

## **Cerebrospinal Fluid Flow and the Circadian Rhythm.**

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The glymphatic system (GS) is a network of ring-shaped tunnels surrounding blood vessels in which cerebrospinal fluid (CSF) flows into the brain and through which waste is cleared (Hablitz et al. 2020). GS tunnels are formed by astrocyte end-feet, which are the end portions of extensions of astrocytes, a type of central nervous system glial cell. The GS tunnels are known as the perivascular space. The glymphatic system consists of three primary segments: 1, CSF inflow within perivascular spaces; 2, dispersal and mixing of CSF with interstitial fluid (ISF) throughout the interstitial space (ISS), a network of minute spaces surrounding cells; and 3, the outflow of ISF within the perivascular space to re-enter the CSF within the subarachnoid space (Mestre et al. 2018). Within the end-feet facing blood vessels, known as perivascular end-feet, are water channels called aquaporin-4 (AQP4). AQP4 promotes CSF movement throughout the brain (Mestre et al. 2018).

Meningeal lymphatic vessels (MLVs) are lymphatic vessels within the dura mater membrane that play an important role in CSF drainage as they clear fluid, molecules, and immune cells from the subarachnoid space and into cervical lymph nodes (Silva et al. 2021, Tavares and Louveau 2021).

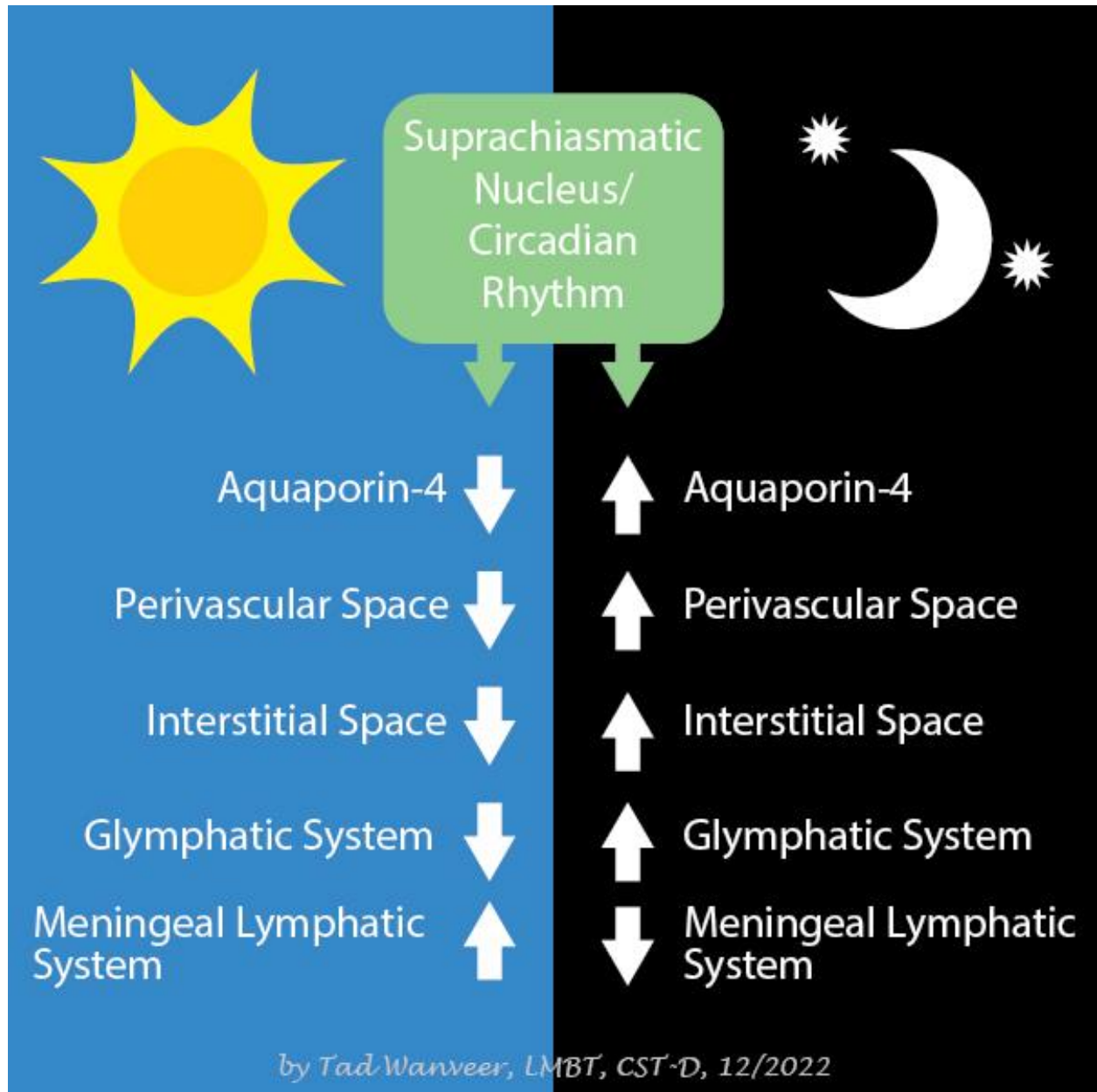
The GS and MLVs of the brain are most active at different times. Glymphatic function is increased during sleep and drainage of CSF to the lymph nodes is increased when awake. Although the mechanisms behind brain-regulated GS activity changes remain unknown, it is linked to the master internal clock, which is the suprachiasmatic nucleus (SCN) (Hablitz et al. 2020). "Glymphatic system function is not solely based on sleep or wakefulness, but by the daily rhythms dictated by our biological clock," Maiken Nedergaard, M.D., D.M.Sc., (Science Daily 2020). The SCN is the central pacemaker of the circadian timing system and regulates most circadian rhythms in the body (Hastings, Maywood, and Brancaccio 2018). The SCN coordinates the daily rhythms of sleep and wakefulness, physiology, and behavior (Hastings, Brancaccio, and Maywood, 2014).

During wakefulness, the brain decreases the size of the perivascular space and the ISS and reduces the number of AQP4s, suppressing the GS CSF flow. In response, the MLVs become more active. (Hablitz et al. 2020, Mestre, Tithof, et al. 2018, Xie et al. 2013). During sleep, the brain increases the size of the perivascular space and ISS and increases the number of AQP4s, increasing the GS CSF flow. In response, the MLVs become less active.

Recent work has provided evidence that astrocytes in the SCN may be responsible for setting circadian behavior, such as rhythmic sleep and wake behavior (Tso et al. 2017). Importantly, research has revealed that astrocytes are equal partners with neurons in the SCN circadian timing network with distinct circadian properties: day-active neurons and night-active astrocytes (Hastings, Maywood, and Brancaccio 2019).

Theoretically, Upledger CranioSacral Therapy practitioners can reach the SCN by way of the interconnection of the astrocyte network with the pia mater membrane, referred to as the pia-glial interface (Wanveer 2015). Facilitating the form and function of SCN astrocytes and the brain-wide

astrocyte network can support improving and fine-tuning the circadian rhythm and its influence on the GS and MLV fluid flow. Improving CSF and ISF flow leads to optimal nourishment and cleansing of brain cells, essential for brain health, healing, and function.



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