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ORIGINAL ARTICLE

3D evaluation of fetal brain structures: reference values and growth curves

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ABSTRACT

Background: The development of the fetal central nervous system is one of the most important fields of research in perinatology. Since the early 1980s, 3 D ultrasound has become one of the major research tools in obstetrics and gynecology.

Objective: The aim of this study was to reconstruct thalamus, cerebellum and Cortex volumes of fetal brain and generate, for these volumes, growth curves related to gestational age.

Methods: We enrolled 344 pregnant women. Using "Tomographic Ultrasound Imaging" (TUI), in all cases we obtained a satisfying 3 D acquisition of fetal brain. We reconstructed offline thalamus, cerebellum and cortex volumes using "Virtual Organ Computer-Aided AnaLysis" (VOCAL) or 4 D View (GE Healthcare).

Results: Among the 344 fetuses examined, we obtained 314 thalamus volumes, 252 cerebellum volumes and 261 cortex volumes and we constructed the reference growth curves.

Conclusion: Our study confirms the reliability of cerebral volumes evaluation using 3 D technology and how these cerebral structures grow through gestation.

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KEYWORDS
Cerebellum; cortex; thalami; TUI; VOCAL

Introduction

Fetal central nervous system (CNS) development is one of the most important fields of research in perinatology. Since the early 1980s, neurosonography with 2 D ultrasound has become a research tool in obstetrics and gynecology, but is has not been incorporated into routine fetal anomaly scanning in most centers [1,2]. Several studies have shown that 3 D ultrasonographic volume evaluation is accurate with an excellent intraobserver and interobserver reliability [3]. Furthermore, previous studies have shown that these volumes can also be used to estimate gestational age [4,5]. Finally, the superiority of 3 D ultrasonography over standard 2 D scanning in the diagnosis of fetal anomalies has been reported [3,6].

The most important fetal CNS structures, such as the thalamus, cerebellum and cortex are of special interest for investigation. Cerebellum is involved in a wide variety of functions such as the control of body movements and in neurocognitive functions [7]. Cerebellar lesions are indeed associated with "cerebellar cognitive affective syndrome" described by Shmahmann [8]. The clinical interest for cerebellum developmental sequence is related to neuropsychiatric disorders, like autism and schizophrenia, which include cerebellar pathologies as part of their phenotype [7]. Thalami nuclei are important for a wide range of sensorimotor and neuropsychic functions as shown in thalamic vascular accidents [9]. Moreover, the disorders in thalamic development and volume are implicated in complex psychiatric syndromes and autism [10]. Previous ultrasound studies of the brain cortex evaluated few cases and never tried to create a model of volumetric growth curves [1–10]. Given the importance of these fetal neurological structures, the aim of this study is to realize the growth volumes curves for thalamus, cerebellum and fetal cortex, and evaluate the correlation between volumetric parameters and gestational age.

Materials and methods

A total of 344 pregnant women attending our diagnostic center (European Medical and Research Center – CEMER) and the Prenatal Medicine Center Hospital in Perugia for routine anatomical scan (20–22 weeks) were included in this prospective observational study and periodically investigated until 39 weeks. All cases were singleton pregnancies. Informed consent was obtained from each patient. All cases included in the

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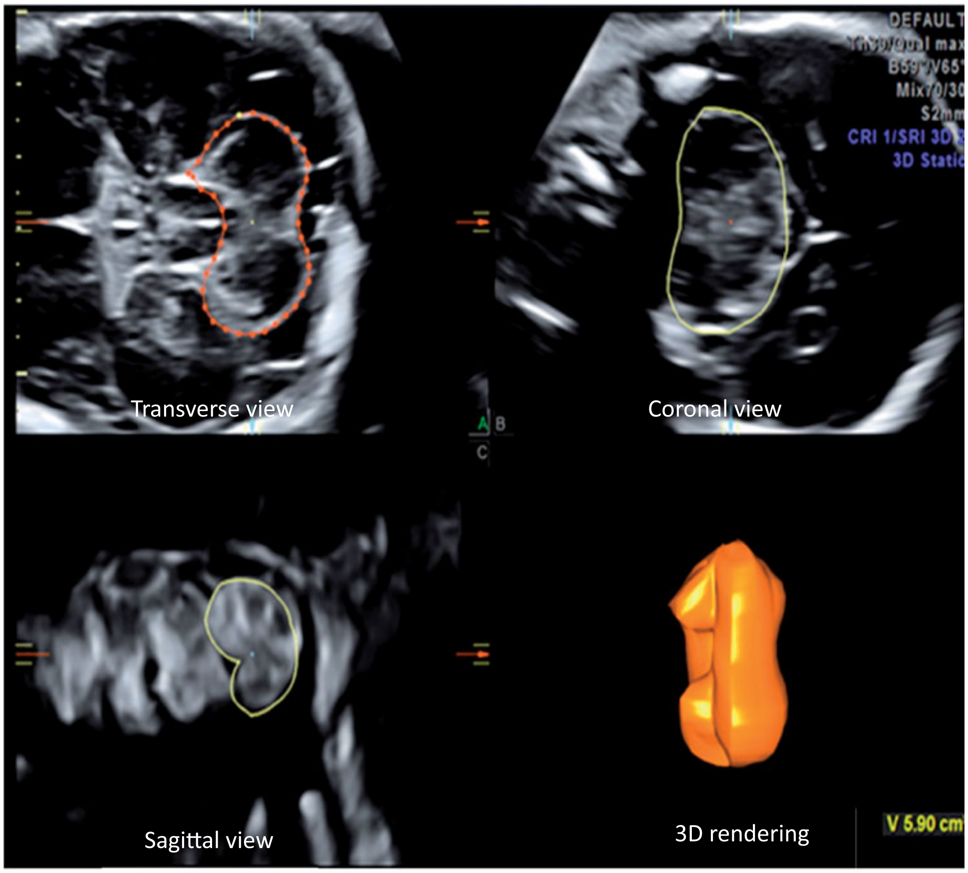

Figure 1. Multi-planar view of the cerebellum: axial (as working plane), coronal and sagittal views and rendering of cerebellum volume expressed in cm^3.

study had a normal fetal brain anatomy and this was confirmed after birth. Only cases without significant abnormal findings in a routine fetal anomaly scan were included in this study. All pregnancies enrolled were correctly dated during the first trimester, by ultrasound. We excluded from the study all the patients for whom it was impossible to obtain a satisfactory 3 D volume capture of the fetal head because of fetal position or maternal habitus.

Ultrasound and sampling techniques

All patients were scanned by two of the authors as trainer operators (GB, GC) using a GE Voluson E10-E6 ultrasound machine with 4–8 MHz curvilinear probe. Brain volumes were stored on a digital device for further analysis. All volumes were acquired in axial view using the "Tomographic Ultrasound Imaging" (TUI) method. The volume sample box was adjusted to include the complete fetal head and no magnification was used by zooming, but only adjusting depth. The angle volume was set at 80° and the highest quality acquisition was chosen. Brain volumes were acquired from each patient, at level of BPD plane. In many cases, this acquisition of volumes allowed the sampling of the thalamus, cerebellum and hemi-cortex. In some cases, to avoid ultrasound shadowing of the petrous process and to obtain a clear image of cerebellum, a second volume data acquisition was necessary. This second acquisition was obtained from the same axial plane tilting the transducer of 15°–20° downward. Fetal volumes were acquired in absence of maternal and fetal movements. The multiplanar acquisition process was repeated until the established criteria were satisfied. Tilting the transducer downward from the transthalamic view made the following parts be visible: midline, both choroid plexus, lateral ventricles, III ventricle, thalami, interhemispheric fissure, distal hemi-cortex, posterior fossa with cerebellar hemispheres, vermis, IV ventricle, cisterna magna and cerebellar peduncles.

Volume calculation was performed by a single operator using the "Virtual Organ Computer-aided Analysis" (VOCAL of GE Healthcare) or using the same application included in the 4 D View software (GE Healthcare) for personal computer. As used in previous studies, we chose a rotation step of 30° obtaining 6 images of reconstruction volume. The rotation process,

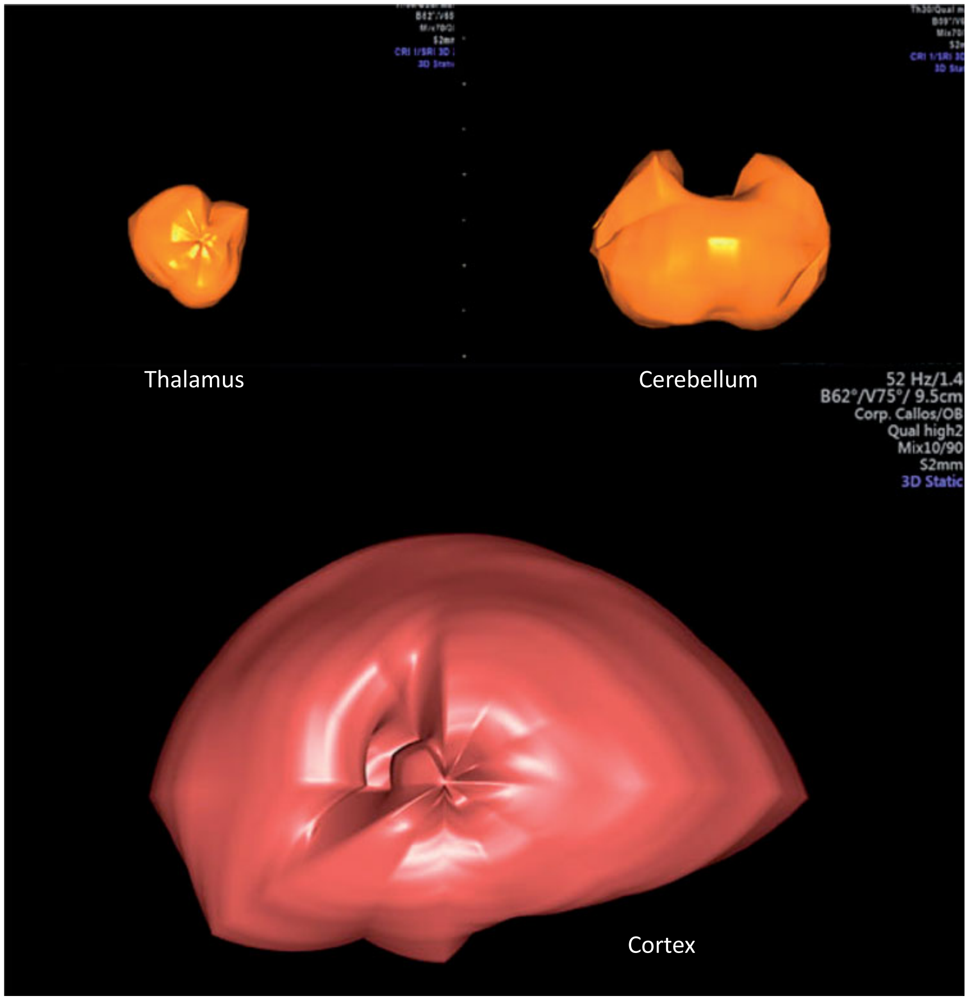

Figure 2. Rendering of cerebellum, thalamic and cortex volumes expressed in cm^3.

necessary to evaluate the volume, was started in an axial view, 0° of rotation, and finished in the same plane at 180° of rotation. In the middle (90° of rotation) we were able to obtain a coronal view of the structures. Because of the shadowing of the fetal skull at the ultrasound examination of the proximal structures, we evaluated the distal brain structures. In relation with the fetal position, we were able to evaluate the right-side brain structures in about half of cases and the left side ones in the other cases, finding not statistically significant differences in the detected volumes. Outlining the contours of the thalamus and cerebellum on six reconstruction planes we obtained a "Region Of Interest" ROI and thus a rendering with a volume expressed in cm^3 (Figures 1 and 2). The same process was realized for hemi-cortex (Figure 2). For the reasons described above, we evaluated the distal hemi-cortex that was easily recognizable. In some patients, for whom it was possible, we detected both hemi-cortex and, observing that there were not significant differences between the two hemi-cortex volumes, we calculated the global cortex volume doubling the volume of a single hemi-cortex.

Statistical analysis

Statistical analysis was performed using SPSS software. We created specific growth curves for thalamus, cerebellum, hemi-cortex and total cortex volumes. Given the inhomogeneity of the sample related to the gestational ages, we plotted the growth percentiles considered (5°, 25°, 50°, 75°, 95°) with nine classes of gestational age (class 1, $21+0$; class 2, $21+1–21^{+2}$; class 3, $21+3–21^{+6}$; class 4, $21+6–22^{+3}$; class 5, $22+4–25^{+5}$; class 6, $25+6–27^{+0}$, class 7, $27+1–29^{+6}$; class 8, $30+0–33^{+1}$; class 9, $33+2–38^{+5}$). We used smoothing techniques and a second polynomial equation for the data processing. The number of the cases for each class were respectively: class 1:36 cases; class 2:48 cases; class 3:34 cases; class 4:38 cases; class 5:37 cases; class 6:41 cases; class 7:35 cases; class 8:40 cases; class 9:35 cases.

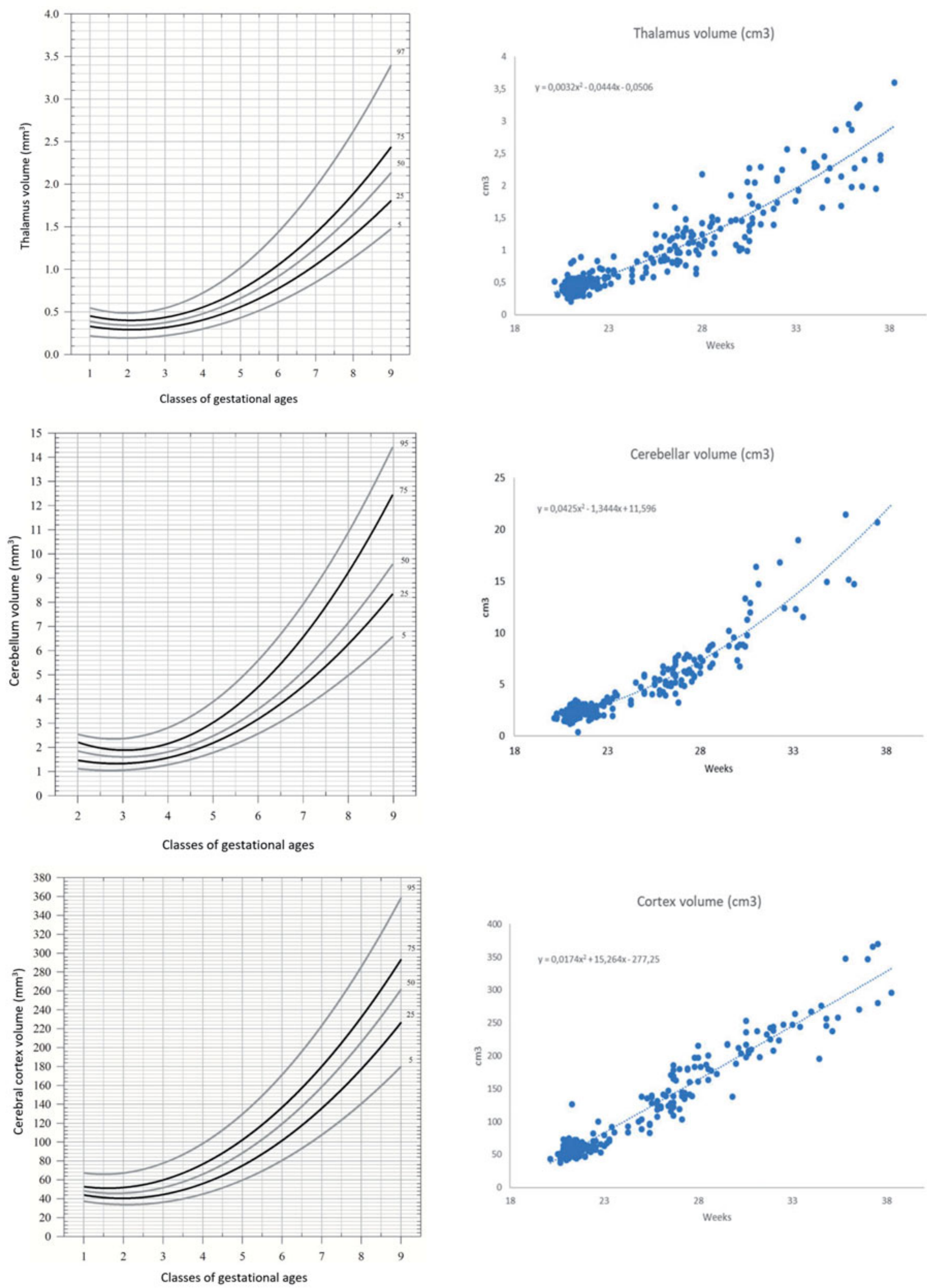

Figure 3. Thalamic, cerebellum and cortex volume growth curves and the dispersion data with polynomial equation (class 1, 21^{+0}; class 2, 21^{+1}–21^{+2}; class 3, 21^{+3}–21^{+6}; class 4, 21^{+6}–22^{+3}; class 5, 22^{+4}–25^{+5}; class 6, 25^{+6}–27^{+0}; class 7, 27^{+1}–29^{+6}; class 8, 30^{+0}–33^{+1}; class 9, 33^{+2}–38^{+5}).

Results

Of the 344 fetuses enrolled in the study, we obtained 314 thalami volumes, 252 cerebellum volumes and 261 Cortex volume. The growth curves and the dispersion data with each polynomial equation for the thalami, cerebellum and cortex volumes are shown in Figure 3. The following are the data with the reference limits for the cerebral structures examined:

Thalamus

Classes	5°	25°	50°	75°	95°
1	0.23850	0.40200	0.44800	0.50400	0.68050
2	0.28940	0.37250	0.42800	0.50800	0.56160
3	0.31855	0.38875	0.43500	0.50000	0.67980
4	0.30440	0.41250	0.48500	0.54225	0.65625
5	0.41045	0.47925	0.58500	0.69775	0.91740
6	0.65100	0.83100	0.97400	1.07000	1.66600
7	0.67285	0.97225	1.17500	1.33500	1.87850
8	0.98180	1.20000	1.45500	1.79000	2.27600
9	1.67200	1.99000	2.31000	2.56100	3.64800

Cerebellum

Classes	5°	25°	50°	75°	95°
2	1.31400	1.94000	2.20000	2.58400	2.91800
3	1.61100	1.98000	2.19000	2.41000	3.09900
4	0.98280	1.95075	2.27500	2.82750	3.15300
5	1.62600	2.22000	2.49000	2.76500	3.08440
6	1.87400	2.55000	3.12000	3.95400	5.83800
7	3.96950	4.83250	5.24000	6.40000	7.42850
8	1.95660	5.69000	6.40000	7.48000	8.56800
9	3.50000	8.03500	8.84500	11.77500	16.31550

Cortex

Classes	5°	25°	50°	75°	95°
1	41.6760	49.6600	53.7600	58.3600	72.2560
2	45.6400	52.2600	55.3600	61.3900	79.4320
3	43.9120	51.7600	58.3600	63.0800	72.3560
4	46.9600	55.1200	58.9000	62.7200	68.0720
5	53.1980	62.1300	70.2400	90.0700	127.1420
6	71.1640	117.8200	128.3600	141.2200	180.9760
7	107.3150	139.4100	163.1000	182.8050	211.2900
8	78.0420	197.5900	209.4200	233.7500	250.3240
9	189.2840	244.3400	260.9400	291.8950	369.6100

Discussion

Our growth curves, constructed using percentiles of fetal growth, confirm the reliability of 3 D ultrasonography in evaluating cerebral volumes and the growth of these structures through gestation [9,11,12]. Previous studies had realized growth curves of fetal brain structures using MRI [13]. Our study is the first using ultrasound technique with, to our knowledge, the largest number of cases ever enrolled. The absence of the 10th class for the curves can be explained by the difficulties of sampling these cerebral structures, due to the shadow of the petrous process and the unfavorable fetal positions at later gestational ages.

In conclusion, our study suggests that it's possible to obtain fetal cerebral structures volumetric growth curves by 3 D ultrasound examination investigating fetuses at a gestational age between 20 and 39 weeks. The use of tissue volumes for the construction of growth curves could add important information to the biometric 2 D curve. For the future it would be interesting to continue sampling the thalamic, cortex and cerebellar volumes by increasing samples and including in the study IUGR cases and/or diabetes cases for the known variations of fetal growth in these pathologies.

Disclosure statement

No potential conflict of interest was reported by the authors.

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References

[1] Correa FF, Lara C, Bellver J, et al. Examination of the fetal brain by transabdominal three-dimensional ultrasound: potential for routine neurosonographic studies. Ultrasound Obstet Gynecol. 2006;27(5):503–508.
[2] Tonni G, Martins WP, Guimarães Filho H, et al. Role of 3-D ultrasound in clinical obstetric practice: evolution over 20 years. Ultrasound Med Biol. 2015;41(5):1180–1211.
[3] Endres LK, Cohen L. Reliability and validity of three-dimensional fetal brain volumes. J Ultrasound Med. 2001;20(12):1265–1269.
[4] Roelfsema NM, Hop WC, Boito SM, et al. Three-dimensional sonographic measurement of normal fetal brain volume during the second half of pregnancy. Am J Obstet Gynecol. 2004;190(1):275–280.
[5] Caetano AC, Zamarian AC, Araujo Júnior E, et al. Assessment of intracranial structure volumes in fetuses with growth restriction by 3-dimensional sonography using the extended imaging Virtual Organ Computer-Aided Analysis method. J Ultrasound Med. 2015;34(8):1397–1405.
[6] Pavlova E, Markov D, Ivanov S. Three-dimensional (3D) ultrasound in evaluation of fetal brain anatomy. Akush Ginekol (Sofiia). 2014;53(2):11–17.
[7] Allin MP. Novel insights from quantitative imaging of the developing cerebellum. Semin Fetal Neonat Med. 2016;21(5):333–338. 26 Jun.
[8] Schmahmann JD. Disorders of the cerebellum: ataxia, dysmetria of thought, and the cerebellar cognitive affective syndrome. JNP. 2004;16(3):367–378.
[9] Sotiriadis A, Dimitrakopoulos I, Eleftheriades M, et al. Thalamic volume measurement in normal fetuses using

three-dimensional sonography. J Clin Ultrasound. 2012; 40(4):207–213.
[10] Tamura R, Kitamura H, Endo T, et al. Reduced thalamic volume observed across different subgroups of autism spectrum disorders. Psychiatry Res. 2010;184(3):186–188.
[11] Chang CH, Chang FM, Yu CH, et al. Assessment of fetal cerebellar volume using three-dimensional ultrasound. Ultrasound Med Biol. 2000;26(6):981–988.
[12] Araujo E, Pires CR, Nardozza LMM, et al. Correlation of the fetal cerebellar volume with other fetal growth indices by three-dimensional ultrasound. J Matern Fetal Neonatal Med. 2007;20(8):581–587.
[13] Kyriakopoulou V, Vatansever D, Davidson A, et al. Normative biometry of the fetal brain using magnetic resonance imaging. Brain Struct Funct. 2017;222(5): 2295–2307.