Neurochemical alterations related to temporal lobe epilepsy

Naffah-Mazzacoratti MG
Departamento de Bioquímica/Neurologia, UNIFESP
naffahmazz.nexp@epm.br

The epilepsy model induced by pilocarpine reproduces in rodents the main characteristics found in human temporal lobe epilepsy. This model is characterized by an acute phase, with long-lasting status epilepticus (SE), a silent period, with normal behavior and by a chronic period, with spontaneous seizures. The epilepsy may occur due to increased excitation, decreased inhibition or both phenomena. Ours previous works showed a neurotransmission completely altered in the hippocampus of animals submitted to pilocarpine model of epilepsy. Thus, we tried to identify molecular markers involved in epileptogenic process such as: a) changes in the expression of proteins related to signal transduction such as phosphotyrosines (PTyP), mitogen activated protein kinase (MAPK) and growth associated phosphoprotein (GAP-43); b) alteration in the components of extracellular matrix; c) study of the mechanisms involved in inflammatory process such as prostaglandins production, generation of free radicals and the involvement of kinin system. The main results found were: a) increased expression of PTyP, mainly in the CA3 region of hippocampal formation after 5 h of SE onset, increased levels of MAPK in several limbic regions, during the first hour of SE and increased hippocampal expression of GAP-43 during the acute, silent and chronic periods b) Increased synthesis of chondroitin sulfate, decreased synthesis of heparan sulfate associated to increased expression of the receptor tyrosine phosphatase beta in the hippocampus c) Increased synthesis of prostaglandins in the hippocampus such as PGE2, PGD2 and PGF2α, decreased superoxide dismutase activity associated to an increased concentration of hydroperoxides during the acute and chronic phases and increased synthesis of kinin B1 and B2 receptors in all hippocampal formation. The B1 knockout mice showed increased latency for the first seizure, decreased number of seizures during the chronic phase, decreased mossy fiber sprouting and reduced hippocampal cell death, when compared with control animals, showing a deleterious function of this receptor. The B2 knockout mice showed minor silent period, increased seizure frequency during the chronic phase, increased mossy fiber sprouting and accentuated cell death when compared with control, showing a protector role of this receptor. These results demonstrated a great change in several hippocampal pathways during epileptogenesis, showing that the epileptic syndrome present high complexity, involving changes in neuronal and glial connections.

PRONEX, FAPESP, CAPES, CNPq and FADA