Glymphatic dysfunction after craniectomy

Plog et al., hypothesized that a craniectomy, without any other pathological insult, is sufficient to alter brain function due to reduced arterial pulsatility and decreased glymphatic flow. Furthermore, they postulated that glymphatic dysfunction would produce activation of astrocytes and microglia; with the reestablishment of a closed cranial compartment, the glymphatic impairment, astrocytic/microglial activation, and neurobehavioral decline caused by opening the cranial compartment might be reversed.

Using two-photon in vivo microscopy, the pulsatility index of cortical vessels was quantified through a thinned murine skull and then again after craniectomy. Glymphatic influx was determined with ex vivo fluorescence microscopy of mice 0, 14, 28, and 56 days following craniectomy or cranioplasty; brain sections were immunohistochemically labeled for GFAP and CD68. Motor and cognitive performance was quantified with rotarod and novel object recognition tests at baseline and 14, 21, and 28 days following craniectomy or cranioplasty.

Penetrating arterial pulsatility decreased significantly and bilaterally following unilateral craniectomy, producing immediate and chronic impairment of glymphatic CSF influx in the ipsilateral and contralateral brain parenchyma. Craniectomy-related glymphatic dysfunction was associated with an astrocytic and microglial inflammatory response, as well as with the development of motor and cognitive deficits. Recovery of glymphatic flow preceded reduced gliosis and return of normal neurological function, and cranioplasty accelerated this recovery.

Craniectomy causes glymphatic dysfunction, gliosis, and changes in neurological function in this murine model of syndrome of the trephined [1].

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Plog BA, Lou N, Pierre CA, Cove A, Kenney HM, Hitomi E, Kang H, Iliff JJ, Zeppenfeld DM, Nedergaard M, Vates GE. When the air hits your brain: decreased arterial pulsatility after craniectomy leading to impaired glymphatic flow. J Neurosurg. 2019 May 17:1-14. doi: 10.3171/2019.2.JNS182675. [Epub ahead of print] PubMed PMID: 31100725.