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Alteration of hippocampal glial support during early postnatal development as a possible premise of Alzheimer's disease

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Recent studies using state of the art diagnostic techniques have confirmed that the preclinical period of sporadic (> 95 % of cases) form of Alzheimer's disease (AD) can last for decades, but the question of when exactly the disease development begins and what contributes to its development remains open. Several epidemiological and experimental studies indicated that the predisposition for accelerated aging, the main risk factor for AD development, can be formed during the early postnatal period of life, at the age of the completion of brain maturation. The results of our work on the senescence-accelerated OXYS rats, a unique model of sporadic AD, have confirmed the validity of this hypothesis. We have identified the features of brain maturation in OXYS rats in the early postnatal period (at the ages P0-P20, P – postnatal day) which can act as prerequisites for the development of initial neurodegenerative changes in the later age. OXYS rats have a lower (comparing with their maternal Wistar strain) body weight at birth, decreased duration of gestation, a delayed physical development and formation of reflexes in the postnatal period against the background of impaired neuronal stem cells differentiation and the formation of mossy fibers in the dentate gyrus of the hippocampus, and a decrease in the efficiency of formation of synaptic contacts in OXYS rats. The completion of brain maturation in OXYS rats occurs against the background of a decrease in astrocytic and microglial support – a key regulator of the neural circuitry function – taking place in the hippocampus and prefrontal cortex. The lack of glial support may be the cause of the decreased efficiency of the formation of synaptic contacts found in OXYS rats, which made it possible to consider it as a key event leading to the development of AD signs in the future.

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