Investigation the effects of orexins on neuronal activity of CA1/CA3 fields of the hippocampus in control and kainate-induced epilepsy rats

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Epilepsy is a chronic disorder of the CNS characterized by the appearance of spontaneous recurrent seizures generated by an imbalance of excitatory/inhibitory synaptic transmissions[1]. Epilepsy is associated with increased risk for many comorbid conditions including sleep disorders[2]. Insufficient sleep can worsening seizure frequency[3] and further reduce the quality of life by promoting other comorbid conditions, including cognitive impairments/psychological disorders. Based on numerous studies the hypothalamic orexinergic system(OX) is involved in various physiological function and the role of this system in pathophysiology of several brain disorders such as narcolepsy and eating disorders are well documented, but data about their role in epileptogeneses is still on debate. OX neurons connected to the seizure-generating hippocampal network [4]. Recently in kainate-rat model of epilepsy we have found a loss of hypothalamic OX-B positive cells and associated with this changes memory disturbance. These changes were in correlation with structural alterations in the hippocampus. To better understand the role of OX system in hippocampal related functions we investigate the effects of OX on neuronal activity of CA1/CA3 fields of the hippocampus in control and kainate-model of epilepsy.

In vivo electrophysiological experiments were performed to investigate the effects of intracerebroventricular application of OX (A and B, 10µl) on background spiking activity and evoked field responses of the hippocampus. Bipolar intrahippocampal single and paired electrical stimulation of CA1/CA3 fields were performed in wild type and Kainic acid-status epilepsy (KA-SE) rats (120-150g). KA-SE was induced by single intraperitoneal injection of kainic acid (15mg/kg). Stainless steel threepolar electrodes were stereotaxically implanted in ketamine anesthetized rats according to maps of Paxinos and Watson (CA1:AP3.8mm, L2.8mm, H2.8mm. CA3: AP3.8mm, L4.1mm, H3.7mm). Intraventricular injections of OX were performed by chemitrodes. Recording and analyses were carried out by Chart5 program. Analyses of several parameters were performed (frequency/amplitude, duration/Tmax.slope of field responses, % of paired pulse facilitation). For statistical analyses was used program PRIZMA.

Our experiment showed that OX-A decreases amplitude and increases the frequency of baseline activity in CA1, no significant changes were observed in CA3. Changes in CA1 were accompanied by concomitant reduction of duration and Tmax.slope of the responses. The amplitude of single evoked responses was increased in CA1 and decreased in CA3 after OX-A injection. OX-B was ineffective, indicating involvement of OX1 receptors in the effects of OX-A. OX-A induces potentiation of paired pulse facilitation in CA1.

Alterations caused by kainite-model of epilepsy were different in CA1/CA3 fields and KA-SE shifts the character of influence of OX-A in these fields. The possible mechanisms are discussed.

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