BL-BL14C/2019G040

Observation of Autism Model Rat Brain by Phase-Contrast X-ray CT

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1 Introduction

Prenatal exposure of antiepileptic drug Valproic acid (VPA) increases the risk of having offspring with autism spectrum disorder (ASD). Noninvasive imaging technique plays an important role for insights into changes in the brain structure of ASD. Conventional absorption X-ray imaging technique cannot depict internal structure of brain without contrast agent due to the small absorption differences between soft tissues of brain. New imaging method phase-contrast X-ray imaging technique, approximately 1000 times higher sensitivity than conventional imaging technique, can clearly depict soft tissue structural changes in various animal models [1-4].

Here we investigate the feasibility of this technique in detailed visualization of morphological structures changes in VPA-induced autistic brain of rat model.

2 Experiment

Autism rat offspring created by exposure of Sprague Dawley pregnant rats to valproic acid (600 mg/ i.p.) on the 12.5th day of gestation. Normal Control rat were given normal saline at the same condition. Brains from 6 VPA and 3 normal rats of 13-week-old were used in this study. Brains were extracted under anesthesia and fixed with 10% formalin for imaging. A two-crystal X-ray interferometer-based phase-contrast X-ray imaging system was used. An X-ray camera with a 2560 × 2100 pixels sensor of pixel size: 6.5 x 6.5 μm^2 was used to detect interference patterns. The data were acquired with monochromatic X-rays of photon energy (17.8 keV). After imaging, Haematoxylin-eosin (H&E) staining was performed to examine abnormal histopathological structures.

The animal experimental protocol was approved by the Ethics Committee of the Animal Care and Experimentation Council of the National Institute for Environmental Studies, Japan

3 Results and Discussion

Phase-contrast X-ray CT clearly depicted the anatomical structures of rat's brain including cortex, corpus callosum, hippocampus, and lateral ventricle depending on different densities. The significantly increased density was shown in hippocampus especially in dentate gyrus (Fig. 1). This increased density might be associated with various neurodegenerative processes leading to ASD. In addition, mild to moderate expansion of lateral ventricle, associated finding of ASD, was found in VPA group. H&E stain also revealed decreased neuronal size and increased cell packing density in dentate gyrus (Fig. 2) that is consistent with increased density on phase-contrast CT image.

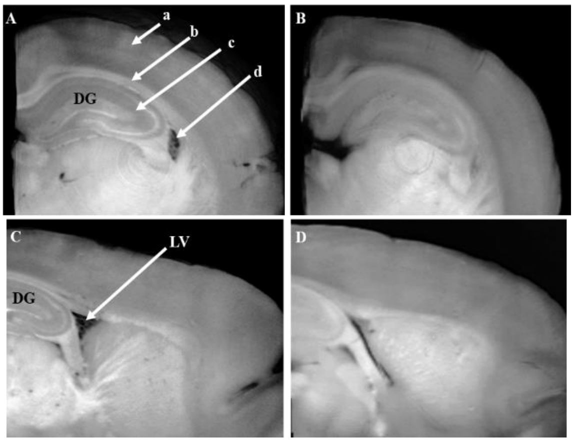

Fig. 1: Phase contrast X-ray CT image of rat brains: Axial image (A; VPA, B; Control), Sagittal image (C; VPA, D; Control), a: cortex, b: corpus callosum, c: hippocampus, d: lateral ventricle. Increased density of hippocampus especially in DG (dentate gyrus), and lateral ventricle (LV) dilatation are found.

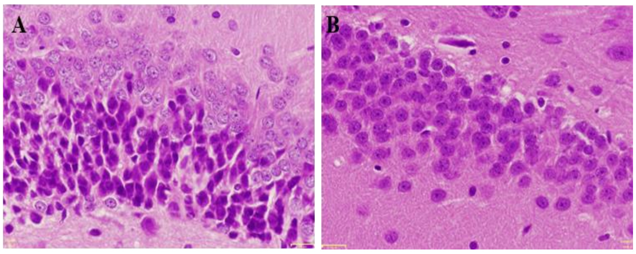

Fig. 2: Dentate gyrus region of hippocampus (×40) (H&E stain); A: VPA, B: Control. Cell density is increased in VPA rat.

References

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