学 位 論 文 の 要 旨

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主論文の題名：

Unilateral hippocampal CA3-predominant damage and short latency epileptogenesis after intra-amygdala microinjection of kainic acid in mice

主論文の要旨

Mesial temporal lobe epilepsy is the most common, intractable seizure disorder in adults. It is associated with an asymmetric pattern of hippocampal neuron loss within the endfolium (hilus and CA3) and CA1, with limited pathology in extra-hippocampal regions. We previously developed a model of focally-evoked seizure-induced neuronal death using intra-amygdala kainic acid (KA) microinjection and characterized the acute hippocampal pathology. Here, we sought to characterize the full extent of hippocampal and potential extra-hippocampal damage in this model, and the temporal onset of epileptic seizures. Seizure damage assessed at four stereotaxic levels by FluoroJade B staining was most prominent in ipsilateral hippocampal CA3 where it extended from septal to temporal pole. Minor but significant neuronal injury was present in ipsilateral CA1. Extra-hippocampal neuronal damage was generally limited in extent and restricted to the lateral septal nucleus, injected amygdala and select regions of neocortex ipsilateral to the seizure elicitation side. Continuous surface EEG recorded with implanted telemetry units in freely-moving mice detected spontaneous, epileptic seizures by five days post-KA in all mice. Epileptic seizure number averaged 1-4 per day. Hippocampi from epileptic mice 15 days post-KA displayed unilateral CA3 lesions, astrogliosis and increased neuropeptide Y immunoreactivity suggestive of mossy fiber rearrangement. These studies characterize a mouse model of unilateral hippocampal-dominant neuronal damage and short latency epileptogenesis that may be suitable for studying the cell and molecular pathogenesis of human mesial temporal lobe epilepsy.

（注）２，０００字以内にまとめて記入すること。