Photostimulation of permeability of blood-brain barrier for beta-amyloid

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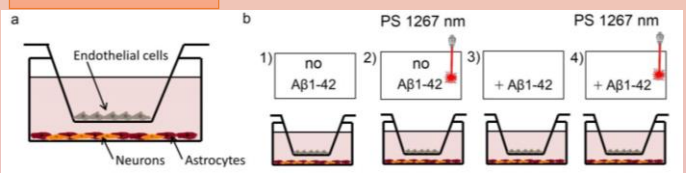
Alzheimer's disease (AD) is marked by a progressive decline in memory and cognition over decades. The beta amyloid (A) hypothesis, which posits A deposition as a key initial step in the pathogenesis of AD, has been the dominant theory driving treatment development. While the role of A in AD remains unclear, A plaque clearance has been a key target of numerous clinical trials. The one recent trial linked a significant reduction in A plaque to the stabilization of the cognitive decline after1 year. The blood–brain barrier (BBB) is a major obstacle for the effective delivery of therapeutic compounds for a treatment of AD. Therefore, the development of a non-pharmacological therapy of AD is actual problem. In our recent pilot study, we proposed transcranialphotostimulation (PS) of clearance of A from the brain via a PS-mediated stimulation along the lymphatic pathway.

Methods

Analysis of beta-amyloid level in the tested tissues

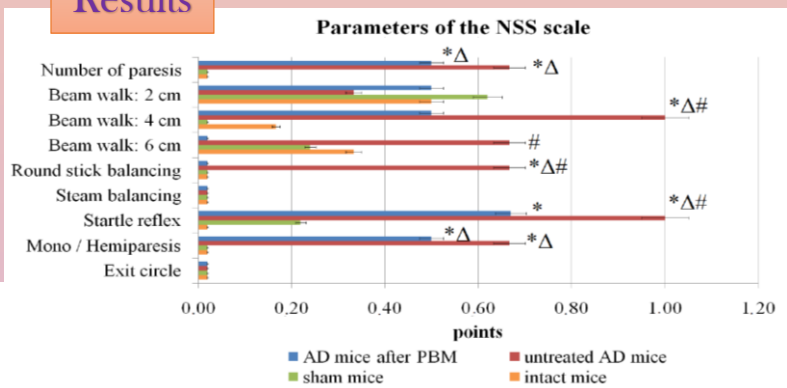


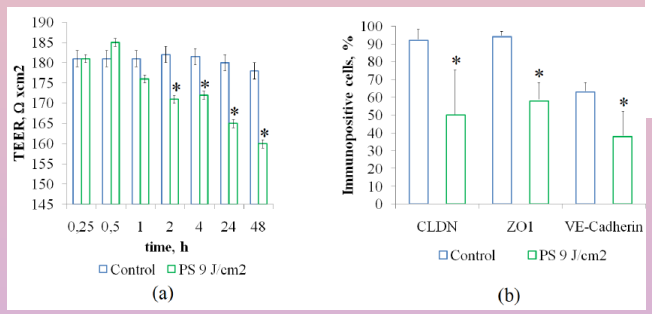
Schematic illustration of a three-cell model of a neurovascular unit (NVU) in vitro: a-the cultivation and differentiation of cells of NVU; b-the experimental groups.

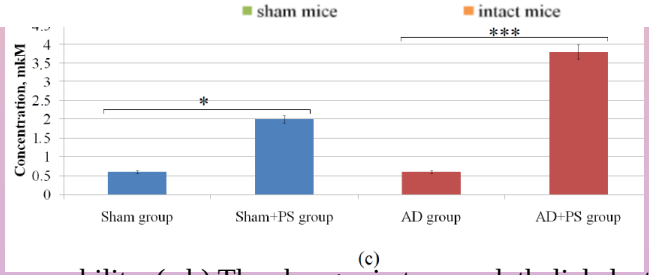
Results

Memory and Neurological Tests

The neurobehavioral status of mice was obtained by the neurological severity score (NSS). It consists of 9 individual parameters in points, including tasks on motor function, alertness and physiological behavior. The new object recognition test was used for memory evaluation.







The PS-mediated effects on the blood-brain barrier (BBB) permeability: (a,b) The changes in transendothelial electrical resistance (TEER) and in the expression of tight junction (TJ) proteins before and after PS in normal mice, respectively; (**c**) The quantitative analysis of PS effects on the BBB permeability for fluorescent A; *—$p < 0.05$; ***—$p < 0.001$ vs. the sham groups, n = 15 for (a,b); n = 10 for (c).

Conclusion

PS 9 J/cm2 attenuates the memory and neurological deficit in mice with AD via activation of lymphatic clearance of A from the brain into the dcLNs. The PS-mediated BBB opening via the PS-decrease TEER and the expression of TJ proteins might be a crucial mechanism underlying therapeutic effects of PS in mice with AD. These pioneering data open new strategies in the development of non-pharmacological methods for AD therapy and contribute to a better understanding of the PS effects on the central nervous system.

This research was supported by grants from Russian Science Foundation 18-75-10033
& RF Government Grant 075-15-2019-1885