Lymphatic system

Cerebrospinal fluid (CSF) surrounds the brain and spinal cord, and may function as a shock absorber for the CNS. It may also serve an immunological function analogous to the lymphatic system (socalled “glymphatics” a portmanteau word from glia and lymphatic) [1) 2)].

The lymphatic system is part of the circulatory system and a vital part of the immune system, comprising a network of lymphatic vessels that carry a clear fluid called lymph (from Latin lympha meaning water) directionally towards the heart. The lymphatic system was first described in the seventeenth century independently by Olaus Rudbeck and Thomas Bartholin. Unlike the cardiovascular system, the lymphatic system is not a closed system. The human circulatory system processes an average of 20 litres of blood per day through capillary filtration, which removes plasma while leaving the blood cells. Roughly 17 litres of the filtered plasma are reabsorbed directly into the blood vessels, while the remaining three litres remain in the interstitial fluid. One of the main functions of the lymph system is to provide an accessory return route to the blood for the surplus three litres.

see Meningeal lymphatic vessels.

Unlike every other organ in the body, the brain parenchyma lacks a traditional lymphatic system to drain fluids and central nervous system (CNS) antigens. It was historically assumed that all brain wastes were removed by endogenous processing, such as phagocytosis and autophagy, while excess fluids drained directly into the blood. However, the twin discoveries of the glial-lymphatic (glymphatic) system and meningeal lymphatics have transformed our understanding of brain waste clearance. The glymphatic system describes the movement of fluids through the subarachnoid space (SAS), the influx along periarterial spaces into the brain parenchyma, and the ultimate efflux back into the SAS along perivenous spaces where it comes into direct contact with the meningeal lymphatics. The dura mater of the meninges contains a bona fide lymphatic network that can drain CSF that has entered the dura. Together, these pathways provide insights into the clearance of molecules and fluids from the brain, and show that the CNS is physically connected to the adaptive immune system. [3)]

In a study of Oshio et al., the MR signal of the extracellular water was decomposed into components with distinct T2's, to obtain some information about distribution of waste material in the brain.

Images were acquired using a Curr, Purcell, Meiboom, Gill (CPMG) imaging sequence. In order to reduce T1 contamination and the signal oscillation, hard pulses were used as refocusing pulses. The signal was then decomposed into many T2 components using non-negative least squares (NNLS) on a pixel-by-pixel basis. Finally, a color map was generated by assigning a different color for each T2 component, then adding them together.

From the multi-echo images, it was possible to decompose the decaying signal into separate T2 components. By adjusting the color table to create the color map, it is possible to visualize the extracellular water distribution, as well as their T2 values. Several observation points include: (1) CSF inside ventricles has very long T2 (~2 s), and seems to be relatively homogeneous, (2) subarachnoid

CSF also have long T2, but there are short T2 component at the brain surface, at the surface of dura, at the blood vessels in the subarachnoid space, etc., (3) in the brain parenchyma, short T2 components (longer than intracellular component but shorter than CSF) exists along the white matter, in the choroid plexus, etc. These can be considered as distribution of macromolecules (waste materials) in the brain.

From T2 component analysis it is possible to obtain some insight into pathways for the transport of large molecules in the CNS, where no lymphatic system is present [4].

1)
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2)
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3)
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4)
Oshio K, Yui M, Shimizu S, Yamada S. The Spatial Distribution of Water Components with Similar T(2) May Provide Insight into Pathways for Large Molecule Transportation in the Brain. Magn Reson Med Sci. 2020 Feb 19. doi: 10.2463/mrms.mp.2019-0138. [Epub ahead of print] PubMed PMID: 32074590.

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