Abstract

Perinatal insult may lead to a permanent impairment of brain function resulting in the development of epilepsy. Status epilepticus (SE) in immature rats leads to hippocampal hyperexcitability. The functional and morphological changes of the hippocampus are similar to those seen in human temporal lobe epilepsy. The excitability may be influenced by adenosine. Adenosine acts its anticonvulsant effect by activation of A1 receptors (A1R). The concentration of adenosine is regulated by adenosine kinase (ADK) present in two isoforms – ADK-L and -S. The main goal of the thesis is to elucidate the changes in A1R and ADK isoforms expression during intact brain development and after SE. A1R agonist 2-chloro-N6-cyclopentyladenosine (CCPA), as well as inhibition of ADK by 5-iodotubercidin (5-ITU), may bolster the anticonvulsant effect, but their action may correspond with the level of A1R and ADK. Hippocampal excitability in immature rats after LiCl-pilocarpine SE was studied by the model of hippocampal afterdischarges (ADs) and correlated with changes of A1R and ADK in the hippocampus. ADs demonstrated significantly decreased hippocampal excitability shortly after SE induction, whereas significant hyperexcitability accompanied by spontaneous seizures in older rats was shown. Increasing ADK-S expression during early brain development was revealed, ADK-L remained unchanged. In SE rats, ADK-L showed an initial decline in expression followed by an increase, whereas ADK-S demonstrated opposite changes. A1R expression gradually decreased in 10-day-old rats. 5-ITU inhibited ADs and decreased the incidence of spontaneous seizures. CCPA decreased hippocampal excitability in immature rats. Age-related differences in hippocampal excitability might be due to the expression of A1R and ADK in the hippocampus. A1R agonists and ADK inhibitors may represent promising approaches to developing a new anticonvulsant and/or preemptive treatment of epilepsy.