The role of orexinergic system of the brain in behavioral changes induced by kainic acid status epilepsy in laboratory rats

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Epilepsy appears to be a widely spread disease having observed in 1% of the world population. Even under conditions of optimal therapeutic treatment the epilepsy is totally controlled only in 75% of the patients The pathophysiology of epilepsy is not clear. It involves a complex interaction of many factors. One possible mechanism is considered a disbalance between excitatory and inhibitory neurotransmiters. Knowledge of epileptogenesis and investigation of the mechanisms of antiseizure action of intrinsic modulatory systems of brain will help to elaborate the right strategy of the therapeutic treatment of this disease. Disbalance between excitatory and inhibitory transmitter systems is considered as a common reason of epileptic activity [Avanzini, G., Franceschetti, S., 2003] and it is well known that several neuromediators in the brain play an important role in controlling of epilepsy [Salgado and Alkadhi, 1995; Harada et al., 2004; Anschel et al., 2004] The functioning of above-mentioned systems is considerably dependent on the activity of orexinergic system. It has been shown that orexin induces modulation of bursting activity of the hippocampal neurons, depression of isolated NMDA responses (Doreulee et al., 2004) and the stimulation of norepinephrine release (Hirota et al., 2001). Basing on these data a consideration was made about a possible involvement of orexinergic system in epileptogenesis.

The behavioral experiments were carried out in open field, passive avoidance and T-maze labyrinth to determinate behavioral changes induced by KA-SE. The experiments have shown that status epilepticus prompts a deterioration of hippocampal associated learning and memory processes as well as strengthening of fair emotion and changes in motor activities of rats.

A morphological analysis of the brain of experimental animals revealed changes at the hippocampal level resulting in decrease of the amount of main glutamatergic pyramidal neurons. Which was in correlation with decrease amount of Glutamicaciddecarboxylase (GAD) – positive neurons in hippocampus. On the other hand our experiment show the statistically significant reduction of orexinergic neurons in periventricular area of the hypothalamus.

Basing on these data we suggest that in KA-SE-laboratory rats disturbance of hypocampal-associated spatial memory is conditioned by massive death of glutamatergic neurons in hippocampus. Disruption of hypothalamo-hippocampal relationship may play additional role for this memory changes. The massive death of hypothalamic orexinergic neurons and accompanied changes in functionality of mesolimbic system throughout deterioration of activity of dophaminergic system should be caused the changes in motor and emotional status of rats which were founded in our study.