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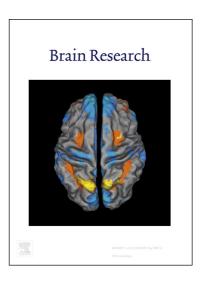
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ACCEPTED MANUSCRIPT

NEURODEVELOPMENT AND BEHAVIOR IN NEONATAL OXYS RATS WITH GENETICALLY DETERMINED ACCELERATED SENESCENCE

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Abstract

Study of the developmental characteristics and mechanisms of senescence is an important field in brain aging research. The OXYS strain was selected from Wistar rats in Novosibirsk, and it serves as a rat model of accelerated aging. Previously, neurodegenerative processes and aberrant behavior were reported in experiments with adult OXYS rats. In our study, neurodevelopmental reflexes, neuronal density in the prefrontal cortex and hippocampus, and global DNA methylation in the hippocampus are compared between OXYS and WAG (Wistar Albino Glaxo) neonatal pups. The development of the righting, forelimb grasp, and cliff avoidance reflexes is delayed, and body weight gain was deferred in neonatal OXYS pups. Neuronal density in the hippocampus does not differ between one-day-old OXYS and WAG pups. On the sixth day, the neuronal density in OXYS pups is reduced in the CA2 hippocampal zone, augmented in CA3 and DG, and unchanged in CA1. Six-day-old OXYS pups have fewer and smaller pyramidal neurons in the prefrontal cortex as compared to WAG controls. Global DNA methylation levels in the hippocampus of OXYS newborns are significantly lower than in the WAG newborn pups. At the age of six days, the global DNA methylation level decreases in WAG pups, but does not change in OXYS pups. Thus, neonatal OXYS rats show delayed neurodevelopment accompanied by changes in the global DNA methylation pattern in the hippocampus and in neuronal density in the hippocampus and the prefrontal cortex. These changes may be related to accelerated senescence in adult OXYS rats.

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