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The Interaction between Blood-Brain Barrier and the Cerebral Lymphatics Proposes Therapeutic Method for Alzheimer’S Disease

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Abstract : The direction for research of Alzheimer's disease is to find an effective non-invasive and non-pharmacological way of treatment. Here we tested our hypothesis that the opening of the blood-brain barrier (BBB) induces activation of lymphatic drainage and clearing functions that can be used as a method for non-invasive stimulation of clearance of beta-amyloid and therapy of Alzheimer’s disease (AD). To test our hypothesis, in this study on healthy male mice we analyzed the interaction between BBB opening by repeated loud music (100-10000 Hz, 100 dB, duration 2 h: 60 sec – sound; 60 sec - pause) and functional changes in the meningeal lymphatic vessels (MLVs). We demonstrate clearance of dextran 70 kDa (i.v. injection), fluorescent beta-amyloid (intrahippocampal injection) and gold nanorods (intracortical injection) via MLV that significantly increased after the opening of BBB. Our studies also demonstrate that the BBB opening was associated with the improvement of neurocognitive status in mice with AD. Thus, we uncover therapeutic effects of BBB opening by loud music, such as non-invasive stimulation of lymphatic clearance of beta-amyloid in mice with AD, accompanied by improvement of their neurocognitive status. Our data are consistent with other results suggesting the therapeutic effect of BBB opening by focused ultrasound without drugs for patients with AD. This research was supported by a grant from RSF 18-75-10033
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