**The activation of the meningeal lymphatics after cerebral hypoxia associated with brain hemorrhages**

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**Abstract:** The meningeal lymphatic vessels were discovered three years ago as a new vascular system in the brain that immediately activated scientific works focused on study of the role of meningeal lymphatics in the brain circulation. In our recent publications1,2 we clearly showed significant role of the meningeal lymphatics in the brain clearing from substances, which crossed the blood-brain barrier (BBB).

Here we analyzed activation of the meningeal lymphatics after intracranial hemorrhages (ICH) in rats and studied the role of hypoxia in these processes.

To induce ICH, we used protocol of sound stress’s impact. The level of the blood oxygen saturation in the brain was monitored using pulse oximetry. The ICH-related opening of BBB was confirmed by spectrofluorometric assay of Evans Blue dye extravasation and confocal imaging of FITC-dextran 70 kDA leakage. For visualization of the meningeal lymphatic vessels were used immunohistochemical method and *in vivo* real-time two-photon laser scanning microscopy with specific marker lymphatic vessel endothelial hyaluronan receptor 1.

Our results showed that pre-hemorrhage time was accompanied by mild hypoxia and diffuse type of weak opening of the BBB in subcortical area. No changes in the meningeal lymphatics were observed. Post-hemorrhage period was characterized by severe hypoxia, vasogenic edema and the strong diffuse BBB disruption in area surrounding ICH. These changes were associated with increase in diameter of the meningeal lymphatic vessels and appearance of hemosiderin (product of degradation of hemoglobin and marker of hemorrhages) in deep cervical lymph node (dCLN, first anatomical station for the exit of lymph from the brain). Note, more hypoxia was presented, larger meningeal lymphatic vessels and more high level of hemosiderin in dSLN were detected.

Collectively, these new fundamental results demonstrate close interaction between severity of cerebral hypoxia associated with ICH and activation of the meningeal lymphatics paying an important role in brain clearing from the blood after ICH.

References: 1doi: 10.1002/jbio.201700287; 2doi: 10.1117/1.JBO.22.12.121719.

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