How does the brain eliminate waste?

- What is lymph?
- The brain has no dedicated lymphatic system
  - Disease and metabolic intermediates
- Cerebrospinal Fluid (CSF) acts as lymph for the brain by eliminating waste.

New Understanding of CSF

- Is CSF produced in the Choroid Plexus?
- Does CSF flow unidirectionally?
- Bulk Flow vs. Diffusion
  - Is brain interstitial fluid (ISF) stagnant?

New Understanding of CSF

- Perivascular spaces and Glial basal membrane
New Understanding of CSF

- Astroglial Water Channel Aquaporin-4 proteins (AQP4)

Glymphatic System

- Term for the lymphatic effect of CSF and ISF exchange and efferent CSF drainage into the lymphatic system

Glymphatic System

Para-arterial influx
Paravenous clearance

Glymphatic System

Para-arterial influx
Paravenous clearance

Data from: lympatic vascular in the Proxl-GFP mouse. Aspelund et al. 2013 / Video 1
Glymphatic System and Sleep

- Sleep aids in metabolic clearance
  - Why?
- Awake vs. Asleep metabolic rate
  - No inhibition of glymphatic system during REM or light sleep
- Sleep increases Interstitial space by up to 60%
- Anesthesia has different effects
  - Can aid or inhibit glymphatic system
- Adrenergic Signaling also modulates interstitial volume

Glymphatic System, Nervous System Disorders, and the Future

- CSF levels of toxins, waste, and metabolic intermediates used to indicate many NS disorders
  - Schizophrenia, Alzheimer’s, Dementia
- Recent advances in understanding of CSF highlights need for new research context
  - How might Glymphatic abnormalities be affecting disease pathologies?
- Further research into dural lymphatic vessels

Questions?

- What two primary factors likely led to both the initial misunderstanding of CSF mechanics, and to the recent discovery of the glymphatic system?
- How could Glymphatic System abnormalities potentially result in, or exacerbate, Nervous System disorder?
- How could understanding the effects of anesthesia on the Glymphatic System potentially help in the treatment of Nervous System disorders?