table 1 and Table 2. The boxplot graph of the variables with significant differences was shown in Figure 2.

Table 1. Descriptive statistics and analysis results of Age, MCL, KI, LC, LSO, PDFC, and PHFC variables

Variable	Gender	G1 (N=100)	G2 (N=100)	G3 (N=100)	p-value
Age	M (n=50)	27.5 (25-34)	38.5 (35-45)	50 (45-55)	<.001⸗
	F (n=50)	29 (25-34)	40 (35-44)	50 (45-55)	
p-value≠		0.088	0.455	0.692	
MCL	M (n=50)	40.39 (28.14-51.35)	38.47 (27.5-49.42)	37.89 (28.7-55.99)	0.018⸗
	F (n=50)	38.72 (28.67-51.54)	37.3 (26.94-45.48)	36.86 (24.06-51.9)	
p-value≠		0.242	0.037	0.079	
KI	M (n=50)	45.75±6.13	45.96±6.68	43.88±7.45	<.001*
	F (n=50)	40.33±5.42	40.82±5.57	40.61±5.69	0.901**
p-value†		<.001	<.001	0.091	0.887***
LC	M (n=50)	36.47 (18.22-51.62)	34.52 (15.72-54.18)	37.92 (18.71-52.54)	0.254⸗
	F (n=50)	31.79 (16.92-47.81)	31.6 (15.86-47.97)	33.8 (16.45-46.47)	
p-value≠		0.009	0.203	0.008	
LSO	M (n=50)	37.91±5.43	38.14±5.36	37.17±6.16	0.807*
	F (n=50)	37.17±4.74	40.07±5.89	35.64±5.46	0.002**
p-value†		0.985	0.503	0.734	0.069***
PDFC	M (n=50)	96.59±6.39	96.06±8.13	94.07±7.33	0.001*
	F (n=50)	93.88±7.22	93.11±5.96	91.71±7.32	0.055**
p-value†		0.396	0.298	0.558	0.955***
PHFC	M (n=50)	62.34±6.1	58.71±7.16	58.52±6.41	<.001*
	F (n=50)	56.69±5.63	56.21±5.92	55.26±7.71	0.012**
p-value†		<.001	0.398	0.128	0.206***

≠: p values from Mann-Whitney U test; †: p-values in the result of the independent t-test; ⸗: the p-value from the Kruskal-Wallis test; *: the p value showing the difference between genders in the two-factor analysis of variance; **: the p value showing the differences among the groups in the two-factor analysis of variance; ***: the p-value indicating the interaction among the groups and between the gender in the two-factor analysis of variance

Table 2. Descriptive statistics and analysis results of LDC, HCL, WCL, HC, ADAC, ACC, RCHD, and LCHD variables

Variable	Gender	G1 (N=100)	G2 (N=100)	G3 (N=100)	p-value
LDC	M (n=50)	105.87±5.11	106.68±3.48	104.88±4.07	<.001*
	F (n=50)	101.98±3.5	101.8±4.43	101.96±5.05	0.404**
p-value†		<.001	<.001	0.01	0.282***
HCL	M (n=50)	52.78±4.54	51.42±5.19	51±4.64	<.001*
	F (n=50)	50.06±3.77	51.36±5.01	48.21±5.08	0.008**
p-value†		0.050	0.999	0.039	0.067***
WCL	M (n=50)	165.94 (142.46-190)	163.16 (147.65-183.71)	168.57 (141.66-181.91)	0.489⸗
	F (n=50)	162.6 (137.18-177.15)	161.17 (70.83-182.05)	159.64 (107.04-176.18)	
p-value≠		0.007	0.090	<.001	
HC	M (n=50)	100.5 (65.15-114.68)	98.72 (67.96-110.2)	96.4 (80.6-111.73)	0.198⸗
	F (n=50)	93.14 (65.03-106.52)	93.76 (10.54-109.65)	93.7 (63.85-104.2)	
p-value≠		<.001	<.001	0.006	
ADAC	M (n=50)	12.35±1.8	12.12±1.56	11.81±1.92	0.185*
	F (n=50)	12.65±2.11	12.4±2.68	12.17±2.15	0.220**
p-value†		0.976	0.985	0.948	0.988***
ACC	M (n=50)	26.22 (20.4-33.85)	26.73 (19.39-33.4)	25.16 (16.34-32.03)	0.319⸗
	F (n=50)	27.91 (20.31-36.8)	26.52 (19-50.13)	26.73 (19.44-33.46)	
p-value≠		0.180	0.917	0.034	
RCHD	M (n=50)	50.21±4.26	49.36±3.47	49.79±5.03	0.001*
	F (n=50)	47.58±4.08	48.18±3.79	49.09±4.01	0.478**
p-value†		0.020	0.710	0.958	0.203***
LCHD	M (n=50)	53 (39.16-59)	52.16 (39.94-61.38)	52.19 (26.44-62.64)	0.689⸗
	F (n=50)	49.64 (32.68-58.22)	50.03 (42.56-56.94)	49.45 (41.7-58.45)	
p-value≠		0.001	0.004	0.002	

≠: p values from Mann-Whitney U test; †: p-values in the result of the independent t-test; ⸗: the p-value from the Kruskal-Wallis test; *: the p value showing the differences between the genders in the two-factor analysis of variance; **: the p value showing the differences among the groups in the two-factor analysis of variance; ***: the p-value indicating the interaction among the groups and between the genders in the two-factor analysis of variance

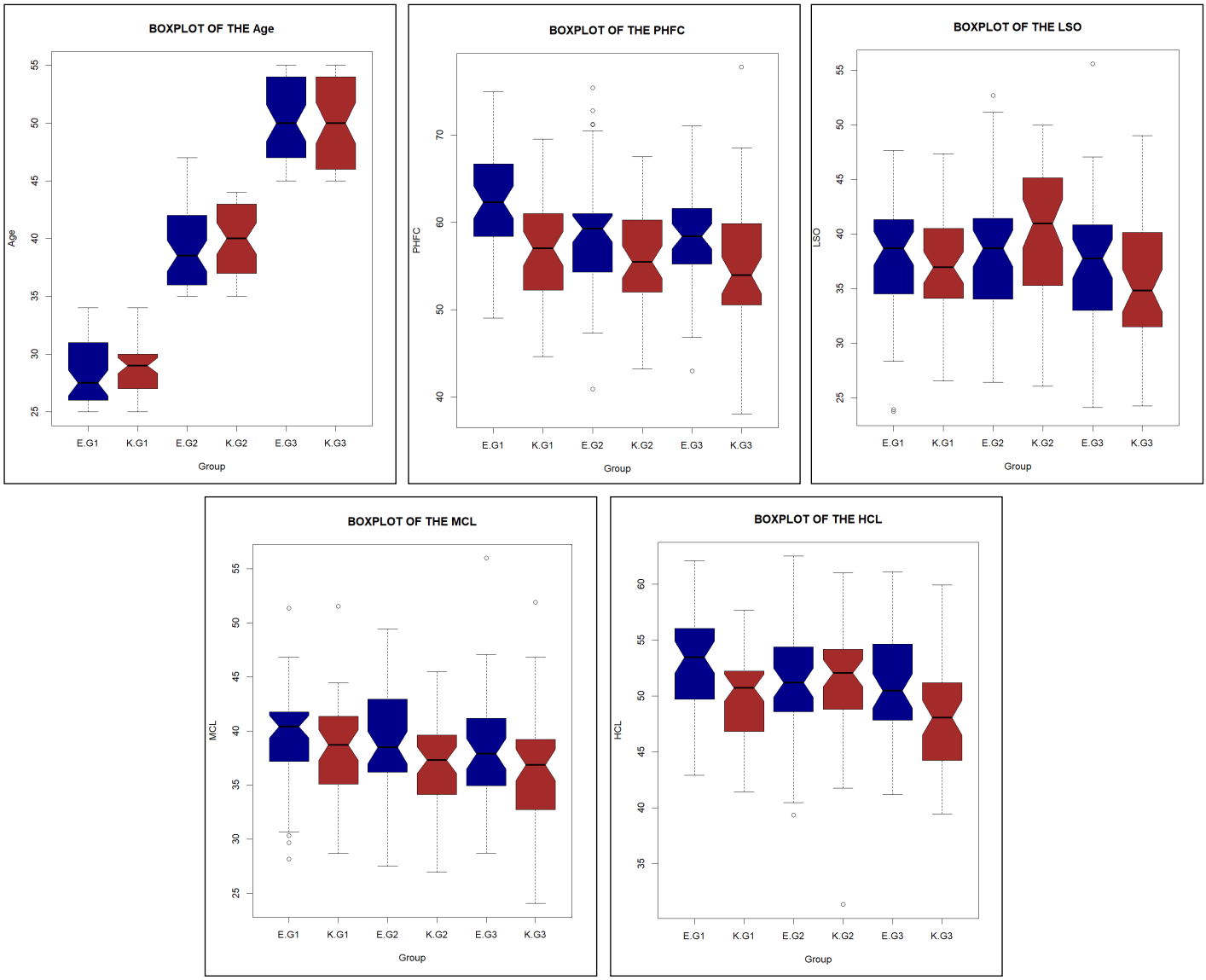

Figure 2. Boxplot for Age, PHFC, LSO, MCL and HCL variables

DISCUSSION

Anatomical and physiological changes in healthy individuals during the life span starting with the birth process and continuing into old age have been the subject of several research. In particular, the evaluation of age-related changes in healthy brain and its parts allows to help detection of pathological conditions and monitoring of changes in the brain caused by the natural aging process (18). The changes seen in the brain with aging are accompanied by deterioration in cognitive functions and this is also affected by gender (19). In this regard, the present study aims to fill the gap in literature by reporting the changes in cerebellum morphometry according to age and gender in healthy adults aged 25-55 years. While age-related changes have been found to be statistically significant for the MCL, LSO, PHFC and HCL variables evaluated in the study, it has also been determined that most variables show gender-related changes within the groups.

This age- and gender-related change observed in the present study is supported by several studies in literature. In a longitudinal study conducted in healthy children and adolescents to examine cerebellum development (3), the cerebellum volume has been found to be higher in males, even when compared to total brain volume. The fact that this difference is larger during adolescence indicates that this organ shows gender dimorphism. Another study (18), which aimed to assess the correlation of volumetric changes in the cerebellum with age and gender in healthy participants, has found a larger volume in males in all age groups, suggesting that this result may reflect gender differences in the body as well. Another research aiming to evaluate the correlation of white and gray matter and volumetric variables with cognitive functions with aging in the brain (19) has found an age-related decrease in the volumes of gray and white matter regions in both sexes. Moreover, differences have been observed between genders in the regions where the volume has decreased and in the slope of the decrease. Another study (20), which aimed to present the effect of aging on cerebellum volume, has grouped participants between the ages of 25 and 65 as early and late adults. As a result of the study, it has been reported that a decrease in cerebellum volume and atrophy

in gray matter have been observed in the late adult group. In a similar study (21), aging-related morphologic changes in the cerebellum in healthy participants between the ages of 20 and 80 have been presented with the convolutional neural network method. It has been found that aging causes a significant decrease in the absolute volumes of cerebellum subregions and atrophies in some cerebellar regions are more pronounced in men. In a study (22) designed with the method of convolutional neural network and aiming to reveal resent the gender differences of the cerebrum and cerebellum, it has been found that some subregions of the cerebellum show gender dimorphism. Another study evaluating brain volume changes in relation to aging has reported a decrease in brain volume and cerebellar atrophy (23). A study involving participants aged between 50 and 95 years (24) has examined the changes in the regions of the cerebellum during normal aging. The findings of the study have indicated that aging-related volumetric atrophy in several subregions of the cerebellum, and in addition, the findings have been affected by gender. In another study designed to reflect the morphometry of the lobules of the cerebellum and its relationship with cognitive status in healthy elderly people (25), segmentation method has been used, suggesting that there is a decrease in lobule volumes and cognition from middle age to old age.

Research involving in the measurements of linear variables of the cerebellum in a Sudanese population (26), contrary to the present study, has found no significant result between the age and the variables. Furthermore, the study findings have been found to be lower compared to the present study. This difference is thought to be due to the different populations, age distribution, and number of participants included in the case. Another study (27) on the evaluation of the variables of the posterior cranial fossa in a healthy population in relation to age and gender, has documented higher LSO variables than the present study while the other variables have been observed to be lower. The difference observed has not been found to be statistically significant, as in the present study, but the gender-related change was significant. Likewise, another report (28) which has analyzed the MCL variable using a bone collection from a South Indian population for the craniovertebral junction analysis, has reached a lower result than the present study. This is thought to be because different populations have been studied and the current study used MR images that also reflect soft tissues as a method. Furthermore, a study investigating the morphometry of the cranium, cerebrum and cerebellum in patients diagnosed with tonsillar herniation (29), has shown lower values of the linear variables in patients, as compared to healthy controls. The morphometric values of the control group have had very similar patterns, in comparison with the values of the present study. Yet, another study (30) performed on the morphometric analysis on brain MR images in patients between the ages of 20 and 65 diagnosed with Chiari malformation and healthy control subjects, has revealed volumetric decreases in the patient group. In the control group, on the other hand, the LC variable has been significantly higher and the MCL and KI variables lower than those in the present study. Finally, another report (31) focusing on the morphometric evaluation of the posterior cranial fossa in patients with Chiari malformation, has found higher values in the LC, LSO and HCL variables for the control group, in comparison with the present study. Although this difference between the studies has not been statistically significant, it may be attributed to the fact that the sample group in the present study consists of more participants.

Consequently, it is of essential to indicate that the study has certain limitations such as the retrospective design, the fact that radiological analyzes have been performed by a single specialist, the lack of participants from advanced age groups in the sample group, and the lack of variables evaluating hormonal processes such as childbirth and breastfeeding process in female participants.

CONCLUSION

The age-related change has been found to be statistically significant for MCL, LSO, PHFC, and HCL variables evaluated in the study. In the analysis of the individuals comprising the groups in terms of gender, it has been determined that the differences in KI, LC, PHFC, LDC, WCL, HC, RCHD, LCHD variables for the first group are statistically significant. For the second group, the differences in MCL, KI, LDC, HC, LCHD variables are statistically significant. For the third group, the differences in LC, LDC, HCL, WCL, HC, ACC, LCHD variables have been found to be statistically significant. It is thought that the present study provides a structural basis for the clinic by presenting atrophic changes in cerebellum morphometry during healthy aging with the effect of gender.

This study was presented orally at the 2nd International Congress of Multidisciplinary Medical and Health Sciences Studies on May 27-28, 2024.

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Conflict of interest: *The authors have no conflicts of interest to declare.*

Ethical approval: *Approval number 2024/61 was obtained from Clinical Research Ethics Committee, Bolu Abant İzzet Baysal University.*

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