31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

3D Ultrasound in Assessment of Growth and Development of Frontal Lobes in Children with Perinatal Brain Injury

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Abstract—**To investigate the functions of cranial 3D ultrasound in the assessment of growth and development of the volume of frontal lobes in children with perinatal brain injury, 226 neonates of different gestational ages and 86 full term with perinatal brain injury were selected as subjects. The volume of frontal lobe of neonate increased with gestational age within 7 days after birth (r=0.676, P<0.05). The volume of frontal lobe in the 33 children with serious brain injury was lower than that in the control group at 1 month and the difference was significant at 3 and 6 months (P<0.01). There was a correlation between the long-term nervous system dysplasia and the slow increase of frontal lobe volume. The volume of frontal lobe increases with gestational age. The brain injury during the perinatal period affects the development of frontal lobe and is related with neural dysplasia. 3D ultrasound is useful for evaluating the normal and abnormal brain development.**

I. Introduction

THE brain of neonate is the continuation and development of the brain of fetus, and the continuous increase of brain volume is both an important index for the development of brain and the histological and anatomical basis for the normal functional state of brain [1-3]. Various brain injuries caused by the high risk factors during perinatal period may influence the normal development of brain tissues, and the serious injury caused nervous system sequel [4-6]. Head circumference is an essential index during the development of different stages in infants. In some brain injury infants, the head circumference of some children increases slowly, and it is most often seen that the forehead becomes small and the coronal sutures of skull are overlapped. Under imaging examination, some children have encephalography of the whole or partial brain, and the atrophy of frontal lobe is especially significant. However, the measurement of head circumference only represents the periphery of skull. When the space outside brain increases, the head circumferences of these children are not small, and the changes of brain are impossible to detect in clinic.

Routine imaging examinations, such as CT and MRI, have been increasingly applied in the department of pediatrics in recent years so that the cerebral structure can be clearly observed in vivo. It has been found that in the children with serious brain injury, the space outside brain often increases in the children with serious brain injury, which is caused by the atrophy and limit in the continuous development of brain parenchyma, especially in the frontal lobe and parietal lobe, indicating there are problems in the development of frontal lobe in these children. However, the increase of the space outside brain in imaging examination may result in some confusion, because the increase of the space outside brain resulting from the mismatch between the rate of brain growth and the development of skull during the development process of normal children often makes parents feel panic.

Tridimensional imaging examination has ideal effects so as to solve this problem. Tridimensional MRI has been established in the study on the development of brain structure from the perspective of tridimensional morphology and quantitative volumetric analysis [7-9]. However, the transportation and operation for the serious disease neonates are difficult, so they have not been widely used in the clinical practice of neonates up to the present. Three-dimensional ultrasound (3D US) has developed into a practical medical diagnostic technique because of such advantages as its non-invasiveness, simplicity and ease for bedside operation.

Since Nagdyman et al [10] used the three-dimensional ultrasound to examine the anatomical structure of skull and brain of neonates, a new application field of 3D ultrasound has been developed, that is, the application in the study on the brain development of neonates. 3D ultrasound has great diagnostic values for perinatal brain injury. It can not only show the 3-D lesions, for example, it can be used to observe intracranial hemorrhage, precisely locate the range of paraventricular white matter lesions, cerebral infarction, cerebral tumor etc, but also quantitative measure the volume of the whole brain or local brain tissues [11-12]. So that the change of the whole brain after injury can be intuitively known and the development of brain can be evaluated. This present study evaluated the effect of perinatal brain injury on the development of the brain of children from a new perspective by measuring the volume of frontal lobe, the main function area of brain with cranial 3D ultrasound.

II. Material and Method

The subjects in this study were the neonates treated in first hospital of Peking University during Sep. 2003 and May 2006. 3D ultrasound was used to observe the increase of the

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978-1-4244-3296-7/09/$25.00 ©2009 IEEE

volume of brain frontal lobe within 7 days after birth and at 1, 3 and 6 months during follow-up in 226 cases of (~34W 57 cases, ~37W 34 cases, all were appropriate for gestational age infants) neonates with different gestational age. According to clinical and imaging examinations, 86 term infants were diagnosed as perinatal brain injury during neonatal period. The volumes of frontal lobes of these infants were measured using 3D US within 7 days after birth and at 1, 3 and 6 months during follow-up. According to the conditions of the 86 children with brain injury, the brain injuries were classified into the following groups: (1) The mild injury group had 53 cases, including the cases of mild, mild moderate hypoxic-ischemic encephalopathy (HIE), intracranial hemorrhage degrees I and II. (2) Serious injury group had 33 cases; including serious, serious moderate HIE cases, III and IV degree intracranial hemorrhage cases, the cases of polycythemia and bilirubin encephalopathy with serious imaging structural changes, hypoglycemic encephalopathy, hereditary metabolic diseases and epilepsy etc.

During the follow-up at scheduled time in infancy, physical and nervous system examinations were performed together with the measurement of brain volume using 3D ultrasound The measured brain volume of the neonates with brain injury two standard deviation lower than that of the normal neonates of the same age was considered abnormal, and the measured brain volume two standard deviation lower was considered essentially normal. The clinical development status of nervous system can be divided into the following classifications: (1) Normal. (2) Mildly abnormal: The muscle tension was mildly abnormal within 6 months after birth, which was improved markedly after physical rehabilitation treatment and might return to normal; the Gesell scores were still lower in some items in varying degrees and DQ was more than 75%. (3) Seriously abnormal: There were obvious early manifestations of cerebral palsy, delayed development, epilepsy etc. about two years old. The DQ was lower than 75% in Gesell examination.

Medison 8000 ultrasonograph was used for cranial three-dimensional imaging and image analysis. Tridimensional volume probe with frequency of 5-8MHz was used; this machine could acquire full-resolution picture by 512 tunnels superelevation frame frequency multi-beams handling. The bregmatic fontanelle of the children was used as the acoustical window for the fixation of probe. 3D function was enabled, the tridimensional sampling volume adjusted, the coronal plane of the third ventricle used as reference and the size was large enough to include the whole brain (at least the whole frontal lobe) (Fig 1). Automatic volume scan program was enabled in order to obtain the data of the tridimensional volumes of brain within 3-6 seconds. The data were saved in the equipment for the tridimensional multiple plane image analysis. Then the built-in tridimensional volume measuring function was enabled for tridimensional volume imaging. In the image of coronal section, the midline of brain was used as the medial axis, and 30-degree rotation was conducted each time so as to obtain 6 planes. Sampling and definition of the images of the 6 planes were performed manually one by one based on the anatomic landmarks (Fig 2), such as lateral fissure, central sulcus, corpus callosum, anterior horn of lateral ventricle, thalami and basal ganglia so as to obtain the tridimensional volume image of frontal lobe and the data of final volume (Fig 3). Due to the form of frontal lobe was irregular shape, and the echo intensity was almost equal between frontal lobe and its surrounding brain tissues, so it was more precise that we manually placed the frontal lobe measuring range according to the anatomic landmarks. There were distinct anatomic landmarks in each plane; the systematic errors should be utmost reduced. The cases quantity was large, so the accidental errors also are utmost reduced. All of them caused the final volume measurement were accurate.

SPSS 13.0 statistical software was used. Measurement data were described as mean ± standard deviation. Student's t test was used for paired comparison and ANOVA for comparison of trilateral comparison. Numeration data were described with number of cases and percentage and tested by chi-square test ($P<0.05$: statistical difference; $P<0.01$: significant difference).

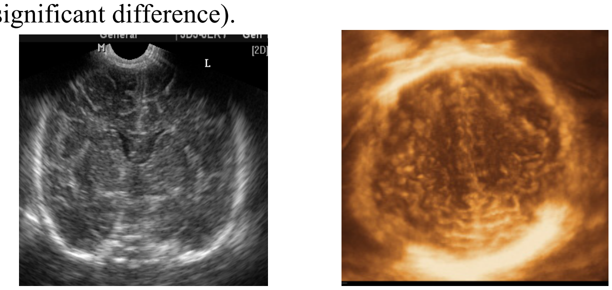

Fig. 1. The two-dimensional image (left) and three-dimensional image (right).

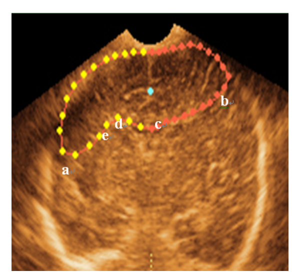

Fig. 2. The scale image of frontal (a.lateral fissure, b.central sulcus, c.corpus callosum, d.anterior horn of lateral ventricle, e.thalami and basal ganglia).

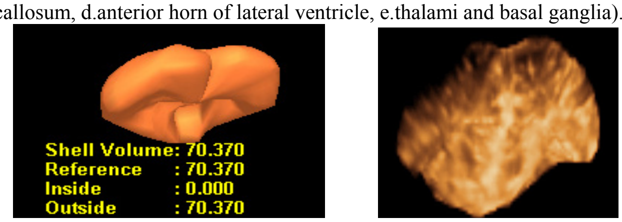

Fig. 3 The data of final frontal lobe volume (left) and three dimensional image of frontal lobe (right).

III. Results

A. Measurement of the Volumes of the Frontal Lobe

3D ultrasound was used to measure the volumes of the frontal lobes of 226 neonates with different gestational ages within 7 days and the results showed obvious regularity. The volume of frontal lobe of neonate increased with gestational age (Fig 4) and there was significant intergroup difference, which agreed with the law of the normal development of human brain (Table 1) and also showed that measuring the volume of brain with 3D ultrasound was of significance for the evaluation of brain development status.

TABLE 1 MEASUREMENTS OF THE VOLUME OF FRONTAL LOBE IN NEONATES WITH DIFFERENT AGES (CM^3)

GestationalWeek	Cases	mean±std [a]
28~33W	57	49.96±11.696
34~36 W	34	59.62±11.189
37~42 W	135	71.59±11.627

[a] , F=73.229, P<0.01

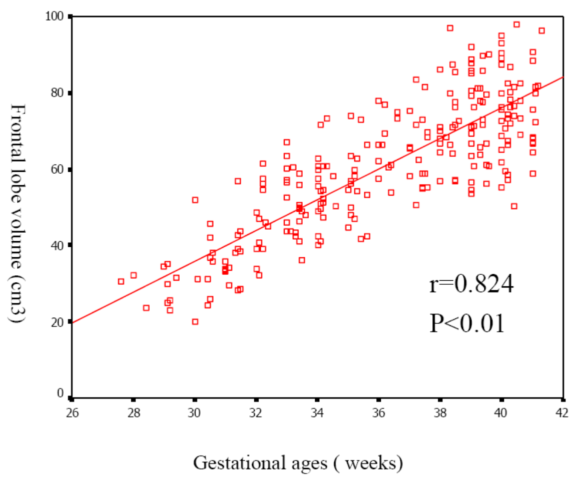

Fig 4 The relationship between different gestational ages and the volume of frontal lobe of neonates

B. Effect of Perinatal Brain Injury on the Development of Frontal Lobe

Tridimensional frontal lobe volume measurement was performed on the 119 normal infants or infants with varying degrees of brain injuries receiving follow-up examinations after discharges (53 cases of normal infants, 36 cases of mild brain injury and 30 cases of serious brain injury). This study indicated there was difference in the volume of diencephalon frontal lobe between different groups with time, which increased with time, and the severity of brain injury and the significance of the slowness of brain volume enlargement also increased with time.

At one month post-birth, the measured volumes of the frontal lobes of the children with serious brain injury were significantly lower than those of normal children, while there was no statistical difference in the measured volume of frontal lobe between the children with mild injury and normal children. With the further development of children, at 3 months, the measured volumes of the frontal lobes of the children with serious brain injury further decreased; At 6 months, the difference of the measured volume of frontal lobe between the children with serious brain injury and normal children of the same age increased, and the volume of frontal lobe of the children with serious brain injury was 2 standard deviations lower than that of the normal group. The measured volumes of the frontal lobes of the children with mild brain injury were lower than that of the normal control group and higher than that of the serious brain injury group, but the differences were not statistically different (Table 2).

TABLE 2 COMPARISON ON VOLUME OF FRONTAL LOBE BETWEEN NEONATES WITH VARYING DEGREES OF BRAIN INJURIES AND NORMAL CHILDREN

Group	Volume of Frontal Lobe (cm^3) 1 month	3 months	6 months
Normal	95.24±13.74	137.5±15.16	174.0±13.27
Mild injury	97.53±20.57	124.16±17.06	156.42±12.61
Serious injury	83.81±16.36 *	100.36±20.10 **	107.82±28.76 **
F value	4.278	15.889	21.907
P value	< 0.05	< 0.01	< 0.01

The serious injury group was respectively compared with the normal group and mild injury group (* P<0.05, ** P<0.01)

C. The Relation between Nervous System Abnormity and the Slow Increase of Frontal Lobe Volume

The relation between the abnormal measured volume of brain and the development status of nervous system during follow-up was observed in this study in order to know the clinical significance of brain volume measurement. The results showed in the 57 children receiving 3D ultrasound examination at months 3 or 6, the incidence of slow increase of frontal lobe volume in the children with nervous system abnormity was higher than that in the children without nervous system abnormity, and the percentage of children with slow frontal lobe volume increase in the children with serious nervous system abnormity was significantly higher than that in the children with mild nervous system abnormity (Table 3).

TABLE 3 THE RELATION BETWEEN NERVOUS SYSTEM ABNORMITY AND THE SLOW INCREASE OF FRONTAL LOBE VOLUME

Development of Nervous System	Cases	Slowness of increase of frontal lobe volume Normal (%)	Abnormal (%)
Normal	26	24(92)	2(8)
Mild abnormal	18	14(78)	4(22)
Seriously abnormal	13	3(23)	10(77)

X^2=21.019，P<0.01. Mild abnormal nervous system development group and normal group (P=0.208). Serious abnormal nervous system development group, normal group and mild abnormal nervous system development group (P<0.01).

IV. DISCUSSION AND CONCLUSION

The brain of neonate is the continuation and development of the brain of fetus. The change in the volume of brain represents the development process of brain. This result agrees with the law of human brain development, which means that with the increase of gestational age, the neuron bodies increase, and the formation of dendrites and synapses and myelinization of white matter and blood vessel hyperplasia increase the content of brain tissues, which appears as the increase of volume in 3D ultrasound image.

Serious perinatal brain injury can lead to the acute necrosis of neurons, lysis and liquification of brain tissues, loss of brain parenchyma, multiplication of dendrites and myelinization of axons, increase apoptosis, and hinder the further development of brain and increase of the cell bodies of neurons. The combined effect of these changes results in the slow increase of brain volume. The volume of frontal lobe was selected as the observation index in this study and the results showed that as time went on, the volume of frontal lobe in the children with serious brain injury was lower than that in normal children at 1 month, and the difference became more significant at 3 and 6 months. The volume of frontal lobe in normal children was about 140cm3 at 3 months and about 170cm3 at 6 months, while the volume of frontal lobe in the serious injury group was about 100cm3 at 3 months and about 110cm3 at 6 months ($P<0.01$). Although the increase of frontal lobe volume in the children with mild brain injury was slower than that in the control group and faster than that in the serious brain injury group, there was no statistical difference. It could be concluded that the slow increase of frontal lobe volume was the result of brain injury and the continual development of brain during infancy might be affected in the children with perinatal brain injury.

The serious hazard of serious perinatal brain injury is the various degrees of nervous system sequel and it has been shown by the researches in recent years the occurrence and degree of sequel depend on the degree of brain injury. As shown above, the increase of brain volume represents the normal development of brain, serious perinatal brain injury may lead to slow increase of brain volume and there are intrinsic correlations between the brain volume changes and the abnormalities of nervous system during the development process of the children with perinatal brain injury. The limited cases receiving follow-up examinations in this study showed that the proportion of serious sequel of nervous system (such as cerebral palsy, delayed development and epilepsy etc.) in the children with abnormal slow increase of frontal lobe volume (77%) was significant higher than that in the children with normal and essentially normal increase of frontal lobe volume (22%, $P<0.05$), and the increase of frontal lobe volume in the children with clinically mild nervous system abnormality was better than that in the children with serious nervous system sequel. This indicated the dynamic monitoring of frontal lobe volume could be used as a new reference index for the evaluation on the normal development of brain and the abnormal development of brain after perinatal brain injury.

This study investigated the value of 3D ultrasound in the evaluation on the early brain development of neonates and infants, and showed the law of development of frontal lobe of the neonates with different gestational ages. Perinatal brain injury resulted in the slow increase of frontal lobe volume during the development process of brain and the trend of changes agreed with the clinical nervous system examination findings. Therefore 3D ultrasound has valuable application prospects in the evaluation and diagnosis of the brain development and brain injury of neonates.

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