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Evaluation of the development of the posterior fossa in normal Chinese fetuses by using magnetic resonance imaging

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Abstract

The posterior fossa is an important brain structure containing the cerebellum, cerebral ventricle, and cistern. Early evaluation of the cerebellar structure and function may be valuable for early detection of fetal deformities. At present, no normal value for the fetal posterior fossa has been established yet. This study is aimed to investigate the development of the posterior fossa in normal Chinese fetuses by using magnetic resonance imaging (MRI).

Pregnant women who need MRI scan were enrolled in our Hospital between January 2012 and December 2014. The fetal supero-inferior diameter (SID), anterio-posterior diameter (APD), cerebellar vermis area, cerebellar width (CW), cerebellar volume (CV), superior cerebellar cistern width, and cerebellomedullary cistern width were measured using MRI. Pearson's correlation analysis was used to detect the relationship between those parameters and gestational age. A regression analysis was performed for all parameters.

A total of 92 participants were retrospectively enrolled finally. The results indicated SID, APD, cerebellar vermis area, CW, and CV were positively associated with gestational age, while no significant correlation was found between the superior cerebellar cistern width and cerebellomedullary cistern width and gestational age. Each equation was established.

Our study demonstrated that MRI has the advantages over ultrasound imaging for prenatal evaluation of the fetal posterior fossa with multiple views. Normal value of the posterior fossa of Chinese fetuses was established in this study.

Abbreviations: APD = anterio-posterior diameter, CM = cistern manga, CNS = central neurology system, CV = cerebellar volume, CW = cerebellar width, GW = gestational week, LMP = last menstrual period, MRI = magnetic resonance imaging, RF = radio frequency, SID = supero-inferior diameter.

Keywords: cerebellum, Chinese, cranial fossa, fetus, magnetic resonance, posterior

1. Introduction

The posterior fossa is an important structure that contains the cerebellum, cerebral ventricle, and cistern. The cerebellum was initially considered to be solely a motor center, however, the later studies revealed that it is also involved in language, socialization, and cognition.[1] The cerebellum develops during the early stage, but matures during the late stages of embryonic development. Fetal posterior fossa is an important component of the fetal central neurology system (CNS). Functional abnormalities of the cerebellum are difficult to detect during gestation and are normally identified ~1 year after birth, early evaluation of cerebellar development may be helpful for the early diagnosis of function abnormalities. Performing imaging studies of the posterior fossa in normal fetuses of different gestational ages may provide useful information for the early detection of fetal deformities.

Ultrasound is a simple, non-invasive, and real-time imaging, which is typically used as the first option for screening. However, ultrasound images are low-resolution, making it difficult to detect fine brain structures. Furthermore, it is difficult to acquire an image of the median sagittal plane of the fetal brain using ultrasound, which is an important plane for evaluating the posterior fossa.[2] A number of factors, such as fetal bone, maternal pelvis, bowel gas, body size, amniotic fluid, and the experience of sonographer, may affect the quality of ultrasound imaging. Compared with ultrasound, MRI has produces higher resolution images without interference from fetal or maternal bone, and is able to provide multiple views, planes, and sequences, resulting in a more accurate measurement of the posterior fossa.[3]

No normal values for the posterior fossa and cerebellum have yet been established for Chinese fetuses of different gestational ages. The present study was performed to establish normal values for the fetal posterior fossa in order to enable early detection of cerebral abnormalities using MRI. We herein hope to establish

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diagnosis criterion for cerebellar abnormalities and provide normal values for the posterior fossa in Chinese fetuses.

2. Materials and methods

2.1. Objectives

This observational study retrospectively enrolled participants who were treated between January 2012 and December 2014. The participants were pregnant women who underwent MRI following ultrasound imaging that suggested potential fetal abnormalities. The inclusion criteria were as follows: No abnormal CNS findings; gestational age established by last menstrual period (LMP) was consistent with ultrasound age; no abnormalities in developmental milestones during follow-up for 1 year after birth and Gesell scale[4] > 85 if development evaluation was necessary. The exclusion criteria were as follows: Abnormal fetal MRI findings, abnormal milestone events in neonates, non-standard scanning results, or obvious artifacts that meant imaging could not be evaluated. The present study was approved by the Ethics Committee of the Hospital. All participants provided written informed consent.

2.2. Method of scan

1. Pre-scan preparation: The participants were screened for contraindications in MRI results. Gestational age was calculated depending on their LMP.
2. Equipment: A GE 1.5 T Signal HD MR was used. A body coil was used for radio frequency (RF) coil, while a torso phased array coil was used as the receiving coil.
3. Scan method: The participants laid down on the examination bed feet first. The topogram covered the whole uterus and fetus to acquire three scout scan view. Images were obtained in the coronal, sagittal, and axial views. The axial scan was performed in parallel with the connecting line between the genu and splenium of corpus callosum. The sagittal scan was performed in parallel with the cerebral longitudinal fissure. The coronal scan was performed vertical to the cerebral longitudinal fissure and in parallel with brain stem. The following pulse sequences and parameters were used.
   (a) FIESTA scan parameters: Repetition time (TR), 6000 ms; TE (echo time), 4.20 ms; flip angle, 70 degrees; bandwidth, 200 Hz; field-of-view (FOV), 36 cm; slice thickness, 3 to 5 mm; slide gap, 0 mm; number of excitations (NEX) = 1; matrix size, 256 × 256.
   (b) T2WI scan parameters: TR, 4000 ms; TE, 240 ms; bandwidth, 83 Hz; FOV, 36 cm; slide thickness, 3 to 5 mm; slide gap, 0 mm; NEX = 1; matrix size, 256 × 256. The number of scan section was determined depending on the size of fetal brain.

2.3. Data acquisition

1. Screening and images evaluation: All images was transferred to Carestream PAC (Ver 11.0) and were evaluated by a radiologist with >5 years of work experience.
2. Measurement of the posterior fossa: All measurements were processed using PACS (Fig. 1). All diameters and areas were measured twice and the mean value was used. The SID of cerebellar vermis was accessed on the median sagittal plane of the fetal brain to measure the distance between the upper and lower margins of the cerebellar vermis.

The APD of cerebellar vermis was accessed on the median sagittal plane of the fetal brain to measure the distance between

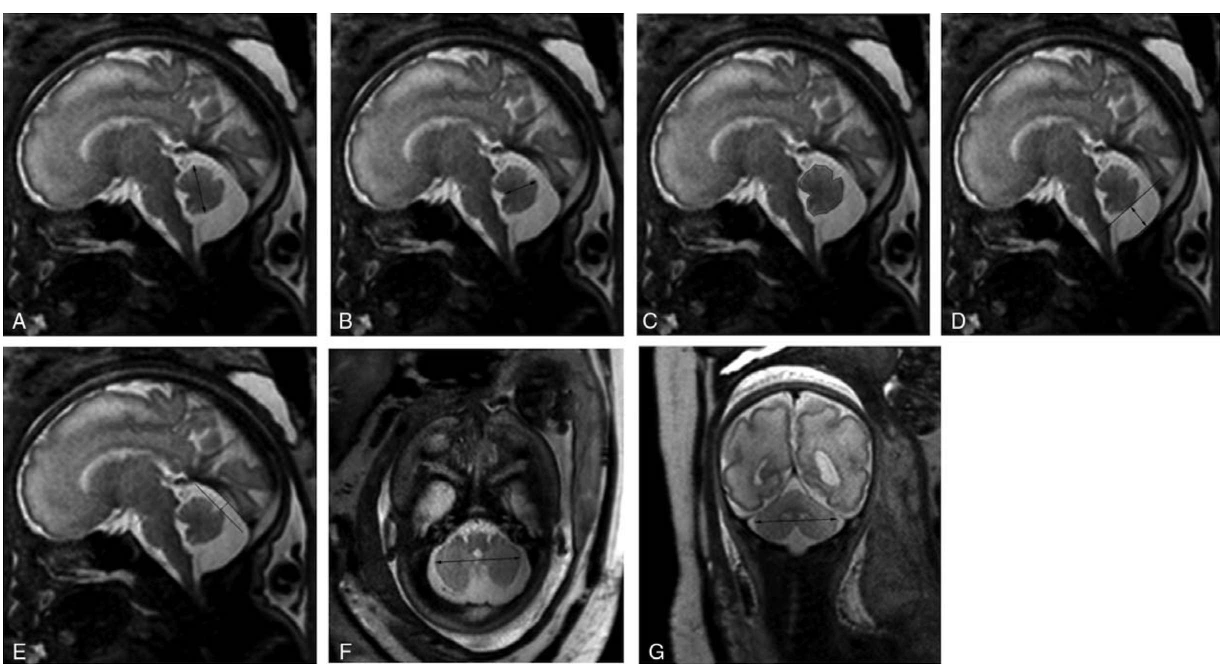

Figure 1. Cerebellar measurements using MR. (A) SID of vermis measured in the sagittal plane; (B) APD of vermis measured in the sagittal plane; (C) area of cerebellar vermis measured in the sagittal plane; (D) width of cerebellomedullary cistern measured in the sagittal plane; (E) width of superior cerebellar cistern measured in the sagittal plane; (F) cerebellar width measured in the axial plane; (G) cerebellar width measured in the coronal plane. APD = anterio-posterior diameter, CW = cerebellum width, CV = cerebellum volume, SID = supero-inferior diameter.

the top of the posterior wall of the fourth ventricle and the most dorsal outer edge of the cerebellar vermis.

The cerebellar vermis area was accessed on the median sagittal plane of the fetal brain to manually outlined. The cerebellar vermis area was automatically calculated using PACS.

CW was accessed on the sagittal, coronal, and axial plane to measure the longest distance between the left margin and right margins of the cerebellum.

CV was accessed on the sagittal, coronal, and axial planes. First, the investigator manually sketched the outline of the cerebellar vermis first, and then added all areas together and multiplied by slides thickness.

The width of cerebellomedullary cistern was accessed on the median sagittal plane of the fetal brain to measure the vertical distance between the upper posterior margin of the cerebellum and the occipital bone plate.

The width of the superior cerebellar cistern was accessed on the median sagittal plane of the fetal brain to measure the vertical distance between the upper posterior margin of the cerebellum and the tentorium cerebelli.

2.4. Statistical analysis

SPSS 20.0 software was used for analysis. Data are presented as the mean ± standard deviation if they are normal distribution. Median is used if the data are not normal distribution. The width and volume of the cerebellum on different planes were compared using paired t tests. One-way ANOVA analysis was used for compare CV on different planes. Pearson's correlation analysis was performed to access the correlation between these parameters and gestational age. A regression equation was established. $P<.05$ was considered to indicate statistically significant differences.

3. Results

3.1. Baseline characteristics of participants

A total of 92 participants were enrolled in this study. The gestational age was 21 to 38 weeks, with a median of 31 weeks. Gestational age distribution is shown in Figure 2. The male: female sex ratio of the fetuses was 43:49.

3.2. Analysis of the parameters of the cerebellar vermis

The association of vermis SID, APD, and vermis area with gestational age is shown in Figure 3. The SID of cerebellar vermis was 18.73 ± 3.91 mm, which was positively associated with gestational age ($r=0.835$, $P<.001$). The APD of the cerebellar vermis was 15.97 ± 3.55 mm and was positively associated with gestational age ($r=0.787$, $P<.001$). Cerebellar vermis area was 249.39 ± 91.11 mm^2 and was positively associated with gestational age ($r=0.859$, $P<.001$).

3.3. Analysis of CW on different view

The width of cerebellum based on axial and coronal view was 38.82 ± 8.15 mm and 38.75 ± 8.08 mm, respectively, without statistical difference ($t=0.633$, $P=.528$; Fig. 4). Axial CW was positively correlated with gestational age ($r=0.931$, $P<.001$). Coronal CW was positively correlated with gestational age as well ($r=0.926$, $P<.001$).

3.4. Cerebellar volume

Figure 5 shows the cerebellar volume (CV) measurements taken in the axial, coronal, and sagittal planes. The axial, coronal, and sagittal CV values were 8674.23 ± 4382.52 mm^3, 8805.43 ±

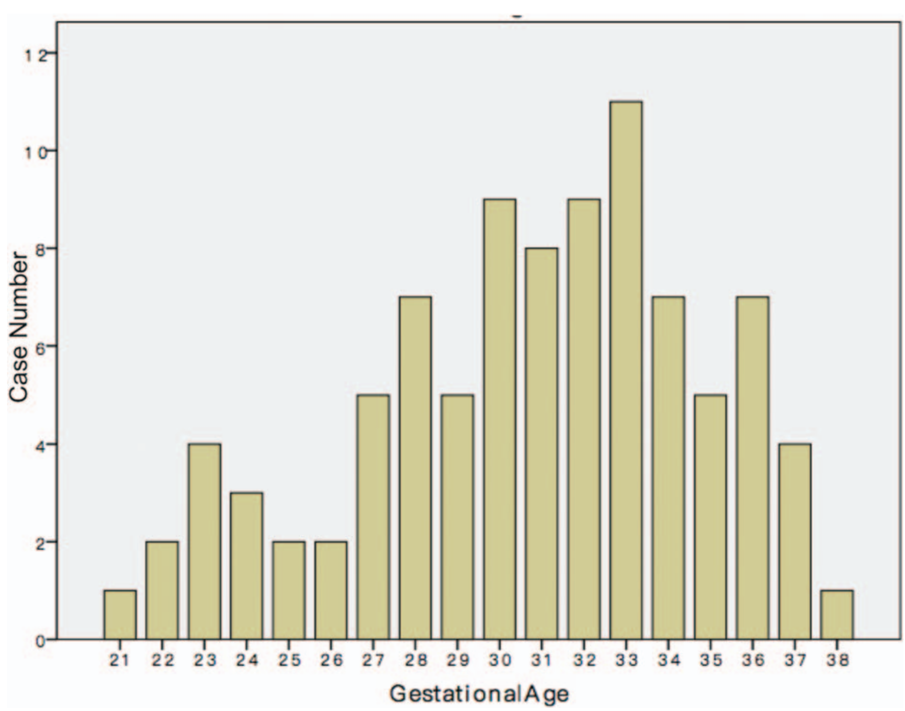

Figure 2. Distribution of gestational age. The horizontal axis presents gestational age and the vertical axis is the number of the participants. N=92. Age range, 21 to 38 weeks; median=31 weeks.

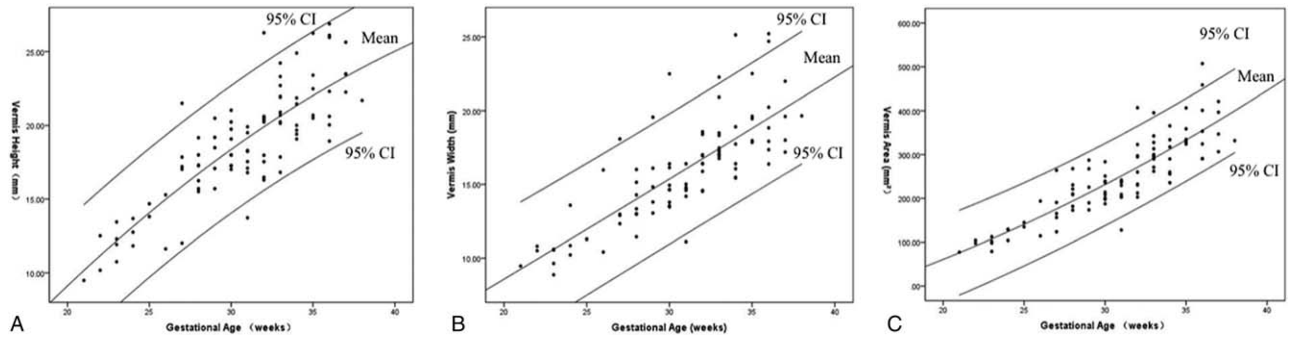

Figure 3. Association of vermis SID, vermis APD, and vermis area with gestational age. The horizontal axis is gestational age and vertical axis is the vermis SID, vermis APD, and vermis area. Mean value and 95%CI is shown. Cerebellar vermis SID, APD, cerebellar vermis area was positively associated with gestational age. (A) Cerebellar vermis SID against gestational age; (B) cerebellar vermis APD against gestational age; (C) cerebellar vermis area against gestational age. APD = anterio-posterior diameter, CI = confidential interval, SID = supero-inferior diameter.

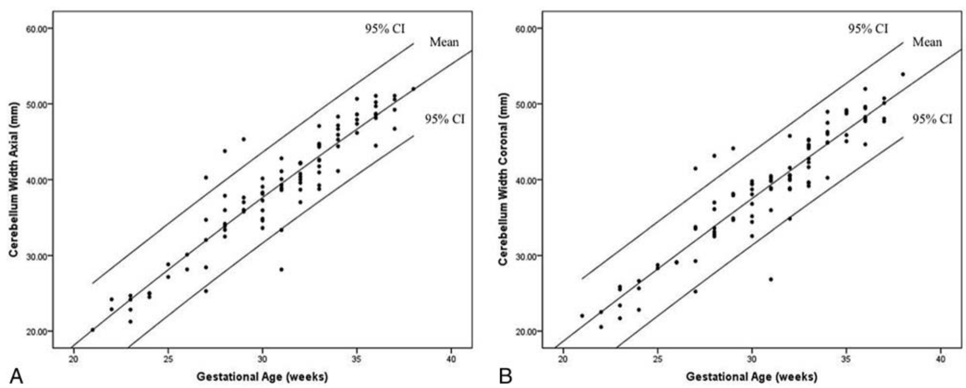

Figure 4. Association between CW and gestational age. The horizontal axis is gestational age and vertical axis is CW in axial and coronal plane. Mean value and 95%CI is shown. Cerebellar width showed positive association with gestational age. (A) Axial cerebellar width against gestational age; (B) coronal cerebellar width against gestational age. CI = confidential interval, CW = cerebellum width.

4383.16 mm^3, and 8956.10 ± 4326.19 mm^3, respectively. No statistically significant differences were observed between the three planes ($F = 0.096$, $P = .908$).

CV on axial view, coronal view, and sagittal view was all positively correlated with gestational age and *r* value was 0.874, 0.873, and 0.875, respectively with $P < .001$. All the regression equations were shown in Table 1. Cerebellar parameters in different gestational groups are shown in Table 2.

3.5. Cerebellomedullary cistern and superior cerebellar cistern width

The association between cerebellomedullary cistern and superior cerebellar cistern width and gestational age is presented in Figure 6. The mean width of cerebellomedullary cistern was 5.03 ± 1.91 mm and no significant correlation was observed with gestational age ($r = -0.103$, $P = .331$). The mean width of the superior cerebellar

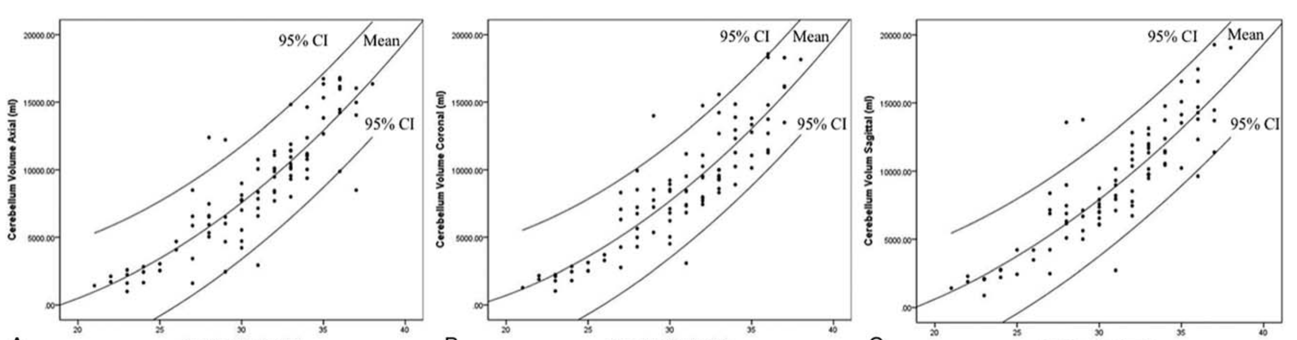

Figure 5. Association between CV and gestational age. The horizontal axis is gestational age and vertical axis is CV in axial, coronal, and sagittal plane. Mean value and 95%CI is shown. CV in axial, coronal, and sagittal plane was positively associated with gestational age. (A) Axial CV against gestational age; (B) coronal CV against gestational age. (C) Sagittal CV against gestational age. CI = confidential interval, CV = cerebellum volume.

Table 1

Equations for different parameters of fetal posterior fossa.

Parameters	Regression equation	Adjusted r^2	Significance test of regression equation	Regression coefficient
Vermis SID	−5.877+0.801*GA	0.694	F=207.337 P<.001	t=14.399 P<.001
Vermis APD	−5.158+0.684*GA	0.615	F=146.658 P<.001	t=12.110 P<.001
Vermis area	−339.777+19.174*GA	0.735	F=253.305 P<.001	t=15.916 P<.001
CW on axial	−18.311+1.859*GA	0.866	F=587.432 P<.001	t=24.237 P<.001
CW on coronal	−17.594+1.834*GA	r^2=0.857	F=544.704, P<.001	t=23.339 P<.001
CV on sagittal	−20175.411+939.963*GA	0.762	F=292.442 P<.001	t=17.101 P<.001
CV on axial	−19998.798+937.385*GA	0.721	F=288.217 P<.001	t=16.977 P<.001
CV on coronal	−19535.032+927.196*GA	0.763	F=293.519 P<.001	t=17.132 P<.001

Equations for vermis SID, vermis APD, vermis area, CW on axial view, CW on coronal view, CV on sagittal view, CV on axial view and CV on coronal view was shown on this table. Significance test of each regression equation and regression coefficient was shown as well.
APD=anterio-posterior diameter, CV=cerebellar volume, CW=cerebellar width, SID=supero-inferior diameter.

cistern was 2.35±0.90 mm and no significant correlation was observed with gestational age (r=−0.130, P=.217).

3.6. Sex difference

No significant differences were observed in vermis SID, APD, axial CW, coronal CW, axial CV, coronal CV, sagittal CV, and superior cerebellar cistern width. However, vermis APD was smaller in male compared with female, while the cerebellomedullary cistern width was significantly larger (Table 3).

4. Discussion

The cerebellum is a region of the brain that plays an important role in motor control and motor learning, contributing to coordination, precision, and accurate timing. It is also involved in a number of cognitive functions, such as attention and language, and has been reported to be involved in some emotional functions.[5,6] However, functional abnormalities of the cerebellum are difficult to detect at the antenatal stage, typically becoming apparent ~1 year after birth. Early evaluation of the cerebellar structure and function is, therefore, of great importance.

Cerebellar development starts as early as gestational week (GW) 5, but continues until after birth.[7,8] The cerebellum originates from the rhombic lip of the dorsal part of metencephalon flange. Two rhombic lips emerge from the midline of the cerebellar plate. On GW 12, the lateral parts of the cerebellar plate enlarge to form the cerebellar hemispheres. The middle of cerebellar plate thins and becomes the vermis. By the end of GW 16, horizontal fissures

Table 2

Cerebellar parameters depending on different gestational groups.

Parameters	GW 21–26 n=14	GW 27–32 n=43	GW 33–38 n=35
Vermis SID (mm) range	9.49–15.29	12.02–26.28	18.82–26.89
Mean±SD	12.45±1.65	18.16±2.31	21.94±2.47
Vermis APD (mm) range	8.87–15.98	11.11–22.49	15.43–25.22
Mean±SD	11.00±1.79	15.05±2.20	18.84±2.61
Vermis area (mm) range	77.30–193.63	123.64–407.02	235.58–507.42
Mean±SD	115.72±29.81	225.62±51.52	332.06±59.10
CW on axial (mm) range	20.18–30.11	25.30–45.34	38.76–51.98
Mean±SD	24.93±2.82	37.24±4.26	46.33±3.47
CW on coronal (mm) range	20.55–29.13	25.23–45.78	39.16–53.91
Mean±SD	25.14±2.98	37.15±4.26	46.16±3.58
CV on sagittal (mL) range	876.57–4213.80	2492.30–13765.97	9475.86–19275.45
Mean±SD	2487.71±949.15	7823.25±2482.26	12935.25±2463.12
CV on axial (mL) range	999–13831.39	1610.09–12404.53	8004.17–16814.73
Mean±SD	2423.54±1011.27	7382.53±2545.51	12761.45±2759.58
CV on coronal (mL) range	1031.91–3696.41	2758.45–14743.70	8316.21–18328.65
Mean±SD	2304.72±750.21	7722.94±2457.17	12735.62±2993.92

Vermis SID, vermis APD, vermis area, CW on axial view, CW on coronal view, CV on sagittal view, CV on axial view and CV on coronal view was divided depending on different gestational week. The range and mean value of those parameters was provided respectively.
APD=anterio-posterior diameter, CV=cerebellar volume, CW=cerebellar width, GW=gestational week, SID=supero-inferior diameter.

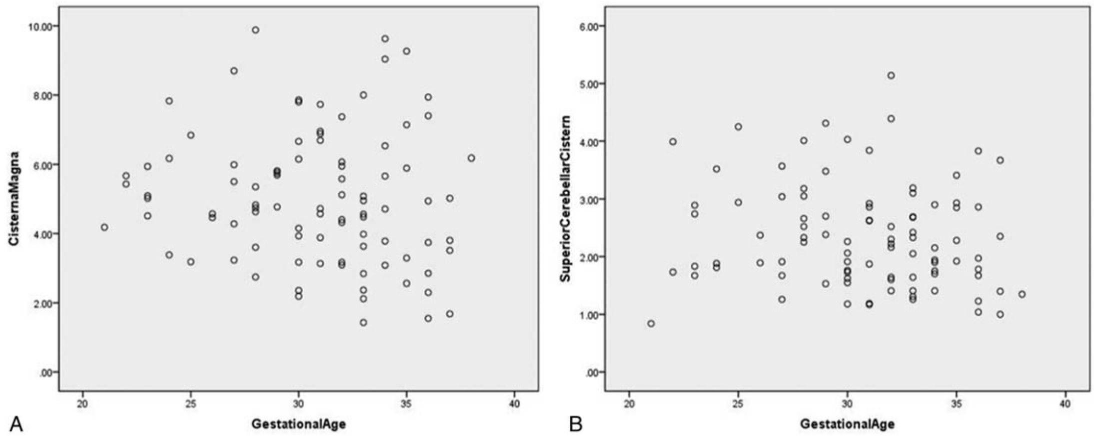

Figure 6. Association of cerebellomedullary cistern width and superior cerebellar cistern width with gestational age. The horizontal axis is gestational age and vertical axis is the width of cerebellomedullary cistern and superior cerebellar cistern. The width of cerebellomedullary cistern and superior cerebellar cistern had no relationship with gestational age. (A) Cerebellomedullary cistern width against gestational age; (B) superior cerebellar cistern width against gestational age.

develop on the smooth cerebellar plate and the nodulus of the cerebellum is pushed anteriorly to indent the inferior aspect of the fourth ventricle.[9] Between GW 20 to 31, the surface of cerebellum undergoes marked structural changes.[10] 3D analytical methods have indicated that the CV increases by ~7-fold during this time, from 2.4% to 3.7%.[11] In contrast, a 4-fold increase (384%) is observed between GW 25 to 37.[12]

The vermis begins to fuse at the midline during GW 8 to 9. By the 3rd month of gestation, the midportion of the vermis and cerebellar hemispheres begin to proliferate more rapidly compared with the rest of the cerebellum, causing central swelling. The vermian growth is soon overtaken by growth of the cerebellar hemispheres, and a significant portion of the vermis is engulfed by the hemispheric bulges.

The rate of cerebellar development varies as a function of the region.[13] Antenatal assessment of the gross features of cerebellar development is routinely performed using ultrasound. Ultrasound is able to provide real time images at relatively low cost; however, its use is limited due to low resolution of space and organization. Obesity, oligoamnios, excessive gas, and pelvic block can influence the resolution. Some CNS malformations may be better defined using MRI. MRI enables viewing the developing brain in more detail, and MR images of the human cerebellum in the immediate postnatal period through to adulthood has been well described.[9,14,15] As developing cerebellar structures are very small, their detection by MRI lags behind histological proof.

A number of studies have investigated the normal fetal cerebellum to provide reference values using ultrasound. A Brazilian study of 3862 pregnant women reported that the mean cistern manga (CM) length ranged from 4.29±0.93 mm at 1 to 24 weeks to 5.58±1.23 mm at 24 to 30 weeks of pregnancy.[16] Of note, the equation for predicting fetal CV among people from Taiwan living in Brazil exhibited lower accuracy compared with the indigenous Brazilian population, which may be due to the strong ethnical differences between the two populations.[17]

Serhatlioglu et al[18] investigated 130 normal fetuses at GW 16 to 38 using transabdominal sonography to provide the reference value for CM. A Dutch study of 27 fetuses at GW 20 to 40 was used to generate a nonlinear growth curve of CV in normal pregnancy. The 2-week cerebellar growth decreased from +51% at GW 20 to a +16% at GW 38.[19] A Japanese study investigated 150 normal fetuses at GW 14 to 36 and 26 cases of trisomy 18 to provide reference values for cerebellar APD.[20] An Israeli study analyzed 215 normal fetal MR images to generate an abnormal biometry curve of each parameter against gestational age.[21]

Table 3

Sex distribution of cerebellar parameters.

	Male (n=43)	Female (n=49)	*t*	*P*
Vermis SID (mm)	18.17±3.41	19.22±4.28	−1.285	.202
Vermis APD (mm)*	15.06±2.92	16.58±3.92	−2.088	.040
Vermis area (mm)	232.87±76.86	263.89±100.55	−1.645	.098
CW on axial (mm)	37.95±8.18	39.59±8.13	−0.964	.338
CW on coronal (mm)	38.07±8.00	39.35±8.18	−0.759	.450
CV on sagittal (mm)	8499.01±4440.17	9357.22±4228.49	−0.949	.345
CV on axial (mm)	8068.86±4203.15	9205.47±4509.74	−1.245	.216
CV on coronal (mm)	8235.83±4236.63	9305.28±4491.30	−1.170	.245
Cerebellomedullary cistern width (mm)*	5.47±1.97	4.64±1.79	2.109	.038
Superior cerebellar cistern width (mm)	2.43±0.96	2.28±0.85	0.801	.425

In this table, vermis width and cerebellomedullary cistern width showed sex difference. All the parameters of male were smaller than female except cerebellomedullary cistern width.
APD=anterio-posterior diameter, CV=cerebellar volume, CW=cerebellar width, SID=supero-inferior diameter.
* $P<.05$.

A retrospective study used three different imaging modalities to measure vermis biometry: 2D ultrasound, 3D ultrasound, and MR imaging. For all 4 biometric parameters, the lowest results were obtained using MRI, while the highest results were measured using 3D ultrasound.[22] Xi et al[23] compared 64 normal and abnormal fetuses at GW 13 to 38. Significant differences were observed in vermis length, inferior vermian distance, and correlation with predicted values based on neurologic outcome. A short, raised vermis length discrepancy 4 mm or an inferior vermian distance 4 mm is associated with abnormal neurologic, syndromic, and developmental outcomes.

In a postmortem study, Liu et al[6] in scanned 40 fetuses of postmortem that had no morphological brain disorder at GW 14 to 22 using 7.0 T MRI to access cerebellar development. The association of gestational age with CV, SID, and APD of the vermis were described using second-order polynomial regression curves. Some Chinese studies have investigated fetal cerebellar values using MRI or other modalities in larger study population,[24–27] and results indicated that SID, APD, vermis area, and CV are associated with GW. However, these studies had no clear enrollment criteria to define the normal fetal brain and did not follow up to access development milestones. A lack of abnormal findings during scanning does not guarantee normal development after birth. In contrast, Chen et al[28] provided a number of parameters for cerebral and cerebellar assessments, as well as prognostic equations; however, that study was not published in English.

Only few studies have compared fetal brain structure according to sex and the results of those that have are controversial. Some studies did not show sex difference of cerebral parameters.[29,30] UK study did not show sex difference of CV by using MR.[31]

The widths of the superior cerebellar cistern and cerebellomedullary cistern were not found to be associated with gestational age. There is no standard normal value for the width of superior cerebellar cistern. Previous studies[32] have suggested that the width of cerebellomedullary cistern is associated with gestational age; however, other studies have reported the opposite.[18,33,34] Enlarged retrocerebellar fluid space, defined as the anteroposterior diameter of the retrocerebellar fluid space exceeding 10 mm, is usually diagnosed on the transverse plane of a routine sonographic examination.[35] Such an enlarged space may be associated with normal cerebellar biometry or abnormal anatomy of a free communication with the fourth ventricle.[3] If no free communication with the fourth ventricle is observed, other potential causes should be considered and completed by a midsagittal plane of ultrasound or MRI scan should be performed.[36] In our study, the median width of cerebellomedullary cistern was 5.0 ± 1.9 mm and was not correlated with gestational age. Some studies have suggested that indicated the width of the cerebellomedullary cistern may be larger in male compared with female fetuses,[32,37] and this is consistent with the results of the present study.

To the best of our knowledge, no previous Chinese study published in English have reported normal values for fetal cerebellar parameters and compared sex differences. We herein defined normal fetal brain using criteria; fetuses must appear normal during scanning and neonates must develop normally until 1 year after birth. These parameters help to decrease the selective bias. However, there are some limitations of this study. First, compared with other studies, sample size is not large enough. Secondly, we did not indicate the qualifications of the different investigators measuring the structures. Lastly, some developmental abnormality may need longer observational period. We are looking forward to performing future studies with larger sample sizes.

5. Conclusion

The results of our study demonstrated that, in Chinese fetal fetuses, the SID, APD, vermis area, CW, and CV are associated with gestational age. The superior cerebellar cistern width and the cerebellomedullary cistern width may not be associated with gestational age. To the best of our knowledge, this is the first study in China to report normal values for fetal cerebellar parameters published in English.

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