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Nanofluidic Approach to Brain Water Metabolism and Related Issues

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ABSTRACT

The brain intercellular communications, transit of the signaling molecules, neurotransmitters, cytokines and substrates, the clearance of pathogenic metabolites, heat exchange are all linked to the brain water metabolism. Many serious neurological conditions arise from or aggravated by the altered brain water metabolism (e.g. Alzheimer's disease, idiopathic normal pressure hydrocephalus, migraine, traumatic brain injury and stroke, tumor migration).

According to the commonly accepted orthodox theory, the nanodimentional brain Interstitial Space (ISS) presents a diffusion barrier admitting only the Fickian mass-transfer mechanism. Contrary to the orthodox theory, in this research the ISS is viewed as a nanofluidic domain where fluid flow is governed by the slip-flow principles of nanofluidics. The water nanochannel aquaporin-4 of the astrocyte end feet membranes ensures kinetic control over water movement across the blood-brain barrier while the pulsatory intracranial pressure presents the driving force behind the transcapillary water flow. A novel computational model of brain water metabolism has been developed and explored. The model demonstrates good predictability in respect to some brain physiological features, mass transfer of glucose, oxygen and carbon dioxide and relevance to some clinical conditions.

The new paradigm and the model may be employed in neurobiological research, development of the AQP4-targeted drug therapy, optimization of the intrathecal drug delivery to the brain tumors and in a research on a broad spectrum of water-metabolic-disorder-related conditions.

Keywords: Brain nanofluidic domain, Computational model of brain water metabolism, Convective mass transfer of glucose, CO_2 and O_2, Implications for nanomedicine

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