Short communication

Morphological features and length measurements of fetal lateral ventricles at 16–25 weeks of gestation by magnetic resonance imaging

First author's surname: Taketani

Short title: **Morphology of fetal lateral ventricles**

Kaori Taketani[1], Shigehito Yamada[1,2], Chigako Uwabe[2], Tomohisa Okada[3], Kaori Togashi[3], Tetsuya Takakuwa[1]

[1]Human Health Science, [2]Congenital Anomaly Research Center, & [3]Diagnostic Imaging and Nuclear Medicine, Graduate School of Medicine, Kyoto University

Corresponding author: Dr. Tetsuya Takakuwa

Human Health Science, Graduate School of Medicine, Kyoto University

606-8507 Sakyo-ku Shogoin Kawahara-cyo 53, Kyoto, Japan

E-mail: tez@hs.med.kyoto-u.ac.jp

Tel/Fax: +81-75-751-3931

Abstract

Normal growth of the lateral ventricles (LVs) was characterized three-dimensionally using magnetic resonance imaging (MRI) data from 16 human fetuses at 16–25 weeks of gestation. The LV was differentiated into 4 primary regions, the anterior horn, central parts, posterior horn, and inferior horn, at 16 weeks of gestation. The LV changed shape mainly by elongation and narrowing, which correspond to the external and internal growth of the surrounding cerebrum. Six length parameters measured in the LV correlated with biparietal diameter by simple regression analysis (R^2 range, 0.56–0.93), which may be valuable for establishing a standardized prenatal protocol to assess fetal well-being and development across intrauterine periods. No correlation was found between biparietal diameter and LV volume (R^2=0.13).

Keywords

Fetal lateral ventricles, morphology, magnetic resonance imaging, three-dimensional reconstruction, length measurements

Introduction

Imaging over intrauterine periods is important for prenatal diagnosis and care. Growth and differentiation of the brain are particularly important issues. Sonography is convenient and low-risk compared to other imaging methods such as magnetic resonance imaging (MRI) and computed tomography. Sonography has additional advantages as a morphometric tool. Many morphometric parameters have been proposed for structural screening of the entire fetal body using sonography. Crown-rump length, abdominal diameter or circumference, nuchal translucency, femur length, and biparietal diameter (BPD) should be determined in the fetus from 10–11 weeks of gestation (Blaas 2014). Among these, BPD is a representative parameter for estimating brain development.

The lateral ventricles (LVs) are among the most easily detectable structures in the fetal brain using sonography. In fact, LVs serve as an anatomical reference to locate the fetal brain and to determine transverse sections in the very early stages of pregnancy. LV widening, narrowing, deviations, or change in intensity may be signs of serious abnormalities in the production and/or flow of cerebral fluids, such as hydrocephalus, brain tumors, and intracranial hemorrhage (Wyldes and Watkinson 2002; Blaas 2014; Blaas and Eik-Nes 2009).

The advent of sonography and MRI has enabled more detailed study of LV morphology, which is potentially useful for prenatal diagnosis (Bulas 2007; Pooh and Kurjak 2011; Glenn 2009; Hata et al. 2011; Girard and Chaumoitre 2012; Li et al. 2011). It is essential to be aware of LV morphological features and their changes during the fetal period and to define the normal limits of ventricular measurements. Ventricular measurement can potentially aid in estimating the growth and regional differentiation of the fetal cerebrum, as LV morphology is influenced by cerebrum growth. The present study thus aimed to identify the features of LVs during the second trimester, and to estimate the morphometric measurements for LVs indicating the growth and regional development of the cerebrum, which may be convenient and clinically relevant indicators of fetal well-being in prenatal care.

Materials and Methods

Approximately 44,000 human embryos and fetuses, comprising the "Kyoto collection," are stored at the Congenital Anomaly Research Center of Kyoto University (Nishimura et al. 1968; Shiota 1991; Yamada et al. 2004). In most cases, pregnancy was terminated for socioeconomic reasons, under the Maternity Protection Law of Japan. Sixteen fetuses at 16–25 weeks of gestation that were diagnosed as externally normal were analyzed in the present study. The samples with apparent deformity and brain shrinkage were excluded from the analysis because prolonged fixation is known to cause MRI artifacts and tissue shrinkage due to dehydration (van Duijn et al. 2011). Body weights and BPD ranged from 80.6–740.0 g and 30.2–59.5 mm, respectively. MRI data from fetuses were acquired from the Kyoto University Hospital (Kyoto, Japan) as DICOM formatted files. The conditions used for data acquisition have been described elsewhere (Hamabe et al. 2013).

Three-dimensional (3D) LV images were reconstructed and assessed morphologically. LV length and volume were then measured with OsiriX™ software (version 3.9, Pixmeo SARL, Geneva, Switzerland). The LVs were divided into four parts: anterior horn, central part, posterior horn, and inferior horn. The formation of each part was influenced by the growth and differentiation of cerebrum regions including frontal lobe, corpus callosum, basal ganglia, thalamus, occipital lobe, and temporal lobe (Fig. 1A). The following lengths indicating the elongation and narrowing of the ventricles were measured: L_{TAP} (total anterior-posterior length), L_{APP} (width between anterior and posterior parts), L_{PH} (length of the posterior horn), L_{HCP}

(intraventricular height at the central part), L_{CI} (length between the central part and inferior horn), and L_{BIH} (width between the bilateral inferior horns) (Fig. 1B).

Simple regression analysis was performed between BPD and the measured lengths. This study was approved by the Committee of Medical Ethics of Kyoto University Graduate School of Medicine, Kyoto, Japan (E986).

Results and Discussion

LV morphology

A 3D image of the LV was reconstructed in all 16 fetuses (Fig. 2). A previous study demonstrated that at the end of the embryonic stage (Carnegie stage 23), the LV formed a simple crescent shape (Shiraishi et al. 2013). At 16 weeks of gestation (BPD = 31.1 mm in Fig. 2a), the LV differentiated into 4 regions in its primary form: anterior horn, central parts, posterior horn, and inferior horn. The three horns were short in length. The ventricle was broad, and narrowing and flattening was not evident. The LV changed in shape mainly by elongation and narrowing, which correspond to the external and internal growth of the surrounding cerebrum.

Growth of the posterior parts of the LV was evident in the posterior and caudal directions. The projections of the posterior and inferior horns elongated over time. The inferior horn elongated caudally and then anteriorly on lateral view, while it elongated laterally on anterior view (arrow in Fig.2b-d). The formation of the inferior horn was notable in that the tip elongated toward the medial direction over the gestational period we observed. A previous paper described that elongation toward the medial direction occurring at a later stage (Corliss 1976). The posterior horn elongated posteriorly but remain broad during the period under observation (asterisk in Fig.2d). The narrowing of the posterior horn may start at a later stage compared to the anterior horn, inferior horn, and central parts.

Length and volume measurement

The results of simple regression analysis (slope and R^2) and distribution of the measured data for the present study are summarized in Table 1 and Fig. 3.

The length parameters measured in LVs correlated with BPD (R^2=0.89 for L_{TAP}, 0.80 for L_{APP}, 0.56 for L_{CI}, 0.82 for L_{HCP}, 0.93 for L_{PH}, 0.78 for L_{BIH}; Fig. 3). L_{PH} (R^2=0.93) may correspond to the growth of the occipital lobe. L_{HCP} may correspond to the growth of the corpus callosum (R^2=0.82), although the slope of the best-fit line may indicate two phases, the anterior half representing BPD < 40 cm, which was steep, and the posterior half, which was gentle (Fig. 3). Additional cases may be necessary to differentiate these periods. L_{CI} and L_{BIH} may be influenced by growth of the temporal lobe and other components such as basal ganglia, thalamus, corpus callosum, and parietal lobe. R^2 was small in these two parameters (0.56 for L_{CI}, 0.78 for L_{BIH}). In the present study, specific parameters for the anterior and temporal lobes were not proposed because anatomical reference points have not been determined for precise and reproducible measurements. Additional research using clinical data may be necessary, as the artifacts due to prolonged storage in formalin in the present study should be taken into account (van Duijn et al. 2011).

No obvious correlation was observed between BPD and LV volume in the present study (R^2=0.13; data not shown). A previous study reported that LV volume was not linearly correlated with fetal gestational week during the second trimester. Kinoshita et al. (2001) observed a linear increase of LV volume from 7 to 23 weeks of gestation, followed by a decrease until 28 weeks of gestation. Huang et al. (2009) reported that volume increased from 13 to 17 weeks of gestation and then decreased until 21 weeks of gestation. The LV becomes complicated in form, as shown in Fig. 2: it elongates, narrows, and flattens in shape. The ventricular volume increase appears not to reflect brain growth except for in embryos and early fetuses (Blaas 1998). In addition, volume measurement is not accurate when the surface area is large compared to the volume. The border between the LV and third ventricle is unclear because the interventricular foramen remains broad in the first and second trimesters. Kinoshita et al. (2001) claimed that sonography may overestimate LV volume in the embryonic and early fetal periods. Therefore, ventricular volume does not appear to a clinically useful due to its limited significance, accuracy, and convenience in comparison to length (one-dimensional data), which appears preferable for clinical applications.

Non-human primates, macaques (Fukunishi et al. 2011) and common marmosets (Hikishima et al. 2013), showed similar developmental changes in the volume and morphology of the lateral ventricle. These studies suggested a linkage between the decrease in the LV volume during fetal periods and explosive neurogenesis and astrogenesis, and the development of the calcarine sulcus. The length measurements in the present study may be worth applying to the evaluation of brain development in non-human primates.

The sophisticated sonographic and MRI techniques have enabled more detailed study of the morphology of LVs, including 3D morphology and cerebrospinal fluid flow (Scott et al. 2013; Mailath-Pokorny et al. 2012; Pooh 2012a, 2012b; Pooh and Kurjak 2011; Girard 2012; Studholme 2011; Gholipour et al. 2012). These images are beautiful, comprehensive and helpful for prenatal diagnosis. However, efficient fetal sonographic examination should be carried out using a standardized protocol for anatomical structures, which take into account the size and developmental stage of the fetus (Blaas 2014). Length measurement is necessary for prenatal diagnosis and monitoring of the fetal cerebrum to 1) establish criteria for systemic screening, 2) distinguish abnormal from normal morphology, and 3) evaluate relevant structures without the use of specialized machines. In these regards, LV morphological features and changes and the length measurements presented in this study may be valuable to establishing a standardized prenatal protocol to assess fetal well-being and development across intrauterine periods.

Acknowledgements

This study was supported by grants #22591199, #24119002, #24790195 and #25461642 from the Japan Society for the Promotion of Science.

Disclosures

None

References

Blaas HG. 2014. Detection of structural abnormalities in the first trimester using ultrasound. Best Pract Res Clin Obstet Gynaecol 28:341-353.

Blaas HG, Eik-Nes SH. 2009. Sonoembryology and early prenatal diagnosis of neural anomalies. Prenat Diagn 29:312-325.

Blaas HG, Eik-Nes SH, Berg S, Torp H. 1998. In-vivo three-dimensional ultrasound reconstructions of embryos and early fetuses. Lancet 352:1182-1186.

Bulas D. 2007. Fetal magnetic resonance imaging as a complement to fetal ultrasonography. Ultrasound Q 23:3-22.

Corliss CE. 1976 The nervous system. In: Corliss CE, editor. Patterns Human Embryology. New York: A Blakiston Publication. p 199-235.

Fukunishi K, Sawada K, Kashima M, Saito S, Sakata-Haga H, Sukamoto T, Aoki I, Fukui Y. 2011. Correlation between formation of the calcarine sulcus and morphological maturation of the lateral ventricle in cynomolgus monkey fetuses. Acta Neurobiol Exp (Wars) 71:381-386.

Gholipour A, Akhondi-Asl A, Estroff JA, Warfield SK. 2012. Multi-atlas multi-shape segmentation of fetal brain MRI for volumetric and morphometric analysis of ventriculomegaly. Neuroimage 60:1819-1831.

Girard NJ, Chaumoitre K. 2012. The brain in the belly: what and how of fetal neuroimaging? J Magn Reson Imaging 36:788-804.

Glenn OA. 2009. Normal development of the fetal brain by MRI. Semin Perinatol 33:208-219.

Hamabe Y, Hirose A, Yamada S, Uwabe C, Okada T, Togashi K, Kose K, Takakuwa T. 2013. Morphology and morphometry of fetal liver at 16-26 weeks of gestation by magnetic resonance imaging: Comparison with embryonic liver at Carnegie stage 23. Hepatol Res 43:639-647.

Hata T, Mori N, Tenkumo C, Hanaoka U, Kanenishi K, Tanaka H. 2011. Three-dimensional volume-rendered imaging of normal and abnormal fetal fluid-filled structures using inversion mode. J Obstet Gynaecol Res 37:1748-1754.

Hikishima K, Sawada K, Murayama AY, Komaki Y, Kawai K, Sato N, Inoue T, Itoh T, Momoshima S, Iriki A, Okano HJ, Sasaki E, Okano H. 2013. Atlas of the developing brain of the marmoset monkey constructed using magnetic resonance histology. Neuroscience 230:102-113.

Huang H, Xue R, Zhang J, Ren T, Richards LJ, Yarowsky P, Miller MI, Mori S. 2009. Anatomical characterization of human fetal brain development with diffusion tensor magnetic resonance imaging. J Neurosci 29:4263-4273.

Kinoshita Y, Okudera T, Tsuru E, Yokota A. 2001. Volumetric analysis of the germinal matrix and lateral ventricles performed using MR images of postmortem fetuses. AJNR Am J Neuroradiol 22:382-388.

Li Y, Estroff JA, Mehta TS, Robertson RL, Robson CD, Poussaint TY, Feldman HA, Ware J, Levine D. 2011. Ultrasound and MRI of fetuses with ventriculomegaly: can cortical development be used to predict postnatal outcome? AJR Am J Roentgenol 196:1457-1467.

Mailath-Pokorny M, Kasprian G, Mitter C, Schöpf V, Nemec U, Prayer D. 2012. Magnetic resonance methods in fetal neurology. Semin Fetal Neonatal Med 17:278-284.

Nishimura H, Takano K, Tanimura T, Yasuda M. 1968. Normal and abnormal development of human embryos: first report of the analysis of 1,213 intact embryos. Teratology 1:281-290.

Pooh RK. 2012a. Neurosonoembryology by three-dimensional ultrasound. Semin Fetal Neonatal Med 17:261-268.

Pooh RK. 2012b. Normal anatomy by three-dimensional ultrasound in the second and third trimesters. Semin Fetal Neonatal Med 17:269-277.

Pooh RK, Kurjak A. 2011. 3D and 4D sonography and magnetic resonance in the assessment of normal and abnormal CNS development: alternative or complementary. J Perinat Med 39:3-13.

Scott JA, Habas PA, Rajagopalan V, Kim K, Barkovich AJ, Glenn OA, Studholme C. 2013. Volumetric and surface-based 3D MRI analyses of fetal isolated mild ventriculomegaly: brain morphometry in ventriculomegaly. Brain Struct Funct 218:645-655.

Shiota K. 1991. Development and intrauterine fate of normal and abnormal human conceptuses. Congenit Anom Kyoto 31:67-80.

Shiraishi N, Nakashima T, Yamada S, Uwabe C, Kose K, Takakuwa T. 2013. Morphogenesis of lateral choroid plexus during human embryonic period. Anat Rec (Hoboken) 296:692-700.

Studholme C. 2011. Mapping fetal brain development in utero using magnetic resonance imaging: the Big Bang of brain mapping. Annu Rev Biomed Eng 13:345-368.

van Duijn S, Nabuurs RJ, van Rooden S, Maat-Schieman ML, van Duinen SG, van Buchem MA, van der Weerd L, Natté R. 2011. MRI artifacts in human brain tissue after prolonged formalin storage. Magn Reson Med 65:1750-1758.

Wyldes M, Watkinson M. 2004. Isolated mild fetal ventriculomegaly. Arch Dis Child Fetal Neonatal Ed 89:F9-13.

Yamada S, Uwabe C, Fujii S, Shiota K. 2004. Phenotypic variability in human embryonic holoprosencephaly in the Kyoto Collection. Birth Defects Res A Clin Mol Teratol 70:495-508.

Figure legends

Figure 1 Length measurements of the lateral ventricle (LV)

(A) Illustration of the LV with the surrounding regions of the cerebrum.

(B) Illustration indicating the length parameters measured. L_{TAP}, total anterior-posterior length; L_{APP}, width between the anterior and posterior parts; L_{CI}, length between the central part and inferior horn; L_{PH}, length of the posterior horn; L_{HCP}, intraventricular height at the central part; L_{BIH}, width between the bilateral inferior horns

Figure 2 Representative three-dimensional images of the fetal lateral ventricles (LVs)

Body weights and biparietal diameter (BPD) were used as indicators of fetal growth. Arrows and arrowheads indicate the noticeable orientations of LV growth over the time course.

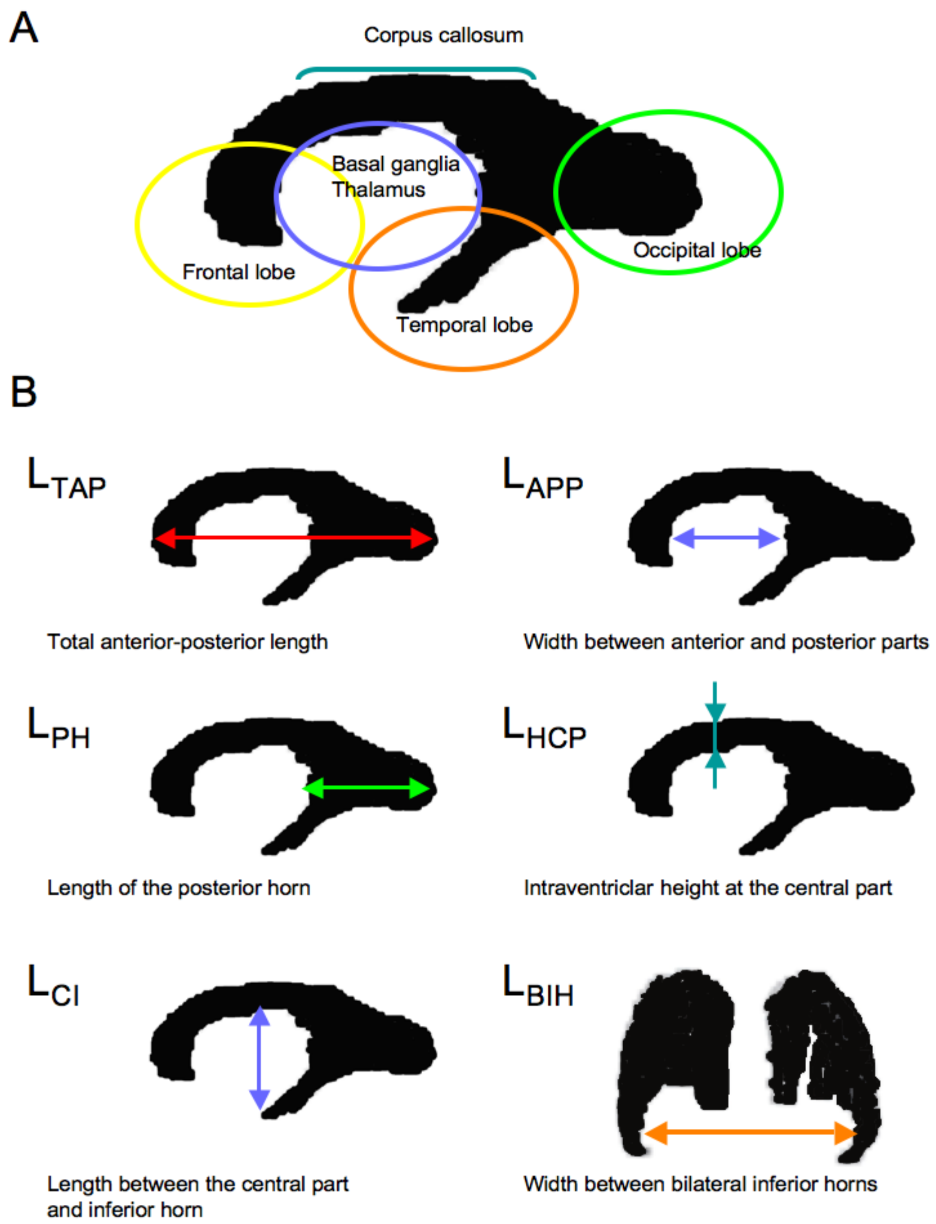
Figure 3 Simple regression diagram between biparietal diameter (BPD) and fetal lateral ventricle (LV) length measurements

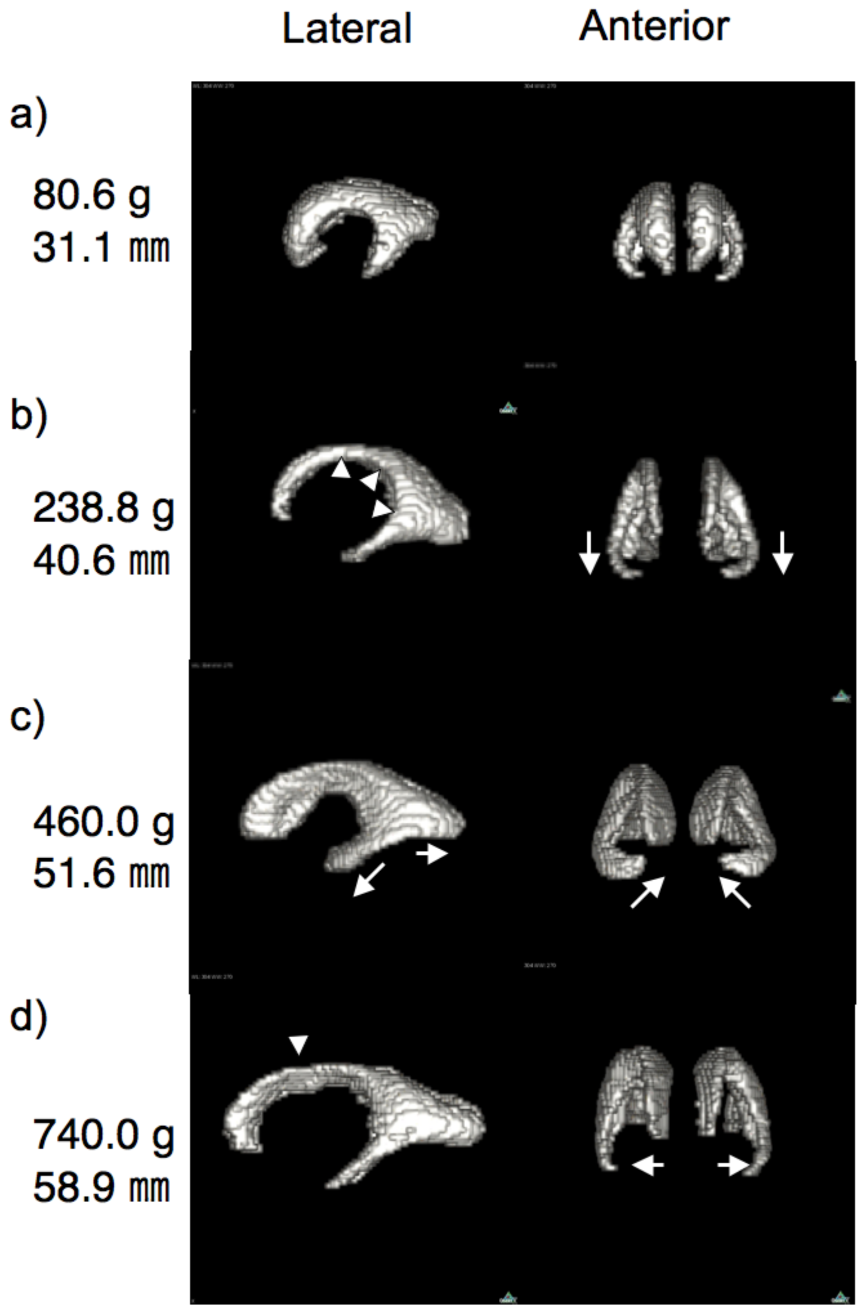
LV length measurements correlated with BPD using simple regression analysis. L_{TAP}, total anterior-posterior length; L_{APP}, width between the anterior and posterior parts; L_{CI}, length between the central part and inferior horn; L_{PH}, length of the posterior horn; L_{HCP}, intraventricular height at the central part; L_{BIH}, width between the bilateral inferior horns

Table 1 Summary of the measurements of the samples and lateral ventricles

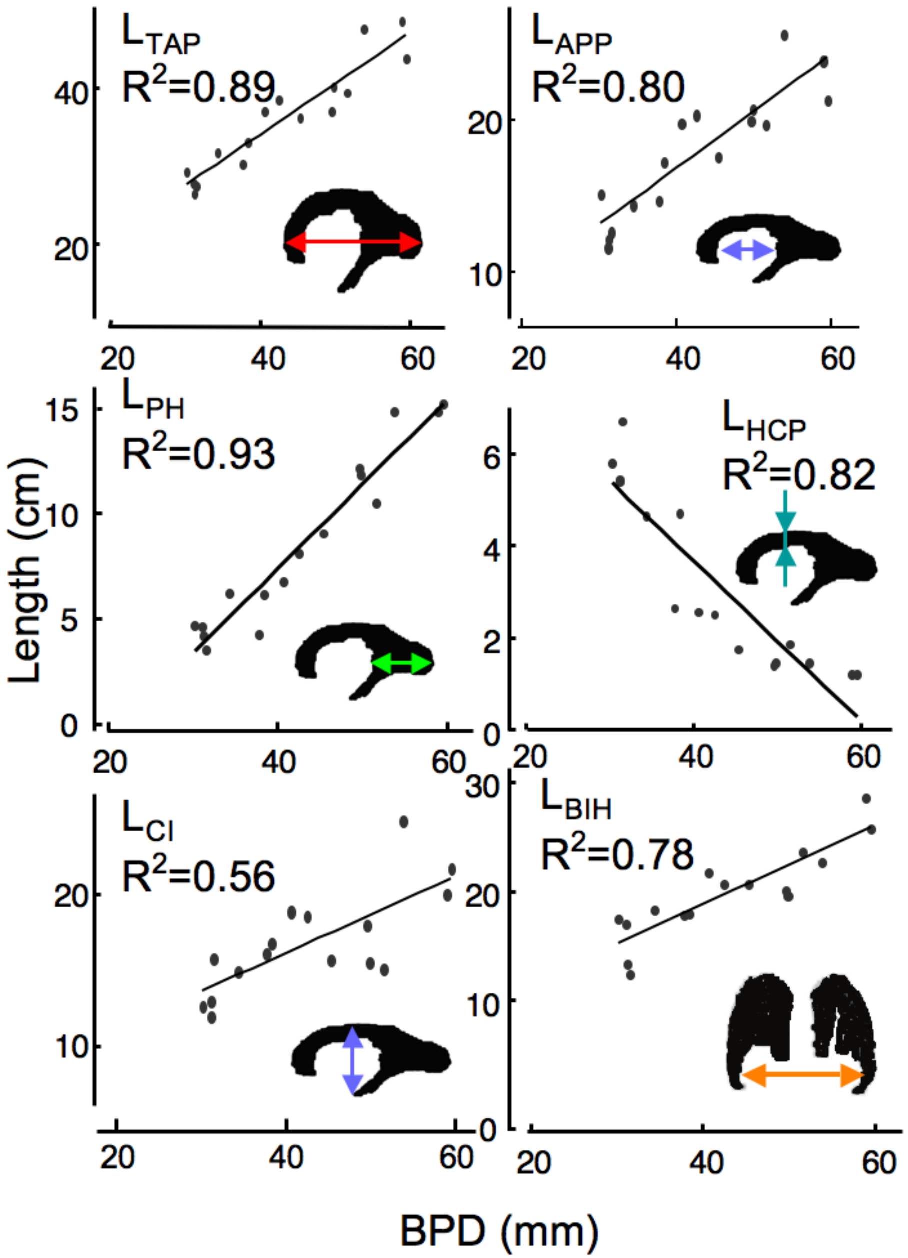
Morphometry	Simple regression analysis			Growth indicator expected
	Slope	R^2	Range	
Measurements of the samples in the present study				
BPD (mm)			30.2–59.5	whole brain
Weeks			16–25	intrauterine period
BW (g)			80.6–740.0	whole body
Measurements of the lateral ventricles				
L_{TAP} (mm)	y = 0.65x + 7.80	0.89	26.4–48.5	whole brain
L_{PH} (mm)	y = 0.40x - 8.60	0.93	3.50–15.2	occipital lobe
L_{APP} (mm)	y = 0.37x + 3.29	0.80	13.0–27.1	basal ganglia, thalamus
L_{HCP} (mm)	y = -0.17x + 10.6	0.82	1.20–6.70	corpus callosum
L_{CI} (mm)	y = 0.25x + 5.99	0.56	12.0–24.9	basal ganglia, thalamus (+temporal lobe)
L_{BIH} (mm)	y = 0.37x + 6.12	0.78	14.3–30.5	temporal lobe (+basal ganglia, thalamus)
V_{LV} (cm^3)	y = 0.012x + 0.92	0.13	0.88–1.98	whole brain

BPD, biparietal diameter; weeks, weeks of gestation; BW, body weight; L_{TAP}, total anterior-posterior length; L_{PH}, length of the posterior horn; L_{APP}, width between the anterior and posterior parts; L_{HCP}, intraventricular height at the central part; L_{CI}, length between the central part and inferior horn; L_{BIH}, width between the bilateral inferior horns; V_{LV}, lateral ventricular volume


A
Corpus callosum
Basal ganglia
Thalamus
Frontal lobe
Occipital lobe
Temporal lobe
B
L TAP
Total anterior-posterior length
L APP
Width between anterior and posterior parts
L PH
Length of the posterior horn
L HCP
Intraventriclar height at the central part
L CI
Length between the central part and inferior horn
L BIH
Width between bilateral inferior horns



Lateral
Anterior
a)
80.6 g
31.1 ㎜
b)
238.8 g
40.6 ㎜
c)
460.0 g
51.6 ㎜
d)
740.0 g
58.9 ㎜



L_TAP
R²=0.89
L_APP
R²=0.80
L_PH
R²=0.93
L_HCP
R²=0.82
L_CI
R²=0.56
L_BIH
R²=0.78
Length (cm)
BPD (mm)