ABSTRACT NO. 27

ALTERATION IN GLAST PROTEIN LEVELS DURING Fe^{+++}-INDUCED EPILEPTOGENESIS

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Repetitive microinjection of glutamate into the amygdala causes seizure propagation similar to that found in both kindling and the $FeCl_3$-induced epilepsy model. This observation suggests that the enhancement of excitatory neurotransmitter levels, especially of glutamate, within the limbic system has a critical role in seizure propagation. Although glutamatergic excitatory synaptic transmission efficiency has been suggested to be important in epileptogenesis, the molecular and cellular events responsible for this potential mechanism remain unknown. An essential component of the transmission process in glutamatergic synapses is its removal from the synaptic cleft. To date, three types of cDNAs, encoding high-affinity sodium-, potassium-dependent glutamate transporters have been cloned, their distribution estimated and their roles proposed. These glutamate transporters are excitatory amino-acid carrier, glutamate-aspartate transporter (GLAST) and glutamate transporter-1. We wondered if enhancement of glutamatergic excitatory synaptic transmission efficacy in the spontaneous seizure model is associated with changes in the levels of glutamate transporter proteins. Severe head injury in humans causes recurrent seizures; this form of epilepsy appears to correlate with occurrence of parenchymal hemorrhage. Injection of ferric cations, one component of hemoglobin, into rat amygdala, causes lipid peroxidation, and recurrent spontaneous seizures. We wondered whether a perturbed regulation of glutamate might be a mechanism for chronic epileptogenesis. Levels of glutamate transporter proteins GLAST were measured in ipsilateral and contralateral hippocampi removed from rats having spontaneous iron-induced limbic seizures. At 15 days and 30 days after injection, when experimental animals were experiencing spontaneous limbic behavioral seizures, GLAST transporter protein was down-regulated. Epileptogenesis may correlate with the impairment of glial glutamate transport, leading to excitation and imbalance of transmitter influences within the hippocampi.