DOI 10.18699/CSGB-2018-30

Effect of ceftriaxone on cognitive deficits caused by amyloid-beta neurotoxicity in mice

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Key words: Alzheimer's disease, ceftriaxone, Aß 25-35, Barnes test

Motivation and Aim: At the moment, there are no effective therapies that can stop or reverse the course of a serious and widely spread neurodegenerative disorder, Alzheimer's disease (AD). One of frequently used animal models of AD is based on the injection of amyloid beta (Aß) or its fragments into the brain that causes neurodegenerative changes and AD-like cognitive deficits. Recently, an antibiotic ceftriaxone that possesses neuroprotective properties was found to correct cognitive deficits in a genetic rat model of accelerated senescence and sporadic AD (OXYS rat strain) has been revealed. [1] The aim of this study was to study the effect of ceftriaxone on cognitive deficits caused by the amyloid-beta neurotoxicity in mice.
Methods and Algorithms: In the experiment, were used sexually mature male mice C57BL/6J. Animals were divided into 4 groups. Groups 1 and 2 received sterile water, and groups 3 and 4 received Aß fragment 25-35 (Aß 25-35) into the lateral ventricles of the brain. Groups 2 and 4 were chronically injected with ceftriaxone (100 mg/kg, i.p., 5 weeks) while groups 1 and 3 were given injections of saline. Open field test, Barnes test and T-maze were performed to assess the behavioral effects of ceftriaxone in mice.
Results: Mice injected with Aß 25-35 had a significant decrease in motor and exploratory activity in the open field test two weeks after the injections, whereas in the later these indicators recovered. Ceftriaxone had a positive effect on a number of parameters in the Barnes test. A significant decrease in the latency to find a target hole in the 4th session of the first day of training (short-term spatial memory index) and an increase in the percentage of goal hole nosepokes on the test day (long-term spatial memory index) were observed in mice of the 4th group. Ceftriaxone also significantly augmented percentage of correct choices (working memory index) in mice of the 4th group in the T-maze test.
Conclusion: The central injection of the fragment Aß 25-35 leads to a disruption in the learning ability and short-term spatial memory in the Barnes test. Chronic administration of ceftriaxone in mice injected with fragment Aß 25-35 caused an improvement in cognitive performance in the Barnes test. Moreover, ceftriaxone administration influenced various indicators in other behavioral tests. Those alterations are apparently related to the neuroprotective properties of ceftriaxone, based on the restoration of glutamate transport in astrocytes and the reduction of excitotoxicity, which plays an important role in the pathogenesis of AD.
Acknowledgements: Supported partially by grant No. 15-04-05593-a from RFBR (Russia). The studies were partially implemented using the Unique scientific installation "Biological collection – Genetic biomodels of neuro-psychiatric disorders" (No. 493387).

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