LINKING SLEEP-WAKE DISTURBANCES, GLYMPHATIC PATHWAY IMPAIRMENT AND POST-CONCUSSIVE SYMPTOMS IN YOUTH WITH TBI

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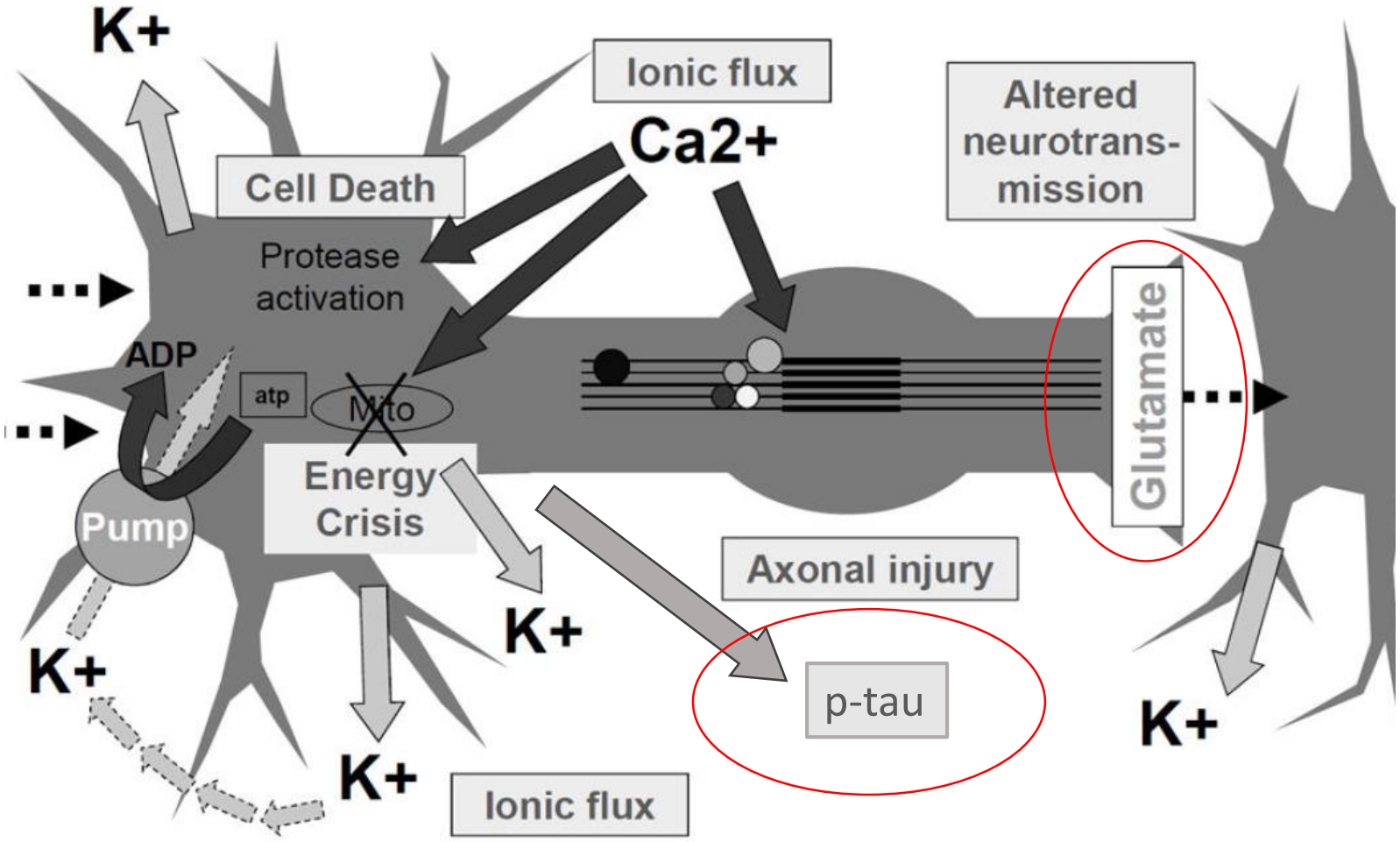
Background – Knowledge gap

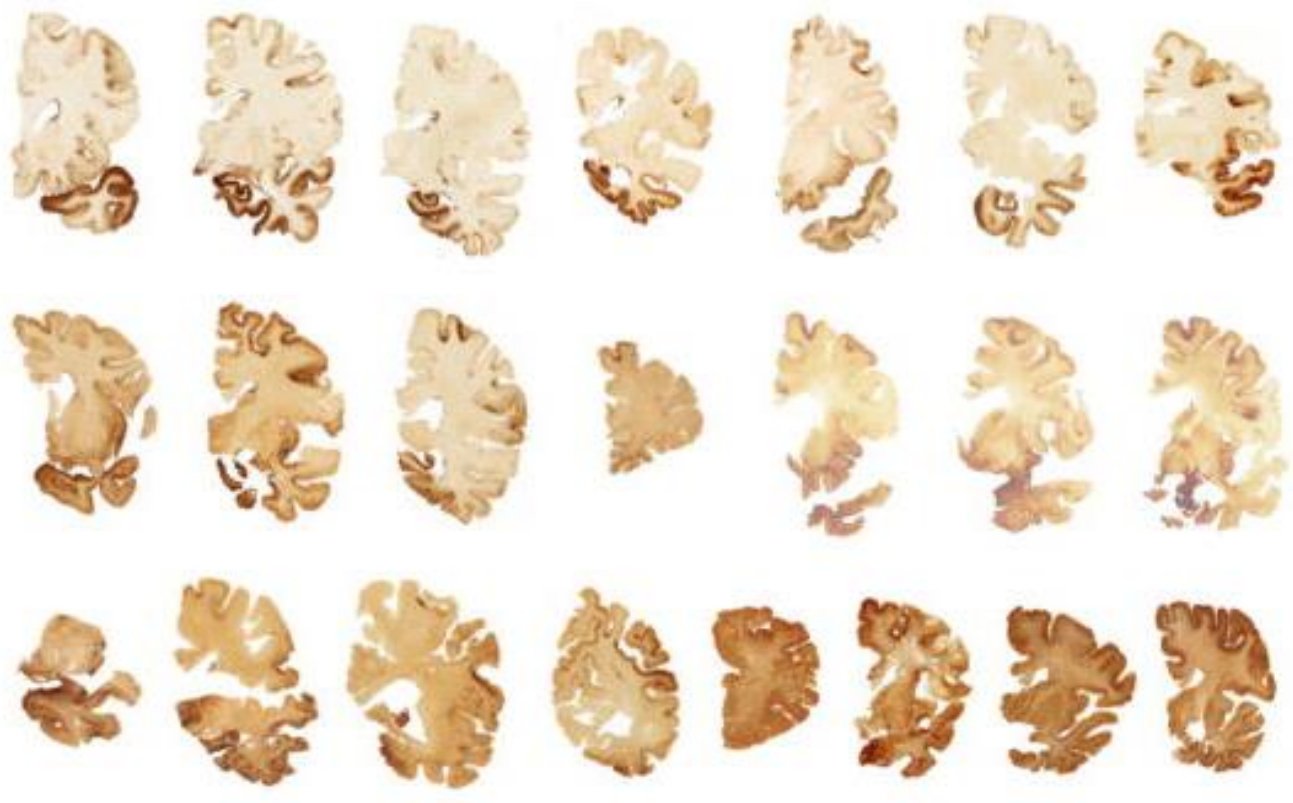
- Sleep disturbances are commonly reported in youth after TBI
- The **impact** of post-injury sleep disturbances on postconcussive symptoms in youth is poorly quantified
- The **mechanisms** by which sleep modulates recovery after mTBI remain unknown
- **Importance**: improving sleep may have a significant impact in post mTBI morbidity.

Background – Neurometabolic cascade of mTBI

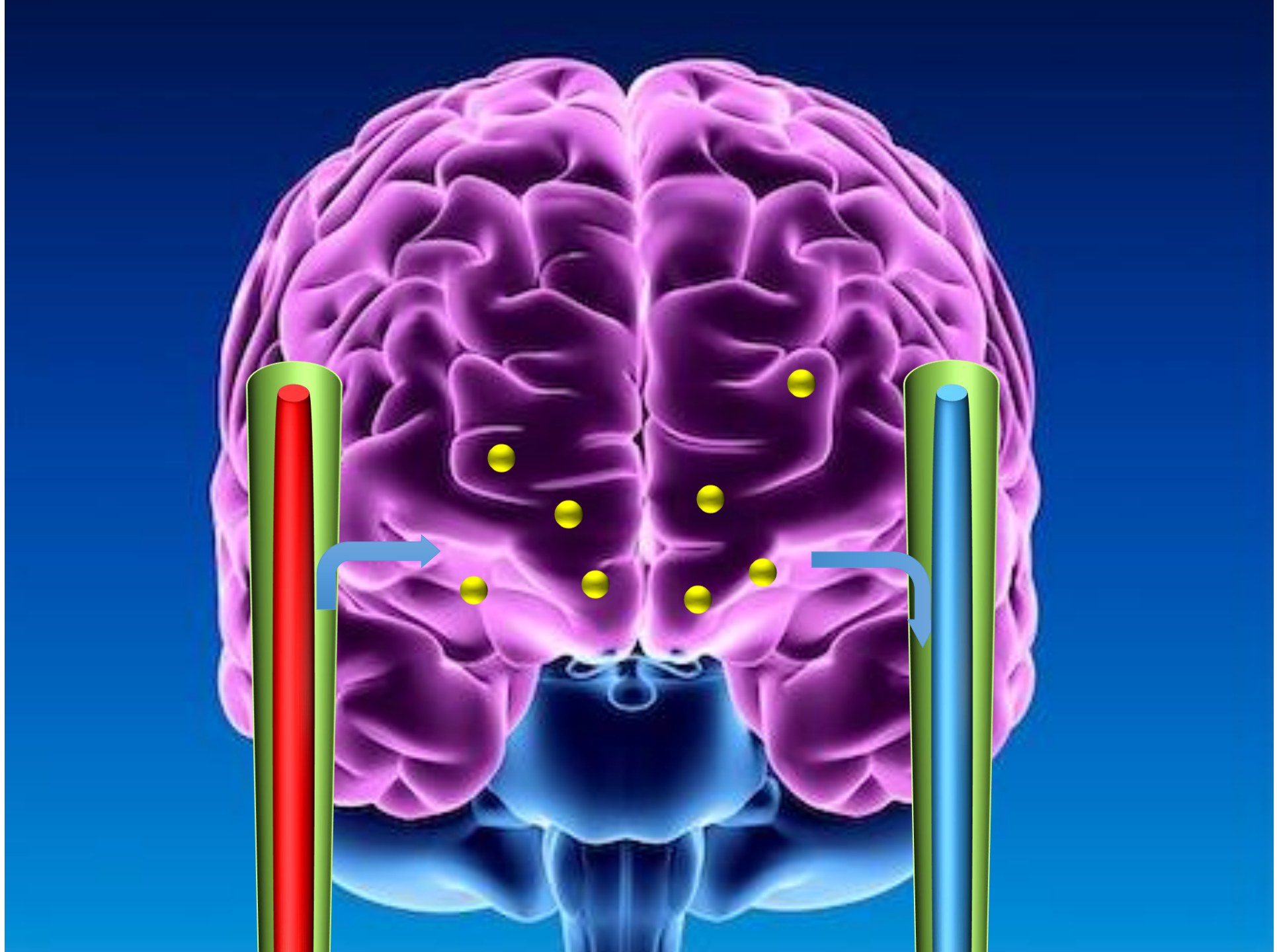


Giza *et al.*, 2014

Background – Chronic traumatic encephalopathy is a tauopathy

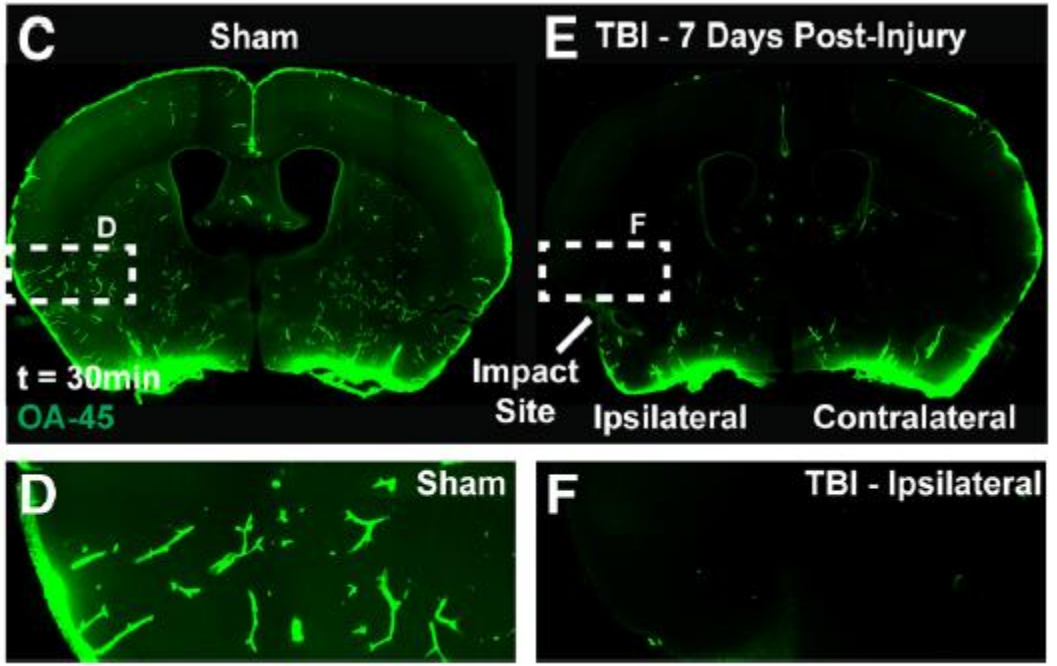


McKee *et al.*, 2015



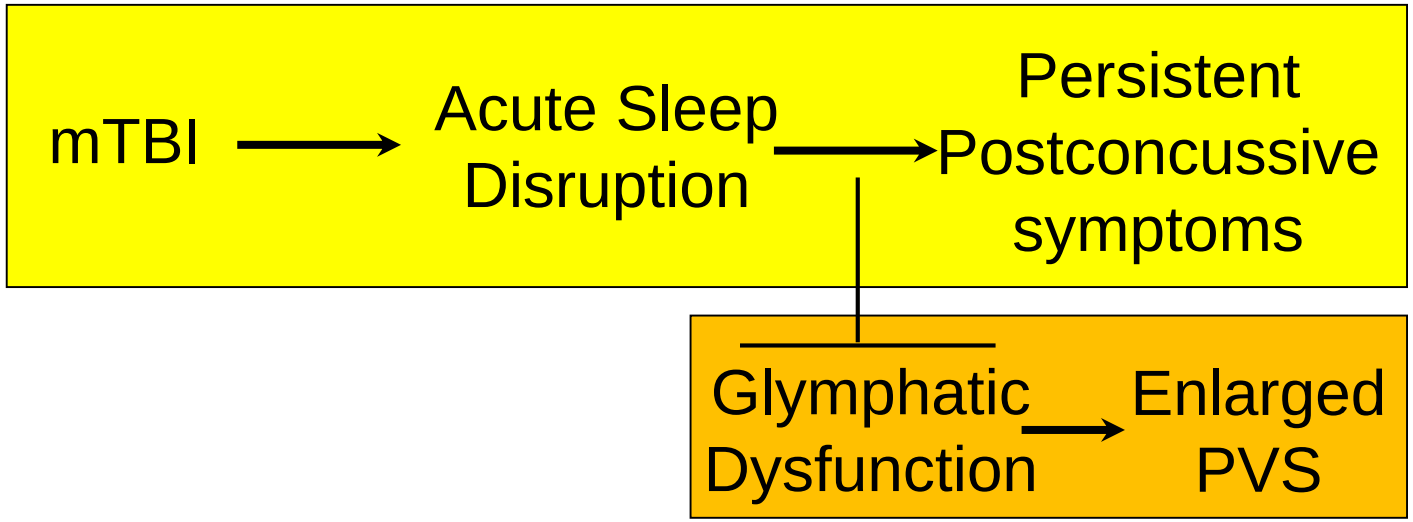
Background – glymphatic function, sleep, and mTBI

- The glymphatic pathway is involved in the clearance of metabolic wastes
- Glymphatic function is more rapid in the sleeping versus the waking brain
- Glymphatic function is impaired after mTBI
- (Glymphatic impairment exacerbates neurocognitive dyfunction)



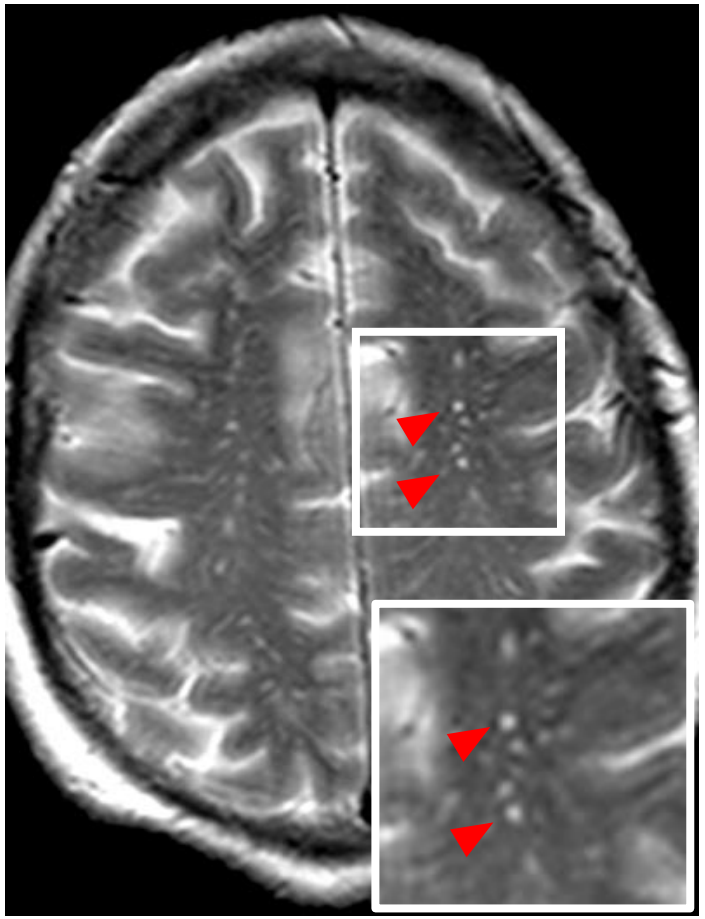
Iliff *et al.* J Neurosci 2014

Proposed framework for mTBI, sleep disturbances, glymphatic impairment and post-concussive symptoms

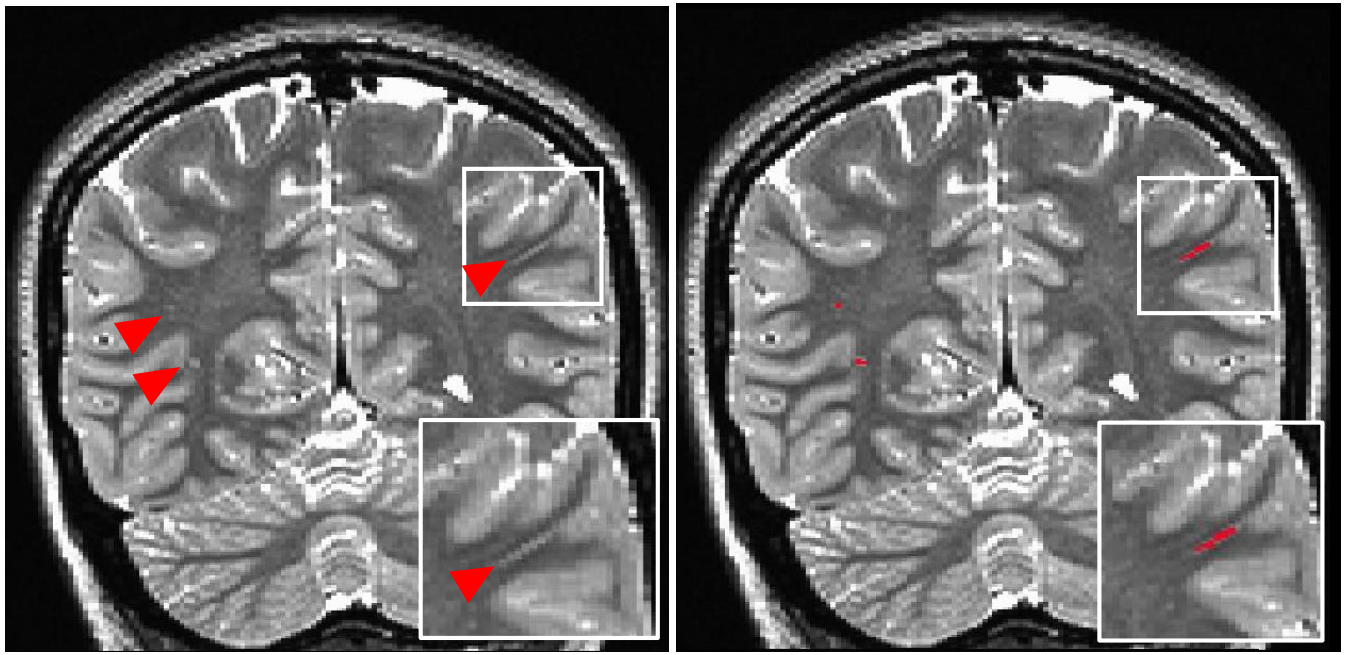


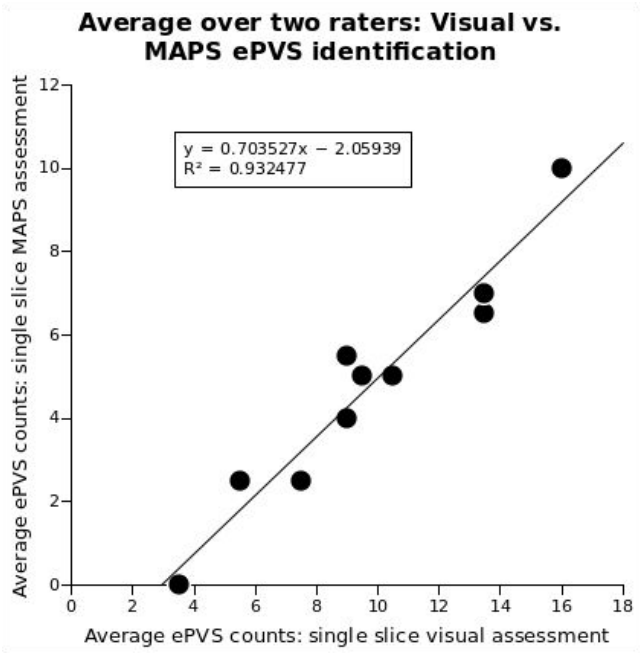
Enlarged perivascular spaces – a putative marker of glymphatic dysfunction

- Glymphatic function assessment in humans is invasive and may lead to complications
- Enlarged perivascular spaces (ePVS) are seen in conditions associated with glymphatic dysfunction
- ePVS are seen in adults after mTBI
- ePVS are seen in adults with sleep problems

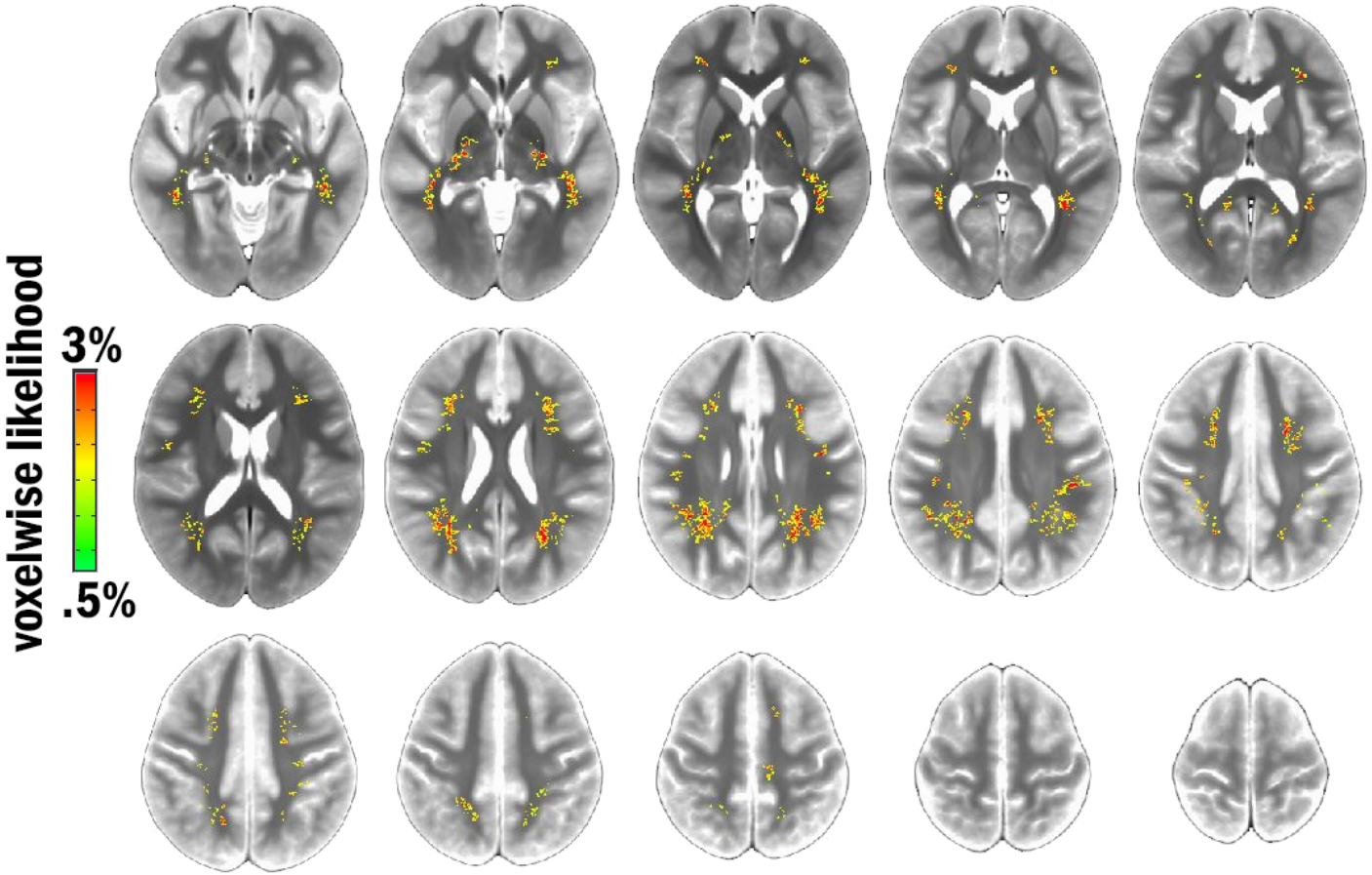


Preliminary data – Automated PVS burden measurement in normal children

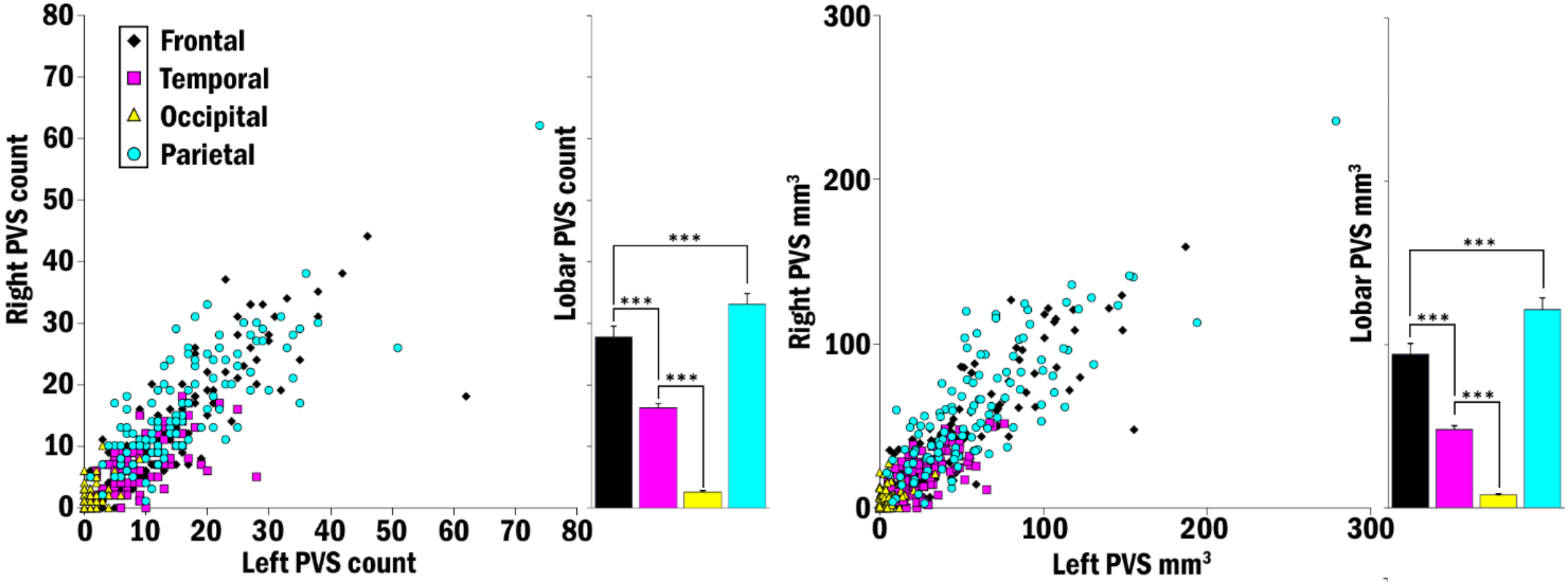




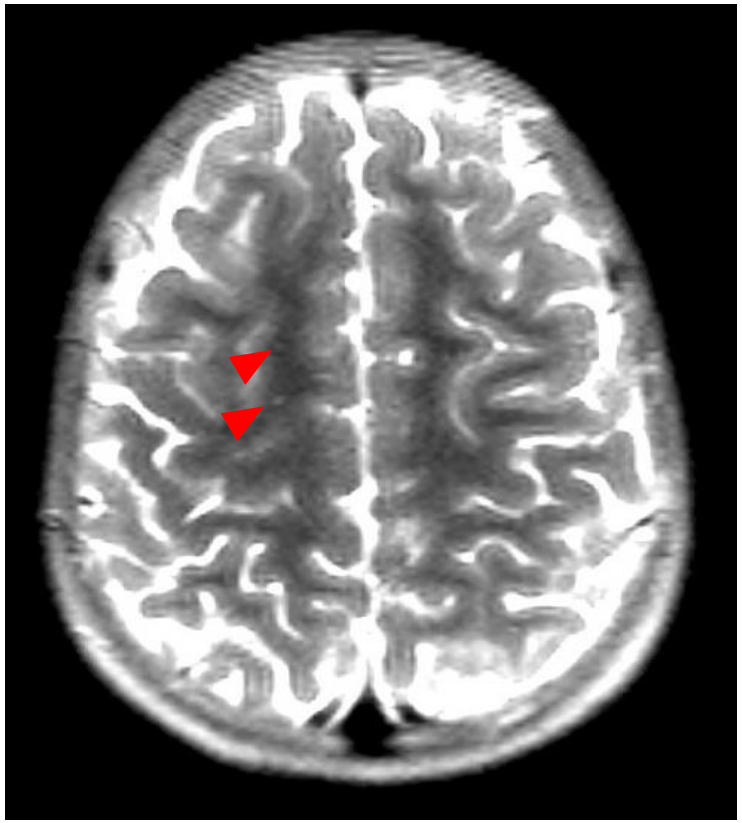
Preliminary data – location of ePVS in normal children



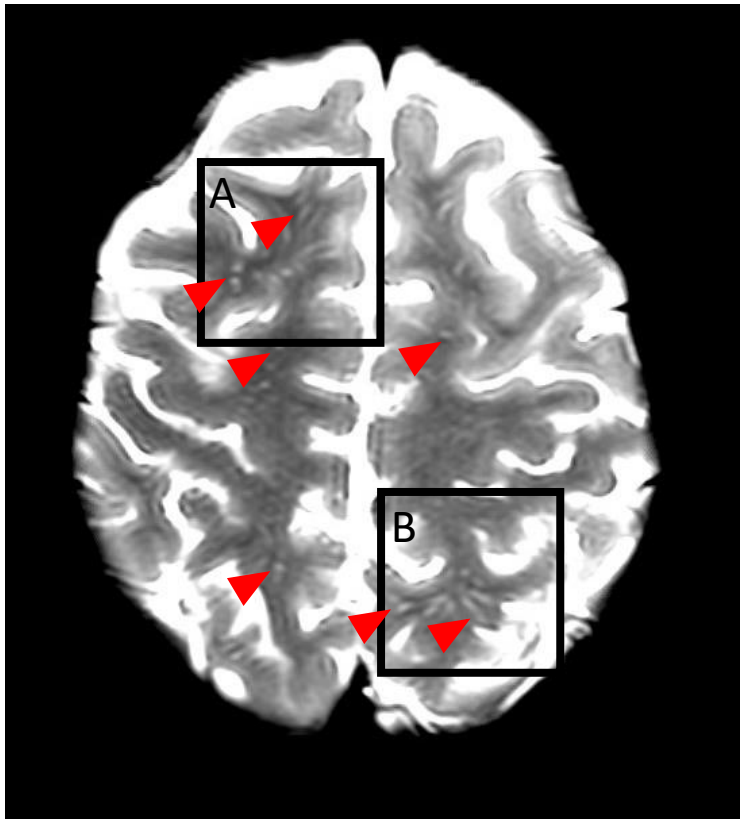
Preliminary data – ePVS are symmetric



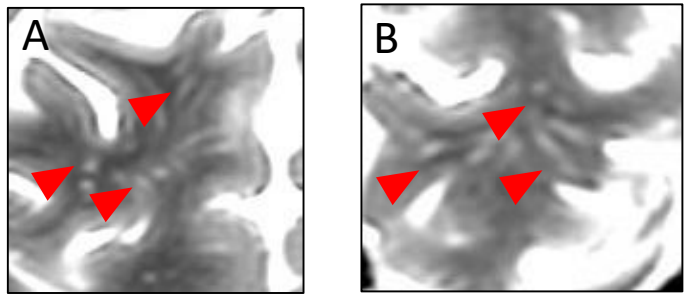
Preliminary data – increased PVS burden in children with mTBI at 1-month follow up

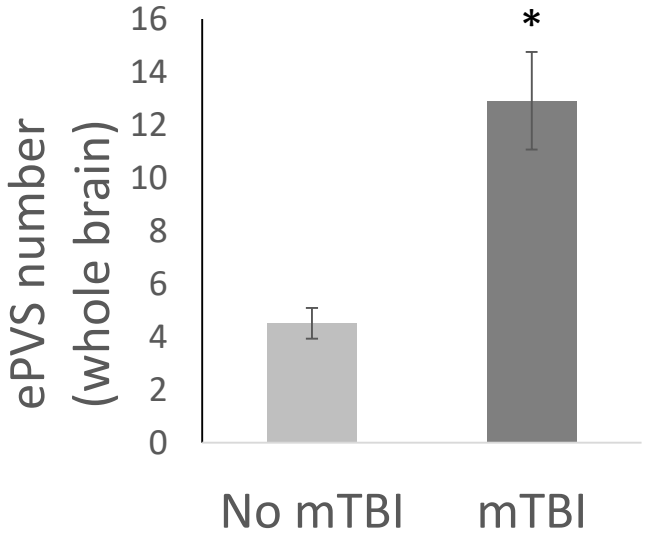


No mTBI

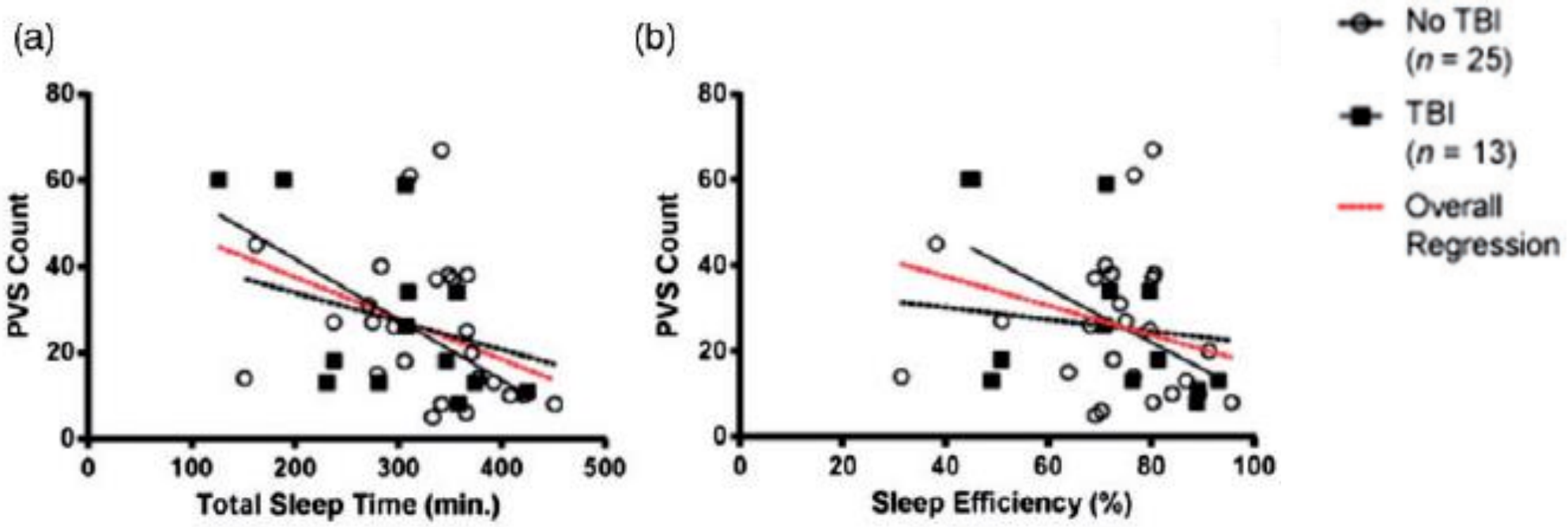


TBI



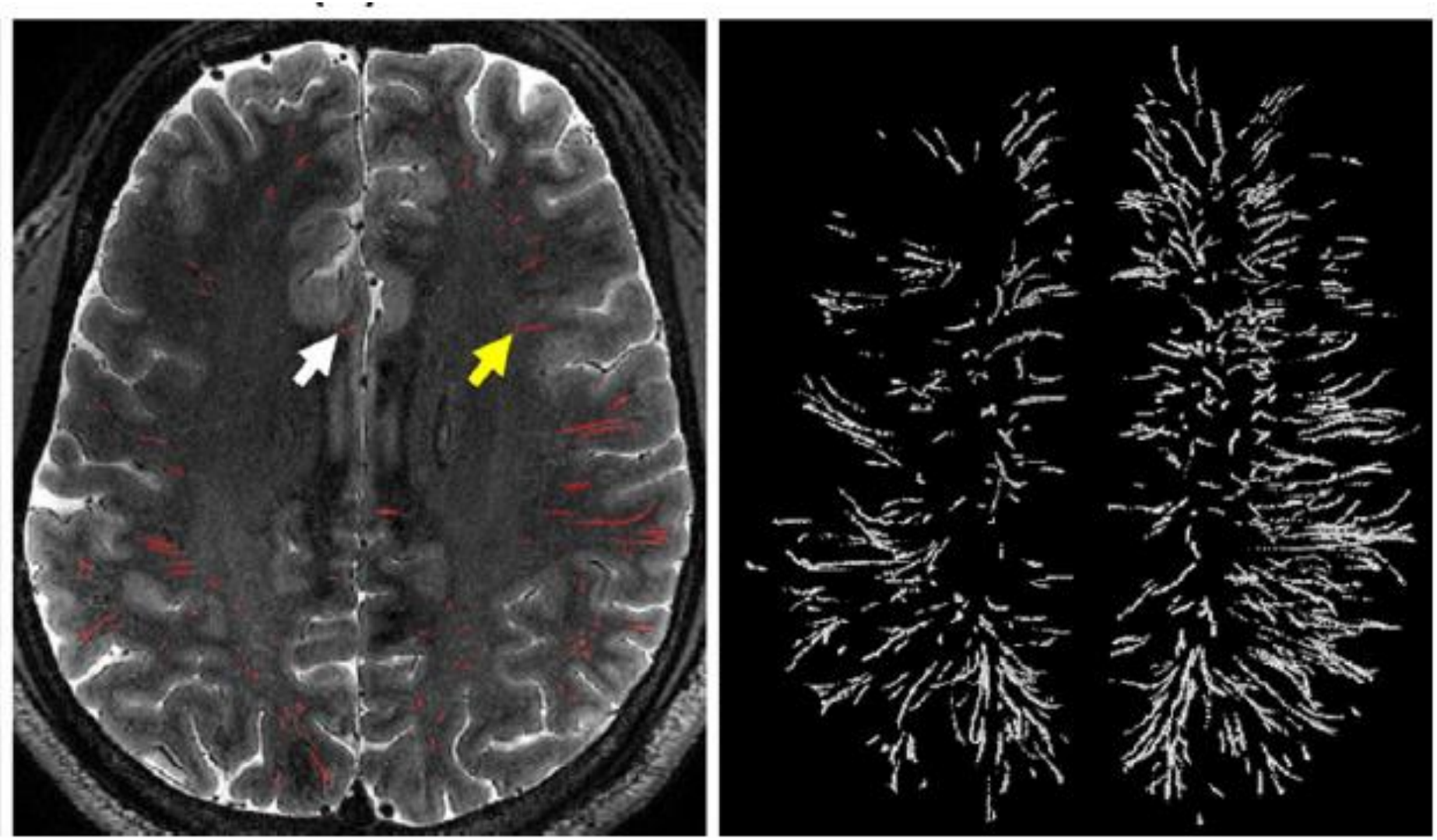


Background – correlation between sleep impairment and enlarged PVS in adults with mTBI



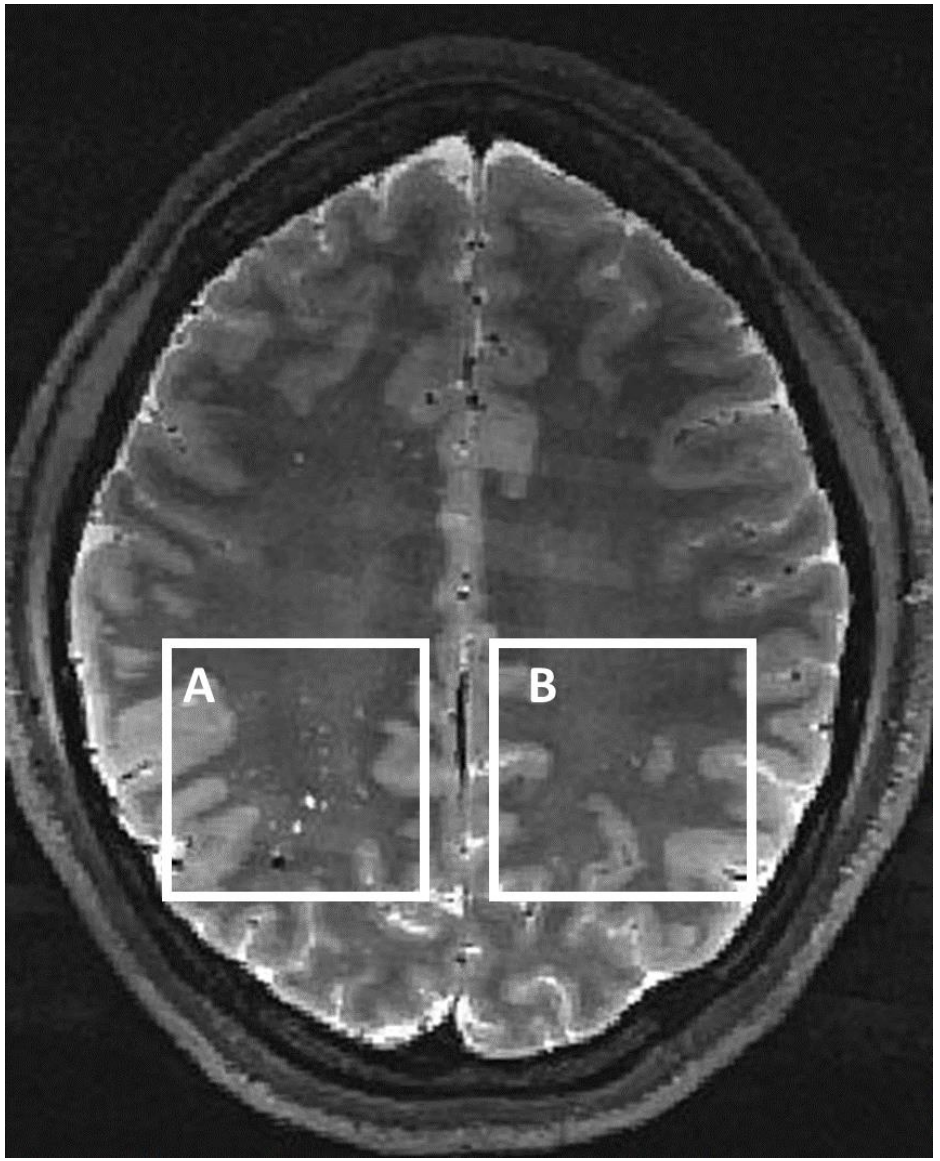
Opel et al., 2018

7 Tesla MRI = better visualization

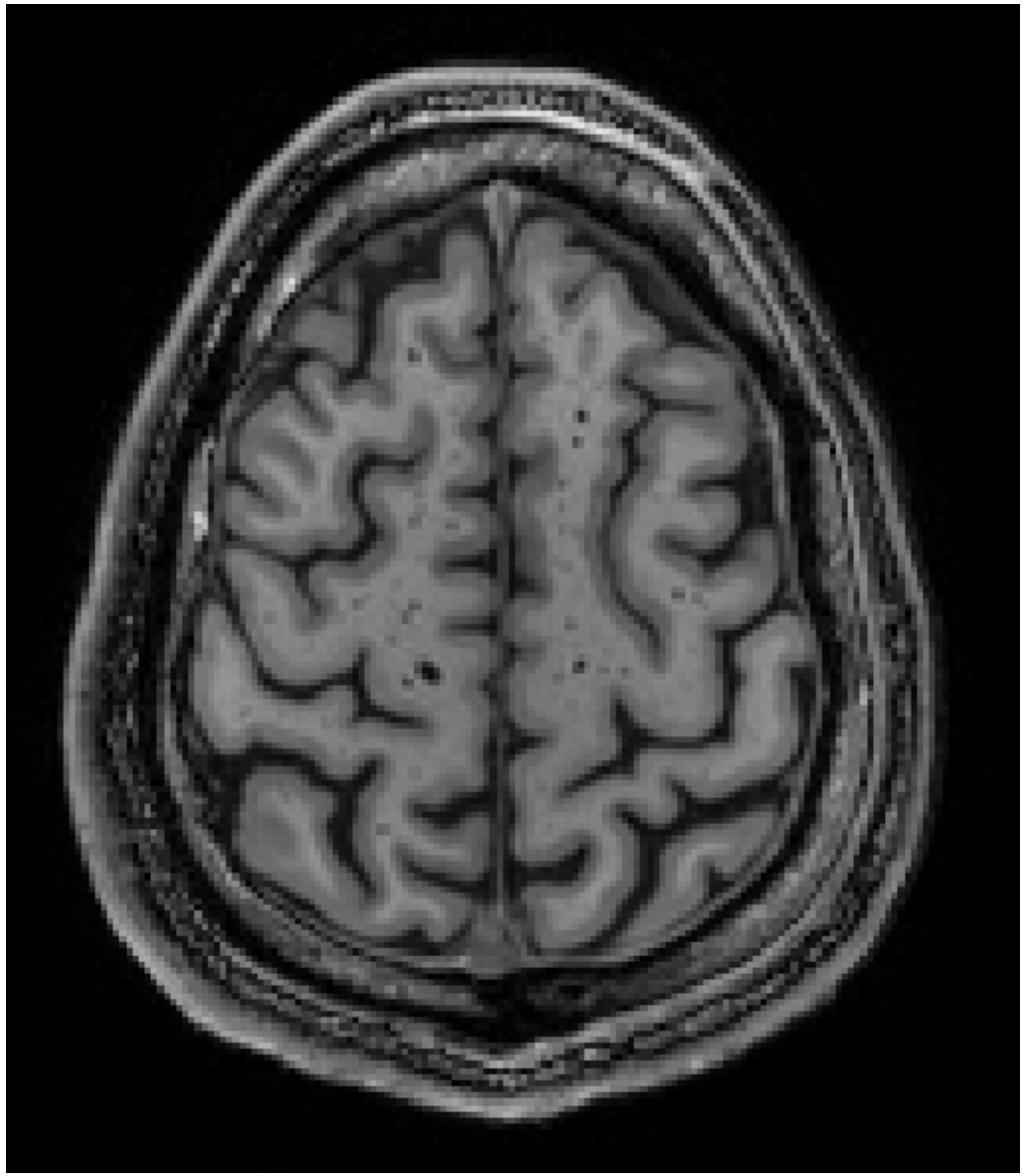


Preliminary data – ePVS asymmetry after TBI

- 16 year old previously healthy girl
- Fell on her back while playing volleyball, hit the RIGHT BACK of her head
- Was seen in an ED, GCS 15, - PECARN criteria, so no imaging was obtained
- Started having headaches, difficulty sleeping
- A month after the injury she continues to have debilitating headaches, sleep problems, dizziness, has been out of school since the accident



Preliminary data – ePVS in veterans with mTBI



Summary

- Sleep disturbances are prevalent among youth with mTBI
- Individuals with sleep disturbances after mTBI report worse post-concussive symptoms
- Glymphatic dysfunction may at least in part explain the relation between mTBI, sleep disturbances, and post-concussive symptoms
- Enlarged perivascular spaces may be a putative marker of glymphatic dysfunction
- Asymmetric perivascular spaces may represent a biomarker of injury in subjects with mTBI

Mentorship team

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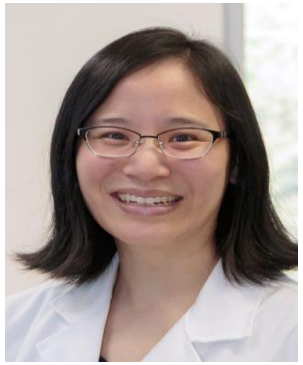

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NIH National Institutes of Health

National Heart Lung and Blood Institute

AHRQ Agency for Healthcare Research and Quality