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Assessment of age- and sex-dependent changes of cerebellum volume in healthy individuals using magnetic resonance imaging

Sağlıklı bireylerde cerebellum hacminin yaş ve cinsiyete bağlı değişiminin manyetik rezonans görüntüleriyle değerlendirilmesi

Ali Haydar Baykan [1], Sibel Ateşoğlu Karabaş [2], Zümrüt Doğan [2], Selma Solgun [3], Gökhan Özcan [1], Şükrü Şahin [1], Fatih Erbay [6], Ali Aydın [2], Fatih Üçkardeş [4], İbrahim İnan [5]

[1] Adiyaman University Faculty of Medicine Department of Radiology, Adiyaman, Turkey
[2] Adiyaman University Faculty of Medicine Department of Anatomy, Adiyaman, Turkey
[3] İnonu University, Department of Anatomy, Master, Malatya, Turkey
[4] Adiyaman University Faculty of Medicine Department of Biostatistics and Medical Informatics, Adiyaman, Turkey
[5] Department of Radiology, Biruni University Hospital, Istanbul, Turkey
[6] Department of Radiology, Gaziantep University Hospital, Istanbul, Turkey

ORCID ID of the author(s)

AHB: 0000-0002-9281-652X
SA: 0000-0002-8469-4518
ZD: 0000-0001-7131-2317
SS: 0000-0003-2827-2158
GÖ: 0000-0002-9046-3070
ŞŞ: 0000-0001-6920-4317
FE: 0000-0003-1747-9989
AA: 0000-0002-2392-2388
FÜ: 0000-0003-0677-7606
İİ: 0000-0003-2136-3604

Corresponding author / Sorumlu yazar:
Ali Haydar Baykan
Address / Adres: Adıyaman Üniversitesi Tıp Fakültesi Radyoloji Anabilim Dalı, Adıyaman, Türkiye
e-Mail: drbaykan@hotmail.com

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Abstract

Aim: Cerebellum is a structure ingrained in fossa cranii posterior and has a great role in contributing to the coordination of motor functions, regulation of muscle tone, and motor learning, as well as precision and accurate timing. This study primarily aimed to establish a cerebellum measurement scale based on age and sex.
Methods: The study was carried out with the approval of Adiyaman Clinical Research Ethics Board and the contributions of Adiyaman University Training and Research Hospital Radiology Department. The data were retrospective cohort study obtained from the magnetic resonance images of 160 individuals (80 female and 80 male). The individuals included in the study were divided into age groups of 0-4, 5-9, 10-19, 20-29, 30-39, 40-49, 50-59 and 60-80 years, each consisting of 10 women and 10 men. All statistical analyses were performed using SPSS program.
Results: The cerebellum volume was 139.23 (11.73) cm^3 for women and 151.14 (12.30) cm^3 for men aged 10-19 years, and the difference was significant (P=0.040). The cerebellum volume of individuals aged 0-4 years was found to be 105.05 (33.28) cm^3 with a significant difference compared to the remaining age groups (P<0.001). The total cerebellum volume was calculated as 128.84 (29.66) cm^3 for individuals aged 0-17 years and 141.91 (15.06) cm^3 for those in the 18-80 years group. It was found to be smaller in the 0-17 age group (P<0.001).
Conclusion: Determining the volumes of brain parts in healthy individuals is very important in assessing the aging process, as well as contributing to the differentiation of normal and pathological conditions.
Keywords: Cerebellar volume, Magnetic resonance imaging, Age, Gender

Öz

Amaç: Serebellum fossa cranii posterior'da yerleşmiş, motor fonksiyonların koordinasyonu, kas tonusunun düzenlenmesi ve motor öğrenmede; ayrıca hassasiyet ve doğru zamanlamanın sağlanmasına katkıda bulunan beyinde önemli rolü olan bir yapıdır. Bu çalışma ile amacımız öncelikle yaşa ve cinsiyete bağlı olarak serebellum ölçüm skalası oluşturabilmektir.
Yötemler: Çalışma Adıyaman Klinik Araştırmalar Etik Kurulu'ndan alınan onay ile Adıyaman Üniversitesi Eğitim ve Araştırma Hastanesi Radyoloji Anabilim Dalı'nın katkılarıyla gerçekleştirilmiştir. Veriler manyetik rezonans görüntüleme yöntemi kullanılarak (80 kadın ve 80 erkek) toplam 160 bireye ait görüntüler üzerinde retrospektif kohort bir çalışma olarak elde edilmiştir. Çalışmaya dâhil edilen bireyler 0-4 yaş, 5-9 yaş, 10-19 yaş, 20-29 yaş, 30-39 yaş, 40-49 yaş, 50-59 yaş ile 60-80 yaş toplam 8 gruba ayrılmış ve her yaş grubu da 10 kadın ve 10 erkek toplam bireylerden oluşmaktadır. Elde edilen verilerin istatistiksel tüm analizleri için SPSS programı kullanılmıştır.
Bulgular: Çalışmamızda serebellum hacmi 10-19 yaş kadınlarda 139,23 (11,73) cm^3 ve erkeklerde 151,14 (12,30) cm^3 idi (P=0,040). 0-4 yaş arası bireylerin serebellum hacmi 105,05 (33,28) cm^3 diğer yaş gruplarına göre daha küçük bulundu ve diğer gruplar ile arasında anlamlı bir farklılık vardı (P<0,001). 0-17 yaş arasındaki bireylerde toplam serebellum hacmi 128,84 (29,66) cm^3,18-80 yaş grubundaki bireylerde toplam serebellum hacmi 141,91 (15,06) cm^3 idi. 0-17 yaş grubunda daha küçük bulundu (P<0,001).
Sonuç: Beyin bölümlerinin sağlıklı bireylerdeki hacimlerinin belirlenmesi; normal ve patolojik durumların ayırt edilmesine katkı sağlamakla birlikte yaşlanma sürecinin değerlendirmesinde de oldukça önemlidir.
Anahtar kelimeler: Serebellar hacim, Manyetik rezonans görüntüleme, Yaş, Cinsiyet

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Introduction

Cerebellum, the second largest part of the encephalon and the largest part of the rhombencephalon [1], is ingrained in the fossa cranii posterior and has important functions for the brain, contributing to the coordination of motor functions, regulation of muscle tone, and motor learning, as well as precision and accurate timing [2]. The external structure of the cerebellum consists of two lateral lobes known as hemispheres and a medial part called vermis cerebelli that connects these lobes [3]. In the median sections of the cerebellum composed of white matter on the inside and gray matter on the outside are corpus medullare cerebelli and the surrounding cortex cerebelli, referred to as arbor vitae (tree of life) since the structure resembles the branches of a tree [2].

Changes in the cerebellum volume are seen in many diseases in the clinic, especially occurring due to neuropsychiatric, neurological, hereditary-idiopathic, developmental, vascular and metabolic diseases, nutrition and infection-related diseases, and physical trauma [4]. Therefore, the total volume and volume ratios are frequently used in experimental studies, as well as in clinical diagnosis, treatment and treatment planning [5].

Stereology, which is now considered to be one of the most reliable methods used to measure the volume of irregularly shaped objects, is a branch of science that provides many numerical values related to a structure, such as the volume and surface area based on two-dimensional sections or section images of that structure [6]. Taking advantage of soft tissue contrast analysis [7], the images obtained by magnetic resonance imaging (MRI), which does not contain ionizing radiation that is harmful to tissues, have an important place in the diagnosis of many neurological and psychiatric diseases and revealing intracranial anatomical structures and pathological changes [8].

In this study, we divided healthy individuals into age groups and measured cerebellum volumes on MRI images using stereology. We consider that this will provide useful data to guide clinicians in the diagnosis, treatment, and monitoring treatment progress in the clinic, as well as pioneering further studies.

Materials and methods

The study was carried out with the approval of Adiyaman Clinical Research Ethics Committee, and the measurements were undertaken by two specialist radiologists with more than 10 years of experience in the Radiology Department of Adiyaman University Training and Research Hospital.

The data were retrospectively obtained from the images of 160 individuals, 80 female and 80 male, recorded in the radiology archive of the hospital. No age limitation was used for the individuals included in the study. For the evaluation, the sample was divided into eight age groups as 0-4 years, 5-9 years, 10-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, and 60-80 years, each containing 20 people (10 female and 10 male).

Included in the study were patients who underwent cranial MRI and were reported to have normal findings. The patients who presented to the hospital due to cardiovascular diseases, neurological diseases, psychiatric diseases, thyroid, transient ischemic attacks, tumor, seizures, dementia, and diabetes were excluded. The parameters used in the MRI and radiological measurements were age, gender, section thickness, section number, surface area, and cerebellum volume.

Imaging technique and volume measurement

MRI imaging was performed using the Philips Achieva 1.5 Tesla (Achieva; Philips Medical Systems, Best, the Netherlands) system, which allows soft tissue analysis. The same protocol was used for the assessment of all MRI data. For the calculation of cerebellum volume, T2-weighted axial images (TR: 4800, TE: 100, slice thickness: 5 mm, FOV: 230, average: 1, matrix: 208x130) were recorded. The volumetric measurements were obtained based on the contour stack principle using MPR View 3D workstation. Cerebellar volume calculations were performed planimetrically according to Cavalieri’s principle (Figure 1).

Figure 1: Volumetric measurement of the cerebellum (shown in red) on a T2-weighted image in the axial plane. The fourth ventricle was not included in the volumetric calculation.

Statistical analysis

Statistical analysis was performed using the SPSS program v. 15.0. Conformance of quantitative variables to normal distribution was evaluated using one-sample Kolmogorov Smirnov test. The independent two-sample t-test was employed for the comparison of two independent groups and the analysis of variance for more than two groups. For the variables found significant, Tukey's Honest Significant Difference binary comparison test was utilized to determine the differences between the groups. The results were given as mean (standard deviation). The minimum level of significance was considered $P<0.05$.

Results

The cerebellar volume of males at 10-19 age group has been detected significantly higher than females ($P=0.004$). For the other age groups the cerebellum volume is higher at males but not significant. Table 1 shows the relationship between age and gender and the mean cerebellar volume calculated using the planimetric method (Figure 2).

In the 0-4 year old group, the total cerebellum volume was found to be 105.05 (33.28) cm^3, which was lower compared to the remaining age groups ($P<0.001$). Table 2 presents the relationship of the mean cerebellum volume with age groups.

The cerebellar volume of the individuals in the 0-17 age group was found to be significantly smaller than that of the 18-80 age group ($P<0.001$) (Table 3).

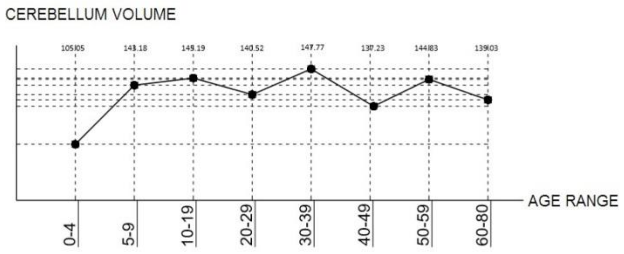

Figure 2: Changes in cerebellum volume according to age groups

Table 1: The relationship of cerebellum volume with age and gender

	Gender	Mean (SD)	*P*-value*
0-4 Years	Female (n = 10)	91.70 (38.55)	0.071
	Male (n = 10)	118.40 (21.34)	
5-9 Years	Female (n = 10)	137.40 (13.83)	0.263
	Male (n = 10)	144.82 (14.84)	
10-19 Years	Female (n = 10)	139.23 (11.73)	0.040
	Male (n = 10)	151.14 (12.30)	
20-29 Years	Female (n = 10)	140.12 (15.90)	0.870
	Male (n = 10)	141.46 (19.83)	
30-39 Years	Female (n = 10)	145.94 (17.15)	0.419
	Male (n = 10)	151.78 (14.31)	
40-49 Years	Female (n = 10)	132.29 (14.99)	0.107
	Male (n = 10)	142.16 (10.68)	
50-59 Years	Female (n = 10)	138.67 (17.20)	0.122
	Male (n = 10)	150.99 (16.69)	
60-80 Years	Female (n = 10)	133.29 (17.13)	0.148
	Male (n = 10)	144.77 (16.82)	

SD: Standard deviation, *: Independent two-sample t-test

Table 2: The relationship of cerebellum volume with age groups

Age Groups	Mean (SD)	*P*-value*
0-4 Years (n = 20)	105.05^{b} (33.28)	<0.001
5-9 Years (n = 20)	143.18^{a} (10.15)	
10-19 Years (n = 20)	145.19^{a} (13.20)	
20-29 Years (n = 20)	140.52^{a} (13.31)	
30-39 Years (n = 20)	147.77^{a} (13.39)	
40-49 Years (n = 20)	137.23^{a} (13.65)	
50-59 Years (n = 20)	144.83^{a} (17.66)	
60-80 Years (n = 20)	139.03^{a} (17.54)	

SD: Standard deviation, *: One-way variance analysis, ^{ab}: The letters in the same column (a-b) refer to the significant differences ($P<0.05$) between the means according to the results of Tukey's Honest Significant Difference test.

Table 3: Cerebellum volume according to the age groups of below and above 18 years

Age Group	Mean (SD)	*P*-value*
0-17 Years (n = 51)	128.84 (29.66)	<0.001
18-80 Years (n = 109)	141.91 (15.06)	

SD: Standard deviation, *: Independent two-sample t-test

Discussion

The various anatomic and physiological changes beginning with the birth of an organism and continuing with aging throughout the life span have attracted the attention of many researchers [9]. The volumes of the brain and its sections in healthy individuals are important in the evaluation of both the clinical pathological condition and the normal aging process [10]. In addition, it has been demonstrated that there is a volumetric decrease in brain tissue and cerebellar atrophy occurs with aging [11,12]. Calculation of the cerebellum volume is important to accurately assess size differences that may later occur and calculate the changes [9].

The volume of intracranial structures can be measured by using different techniques. Similarly, in the current study, the cerebellum volume measurements were undertaken using planimetry in accordance with Cavalieri principle. In planimetry, the boundaries of structures of interest on sectional images are manually drawn for each section individually in the electronic environment. The sum of the measured cross-sectional areas is multiplied by section thickness to obtain the volume of the structure [13,14].

Knickmeyer et al. [15] found the volume of cerebellum to be 91.962 cm^3 in one-year-olds and 105.154 cm^3 in two-year-old. In our study, the cerebellum volume was calculated as 91.70 (38.55) cm^3 for girls and 118.40 (21.34) cm^3 for boys aged 0-4 years, with a mean of 105.05 (33.28) cm^3. In the literature, the measurements of cerebellar hemispheres, transcerebellar diameter, and anterior-posterior dimension in individuals aged 0-4 years were previously reported [16]. However, we did not find an enough studies on the cerebellar volumes of different age groups; thus, we consider that there is a need for further research in this area.

In many studies it has been observed that the cerebellum volume of males is higher than females for all age groups [17]. It was reported that men had a larger cerebellum than women of the same age, and these differences might also reflect sexual dimorphism in the body structure [18]. Cerebellum volume of males has been calculated as higher than females in this study too for all age groups. But these differences are not statistically significant except for 10-19 age group.

Mas [19] has been stated that cerebellar volume is greater in males than in females between the ages of 10-19 years. Similarly, it has been determined that the cerebellar volume was greater in males than in females in the 10-19 age group in this study. It has been considered that this difference may be associated with the hormones released in adolescence.

Comparative studies investigating the volume of the cerebellum may constitute valuable references for other research demonstrating physiological and pathological conditions, and cerebellum volumes in different races [20,21]. Mas [19] performed the volumetric analysis of cerebrum-diencephalon, cerebellum and total intracranial structures using the MRI method in a healthy sample consisting of 42 male and 42 females aged 10 to 86 years according to gender and decade and found a significant volumetric decrease in these structures with increased decades. He noted that the cerebellum volume did not significantly differ between men and women at the age of 60 years or older, with the latter having a smaller cerebellum for each decade. In another study, Woodruff-Pak et al. [22] investigated age-related cerebellar volume changes in healthy subjects and found no relationship between age and cerebellar volume. Luft et al. [23] investigated the effects of age on cerebellar volume using the MRI images of 48 volunteers aged 19.8-73.1 years. The results revealed that the total cerebellar volume remained constant until the age of 50 and showed a linear decrease after this period. Many studies investigating age-dependent changes in cerebellum volume provide controversial results. Some researchers detected a decrease in cerebellum volume with aging [17], while others reported no significant decrease in older groups [24]. In the current study, we found that the cerebellum volume was smaller in the 0-4 years group, but there was no significant change in the remaining age groups. Furthermore, women aged 60 to 80 years had a smaller cerebellum than men in the same age group, but the difference was not statistically significant. However, since the gaps between the cerebellar sulci were included in the total volume calculation, further studies are needed to perform measurements by considering sulcal dilatations that develop in the background of early-stage atrophy, especially after the age of 60 years.

This study has certain limitations. The first is the retrospective design; i.e., retrospective collection of data. The second limitation concerns the relatively small number of cases and radiological analyses being undertaken by a single radiologist. In addition, the ages at which adolescence began and individuals reached adulthood were not known. Lastly, the parameters that can change the hormonal status of women of reproductive age, such as the number of births and breastfeeding period were not investigated.

Conclusion

Cerebellum volume of males has been found to be significantly higher than females for all age groups. Furthermore, it has been found lower in the 0-4 age group when compared to the other age groups. In the 10-19 age group, the cerebellum level of males has been observed considerably higher when compared with females, this phenomenon may be related with the adolescence period hormonal changes.

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