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Cystatin C as regulator of autophagy in brain of transgenic mice with model of Parkinson's disease

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Motivation and Aim: Autophagy was shown to be suppressed in striatum of transgenic mice with model of Parkinson's disease [1]. Cystatin C is one of the potent regulators of autophagy [2]. Changes in the expression and secretion of Cystatin C in the brain have been shown in amyotrophic lateral sclerosis, Alzheimer's and Parkinson's diseases and in some animal models of neurodegeneration, demonstrating protective role of Cystatin C [3]. It was suggested that Cystatin C plays the primary role in amyloidogenesis and perspective as treatment of neurodegenerative diseases. Cystatin C colocalizes with amyloid beta-protein in brain in Alzhemer's disease. Controlled expression of a cystatin C-peptide was suggested as a new approach to therapy for Alzheimer's disease. In Parkinson's disease serum Cystatin C levels can predict disease severity and cognitive dysfunction, although the exact role of Cystatin C remains unclear. The aim: to evaluate expression of Cystatin C in transgenic mice with model of Parkinson' disease in early pathological state of disease (5 months) and evaluate results as related to mechanism of development of autophagy.
Methods and Algorithms: 5-month-old male mice of B6.Cg-Tg(Prnp-SNCA*A53T)23Mkle/J) (further – B6.Cg-Tg) and control C57Bl/6J strain were used. Total RNA was purified from mouse brain areas (striatum, amygdaloid complex, hypothalamus, hippocampus) using RNeasy Plus mini kit (Qiagen). qPCR was performed in a CFX96 Real-Time PCR Detection System (Bio-Rad, USA) using HS-qPCR Mix SYBR Green (2x) (Biolabmix, Russia), 200 nM real-time PCR primers (Forward Primer (5′→3′) AGGAGGCAGATGCCAATGAG; Reverse Primer (5′→3′) GGGCTGGTCATGGAAAGGA), 5 µl template (1:50 diluted cDNA).
Results: Cystatin C (*Cst3*) gene expression analysis in *striatum and*, especially in *amygdaloid complex*, in mice with transgenic model of Parkinson's disease (5 months) revealed statistically significant ($p = 0.0168$) decrease vs control; there was a correlation between the *Cst3* expression and marker of autophagy *LC32* level (immunohistochemistry). Cystatin C concentration in serum (ELISA) of transgenic mice was not changed *vs* control.
Conclusion: The data obtained confirms that *Cst3* expression in striatum correlates with autophagy. Cystatin C can play a protective role in multiple neurodegenerative disorders, including Parkinson's and Alzheimer's diseases.
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