

CSF and ISF Flow – Open Questions

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ASNR CSF Flow Group and IHIWG Meeting
Montreal, Mai 22, 2014

Background

Request by Dr. Rekate to have a ...

- summary of the key points of the previous talks, and
- a list of open questions for the following round table discussion.

Background

Organization of key points

- Common points
- Talk specific points not contested in other talks
- Disparate points

Background

Selection of open questions

- Based on disparate key points
- Additional questions with interdisciplinary audience in mind
- Not exhaustive

Common Key Points

- There is paravascular solute transport
- Arterial pulsation drives para- / perivascular flow
- Amyloid β clearance rate is reduced as the brain ages



Talk Specific Key Points

Jonathan Stone

- Visualization of paravascular tracer transport in mouse brain using two-photon microscopy. Coining of the term *glymphatic system*.
- Interstitial space volume increases during sleep.
- Increased paravascular tracer transport during sleep.
- Possibly reduced clearance of tracer in kaolin induced hydrocephalus

Talk Specific Key Points

Jeffrey Iliff

- Paravascular CSF influx is impaired in the aged mouse brain.
- Glymphatic pathway impairment is accompanied by AQP4 mis-localization in the aging mouse brain.
- AQP4 mis-localization is a feature of the aging human brain, and is more prominent in patients with Alzheimer's disease.

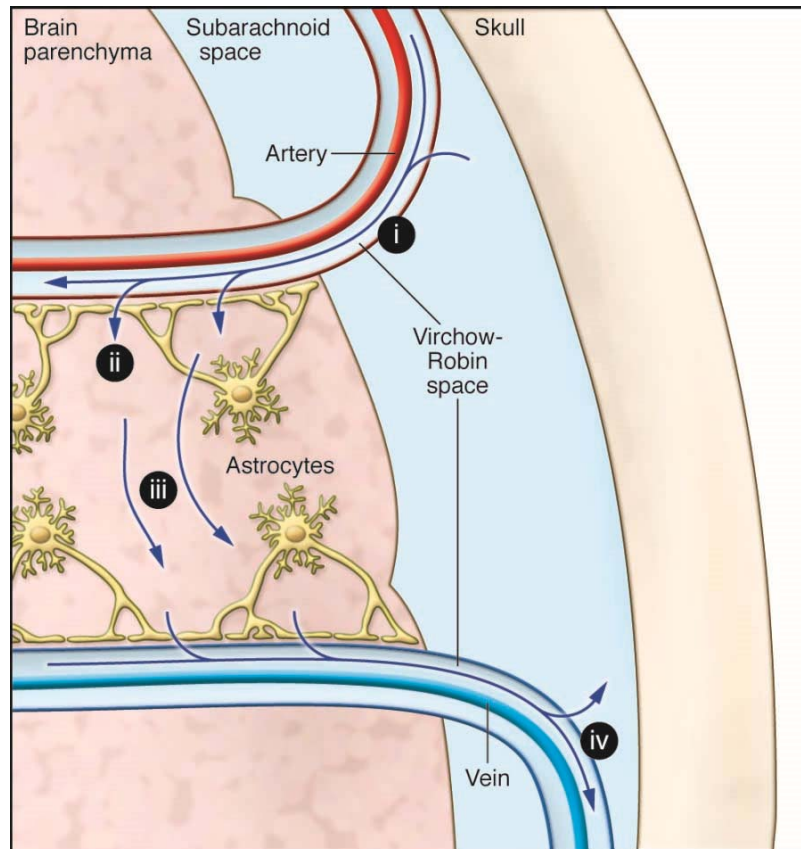
Talk Specific Key Points

Roy Weller

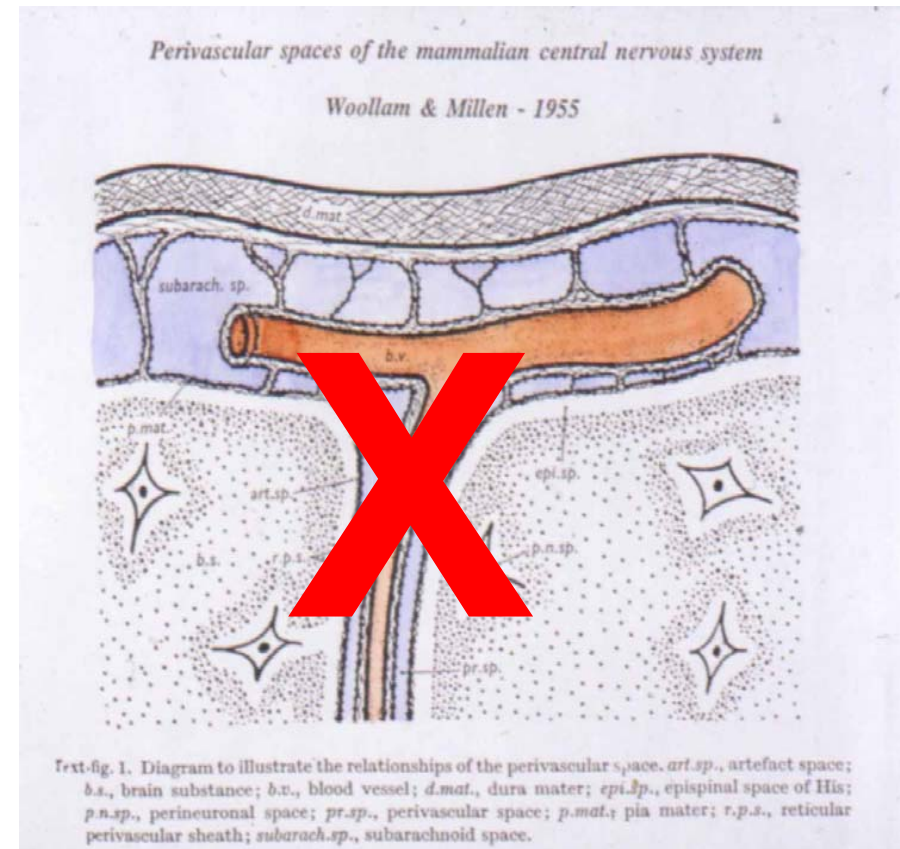
- Juxtaposition of ISF and CSF elimination pathways to convective / glymphatic system
- Differentiation between specific ISF elimination via arterial basement membrane and non-specific transport via the convective / glymphatic system
- Impaired ISF drainage due to deposition of amyloid β in arterial basement membrane
- No pathological lesions have been identified that relate to the convective / glymphatic system. It is thus difficult to determine its function.

Disparate Points

- Importance / Existence of Virchow-Robin spaces in the human cortex



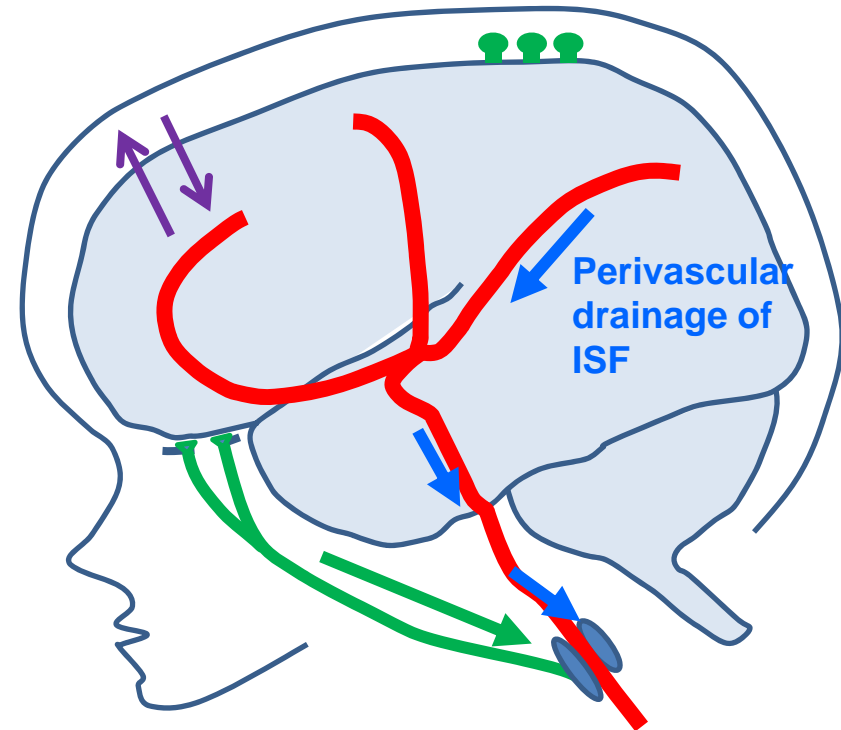
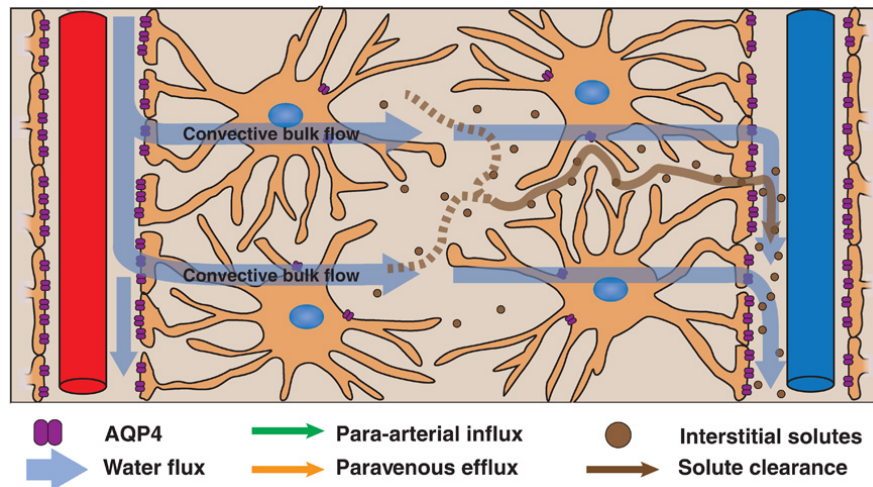
From Dr. Iliff's talk



From Prof. Weller's talk

Disparate Points

- Location (peri- vs. paravascular) and direction of solute transport along arteries



Iliff et al, 2012

From Prof. Weller's talk

Disparate Points

- Terminology: *Convective System* vs. *Glymphatic System*
- The terminology is important, as it suggests a certain function



Open Questions

- To what extent do results obtained in rodents reflect human physiology?
- How does CSF enter the arterial paravascular space in the glymphatics theory?
- Where does the venous paravascular fluid drain?
- How does arterial pulsation drive para- / perivascular flow?
- How do the astrocytes transport the water entering through AQP4, and how do they distribute it?
- Is there a bulk flow in the glymphatics theory and what is the directionality of this bulk flow?
- How does the tracer transport relate to actual water flow?

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