Pathophysiological Analysis of the Epileptogenic Zone in Familial Spontaneous Epileptic Cats: Electroencephalographic, Imaging, and Pathological Studies

Abstract of Doctoral Thesis

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Epilepsy is the most common cerebral disease in human and veterinary medicine. Familial spontaneous epilepsy cats (FSEC) have 2 types of seizure (spontaneous and induced) and are considered to be a model of human mesial temporal lobe epilepsy (MTLE) from their ictal semiology. In the present study, we identified the epileptogenic zone and performed pathophysiological analysis in FSEC using electroencephalographic, diagnostic imaging, and histopathological techniques. Chronic video electroencephalographic recordings with depth electrodes demonstrated spontaneous seizures originating in the hippocampus and amygdala. The location of the symptomatogenic and ictal onset zones suggested the presence of the epileptogenic zone in the hippocampus and amygdala. Measurement of hippocampal volume (HV) with magnetic resonance imaging (MRI) demonstrated a significant expansion in the difference of HV between the left and right sides and significant shrinkage of the smaller HV in FSECs than in control animals. It also revealed a long-term tendency for an increase of hippocampal asymmetry and long-term decrease of HV in FSECs. These results indicated the presence of structural abnormal zones in the hippocampus of FSECs. Examinations of imaging parameters from diffusion and perfusion MRI, which is a cerebral function imaging technique, demonstrated a significant elevation of diffusibility and reduction of anisotropy, hypoperfusion in the hippocampus and amygdala during interictal periods, and reduced diffusibility and hyperperfusion in these regions in postictal periods. These results suggested microscopic changes in tissue structures and the presence of functional deficit zones in the hippocampus and amygdala. Furthermore, pathological analysis revealed extensive neuronal cell loss without gliosis in the hippocampus and amygdala in homozygous and heterozygous FSECs. The abnormalities in the hippocampus of FSECs were not consistent with the findings of hippocampal sclerosis in patients with sporadic typical human MTLE, but resembled the pathology of human familial MTLE. From the results of the invasive and non-invasive detection of the epileptic focus in this study, it is considered that the epileptogenic zones are located in the hippocampus and amygdala in FSEC, and hippocampal atrophy and neuronal cell loss in FSEC are considered to be a possible congenital (genetic) malformation similar to human familial MTLE. The presence of these abnormalities in the hippocampus suggests a variety of pathology involved in the development of epilepsy in FSEC. Therefore, it will be necessary to elucidate the underlying mechanism of epileptogenicity, including the identification of

responsible genes, in the future. FSEC are the sole model of genetic epilepsy in cats and can be a good tool with which to study human familial MTLE. It is expected that the elucidation of the pathogenic mechanism for epilepsy in FSEC will play an important role in the analysis of pathology that is common between veterinary and human medicine.