Evaluation of Cerebellar Asymmetry with Vertigo Cases: A Stereological Study

Vertigolu Olgularda Cerebellar Asimetrinin Değerlendirilmesi

H. Selim KARABEKİR[1]
Nuket GÖÇMEN MAS[2]
Özge KÜSPECİ YILMAZ[3]
Orhan BAŞ[4]
Tolga ERTEKİN[5]
A. Canan YAZICI[6]
Sevda SENAN[7]

1 Afyon Kocatepe University, School of Medicine, Neurosurgery Department, Afyonkarahisar, Turkey
2 Afyon Kocatepe University School of Medicine, Anatomy Department, Afyonkarahisar, Turkey
3 Afyon Kocatepe University School of Medicine, Neurology Department, Afyonkarahisar, Turkey
4 Rize University School of Medicine, Anatomy Department, Rize, Turkey
5 Afyon Kocatepe University Ataturk Vocational School of Health Services, Anatomy Department, Afyonkarahisar, Turkey
6 Baskent University School of Medicine, Biostatistics Department, Ankara, Turkey
7 Turkish Geriatric Foundation, Ankara, Turkey

ABSTRACT

AIM: We aimed to evaluate the relevant methods of stereology to estimate cerebellar asymmetry according to gender in both adult right-handed vertigo cases and healthy cases.

MATERIAL and METHODS: The study included 14 adult control subjects and 18 patients with vertigo. The volumes of the cerebellar hemispheres were determined on MRI using the point-counting approach of stereological methods.

RESULTS: The mean (±SD) of the right cerebellar hemispheres in the patients with vertigo were 52.49±5.42 cm^3 in males, 50.11±4.02 cm^3 in females. The mean (±SD) of the left cerebellar hemispheres in the patients with vertigo were 53.11±3.70 cm^3 in males and 49.73±4.69 cm^3 in females. There was no significant quantitative evidence detected in terms of cerebellar asymmetry between sagittal plane estimates in the cases with vertigo in both genders (p>0.05). There were no statistically significant differences by genders between vertigo and control subjects (p>0.05). There was statistical significance only between right and left hemispheres in male control subjects (p=0.039)

CONCLUSION: There was no cerebellar asymmetry between control and vertigo cases by gender. The stereological evaluation of cerebellar asymmetry or atrophy in humans in correlation with gender is of importance both for clinicians and anatomists. The technique is simple, reliable, inexpensive and unbiased.

KEYWORDS: Cavalier principle, Stereology, Cerebellar asymmetry, Magnetic Resonance, Imaging, Vertigo

ÖZ

AMAÇ: Çalışmada sağ elini kullanan vertigolu ve sağlıklı olguların karşılaştırmalı olarak serebellum asimetrilerinin stereolojik metotla cinsiyete göre değerlendirilmesini amaçladık.

YÖNTEM ve GEREÇ: Çalışmada 14 erişkin kontrol ve 18 vertigolu hasta dahil edildi. Serebellar hemisfer hacimleri, MR görüntülerde, stereolojik olarak nokta sayım yöntemi kullanılarak saptandı.

BULGULAR: Vertigolu olgularda ortalama sağ hemisfer hacimleri (±SD), erkeklerde 52.49±5.42 cm3, kadınlarda 50.11±4.02 cm3 olarak bulundu. Vertigolu olgularda ortalama sol hemisfer hacimleri (±SD), erkeklerde 53.11±3.70 cm3, kadınlarda 49.73±4.69. Vertigolu olgularda her iki cinsiyette de sagital planda serebellar asimetriye ilişkin anlamlı kantitatif kanıt saptanmadı (p>0.05). Vertigolu ve kontrol olgular arasında cinsiyete göre anlamlı istatistiksel fark yoktu (p>0.05). Kontrol grubunda yalnızca sağ ve sol hemisferler arasında istatistiksel olarak anlamlı fark bulundu (p=0.039)

SONUÇ: Vertigolu ve kontrol olgular arasında cinsiyetler arasında serebellar asimetri saptanmadı. İnsanlarda cinsiyetle korele serebellar asimetri veya atrofinin değerlendirilmesi klinisyen ve anatomistlerin her ikisi için de önem taşır. Teknik basit, ucuz, güvenilir ve tarafsızdır.

ANAHTAR SÖZCÜKLER: Cavalieri prensibi, Stereoloji, Serebellar asimetri, Manyetik Rezonans Görüntüleme, Vertigo

Received : 10.11.2008
Accepted : 08.01.2009

Correspondence address:
H. Selim KARABEKİR
E-mail: hskarabekir@hotmail..com

INTRODUCTION

Vertigo is an illusion of movement, usually rotation, although patients occasionally describe a sensation of linear displacement or tilt. It occurs when an imbalance or disturbance in vestibular function occurs anywhere in the peripheral and central vestibular system and it is associated with several different disorders. The most common causes of vertigo are peripheral vestibular disorders, but central nervous system disorders must be excluded. Central vestibular lesions affecting the pons, medulla, or the cerebellum cause vertigo and the central causes of vertigo are cerebrovascular disorders, migraine, multiple sclerosis, epilepsy, craniocervical junction disorders, neoplastic, inherited ataxia, psychophysiological problems, global cerebral hypoperfusion and hypometabolism, neurodegenerative disorders, and posttraumatic and toxic conditions [21].

Asymmetry of neural activity between the left and right vestibular nuclei is the most important reason of true rotatory vertigo, whereas more nonspecific vertigo symptoms are caused by cerebellar dysfunction, vasodepressor syncope, postural hypotension, cardiac disrhythmia, peripheral neuropathy, anxiety, and hypoglycemia. Vertigo is always temporary and abates within a few days as central compensation occurs [10,34]. Signs and symptoms of dysfunction of neighboring structures can belong to the central brainstem and cerebellar structures in central causes of vertigo [9].

Several studies have focused on the determination of brain compartments and tried to find MRI-detectable discriminators of healthy and pathological aging in neurodegenerative diseases [8,14,19]. Asymmetric and volumetric changes in cerebellar anatomy have been an interesting subject for researchers [17,26]. MRI-based volume quantification is now being increasingly used to investigate neuroanatomical structures in neurological and psychiatric disorders, e.g. schizophrenia, Alzheimer's disease, and epilepsy [8,19,24]. MRI is useful in the quantitative evaluation of asymmetrical changes of cerebella because the superior contrast resolution facilitates separation of gray and white matter. Quantitative assessment of cerebellar asymmetry has mainly been performed by manual measurement, which requires considerable time and effort to determine the cerebella volume.

Some authors investigated volumetric analysis of different cerebellar regions as the anterior and posterior lobe, the vermis and the flocculonodular lobe. They found that total cerebellar volume loss was seen during the aging process but they included only male subjects and did not evaluate cerebellar asymmetry [3,4]. The cerebellum does not have a symmetrical morphology according to many authors. As an example, dextrals show more asymmetry than non-dextrals [30]. On the other hand some pathological disorders such as schizophrenia, epilepsy, cerebellar hypoplasia, hemimegalencephaly, dyslexia, autism, alcoholism, drug abuse, bipolar disorder, brain injuries or tumors can also cause asymmetrical changes in the cerebellar morphology [2,7,18,26,30,31]. Thus, a detailed knowledge on the asymmetrical structure of the cerebellum and changes in this morphology related with gender in the sagittal plane would be of importance for a reliable diagnoses and neurosurgical approach.

It is important to evaluate cerebellar asymmetry based on gender in both axial and sagittal cross-sectional images of MRI combined by stereological technique and it is also of crucial importance for both anatomists and neurologists [3,4,10,33]. Our aim was to enable the comparison of different pathologies in brain tissue defined by clinicians to the stable database in the present study in this way.

We therefore aimed to evaluate the cerebellar asymmetry of the patients with vertigo disease using a stereological technique depending on gender in the sagittal plane. The requirement for the application of the stereological method is an entire set of two-dimensional slices through the object, provided they are parallel, separated by a known distance, and begin randomly within the object, all criteria that are met by standard MR imaging technique [25,29]. There are no current data on the evaluation of cerebellar asymmetry in vertigo disease using stereological technique in the literature.

MATERIALS and METHODS

1. Clinical data

The subjects consisted of 14 (7 males, 7 females) healthy controls and 18 (8 males, 10 females) right-handed adult patients with vertigo, aged between 26-50 years. They were admitted to the Department of Neurology and Neurosurgery in Afyon Kocatepe University Faculty of Medicine with severe dizziness. All the patients underwent oto-neurological examination, auditory evoked potentials registration and MRI. Patients with cerebrovascular disease, multiple sclerosis, epilepsy, cerebellar or cerebellopontine angle tumors, spondylosis, depressive state, poor vision, orthostatic hypotension, whiplash injury, vestibular disorders such as neuritis, peripheral cochleovestibular syndromes etc. or low cerebrospinal fluid syndrome were excluded. Informed contents of all subjects in both the study and control groups were obtained. Diagnosis was made on the basis of history and physical, otolaryngological and neurological examination and confirmed by relevant investigations including laboratory, radiological and audiovestibular tests. We also excluded patients who had peripheral vertigo from the study.

2. Magnetic resonance image data

The MR images of all subjects were examined retrospectively. Standard T1-weighted axial and sagittal plane (5 mm) slices were obtained according to the opinion of radiology specialist, and were used to compute cerebellar hemisphere volumes in a 1.5-T MR machine (Philips Systems, the Netherlands). A spoiled pulse gradient recalled (SPGR) acquisition in the steady state was used. This is a three-dimensional volume gradient echo pulse sequence that is radiofrequency spoiled. A sagittal localizer was first acquired, and the volume of interest was then arranged to include the whole brain. The three-dimensional SPGR sequence was acquired over a period of 14 min. The MRI parameters were as follow; time of repetition (TR) of 35 ms and a time echo (TE) of 15 ms; the echo was 1/1 with 16 kHz. The flip angle was 350. Because image data were collected retrospectively, the data set contained an image matrix of 256x256 pixels x 124 slices for a FOV of 24x24x18.6 cm, respectively. Thus, image voxels are 0.09375x0.09375x1.5 cm.

3. Stereological analysis

Both whole and hemicerebellar volumes computed from each image were measured three times by three observers using a stereological method. All measurements were performed blinded to subject details and the results of any other measurements. An optimal plan was taken as the smallest diameter of anisotropic structures that can be measured in volumetric analysis of sagittal and axial cranial MRI sections. Original MR Images were exported as tif image files and further stereological analysis was done using these image sets with the aid of Image-J software. A uniform point-grid with a point-associated area of 0.625 cm^2 was randomly superimposed on each MR image using the “Grid” plug-in installed with Image-J. Points hitting the cerebella were manually counted for volume estimation. Volume estimation was accomplished by Cavalier’s principle as described previously [1,15,20] using the formula given below:

$$V = t \times [((SU) \times d)/SL]2 \times \sum P$$

where, t is the section thickness, SU is the scale unit (the real length of the scale marked on the MRIs), d is the distance between two points in the point grid, SL is the scale length (the actual measure of the scale on MRIs) and P is the number of points counted. All data were entered to a previously-prepared Microsoft Excel spreadsheet for automatic calculation of both the results of the above Formula and the statistical evaluation parameters including the nugget variance and the coefficient of error (CE).

In order to evaluate the hemispheric asymmetry between cerebellar hemispheres, the middle sections were identified by the clear visualization of the cerebral aqueduct. The point counts belonging to the middle section was divided by two and the results were added to the total point counts for each hemisphere separately, and thus, a volume value for each cerebellar hemisphere was estimated. The stereological point counting method has been demonstrated in Figure 1. Statistical analyses were

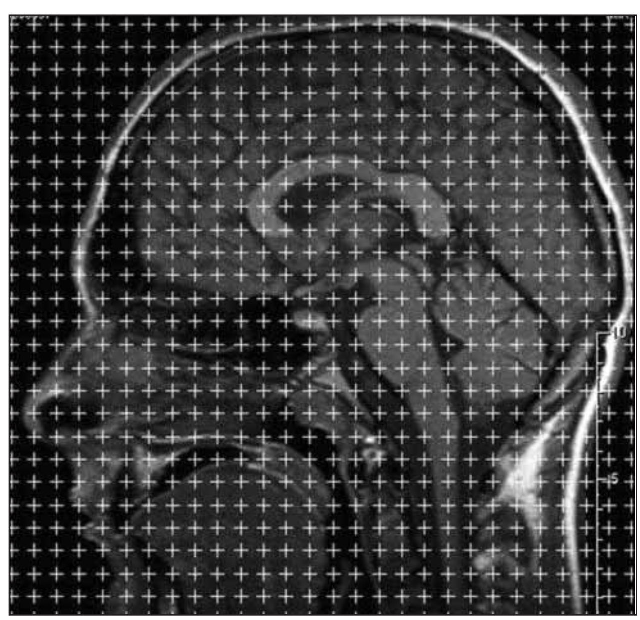

Figure 1. *The stereological point counting method.*

performed afterwards and the results were standardized to generate a normal database.

4. Statistical Analysis

Distributions of the variables were analyzed using the Shapiro-Wilk normality test. Homogeneity of the groups' variances was controlled by Levene's test. Parametric test assumptions were satisfied, and differences between the left and right cerebellum volume means of control and vertigo groups according to sex were analyzed by Three Factorial Repeated Measures Analysis of Variance. Results have been expressed as number of observations (n) and mean ± standard deviation (SD). A p value less than 0.05 was considered as statistically significant. All statistical analyses were performed with the SPSS software (Statistical Package for the Social Sciences, version 13.0, SSPS Inc, Chicago, IL, USA).

RESULTS

Mean values for hemispheres of cerebellar volume calculated according to the stereological point counting method are listed in Table 1. The mean (±SD) of right cerebellar hemispheres (RCH) in the control group were 46.50±4.84 cm^3 in males, 48.47±9.56 cm^3 in females in the sagittal plane. The mean (±SD) of the left cerebellar hemispheres (LCH) in the control group were 51.56±4.17 cm^3 in males, 52.33±5.52 cm^3 in females in the sagittal plane. The mean (±SD) of the RCH in the patients with vertigo were 52.49±5.42 cm^3 in males, 50.11±4.02 cm^3 in females in the sagittal plane. The mean (±SD) of the LCH in the patients with vertigo were 53.11±3.70 cm^3 in males, 49.73±4.69 cm^3 in females in the sagittal plane. There was no significant quantitative evidence detected in terms of cerebellar asymmetry between sagittal plane estimates in the cases with vertigo ($p>0.05$). There were also no statistically significant differences by gender in both vertigo and control subjects ($p>0.05$). There was only statistical significance between the right and left hemispheres in male control subjects ($p=0.039$).

DISCUSSION

Dizziness and vertigo rank among the most common complaints in medicine, affecting approximately 20% to 30% of patients in the general population [12]. Vertigo is a subtype of dizziness, defined as an illusory sensation of movement, and may occur in peripheral and/or central vestibular disorders. The vestibular system consists of the peripheral and central parts. The semicircular canals, the otoliths, and the vestibular nerve are peripheral parts of the vestibular system. The vestibular nuclear complex, vestibulocerebellum, brainstem, spinal cord, and vestibular cortex are central parts of the vestibular system [6].

Neuroanatomical, neuroimaging and behavioral reports of cerebella in cognitive and language functions increasingly define the cerebellum as the site of morphological changes occurring in neuropsychiatric disorders [10,33,34].

MRI analysis allows quantitative analysis of the cerebella and morphological evaluation of the brain in vivo [1]. Many authors have evaluated volume changes of the cerebellum according to age and gender in healthy subjects. They claimed that female subjects had significantly smaller cerebellar volumes compared with males of similar age [11,32]. Gocmen-Mas et al found that the reduction of the cerebellar volume was not statistically significant and there was no cerebellar asymmetry according to age and gender in healthy subjects [17]. The relationship of the gender of the subject and cerebellar size is not clear and there are conflicting reports in the literature [1,16,28]. Although the literature has many studies about volume changes of cerebellum according to age and

Table I: Mean values of control and study groups cerebellum hemispheres by gender

Cerebellum	Control Mean ± SD		Vertigo Mean ± SD	
	Left side	Right side	Left side	Right side
Male	n=7 51.56±4.17*	n=7 46.50±4.84	n=8 53.11±3.70	n=8 52.49±5.42
Female	n=7 52.33±5.52	n=7 48.47±9.56	n=10 49.73±4.69	n=10 50.11±4.02

*$p<0.05$

gender, there are no data about cerebellar asymmetry related to gender in adult cases of vertigo. Some pathological conditions such as cerebellar hypertrophy, atrophy, agenesis and architectural alterations could also cause asymmetrical changes between the right and left hemispheres [17,30]. Asymmetric alterations of cerebella can lead to many different pathologies. Hemicerebellar asymmetric enlargement has been reported in intractable epilepsy [30]. Unilateral atrophy of a cerebellar hemisphere occurring as a sequel of ischemic or destructive injury has also been reported. The age-related atrophy of the cerebellum has been investigated by MRI using stereological methods in the elderly [27,32]. We aimed to evaluate whether cerebellar hemispheric asymmetry was present or not in cases of vertigo. The mean values for hemispheres of cerebellar volume were therefore calculated using the stereological point counting method.

In morphometric studies, the volume of an organ or its components and the volume of the variable component in a structure are frequently investigated via different measurement techniques [5,20,22,23]. In the present study, we used the stereological method for the estimation of cerebellar asymmetry according to gender in the adult cases with vertigo since a previous study showed the method [1,17]. The Cavalier principle of stereological approaches by point counting consists of overlying each selected section with a regular grid of test points, which is randomly positioned [1,17]. The Cavalier theorem of systematic sampling in combination with point counting is considered a reliable, simple, inexpensive and efficient method for estimating volumes in MRI [13]. However, the safest method is undoubtedly to reduce section thickness as much as technically possible while maintaining an acceptable image quality.

Ekinci et al used MRI obtained from 24 normal volunteers ranging from 20-25 years of age and measured total brain, cerebrum and cerebellum volume. They found that the mean (+/-SD) cerebellum volumes were 117.75±10.7, 111.83±8.0 cm^3 in males and females, respectively [15]. They also claimed that cerebellar volumes were slightly larger in females but smaller in males than those reported by Escalona et al as 104±10 cm^3 in females and 122±16 cm^3 in males and by Rhyu et al, as 115.4±11.29 cm3 in females and 126±10.3 cm^3 in males, smaller than those reported by Luft et al, with a mean value of 134.3±14.9 cm^3 in both sexes and similar to Dupuis [15,16,22,23,28]. It is not clear whether the discrepancy is due to the racial difference or the variation resulting from different scanning protocols and measuring methods used. Ekinci's results revealed that the volumetric composition of the cerebellum does not show sexual dimorphism [15]. We found that the right hemisphere of the cerebellum was smaller than the left in control male subjects. There were no asymmetric differences in vertigo for both genders. Asymmetric involvement of the vestibular system has been reported to lead to vertigo [21]. In contrast, we found no correlation between cerebellar asymmetry and vertigo. According to our clinical observations and the findings of the present study, we believe that cerebellar asymmetry is not a basic factor for vertigo etiology.

The present evaluation of cerebella hemisphere volumes can be done on any complete set of MRI where plane scan distance and magnification factor is known, which already are present on MRI. The stereological evaluation of cerebella asymmetry or atrophy in humans correlating with gender is of importance for both clinicians and anatomists. The technique is simple, reliable, unbiased and inexpensive.

The data of the present study can large enough to be meaningful for anatomists and clinicians. Further studies are required with larger samples in order to support these data.

REFERENCES

1. Acer N, Sahin B, Usanmaz M, Tatolu H, Irmak Z: Comparison of point counting and planimetry methods for the assessment of cerebellar volume in human using magnetic resonance imaging: A stereological study. Surg Radiol Anat. 30:335-339, 2008
2. Ammerman JM, Lonser RR, Oldfield EH: Posterior subtemporal transtentorial approach to intraparenchymal lesions of the anteromedial region of the superior cerebellum. Neurol Neurochir Pol. 41:436-444, 2007
3. Andersen BB, Gundersen HJ, Pakkenberg B: Aging of the human cerebellum: a stereological study. J Comp Neurol 17,466:356-365,2003
4. Andersen BB, Pakkenberg B: Stereological quantitation in cerebella from people with schizophrenia. Br J Psychiatry 82:354-361, 2003
5. Andreasen NC, Rajarethinam R, Cizadlo T, Arndt S, Swayze VW 2nd, Flashman LA, O'Leary DS, Ehrhardt JC, Yuh WT: Automatic atlas-based volume estimation of human brain regions from MR images. J Comput Assist Tomogr. 20: 98-106, 1996

6. Baloh RW. Vertigo. Lancet. 352:1841-1846, 1998
7. Benegal V, Antony G, Venkatasubramanian G, Jayakumar PN: Gray matter volume abnormalities and externalizing symptoms in subjects at high risk for alcohol dependence. Addict Biol 12:122-132, 2007
8. Bernasconi F, Andermann DL, Bernasconi AA: Entorhinal cortex MRI assessment in temporal, extratemporal, and idiopathic generalized epilepsy, Epilepsia 44:1070–1074, 2003
9. Brazis Paul W, Masdeu Joseph C, Biller Jose: Localization in clinical neurology. Ch 10.Ed: Jose Biller, Paul Brazis: The localization of lesions affecting cranial nerve VIII. 2nd ed. Little, Brown and Company, Boston: 1990:229-233
10 Bruzzone MG, Grisoli M, De Simone T, Regna-Gladin C: Neuroradiological features of vertigo. Neurol Sci 24:20-23, 2004
11. Carne RP, Vogrin S, Litewka L, Cook MJ: Cerebral cortex: An MRI-based study of volume and variance with age and sex. J Clin Neurosci 13:60-72, 2006
12. Chu YT, Cheng L. Vertigo and dizziness [Chinese]. Acta Neurol Taiwan. 16:50-60, 2007
13. Cruz-Orive LM: Distribution-free estimation of sphere size distributions from slabs showing overprojection and truncation, with a review of previous methods, J. Microsc. 131: 265–290, 1983
14. Edland SD, Xu Y, Plevak M, O'Brien P, Tangalos EG, Petersen RC, Jack CR: Total intracranial volume: Normative values and lack of association with Alzheimer's disease. Neurology 59: 272–274,2002
15. Ekinci, N, Acer, N, Akkaya, A, Sankur, S, Kabadayi, T, Sahin, B: Volumetric evaluation of the relations among the cerebrum, cerebellum and brain stem in young subjects: A combination of stereology and magnetic resonance imaging. Surg Radiol Anat 30:489-494, 2008
16. Escalona PR, McDonald WM, Doraiswamy PM, Boyko OB, Husain MM, Figiel GS, Laskowitz D, Ellinwood EH Jr, Krishnan KR: Invivo stereological assessment of human cerebellar volume: Effects of gender and age. Am J Neuroradiol. 12:927-929, 1991
17. Gocmen-Mas N, Pelin C, Canan S, Yazici AC, Zagyapan R, Senan S, Karabekir HS, Sahin B: Stereological evaluation of volumetric asymmetry in healthy human cerebellum. Surg Radiol Anat. Oct 22, 2008 [Epub ahead of print]
17. Guerrini L, Lolli F, Ginestroni A, Belli G, Della Nave R, Tessa C, Foresti S, Cosottini M, Piacentini S, Salvi F, Plasmati R, De Grandis D, Siciliano G, Filla A, Mascalchi M: Brainstem neurodegeneration correlates with clinical dysfunction in SCA1 but not in SCA2. A quantitative volumetric, diffusion and proton spectroscopy MR study. Brain. 127:1785-1795, 2004
19. Ho NC, Andreasen P, Nopoulos S, Arndt V, Flaum M: Progressive structural brain abnormalities and their relationship to clinical outcome: A longitudinal magnetic resonance imaging study early in schizophrenia, Arch. Gen. Psychiatry 60: 585–594, 2003
20. Kalkan E, Cander B, Gul M, Karabagli H, Girisgin, S, Sahin B: A new stereological method for the assessment (prediction) of prognosis in patients with epidural hematoma: the hematoma to total brain volume fraction. The Tohoku Journal of Experimental Medicine 211:235-242,2007
21. Karatas M. Central Vertigo and Dizziness Epidemiology, Differential Diagnosis, and Common Causes. The Neurologist 14:355-364, 2008
22. Luft AR, Skalej M, Welte D, Kolb R, Bürk K, Schulz JB, Klockgether T, Voigt K: A new semiautomated, three-dimensional technique allowing precise quantification of total and regional cerebellar volume using MRI. Magn. Reson. Med. 40:143-151, 1998
23. Luft AR, Skalej M, Welte D, Voigt K, Klockgether T: Age and sex do not affect cerebellar volume in humans. Am J Neuroradiol 18:593-596, 1997
24. Murphy TL, Jernigan TL, Fennema-Notestine C: Left hippocampal volume loss in Alzheimer's disease is reflected in performance on odor identification: A structural MRI study, J. Int. Neuropsychol. Soc. 9: 459-471, 2003
25. Roberts, N., Puddephat, M.J., McNulty, V: The benefit of stereology for quantitative radiology. Br J Radiol. 73: 679–697, 2000
26. Robins JB, Mason GC, Watters J, Martinez D: Case Report: Cerebellar Hemi-Hypoplasia. Prenat. Diagn. 18: 173–177, 1998
27. Rollins NK, Wen TS, Dominguez R: Crossed cerebellar atrophy in children: a neurologic sequela of extreme prematurity. Pediatr Radiol. 25:20-25, 1995
28. Rhyu IJ, Cho TH, Lee NJ, Uhm CS, Kim H, Suh YS: Magnetic Resonance Image-based cerebellar volumetry in healthy Korean adults. Neurosci Lett 270:149-152, 1999
29. Sahin B, Ergur H: Assessment of the optimum section thickness for the estimation of liver volume using magnetic resonance images: a stereological gold standard study. Eur J Radiol 57: 96 –101, 2006
30. Sato N, Yagishita A, Oba H, Miki Y, Nakata Y, Yamashita F, Nemoto K, Sugai K, Sasaki M: Hemimegalencephaly: A Study of Abnormalities occurring outside the involved hemisphere. AJNR Am J Neuroradiol. 28:678-82, 2007
31. Sim ME, Lyoo IK, Streeter CC, Covell J, Sarid-Segal O, Ciraulo DA, Kim MJ, Kaufman MJ, Yurgelun-Todd DA, Renshaw PF: Cerebellar Gray Matter Volume Correlates with Duration of Cocaine Use in Cocaine-Dependent Subjects. Neuropsychopharmacology. 32: 2229-2237, 2007
32. Tang Y, Whitman GT, Lopez I, Baloh RV: Brain changes on longitudinal magnetic resonance imaging in normal older people. J. Neuroimaging. 11: 393-400, 2001
33. Traccis S, Zoroddu GF, Zecca MT, Cau T, Solinas MA, Masuri R: Evaluating patients with vertigo: Bedside examination. Neurol Sci. 24:16-19, 2004
34. Weinberger DR, Kleinman JE, Luchins DJ, Bigelow LB, Wyatt RJ: Cerebellar pathology in schizophrenia: A controlled post-mortem study. American Journal of Psychiatry 137: 359-361, 1980