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Effects of Ceftriaxone on cognitive and neuromolecular deficits in A53T mouse genetic model of Parkinson's disease

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Objectives: In addition to typical motor dysfunction, Parkinson's disease (PD) is characterized by dementia affecting about 30% of PD patients (PDD). Memory impairment, decreased attention and visuospatial skills are among the most common cognitive deficits in PDD. Current treatment of PD does not cover all manifestations of the disease focusing mainly on motor symptoms. Ceftriaxone (CEF), which has been used for decades as an antimicrobial agent, recently attracted attention as a neuroprotective agent due to its ability to reduce glutamate-mediated neurotoxicity and to enhance the degradation of misfolded proteins. This study was aimed to investigate the effects of CEF administration on cognitive impairment and neuromolecular parameters such as autophagy intensity and expression of neurotrophic factors in a genetic model of PD (B6.Cg-Tg(Prnp-SNCA*A53T)23Mkle/J mouse strain).

Methods: To estimate neuroprotective effects of CEF, the animals of experimental groups (B6.Cg-Tg and C57Bl/6j) were injected chronically with the drug (100 mg/kg/day, i.p., 35 days). The behavioral testing included open-field test, Barnes test and T-maze. RT-PCR examination of gene expression levels was conducted as well.

Results: CEF administration diminished memory deficits associated with alpha-synuclein overexpression in Barnes test, as evidenced by improved dynamics of the latency to find the target hole, decreased value of weighted mean distance and increased percentage of visits to the target hole. Besides, CEF increased the ratio of correct choices to all choices in T-maze in A53T mice. Finally, we assessed the impact of CEF on the expression levels of neurotrophic factors genes (BDNF, GDNF, CDNF) and some of the key autophagy-related genes (p62 and Becn1) in brain.

Conclusions: CEF treatment improved some of the impaired cognitive features and exerted positive effects against neurodegeneration-related processes in A53T genetic model of PD. Obtained results provide notable evidence that CEF is a multipotent agent for therapy of various manifestations of PD including dementia.

Biography

Anastasiya S Ryzhkova graduated from Novosibirsk State University in 2015 with a Bachelor of Biology degree. Her BS thesis is related to the effects of new psychotropic drug TC-2153 on serotoninergic system and its potential activity as an antidepressant (Institute of Cytology and Genetics SB RAS (Novosibirsk, Russia). Currently, she is in Master's Program of Physiology at Novosibirsk State University and working on her MS thesis in the Scientific Research Institute of Physiology and Basic Medicine. Her research interests are focused on neurodegeneration, synucleinopathies, neuropharmacology, animal models of neurodegeneration, aging, and autophagy.

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