ABSTRAKT (EN)

The formation of brain oedema, which accompanies ischemic or traumatic brain injuries, originates from a disruption of ionic/neurotransmitter homeostasis that leads to extracellular K^+ elevation and neurotransmitter accumulation in the extracellular space. An increased uptake of these osmotically active substances, predominantly provided by astrocytes, is accompanied by intracellular water accumulation via aquaporin-4 (AQP4). Since it has been shown that the removal of perivascular AQP4 via the deletion of α-syntrophin, which is the protein responsible for anchoring AQP4 on the astrocytic membrane (Neely et al. 2001), delays oedema formation and K^+ clearance (Amiry-Moghaddam et al. 2003), we aimed to elucidate how the alpha-syntrophin deletion affects astrocyte volume changes in the cortex during pathological states, such as hypoosmotic stress or oxygen-glucose deprivation (OGD), using three-dimensional (3D) confocal morphometry in situ. In order to visualize individual astrocytes that lack alpha-syntrophin, double transgenic mice (GFAP/EGFP/α-Syn$^{-/-}$) were generated by crossbreeding GFAP-EGFP mice with α-syntrophin knockout mice. 3D-confocal morphometry revealed that alpha-syntrophin deletion did not alter astrocyte swelling during hypoosmotic stress or their recovery in isotonic solution; however, astrocytic swelling was slower in hyperosmotic solution containing mannitol. During OGD a-syn deletion resulted in the slower swelling of astrocytes and slower volume recovery following OGD when compared to astrocyte volume changes in the cortex of GFAP/EGFP mice (controls). Interestingly, astrocyte swelling of GFAP/EGFP/α-Syn$^{-/-}$ mice evoked by 30-minute application of 10 mM K+ was comparable with that observed in controls however, astrocytes of GFAP/EGFP/α-Syn$^{-/-}$ mice recovered their volume during washout in isotonic solution more effectively. Similarly to our previous findings (Benesova et al. 2011), we have confirmed the existence of two astrocytic subpopulations also in the cortex of GFAP/EGFP/α-Syn$^{-/-}$ mice that significantly differed in their responses to stress conditions. The individual subpopulations identified in GFAP/EGFP/α-Syn$^{-/-}$ mice displayed distinct volume changes as well as the incidence when compared to controls.

SEZNAM POUŽITÉ LITERATURY

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