Effects of long-term chemotherapy on elderly Wistar rats in experimental model in vivo

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Conventional anti-glioblastoma chemotherapy includes temozolomide (TMZ) and dexamethasone (DXM) to prevent brain oedema, but patients often suffer from the side effects on the nervous system, and the molecular mechanisms of them are poorly understood. Major components of brain tissue extracellular matrix are chondroitin sulfate proteoglycans (CSPGs) which are involved in the development of various brain pathologies. The aim of this work was to study the effect of long-term administration TMZ and/or DXM on behavior of experimental animals and the expression of the CSPGs in the brain tissue. TMZ (150 mg/m2) and/or DXM (2,5 mg/kg) were administrated to elderly Wistar rats for 4 months. To investigate the general locomotor activity and anxiety-related behavior, open field and the elevated plus maze tests were used. Expression of the main CSPGs (Cspg4/Ng2, brevican, aggrecan, versican, neurocan, biglycan, Cspg5, phosphacan) was studied using RT-PCR. TMZ administration resulted in a decrease of horizontal locomotor activity, increase anxiety levels of rats and reduced expression of aggrecan by 7,8-fold ($p< 0,05$) in rat brain tissue. DXM treatment led to an increase in total locomotor activity and down-regulation of aggrecan (35-fold) and neurocan (1,8-fold, $p< 0,05$) mRNA levels. The combined treatment TMZ and DXM increased the vertical locomotor activity and decreased aggrecan transcription level (19,5-fold, $p< 0,05$). Taken together, obtained results demonstrate that long-term TMZ administration reduces the general locomotor activity of adult rats and induced anxiety-related behavior. Downregulation of aggrecan and neurocan expression upon TMZ treatment might be involved into these changes in the behavior characteristics of the experimental animals. This study was funded by the Russian Science Foundation, grant number 19-75-00051. AVS was supported by a scholarship of Russian Federation President for young scientists (SP-1816.2019.4).