FEATURES OF NEUROINFLAMMATION IN TRANSGENIC RAT EXPRESSING MISFOLDED TAU PROTEIN VARY WITH GENETIC BACKGROUND AND INFLUENCE THE VULNERABILITY TO THE NEURODGENERATION

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Epidemiology of Alzheimer's disease and other neurodegenerative disorders shows that inflammation is one of the most important and genetically variable factors influencing the course of neurodegeneration. In previous work we described tau-induced neurodegeneration accompanied by inflammation in SHR 72-transgenic rat model on the background of spontaneously hypertensive strain (SHR). To assess the role of genetic background in tau-induced neurodegeneration, SHR transgenic rats were back-crossed to Wistar-Kyoto (WKY) strain. We monitored the motor impairment in transgenic rats by the set of basic behavioural tests. Brainstems of SHR and WKY transgenic rats in terminal stage with age-matched controls were examined by the means of immunohistochemistry and unbiased stereology.

Both transgenic lines showed the same tau neurodegenerative cascade including AT8-positive neurofibrillary tangles, increase of microglial numbers and signs of microglial activation (increased CD11b/CD18, CD4, CD68) in the same regions. Surprisingly, WKY transgenic rats develop motor symptoms earlier (despite lacking chronic hypertension and other pathologies of SHR strain) and bear significantly less tangles than SHR transgenic line. However, WKY transgenic rats demonstrate different features of inflammatory response: lower density of Iba1-positive microglia with less phagocytic morphology, but 12-times higher ratio of MHCII-positive microglia than their SHR counterparts.

These results suggest that the neurodegeneration in our model is driven by neurofibrillar pathology, but the nature of inflammatory reaction in the tissue determines the vulnerability of the organism or its ability to resist the neurodegeneration.

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