DOI 10.18699/SBB-2022-422

Effects of two types of the central (intracerebroventricular vs. intrahippocampal) administration of $A\beta_{25-35}$ on the induction of Alzheimer's disease-like pathology in mice

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Key words: models of Alzheimer's disease, $A\beta O_{25-35}$, mice, neuroinflammation, microglia, autophagy, neurodegeneration

Motivation and Aim: Identification of key pathogenetic mechanisms of Alzheimer's disease (AD) using adequate animal models that reproduce various signs of the pathology seems to be a priority area of research. Animal models of AD induced by intracerebroventricular (ICV) or intrahippocampal (IH) administration of oligomeric forms of amyloid-beta (Aβ) to laboratory rodents are widely used in current research [1]. It remains unclear whether these models provide similar outcomes or mimic core pathological mechanisms of AD equally. The aim of the work was to compare two models of AD induced by ICV or IH administration of $A\beta_{25-35}$ oligomers ($A\beta O_{25-35}$) to C57BL6 mice (3 m.o.). *Methods and Algorithms*: The analysis was performed using parameters characterizing behavior (passive avoidance test, open field test), protein content (IBA1, Aβ, LC3-II), and expression of genes for neuroinflammation (*Aif1*, *Lcn2*, *Nrf2*), autophagy (*Atg8*, *Becn1*, *Park2*), and markers of neurodegeneration (*Cst3*, *Insr*, *Vegfa*). *Results*: Similar severity of cognitive deficits was found in both models of $A\beta O_{25-35}$ administration. The detected deposits of Aβ were associated with the activation of microglia and neuroinflammatory response in the frontal cortex and hippocampus. Autophagy activity was increased in the hippocampus (LC3-II, ICV, IH) and frontal cortex (LC3-II, IH). The mRNA levels of genes related to neuroinflammation were elevated in the hippocampus (*Lcn2*, ICV) and amygdala (*Aif1*, ICV). Mitophagy activity (*Park2*) was suppressed in the cortex (IH) and increased in the amygdala (ICV). Neurodegenerative alterations were revealed by the reduced mRNA levels in the hippocampus (*Vegfa*, ICV, IH), frontal cortex (*Cst3*, ICV; *Insr*, IH; *Vegfa*, ICV), and amygdala (*Vegfa*, ICV). *Conclusion*: Despite similar effects on behavior, there were certain differences in the course of AD-like pathological processes induced by ICV or IH, which should be taken into account while modeling various aspects of AD.

Acknowledgements: The study was supported by budgetary funding for basic scientific research of the Scientific Research Institute of Neurosciences and Medicine (theme No. 122042700001-9 (2021-2025)). The studies were partially implemented using the Unique scientific installation "Biological collection – Genetic biomodels of neuro-psychiatric disorders" (No. 493387) at the Scientific Research Institute of Neurosciences and Medicine.

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