# Wearable fNIRS on studies of neurohydrodynamics

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# OUTLINE

- Neurohydrodynamics and cerebral circulation
- fNIRS method to study human hydrodynamics
- Ongoing fNIRS studies on neurohydrodynamics

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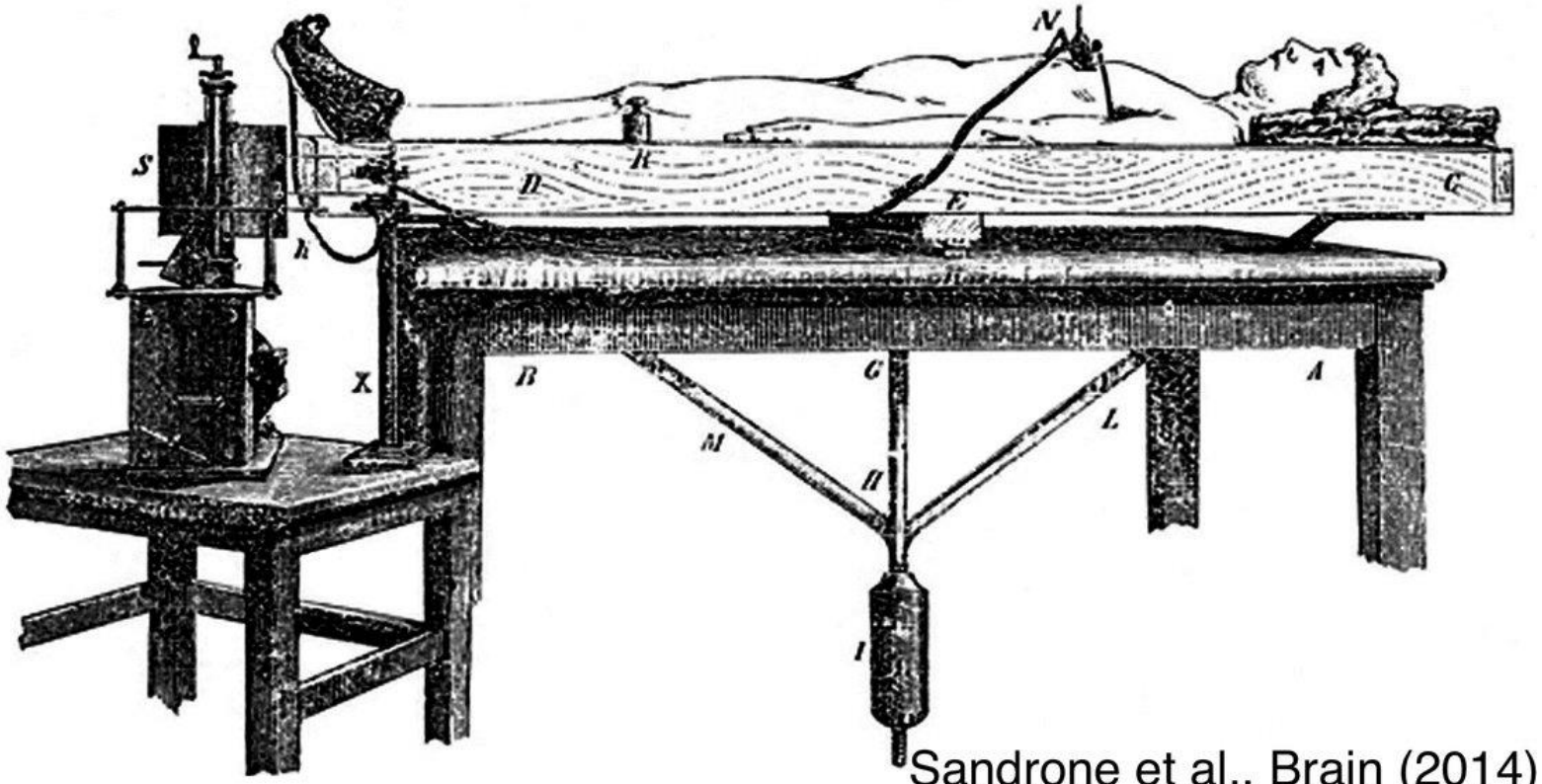
# Probably the first brain monitoring device, invented 140 years ago!



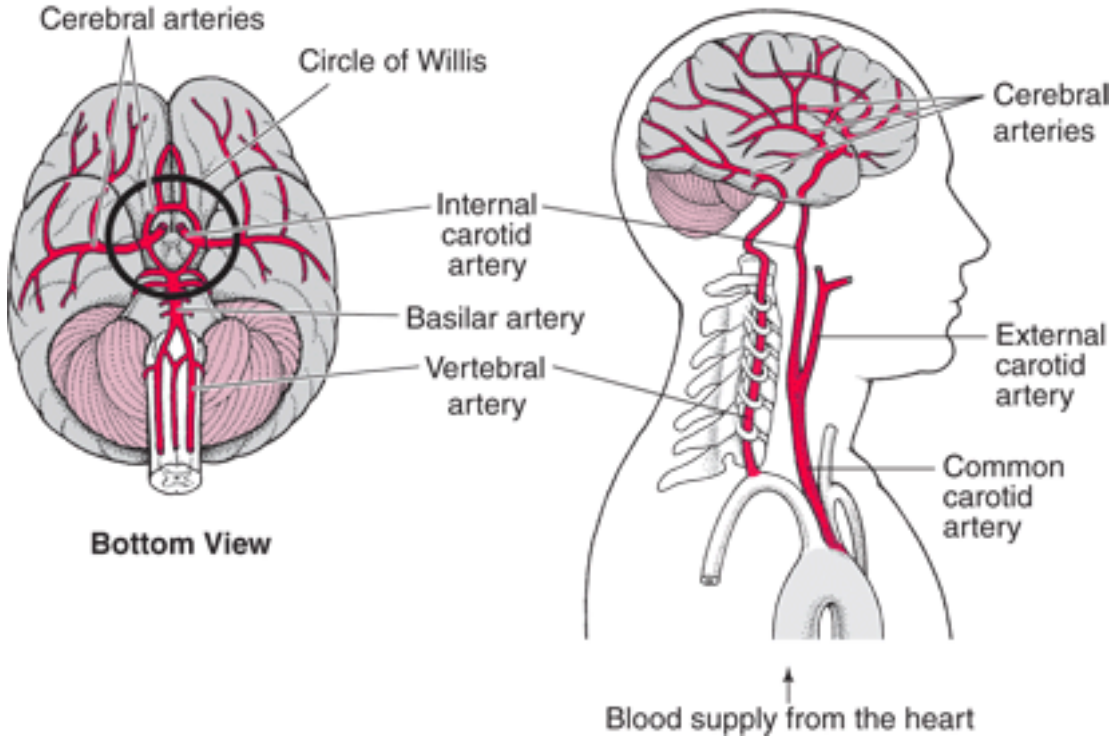

Sandrone et al., Brain (2014)

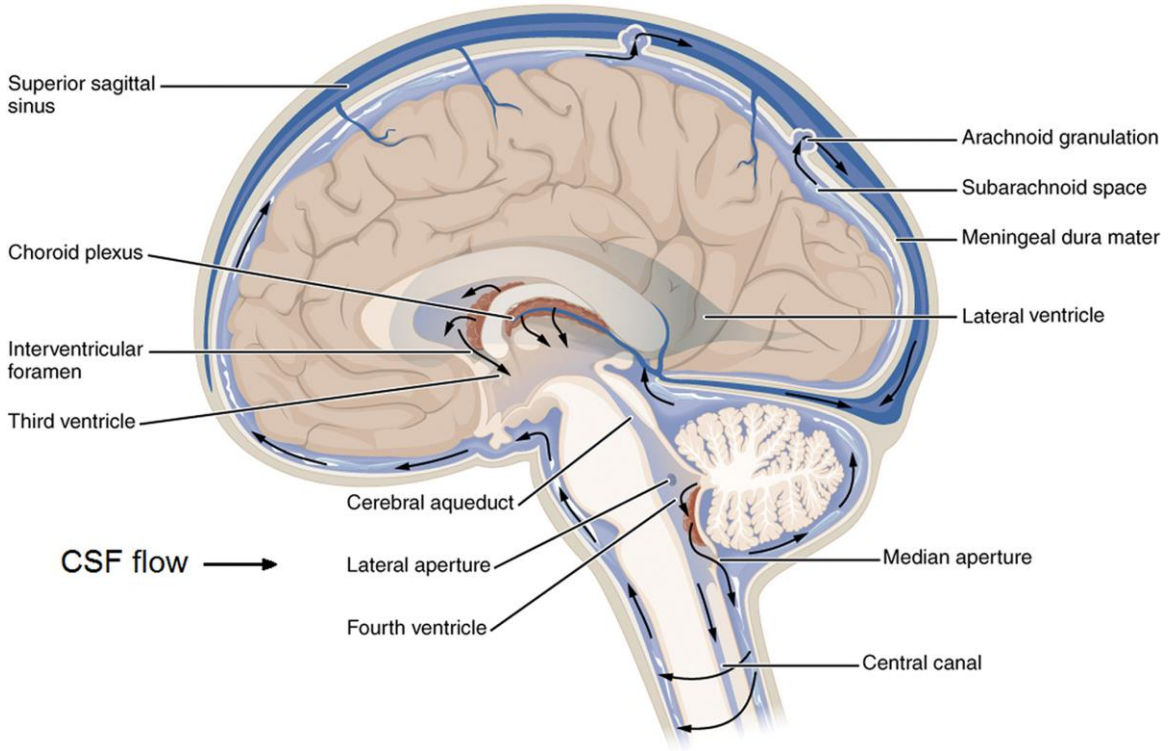
Weighing brain activity - 'human circulation *balance,* Angelo Mosso, 1882

# Cerebral circulation and neurohydrodynamics

- **Neurohydrodynamics investigates the role of intracranial fluid hydrodynamics** (e.g. **cerebrospinal fluid (CSF)**, cerebral blood flow, and interstitial fluid) in the pathophysiology of neurological disorders such as hydrocephalus, Chiari malformation, syringomyelia, pseudotumor cerebri, cerebral vasospasm, *Alzheimer's disease*, multiple sclerosis and cerebral aneurysm.
- **Cerebral (blood) circulation ensures energy and oxygen supply to the brain**. The most important parameters reflecting cerebral circulation are **cerebral blood flow (CBF), cerebral perfusion pressure (CPP), cerebrovascular resistance (CVR), and intracranial pressure (ICP)**. These have also an important role in diagnostics of many brain disorders, such as *stroke, hemorrhage*, head trauma, and carotid artery disease.

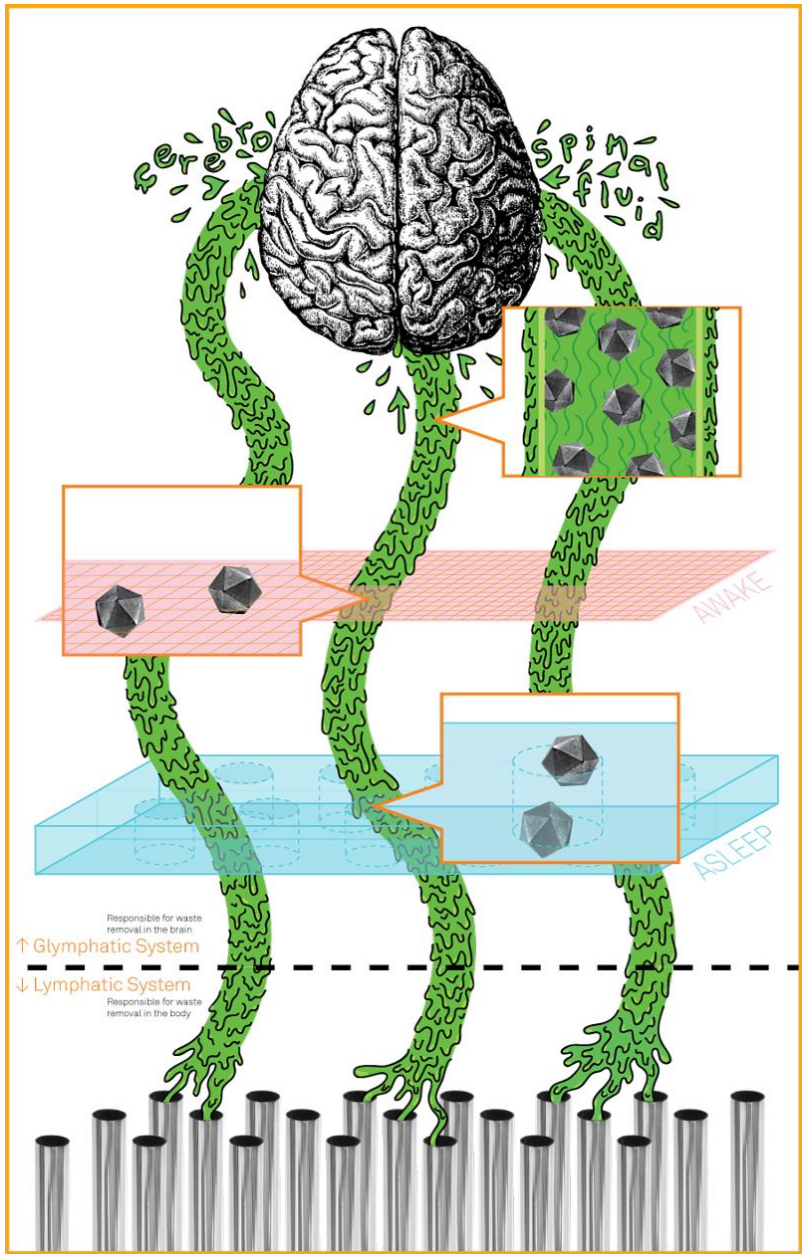
# Cerebral circulation and neurohydrodynamics



# Glymphatic system and brain clearance

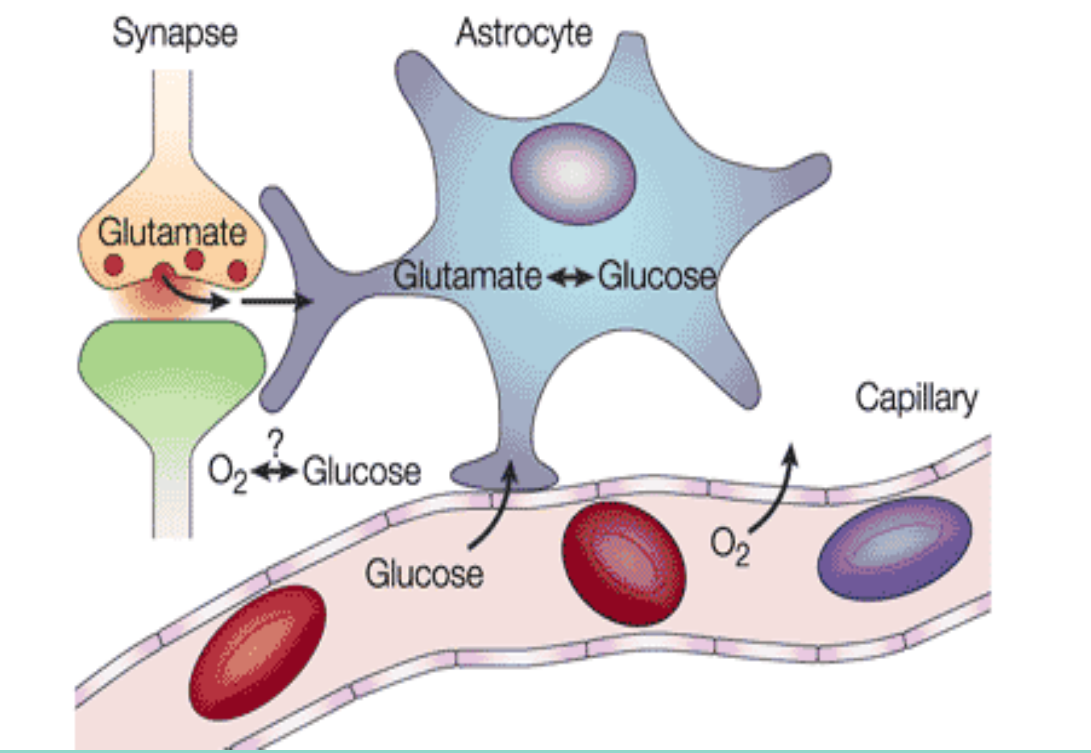
- The Glymphatic system is the counterpart of the lymphatic system elsewhere in the body.
- As a whole, it is responsible for flushing out toxins, metabolic waste products, soluble proteins and other harmful fluids from the body system into the CSF drainage
- Its function is closely related to neurohydrodynamics!




Source: *http://www.samanthamonarch.com/*

Raper, Daniel, Antoine Louveau, and Jonathan Kipnis. "How Do Meningeal Lymphatic Vessels Drain the CNS?." Trends in Neurosciences 39.9 (2016): 581-586.

# Neurohydrodynamics - Neurovascular coupling




HbO and HbR are correlates of brain activity through oxygen consumption **by neurons**

Neurons consume energy (glucose) when activated

Oxygen is required to metabolize the glucose

As clusters of neurons are activated, there is an increased need for oxygen in that area

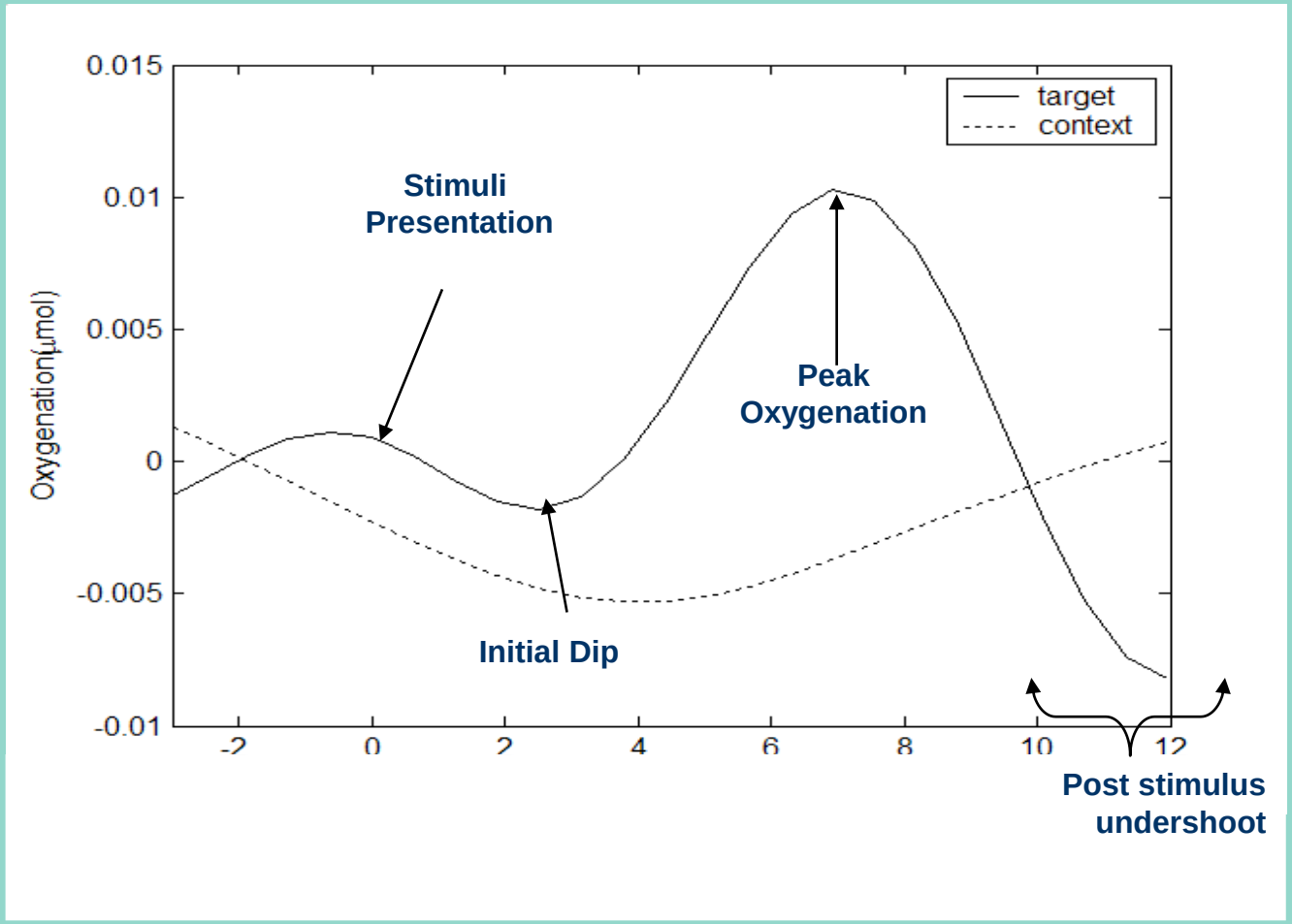
Oxygen is transported to neural tissue via oxy-hemoglobin (HbO or $HbO_2$) in the blood

The oxygen exchange occurs in the capillary beds

As oxy-hemoglobin gives up oxygen to the neural tissue, it is transformed into deoxygenated (Hb or HbR) hemoglobin

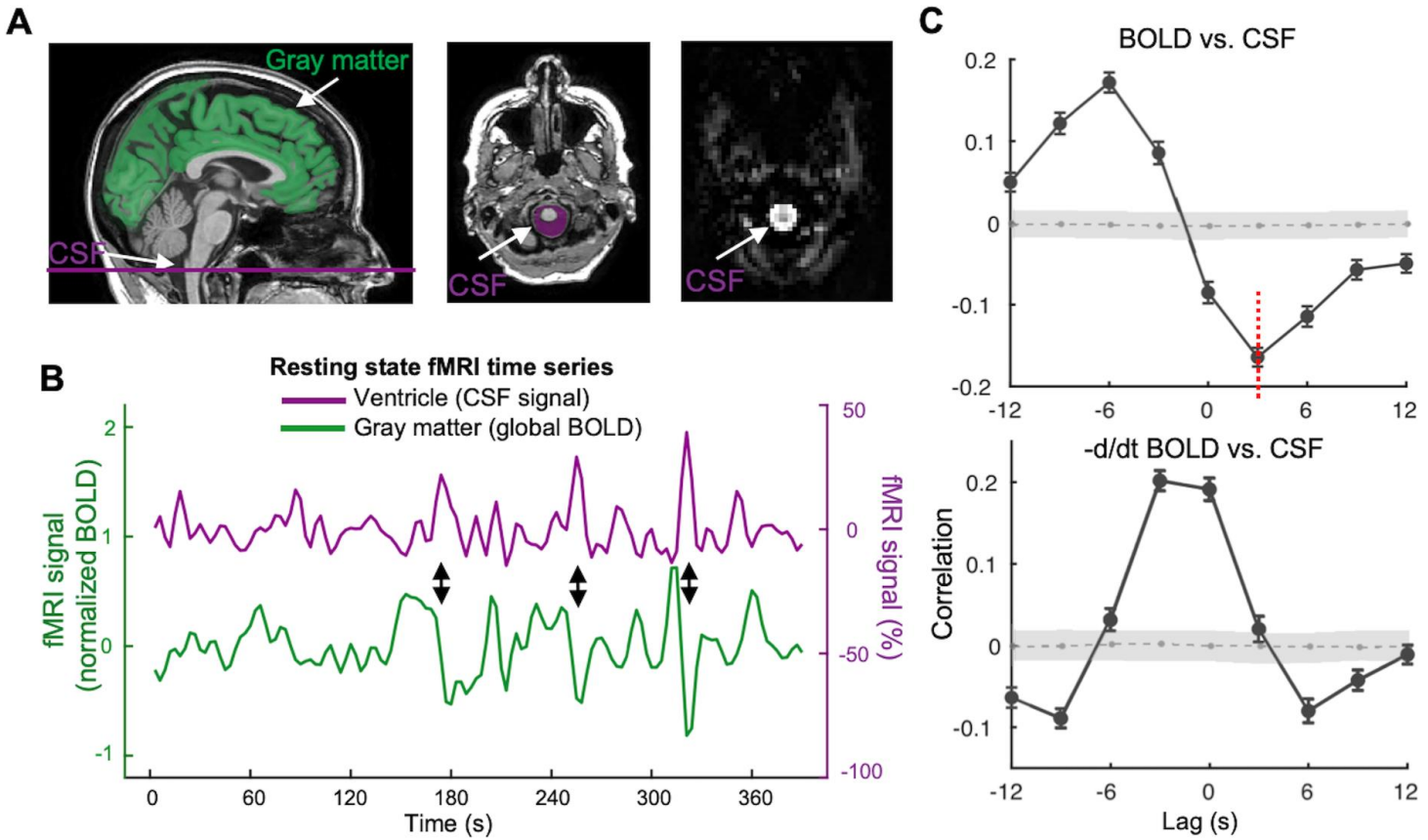
David J. Heeger & David Ress. (2002)What does fMRI tell us about neuronal activity? Nature Reviews Neuroscience 3, 142-151

# Neurohydrodynamics - Neurovascular coupling




**Neurovascular** coupling refers to the relationship between local neural activity and subsequent changes in cerebral blood flow (CBF) and hemodynamic response

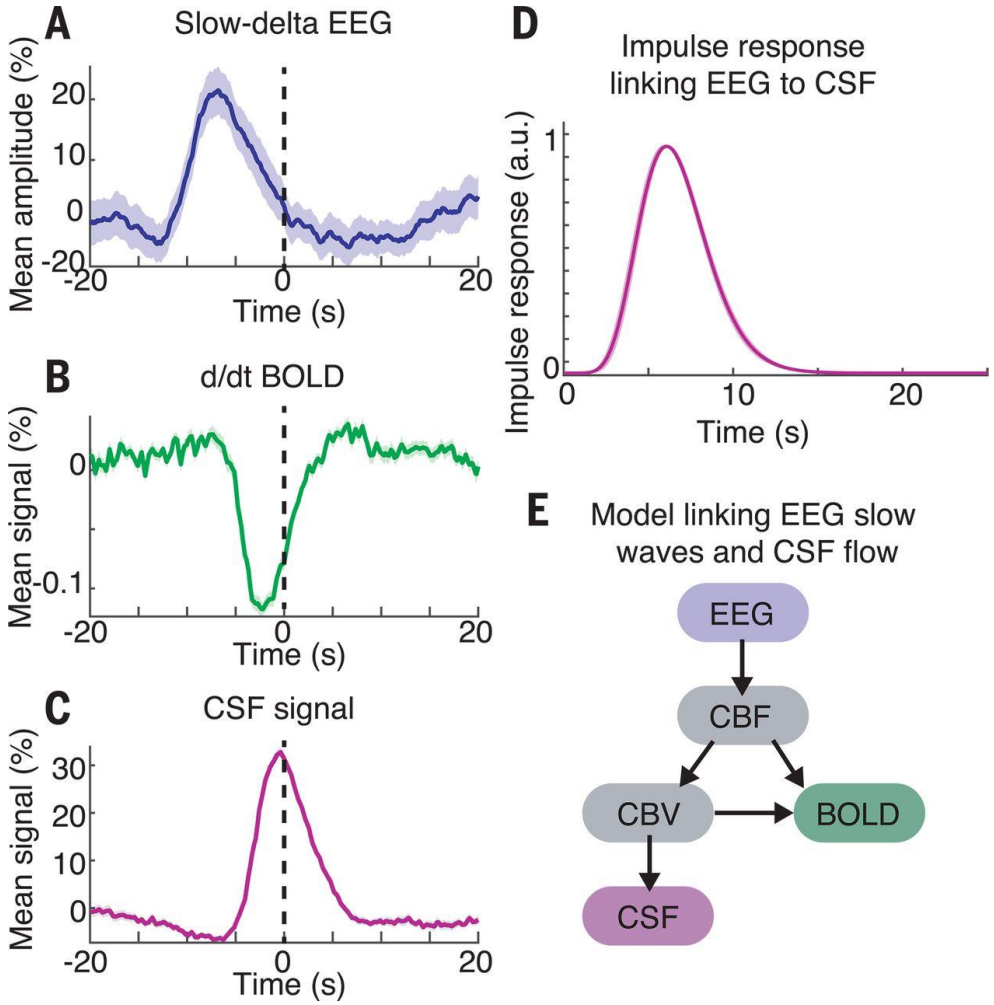
# Neurohydrodynamics
# - Neurovascular - CSF coupling



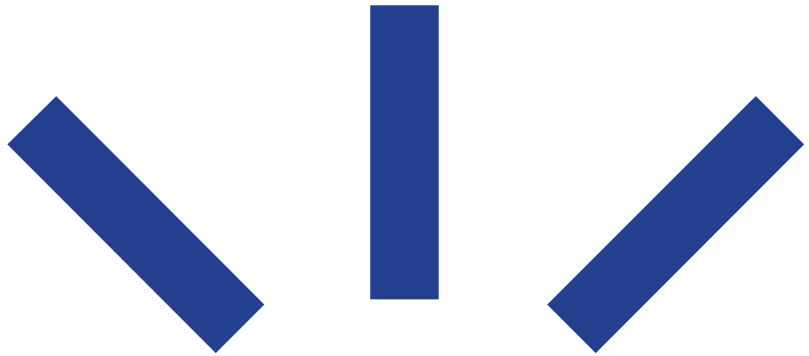

**In AD, reduced coupling between cerebrospinal fluid flow and global brain activity**

Han, F., Chen, J., Belkin-Rosen, A., Gu, Y., Luo, L., Buxton, O. M., ... & Alzheimer's Disease Neuroimaging Initiative. (2021). Reduced coupling between cerebrospinal fluid flow and global brain activity is linked to Alzheimer disease–related pathology. PLoS biology, 19(6), e3001233.

# Neurohydrodynamics
# - Neurovascular - CSF coupling

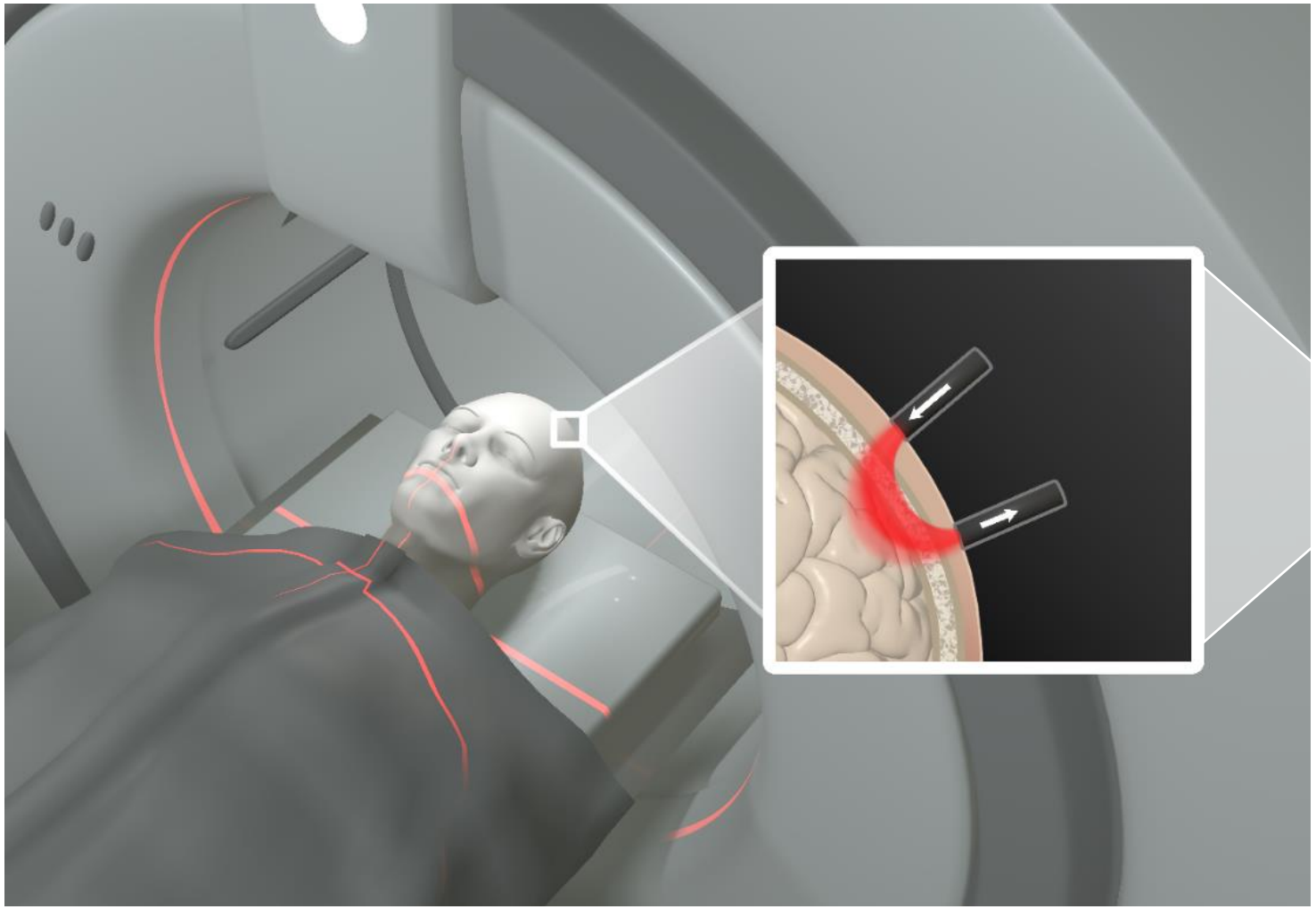


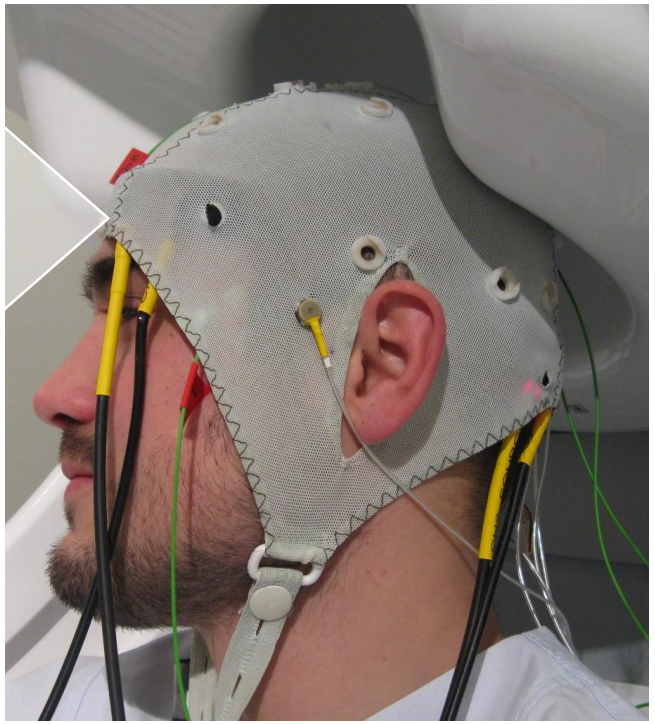

Fultz, N. E., Bonmassar, G., Setsompop, K., Stickgold, R. A., Rosen, B. R., Polimeni, J. R., & Lewis, L. D. (2019). Coupled electrophysiological, hemodynamic, and cerebrospinal fluid oscillations in human sleep. Science, 366(6465), 628-631.



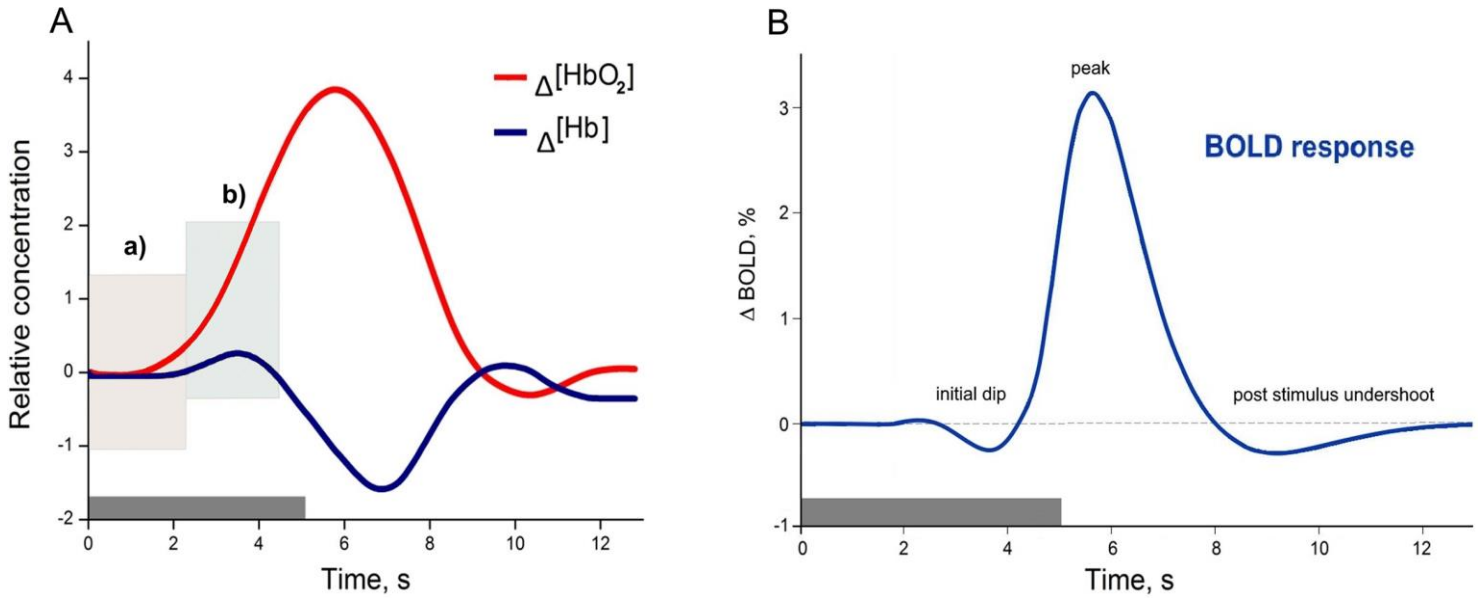
# fNIRS method to study human cerebral hydrodynamics

# fNIRS in multimodal neuroimaging





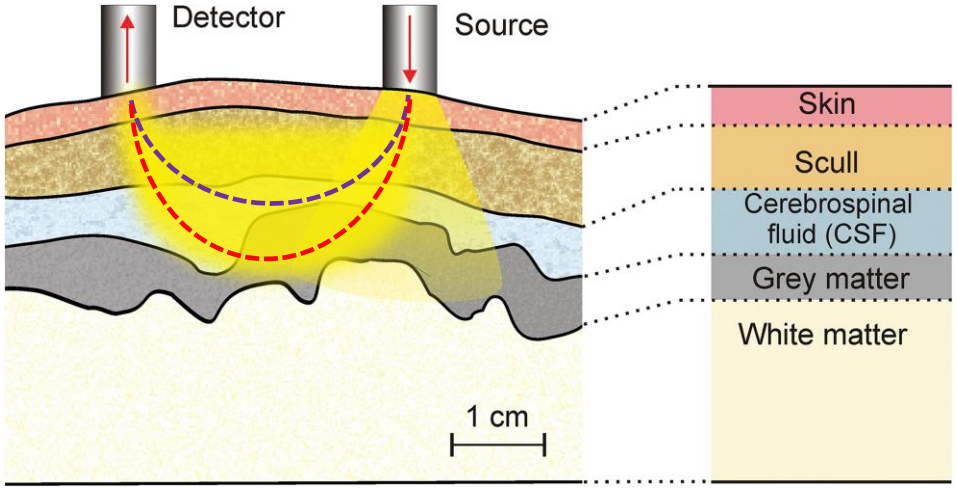
# Oxygen level changes can be measured optically (fNIRS) and magnetically (fMRI)

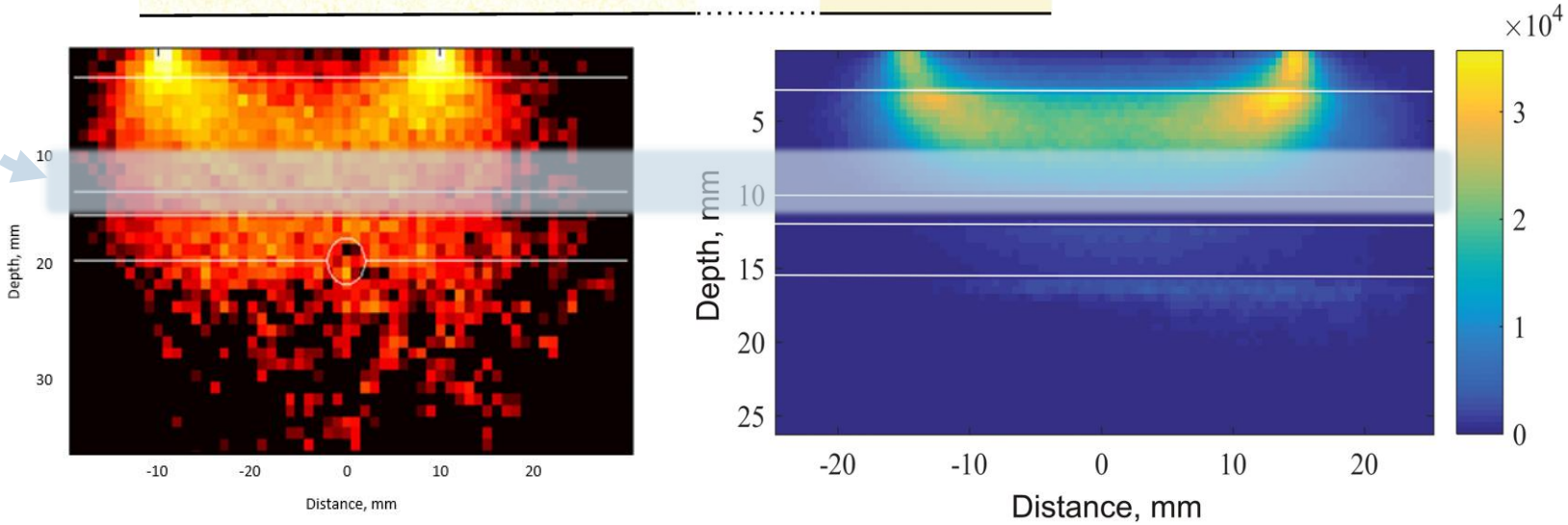



**Examples of fNIRS hemodynamic response (A), and fMRI hemodynamic response function (B).**

Cinciute, Sigita. "Translating the hemodynamic response: why focused interdisciplinary integration should matter for the future of functional neuroimaging." *PeerJ* 7 (2019): e6621.

# Functional Near-Infrared Spectroscopy (fNIRS) for measuring brain fluid concentrations



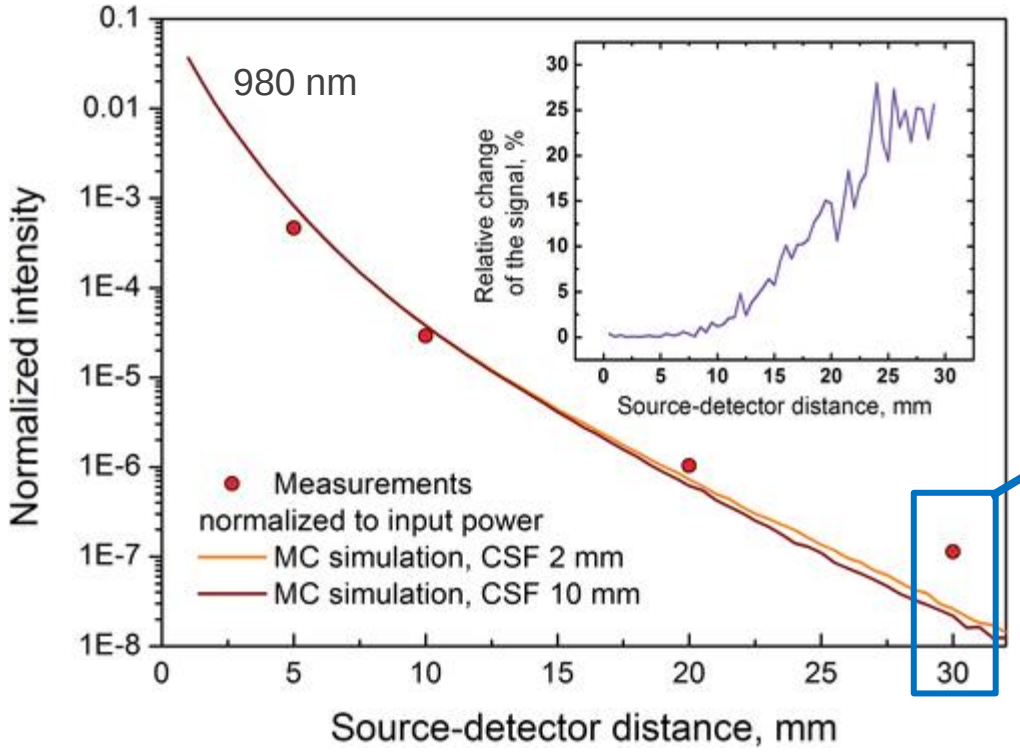




Monte Carlo (MC) simulated scattering map for photons propagating inside the human head model at the source-detector distance of 30 mm for 830nm (left) and 980 nm (right).

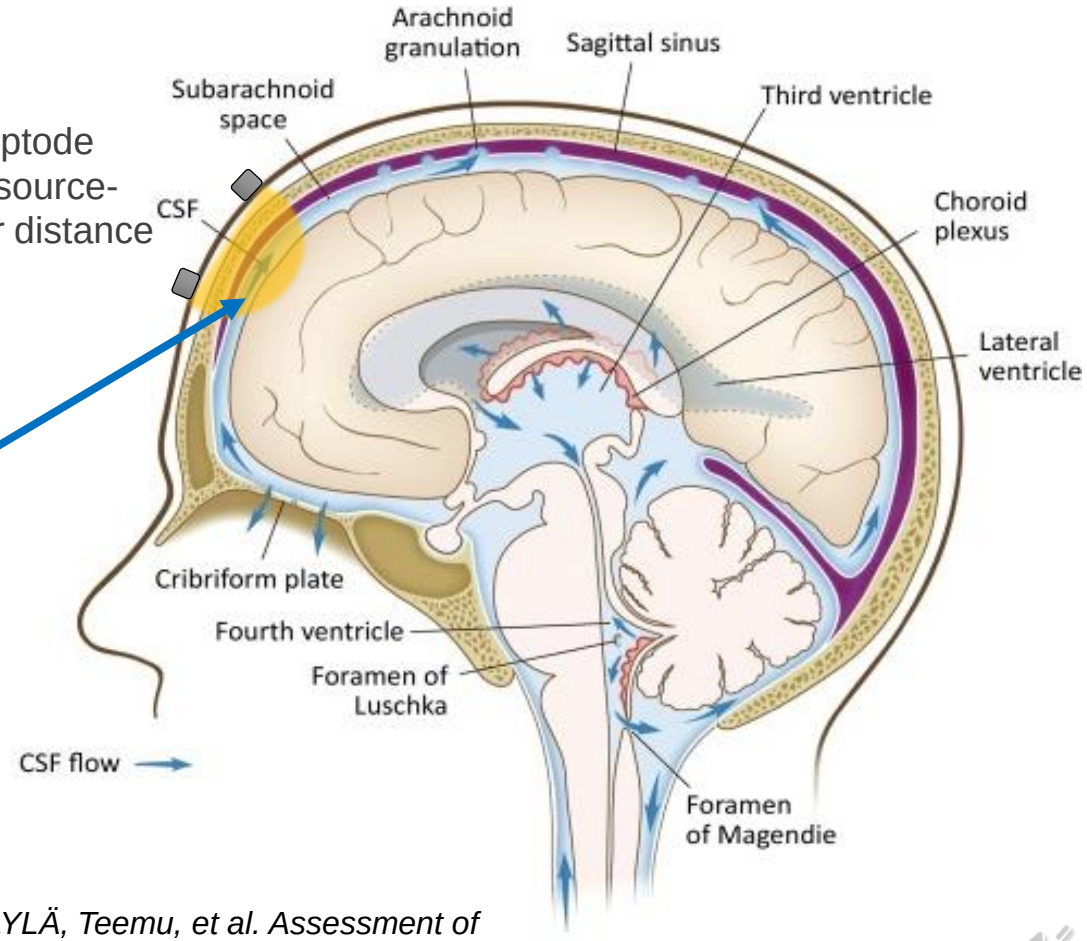

*KORHONEN, Vesa O., et al. Light propagation in NIR spectroscopy of the human brain. IEEE Journal of Selected Topics in Quantum Electronics, 2013, 20.2: 289-298.*

*MYLLYLÄ, Teemu, et al. Assessment of the dynamics of human glymphatic system by near-infrared spectroscopy. Journal of biophotonics, 2018, 11.8: e201700123.*

# Our previous MC simulation study indicates that CSF volume changes can be detected optically

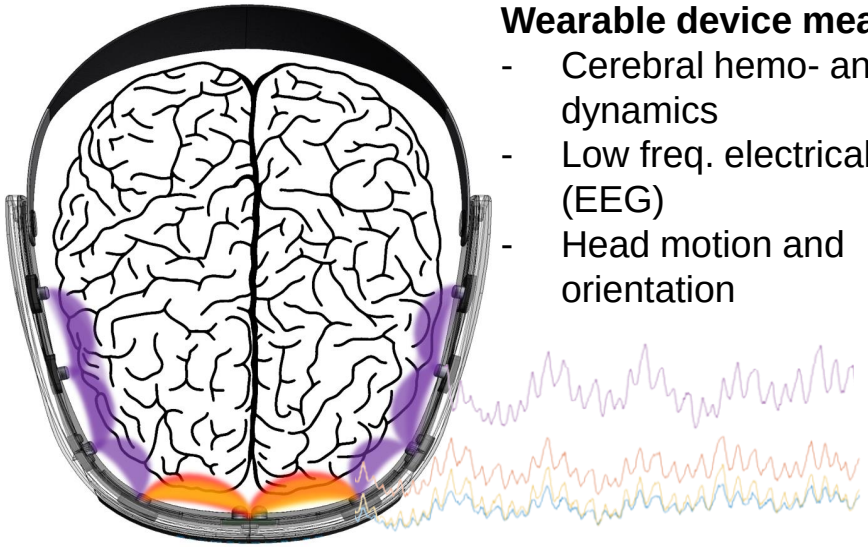



NIRS, optode
30 mm source-
detector distance



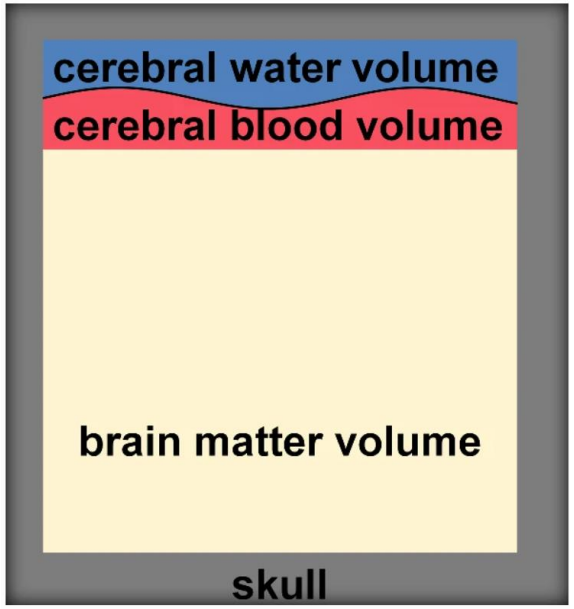

*MYLLYLÄ, Teemu, et al. Assessment of the dynamics of human glymphatic system by near-infrared spectroscopy. Journal of biophotonics, 2018, 11.8: e201700123.*

# Wearable fNIRS device for measuring cerebral hemo- and water volume dynamics



**Wearable device measures:**

- Cerebral hemo- and water dynamics
- Low freq. electrical activity (EEG)
- Head motion and orientation



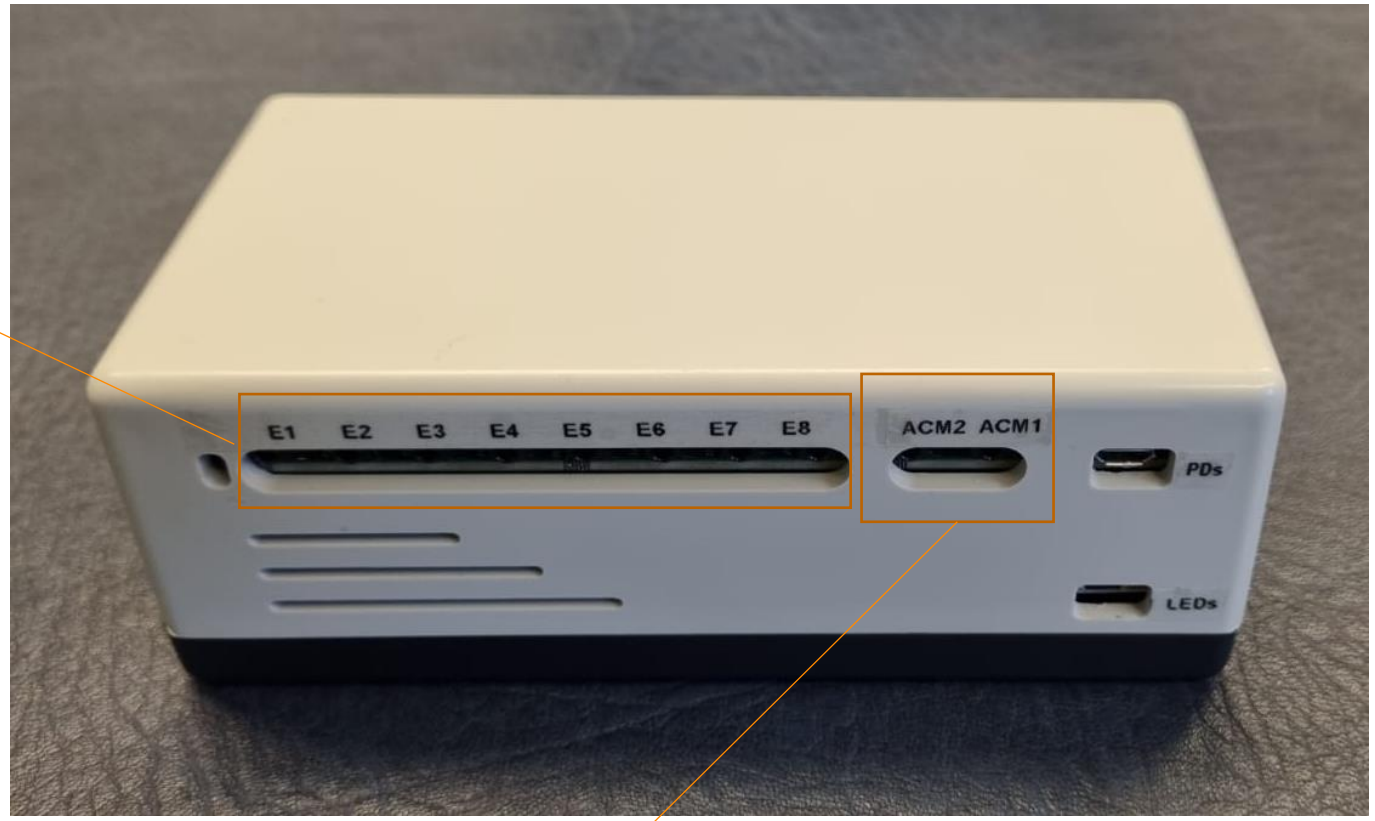

Schematic representation of the observed relationships in the context of **the Munro–Kellie doctrine:**
**The sum of volumes of brain, CSF, and intracranial blood is constant.**

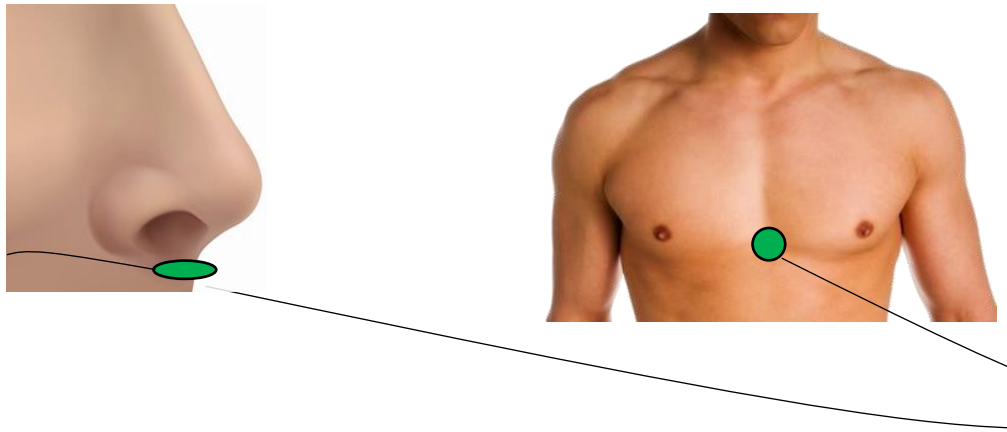
Prototype of the wearable fNIRS.

*MOKRI, Bahram. The Monro–Kellie hypothesis: applications in CSF volume depletion. Neurology, 2001, 56.12: 1746-1748.*
*BORCHARDT, Viola, et al. Inverse correlation of fluctuations of cerebral blood and water concentrations in humans. The European Physical Journal Plus, 2021, 136.5: 1-14.*

# Wearable multimodal brain monitoring device

4 EEG electrode to record brain's activity.



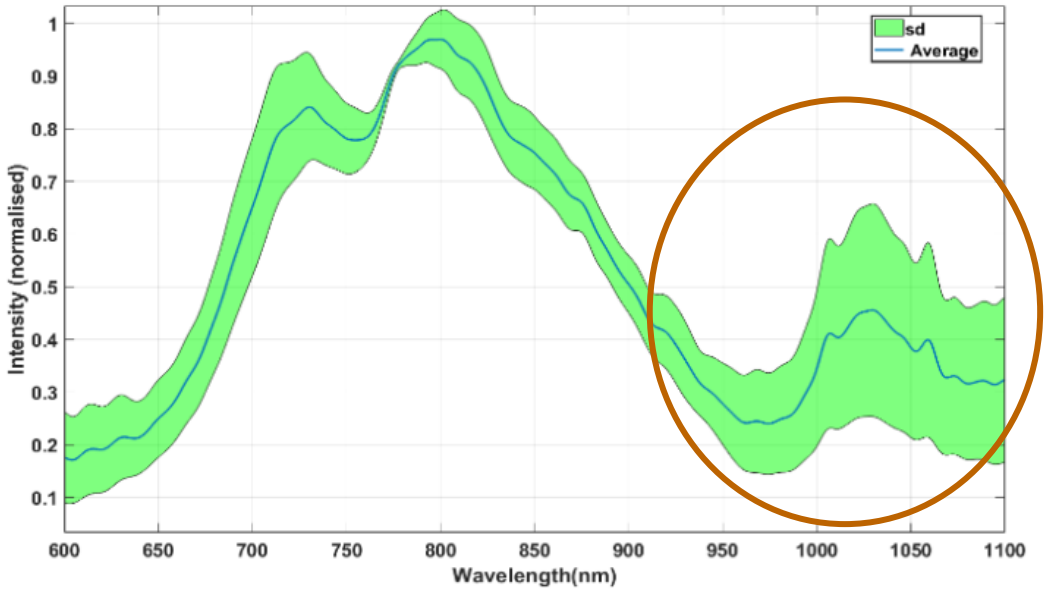



Two Analog inputs to connect Accelerometer and Thermistor sensors.

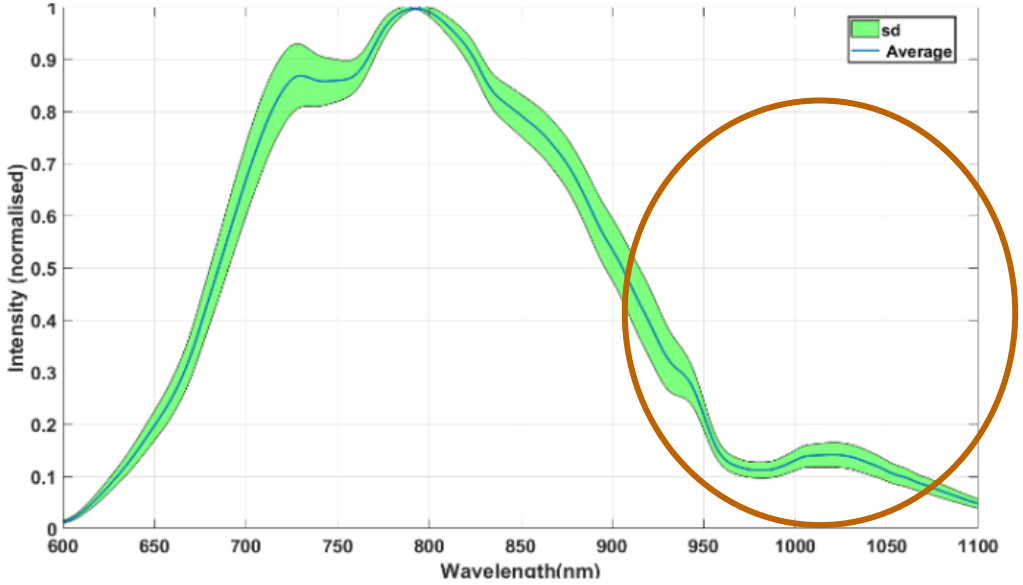
# Ongoing fNIRS studies on neurohydrodynamics

# NIRS spectra shows sensitivity to CSF layer thickness changes with wavelengths > 960 nm when using long source-detector distance

**Long (~30 mm) source-detector distance**




**Short (~18 mm) source-detector distance**

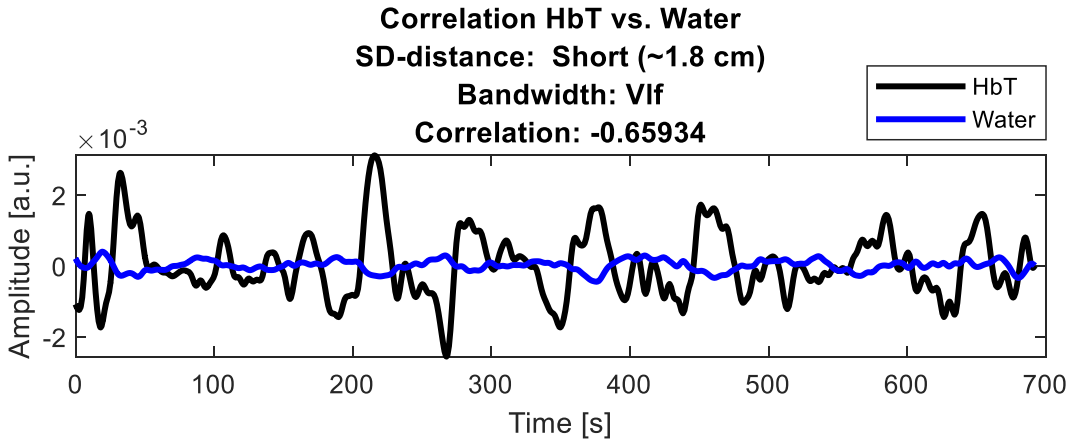


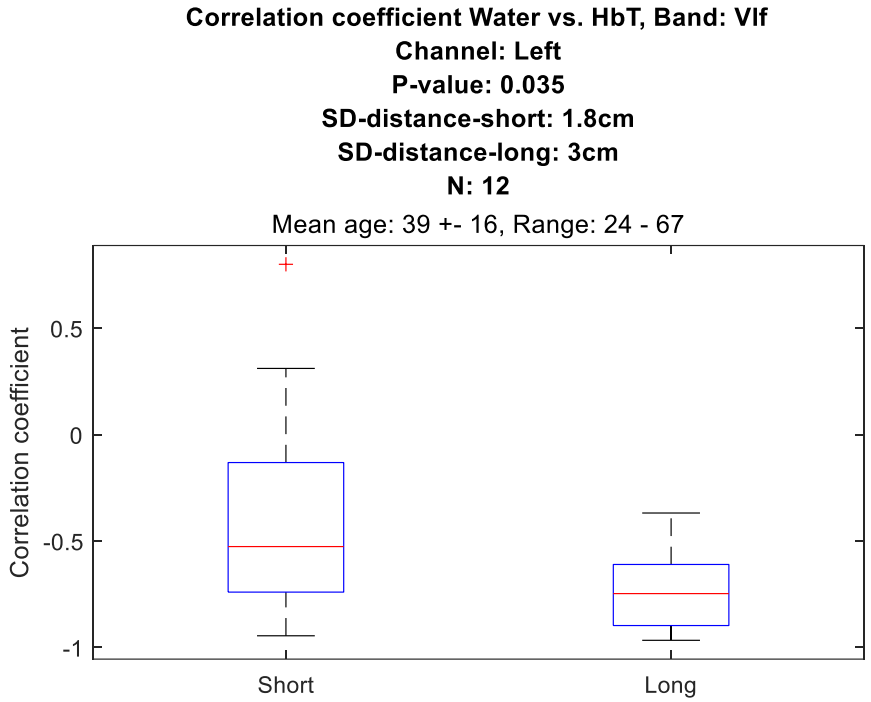

- In the selected group of volunteers, all subjects had approximately same skin and skull layer thicknesses, but CSF layer thickness variation between 1 mm - 9 mm.

- Spectral changes due to changes in dura + CSF thickness assessed by MRI.

- Standard deviation in wavelengths above 960nm is visibly greater when measured with long source-detector separation distance in comparison to short.

# Anti-correlation between HbT and Water stronger with long source-detector separation in VLF frequency band




Requires further validation with more data but initial results seem promising. Anti-correlation could provide an useful metric for validating NIRS penetration depth when using optodes with different source-detector distances.

# Current study: Could body posture affect neurohydodynamics and how brain clears waste?

## Breath hold test while lying back

## Body position test

# Current study: Could body posture affect neurohydodynamics and how brain clears waste?

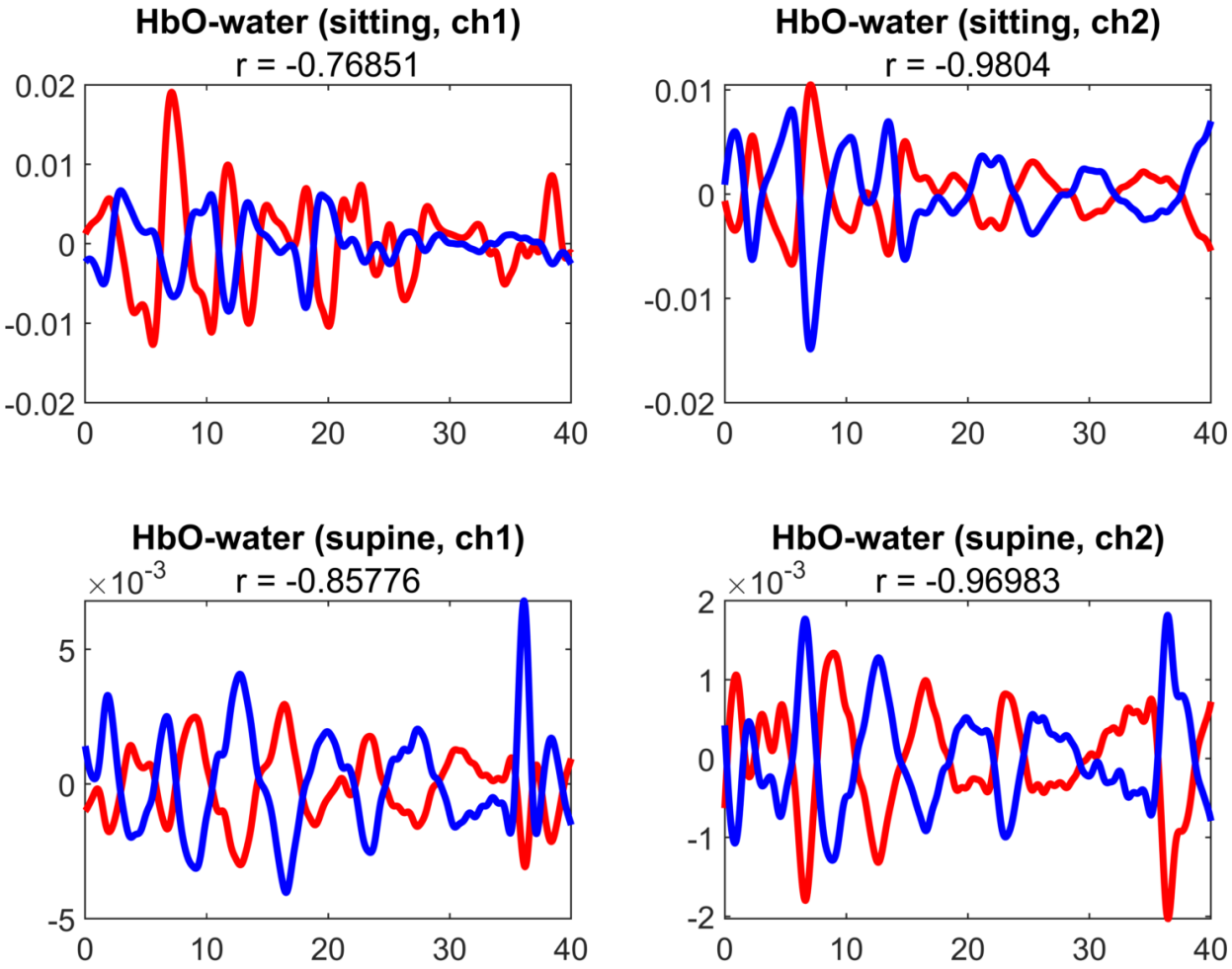
Head tilting test

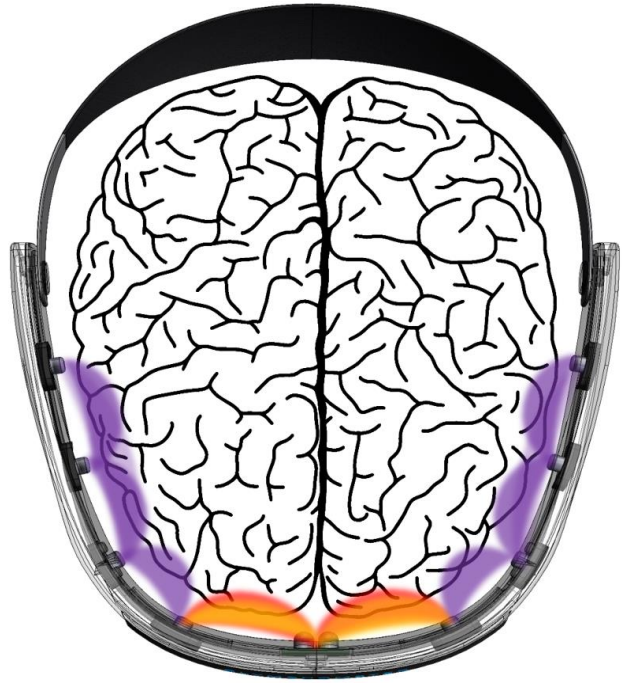
Tilt to right

Normal

Tilt to left

# Preliminary results



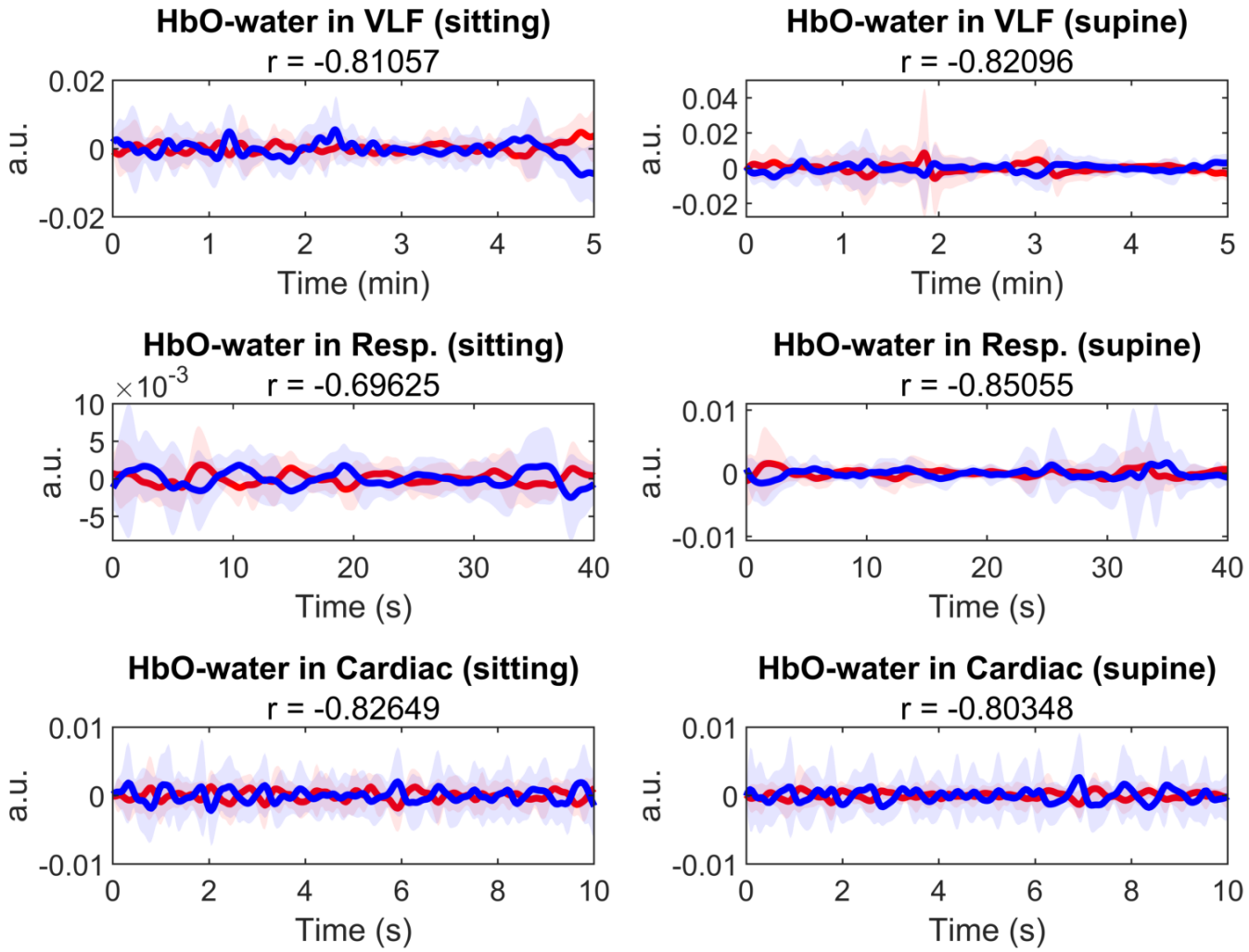



**ch2** **ch1**

NIRS measurement volumes (illustrated in orange) for **ch1** and **ch2**.

Comparison between cerebral oxyhemoglobin (HbO) and water (CSF) responses and their correlations in **sitting** and **supine** positions during normal breathing, in the **respiration freq. band**, measured from the same subject.

# Preliminary results




**The fNIRS study based on 20 measurements of healthy subjects supports the Munro–Kellie doctrine.**

Average response of HbO and water and their correlations measured in **sitting** and **supine** positions, in the **very low freq. (VLF), respiration (Resp.) and cardiac bands**.

# Thank you!

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