A Longitudinal Comparison of Fetal Brain Development between Chimpanzees and Humans

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It is argued that the extraordinary brain enlargement observed in humans is due to not only the human-specific pattern of postnatal brain development, but also to that of prenatal brain development [1] and [2]. However, the prenatal trajectory of brain development has not been explored in chimpanzees (Pan troglodytes), even though they are our closest living relatives. To address this lack of information, we tracked fetal development of the chimpanzeebrain from approximately 14 to 34 weeks of gestation (just before birth) in utero using three-dimensional ultrasound imaging. The results were compared with those obtained for the human brain during approximately the same period. We found that the brain volume of chimpanzee fetuses was only half that of human fetuses at 16 weeks of gestation. Moreover, although the growth velocity of brain volume increased until approximately 22 weeks of gestation in both chimpanzees and humans, chimpanzee fetuses did not show the same accelerated increase in brain volume as human fetuses after that time. This suggests that maintenance of fast development of the human brain during intrauterine life has contributed to the remarkable brain enlargement observed in humans.

Earlier studies have suggested that, compared with other primates, human neonates show a more immature brain size relative to that of the adult, followed by a rapid rate of brain development after birth [1] and [2]. This has been attributed to the constraints imposed on neonate head size by the structure of the maternal pelvis [3]. But although gestational length is slightly longer in humans than in chimpanzees (human, 38 weeks; chimpanzee, 34–35 weeks) [4], human neonates do have larger brains than chimpanzee neonates [2]. It has been suggested that the extraordinary brain enlargement in humans is due to unique features in the human pattern of brain development during both the prenatal and postnatal periods [1] and [2]. It has been argued that all primates conform to a 12%

ratio of brain mass to body mass from the fetal period to birth [5] and [6], though a recent study [7] suggested that the brain of a chimpanzee neonate accounts for 10% of its body weight, whereas that of a human neonate, on average, accounts for 12.3%, an increase due to accelerated brain growth, known as encephalization, in humans.

We looked for empirical evidence for the remarkable enlargement of the human brain during the fetal period. We performed three-dimensional ultrasound imaging on two chimpanzee fetuses from approximately 14 to 34 weeks of gestation (Figure 1A and Tables S1–S4 in the Supplemental Information) and compared the results with previously estimated numerical data from human fetuses from 16 to 32 weeks of gestation [8] — up until a few weeks before birth (Tables S5 and S6; see the Supplemental Experimental Procedures for details).

The chimpanzee fetuses used in our study showed a significant age-related change in brain volume over the course of the study period (Figure 1B,C). The volume of the chimpanzeebrain increased nonlinearly from 14 to 34 weeks of gestation ($F = 634.28$; cubic effect, $p < 0.0001$) (Figure 1C). The brain volume of the chimpanzee was only half that of the human fetus at 16 weeks of gestation (15.8 cm3; Figure 1C). The estimated volume of the human brain at the same gestational age is 33.6 cm3[8]. At 32 weeks of gestation (just before birth), the volume of the chimpanzeebrain reached approximately 40.3% of the adult volume. By contrast, the corresponding value for humans was 23.4%. However, the volume of the fetal human brain appears to continue to increase after this gestational age, as the volume of the human neonatal brain is ~ 30% of the adult volume (see Supplemental Experimental Procedures for details).

Chimpanzee fetal brain growth velocity continued to increase from ~ 17 to 22 weeks of gestation (as also observed in human fetuses), although it was slower than that in human fetuses during this period. However, the velocity of brain growth in chimpanzee fetuses did not continue to increase after 22 weeks, whereas it did in human fetuses (Figure 1D). At 32 weeks of gestation, the velocity of chimpanzeebrain growth slowed down to approximately 20% of that observed in humans (Figure 1D). The estimated rate of chimpanzeebrain growth was 4.1 cm3/week at ~ 32 weeks of gestation (Figure 1D); in humans, the corresponding value was 26.1 cm3/week at the same gestational age (Figure 1D).

These results demonstrate that the remarkable enlargement of the human brain already begins before ~ 16 weeks of gestation. Moreover, the growth velocity of brain volume increased until ~ 22 weeks of gestation in both chimpanzees and humans; however, after that time, brain growth in the chimpanzee fetus slowed down as birth approached. By contrast, brain growth in the human fetus continued to accelerate until around 32 weeks of gestation. Therefore, we infer that prenatal patterns of human neuronal enhancement changed from those of the chimpanzee during the rapid brain evolution of modern humans [9] and [10]. These ontogenetic patterns during intrauterine life appear to have emerged after the split of humans from chimpanzees and have contributed to the more marked brain size in our species.

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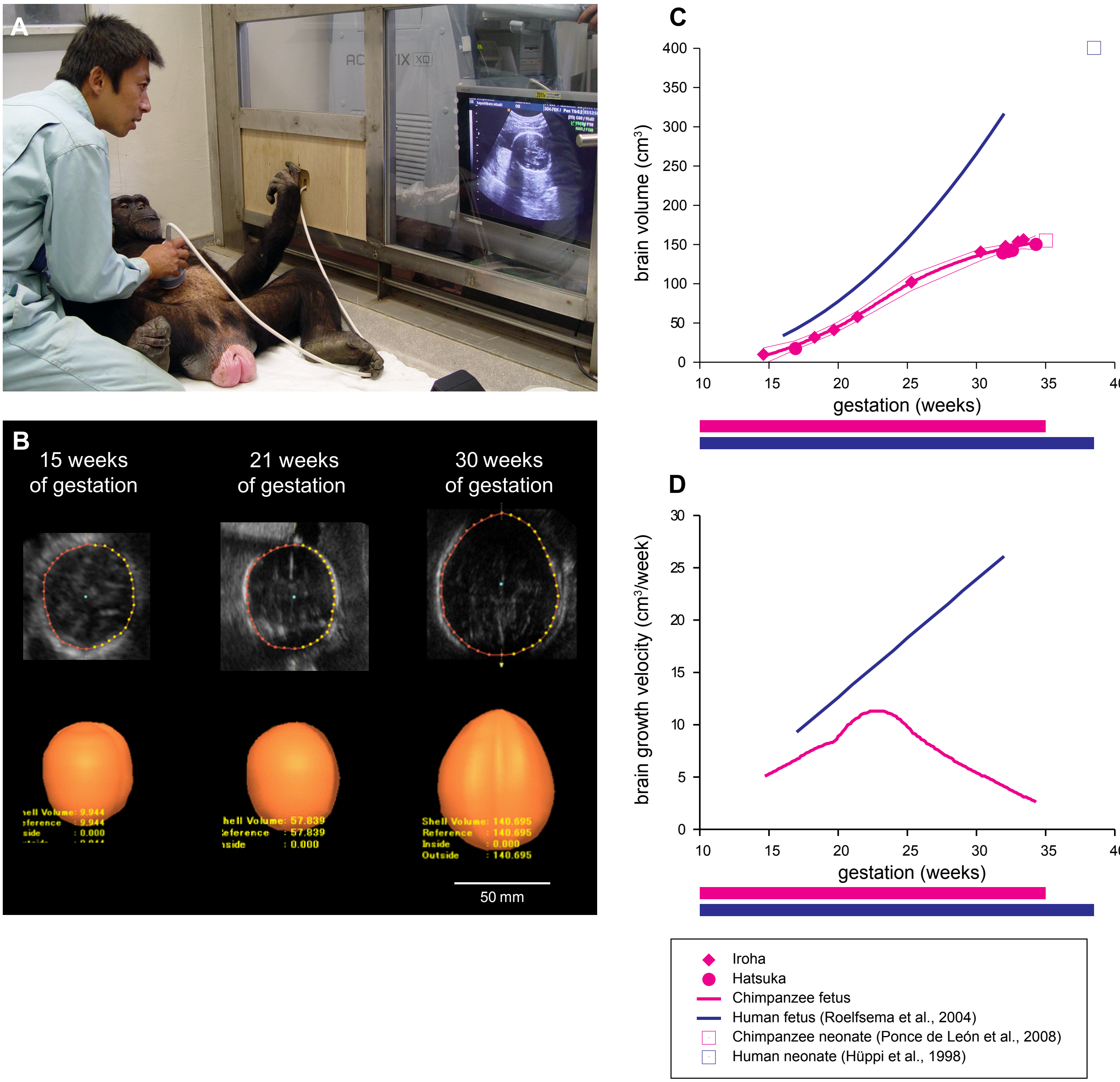
Figure Legend

Figure 1. Evaluation of Fetal Brain Volume Relative to Gestational Age

Three-dimensional (3D) ultrasound images were acquired from two chimpanzee fetuses as they developed from 14 to 34 weeks of gestation. (A) 3D ultrasound scanning of a chimpanzee fetal brain. At 21 weeks of gestation, the mother (Mizuki) was placed on the floor in a supine position in the experimental booth without anesthesia. She was relaxed throughout the scans. Trained operators (S.H. and K.F.), who are both familiar with the chimpanzee, obtained the 3D ultrasound brain images of the fetus (Iroha). (B) An ontogenetic series of images of the chimpanzee fetal brain. 3D ultrasound brain images from one chimpanzee fetus (Iroha) at 14 weeks, 21 weeks, and 30 weeks of gestation are shown. The upper row shows sonographic axial images of the brain. The lower row shows three-dimensional renderings of the brain. (C) Gestational age-related changes in the brain volume in chimpanzee fetuses (Hatsuka and Iroha) and human fetuses (n = 68). The magenta solid line represents the LOESS fit of the chimpanzee fetus. The blue line represents the linear fit of the human fetus. The fine magenta lines represent the 95% confidence band of the LOESS fit. (D) Gestational age-related changes in the growth velocity of brain volume in chimpanzee fetuses (Hatsuka and Iroha) and human fetuses (n = 68). For comparison with human fetuses, we analyzed the median value (50th percentile) of brain volume ($\sqrt{\text{brain volume}} = 0.75 \times \text{gestational age} - 7.71$) from 68 normal human fetuses during the corresponding gestational period from 16 to 32 weeks of gestation based on the time of conception (see details in [8]). The color bars below the graphs represent the gestational time based on the time of conception in chimpanzees (magenta) and humans (blue), respectively. See also “Supplemental Experimental Procedures” for estimates of neonate brain volume in chimpanzees and humans, estimates of adult brain volume in chimpanzees and humans, a more detailed description of the developmental trajectories in chimpanzees and humans, and statistical analysis; see Tables S1, S2, S3, S4, S5, and S6 for more detailed results about the brain volume in chimpanzee and human fetuses.

Figure 1


A
B
15 weeks of gestation
21 weeks of gestation
30 weeks of gestation
Shell Volume: 140.695
Reference : 140.695
Inside : 0.000
Outside : 140.695
50 mm
C
brain volume (cm³)
400
350
300
250
200
150
100
50
0
10
15
20
25
30
35
40
gestation (weeks)
D
brain growth velocity (cm³/week)
30
25
20
15
10
5
0
10
15
20
25
30
35
40
gestation (weeks)
Iroha
Hatsuka
Chimpanzee fetus
Human fetus (Roelfsema et al., 2004)
Chimpanzee neonate (Ponce de León et al., 2008)
Human neonate (Hüppi et al., 1998)

Current Biology

Supplemental Information

A Longitudinal Comparison of

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Supplemental Inventory

Table S1. Gestational Age and 3D Ultrasound Measurements of the Volume of Fetal Chimpanzee Brains

Subject	Gestational age based on conception (weeks)	Brain volume (cm^3)
Hatsuka	16.9	17.6
	31.9	139.1
	32.3	141.0
	32.6	142.3
	34.3	150.4
Iroha	14.6	9.9
	18.3	31.7
	19.7	41.3
	21.4	57.8
	25.3	102.0
	30.3	140.7
	32.1	147.7
	33.0	153.4
	33.4	156.3

Table S2. Comparison of Actual Phantom Volume with 3D Ultrasound Measurements of Phantom Volume

Actual volume (cm^3)	Measured volume (cm^3)
10.0	9.4
20.0	19.7
30.0	29.6
40.0	39.9
50.0	50.0
60.0	59.9
70.0	69.9
80.0	79.9
90.0	89.9
100.0	99.9
110.0	109.7
120.0	119.9
130.0	129.9
140.0	139.6
150.0	149.9

Table S3. Comparison of the First 3D Ultrasound Measurement of Fetal Chimpanzee Brain Volume with a Second Measurement Made by the Same Rater

Subject	Gestational age based on conception (weeks)	First measurement (cm^3)*	Second measurement (cm^3)*
Hatsuka	16.9	17.6	16.9
	31.9	139.1	139.1
	32.3	141.0	141.1
	32.6	142.3	142.3
Iroha	14.6	9.9	9.9
	18.3	31.7	31.7
	19.7	41.3	41.3
	21.4	57.8	57.8
	25.3	102.0	102.0
	30.3	140.7	140.7
	32.1	147.7	147.7
	33.0	153.4	153.2
	33.4	156.3	156.3

*3D ultrasound measurement of the fetal chimpanzee brain was conducted twice by T.S.

Table S4. Comparison of 3D Ultrasound Measurements Fetal Chimpanzee Brain Volume Made by Different Raters

Subject	Gestational age based on conception (weeks)	Measurements made by T.S. and H.M. (cm^3)	Measurements made by T.E. (cm^3)
Hatsuka	16.9	17.6	16.7
	31.9	139.1	139.5
	32.3	141.0	141.2
	32.6	142.3	141.3
Iroha	14.6	9.9	10.4
	18.3	31.7	30.8
	19.7	41.3	41.3
	21.4	57.8	58.0
	25.3	102.0	102.4
	30.3	140.7	140.7
	32.1	147.7	146.9
	33.0	153.4	153.7
	33.4	156.3	156.7

Table S5. Corresponding gestational Age based on the Time of Conception and 3D Ultrasound Measurements of Human Fetal Brain Volume

Corresponding gestational age based on conception* (weeks)	Median brain volume** (cm^3)
16.0	33.6
17.0	42.9
18.0	53.3
19.0	64.8
20.0	77.4
21.0	91.2
22.0	106.1
23.0	122.1
24.0	139.2
25.0	157.5
26.0	176.9
27.0	197.4
28.0	219.0
29.0	241.8
30.0	265.7
31.0	290.7
32.0	316.8

*The corresponding human gestational age based on the time of conception was calculated by subtracting 2 weeks (the average time from menstruation to ovulation) from the human gestational age based on the last menstrual period (LMP).

**We used the median (50^{th} percentile) brain volume ($\sqrt{\text{brain volume}} = 0.75 \times \text{gestational age} - 7.71$) calculated from 68 normal human fetuses (see details in [8]) to compare the developmental trajectories of chimpanzee and human fetuses.

Table S6. Comparison of 3D Ultrasound Measurements of Human Fetal Brain Volume by Chang et al. (2003) with Those by Roelfsema et al. (2004)

Corresponding gestational age based on conception* (weeks)	Median brain volume Measured by Chang et al. (2003)** (cm^3)	Median brain volume Measured by Roelfsema et al. (2004)** (cm^3)
18.0	42.8	53.3
19.0	59.7	64.8
20.0	77.2	77.4
21.0	95.3	91.2
22.0	114.0	106.1
23.0	133.2	122.1
24.0	153.1	139.2
25.0	173.5	157.5
26.0	194.6	176.9
27.0	216.2	197.4
28.0	238.5	219.0
29.0	261.3	241.8
30.0	284.7	265.7
31.0	308.7	290.7
32.0	333.3	316.8

*The corresponding human gestational age based on the time of conception was calculated by subtracting 2 weeks (average time from menstruation to ovulation) from the human gestational age based on the last menstrual period (LMP).

**The median (50^{th} percentile) brain volume (brain volume = 171.48036 + 4.8079 × gestational age + 0.29521 × gestational age^2) was calculated from 203 normal human fetuses (see details in [11]).

***We used the median value (50^{th} percentile) for brain volume (√brain volume = 0.75 × gestational age–7.71) calculated from 68 normal human fetuses (see details in [8]) to compare the developmental trajectories of chimpanzee and human fetuses in this study.

Supplemental Experimental Procedures

Subjects

Two female chimpanzees, named Misaki and Mizuki, participated in this study. The two chimpanzees lived with four other individuals (two males and two females) in an enriched environment at the Great Ape Research Institute of Hayashibara Biochemical Laboratories, Inc. Misaki gave birth to Hatsuka (female) on 20 June, 2008. Mizuki gave birth to Iroha (female) on 5 September, 2008 (see [4] for a more detailed account of the subjects). In both cases, the father was Loi, one of the group's males; paternity was confirmed by DNA analysis. Based on daily monitoring of urine samples from these female chimpanzees using an ovulation test kit (Check One LH, ARAX Co., Ltd.), we determined the date of ovulation. The gestational periods of the two chimpanzee mothers were 34.4 weeks and 33.4 weeks, respectively, based on the time of conception. The chimpanzee fetuses did not show any abnormalities on ultrasound scans. This research was conducted in accordance with the Guide for the Care and Use of Laboratory Animals of Hayashibara Biochemical Laboratories, Inc., and the Weatherall report ("the Use of Nonhuman Primates in Research"), in that only a noninvasive 3D sonography technique was used to measure the brain volume of the chimpanzee fetuses in *utero*. All protocols were approved by the Animal Welfare and Animal Care Committee of Hayashibara Biochemical Laboratories, Inc. (GARI-051101).

Image Acquisition

3D ultrasound (Accuvix XQ, Medison, Co, Ltd.) was used to measure the brain volume of the two chimpanzee fetuses (Hatsuka and Iroha). Measurements were made using a 3–5 MHz curvilinear probe and an internal device for automatic acquisition of frames for volume reconstruction (Figure 1A).

For each pregnancy, 3D ultrasound measurements of brain volume were acquired at scheduled intervals as a part of an ongoing longitudinal behavioral and cognitive study of serial four-dimensional (4D) ultrasound imaging (see [4] for the details of pregnancy detection and estimation of conception date). However, because 3D ultrasound examination was conducted from late April to early September (2008), and it is difficult to scan the whole head of chimpanzees fetuses to fully measure the brain volume, the 3D ultrasound data regarding the brain volume of the two fetuses were collected during a limited gestational period. There was also a difference in the scan period between the two subjects (Hatsuka, gestational period 16.9–34.3 weeks; Iroha, gestational period 14.6–33.4 weeks). Future studies will need to ensure that the limited and different data points do not lead to contradictory results in the future. Nonetheless, at the present time, our experiment is the first to measure the brain size of chimpanzee fetuses using 3D ultrasound imaging in *utero*.

Prior to scanning, the mother chimpanzees were placed on the floor in a supine position in the experimental booth without anesthesia. The mothers were relaxed throughout the ultrasound scans. Trained operators (S. H. and K. F.), who were familiar with the chimpanzees, obtained the 3D ultrasound brain images. The volume sample box was adjusted to include the complete fetal head and no zoom magnification was used. The volume sweep angle was set at 80° and the highest quality acquisition was selected. All volumes were acquired by an axial scan of the head and displayed in three perpendicular planes on the monitor. The 3D images were then stored on digital devices for later analysis. The acquisition process was repeated until the operators were satisfied with the 3D data. The scanning time for one recorded volume ranged between 4 and 8 seconds, depending on the fetal movement and the size of the recorded data. Fetal brain scans were performed in the absence of maternal and fetal movement.

Image Processing

The 3D ultrasound data were analyzed with a SonoView Pro (Medison, Co, Ltd.) on a personal computer using a series of manual and automated procedures. 3D brain volume was measured by rotating the recorded volume until the axial plane was displayed on the upper right panel. Using the VOCAL mode (a method for measuring volume), the internal borders of the head were traced manually with stepwise rotations of 30 degrees, taking the skull base (defined as the line between the glabella and opisthion) as the lower border in accordance with a previous study [8] (Figure 1B). The absolute brain volume of the chimpanzee fetus was then measured and expressed in cm^3 (Table S1).

Three image analysts (T.S., H.M., and T.E.), all trained in 3D ultrasound analysis and all blind to the gestational age of the subjects, semi-manually traced and measured the entire brain. T.S. and H.M. identified the anatomical landmarks (glabella and opisthion) used to delineate the brain volume in all brain images. The segmentation results at each gestational stage were reviewed by an expert in ultrasound diagnostics and anatomy (S.Y.) to ascertain whether the brain border determined by T.S. and H.M was accurate.

Accuracy of the 3D Ultrasound Volume Measurements

The accuracy of the 3D ultrasound measurements made in this study was evaluated using 10% agarose phantoms ranging in volume from 10 cm^3 to 150 cm^3 (10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, and 150 cm^3), which corresponded with the range of brain volumes measured in the chimpanzee fetus. Then, the operators (S. H. and K. F.) scanned the phantoms with the same ultrasound equipment used in the actual experiment. The image analyst (T.S.) then analyzed these images using the same techniques used to measure the chimpanzee fetal brain volume. Retrospective analysis of the accuracy of the ultrasound measurements was performed by calculating the absolute percentage error (absolute value {actual volume–ultrasound volume}/actual volume × 100%) for each phantom. The results showed that the absolute percentage error for the ultrasound measurements was 0.7±1.4% (Table S2).Therefore, it can be concluded that that volume of the phantoms could be accurately estimated using the same image acquisition and analysis procedures used to study the chimpanzee fetal brains.

Reliability of the 3D Ultrasound Measurements of Chimpanzee Fetal Brain Volume

The intra-rater and inter-rater reliability of the ultrasound measurements used in this study were also evaluated. An analysis of intra-rater reliability was conducted by comparing two sets of brain measurements obtained by T.S. The variability of the intra-rater was expressed as the absolute percentage error (absolute value {the first brain volume measurement–the second brain volume measurement}/the first brain volume measurement × 100%) for each brain volume (Table S3). The intra-rater reliability was 0.3±1.0%.

The inter-rater reliability was also analyzed by comparing brain measurements obtained by T.S. and H.M. from a sample of brain scans measured by T.E, who was blind to the measurements made by T.S. and H.M. The variability of the inter-rater was expressed as the absolute percentage error (absolute value {brain volume measurement by T.S. and H.M.–brain volume measurement by T.E.}/brain volume measurement by T.S and H.M. × 100%) for each brain volume (Table S4). The inter-rater reliability was 1.1±1.8%.

The results showed that the intra-rater and inter-rater reliability of the ultrasound measurements in this study were within an acceptable range.

Comparison of the Developmental Trajectory of Chimpanzee Fetal Brains with That of Human Fetal Brains

Direct comparison of the developmental patterns of chimpanzees and humans allowed the identification of human-chimpanzee shared features and human-specific features. We analyzed the median (50^{th} percentile) brain volumes ($\sqrt{\text{brain volume}} = 0.75 \times \text{gestational age} - 7.71$) of 68 normal human fetuses between 16 and 32 weeks of gestation (i.e. up until a few weeks before birth) obtained from a previous human 3D Ultrasound study. These were then used as the estimated brain volumes for the human fetuses (see details in [8] and Table S5).

The gestational time of the 68 human mothers was between 18 and 34 weeks of gestation. The gestational age of the human fetuses was calculated to match that of the chimpanzee fetuses, which was based on the estimated time of conception. However, the gestational age of the human fetuses in the original study [8] was measured from the last menstrual period (LMP), or by ultrasound in the first trimester of gestation; the date of conception was not formally examined. Therefore, the corresponding human gestational age based on the time of conception was calculated by subtracting 2 weeks (the average time from menstruation to ovulation) from the human gestational age based on the LMP.

The human fetuses in the previous study showed a statistically significant linear increase in brain volume during the corresponding human gestational period (between 16 and 32 weeks) based on the time of conception (Figure 2).

All protocols used in the study [8] were approved by the Hospital Ethics Review Board of the University Medical Center, Rotterdam. For the statistical analyses in the present study, we performed the same procedures to analyze data from chimpanzees and humans.

Validity of the 3D Ultrasound Measurements of Human Fetal Brain Volume Reported by Roelfsema et al (2004)

To evaluate the validity of the previous ultrasound volume measurements for use as control data in our ultrasound study of the chimpanzee brain, data obtained between 18 and 32 weeks of gestation [8] was compared with measurements of fetal brain volume assessed by 3D Ultrasound sonography during the same gestational period in another study [11] (Table S6).

According to the results, all of the median values for brain volume reported in [8] are within a confidence interval of 95% of the median values reported by Chang et al (2003) [11]. Furthermore, although the difference between the two data sets at 18 weeks of gestation (based on the time of the last menstrual period) was 24.6%, the differences between the two data sets obtained for the other gestational weeks was 7.0±2.4%, i.e. less than 10%. Moreover, the developmental change in the brain volume reported by Roelfsema et al (2004) [8] shows almost the same tendency as the estimated brain volume calculated using the formula: 0.12 × estimated fetal weight [5-6, 12].

Furthermore, in our study, methodological validity of the 3D ultrasound measurements of the chimpanzee fetal brain was demonstrated, even though an expert in ultrasound diagnostics (S.Y.) performed the technique slightly differently each time.

NB: At the present time, the paper by Roelfsema et al (2004) is the only publication that provides actual numerical data corresponding to the gestational period we studied.

Therefore, it was reasonable and important to use the median values for human fetal brain volume based on the numerical data published by Roelfsema et al (2004) [1] as control data when comparing the developmental changes in fetal brain volume between chimpanzees and humans in our study.

Statistical Analysis

Fetal Brain Volume

All statistical analyses were performed using SPSS 19 (SPSS, Chicago) and R 2.11.1 (http://www.r-project.org/) software. Hypothesis tests for model building were based on F statistics. At first, linear, quadratic, or cubic polynomial regression models were fitted by age (using SPSS 19) to identify the developmental patterns in brain volume. If a cubic model did not yield significant results, a quadratic model was tested; if a quadratic model did not yield significant results, a linear model was tested. Thus, a growth model was polynomial/nonlinear if either the cubic or the quadratic term significantly contributed to the regression equation. The Akaike information criterion (AIC; a log-likelihood function) [13] was used to ensure effective model selection.

Secondly, R 2.11.1 was used to fit data showing nonlinear trajectories by locally-weighted polynomial regression (LOESS) [14]. In this way, even if the data points are relatively small, it was possible to delineate gestational age-related volume changes by applying the curve fitting suggested by previous human studies [15-16] and a previous chimpanzee study [17], without enforcing a common parametric function on the full data set, as is the case with linear polynomial models. Therefore, the paucity of available data around 20 weeks of gestation is unlikely to appreciably influence the developmental trajectory of the chimpanzee brain. The fit at gestational age X was made using values in a neighborhood that included a proportion, alpha, and for alpha < 1, the neighborhood included a proportion, alpha, of the values. Data were fitted in four interactions with alpha = 0.75. The observed and fitted values for the brain volume were plotted as a function of gestational age to display gestational age-related changes. All statistical tests were conducted at a significance level of 0.05.

To compare the neonatal brain volume between chimpanzees and humans, we referred to previously published numerical data (chimpanzees, 155cm^3 [18]; humans, 400cm^3 [18-19]) Furthermore, to compare the adult brain volumes between the two species, we also used previous data (chimpanzees, 378cm^3 [20]; humans, 1355cm^3 [21]).

The Growth Velocity of Fetal Brain Volume

The growth velocity of the chimpanzee fetal brain was analyzed. Growth velocity was calculated by dividing the difference in predicted brain volumes (Y) by the difference in gestational ages (X). This procedure was used in previous human and nonhuman primate studies to identify growth spurts in body and brain mass [1, 22-23].

Supplemental Discussion

Limitations in the Spatial Resolution of 3D Ultrasound Fetal Brain Imaging and Accuracy of the Volume Measurements of the Chimpanzee Fetal Brain

The spatial resolution of the 3D ultrasound brain images of chimpanzee fetuses was as high as that of the human fetuses until approximately 20–25 weeks of gestation. However, after this time, the special resolution of the 3D ultrasound brain images of chimpanzee fetuses was lower than that of human fetuses during the equivalent pregnancy period. This difference appears to be caused by a difference in the intrauterine space between chimpanzees and humans during the latter stages of gestation (after approximately 20–25 weeks). However, an expert in ultrasound diagnostics and anatomy (S.Y.) reviewed all the ultrasound brain images taken at each week of gestation and concluded that the images of the chimpanzee fetuses after approximately 20–25 weeks gestation had sufficient spatial resolution to clearly delineate the brains of fetal chimpanzees as clearly as in the images taken earlier. Therefore, although the spatial resolution of the 3D ultrasound brain images of chimpanzee fetuses became lower as intrauterine life progressed, the analysis still provided an accurate measurement of brain volume throughout the study period.

Homologous Anatomical Landmarks Used for 3D Ultrasound Measurement of Fetal Brain Volume in Chimpanzees and Humans

Most comparative studies looking at the development of cranial morphology in primates use anatomical landmarks on the human skull such as the glabella and opisthion; the cranial morphology of nonhuman primates is considered homologous with that of humans [24-26]. Therefore, it is appropriate and reasonable to define the brain of chimpanzee fetuses using these human anatomical landmarks (glabella and opisthion) using data obtained in a previous ultrasound study of the human fetus [8].

Limitations in the Demarcation of the Fetal Brain on the 3D Ultrasound Measurement of Brain Volume in Chimpanzees and Humans

As mentioned above, the brain of the chimpanzee fetus was delineated by taking the glabella and opisthion (on radiographic images) as the anterior and the posterior border, respectively, in accordance with a previous ultrasound study of the human fetal brain [8]. The anatomical definition of the brain does not include the part that is below the level of the skull base because this part of the skull is not well visualized by ultrasound. Therefore, this proxy measure of the brain may, in fact, underestimate the extent of the actual brain in chimpanzee fetuses and human fetuses [8]. Nonetheless, this underestimation is unlikely to appreciably influence the comparison of brain development patterns between chimpanzee and human fetuses because the ultrasound measurements are obtained using the same demarcation points in both species.

Limitations in the Evaluation of the Validity of 3D Ultrasound Measurements of Fetal Brain Volume between Chimpanzees and Humans

The developmental pattern of brain volume was compared between chimpanzee and human fetuses with reference to previously published numerical data for the human fetal brain [8]. This data set [8] was compared with the results of another study [11]. It was concluded that it is reasonable to use the data published [8] as the control data for comparison in the present chimpanzee study. However, the human data set by Chang et al. (2003) [8] has lower brain volumes in early gestation compared with those by Roelfsema et al. (2004) [11]. There is more uncertainty in the earliest estimated brain volumes for the human fetuses.

Therefore, it is important to demonstrate the validity of the 3D ultrasound measurement method for measuring fetal brain volume in chimpanzee and human fetuses by using the original ultrasound imaging data from the two species, and to ensure the results of these comparisons are not contradictory. Nonetheless, at the present time, the present study is the first to directly compare the fetal developmental trajectories of the two species.

Supplemental References

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