

STRESSFUL LIFETIME RESULTS IN NEUROINFLAMMATION

Horváth, K.¹, Winkler, Zs.², Kuti, D.², Kővári, D.², Polyák, Á.², Ferenczi, Sz.², Kovács, J.K.²

¹ Institute of Biology, University of Veterinary Medicine, Budapest, Hungary

² Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest, Hungary

Modern stressful lifestyle poses psychosocial and physical stressors, thereby induces centrally mediated complex adaptive changes referred to as systemic stress response. In addition to changes in metabolism and immunoregulation, chronic stress results in significant rearrangements in the neuroendocrine system. Microglia play a main role in generating neuroinflammation, and contribute to the formation, operation and adaptation of neuronal circuitry in health and disease. Fractalkine is a key regulator of microglial activity and neuron-microglia communication. Its receptor (CX3CR1) is mainly expressed in microglial cells. We aimed to characterize chronic variable stress (CVS) - induced metabolic changes, and associated microglial alterations in metabolic-related brain regions.

Experiments were performed on C57Bl6 (control) and transgenic mice CX3CR1^{-/-} in which fractalkine signaling is impaired. Half of the animals from each genotype were exposed to chronic variable stress for four weeks (n=10/9, CVS). Control animals were not stressed. Body weight of the animals and the main metabolic parameters were analyzed by indirect calorimetry. Iba-1 immunohistochemistry followed by morphometrical analysis was used to visualize morphological changes of microglia in the arcuate nucleus.

Changes were detected in body composition, home cage locomotor activity and metabolic parameters after CVS. Chronic stress resulted in increased respiratory exchange ratio (RER) in wild type but not in CX3CR1^{-/-} animals. CVS procedure significantly increased the weight of the adrenal glands and plasma corticosterone. Furthermore, CVS resulted in microglia activation in the arcuate nucleus, the main energy sensor in the brain, but this activation was not seen in stressed CX3CR1^{-/-} mice.

In conclusion, we provided evidence for chronic stress induced metabolic changes in mice which were parallel with activation of microglia in the arcuate nucleus, in which fractalkine signaling had an important role.