

ORIGINAL RESEARCH

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Quantitative analysis of normal cerebellar volume and sagittal pons dimensions on MRI in pediatric population

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Abstract

To determine the normal reference values for cerebellar volume and sagittal pons dimensions in pediatric population with routine magnetic resonance imaging (MRI) and compare relationships with gender and age. **Material and Methods:** This retrospective study evaluated 120 cases (61 male, 59 female) with normal brain MRI (age range: 0-18 years). The cases were divided into four subgroups based on age as 0-2 years (infants; n=21), 3-6 years (young children; n=35), 7-12 years (children; n=35) and 13-18 years (adolescents; n=29). Demographic data like sex and age were recorded. Cerebellar volumes were calculated with semi-automatic volumetric software. Pons CC and AP dimensions were measured manually. Cerebellar volumes and pons dimensions comparisons were made for gender and age groups. Statistical analysis used the Mann-Whitney U test, Pearson's correlation analysis and Tamhane test. The median cerebellar volumes, pons CC and pons AP dimensions were 103.3 cm³, 20.9 mm, 13.3 mm for infants; 134.4 cm³, 24.6 mm, 15.3 mm for young children; 148.8 cm³, 25.5 mm, 15.6 mm for children; 153 cm³, 26.2 mm, 16 mm for adolescents, respectively. There was no significant difference identified for cerebellar volumes, pons CC and pons AP dimensions between the genders in all age groups. There was a positive significant correlation between age and cerebellar volumes, pons CC and pons AP dimensions. As age group increased, there were significant increases in normal cerebellar volume, pons CC and AP dimensions. Quantitative reference values for normal cerebellar volume, pons CC and AP dimensions were revealed for pediatric population using MRI. These results could be promising for clinical practice in pediatric neurology and/or neuroradiology.

Keywords: Adolescent, cerebellar volume, children, magnetic resonance imaging, pediatric, pons

Introduction

The cerebellum, found in the posterior cranial fossa, is the second largest volume in the encephalon and the largest volume in the rhombencephalon [1]. It comprises two lateral lobes and the vermis linking them in the center. Though it comprises nearly 10 percent of the central nervous system weight, the number of neurons is more than half of all neurons. It has many functional roles such as motor coordination, muscle tonus, sensitivity, ensuring accurate timing, attention and language skills, fear and satisfaction [2,3].

The brain stem is the most caudal section of the brain has structural continuity with the spinal cord. The midbrain (mesencephalon) comprises the pons (part of the metencephalon) and the medulla oblongata (myelencephalon) [4]. Through the cranial nerves, they ensure motor and sensory innervation of the face and neck. They regulate the heart, respiratory functions, consciousness, sleep cycle and the central nervous system.

Magnetic resonance imaging (MRI), allowing morphometric assessment of the brain and sections, is a radiological method providing multiplanar two-dimensional images of three-dimensional structures in reality. Due to high contrast resolution power for soft tissue, MRI has very high sensitivity to reveal intracranial anatomic structures and pathologic changes. A very important element is that it does not involve harmful ionizing radiation. This makes it popular for use in the pediatric era.

Many diseases can change the morphometric structure of the cerebellum and pons. Among these are neuro-psychiatric, neurologic, genetic-developmental, vascular and metabolic diseases, nutrition, infection and trauma. Quantitative MRI has significantly advanced our understanding of brain development during childhood and adolescence. Assessment of size changes by visual inspection is subjective. As a result, knowing some normal quantitative values may contribute to diagnosis and treatment. With this aim, in the last twenty-five years brain MRI of the adult and pediatric populations have been obtained and analyzed in terms of diagnosis, gender, genetics and/or psychological variables like IQ [5-7]. Cerebellar volume changes, especially,

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have been compared in pathologic situations such as Parkinson's syndrome, epilepsy, neurometabolic diseases, sleep apnea, brain atrophy, neurodevelopmental disorders such as attention deficit/hyperactivity disorder, autism, and schizophrenia [8-12]. However, it is necessary to collect the plentiful, but scattered, information in the literature related to the cerebellum and pons, which have a close relationship, in a single study and to update some aspects of this information. As a result, we decided to re-determine and review the normal reference values for cerebellar volume and sagittal pons dimensions (craniocaudal [CC] and anteroposterior [AP]) using MRI for the pediatric population. At the same time, we aimed to compare our results with literature information.

Material and Methods

Subjects

This study included 120 cases aged from 0-18 years with normal brain MRI taken from January 2016 to December 2018 for a variety of reasons. The study was conducted with ethics approval from the Ethics Committee. "Informed consent" was not obtained from parents as the study was retrospective. Cases included in the study did not provide personal information and were presented anonymously. Cases were divided into groups as 0-2 years (infants), 3-6 years (young children), 7-12 years (children) and 13-18 years (adolescents). Comparisons were made between girl-boy gender and age groups in terms of cerebellar volume, pons CC and AP dimensions. Data were retrospectively obtained from images recorded in the radiology archive of our hospital. Pediatric cases with normal reports for non-enhanced brain MRI and good MRI quality were included in the study. Elements not related to brain parenchyma like sinusitis, mastoiditis and adenoid hypertrophy were ignored and accepted as normal. These brain MRI were re-evaluated by a radiologist with more than 10 years-experience of pediatric brain MRI. Cerebellar volume and pons dimension measurements were performed by the same radiologist. Cases with pathologic MRI findings like tumor, hemorrhage, infarcts, atrophy and hydrocephalus who were understood to have been monitored and treated in the hospital system were excluded. Individuals with cardiovascular, neurologic, metabolic and psychiatric disease or epilepsy were not included in the study.

MRI protocol

All studies were performed using a 1.5 T system (Achieva; Philips Medical Systems, Best, the Netherlands) using T1-weighted (T1W) sagittal spin-echo [repetition time (TR), 500 msec; echo time (TE), 15 msec], T2-weighted transverse fast spin-echo (TR, 4,800 msec; TE, 100 msec), fluid attenuated inversion recovery (FLAIR) coronal (TR, 8,000 msec; TE, 110 msec; T1, 2,400 msec) sequences with head coil. Contrast material was not used. These images were used for volumetric and morphometric measurements. The positioning at our institute is done parallel to the inferior border of the corpus callosum on the axial plane and perpendicular to the hippocampus on the craniocaudal plane.

Image analysis

For cerebellar volume calculations, T1 axial images with 5 mm slice thickness were used. Estimated cerebellar volume measurements were calculated using 5-8 slices of the axial MR images. The measurement of cerebellar volume took approximately 3-4 minutes for each patient. The cerebellum was drawn based on joining contour points so as not to include the fourth ventricle. Volume measurements were obtained on an MPR View 3D work

station semi-automatically based on the contour stack principle. In our study, cerebellar volume calculations were performed planimetrically according to the Cavalieri principle. Total volume was calculated to include right and left lobe and vermis (Figure 1).

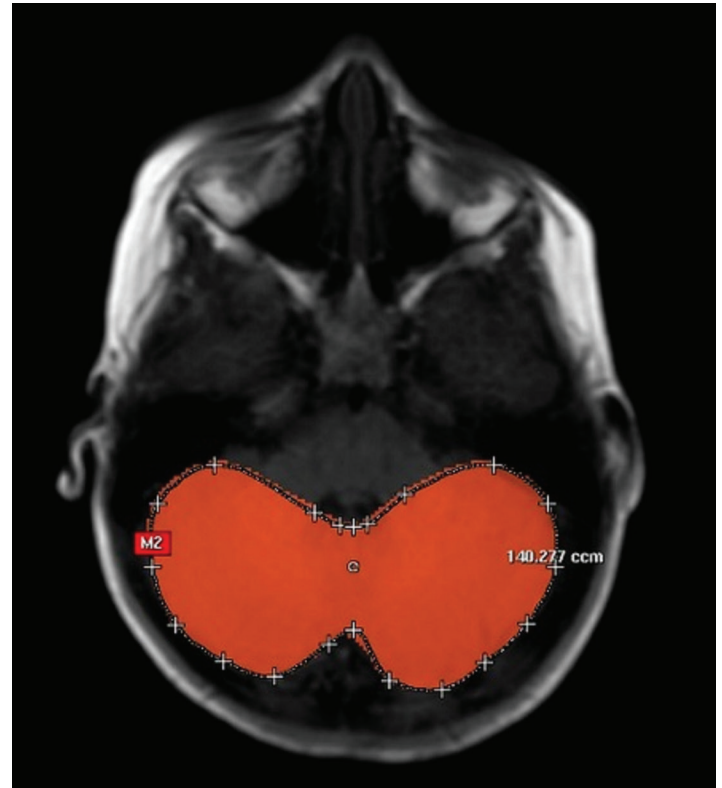


Figure 1. Example showing cerebellar volume measurement on MRI using axial T1 sequence. The boundaries of the cerebellum are manually drawn on a single slice. The fourth ventricle is not included. Volume (red area) is automatically calculated by software. This process is repeated for all slices and total volume is determined

T1 sagittal images were used for pons dimension measurements. The pons, with two main components of the basis pontis (basal/ventral part) and the pontine tegmentum (dorsal part) had a bulbous shape on MRI. The pons is the middle of the three parts of the brainstem, sitting above the medulla and below the midbrain. It acts as a relay between the cerebellum and cerebral hemispheres. The oval-shaped pons was measured manually in millimeters using a straight line from the upper and lowermost edges for the CC dimension and a straight line between the most anterior and posterior edges for the AP dimension (from the surface to the floor of the fourth ventricle at the midpoint and perpendicular to its long axis) (Figure 2).

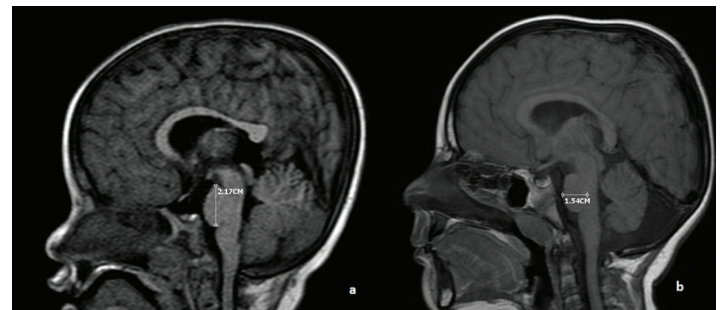


Figure 2. On MRI, sagittal T1 sequence shows the pons measurements. Measurement of pons CC dimension in a 5-year old male (a) and pons AP dimension in a 6-year old female (b) are shown.

Statistical Method

SPSS 22.0 was used for statistical analysis. All data were managed, processed, and compiled in Microsoft Office Excel. The compliance of the cerebellar volume and pons dimensions data with normal distribution was assessed with the Kolmogorov-Smirnov test and Kruskal Wallis test. Comparisons between gender and age groups used the Mann-Whitney U test and Tamhane test due to non-normal distribution. Additionally, the correlation between age with cerebellar volume and pons dimension data was assessed with Pearson's correlation analysis. Quantitative variables are shown as median range (maximum-minimum) in the tables. Variables were investigated at the 95% confidence interval with p values below 0.05 accepted as significant.

Results

One hundred and twenty cases with the median age of 7 (0-18) years were included in the study. Sixty-one of them were male and 59 of them were female. The infants group included 21 subjects (median age: 1 [0-2] years); the young children group included 35 subjects (median age: 5 [3-6] years); the children group included 35 subjects (median age: 8 [7-12] years) and the adolescents group included 29 subjects (median age: 17 [13-18] years).

Descriptive statistics of the demographic data including cerebellar volumes, pons CC and pons AP dimensions belonging to all participants and also age groups are given in Table 1.

Table 1. Descriptive statistics of the demographic data belonging to all participants and also age groups

n=120	Cerebellar volume (cm ³)			Pons CC dimension (mm)			Pons AP dimension (mm)		
	Min.	Max.	Median	Min.	Max.	Median	Min.	Max.	Median
All subjects	58	178	140	18.5	30.2	24.3	10	19.4	15.4
Infants	58	124	103.3	18.5	22.6	20.9	10	14.7	13.3
Young children	98.8	162	134.4	20	28	24.6	13	17.2	15.3
Children	129	171	148.8	20.5	29	25.5	13.4	18	15.6
Adolescents	132	178	153	21.2	30.2	26.2	13.2	19.4	16

AP: Anteroposterior; CC: Craniocaudal; cm: centimeter; Max.: Maximum; Min.: Minimum; mm: millimeter; n: number of subjects

There was no significant difference identified for cerebellar volume, pons CC and pons AP dimensions between the genders in all subjects and also in all age groups (Table 2).

Table 2. Comparisons of the data between genders in all subjects and also in all age groups.

	Cerebellar volume Girls-boys	Pons CC* dimension Girls-boys	Pons AP** dimension Girls-boys
All subjects	0.112	0.193	0.183
Infants	0.064	0.099	0.211
Young Children	0.264	0.433	0.854
Children	0.128	0.140	0.089
Adolescents	0.116	0.164	0.124
P value			
Mann-Whitney U test *Craniocaudal ** Anteroposterior			

There was a positive significant correlation between age with cerebellar volume, pons CC and pons AP dimensions ($p=0<0.001$ for all variables) (Figure 3). There were significant differences between the cerebellar volumes, pons CC and pons AP dimensions in the infants, young children, children and adolescents groups (Table 3). The cerebellar volumes, pons CC and pons AP dimensions significantly increased from infants to young children, young children to children and children to adolescents age groups.

Table 3. Comparisons between age groups in terms of cerebellar volumes, pons CC and pons AP dimensions.

	Cerebellar volume	Pons CC* imension	Pons AP** dimension	P value
Infants-young children	<0.001	0.002	0.003	
Young children-children	0.002	0.033	0.04	
Children-adolescents	0.01	0.03	0.043	
Tamhane Test *Craniocaudal ** Anteroposterior				

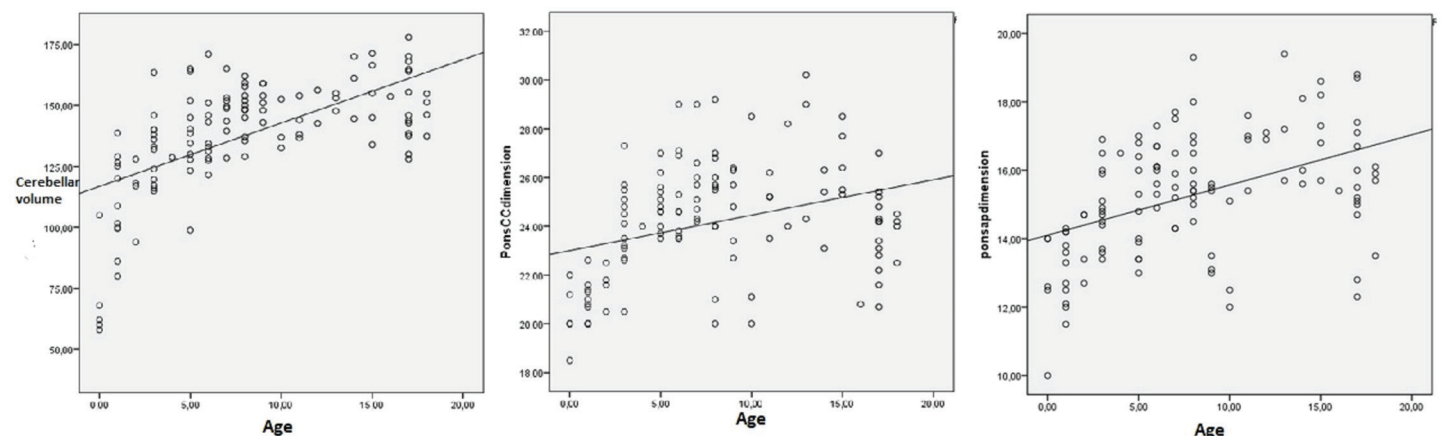


Figure 3. Scatter plots shows the significant positive correlations between age and cerebellar volumes, pons dimensions

Discussion

In this study, quantitative reference values for normal cerebellar volume, pons CC and AP dimensions were revealed for pediatric population using MRI. As age group increases, there were significant increases in cerebellar volume, pons CC and pons AP dimensions. Gender did not have a significant effect on these variables. This study is unique as it collects different data in a single study and is based on commonly-used practical pediatric age groups.

The cerebellum is a very late developing region of the brain in terms of longitudinal evolution. Compared to other mammals, it is one of the clearest expanded brain regions in humans. With a deep role in balance, coordination and other motor skills, the cerebellum is becoming accepted as providing important contributions to a variety of cognitive and emotional functions [2,3]. The pons ensures main motor and sensory innervation of the face and neck through the cranial nerves. Additionally, it ensures links to the brain, basal ganglions, diencephalon, cerebellum and spinal cord. It also contains other brain stem nuclei. It contains multiple white matter tracts (e.g. medial longitudinal fasciculus, medial lemniscus, lateral lemniscus, etc) and grey matter nuclei (e.g. cranial nerves) [4]. All of these are proof that the cerebellum and pons are very important in the pediatric era.

For some diseases, for example x-linked adrenoleukodystrophy and metachromatic leukodystrophy, Pelizaeus–Merzbacher's disease, and 4H syndrome (hypomyelination, hypodontia, and hypogonadotropic hypogonadism), MRI is a routine part of assessment [13,14]. MRI images can be assessed for determined criteria like localization of lesions, progression or regression of disease, along with changes in brain volume. In addition to this, linear parameters may be useful as surrogate markers of brain volume, for example, the bicaudate ratio or the maximum anteroposterior pons diameter. In the last ten years the use of linear parameters has been investigated for diseases like hydrocephalus, atrophy, Huntington's and Parkinson's diseases, progressive supranuclear palsy, human immunodeficiency virus (HIV) related leukoencephalopathy, and multiple sclerosis [15,16].

In this study, the median age and cerebellar volume were found to be 7 years and 140 cm³. A study published by the Brain Development Cooperative Group determined the mean cerebellar volume as 132.82 ± 15.40 cm³ in a total of 325 children and adolescents with median age of 10.5 years (4.5-18) [17]. The same study gave normative values for other brain structures like the frontal, temporal, parietal and occipital lobes. In our study, the inclusion of infants and the lower median age led to expectations that the total volume would be lower. However, though the results of the studies are close, these small volume changes may involve multifactorial factors like race, sociocultural level and IQ. In our study, there was a positive significant correlation found between age and cerebellum volume. Similarly, as stated in other studies above, the best-fitting models of age-related changes in brain volume were predominantly linear for males and quadratic, also in the shape of an inverted-U curve, for females.

Gender differences are less well-characterized for the cerebellum compared to the brain. Many studies have reported larger cerebellum volumes for males in the adult population. In our study,

there were no significant differences in cerebellar volume on MRI for girls and boys in the infant, young children, children and adolescent groups. These results are different from some studies in the literature. Caviness et al. in a study of fifteen males and fifteen females aged 7-11 years reported the cerebellum in girls was at adult volumes [18]. However, they stated that in this age interval the male cerebellum had not yet reached adult volumes. The reason for this was proposed to be the later development and cerebellar maturation of males. Tiemeier et al. in a study of children and adolescents aged 5-24 years published that cerebellar volume was 10% to 13% larger in males depending on the age of comparison and the sexual dimorphism remained significant after covarying for total brain volume [19]. The reason for these different results in our study is not clear. It may be due to the age group and race differences chosen in the studies. It may guide more comprehensive studies comparing different races and using more rational age groups, as in our study.

In our study, pons CC and pons AP dimensions significantly increased from infants to young children, young children to children and children to adolescents age groups. There was no significant difference identified for pons CC and pons AP dimensions between the genders in all subjects and also in all age groups. Similarly, Garbade SF et al. published that maximal sagittal AP brainstem diameters on MRI rapidly increased during the first decade, which, in pons and medulla oblongata, was followed by a plateau and a subsequent slow decrease beyond the sixth decade [20]. Raininko R et al. published that pontine dimensions increased until the age of 20 years and did not subsequently decrease [21]. Similar to our study, Rajaei et al. in a study of children and adults found the length of pons was 21.40 mm in men and 21.10 mm in women, with no difference between males and females [22]. They also published that when age increases by 1 year, a value of 0.01 mm will be added to the size of the transverse length of pons.

Our study results may be beneficial for radiological diagnosis, treatment and monitoring of some neurologic diseases progressing with changes to the cerebellar volume and pons dimensions. Among these, congenital malformations (microcephaly, lissencephaly, polymicrogyria, heterotopic gray matter, etc.), metabolic and vascular disorders (osmotic demyelination syndrome, hypomyelination, Wilson, MELAS, hypoxic-ischemic encephalopathy, stroke, etc.), tumors (pons glioma, medulloblastoma, cerebellar hypoplasia, pilocytic astrocytoma, Lhermitte-Duclos syndrome, etc.), and infection/inflammation (CMV, HIV, Rasmussen encephalitis, etc.) may be listed. For example, small pons glioma with no contrast involvement on MRI may present as changed pons dimension. It may be used as a helpful parameter for conventional MRI sequences. If cerebellar atrophy is mild, the normal cerebellar volume values may be referenced for normal/abnormal differentiation. Or while monitoring an operated medulloblastoma, residual monitoring may be performed based on initial and normal volume values.

There are some limitations in this study. The first is the low number of subjects and the retrospective nature of the study. The second is that clinical and laboratory data leading to the consideration that cases were healthy was only accessed through the archives. The third is that measurements were performed by a single radiologist and reliability between measurements was not assessed. The fourth limitation is that cerebellar sulcus was ignored for volume

measurements and included in total volume.

Conclusion

This study identified reference basal data for cerebellar volume and sagittal pons dimensions on MRI for well-known age groups in the pediatric period. As age group increased, there were significant increases in cerebellar volume, pons CC and pons AP dimensions. Gender did not have a significant effect on these changes. Use of this data in routine practice may be a radiologic guide in terms of diagnosis or monitoring of disease status in the posterior fossa and brain stem.

Competing interests

The authors declare that they have no competing interest.

Financial Disclosure

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Ethical approval

Ethics committee approval was obtained.

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