Human Brain Solute Transport Quantified by Glymphatic MRI-informed Biophysics during Sleep and Sleep Deprivation

Vegard Vinje[1], Bastian Zapf[2,*], Geir Ringstad[3,4], Per Kristian Eide[3,5], Marie E. Rognes[1] and Kent-Andre Mardal[1,6]

[1] Simula Research Laboratory, 0164 Oslo, Norway

[2,*] Department of Mathematics, University of Oslo, 0373 Oslo, Norway
e-mail: bazapf@math.uio.no,

[3] Department of Neurosurgery, Oslo University Hospital – Rikshospitalet, 0372, Oslo, Norway

[4]Department of Geriatrics and Internal Medicine, Sørlandet Hospital 4838 Arendal, Norway

[5] Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, 0372 Oslo, Norway

[6] Department of Mathematics, University of Oslo, 0372 Oslo, Norway

ABSTRACT

Whether you are reading, running or sleeping, your brain and its fluid environment continuously interacts to distribute nutrients and clear metabolic waste. Yet the precise mechanisms for transport of solutes (such as metabolic by-products) within the human brain are still not properly understood [2]. The relative importance of different mechanisms such as diffusive and advective transport of solutes have remained hard to quantify using imaging techniques alone. From multi-modal human brain MRI data sets in sleeping and sleep-deprived subjects [1], we identify and quantify CSF tracer transport parameters using forward and inverse subject-specific PDE-based computational modelling. While the available data is sparse in both space and time and subject to noise, we are able to obtain numerically robust estimates of the parameters underlying different solute transport models.

Our findings support the notion that extracellular diffusion alone is not sufficient as a brain-wide tracer transport mechanism. Instead, we show that human MRI observations align well with transport by either substantially enhanced extracellular diffusion in combination with local clearance rates, or by extracellular diffusion augmented by advection. Reduced advection fully explains reduced tracer clearance after sleep-deprivation, supporting the role of sleep and sleep deprivation on human brain clearance.

REFERENCES

[1] Per Kristian Eide, Vegard Vinje, Are Hugo Pripp, Kent-Andre Mardal, and Geir Ringstad. Sleep deprivation impairs molecular clearance from the human brain. *Brain*, 144(3):863–874, 2021.

[2] Douglas H Kelley, Tomas Bohr, Poul G Hjorth, Sebastian C Holst, Sabina Hrabětová, Vesa Kiviniemi, Tuomas Lilius, Iben Lundgaard, Kent-Andre Mardal, Erik A Martens, et al. The glymphatic system: Current understanding and modeling. *Iscience*, page 104987, 2022.