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ER stress in mice prefrontal cortex pyramidal neurons in peripheral tumor growth

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Motivation and Aim: Endoplasmic reticulum (ER) plays an important role in the synthesis, processing and transport of many proteins, the biosynthesis of membrane lipids, the regulation of carbohydrate metabolism, the maintenance of calcium homeostasis, and other important cellular processes. Under pathological conditions leading to oxidative stress, including oncology, protein folding is disrupted and ER stress is triggered [1]. Purpose: to investigate the structure of endoplasmic reticulum of prefrontal cortex pyramidal neurons under conditions of peripheral tumor growth.
Methods and Algorithms: For tumor induction, cultured B16 cells were subcutaneously injected into the right inguinal area of mice. The material was sampled at 7 days. Transmission electron microscopy was used to examine the ultrastructural organization of prefrontal cortex pyramidal neurons in brain of C57BL/6 male mice from two groups: a tumor growth model and an intact control. Ultrathin sections thick 70–100 nm were studied using an microscope electron JEM 1400 (Japan). Morphometry was performed using Image J software (Wayne Rasband, USA) with an opened test system at x30K magnification. The mean (M) and standard deviation (SD) were calculated using Microsoft Excel software. The significance of differences between the parameters was determined by Statistica 6.0 software (StatSoft, Inc.) with Mann-Whitney U-test. The differences were considered significant at $p<0.05$.
Results: Morphometric analysis of neurons in animals with a tumor revealed a significant increase in the volume density of the ER with widening of its cisterns and tubules (V_V = 5.97 %), which is a structural sign of ER stress (Fig. 1, A). In addition, in the neurons of animals with a tumor, a high level of volume density of mitochondria with destructive changes of cristae was noted (V_V = 5.38 %), this is 46.6 % of the total number of mitochondria (see Fig. 1, B). It is known that ER and mitochondria are functionally related to each other; they provide exchange of calcium, delivery of reactive oxygen species, and lipid sorting [2]. Cellular stress caused by external or internal signals activates processes aimed either at restoring cellular homeostasis or at cell death. These processes include unfolded protein response (UPR), autophagy, hypoxia, and mitochondrial function, which are part of the global ER response to stress [3]. Activation of autophagy limits the inflammatory response and provides cytoprotection by reducing ER stress [1]. Decreased levels of autophagy result in disruption of the intracellular homeostasis of neurons.

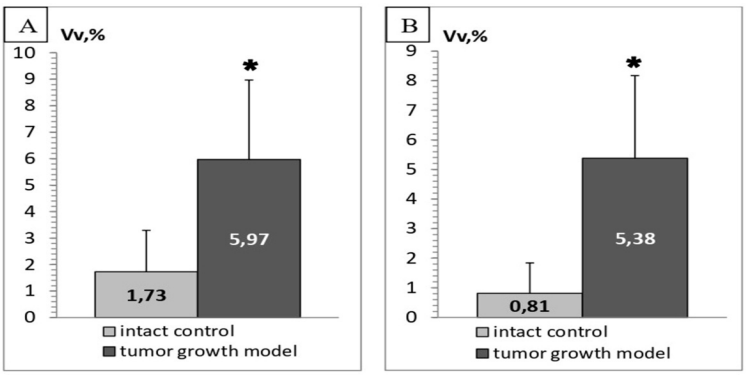

Fig. 1. Volume density of organelles in prefrontal cortex pyramidal neurons. A – V_V of ER with widening of its cisterns and tubules; B – V_V of mitochondria with destructive changes of cristae

Conclusion: The data obtained indicate an increase in ER stress in conditions of peripheral tumor growth. Further study of the structural features of pyramidal neurons will contribute to a more detailed understanding of the effect of peripheral tumor growth on them, and will also help to identify signaling pathways and targets for therapeutic use.

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