Characterizing the glymphatic peri-vascular connectome and its disruption in Alzheimer’s disease

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Research Abstract

Except for hereditary cases of Alzheimer’s disease (AD) where excessive amyloid production and deposition clearly drives cognitive decline, there is limited evidence in the majority of AD cases that amyloid beta (Aß) accumulation is driven by Aß overproduction. In fact, current literature suggests that Aß accumulation in AD is driven by reduced Aß clearance. The peri-vascular space of the central nervous system was recently discovered to function as a

clearance pathway for toxic waste proteins including Aß and designated the ‘glymphatic’ system. The glymphatic pathway is thus a prime candidate for linking disruptive clearance of Aß to AD. Although, there is clear evidence of the glymphatic pathway’s importance for brain waste removal during sleep and a decline in sleep quality precede AD there is limited information on its role in AD. There is also a gap in our knowledge on how amyloid angiopathy contributes to AD progression via a potential glymphatic pathway disruption. In other words, the key physiological and biochemical components involved in peri-vascular, glymphatic dysfunction and declining Aß clearance in the course of AD is unknown and clarifying these elements are the prime goals for the current proposal. Optical or magnetic resonance imaging (MRI) in combination with tracers administered into the cerebrospinal fluid (CSF) has been very informing on the various anatomical components of the glymphatic pathway including information on its spatial and temporal domains. However, none of the current approaches allow real-time visualization of the collective ‘macroscopic’ dynamic forces of 1) CSF and interstitial fluid exchange (so-called ‘streaming’) from the peri-arterial space into the interstitial space and 2) clearance from the live brain. The current proposal is explicitly aimed at building an MRI based imaging and computational tool box for characterizing the glymphatic pathway as a brain-wide dynamic unit and to track its disruption in progressing AD.

Further information available at:

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