nencki institute
of experimental biology

PRESS RELEASE

1.09.2009

Novel mechanism of epileptogenesis involves action of extracellular proteolytic enzyme at the synapse.

Epilepsy is a chronic neurologic disorder affecting up to 1% of mankind. It is defined by recurrent spontaneous seizure-attacks which, in a proportion of patients, are generated by synchronous firing of localized groups of neurons – so called epileptic foci. Temporal lobe epilepsy (TLE) is the most common type of epilepsy in adults that also affects children. It is characterized by the presence of epileptic foci located within hippocampal formation, amygdala or temporal neocortex. In most patients, TLE appears to be caused by a single brain insult, such as seizure episode, trauma or infection, occurring early in life. This is followed by a seizure-free (latent) period, that can last for many years. At some point, a fully expressed epileptic disorder occurs and, if not properly controlled, it leads, over time, to progressive cognitive impairment. Unfortunately, in as much as 70% of patients, TLE is intractable by pharmacologic treatment and requires brain surgery for seizure control.

Temporal lobe epilepsy is frequently associated with a distinctive histological alteration, called hippocampal sclerosis. This is characterized by massive loss of the hippocampal pyramidal neurons. On the other hand, there is no loss of the granule neurons; instead there is pronounced aberrant sprouting of their axons (mossy fibers) that reenter the granule cell layer and likely make recurrent excitatory connections. The latter phenomenon is a prominent example of aberrant neuronal plasticity. In animals, the condition that closely resembles human TLE models is a rodent epilepsy that follows kainate-induced status epilepticus or chronic subthreshold excitatory stimulation called kindling.

In order to explore novel therapeutic avenues for TLE, scientists from the laboratories of Neuromorphology, and Molecular Neurobiology, of the Nencki Institute, investigated the role of extracellular proteolysis in the brain of animals subjected to experimental epilepsy. Synaptic extracellular proteolysis is a novel important mechanism mediating plasticity of synapses. The major proteolytic enzyme in the brain is matrix metalloproteinase 9 (MMP-9). Researchers from the Nencki Institute have discovered that MMP-9 is a synaptic enzyme playing key role in the development of epilepsy in rats and mice. (Wilczynski i wsp. 2008). In particular, mice that had been genetically engineered to be deficient of MMP-9 were more resistant to epileptogenesis than normal mice. Conversely, rats with increased levels of MMP-9 in neurons were more prone to develop epilepsy than normal ones. The findings significantly increase our knowledge about the epilepsy pathogenesis, and indicate possible new directions of research on TLE therapy.
http://wyborcza.pl/1,76842,5008848.html

For more information contact Dr Grzegorz Wilczyński
tel. (22) 58 92 355, e-mail: g.wilczynski@nencki.gov.pl

Prof. Leszek Kaczmarek
tel. (22) 58 92 240, e-mail: l.kaczmarek@nencki.gov.pl