Assessment of Cerebellar Dimensions Using Magnetic Resonance Imaging in Children Aged 0-4 Years

0-4 Yaş Arası Çocukların Serebellum Boyutlarının Manyetik Rezonans Görüntüleme ile Değerlendirilmesi

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ABSTRACT Objective: Several diseases progress with cerebellar atrophy and hypoplasia. Cerebellum dimension measurements facilitating the assessment of decreases in cerebellum size on radiological images between the ages of 0 and 4 years in particular, when the cerebellum is still growing, will be of considerable use in clinical practice and appropriate for measurement value standardization. This will allow easier interpretetation of findings, together with more accurate diagnosis or a decrease in delays caused by false diagnosis. This study, the purpose of which was to obtain a database suitable for clinical use by performing cerebellar development dimension measurements in normal individuals aged 0-4 years, investigated the effect on cerebellar dimensions of parameters such as height, weight, head circumference and birth week. **Material and Methods:** One hundred fourty children aged 0-4 years, 56 girls and 84 boys, undergoing magnetic resonance imaging of the brain at the Karadeniz Technical University Farabi Hospital Radiology Department with no structural cerebral or cerebellar abnormalities were included in the study. **Results:** In this study of cerebellar dimensions in healthy children, these were positively correlated with weight, head circumference and height in both genders. Preterm birth had a significant effect on cerebellar dimensions. **Conclusion:** In conclusion, this scale developed by measuring the cerebellar dimensions of healthy children aged 0-4 years will be of considerable practical assistance in terms of assessing measurements performed in a clinical environment.

Key Words: Magnetic resonance imaging; child

ÖZET Amaç: Serebellumun atrofisi ve hipoplazisi ile giden birçok hastalık mevcuttur. Özellikle serebellumun büyümeye devam ettiği 0-4 yaş arasında radyolojik görüntülerde serebellum boyutlarındaki azalmanın değerlendirilebilmesi için serebellum boyutlarının ölçümleri, klinikte pratik olarak yararlı olacak ve ölçüm değerlerinin standardizasyonu için uygun olacaktır. Böylece bulguların daha kolay tanımlanabileceği ve doğru tanı konulamaması ya da tanı konulmasındaki gecikmelerin azalacağı öngörülmektedir. Bu nedenle 0-4 yaş arası normal bireylerde serebellum gelişimi boyut ölçümleri ile yaparak klinik kullanıma uygun bir veri dökümü elde etmeyi amaçladığımız bu çalışmada boy, kilo, baş çevresi, doğum haftası gibi parametrelerin serebellum boyutları üzerine etkilerini de değerlendirdik. **Gereç ve Yöntemler:** Araştırmaya Karadeniz Teknik Üniversitesi Radyoloji Bölümünde beyin manyetik rezonans görüntülemesi yapılan ve serebral ve serebellum anomalisi olmayan 0-4 yaş arasındaki 56 kız, 84 erkek çocuk dahil edilmiştir. **Bulgular:** Sağlıklı çocuklarda serebellum boyutlarını saptadığımız bu çalışmada, serebellum boyutlarının her iki cinsiyette boy, kilo ve baş çevresi ile pozitif korelasyon olduğu ve erken doğumun serebellum boyutları üzerine önemli etkileri olduğu belirlendi. **Sonuç:** Sonuç olarak 0-4 yaş arası sağlıklı çocukların serebellum boyutlarını ölçerek geliştirdiğimiz bu skala klinik ortamda yapılan ölçümlerin değerlendirilmesinin yapılabilmesi açısından oldukça pratik bir kolaylık sağlayacaktır.

Anahtar Kelimeler: Manyetik rezonans görüntüleme; çocuk

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In the embryological period, the central nervous system that develops from the ectoderm begins to form at the start of the 3rd week. Neural tube development is completed toward the middle of the 4th embryological week. This neural tube subsequently differentiates in the rostral area to form the cerebrum and cerebellum. Development of the cerebellum begins in days 40-45, and the fissurae cerebelli and folia cerebelli appear in the cerebellum at the end of the 4th month. The cerebellum is part of the hindbrain, located below the temporal and occipital lobes. Despite being a structure where many impulses from sensory receptors terminate, it is regarded as one of the motor components of the central nervous system (CNS). Its volume represents approximately 10% of the entire brain, but it consists of more than 50% of all neurons.[1]

The basic functions of the cerebellum are the motor control of coordination, balance and speech functions. Recent neuroanatomical and clinical studies and imaging of the CNS have proved that the cerebellum also has cognitive, affective and executive functions.[2-4] New studies are revealing further cerebellar functions, and this is increasing the amount of research into the cerebellum. One of these studies reported a relation between higher cognitive function, speech memory, consecutive learning and language functions and the cerebellar hemispheres and vermal lobules IV-VII.[5] One study involving functional magnetic imaging showed that activity in the anterior lobe of the cerebellum increased with speed of motor activity.[6] Another study evaluating cerebellar size determined a significant relation between a reduced intelligence function and decreased cerebellar dimension.[7] These studies all reveal the importance of measuring cerebellar dimensions.

Several previous studies have measured cerebellar volume, but none of these developed an average volume scale for age groups between 0 and 4 years. [3, 8-16] One study that measured cerebellar volume between 0 and 2 years identified a 253% increase in cerebellar volume between birth and 2 years.[17] Another study measured cerebral and cerebellar volume using magnetic resonance imaging (MRI) images in children between 4 and 18 years and reported that cerebral and cerebellar volumes did not change in this age range.[18] We therefore included children aged between 0 and 4 years in this study, hypothesizing a potential change in cerebellar dimensions.

Several diseases progress with cerebellar atrophy and hypoplasia, including attention deficit hyperactivity disorder, autism, macrocephaly, cleft lip and palate, Down syndrome, schizophrenia, bipolar disorder, cerebral palsy and epilepsy. [19-31] The cerebellar dimensions obtained in the study will be useful in clinical practice by making it possible to assess a decrease in cerebellum dimensions on radiological images between the ages of 0 and 4 years, when the cerebellum is still growing, and will also be applicable for the standardization of measurement values. The purpose of this study was therefore to obtain a database suitable for clinical use by performing cerebellar development dimension measurements in normal individuals aged 0-4 years. We also assessed the effect of parameters such as height, weight, head circumference and weeks of gestation on cerebellar dimensions.

MATERIAL AND METHODS

One hundred forty children aged 0-4 years, 56 girls and 84 boys, undergoing MRI of the brain at the Karadeniz Technical University Farabi Hospital Radiology Department for reasons such as headache, sleeplessness, delayed speech and walking, preliminary diagnoses of meningitis and hypoxic-ischemic encephalopathy and seizures and with no structural cerebral or cerebellar abnormality, as confirmed by a specialist radiologist, were included. Families were told not to permit their children to sleep during the preceding night, thus ensuring they would sleep and remain immobile during MRI. Images from children who woke or moved during MRI were excluded from the research for lacking sufficient clarity. MRIs were taken of all sections requested by radiology specialists, but only midsagittal and axial images were used in this study. Local ethical approval was granted and written consent was obtained from parents. Children's height, weight and head circumferences at MRI were measured in order to investigate correlations with cerebellar dimensions. Families were administered a questionnaire containing questions about factors that might affect cerebellar development, such as children's weeks of gestation, whether they cried at birth, cyanosis during birth, history of intubation and maternal exposure to viral infection during pregnancy.

Children were divided into premature (<37 weeks of gestation) and term (≥37 weeks of gestation).

MEASUREMENTS

Measurements were performed using a 1.5T MRI system (Simens Magnetom Symphony, Germany). Two-dimensional T_1 weighted sagittal images (TR: 400 ms, TE: 8.6 ms, slice thickness: 5 mm, FOV: 230x230 mm, Dist factor: 40%, Average: 1, Matrix: 256x192) and two-dimensional T_2 axial images (TR: 6800 ms, TE: 121 ms, slice thickness: 5 mm, FOV: 230x168 mm, Dist factor: 30%, Average:1, Matrix: 256x156) were recorded. Cerebellar dimensions were measured personally by one of the authors using automatic calibrations on a work station (Leonardo, Siemens).

Vermis height (VH) was measured on the vertical axis, and vermis anterior-posterior dimension (VAPD) on the transverse axis by accurate determination of cerebellar vermis margins on T_1 weighted midsagittal images (Figure 1).

Right cerebellar hemisphere height (HH_{RIGHT}) was measured on the vertical axis on that section where the right cerebellar hemisphere was largest and left hemisphere height (HH_{LEFT}) was measured on the section where that hemisphere was largest by accurate determination of hemisphere margins on T_1 weighted midsagittal images (Figures 2, 3).

Transcerebellar diameter (TCD) was measured between the two lateral margins of the cerebellum from the section in which the cerebellum appeared largest on T_2 weighted axial images (Figure 4) and cerebellar hemisphere anterior-posterior dimensions ($HAPD_{RIGHT-}$ and $HAPD_{LEFT}$) were measured perpendicular to that length (Figure 5).

FIGURE 1: VH measurement (1), VAPD measurement (2).

FIGURE 2: HH_{RIGHT} measurement

STATISTICAL ANALYSIS

Data were analyzed and compared on SPSS 13.0 software. Median, arithmetic mean, standard deviation and standard error values were determined. The parametric Student's t test and paired t test were used to compare means of normally distributed data and the Mann Whitney U test for non-normally distributed data. P<0.05 was considered statistically significant.

STUDY LIMITATIONS AND RECOMMENDATIONS

Thirty-two of the children in the study were premature, and 108 were term. Due to the small case

FIGURE 3: HH_{LEFT} measurement

FIGURE 4: TCD measurement.

number in this study, no comparison for preterms on the basis of weeks of gestation was possible, and we were unable to determine whether or not cerebellar dimensions of these babies after the 37th week were comparable to those of normal newborns. In addition, cerebellar dimensions increased rapidly in the 0-1 years age range. We therefore think that it will be useful for change in cerebellar dimensions in preterms and rate of cerebellar growth in the 0-1 age range to be evaluated in greater detail by increasing the numbers of children aged 0-1 years in future studies on the subject.

RESULTS

Children's mean age was 48±15.39 months, mean height 70.25 ± 19.78 cm, mean weight 8563.86 ± 5283.15 g and mean head circumference 42.50±6.87 cm. Correlation analysis revealed that cerebellar dimensions increased with height, weight, head circumference and age (Table 1).

Children born on term and aged 0-4 years were divided into 7 groups 0-3, 4-6, 7-9, 10-12, 13-24, 25-36 and 37-48 months. Mean cerebellar dimensions (cm) of these 7 groups are shown in Table 2.

No statistically significant difference was determined between male and female term children in terms of cerebellar dimensions (Table 3).

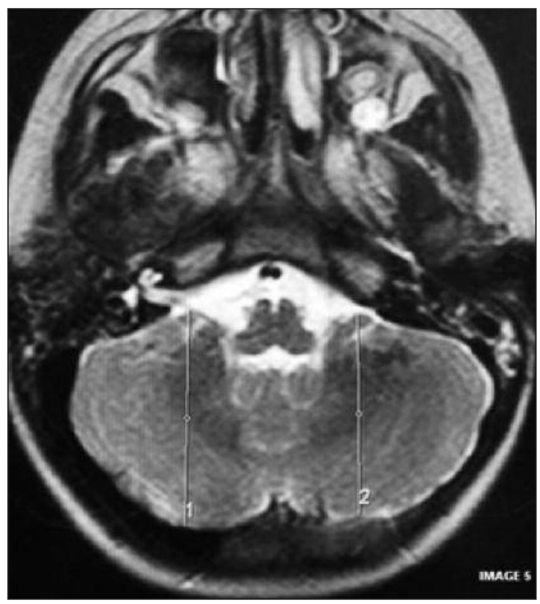

FIGURE 5: $HAPD_{RIGHT}$ (1) and $HAPD_{LEFT}$ measurement (2)

Comparison of cerebellar dimensions between premature and term children revealed statistically significantly lower VH, VAPD, HH_{RIGHT}, HH_{LEFT}, TCD, $HAPD_{RIGHT}$ and $HAPD_{LEFT}$ parameters in prematurely born children compared to those born on term ($p< 0.001$) (Table 4).

DISCUSSION

Several studies in the literature have assessed cerebellar dimension with volume measurement.

TABLE 1: Cerebellar dimension correlations with height, weight, head circumference and age.

		VH	VAPD	TCD	$HAPD_{RIGHT}$	$HAPD_{LEFT}$	HH_{RIGHT}	HH_{LEFT}
Height	r	0.872	0.797	0.927	0.881	0.856	0.877	0.889
	p	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Weight	r	0.842	0.775	0.916	0.864	0.848	0.848	0.863
	p	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Head circumference	r	0.897	0.852	0.956	0.921	0.898	0.897	0.915
	p	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Age	r	0.751	0.715	0.819	0.759	0.748	0.761	0.780
	p	0.000	0.000	0.000	0.000	0.000	0.000	0.000

TABLE 2: Mean cerebellar dimensions at 0-3, 4-6, 7-9, 10-12, 13-24, 25-36 and 37-48 months.

		VH	VAPD	HH_{RIGHT}	HH_{LEFT}	TCD	$HAPD_{RIGHT}$	$HAPD_{LEFT}$
Age Interval	n	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean± SD
0-3 months	32	2.57±0.34	2.10±0.27	2.64±0.40	2.55±0.31	5.85±0.66	3.62±0.39	3.46±0.38
4-6 months	10	3.40±0.25	2.57±0.24	3.49±0.37	3.42±0.30	7.59±0.43	4.28±0.33	4.12±0.37
7-9 months	7	3.85±0.51	2.94±0.47	3.87±0.34	3.66±0.48	8.06±0.94	4.62±0.40	4.10±0.46
10-12 months	9	3.99±0.31	3.13±0.43	4.35±0.30	4.10±0.32	8.92±0.39	5.23±0.37	4.84±0.40
13-24 months	12	4.08±0.40	3.13±0.28	4.15±0.40	4.07±0.36	9.28±0.47	5.32±0.40	4.92±0.45
25-36 months	14	4.20±0.32	3.23±0.30	4.51±0.37	4.38±0.39	9.77±0.41	5.48±0.23	5.14±0.30
37-48 months	24	4.22±0.36	3.34±0.46	4.45±0.34	4.34±0.30	9.85±0.45	5.41±0.31	5.09±0.43

n: Specimen number. All values are given in centimeters.

One study measuring cerebellar vermis dimensions assessed vermis size in individuals aged 0-60 years, but no mean vermis dimensions were given for the 0-4 age group.[32] Another study measured cerebral and cerebellar volumes at MRI in children aged 4-18 years and determined no change in volumes in this age group.[18] Our research therefore involved the 0-4 age group, in which we predicted a possible change in cerebellar dimensions, and these were observed to increase up to the age of 4 years.

Analysis of the rate of increase in cerebellar dimensions between 0 and 4 years determined quite rapid growth in the first year of life. Similarly, a study in which dimensions of the cerebellar vermis were measured reported a marked increase in cerebellar vermis size between the ages of 0 and 1.[32] One study performed with volume measurement paralleled our own research finding by determining rapid growth in cerebellar volume in the first year of life.[17]

TABLE 3: Comparison of male and female children in terms of cerebellar dimensions.

	Female (n: 46)	Male (n: 62)	
	Mean±SD	Mean±SD	p
VH	3.39±0.76	3.67±0.79	0.250
VAPD	2.71±0.56	2.90±0.65	0.117
HH_{RIGHT}	3.63±0.89	3.84±0.83	0.203
HH_{LEFT}	3.47±0.86	3.75±0.80	0.084
TCD	7.89±1.80	8.41±1.71	0.131
$HAPD_{RIGHT}$	4.61±0.87	4.79±0.85	0.284
$HAPD_{LEFT}$	4.32±0.80	4.49±0.81	0.271

All values are given in centimeters.

The difference in cerebellar size between the sexes is unclear in the literature, and conflicting opinions exist. Some authors have suggested that gender variations in cerebellar size may be attributed to sex hormones.[32] No difference in cerebellar dimensions was determined between the sexes in this study. Various studies involving individuals in different age groups (newborn-86 years) have reported,

TABLE 4: Comparison of cerebellar dimensions in children born prematurely or at term.

	Premature (n:32) Mean±SD	Term (n: 108) Mean±SD	p
VH	2.85±0.83	3.59±0.78	0.000
VAPD	2.33±0.57	2.82±0.62	0.000
HH_{RIGHT}	2.98±0.77	3.75±0.86	0.000
HH_{LEFT}	2.87±0.68	3.63±0.83	0.000
TCD	6.32±1.62	8.19±1.76	0.000
$HAPD_{RIGHT}$	3.75±0.88	4.71±0.86	0.000
$HAPD_{LEFT}$	3.48±0.85	4.42±0.81	0.000

All values are given in centimeters.

in agreement with our research, no difference between the genders in terms of cerebellar dimension.[8,11,16,32] However, studies involving individuals from different age groups across a broad range of ages (4-77 years) have reported a greater cerebellar volume in men compared to women.[9,10,18,33,34] Volumetric analysis of organ and tissue dimensions is without doubt more reliable that dimensional measurements. However, analysis of the findings of various studies that have compared gender and volume size [8-11,16,18,32-34] reveals no definitive conclusion regarding whether cerebellar size differs between the sexes.

Several previous studies have reported that fetal cerebellar dimensions increase with weeks of gestation.[14,35-42] Premature births can interrupt cerebellum growth. Investigation of whether the adverse effect or prematurity on cerebellar dimensions persists after birth has shown smaller cerebellar dimensions in children born prematurely compared to those born at term.

One study in which fetal cerebellar dimensions were evaluated using ultrasound reported that head circumference, TCD, cerebellar circumference, vermis surface area, VAPD and VH increased in a linear manner with week of gestation. Another study that employed ultrasound to evaluate the fetal cerebellum also revealed a parallel increase in TCD and head circumference.[36] At analysis of increases in cerebellar dimensions with head circumference, height, weight and age, this increase was reported to persist in a parallel manner also after birth. Another similar study determined that cerebellar circumference and area were positively correlated with head circumference, humerus length and weight.[41] One study comparing cerebellar volume and head circumference supports this research by reporting a positive correlation.[39]

Varying degrees of cerebellar atrophy have been determined in studies involving individuals with attention deficit hyperactivity disorder,[29,43] autism,[23, 30] cleft palate or cleft lip,[31] Down syndrome,[20] cerebral palsy,[28] and epilepsy[26]. In the context of the findings in the literature, this study provides a database suitable for clinical use by measuring cerebellar dimension development in healthy individuals aged 0-4 years in order to for it to be possible for such anomalies to be identified in the early period.

CONCLUSIONS

The findings from this study reveal a rapid increase in cerebellar dimensions between the ages of 0 and 4 years. We think that a scale drawn up for these ages when the cerebellum is growing will be of considerable use in the assessment of cerebellar size in clinical practice.

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