Abstract:

Alzheimer´s disease is a neurodegenerative disorder with the highest prevalence in the population and for which we do not have a cure so far. The aim of this thesis was to test the mediator system of the N-methyl-D-aspartate receptor and nitric oxide in an animal model of sporadic form of Alzheimer´s disease (Samaritan Alzheimer's Rat Model; Taconic Pharmaceuticals, USA). Then compare these results with changes in hippocampal cholinergic system and cognitive tests. The Samaritan rat model is based on the unilateral in vivo application of β-amyloid$_{42}$ and the pro-oxidative substances (ferrous sulfate heptahydrate and L-buthionine-(S,R)-sulfoximine). Neurochemical methods included testing of the NR1/NR2A/NR2B subunits of the N-methyl-D-aspartate receptor and activity of nitric oxide synthases (neuronal, endothelial, inducible) in the cortex, in both cases in the right and left hemisphere separately. Our results show that Samaritan rats exhibited significant changes in expression of NR2A/NR2B subunits of the N-methyl-D-aspartate receptor and activity of inducible nitric oxide synthase in cortex compared to control rats. The results of glutamatergic system are consistent with changes in activity of cholinergic transporter and cognitive tests (Morris water maze and active allothetic place avoidance). Our results support the two-stage mechanism of the glutamatergic system and mimicking the situation of early stages of AD.

Key words: Alzheimer´s disease, NMDA receptor, Samaritan rat model, nitric oxide synthases