

Effects of Age and Sex on Cerebellum and Ventral Pons Volume - MRI Study

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Abstract

Magnetic resonance image (MRI) has much importance in terms of searching aging and gender effects on brain. In this study, age and gender differences were aimed to be found out on cerebellar and ventral pons volumes. It is totally studied on nine cross-section images from MRI; three at transvers plane (top, middle, and bottom), three at frontal plane (front, middle, back), and three at sagittal plane (right, middle, left). T1 transvers, frontal and sagittal MRI was taken from 43 men and 57 women any of whom do not display any pathological symptom. Both gender groups were separated into age groups as young, middle aged and elderly in order to understand effects of aging. Areas of the cerebellum and ventral pons formation were calculated by transferring selected images to NETCAD software. The volumes were calculated in Excel program by using the values obtained from MRI and analysed by SPSS. No significant difference between genders in the ventral pons volumes. A significant size in men's right and left hemisphere volumes at transverse and frontal planes. It was determined a significant size in women's vermis of cerebellum volumes at the sagittal plane. Also, a significant reducing was observed in right hemisphere volumes, in frontal plane right – left hemisphere volumes owing to aging and, so it was found that the reducing was much more in men. The results were comparable with previous ones. NETCAD is concluded to be suitable in volume calculating with MRI.

Keywords: Cerebellum, Ventral Pons, MRI, Volumetry, NETCAD

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Introduction

Morphological changes are expected to occur in different anatomical areas of the brain due to gender and aging. The aging of the brain is characterized by regional shrinkage in the gray and white matter regions (1). Magnetic resonance imaging (MRI) shows the morphological and pathological changes of intracranial anatomy. It also gives the opportunity to examine the changes that occur with aging in healthy individuals (2). The cerebellum plays an important role in normal brain function and it has structural and functional involvement in a number of neurological diseases associated with impairment of functions such as both motor and cognition, mood, and behaviour (3). In different disease states and after damage, it has become important to find concrete ways to evaluate the cerebellum. There are studies in cerebellum, which examine: 21-hydroxylase deficiency (21OHD) (4), effect of steroid hormones in congenital adrenal hyperplasia (5), the volume of cerebellum in normal fetal brain (6), the volume of cerebellum in glioma inactivated protein 1 (LGII), the volume of cerebellum in encephalitis (7), in neurometabolic diseases such as cerebrotendinousxanthomatosis, the volume of the cerebellum nuclei (8) and the volumes of the cerebellum and cerebellar peduncles to distinguish progressive supranuclear Palsy-Richardson Syndrome from Parkinson's disease (9). As Murshed (2003) has carried out, manual drawings on MR images for the volume of cerebellum studies will take more time and subjective data will be obtained. In this study, it was aimed to calculate the cerebellum and the volume of ventral pons

changes on the MR images of healthy individuals over the areas obtained with the NETCAD program.

Method

For the present study, approval was obtained from Selçuk University Faculty of Medicine Ethics Committee with the decision number 2007/091 dated 25.04.2007.

The study was performed on the MR images of patients who applied to the neurology and neurosurgery outpatient clinics of Afyonkarahisar State Hospital for various reasons in 2007. Radiologists studied MR images of 100 adult individuals (43 males - 57 females) (aged between 15-70 years) who were not reported any disease, anomaly or damage and were evaluated as normal. Both sexes were divided into three groups according to their ages:

- 1- Young age group; 23 individuals (13 males, 10 females) between the ages of 15-29.
- 2- Middle age group; 36 individuals (12 males, 24 females) between the ages of 30-49.
- 3- Advanced age group; 41 individuals (18 males, 23 females) between the ages of 50-70.

For the images; spin-echo transverse using 1.5 tesla Siemens Maestro Glast brand device (TR: 475 TE: 8,1), sagittal (TR: 375 TE: 113), frontal (TR: 8770 TE: 113); thickness in sections: transverse and frontal (4,5mm), sagittal (5mm); FOW: 500mm MATRIX: 512 * 512 GAP: 2,2 m.tesla values were received. T1-weighted

transverse, frontal and sagittal MR images were evaluated, since the anatomical structures of the cerebellum and pons without pathology were examined. NETCAD 4.0 GIS software was used to calculate the area and volume of the images included in the research.

A total of 9 images were selected from transverse, frontal and sagittal planes. These images were transferred to the

NETCAD program in bitmap format. First, the borders of the hemisphere of cerebellum, vermis of cerebellum and ventral pons were drawn (Figures 1, 2, 3). The area accuracy of the software on the images was chosen as 0.01 mm². Numerically determined areas were recorded in Excel and the volumes of the following regions were calculated.

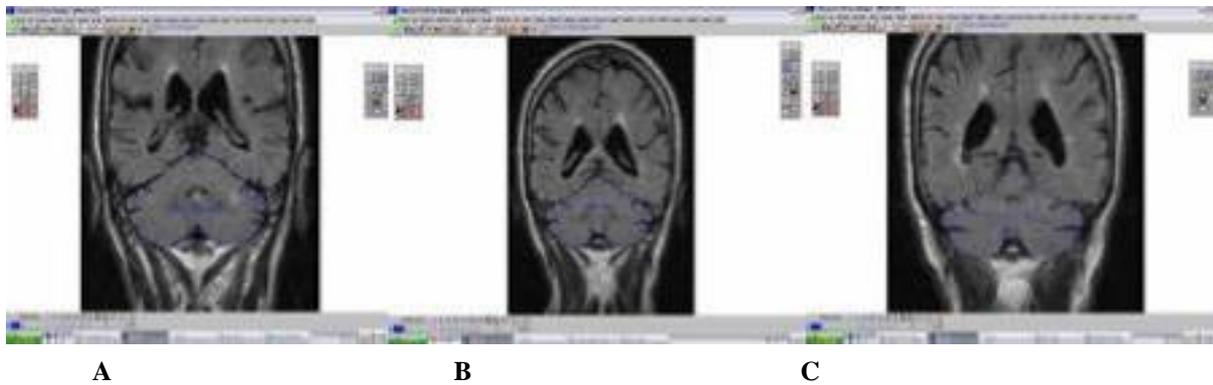


Figure 1: Field plot of the hemisphere of cerebellum (A, a lower section from the middle section; B, middle section; C, upper section from the middle section) on the cranial MRI in the transverse plane transferred to the NETCAD program.

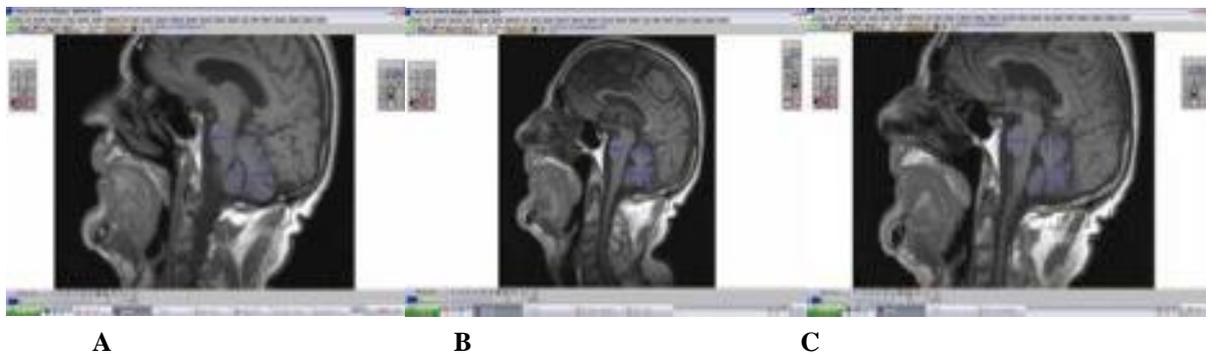


Figure 2: Field plot of the hemisphere of cerebellum (A, the previous section from the middle section, B, the middle section, C, the next section from the middle section) in the cranial MRI in the frontal plane transferred to the NETCAD program.

- 1- Right hemisphere of cerebellum in the transverse plane.
- 2- Left hemisphere of cerebellum in the transverse plane.

- 3- Right-left hemisphere of cerebellum in the frontal plane.
- 4- Vermis of cerebellum in the sagittal plane.
- 5- Ventral pons in the sagittal plane.

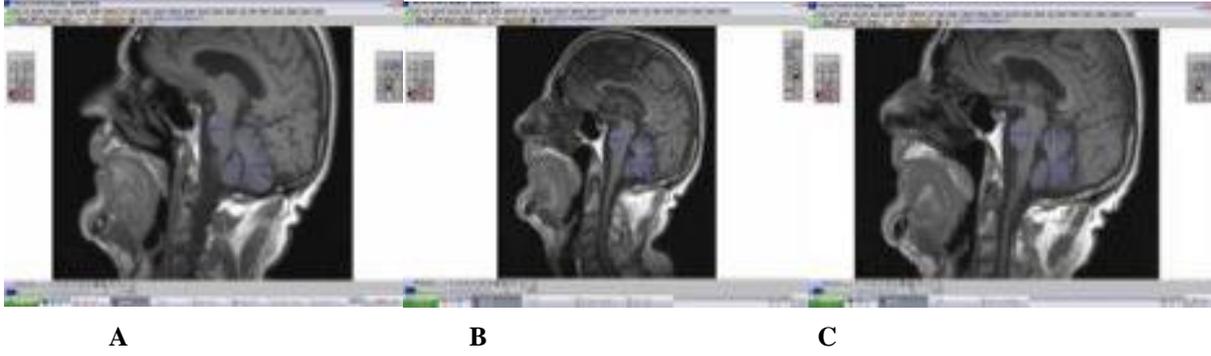


Figure 3: Field plot of the vermis of cerebellum and ventral pons (A; the previous section from the middle section, B; the middle section, C; the next section from the middle section) in the cranial MRI in the sagittal plane transferred to the NETCAD program.

Statistical analysis of parameters according to age groups and gender was performed in SPSS 15.0 (for Windows) program. A two-way analysis of variance was used to evaluate the combined effect of age and gender. If there was a difference in terms of age groups, the bonfer's corrected one-way analysis of variance and Tukey HSD test were performed to determine in which age group the difference originated from. A student-t test was applied to determine, which age group caused the difference in gender. Spearman correlation test, which is used in non-homogeneous data, was used to determine the relationship between the values obtained from the study.

Results

According to the volume calculations made in all three planes in the study, it was found that the right and left cerebellar volume were larger in men and the vermis of cerebellum volumes in women ($p < 0.05$) (Table 1). Also; It was determined that the volume decrease between the middle age group and the advanced age group was greater in males, and the volume decreases between the younger and middle age group in females (Table 2). No gender and age-related changes were observed in ventral pons volume. When analysed by age groups, although the decrease in right cerebellar volume was not found to be statistically significant, it was found that there was a greater decrease in men with increasing age compared to women.

Table 1: Comparison of cerebellar volumes (mean $\text{mm}^3 \pm \text{SD}$) by sex.

Parameters	Male (n=43)	Female (n=57)
Right hemisphaerium	10124 \pm 1959 *	9436 \pm 1714
Left hemisphaerium	10452 \pm 1193 **	9390 \pm 1210
Total hemisphaerium	17613 \pm 15494 *	13741 \pm 1478
Vermis	6264 \pm 1534 **	7120 \pm 1227

SD; Standart deviation, *: $p < 0.05$, **: $p < 0.001$.

Table 2: Comparison of cerebellar volumes (mean mm³ ± SD) by age groups and sex.

	Young age (15-29 age)		Middle age (30-49 age)		Late age (50-70 age)	
	M (n=13)	F (n=10)	M (n=12)	F (n=24)	M (n=18)	F (n=23)
RH	10257 ± 2954	9755 ± 1402	10157 ± 1668*	9422 ± 1325	9958 ± 1218	9311 ± 2185
LH	10611 ± 865	9523 ± 1198	10571 ± 1405**	9147 ± 1175	10257 ± 1280	9085 ± 1259
TH	15815 ± 1598*	14367 ± 1634	13966 ± 1669 ^a	13990 ± 1360	13800 ± 2097 ^a	13317 ± 1223
Vermis	7225 ± 2034	7367 ± 695	6002 ± 1129	7321 ± 1315**	6802 ± 1285	5745 ± 1014 ** ^a

SD; Standart deviation, *: p<0.05, **: p<0.001, ^a; Significantly different from the young age group. RH; right hemisphaerium, LH; left hemisphaerium, TH; total hemisphaerium, M; male and F; female.

Discussion

Thanks to the morphological measurements made in normal people, the changes in the cerebellum and subcortical structures in both aging and neurodegenerative diseases are successfully demonstrated. While MRI is widely used for brain and cerebellar morphological evaluation, advanced MRI techniques allow investigation of cerebellar microstructural and functional features. A group of researchers who calculated the volume on MR images in mice showed that the lateral cerebellar volume was higher in female mice and the medial cerebellar volume was higher in male mice (11). As a result of volumetric analysis performed on healthy people, it was shown that there was no difference between genders in the gray matter of the cerebellum, but there was a decrease in gray matter volume with aging (12).

Volumetry, voxel-based morphometry, diffusion MRI based tractography, functional MRI, perfusion, and proton MR spectroscopy are among the most commonly used techniques in the cerebellum study (3). Sumiyoshi et al. (2017) reported an increase in brain gray matter in adolescent rats in their study by using voxel-based morphometry in MRI. The highest increase was observed in the occipital cortex, amygdala, hippocampal

formation and cerebellum. Voxel-based morphometry, one of the current methods used in volume calculation, is mostly preferred by T1-weighted MRI to define volume changes in normal aging and regional brain atrophy in various neurological and psychiatric diseases (14,15). Unlike previous studies, there are also studies using a Freesurfer 5.1. fully automated technique to measure the volumes of T1-weighted MR images obtained from 3T MR scanners (16). There are studies reporting that the poster inferior part of the cerebellum differs in cognitive criteria in the cerebellar volume measurements performed using the Spatially Un-neutral Infratentorial Toolbox (SUIT) in the Statistical Parametric Matching (SPM12) program of MS patients and healthy individuals, while the anterior part creates the variance in the motor-performance level (17). It was also reported that cerebellar volumetric abnormalities can make an important contribution to explain motor and cognitive performance in MS patients. Vurdem et al. (2012), who measured posterior cranial fossa and cerebellar volume in patients with type I Chiari malformation using a different method: the stereological method, could not find any statistical difference between patients with type I Chiari malformation and healthy individuals in

terms of cerebellar volumes.

Cerebellar volume is important in neurological and some genetic diseases. In a study conducted on patients with schizophrenia, it was observed that posterior vermis of cerebellum volumes decreased significantly in men (19). In a study examining the cerebellar volumes in patients with Prader-Willi syndrome (PWS), a decrease in all parts of the cerebellum was shown in patients compared to the control group, and it was suggested that this would be an important evidence for behavioural change in individuals with PWS (20). It has been reported that there is a significant decrease in white matter of the cerebellum in the volume calculations made on 7-tesla MRI images in patients with Friedreich's ataxia (FRDA), another genetic disease (21).

In a study conducted to differentiate migraine and tension-type headache, it was shown that there was a decrease in the gray matter of the cerebellum in the migraine group, thus it was reported that the cerebellar volume could be the differential diagnosis between the two types of diseases (22). Decreased cerebellar volumes were observed in both genders in smokers compared to non-smokers (23).

In our study, unlike these methods, MR images obtained from 3 planes were transferred to the NETCAD program and measurements were made. The similarity of the results obtained in our study with the results of other studies supports that the NETCAD program can be used in area and volume calculations over MRI.

Conflict of interest

The authors declare that no conflict of interest exists.

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References

1. Persson N, Wu J, Zhang Q, et al. Age and sex related differences in subcortical brain iron concentrations among healthy adults. *Neuroimage*. 2015;122:385-398. doi:10.1016/j.neuroimage.2015.07.050.
2. Szabo CA, Lancaster JL, Xiong J, et al. MR imaging volumetry of subcortical structures and cerebellar hemispheres in normal persons, *Am J Neuroradiol*, 2003;24, 644-7.
3. Mormina E, Petracca M, Bommarito G, et al. Cerebellum and neurodegenerative diseases: Beyond conventional magnetic resonance imaging. *World J Radiol*. 2017;9(10):371-388. doi:10.4329/wjr.v9.i10.371.
4. Webb EA, Elliott L, Carlin D, et al. Quantitative Brain MRI in Congenital Adrenal Hyperplasia: In Vivo Assessment of the Cognitive and Structural Impact of Steroid Hormones. *J Clin Endocrinol Metab*. 2018;103(4):1330-1341. doi:10.1210/je.2017-01481.
5. Serrano NL, De Diego V, Cuadras D, et al. A quantitative assessment of the evolution of cerebellar syndrome in children with phosphomannomutase-deficiency (PMM2- CDG). *Orphanet J Rare Dis*. 2017;12(1):155. doi:10.1186/s13023-017-0707-0.
6. Ber R, Hoffman D, Hoffman C, et al. Volume of Structures in the Fetal Brain Measured with a New Semiautomated Method. *AJNR Am J Neuroradiol*. 2017;38(11):2193-2198. doi:10.3174/ajnr.A5349.
7. Szots M, Blaabjerg M, Orsi G, et al. Global brain atrophy and metabolic dysfunction in LGII encephalitis: A prospective multimodal MRI study. *J Neurol Sci*. 2017;376:159-165. doi:10.1016/j.jns.2017.03.020.
8. Rosini F, Pretegianni E, Mignarri A, et al. The role of dentate nuclei in human oculomotor control: insights from cerebrotendinousxanthomatosis. *J Physiol*. 2017;595(11):3607-3620. doi:10.1113/JP273670.
9. Murshed KA. Volume analysis in normal adult human brains: evaluation by magnetic resonance imaging. PHD Thesis. 2003.
10. Sumiyoshi A, Nonaka H, Kawashima R. Sexual differentiation of the adolescent rat brain: A longitudinal voxel-based morphometry study. *NeurosciLett*. 2017;642:168-173. doi:10.1016/j.neulet.2016.12.023.
11. Ashburner J, Friston KJ. Unified segmentation. *Neuroimage*. 2005;26(3):839- 851. doi:10.1016/j.neuroimage.2005.02.018.

12. Lindig T, Kotikalapudi R, Schweikardt D, et al. Evaluation of multimodal segmentation based on 3D T1-, T2- and FLAIR-weighted images – the difficulty of choosing. *Neuroimage*. 2018;170:210-221. doi:10.1016/j.neuroimage.2017.02.016.
13. Wyciszkievicz A, Pawlak MA, Krawiec K. Cerebellar Volume in Children With Attention-Deficit Hyperactivity Disorder (ADHD). *J Child Neurol*. 2017;32(2):215-221. doi:10.1177/0883073816678550.
14. D'Ambrosio A, Pagani E, Riccitelli GC, et al. Cerebellar contribution to motor and cognitive performance in multiple sclerosis: An MRI sub-regional volumetric analysis. *MultiScler*. 2017;23(9):1194-1203. doi:10.1177/1352458516674567.
15. Vurdem ÜE, Acer N, Ertekin T, et al. Analysis of the volumes of the posterior cranial fossa, cerebellum, and herniated tonsils using the stereological methods in patients with Chiari type I malformation. *Scientific World Journal*. 2012;2012:616934. doi:10.1100/2012/616934.
16. Zanigni S, Calandra-Buonaura G, Manners DN, et al. Accuracy of MR markers for differentiating Progressive Supranuclear Palsy from Parkinson's disease. *Neuroimage Clin*. 2016;11:736-742. doi:10.1016/j.nicl.2016.05.016.
17. Womer FY, Tang Y, Harms MP, et al. Sexual dimorphism of the cerebellar vermis in schizophrenia. *Schizophr Res*. 2016;176(2- 3):164-170. doi:10.1016/j.schres.2016.06.028.
18. Meyer CE, Kurth F, Lepore S, et al. In vivo magnetic resonance images reveal neuroanatomical sex differences through the application of voxel-based morphometry in C57BL/6 mice. *Neuroimage*. 2017;163:197-205. doi:10.1016/j.neuroimage.2017.09.027.
19. Yu T, Korgaonkar MS, Grieve SM. Gray Matter Atrophy in the Cerebellum-Evidence of Increased Vulnerability of the Crus and Vermis with Advancing Age. *Cerebellum*. 2017;16(2):388-397. doi:10.1007/s12311-016-0813-x.
20. Yamada K, Watanabe M, Suzuki K, et al. Cerebellar Volumes Associate with Behavioral Phenotypes in Prader-Willi Syndrome [published online ahead of print. *Cerebellum*. 2020;10.1007/s12311-020-01163-1. doi:10.1007/s12311-020-01163-1.
21. Straub S, Mangesius S, Emmerich J, et al. Toward quantitative neuroimaging biomarkers for Friedreich's ataxia at 7 Tesla: Susceptibility mapping, diffusion imaging, R₂ and R₁ relaxometry. *J Neurosci Res*. 2020;10.1002/jnr.24701. doi:10.1002/jnr.24701.
22. Chen WT, Chou KH, Lee PL, et al. Comparison of gray matter volume between migraine and "strict-criteria" tension-type headache. *J Headache Pain*. 2018;19(1):4. doi:10.1186/s10194-018-0834-6.
23. Vňuková M, Ptáček R, Raboch J, et al. Decreased Central Nervous System Grey Matter Volume (GMV) in Smokers Affects Cognitive Abilities: A Systematic Review. *Med Sci Monit*. 2017;23:1907-1915. doi:10.12659/msm.901870.