DOI 10.18699/SBB-2022-622

Morphological feature of the postnatal blood-brain barrier formation as one of predictors of AD-like pathology development in rats

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Key words: blood-brain barrier, postnatal brain development, tight junctions, OXYS rats

Motivation and Aim: Alzheimer's disease (AD) is destructive neurodegenerative disorder which development is conjugated by dysfunction of the blood-brain barrier (BBB) and decline of the cerebral blood flow. Preconditions of these alterations may originate at early age during BBB formation; nonetheless a probable linkage among altered BBB formation and its dysfunction later in life is studied insufficiently. Difficulties in exploration of this relationship are associated with a deficiency of suitable biological models of the most common sporadic form of AD. Senescence-accelerated OXYS rats are esteemed as an adequate model of the most common sporadic form of AD due to development of all key signs of the disease without mutations in App, Psen1 and Psen2 genes.
Methods and Algorithms: Here we investigated the formation of BBB in the hippocampus and frontal cortex of OXYS and Wistar (control) rats during early postnatal development. We studied the number and length of tight junctions (TJ) between endothelial cells together with the distance between TJ using electron microscopy and levels of occludin and claudin 5 as the main TJ proteins by Western blot analysis. Moreover, we evaluated the size and shape of capillary lumens as well as the integrity of a basement membrane.
Results: We found that the level of occludin did not significantly change with age in the hippocampus of OXYS and Wistar rats; however the occluding level naturally increased from birth to the end of the second postnatal week (postnatal day 14) in the frontal cortex of rats of both strains. Besides, we found a trend of decreased occludin level in the cortex of OXYS rats ($p = 0.067$). Additionally we found that ultrastructure of capillaries was altered in the hippocampus of OXYS rats at early postnatal age.
Conclusion: Alterations of the BBB formation may result in cerebrovascular dysfunction observed previously in OXYS rats even at the early stage of AD-like pathology which therefore may contribute to the development and progression of neurodegeneration late in life.
Acknowledgements: This work was supported by Russian Science Foundation (grant No. 19-15-00044).