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Evaluation of the lateral ventricle using MRI in normal micropigs

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Abstract : This study was undertaken to assess the lateral ventricle, which was some portion of brain and related to congenital anomalies, from 1, 2, 4, and 8 months of age in healthy micropigs. They were induced general anesthesia and performed magnetic resonance imaging (MRI) with a 0.3 Tesla magnet. Each age group was evaluated by three subjects such as lateral ventricular volume, ventricular volume ratio and asymmetry. T1 weighted transverse images were acquired for calculation of lateral ventricular and corresponding brain parenchyma areas. The ratio of bilateral ventricle areas used to analyze the asymmetry. The mean ventricular volumes of each month were 676.74 ± 25.58 mm^3 (1 month-old), 630.64 ± 143.84 mm^3 (2 month-old), 992.12 ± 106.03 mm^3 (4 month-old) and 1172.62 ± 237.57 mm^3 (8 month-old), respectively. The ventricular volume ratio was the smallest at 2 month-old and re-increased from that age. The ratio was significantly different between 2 month-old and other age groups ($p < 0.05$). The value of bilateral area ratio showed within 1.5 in all experimental animals. Consequently the lateral ventricle showed a positive correlation with aging and symmetric shapes in both sides. The developmental pattern of the lateral ventricle provides basic data in micropigs as an experimental animal model for physiological and neurosurgical approach.

Keywords : brain, lateral ventricle, micropigs, MRI

Introduction

Magnetic resonance imaging (MRI) provides important information about the brain and it has been used to evaluate central nervous system (CNS) diseases of animals [7, 17].

Micropigs are steadily gaining importance as animal models in the field of neurologic research, including dementia, stroke, and congenital anomalies and so on [8, 10]. The micropigs brain, which is gyrencephalic, resembles the human brain more in anatomy, growth and development than do the brains of commonly used small laboratory animals [9]. Important practical aspects of the use of the animals are objective data for comparing normal and disease status. To date, there is few study of the pig brain with MRI. The purpose of this study is to assess the micropigs ventricle from 1 to 8 months of age with MRI. Especially, the onset of ventricular expansion, ventricular symmetry and the developmental change of ventricular volumes and ratios were evaluated.

Materials and Methods

Animals

Sixteen healthy micropigs at 1, 2, 4 and 8 months of age were used in this study. All animals (PWG micropig, PWG Genetics Korea, Korea) were raised under strict SPF barrier system and microbiologically well defined conditions. The micropigs were individually housed indoors in cages, fed dry pig food, and provided with water *ad libitum*. This study adhered to the strict to the guide line of the 'Guide for the Care and Use of Laboratory Animals' of Seoul National University, Korea.

Methods

MR images of the brain were acquired under general anesthesia. MR images were obtained with a 0.3 Tesla magnet (Airis Vento; Hitachi Company, Japan). Micropigs were placed in dorsal recumbency on the scanning table. T1 weighted images were acquired in transverse, sagittal

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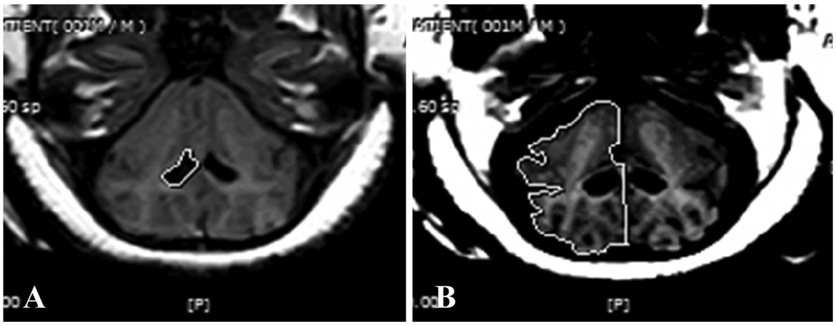

Fig. 1. The areas of the hemisphere (A) and corresponding lateral ventricle (B) were manually calculated on T1 weighted transverse images.

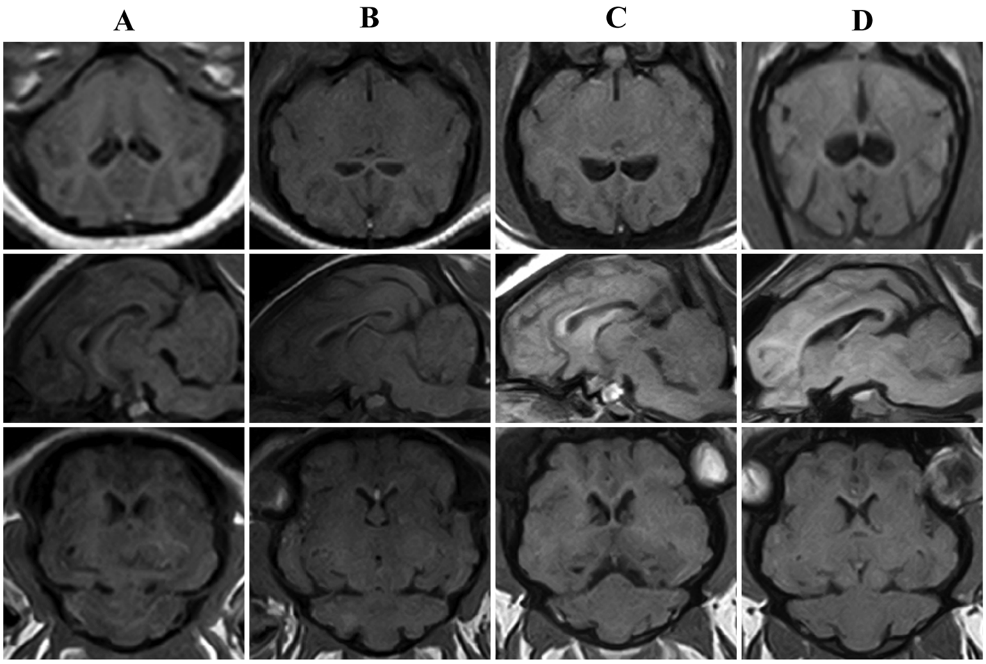

Fig. 2. T1 weighted axial images of three planes at each month-aged. 1 month (A), 2 month (B), 4 month (C) and 8 month (D) age old in micropigs.

and coronal plane using repetition time (TR) of 410 ms and an echo delay time (TE) of 23 ms. Slice thickness for the all planes was 1.5~2 mm.

Each month-aged group was evaluated by three values as lateral ventricular volume, ventricular volume ratio and asymmetry. T1 weighted transverse images were acquired for calculation of lateral ventricular and corresponding brain parenchyma areas (Fig. 1). Lateral ventricular volume was the sum of areas on each transverse plane multiplied by slice thickness and volume ratio was calculated by dividing the ventricular areas by brain parenchyma. The ratio of bilateral ventricular areas used to analyze the symmetry, dividing the volume of the right side by that of the left lateral ventricle. In addition, degree of asymmetry was arbitrarily categorized on the basis of the ratio as normal to mild (value < 0.5), moderate ($1.5 <$ value < 2.0), or severe (value > 2.0). The images were measured by two observers.

Statistical analysis was performed using SPSS Significant differences among each month-aged groups were determined with independent *t*-tests and *p*-values of < 0.05 were considered statistically significant. Inter-observer agreement was assessed with the kappa statistic with values closest to 1 indicating perfect agreement.

Table 1. Quantitative ventricular volume analysis

Minipig	LLV	RLV	Total LV	RLV/LLV	BPV
1 month	318.86 ± 18.88	357.88 ± 6.70	676.74 ± 25.58	1.13 ± 0.05	5920.58 ± 590.16
2 month	319.38 ± 78.92	311.26 ± 65.02	630.64 ± 143.84	0.98 ± 0.04	20067.28 ± 2403.28
4 month	490.97 ± 39.88	501.13 ± 68.09	992.12 ± 106.03	1.02 ± 0.07	21141.27 ± 1135.12
8 month	593.15 ± 112.33	579.46 ± 129.86	1172.62 ± 237.57	0.98 ± 0.09	23290.16 ± 1581.56

LLV: Left lateral ventricular volume, RLV: Right lateral ventricular volume, LV: Lateral ventricular volume, BPV: Brain parenchymal volume.
All data represent mean ± SD (mL).

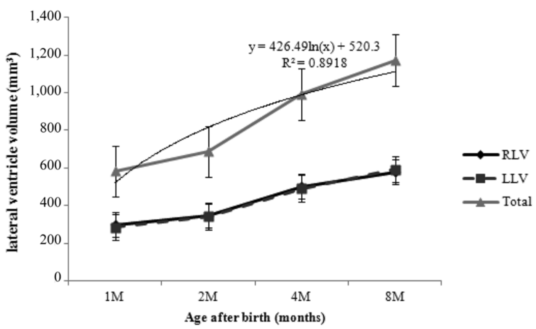

Fig. 3. Changes of the lateral ventricular volume at 1, 2, 4 and 8 month age.

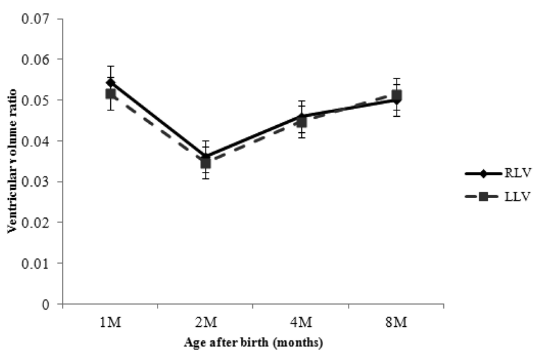

Fig. 4. Changes of the ventricular volume ratio at 1, 2, 4 and 8 month age.

Results

As the micropigs grow, the size of the lateral ventricles was increased (Figs. 2 and 3). The mean ventricular volumes of each month were 676.74 ± 25.58 mm^3 (1 month-old), 630.64 ± 143.84 mm^3 (2 month-old), 992.12 ± 106.03 mm^3 (4 month-old) and 1172.62 ± 237.57 mm^3 (8 month-old), respectively. The value of bilateral area ratio showed within 1.5 in all experimental animals (Table 1).

The ventricular volume ratio was the smallest at 2 month-of-age and re-increased from that age. The ratio was significantly different between 2 month-old and other age groups ($p < 0.05$, Fig. 3). The value of bilateral area ratios showed within 1.5 in all experimental animals. The inter-observer reproducibility was excellent for all measured images ($k > 0.9$).

Discussion

MR images provide exact assessment of the size of the lateral ventricles and brain images [1, 2]. Especially, as the enlargement of the lateral ventricles is closely related to neurological disease such as hydrocephalus in clinics, some studies have been reported about this [11, 14, 15, 17]. But in the micropigs, to date this study was not well established. But Watanabe *et al.* [16] demonstrate that the volume of MR-based lateral ventricles in young adult male Gottingen micropigs show about 740~830 mm^3, which is similar volume in 4 months of age or over that age group in our experiment. This difference seems to be due to genetic characteristics in the micropigs.

Kii *et al.* [5] reported that in Beagle-type dogs, the expansion of lateral ventricles were first detectable at 3~4 weeks-old. In this experiment, the lateral ventricles were visible from the 1 month of age, and have been increase as age advanced. In human infants, ventricular size gradually increase up to 6 months of age [13] and it has been reported that by the end of the 1st week of life a rapid increase in ventricular size occurred [12]. Micropigs also show that the size of the lateral ventricle increase up to 8 months of age, which is to be related to an increase in volume of CSF because of a change from fetal low pressure to the neonatal high pressure circulatory state in human [12]. Gonzalez-Soriano *et al.* [4] have shown that the enlargement which takes place in the ventricular system with age, which is probably related to a general age-related atrophy of neural tissue using dog brain. But in our experiment in which young animals was used, this finding was not revealed and it remains further study.

About the size of the lateral ventricle size and symmetry, Kii *et al.* [6] and Vullo *et al.* [15] reported that clinically insignificant ventricular enlargement and asymmetry was common in this group of Beagle dog. These findings are also found in the Labrador Retriever dogs [2].

In the different canine breeds such as Yorkshire Terrier and German Shepherd dogs, relative ventricle area ([ventricle area/ hemisphere area] × 100) shows different values (5.3 *vs.* 1.7) [3]. But we have found that the symmetry of the lateral ventricles in the micropigs was not apparent and the ventricular volume ratio was within 1.17 during the experimental period.

In our experiment, we have found that at 2 months old, the ventricular volume ratio shows the smallest value. This may be caused by the rapid increase of brain size compare to the ventricle size at this time.

Conclusions

MR imaging is a noninvasive imaging technique to assess morphometric analysis of the ventricular system in micropigs. In normal cases, lateral ventricle showed a positive correlation with aging and symmetric shapes in both sides. The change of ventricular ratio showed 'V' shaped graph, which inferred growth of brain parenchyma is faster than lateral ventricle especially until 2 month-old. The developmental pattern of the lateral ventricle provides basic data in micropigs as an experimental animal model for physiological and neurosurgical approach.

Acknowledgments

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