

# Morphometric assessment of brain stem and cerebellar vermis with midsagittal MRI: the gender differences and effects of age

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## ABSTRACT

Since the development of MRI techniques, many neuroanatomical studies of normal brain growth and atrophy have been reported. Investigations of aging effects on the brain stem and cerebellum are important, not only to understand normal aging process, but also for comparative study of the pathophysiology of degenerative brain disorders. Sex differences in gross cerebellar neuroanatomy have been observed in several studies.

In this study, our purpose was to assess the sex differences and the age-related morphological changes of the brain stem and the cerebellar vermis on midsagittal MRIs. According to radiologists' reports, midsagittal MRIs of 120 normal individuals were evaluated in this study.

There were 50 males and 70 females. By tracing the outline contour of the cerebellar vermis and the brain stem, both brain regions were drawn in a transparent paper, scaled for the real size and saved in the computer. Calculation of the areas of both regions was performed by utilizing NETCAD for Windows program, and the collected data were statistically analysed by using SPSS software. Students' t test was applied for gender comparisons. To determine the associations between age and both areas, Pearson correlation coefficients were calculated.

Significant sex difference was found in the brain stem area favouring males ( $p < 0.05$ ) whereas no significant difference was recorded in the cerebellar vermis area. Non-significant age-associated decrease in brain stem and cerebellar vermis areas were found. The age-related changes in the brain stem and cerebellar vermis remains speculative, though some authors suggest a selective vulnerability of specific posterior fossa structures to the effects of aging and sex.

**Key words:** brain stem, cerebellar vermis, magnetic resonance imaging, measurement

## Introduction

There are many studies in the literature where anatomical structures in brain are measured quantitatively in terms of volume, area, width and length [1]. Investigations of aging effects on the brain stem and cerebellum are important, not only to understand normal aging, but also for comparative study of the pathophysiology of degenerative brain disorders. Since the development of MRI, many neuroanatomical studies of normal brain growth and atrophy have been reported [2-5]. Sex differences in cerebral and brain stem shrinkage with aging might result from intrinsic or extrinsic factors such as hormones [6] and hypertension [7]. Interactions with environmental factors, such as acquired disease, exposure to toxins, and trauma, however, can lead to developmental aberrations and can also result in loss of brain tissue [8]. Several studies have focused on structural changes in the midbrain that contains nuclei which are important for voluntary or involuntary movements and also nerve fibres conducting sensory and motor information [9, 10]. Sex differences in gross cerebellar neuroanatomy have been reported in several studies [11-14]. Moderate

shrinkage of the cerebellar hemispheres and the vermis has been noted in post-mortem studies [15, 16] and in some in vivo investigations [11-13, 17-19]. However, other volumetric studies based on MR imaging yielded no effects of age on the size of the cerebellum [20, 21] or showed non-significant trends [14]. Hayakawa et al. [22] found no significant difference in the midsagittal area of either the pons or cerebellar vermis between the 21-40 and 51-60 age groups. MRI studies have correlated midbrain morphology with symptomatology in several disorders, including Parkinson disease [23] and Wilson disease [24], suggesting that morphometric data may indirectly reflect underlying neurochemical or pathologic process. Coffman et al. [25] found no differences between schizophrenics and controls, whereas Nasrallah et al. [26] reported that schizophrenics have larger cerebellar structures than controls. However, a number of MRI studies could not confirm the vermal atrophy in schizophrenic patients [27-30]. To further characterize the gender differences and effects of age on posterior fossa structures, we examined midsagittal high field (1.5T) MR images and calculated the cross



Figure 1 | Midline sagittal MRI scan shows the brain stem and cerebellar vermis.

sectional areas of the brain stem and cerebellar vermis in 120 normal individuals.

## Material and Methods

The midsagittal MRIs of 120 individuals were obtained from Radiology Department in Meram Faculty of Medicine, Selçuk University. According to psychiatrists and neuroradiologists' reports, none of the individuals was complaining of any symptoms of pathology in the brain, and only subjects with normal routine scans were included. There were 50 males and 70 females. The age range was 13-77 years. Every sex group was distributed in a sequence manner into three age subgroups; the age range of the first subgroup was 13-25 years (10 males, 10 females); the second was 26-50 years (28 males, 40 females); the third was 51-77 years (12 males, 20 females). The midsagittal MRIs had been performed on 1.5 Tesla superconducting unit (Picker Internationals, Highlands Heights, OH Cleveland, USA), with spin-echo sequences. The images were T1 weighted sagittal scout images (TR: 600-300, TE: 16). Slice thickness was 5 mm, gap 2 mm. Field of view 250 mm and display matrix 192x256. The midsagittal section was identified with such landmarks as the corpus callosum, pituitary gland, pineal body and the peaked roof of the fourth ventricle (Fig.1). With a careful tracing, the midsagittal outline contours of the brain stem and cerebellar vermis of the studied subjects were drawn in a transparent paper by the same researcher. Depending on the millimetric scale gradation recorded on the film margins of the scanned subject, the measurement ratio between the image size and the actual (proper) size was recorded. Therefore, the magnification factor for each one of the scanned subjects was identified to obtain a real estimation of the measurements. The actual dimensions of the scanned images were recorded on the margins of the drawn images. All brain stem and cerebellar vermis drawings were serially numbered, scanned and saved

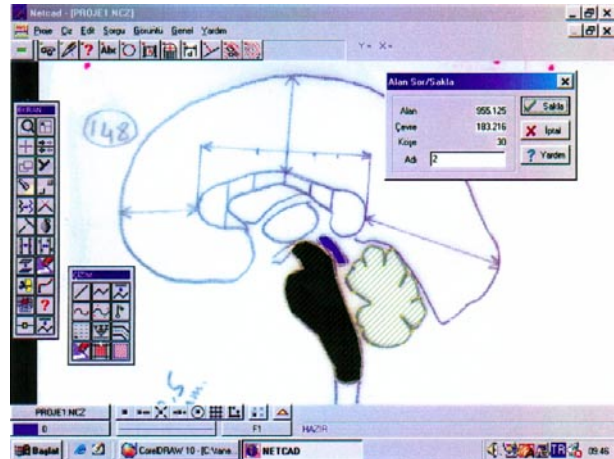


Figure 2 | Diagram of the outline contours of the midsagittal sections of the brain stem and cerebellar vermis showing the calculations of the areas.

in the computer. The midsagittal areas of the brain stem and the cerebellar vermis were quantified. Both measurements were calculated to the nearest 0.01 mm. For quantifying the above mentioned measurements, NETCAD for Windows program was utilized and the collected data for every subject were recorded in an independent file (Fig. 2). Data were summarized as means  $\pm$  standard deviations. The SPSS for Windows 10.0 program was used for statistical analysis. To determine the sex and age differences, Student's t test was used. To determine the degree of associations between the studied measurements, Pearson correlation coefficients were calculated.

## Results

In Table 1, gender comparative results in the first and second age subgroups show that non-significant differences were found between males and females in brain stem and cerebellar vermis areas ( $p>0.05$ ), but in the third age subgroup, significant difference was found between males and females in brain stem area ( $p=0.05$ ). In general, with a combined data in every sex group, the gender comparative results showed that midsagittal brain stem area was significantly greater in males than in females ( $p<0.05$ ) whereas in the cerebellar vermis area, significant difference was not seen ( $p>0.05$ ) (Table 2).

Correlation coefficients between age and both of midsagittal brain stem and cerebellar vermis areas in male and female subgroups are shown in tables 3 and 4, respectively. Significant associations were not seen

Table 1 | Midsagittal brain stem and cerebellar vermis areas – Subgroup (SG) gender comparative results (Mean $\pm$ SD, t and p values)

SG	REGION	MALES		FEMALES	
		Mean $\pm$ SD (mm <sup>2</sup> )	Mean $\pm$ SD (mm <sup>2</sup> )	t	P
(1)	Brain stem	1151.67 $\pm$ 178.22	1111.92 $\pm$ 130.86	0.569	0.577
	Cerebellar vermis	1320.57 $\pm$ 318.73	1289.19 $\pm$ 226.75	0.254	0.803
(2)	Brain stem	1197.67 $\pm$ 123.15	1152.28 $\pm$ 98.01	1.690	0.096
	Cerebellar vermis	1274.23 $\pm$ 226.91	1280.53 $\pm$ 206.17	0.119	0.906
(3)	Brain stem	1227.42 $\pm$ 43.02	1140.97 $\pm$ 143.34	2.023	0.052*
	Cerebellar vermis	1190.18 $\pm$ 155.00	1194.72 $\pm$ 278.04	0.052	0.959

\* p=0.05

**Table 2 |** Midsagittal brain stem and cerebellar vermis areas – General gender comparative results (Mean±SD, t and p values)

REGION	MALES Mean ± SD (mm <sup>2</sup> )	FEMALES Mean ± SD (mm <sup>2</sup> )	t	p
Brain stem	1195.61 ± 123.49	1143.28 ± 116.24	2.369	0.019*
Cerebellar vermis	1263.33 ± 233.39	1257.25 ± 231.55	0.141	0.686

\* p<0.05

**Table 3 |** Correlation coefficients (r) between age, midsagittal brain stem and cerebellar vermis areas in male subgroups.

Subgroup 1		Cerebellar vermis	Brain stem
	Age	0.005	0.22
Brain stem	0.544	-	
Subgroup 2		Cerebellar vermis	Brain stem
	Age	-0.015	-0.086
Brain stem	0.767*	-	
Subgroup 3		Cerebellar vermis	Brain stem
	Age	-0.032	-0.388
Brain stem	0.159	-	

\* p<0.01

**Table 4 |** Correlation coefficients (r) between age, midsagittal brain stem and cerebellar vermis areas in female subgroups.

Subgroup 1		Cerebellar vermis	Brain stem
	Age	-0.329	-0.150
Brain stem	0.715*	-	
Subgroup 2		Cerebellar vermis	Brain stem
	Age	0.154	0.125
Brain stem	0.25	-	
Subgroup 3		Cerebellar vermis	Brain stem
	Age	-0.233	-0.210
Brain stem	0.825**	-	

\* p<0.05, \*\* p<0.01

between age and both studied areas in all male and female subgroups (p>0.05). In male subgroup 2 (Table 3), significant intercorrelation was found between cerebellar vermis and brain stem areas (r=0.767, p<0.01). Significant associations were found (Table 4) between brain stem and cerebellar vermis areas in female subgroup 1 and 3 (r=0.715, p<0.05), (r=0.825, p<0.01), respectively.

## Discussion

The results of this study showed larger brain stem in males, this may explain the correlation between supratentorial larger brain size in males and the brain stem structures, or might mean that there is a correlation in the common physiological process between supratentorial brain and brain stem structures either in their growth or in their atrophy. Some researchers speculated that sexual dimorphism in cerebellar size can be attributed to the effects of sex hormones [14, 20]. Escalona et al. [11] observed that women have a significantly smaller cerebellar volume than men, but indicated no aging effect on cerebellar volume in either sex. However, our findings showed that there was no significant sex difference in the cerebellar vermis. This result is in agreement with that obtained by Hayakawa et al. [22]. Computed tomography studies of the posterior fossa

have generally found no relationship between posterior fossa structures and aging [12]. Koller et al. [31] reported higher subjective ratings of vermian atrophy by age. The trend towards atrophy is probably related to loss of Purkinje cells in the vermis [32]. Others were reported a significant-associated shrinkage of the cerebellar vermis in men after the age of 70 years [33]. Shah et al. [12] reported that the dimension of the posterior cerebellar vermis does not significantly change with age. Although, our results showed non-significant-associated decrease in the cerebellar vermis with age, a moderate shrinkage was found in men and women in this study. This result is in agreement with a previous studies [11-13, 15-17, 19]. Luft et al. [14] suggested that women might show steeper age-related decline in the area of the vermis than do their male counterparts. A few groups have reported on aging of the brain stem. Doraiswamy et al. [9] reported that the volume of the midbrain decline with age in both sexes, but found no differences between men and women. Significant decline in the cross-sectional area of the midbrain was reported by Shah et al. [12], Oguro et al. [33] and Sohmiya et al. [34]. Raininko et al. [35] found minimal reduction in the midsagittal diameter of the midbrain and in the volume of the pons after the age of 50 years, but no sex differences in linear measurements. Shah et al. [12] stated that the age-related decline in midbrain size could be accounted for in part by neuronal death or degeneration with nuclei and/or tracts of the midbrain. Mc Geer et al. [36] have reported a decrease in the number of neurons in the substantia nigra between the age of 20 and 80. Chida et al. [37] studied pontine atrophy using CT and an autopsy series, and reported no correlation with age and sex. Non-significant age-related changes in the mid-sagittal area of pons was reported by Oguro et al. [33], similarly, of pons and medulla oblongata was reported by Shah et al. [12]. With the exception of the significant age-associated shrinkage of the midbrain [12, 33, 34], the determination of non-significant association between age and midsagittal brain stem area in this study is in accordance with those obtained by Shah et al. [12], Oguro et al. [33] and Chida et al. [37].

Data on age-related changes of the brain stem and cerebellar vermis in normal subjects will facilitate further investigation of the relation between brain stem and cerebellar vermis changes and the neuromotor decline with normal aging. This normative data can also be used to compare the findings in patients with neurologic disorders such as Parkinson disease, Alzheimer disease and schizophrenia. A longitudinal study may support the findings of this cross-sectional study on morphometrical sex differences and age-related changes. However, discrepancies in the results concerning the age-related changes in the brain stem and cerebellar vermis remains speculative, though some authors suggest a selective vulnerability of specific posterior fossa structures to the effects of aging and sex.

Further studies on the assessments of sex differences and age-related changes in the brain stem parts i.e, midbrain, pons and medulla oblongata and their correlations with midsagittal cerebral and callosal areas were recently planned by us for collecting data on brain growth and atrophy.

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