

Neural and fluid dynamics of sleep

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Disclaimer and Disclosures

Disclaimer

This certifies that the views expressed in this presentation are those of the author and do not reflect the official policy of the NIH.

Disclosure

This certifies that I, Laura Lewis, have no financial relationship that is relevant to the subject matter of this presentation.

I, Laura Lewis, have a pending patent application on a technique for CSF flow imaging.

Multiple forms and origins of fatigue

Sleep
deprivation

Multiple
sclerosis

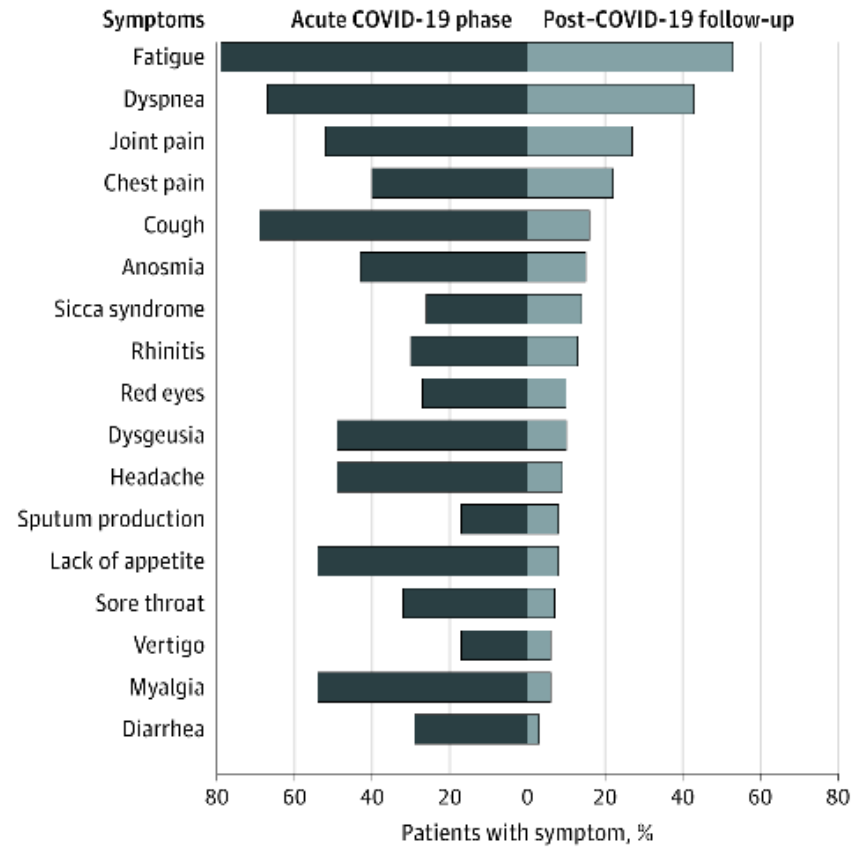
Chronic
fatigue

Depression

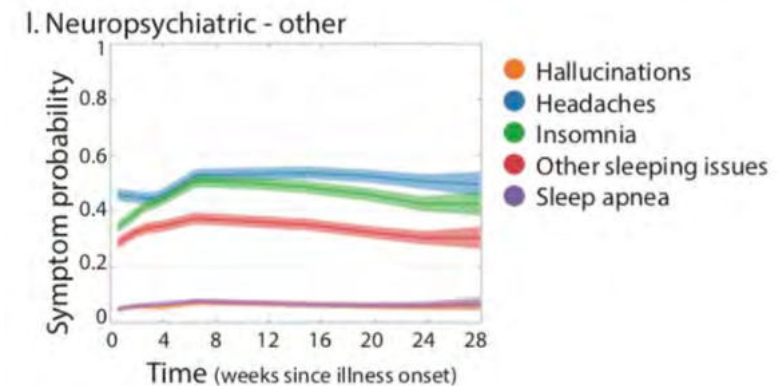
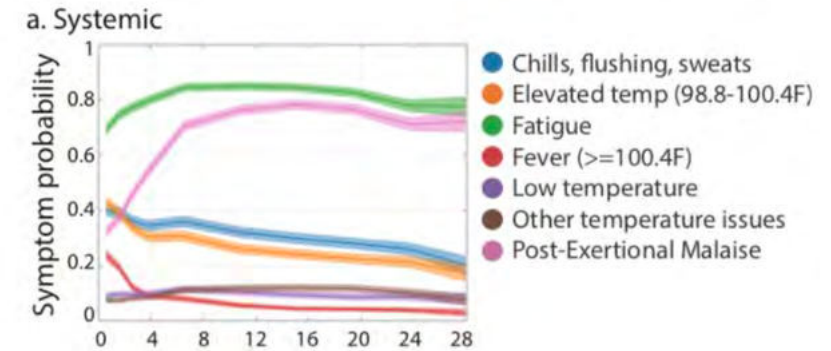
Stroke

- In addition to many other conditions

Persistent fatigue in Long COVID



Carfi et al., JAMA. 2020



Davis et al., medRxiv, 2021

Sleep in individuals with fatigue

- Fatigue can result from sleep disturbances
- Patients with fatigue can have disturbed sleep or may spend as much or more time asleep as is typical (Mariman et al., 2013)



Sleep serves diverse functions for the brain and body

- Cognitive



Sleep serves diverse functions for the brain and body

- Cognitive
- Electrophysiological

Human EEG in NREM:

Wakefulness



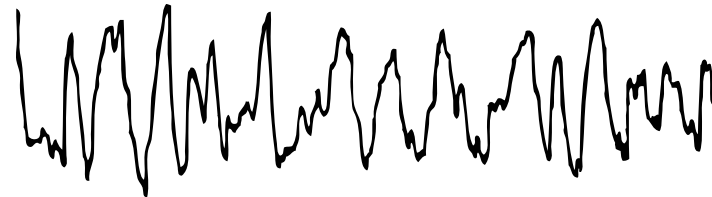
NREM (stage 1)



NREM (stages 2/3)

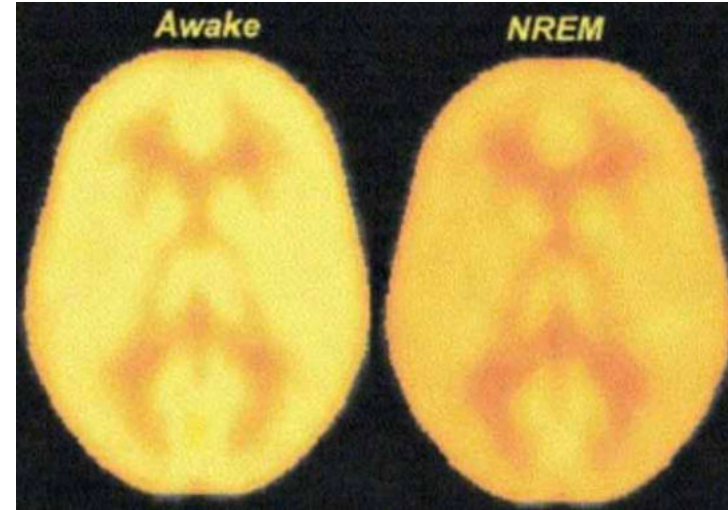


NREM (stage 4)



Sleep serves diverse functions for the brain and body

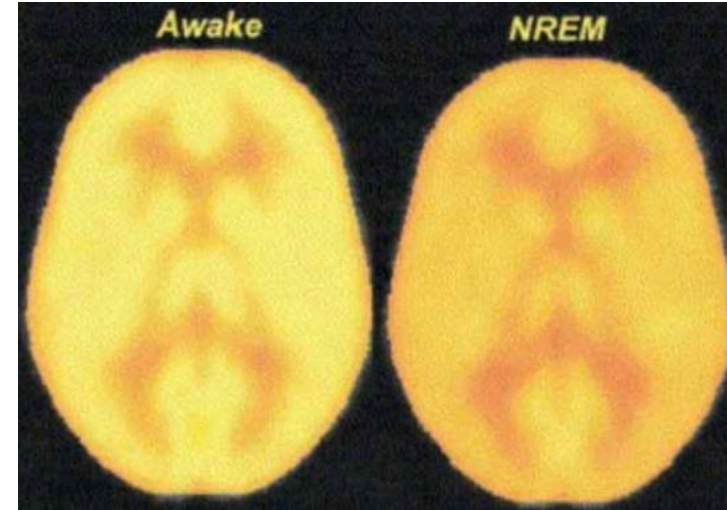
- Cognitive
- Electrophysiological
- Metabolic



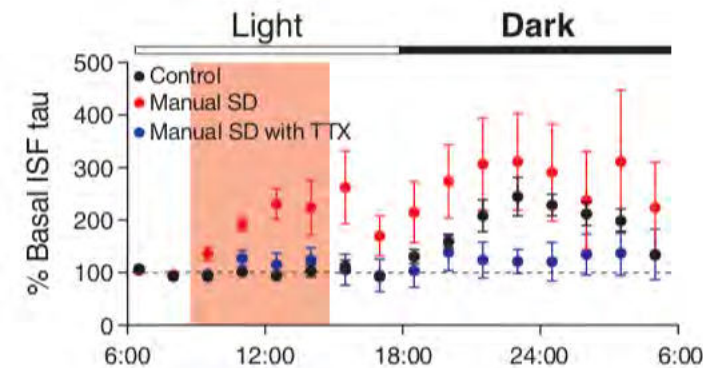
Buchsbaum et al., 2001

Sleep serves diverse functions for the brain and body

- Cognitive
- Electrophysiological
- Metabolic



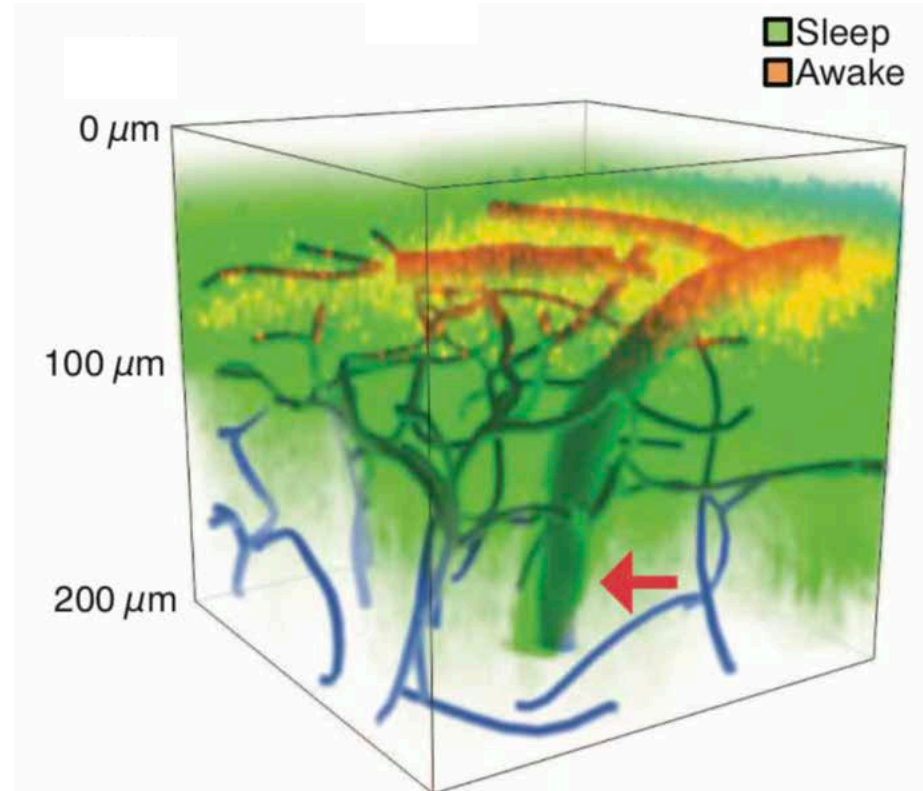
Buchsbaum et al., 2001



Holth et al., 2019

Sleep serves diverse functions for the brain and body

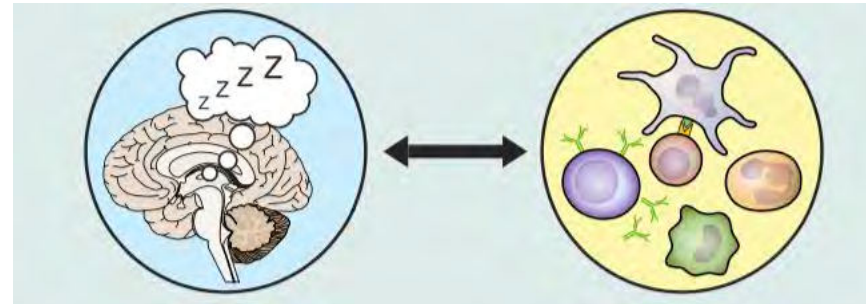
- Cognitive
- Electrophysiological
- Metabolic
- Waste clearance



Xie et al., 2013

Sleep serves diverse functions for the brain and body

- Cognitive
- Electrophysiological
- Metabolic
- Waste clearance
- Immune/inflammatory

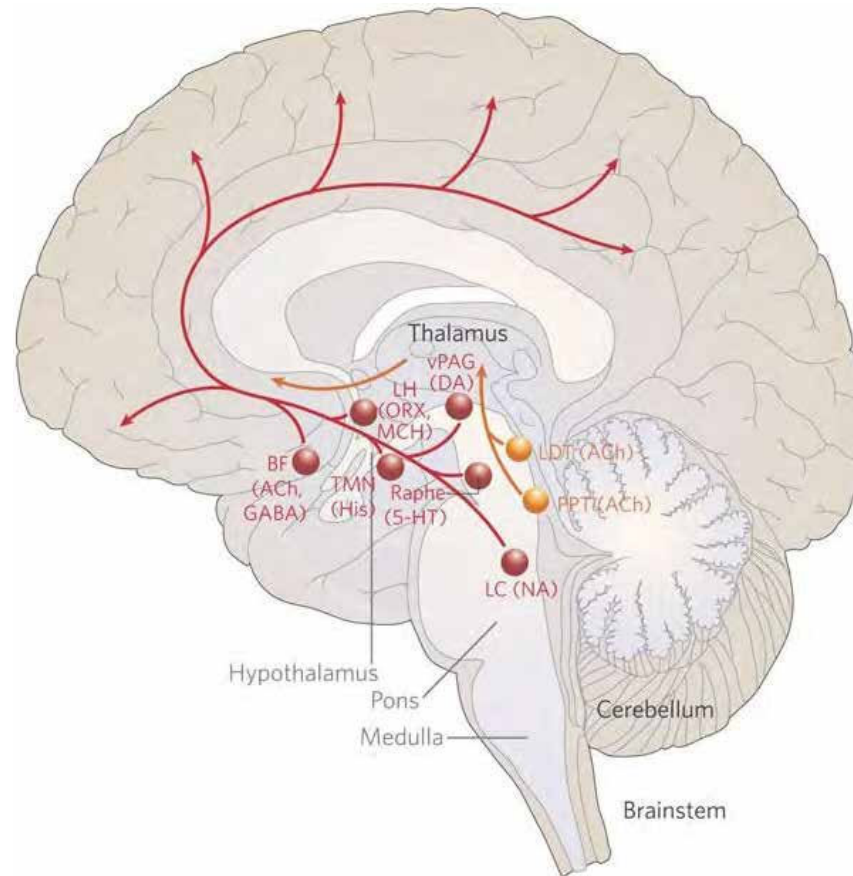


Besedvosky et al., 2017

What neurobiological factors could cause arousal dysregulation?

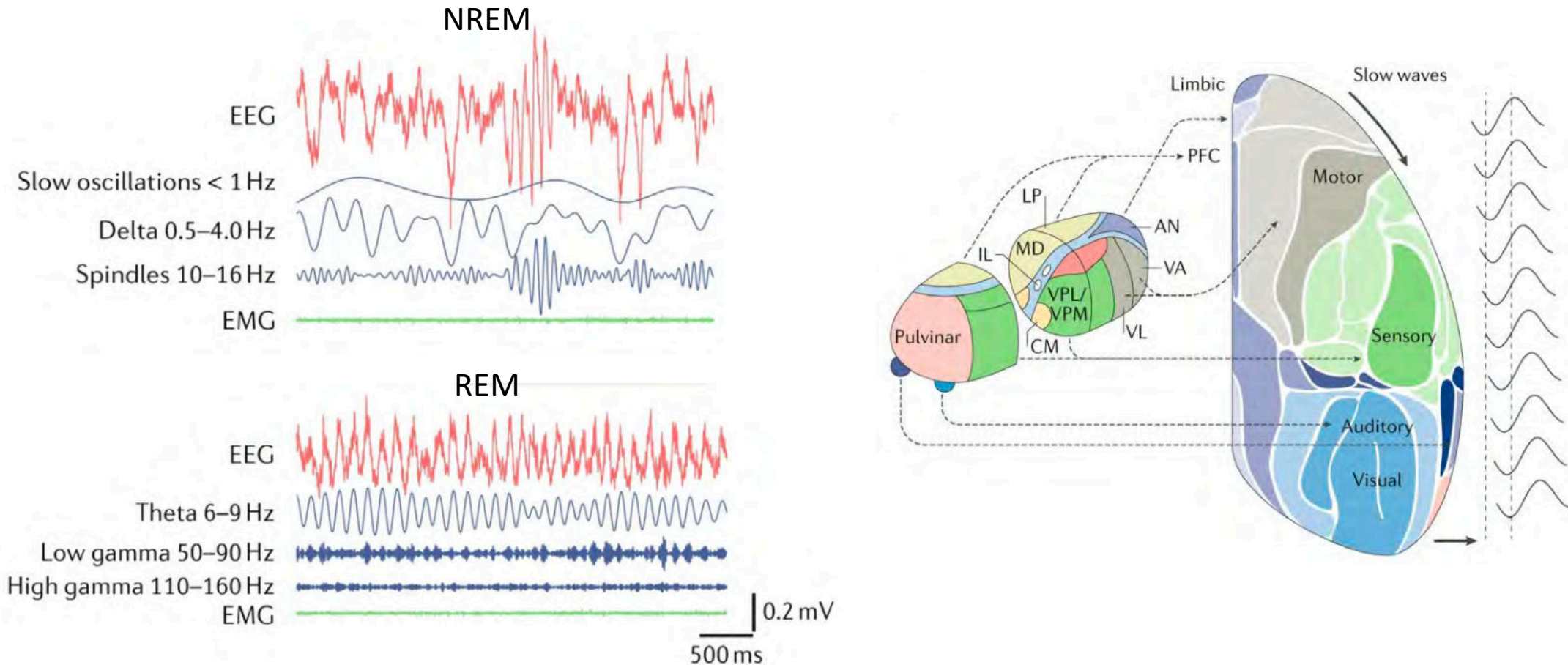
- Is sleep less restorative?
- Are arousal regulatory circuits disordered?
- Is waste removal impaired?
- Is there a widespread dysregulation of neural activity/inflammation?

Subcortical circuits regulate arousal state



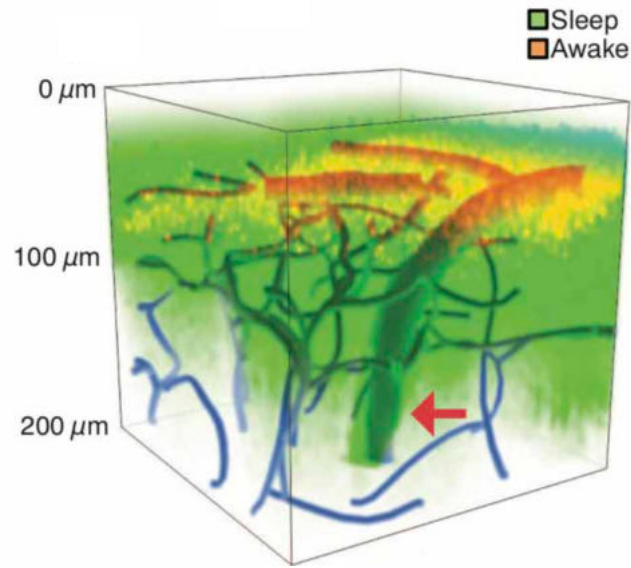
Saper et al., 2005

Sleep-defining EEG rhythms reflect thalamocortical oscillations

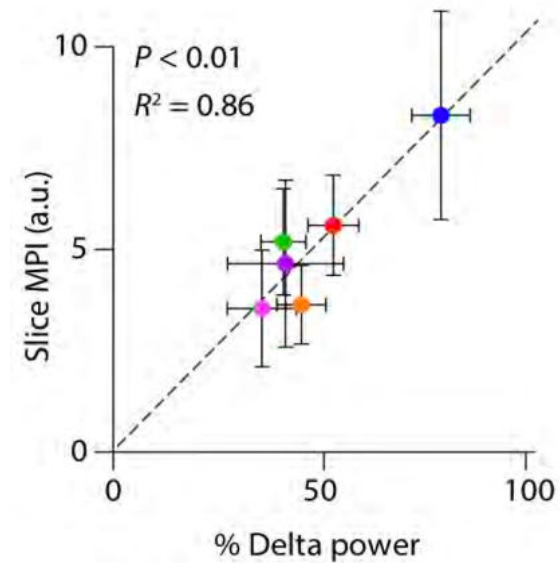


Adamantidis et al., 2019

Heightened clearance during states with neural slow wave activity

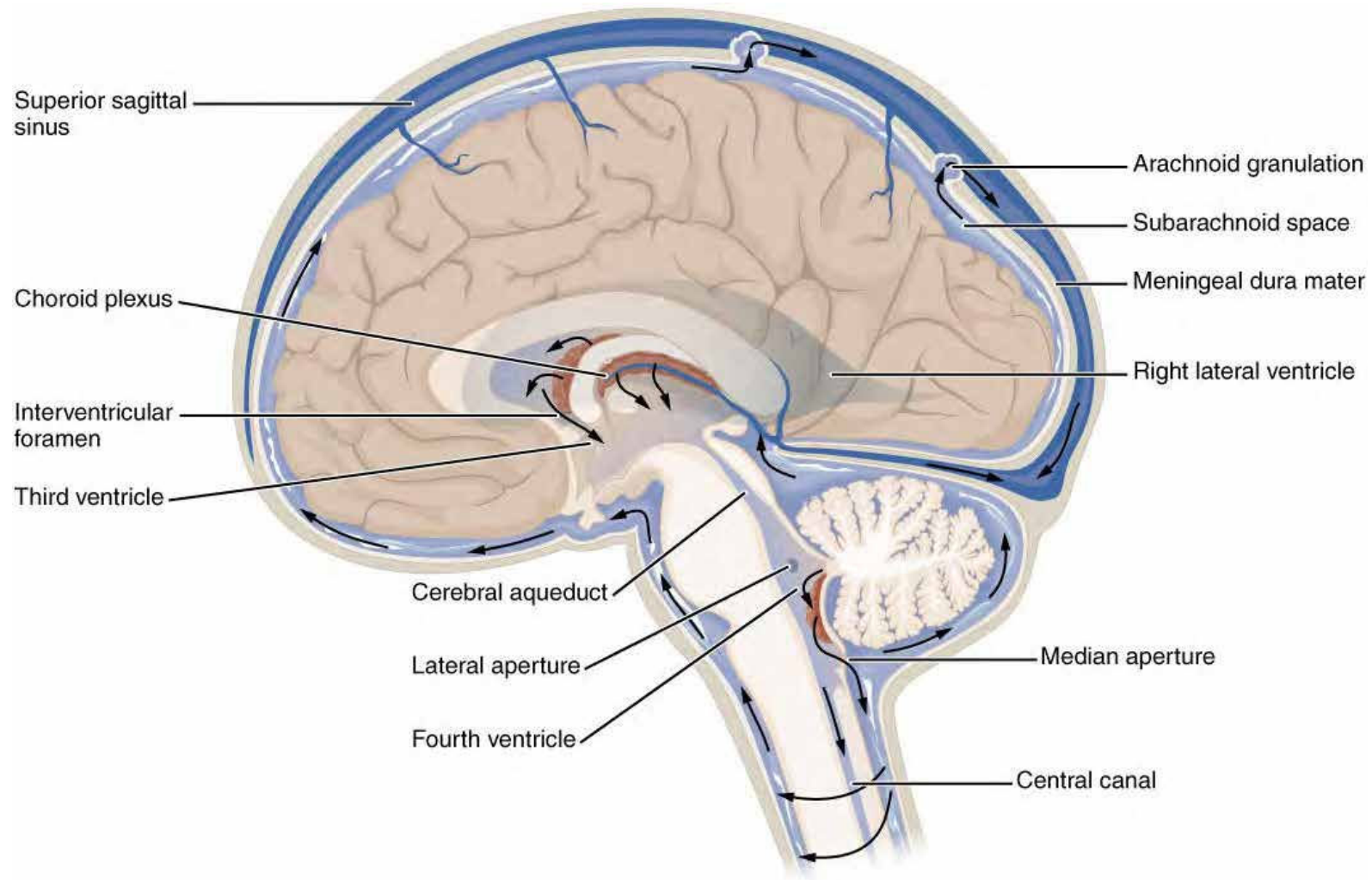


Xie et al., *Science*, 2013

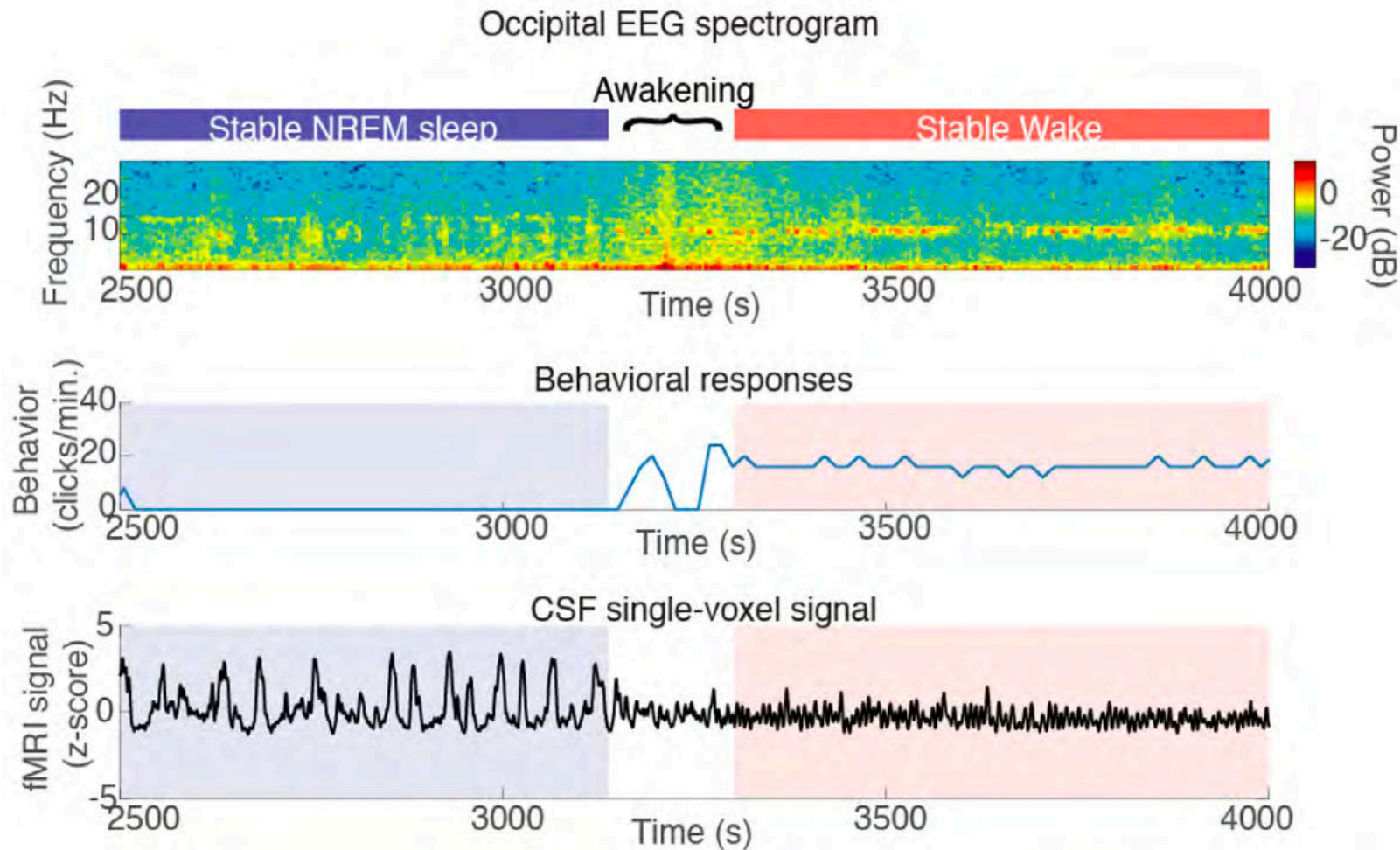


Hablitz et al. *Science Advances*, 2019

Cerebrospinal fluid flow in sleep

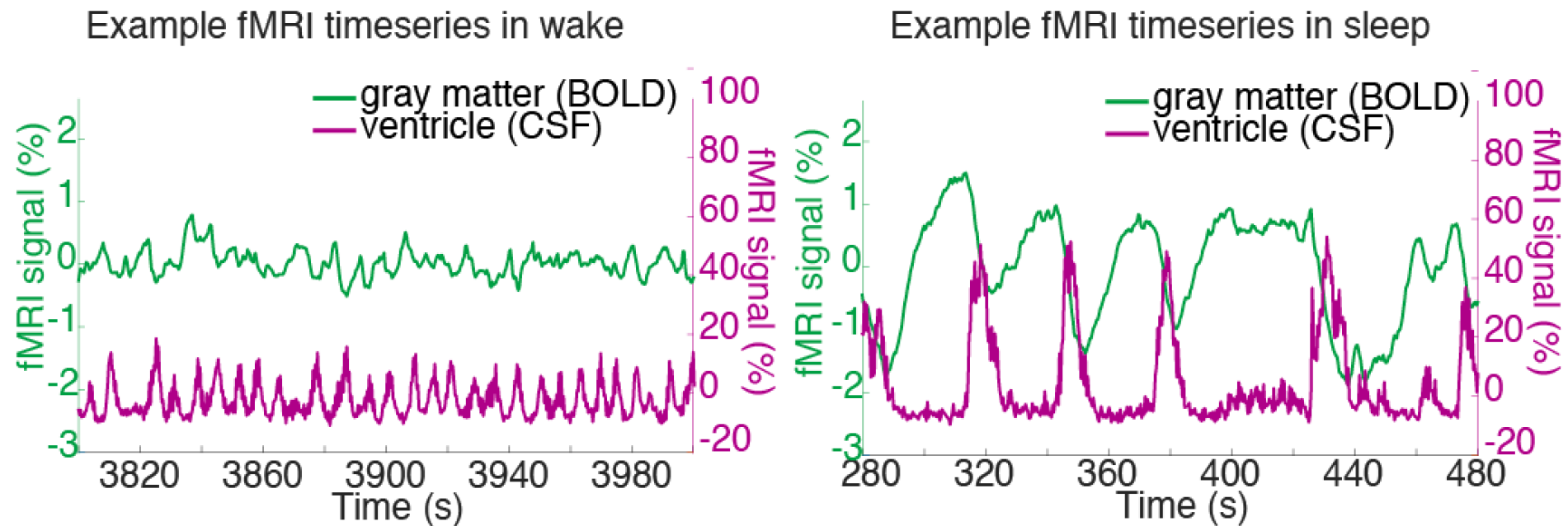


CSF flow waves appear during sleep

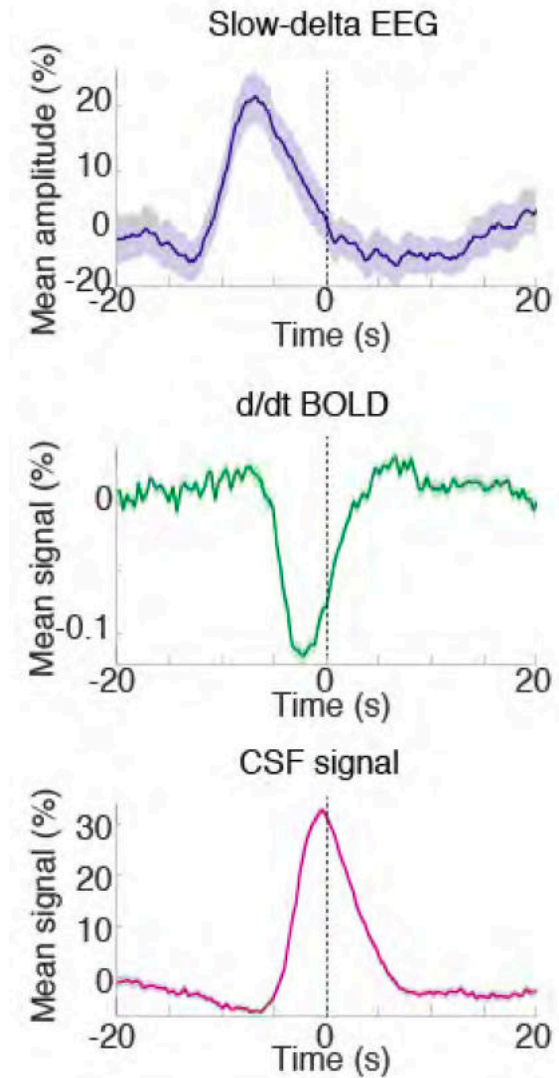


Fultz et al., 2019

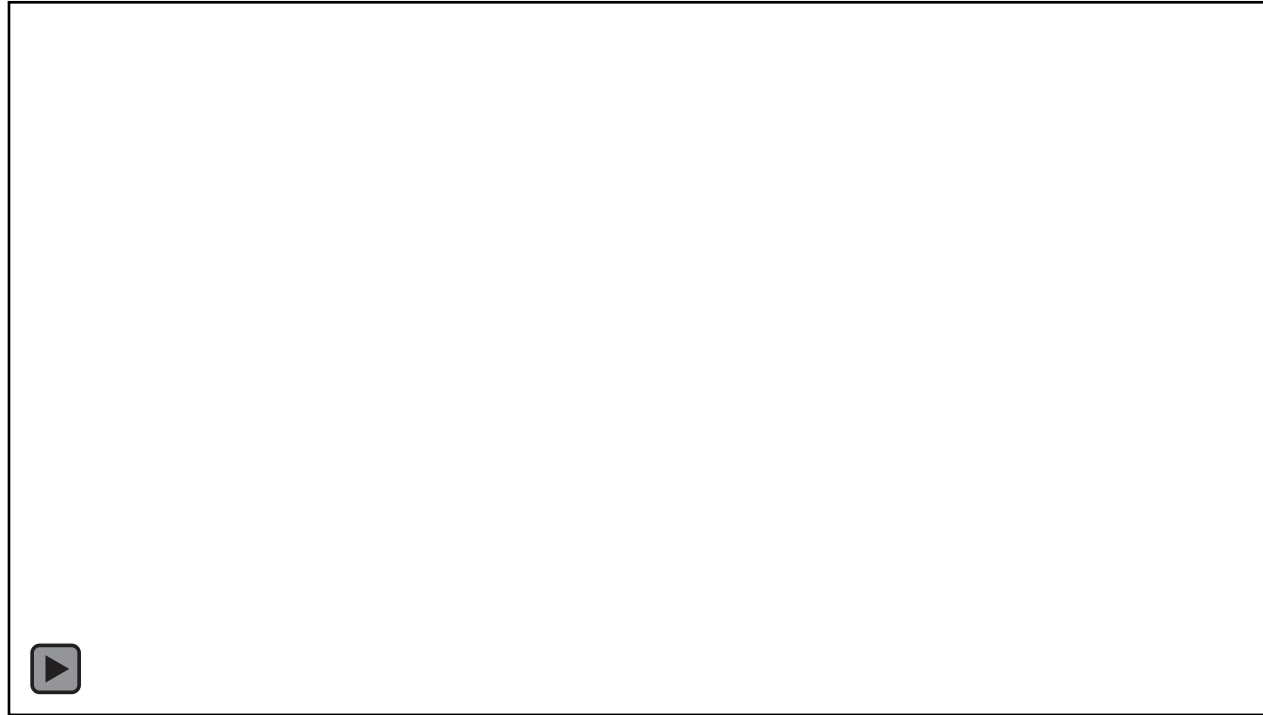
Cerebrospinal fluid flow is coupled to hemodynamic waves during sleep



CSF waves are coupled to neural slow waves



Coupled hemodynamic and CSF flow waves during sleep



Multiple points of vulnerability in sleep

- Sleep loss or fragmentation could impair restorative effects of sleep
- The neural, metabolic, and fluid consequences of sleep are coupled
- Sleep with disrupted neural, glial, vascular, or fluid dynamics may have distinct outcomes for CSF and clearance
- Direct impairment of arousal regulatory circuits as a parallel pathway
- Sleep serves multiple functions and affect multiple components of brain physiology

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