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 dysfunction)

Iliff et al. J Neurosci 2014
Proposed framework for mTBI, sleep disturbances, glymphatic impairment and post-concussive symptoms

- mTBI
- Acute Sleep Disruption
- Persistent Postconcussive symptoms
- Glymphatic Dysfunction
- Enlarged PVS
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
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
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