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SHORT COMMUNICATION

Magnetic resonance volumetry of the hippocampus in familial spontaneous epileptic cats

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Summary A strain of familial spontaneous epileptic cats (FSECs) with typical limbic seizures was identified in 2010. The electroencephalographic features suggested that an epileptogenic zone is present in the mesial temporal structures (i.e., amygdala and/or hippocampus). In this study, visual evaluations and quantitative analyses were performed by using 3D MR hippocampal volumetry in comparing FSECs with age-matched controls. Visual hippocampal asymmetries were seen in 8 of 14 (57.1%) FSECs. The FSEC group showed a significantly higher asymmetric ratio (4.15%) than the control group (0.99%). The smaller side of hippocampal volume (HV) (0.206 cm^3) in FSECs was significantly smaller than the mean HV in controls (0.227 cm^3). However, the means of left and right HVs and total HVs in FSECs showed no differences because the laterality of hippocampal atrophy was different in each individual. Therefore, since FSECs represent a true model of spontaneous epilepsy, hippocampal volumetry should be evaluated in each individual as well as in human patients. The significant asymmetry of HV suggests the potential for hippocampal atrophy in FSECs.

Abbreviations: FLAIR, fluid-attenuated inversion recovery; FSE, fast spin echo; FSEC(s), familial spontaneous epileptic cat(s); HS, hippocampal sclerosis; HV, hippocampal volume; MTLE, mesial temporal lobe epilepsy; T2W, T2-weighted.

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Introduction

Mesial temporal lobe epilepsy (MTLE) is the most common intractable epilepsy in humans, and hippocampal sclerosis (HS) is the most common underlying pathologic abnormality consisting of neuronal loss and gliosis leading to hippocampal atrophy (Engel et al., 1975; Duncan and Sagar, 1987). The MR features of HS include reduced one-sided hippocampal volume and increased signal intensity on T2-weighted (T2W) and/or fluid-attenuated inversion recovery (FLAIR) images (Jackson et al., 1990; Wieser, 2004). Hippocampal volumetry increases the sensitivity of MRI in diagnosing hippocampal atrophy in MTLE patients, and is used as a noninvasive preoperative assessment (Jack et al., 1990; Van et al., 1996).

Recently, we identified a novel model of genetic epilepsy in a familial strain of spontaneous epileptic cats (FSECs) that is maintained at our institute (Kuwabara et al., 2010; Hasegawa et al., 2014). The FSECs showed spontaneous limbic seizures (± secondarily generalization) and stimulation-induced generalized seizures, and electroencephalograms suggested the presence of an epileptogenic zone in the mesial temporal structures, i.e., amygdala and/or hippocampus (Hasegawa et al., 2014). Therefore, these FSECs are considered as a true spontaneous and genetic (autosomal recessive) model of MTLE.

In this study MR hippocampal volumetry was performed using a 3.0 tesla (T) system and 3D sequence to investigate whether or not hippocampal volume changes exist in FSECs.

Materials and methods

This study, including maintenance of the FSEC colony, was approved by the Animal Care and Use Committee of Nippon Veterinary and Life Science University (accession nos. 09-1, 10-3, 11-51, 12-42, 13-22; representative researcher is D.H.).

Animals

Animals were divided into two groups: the control group of clinically healthy cats and the FSEC group. The control group consisted of eight age-matched cats (six males, two females) with no history of seizures and no apparent intracranial structural lesions on MRI. The median age (range) of the control cats was 56.0 months (40—119 months) and mean weight was 4.0 kg (3.3—5.0 kg). The FSEC group consisted of 14 FSECs (nine males, five females). These FSECs were selected from the colony that is maintained by our institute as age-matched to the control cats and all of these had recurrent seizures and EEG abnormalities. Twelve of 14 were the first generation (original found) and the remaining two were of the second generation (F1 cats between the first generations). The median age of the FSEC group was 52.0 months (30—90 months) and mean weight was 3.5 kg (2.6—4.6 kg).

MRI

MRI was performed using a 3.0 T MRI unit (Signa® HDxt, GE Healthcare). All images were acquired using a human knee coil (8 ch HE T/R Knee Array coil, GE Healthcare) that is suitable for the feline head as a RF coil. All cats were anesthetized by propofol and were maintained with isoflurane during MR examination. Fast spin echo (FSE) 3D-T2 Cube images (TR/TE = 3200/78—90 (auto) ms, slice thickness = 0.6 mm, slice gap = 0 mm, FOV = 15 × 15 cm, matrix size = 512 × 512, number of excitation (NEX) = 1) were acquired for 3D volumetry. In addition, FSE T1 FLAIR (TR/TE = 2800/8.2—8.4 (auto) ms, matrix = 320 × 224, NEX = 2), FSE T2 W (TR/TE = 7000/85 ms, matrix = 384 × 288, NEX = 1), and FLAIR (TR/TE/TI = 11000/140/2400 ms, matrix = 256 × 192, NEX = 2) and post contrast T1 FLAIR (Gd-T1 FLAIR: after IV administration of 0.1 mmol/kg of gadodiamide) images were also acquired in the transverse plane to evaluate visual hippocampal changes and to detect or exclude other structural changes. The visual evaluation of hippocampus was performed in each individual. The criteria of hippocampal abnormalities were as follows: presence of significant visual asymmetry of the hippocampus (dorsal and/or ventral hippocampus) and/or the lateral ventricles surrounding the hippocampus (i.e., unilateral atrophy of the hippocampus or unilateral enlargement of the lateral ventricle) on T1 FLAIR and T2W/FLAIR, and abnormal signal intensities of hippocampus such as T2W/FLAIR hyperintensity, T1 FLAIR hypointensity and contrast enhancement.

3D volumetry

Hippocampal volumes (HV) were traced from the 3D-T2 Cube images. Quantitative hippocampal volumetry was determined by semi-automatic traces of the left and right hippocampal regions on each slice using an imaging workstation (Virtual Place® Fujin, AZE) (Figure 1B—D). After semi-automatic tracing, hippocampal regions were corrected manually to improve accuracy. Determinations of anatomic landmarks and borders of the hippocampus were based on the feline anatomic atlas (Snider and Niemer, 1961). The left and right HVs and their means (mean HV) and sums (total HV) were calculated (cm^3). The asymmetric ratio (%) of the hippocampus was obtained by dividing the absolute volume difference between the left and right HV by the larger side of HV.

Two observers, blinded to individual information, performed all measurements. The inter-observer errors of LHV and RHV and total HVs were calculated in each group and were within the SD range of each observer. Therefore, HVs and asymmetric ratios of each group were analyzed using the average of two independent observers.

Statistical analysis

For each group, the mean and SD were calculated for the left HV, right HV, mean HV, total HV and asymmetric ratio. The HV in each group was compared with the left and right sides using Mann—Whitney *U*-test. In addition, the mean HV, total HV and asymmetric ratios were analyzed for statistical correlations of body-weight and age (Spearman's correlation coefficients) in each group. The left HV, right HV, mean HV, total HV and asymmetric ratio respectively for FSECs and controls were compared using the Mann—Whitney *U*-test.