Orexin causes blocking of epileptiformal activity in hippocampal slices of rat

Giorgi Vashalomidze, Nanuli Doreulee

giorgi.vashalomidze611@ens.tsu.edu.ge

Human and Animal physiology, Ivane Javakhishvili Tbilisi State University

Epilepsy is a very common disorder, affecting approximately 0,5% of the population. Even under optimal therapeutic treatment, epilepsy is controlled only in 75% of patients. The pathophysiology of epilepsy is not fully understood. In the treatment strategy of epilepsy it is very important to determine the role of endogenous modulators. Inhibitory role of biogenic amines on epileptiform activity is well known. The functioning of these neurotransmitters considerably depends on the activity of hypocretin/ Orexinergic system of the brain. It has been shown that orexins evoke norepinephrine release (Hirota et al., 2001) and synaptic plasticity in CA-1 of hippocampus (Selbach, Doreulee et al., 2004). Based on these data, a possible antiepileptic action of orexins has been suggested. The aim of our work was to determine the role of orexinergic system in the epileptic activity of the brain. To investigate the antiepileptic action of orexin A in in vitro experiments different approaches were used. The effects of orexins were analyzed on 1. multiple discharges of field population-spike induced by GABA – antagonists; 2. isolated NMDA responses in CA-1 field of hippocampus; 3. spontaneous activity of bursting neurons in CA-3 of hippocampus. Analyses of the results has revealed that orexin-A a) inhibits multiple discharges of pop-spikes (decreases duration/amplitude of discharges and inhibits of spontaneous epileptic afterdischarges); b) induces a long-term depression of isolated NMDA responses in CA-1 field; c) modulates the frequency of bursting neurons in CA-3 field of hippocampus. These effects are indices of antiepileptic action of orexin.