## Pioneering Technology of Night Photo-Stimulation of the Brain Lymphatic System: Therapy of Brain Diseases during Sleep

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Abstract: In modern neurobiology, sleep is considered a novel biomarker and a promising therapeutic target for brain diseases. This is due to recent discoveries of the nighttime activation of the brain lymphatic system (BLS), playing an important role in the removal of wastes and toxins from the brain and contributes neuroprotection of the central nervous system (CNS). In our review, we discuss that night stimulation of BLS might be a breakthrough strategy in a new treatment of Alzheimer's and Parkinson's disease, stroke, brain trauma, and oncology. Although this research is in its infancy, however, there are pioneering and promising results suggesting that night transcranial photostimulation (tPBM) stimulates more effectively lymphatic removal of amyloid-beta from mouse brain than daily tPBM that is associated with a greater improvement of the neurological status and recognition memory of animals. In our previous study, we discovered that tPBM modulates the tone and permeability of the lymphatic endothelium by stimulating NO formation, promoting lymphatic clearance of wastes and toxins from the brain tissues. We also demonstrate that tPBM can also lead to angio- and lymphangiogenesis, which is another mechanism underlying tPBM-mediated stimulation of BLS. Thus, photo-augmentation of BLS might be a promising therapeutic target for preventing or delaying brain diseases associated with BLS dysfunction. Here we present pioneering technology for simultaneous tPBM in humans and sleep monitoring for stimulation of BLS to remove toxins from CNS and modulation of brain immunity. The wireless-controlled gadget includes a flexible organic light-emitting diode (LED) source that is controlled directly by a sleep-tracking device via a mobile application. The designed autonomous LED source is capable of providing the required therapeutic dose of light radiation at a certain region of the patient's head without disturbing of sleeping patient. To minimize patients' discomfort, advanced materials like flexible organic LEDs were used. Acknowledgment: This study was supported by RSF project No. 23-75-30001.

Keywords: brain diseases, brain lymphatic system, phototherapy, sleep

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