Ultra-slow fMRI fluctuations in the fourth ventricle as a marker of drowsiness

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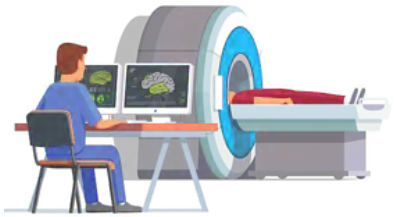
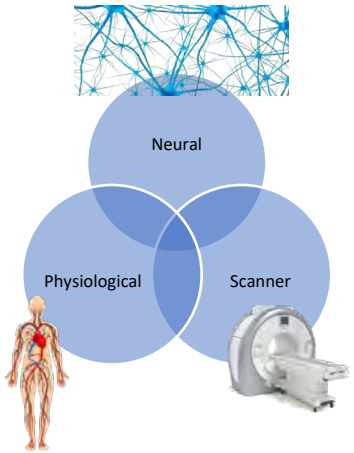
National Institute of Mental Health

Introduction | Overall Research Goals

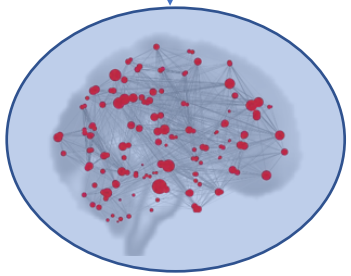


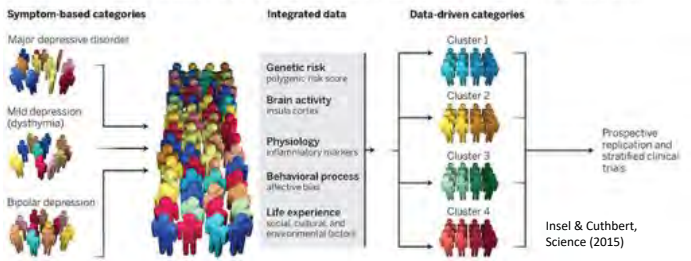
fMRI Methods Development Lab



Resting-State

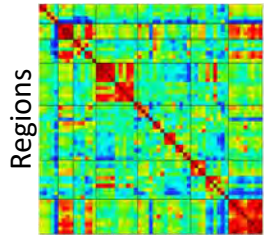
Functional Connectome



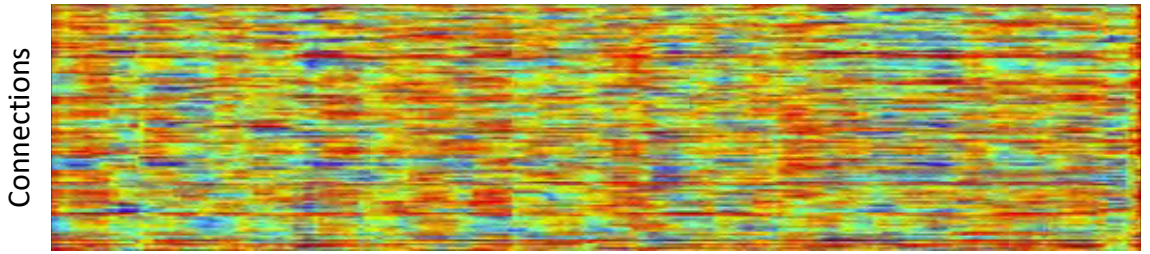


Cognitive Abilities | Personality Traits | Disease

Static FC



Time-varying Functional Connectivity



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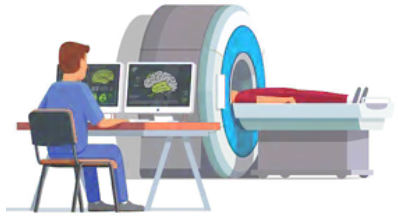
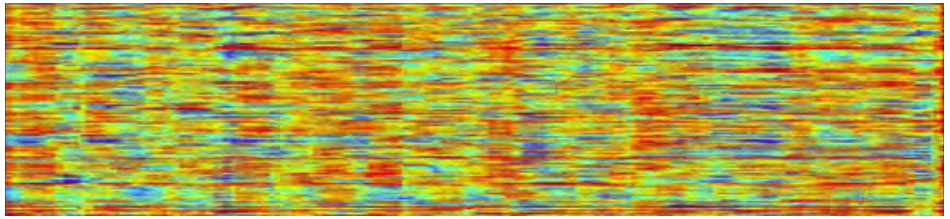
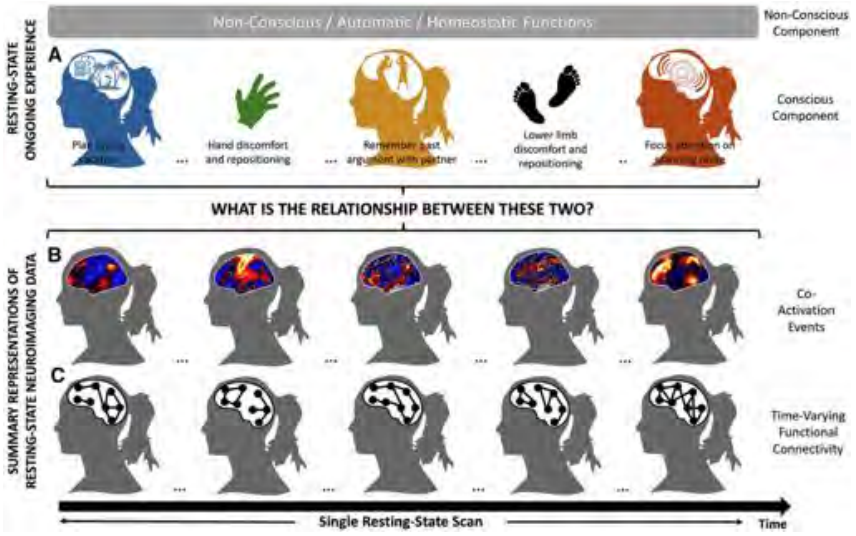
Introduction | Overall Research Goals

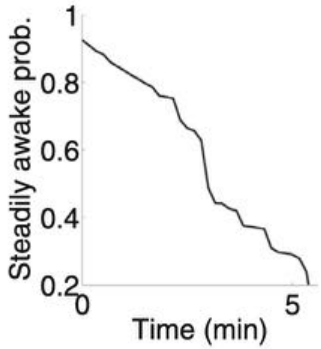


10 mins

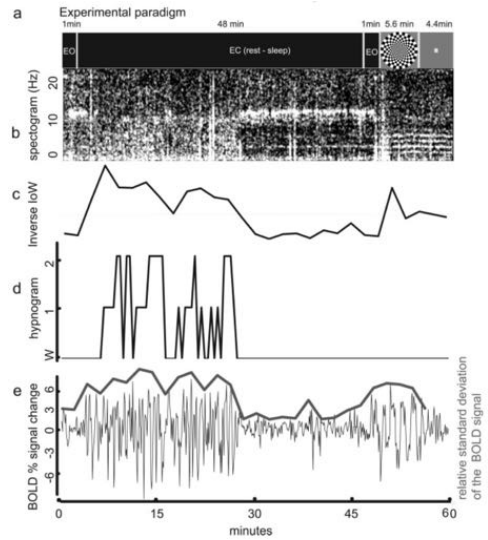




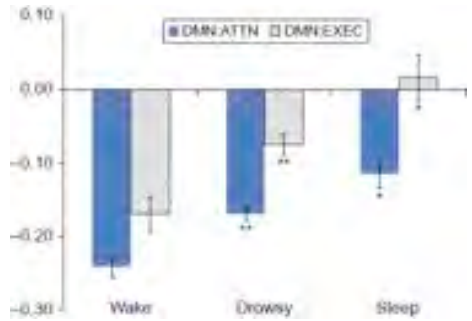
Gonzalez-Castillo et al., J. Neuroscience (2021)



Tagliazucchi et al. Neuron (2014)



Horovitz et al. Human Brain Mapping (2008)



Larson-Prior et al. Progress in Brain Research (2011)

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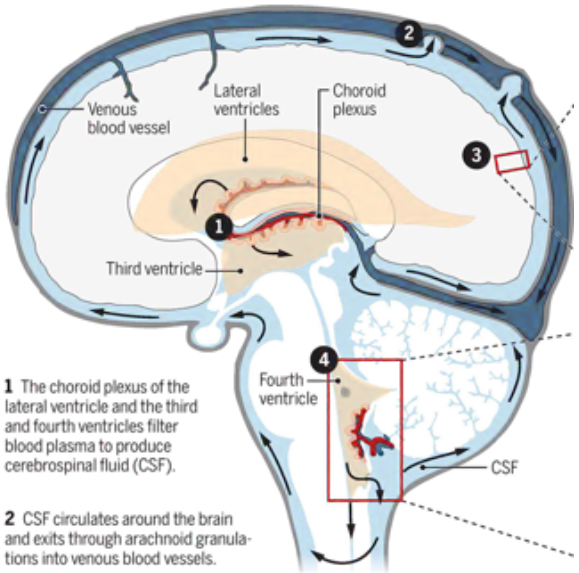
Sleep & CSF Flow

AWAKE → Light SWS → Deep SWS → Light SWS → REM

Slow Wave Sleep (SWS) | NREM

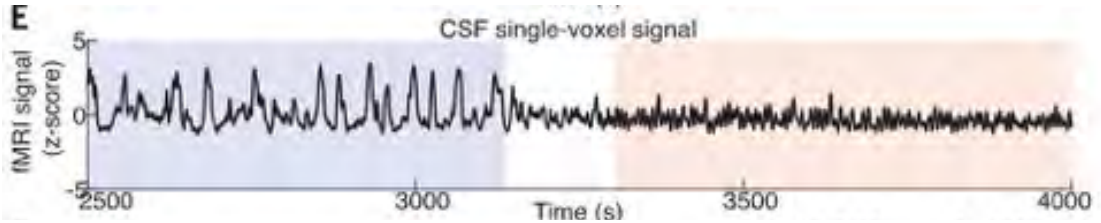
[CBF ↓ ~25%] & [CBV ↓~10%]



Grubb & Lauritzen Science (2019)

CSF FLOW

- 3rd Ventricle
- 4th Ventricle
- Subarachnoid Sp.



Fultz et al. Science (2019)

CSF FLOW

- Lat. Ventricles
- 3rd Ventricle
- 4th Ventricle
- Subarachnoid Sp.
- Top of Brain
- Dural Sinuses

Neural Slow Waves (EEG)

Hemodynamic Oscillations (fMRI: BOLD GS)

CSF Flow (fMRI: Inflow)

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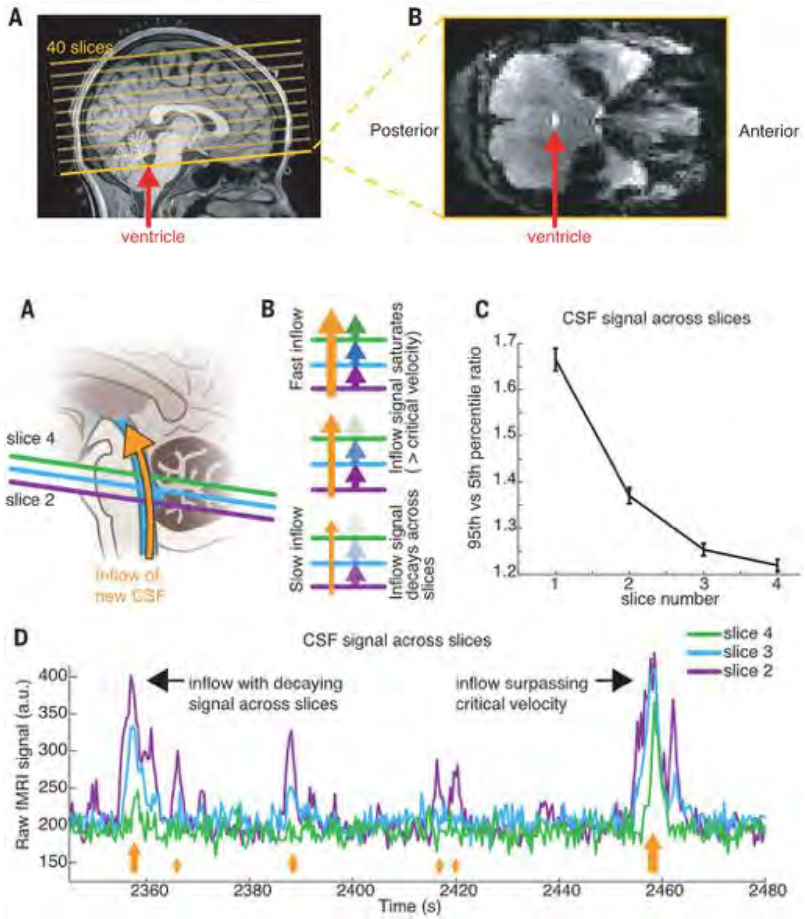
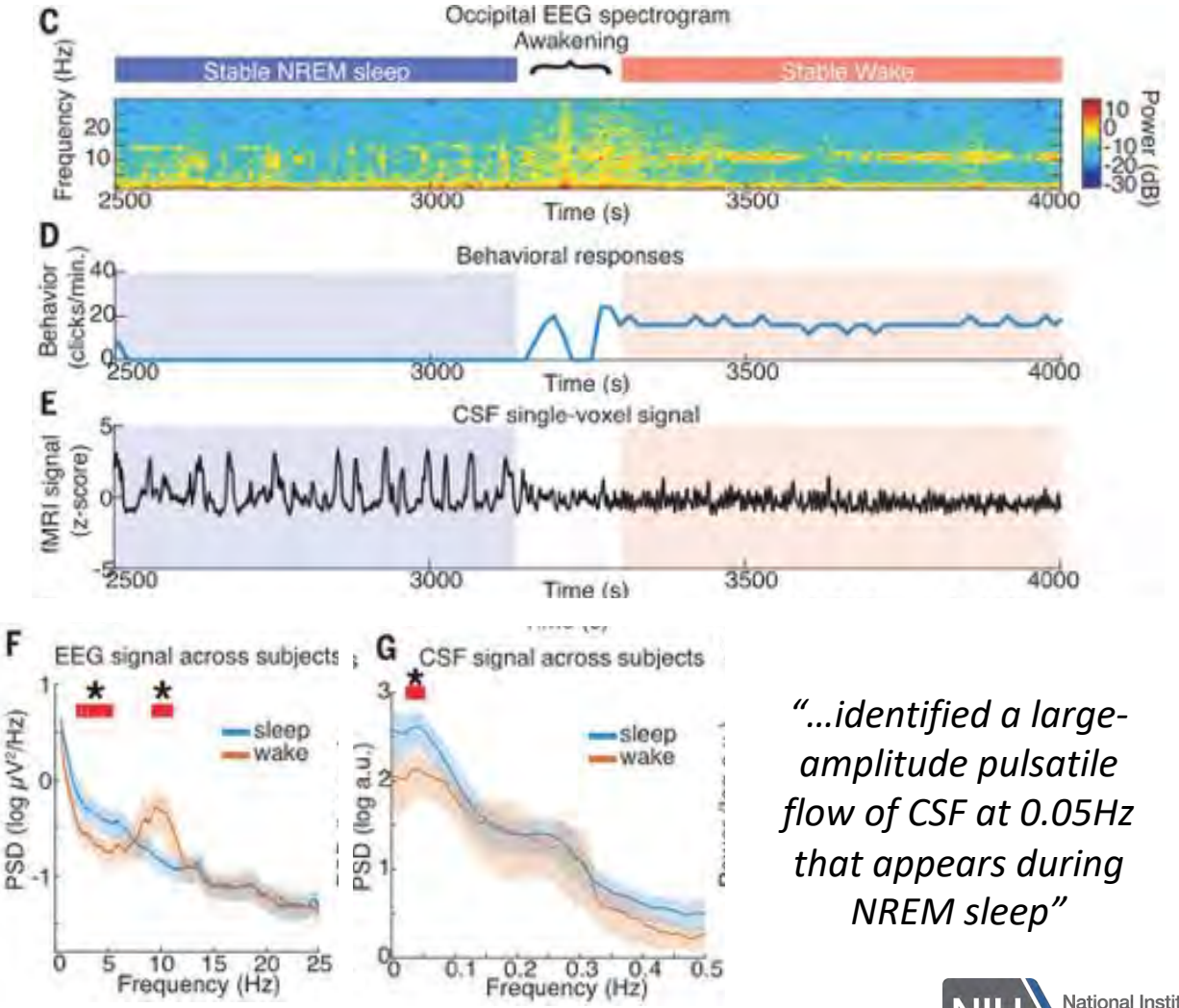
Introduction | Fultz et al. Science (2019)

fMRI / EEG | 13 Subjects | Press Button | 3T | 400ms



Distinct Flow Dynamics during Sleep



"…identified a large-amplitude pulsatile flow of CSF at 0.05Hz that appears during NREM sleep"

Fultz et al. Science (2019)

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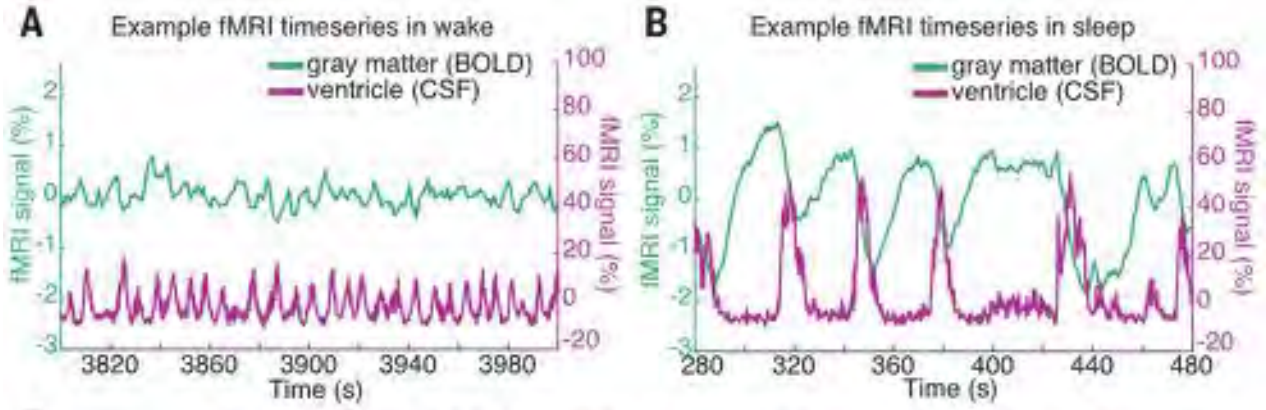
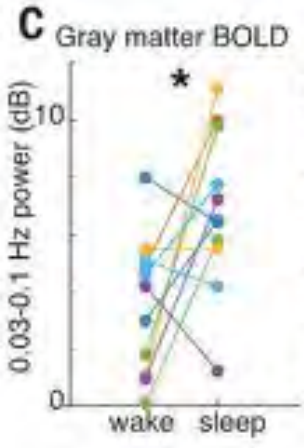
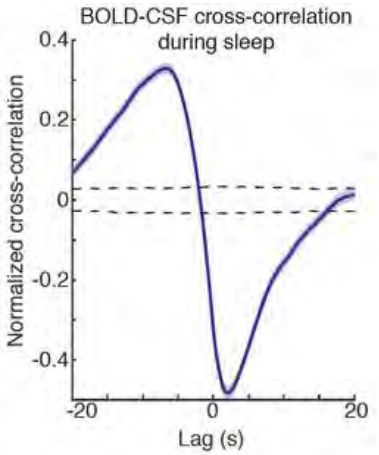
Introduction | Fultz et al. Science (2019)

Link between CSF Fluctuations and Hemodynamic Signals







⬆ BOLD GM Signal during sleep

BOLD Signal and CSF Inflow are tightly anti-correlated

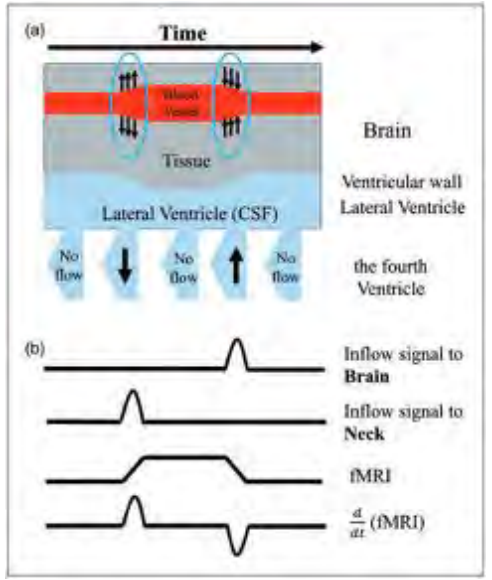
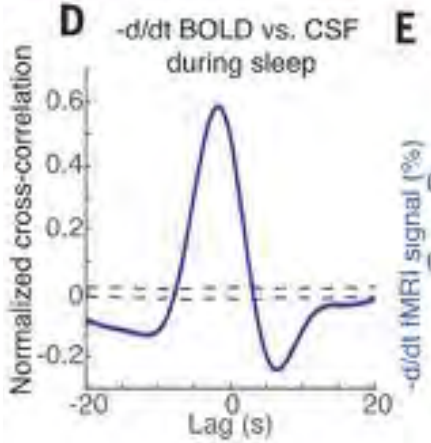
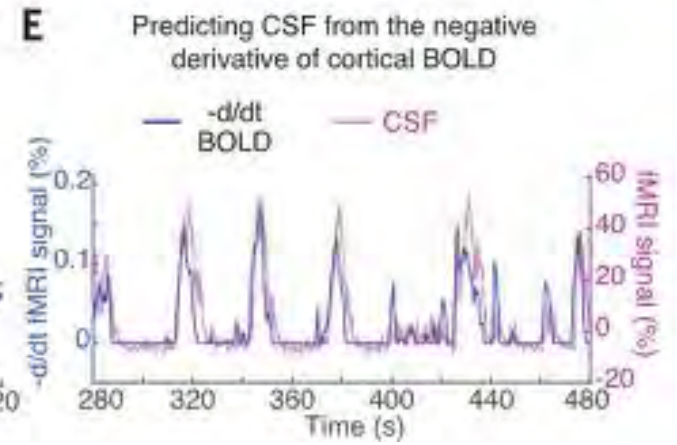


Figure from: Ho-Ching et al. J Cerebral Blood Flow and Metabolism (2022)





Fultz et al. Science (2019)

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Introduction | Our Research Questions

Q1. Can this 0.05Hz fluctuation be found on other datasets not necessarily optimized for detecting in-flow?

Q2. If so, can this signal be used as a simple marker of wakefulness in existing fMRI datasets that lack concurrent EEG and/or eye tracker measurements?

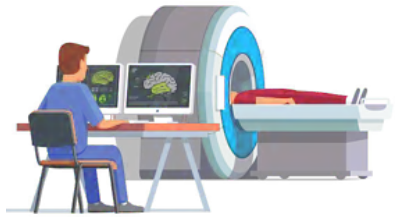
Q3. Do these fluctuations appear anywhere else in the brain (e.g., contribution to GS) and, if so, how do they affect FC estimates?

Dataset

HUMAN Connectome PROJECT

723 Scans / 184 Subjects | 15 mins long | TR = 1s | MB = 5 | 1.6x1.6x1.6mm

7T Resting-state Sample



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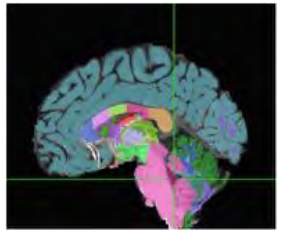

Elimination Criteria	Scans Removed	Scans Remaining
Automatic parcellation for 4th ventricle failed	4	719
ET data not available	149	570
Error while loading ET data	2	568
ET data lacks onset information for synchronization to fMRI scans	4	564
ET data not available for the full fMRI scan	3	561
Scans that do not meet criteria to be labeled as "awake" or "drowsy"	157	404

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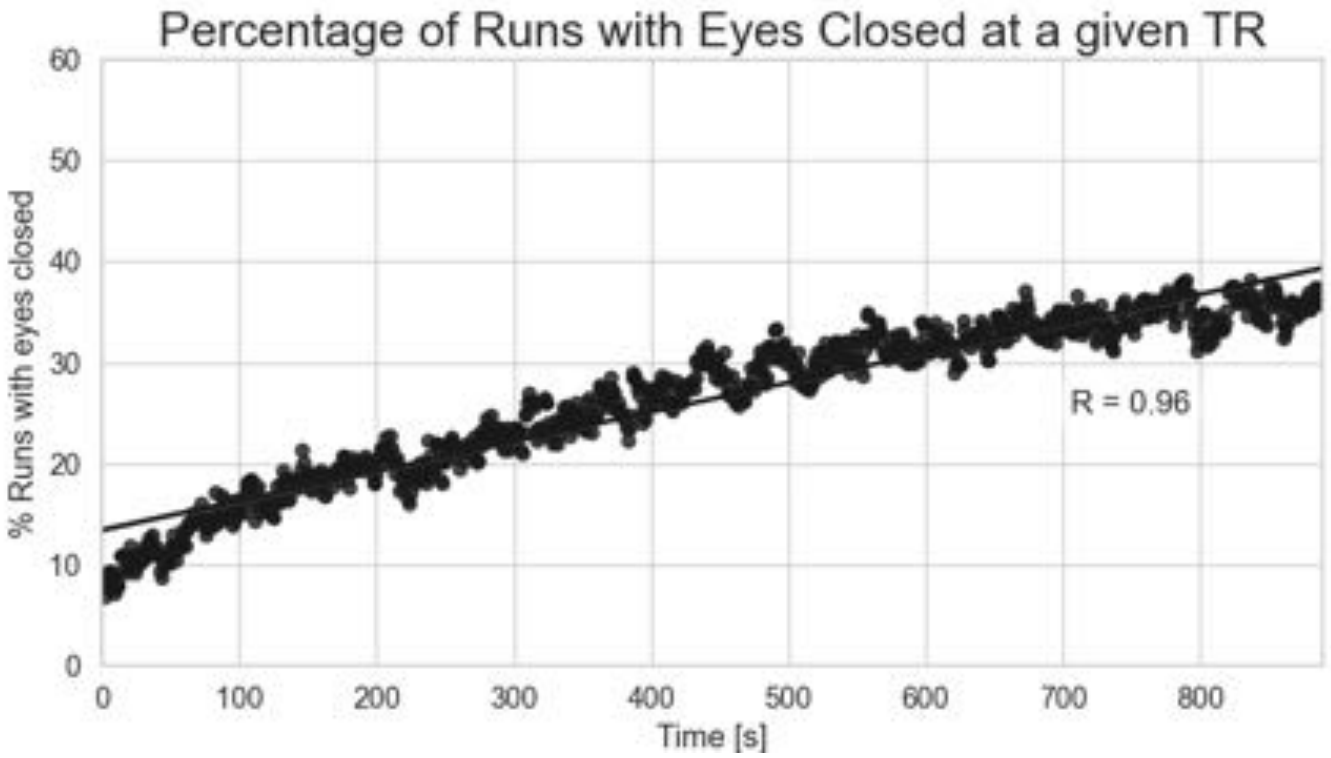
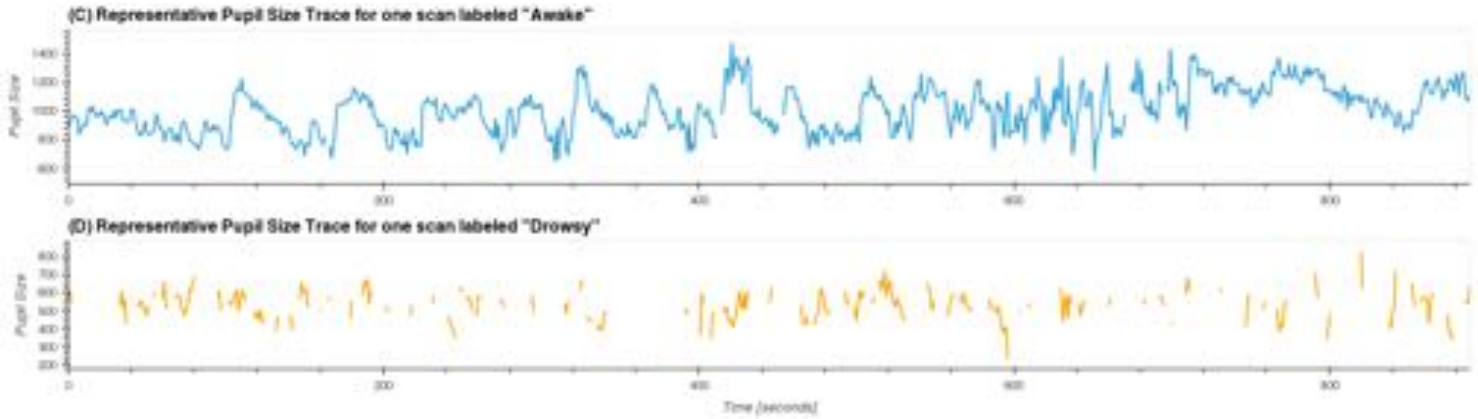
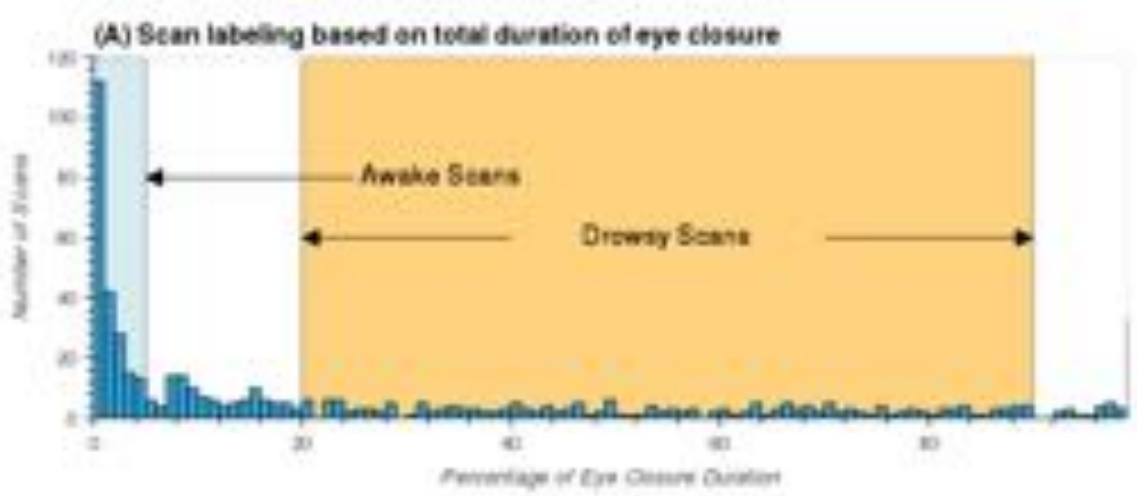
Eye Tracking – Tendency to close eyes as scanning progresses



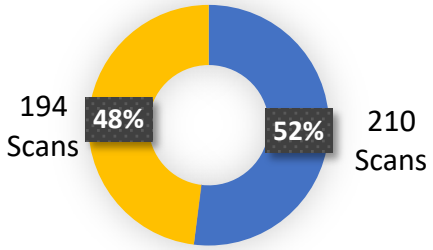
Eye Tracking – Label Scans [Awake / Drowsy]





"*Awake*" scans: defined as those for which pupil size traces indicate subjects had their eyes closed less than 5% of the scan duration.

"*Drowsy*" scans: defined as those for which pupil size traces indicate subjects had their eyes closed between 20% and 90% of the scan duration.



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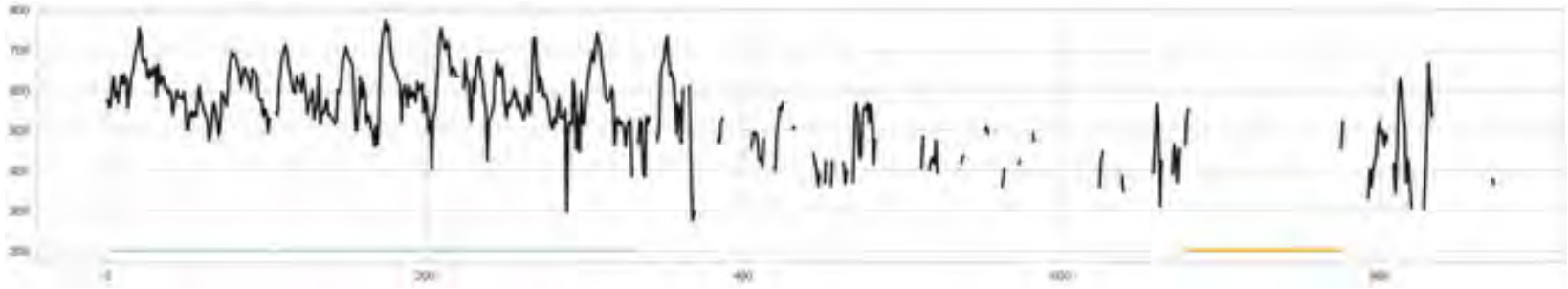
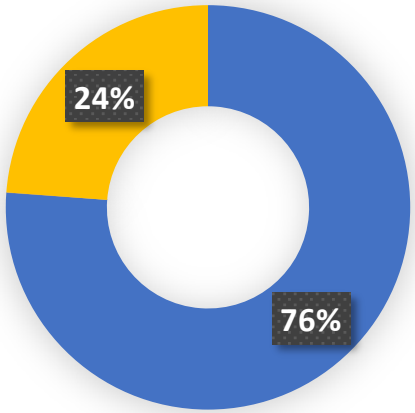
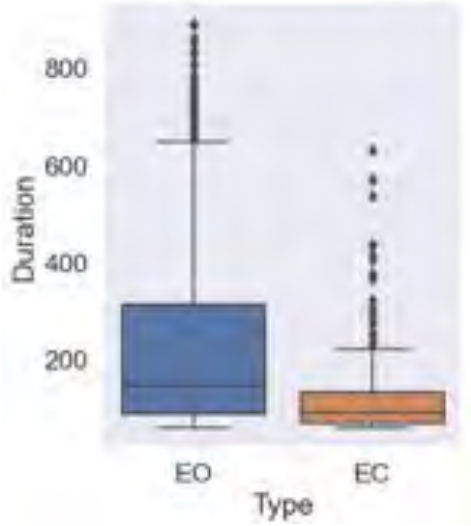
Eye Tracking – Label Scan Segments [E Open/E Closed]



EC Periods = Those with eyes continuously closed for 60s or more

EO Periods = Those with eyes continuously closed for 60s or more





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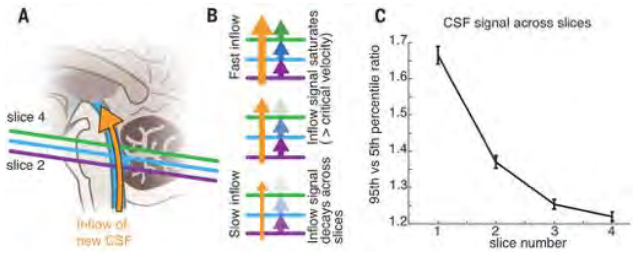
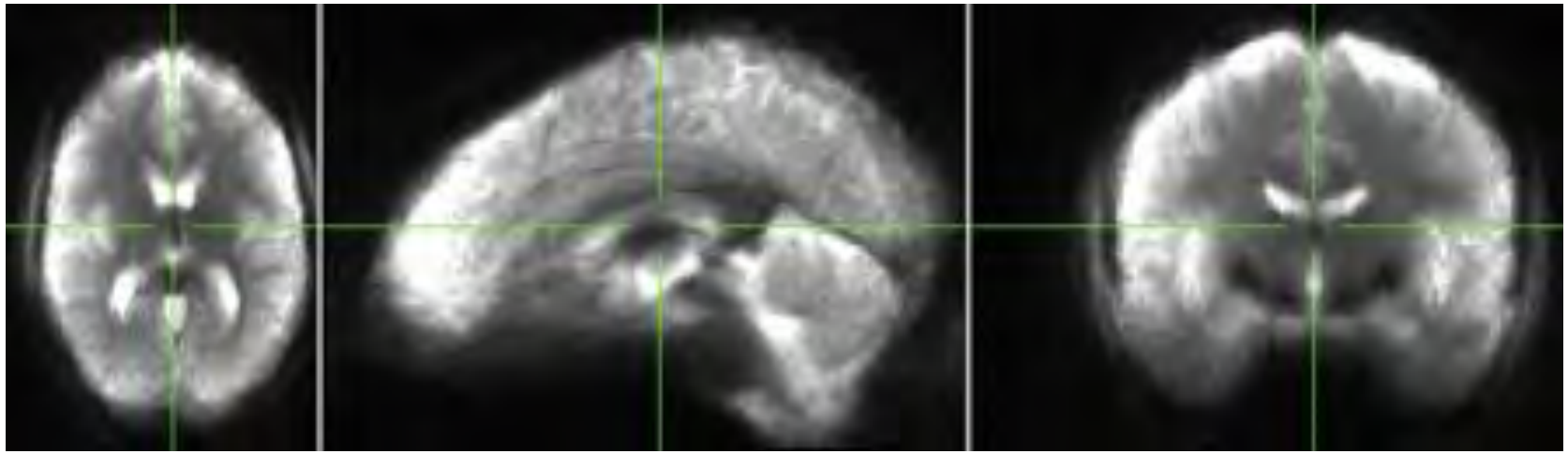
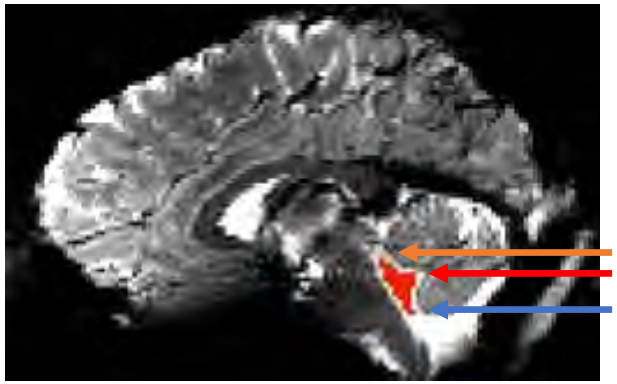
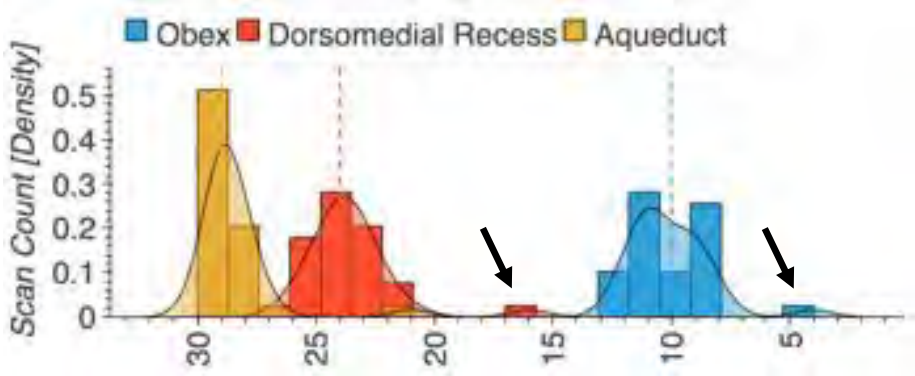
fMRI – Confirm Inflow Profile in 4th Ventricle



30 Scans | Drowsy | FD < 0.1mm







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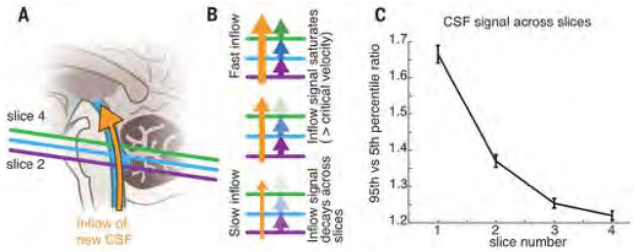

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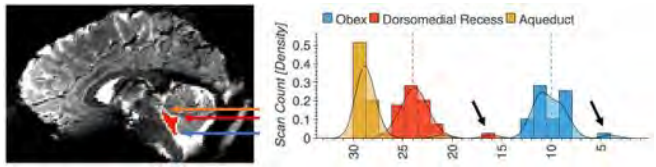

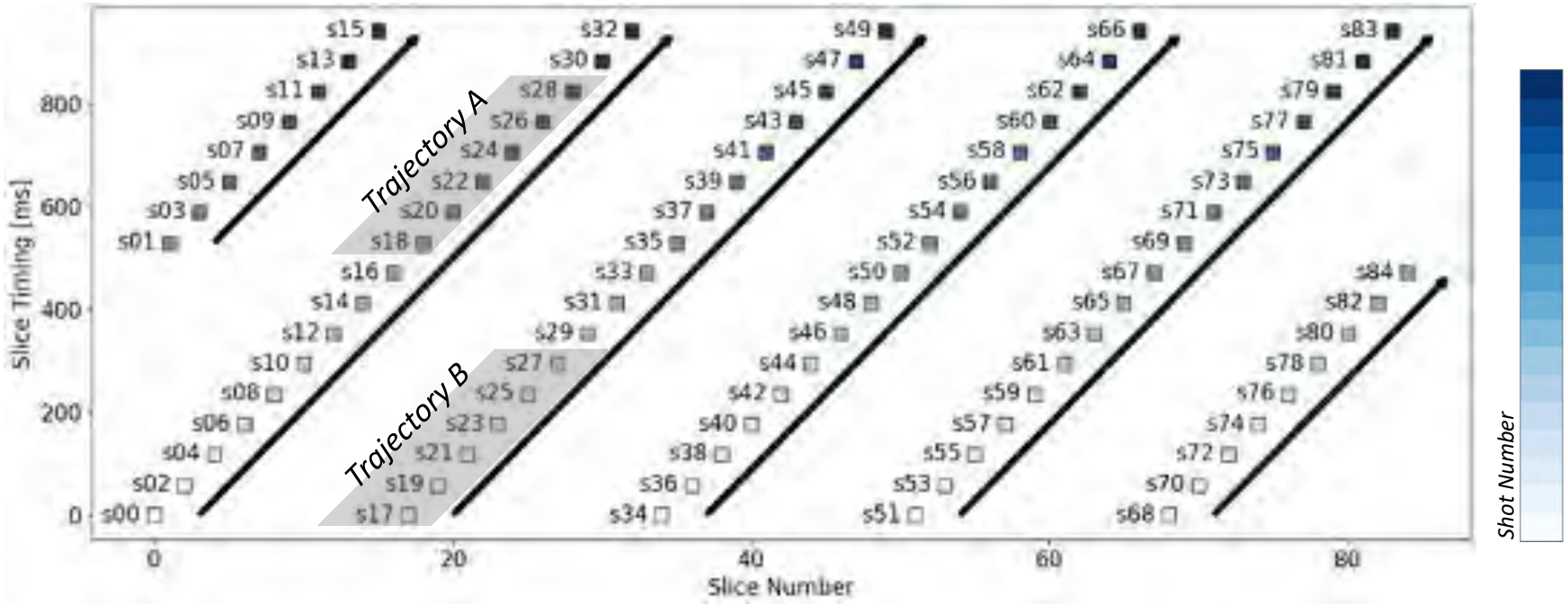

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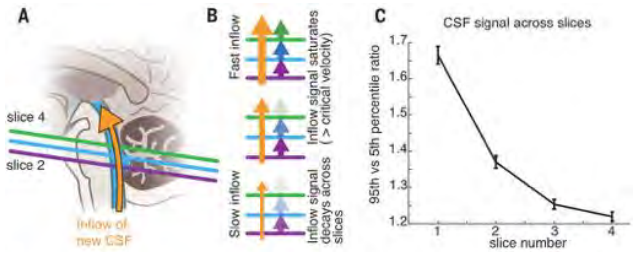

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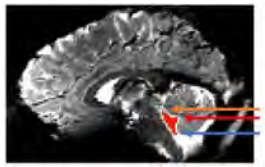

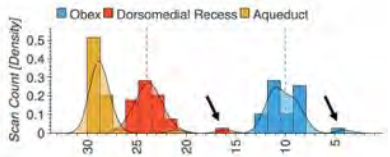

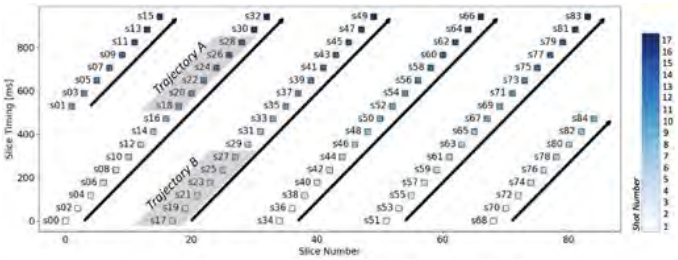

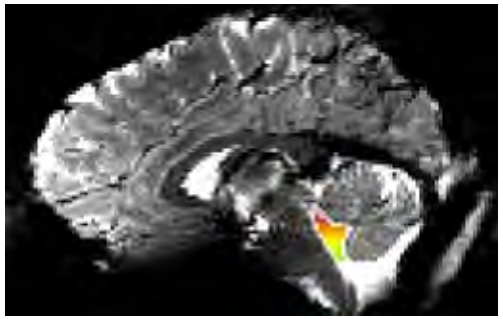

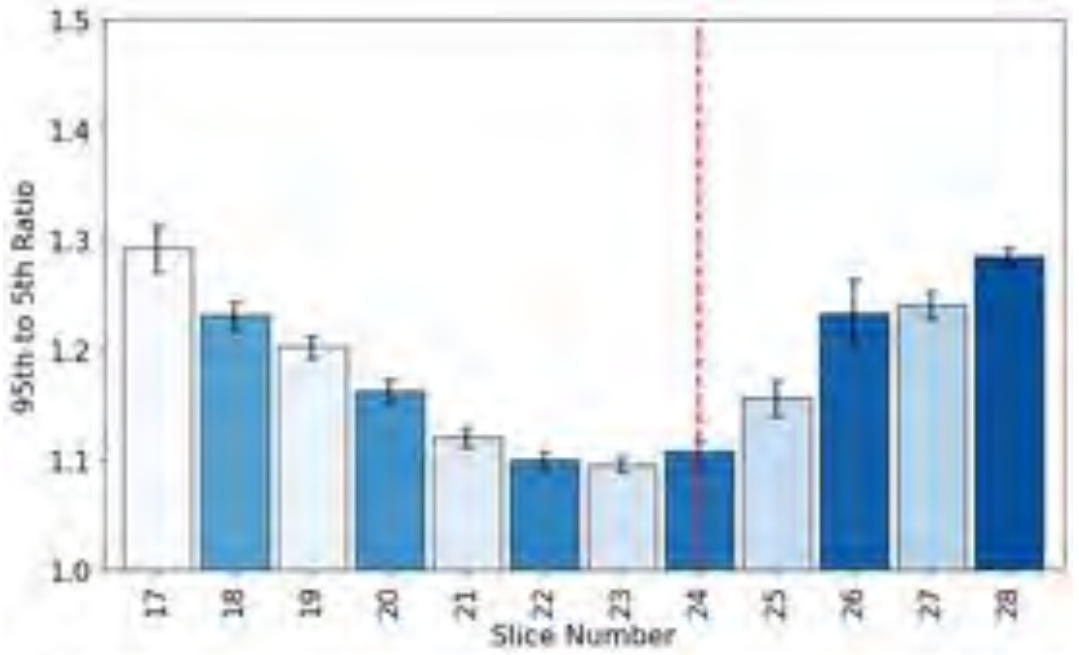

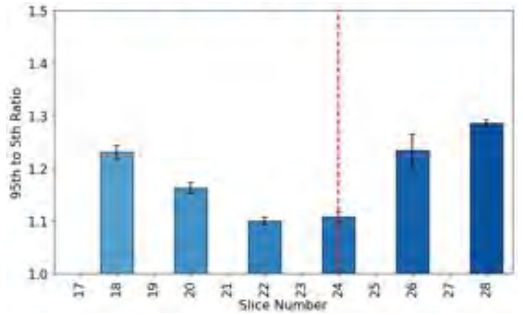

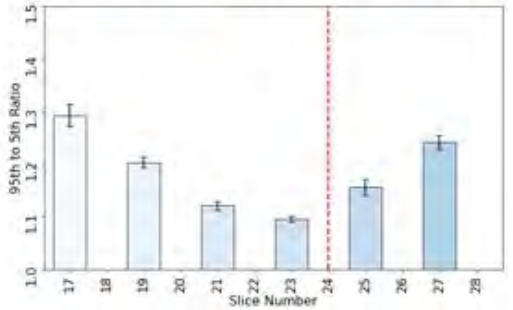

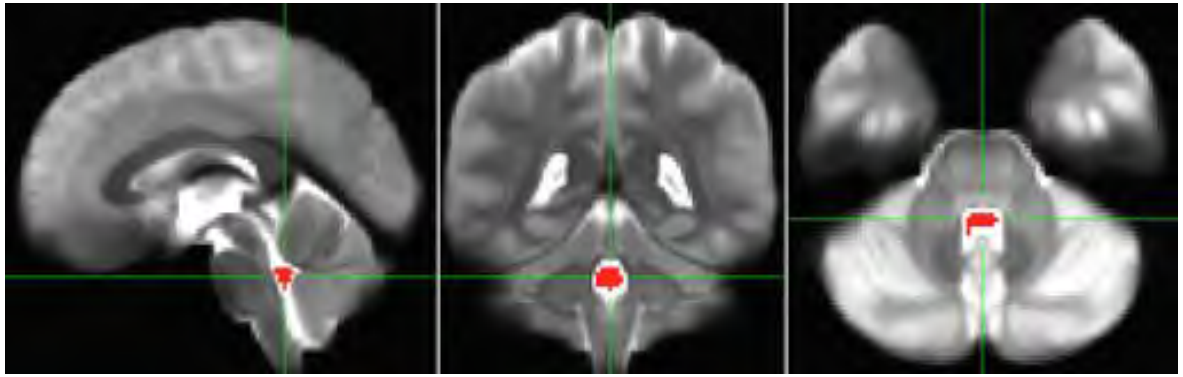

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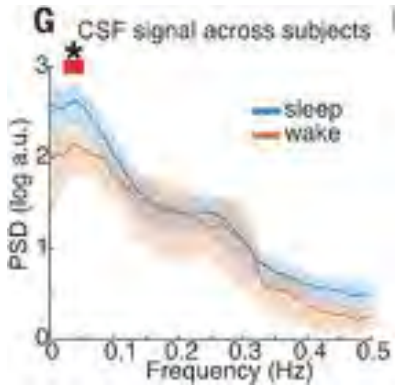
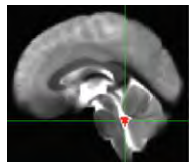
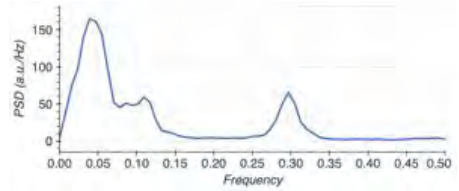
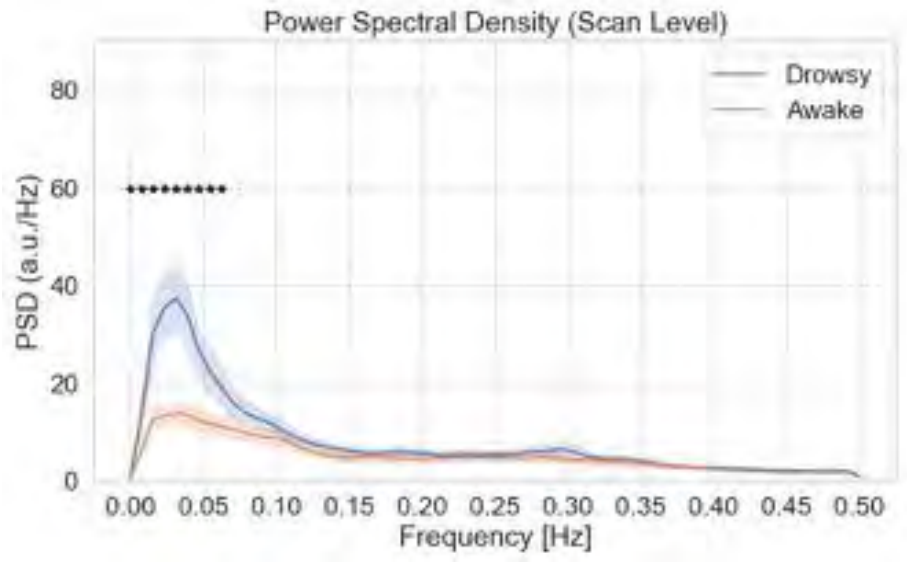
fMRI – Differences in Power between scan and segment types



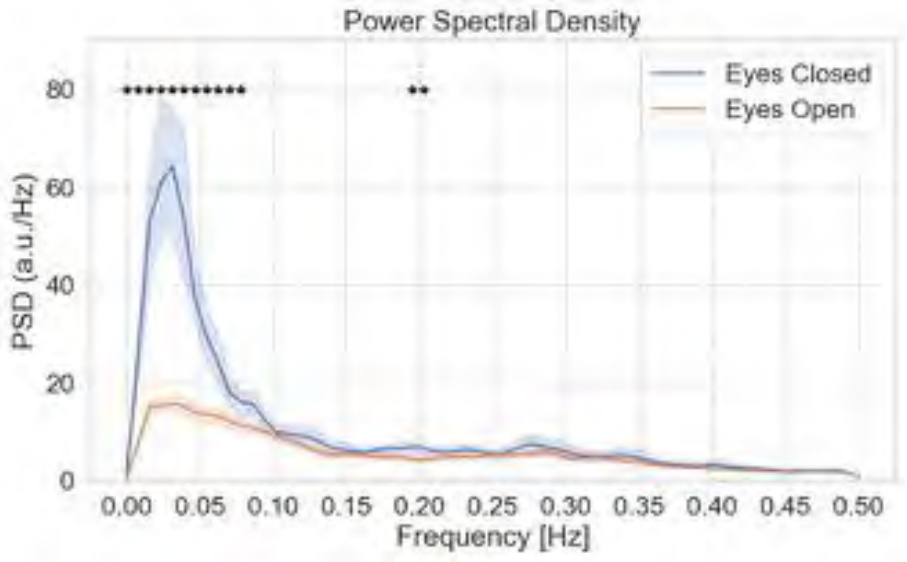




Scan Level [Drowsy / Awake]



Segment Level [Eyes Open / Eyes Closed]



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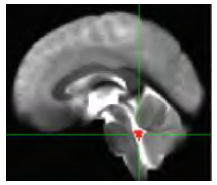
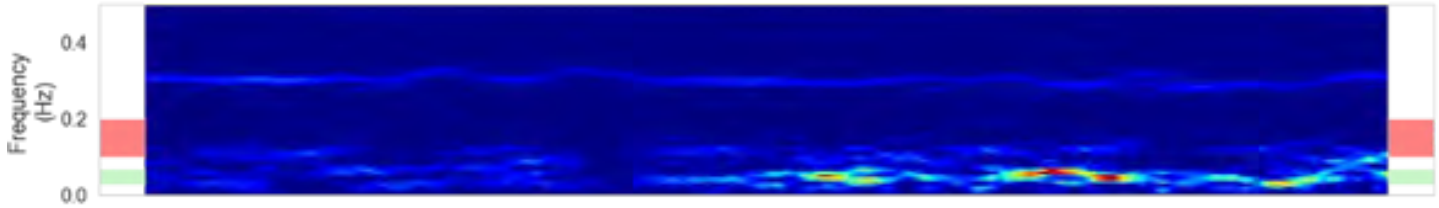
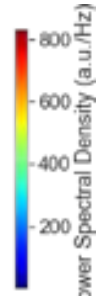
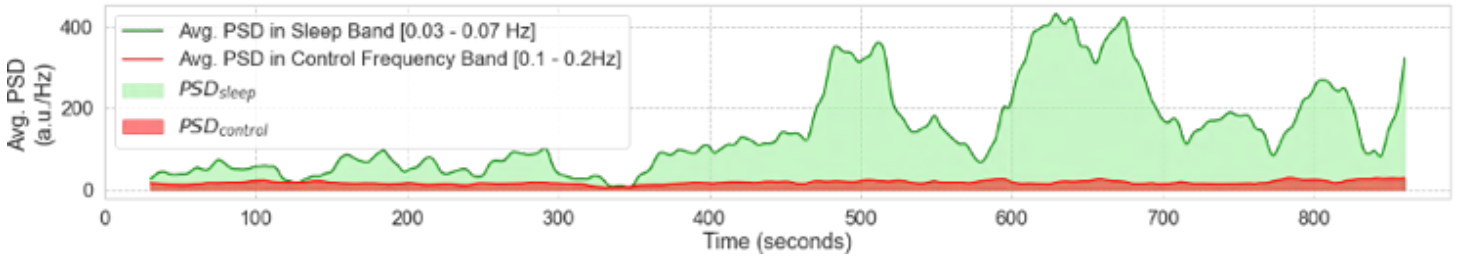
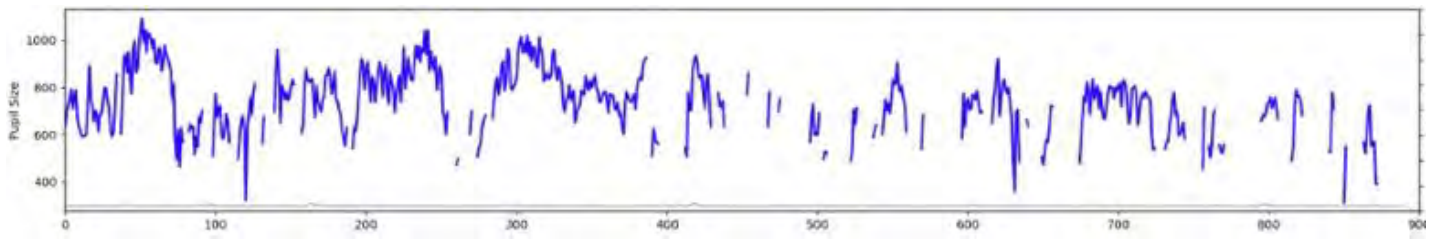
fMRI – Temporal Evolution of Power in 4th Ventricle











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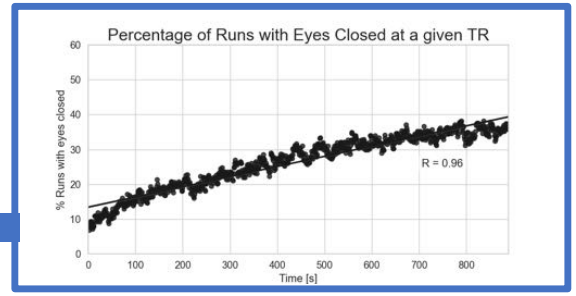
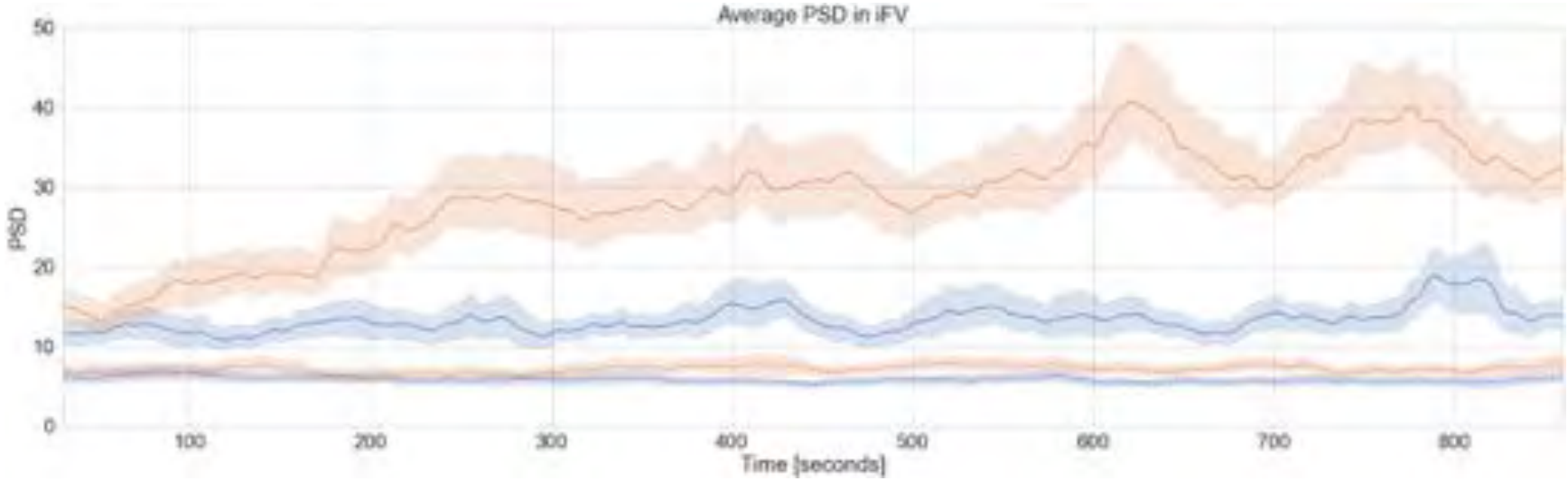
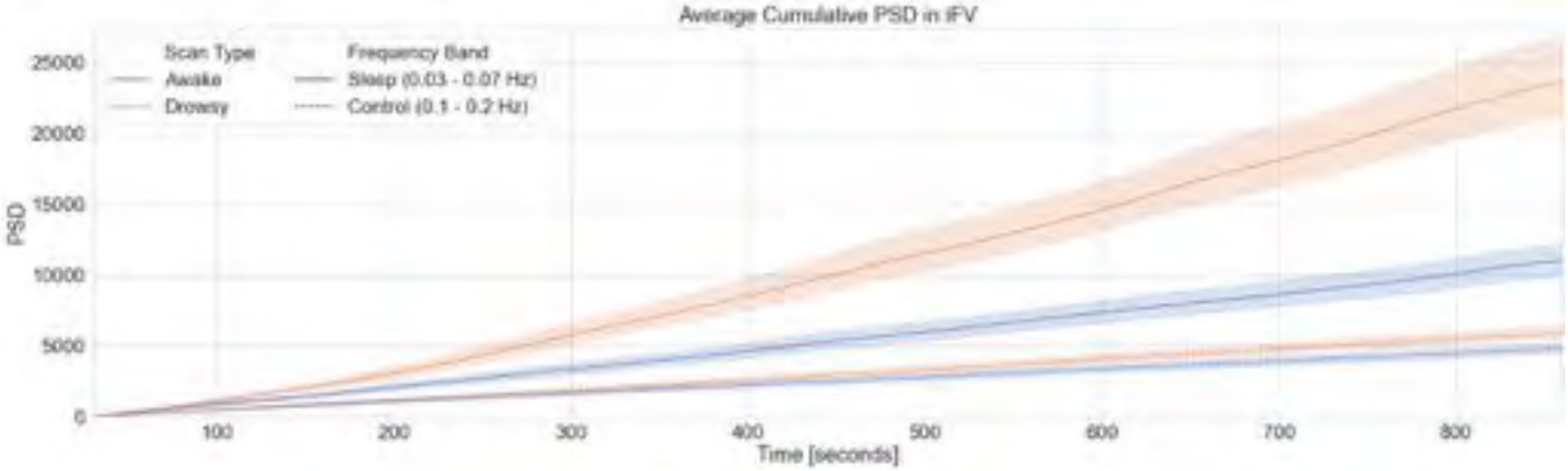
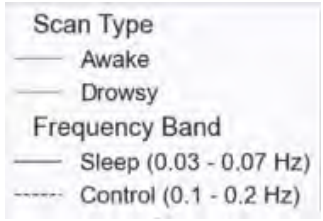
fMRI – Temporal Evolution of Power in 4th Ventricle









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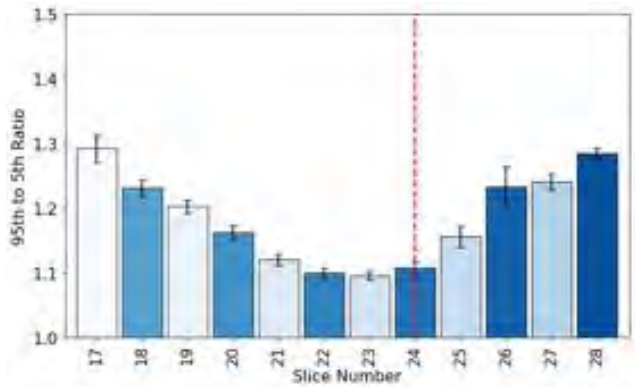
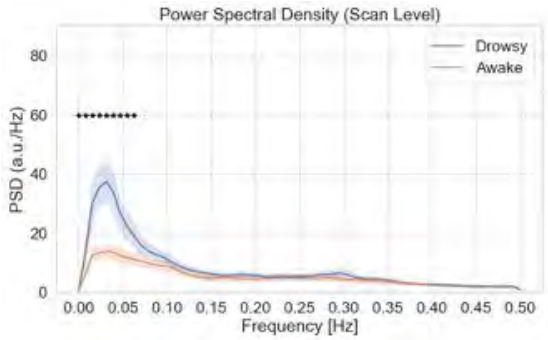
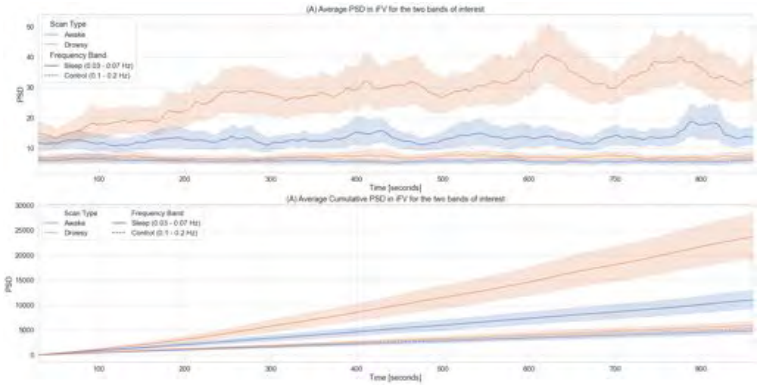
Our Particular Questions

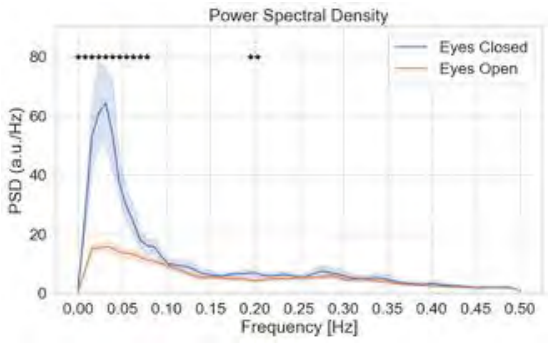
Q1. Can this 0.05Hz fluctuation be found on other datasets not necessarily optimized for detecting in-flow?

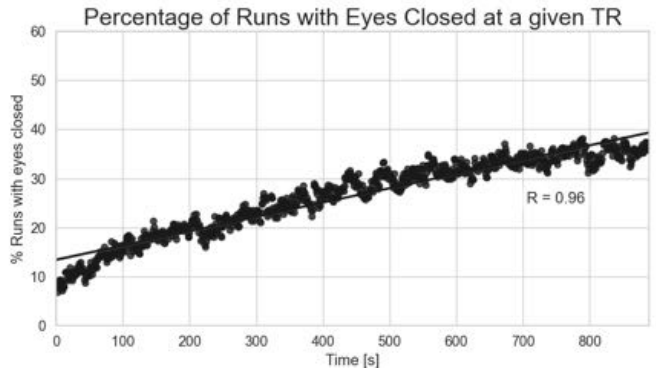






YES





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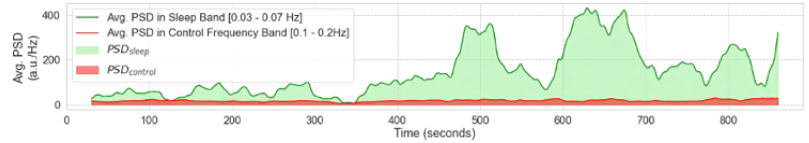
Our Particular Questions

Q1. Can this 0.05Hz fluctuation be found on other datasets not necessarily optimized for detecting in-flow?

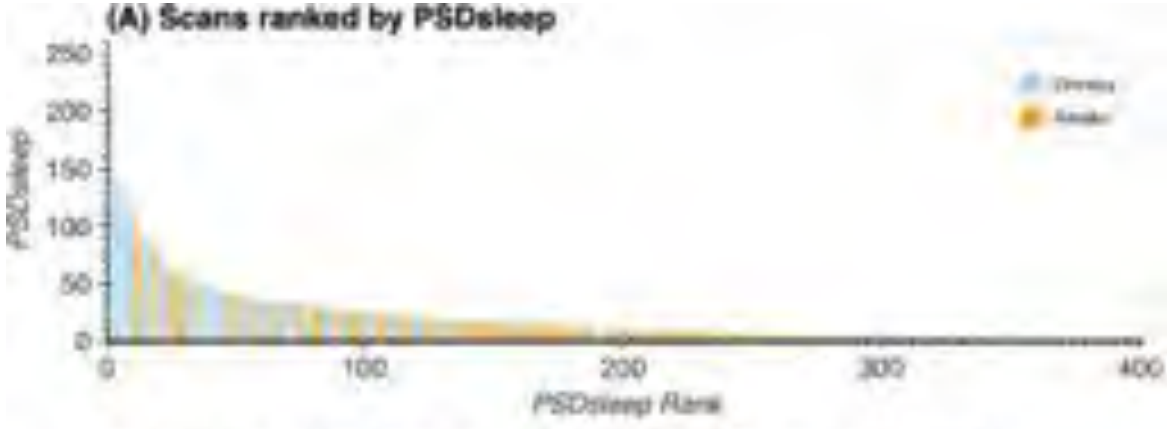
YES

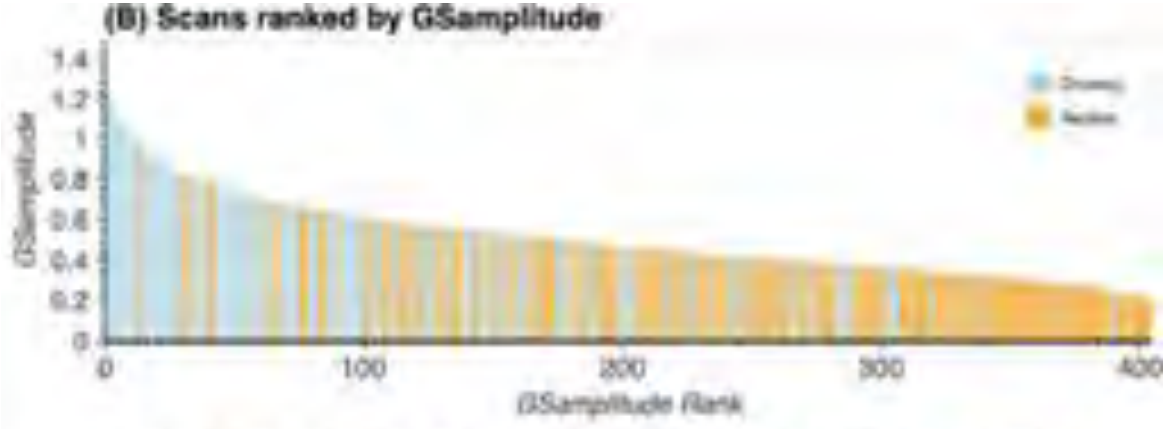
Q2. If so, can this signal be used as a simple marker of wakefulness in existing fMRI datasets that lack concurrent EEG and/or eye tracker measurements?

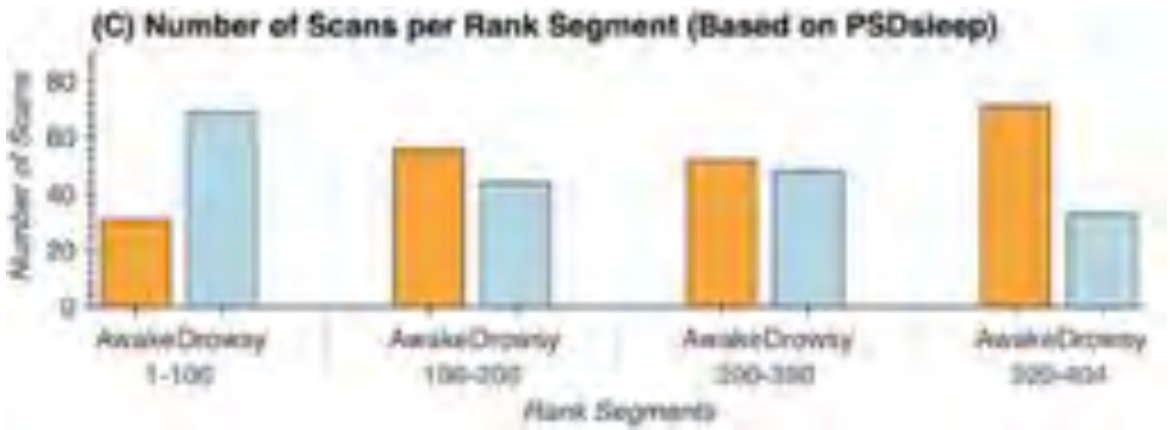
Avg. PSD_{Sleep} as a marker of drowsiness [Scan – Level]



Global Signal







Gonzalez-Castillo et al. NeuroImage (2022)

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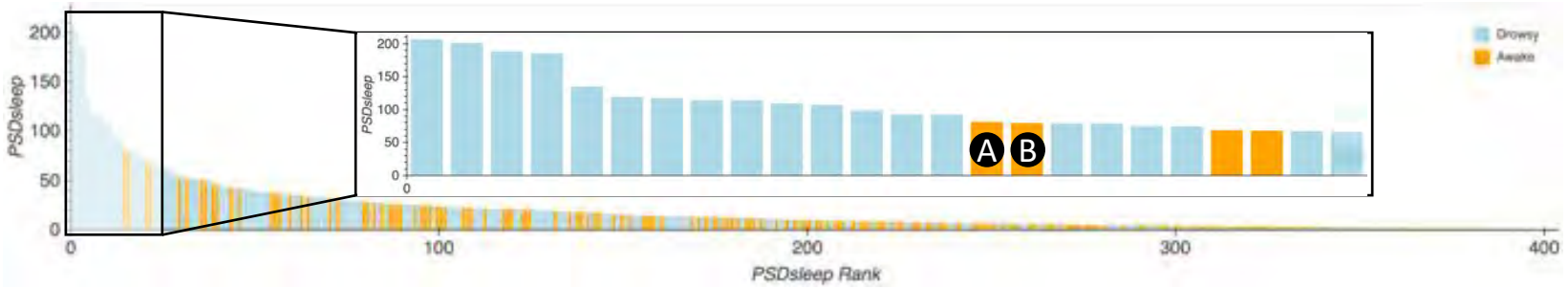
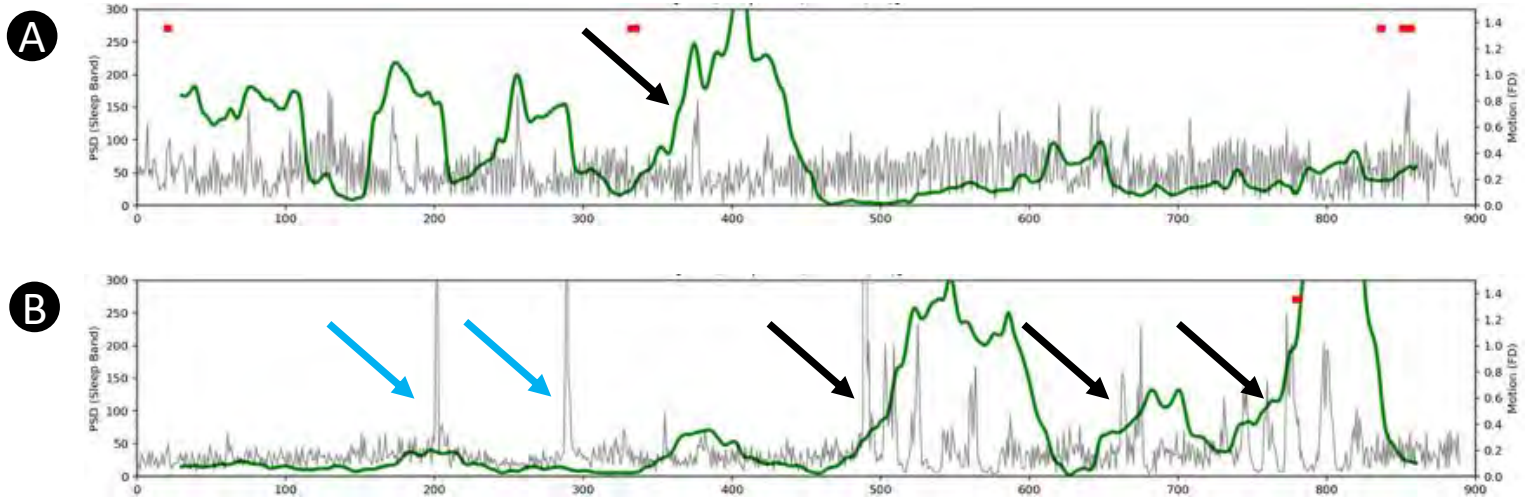
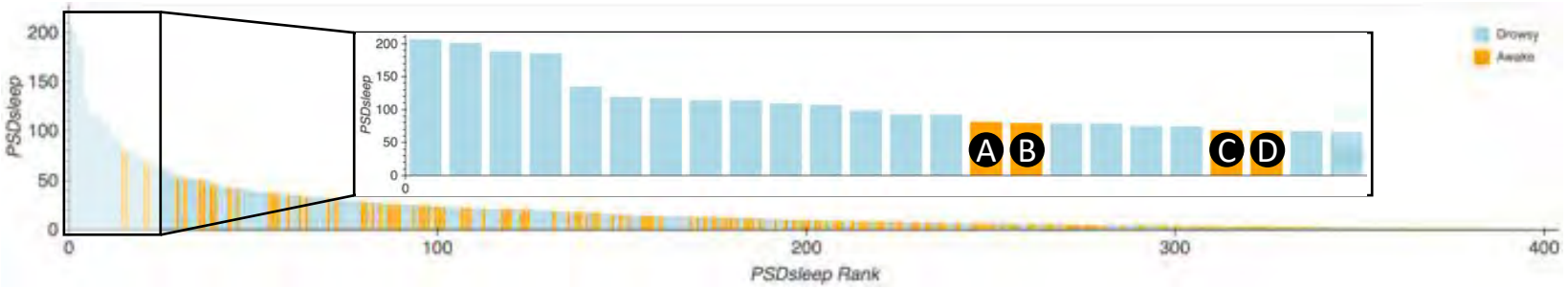
Examine Failures in PSD_{Sleep} Ranking

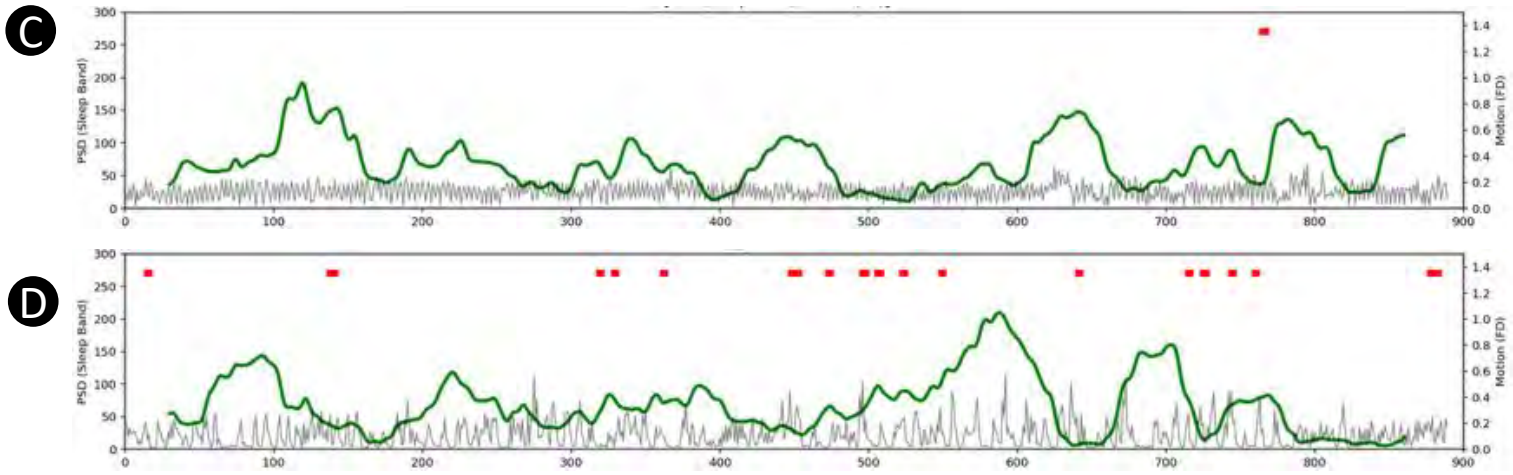




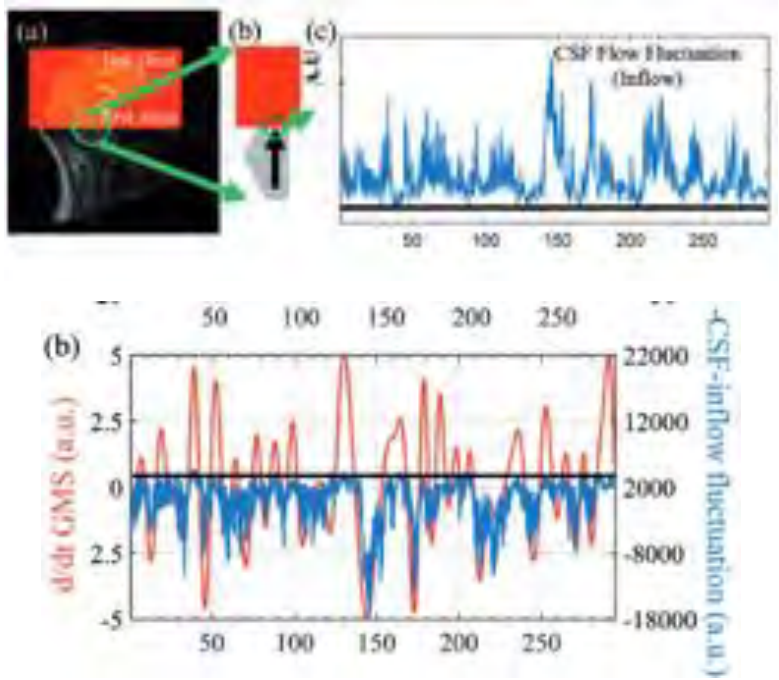
Periods of Eye Closure — PSD_{sleep} — Motion (Framewise Displacement)

Examine Failures in PSD_{Sleep} Ranking





Periods of Eye Closure — PSD_{sleep} — Motion (Framewise Displacement)



Ultra-slow Inflow Fluctuations in CSF in awake subjects

Ho-Ching et al. J Cerebral Blood Flow and Metabolism (2022)

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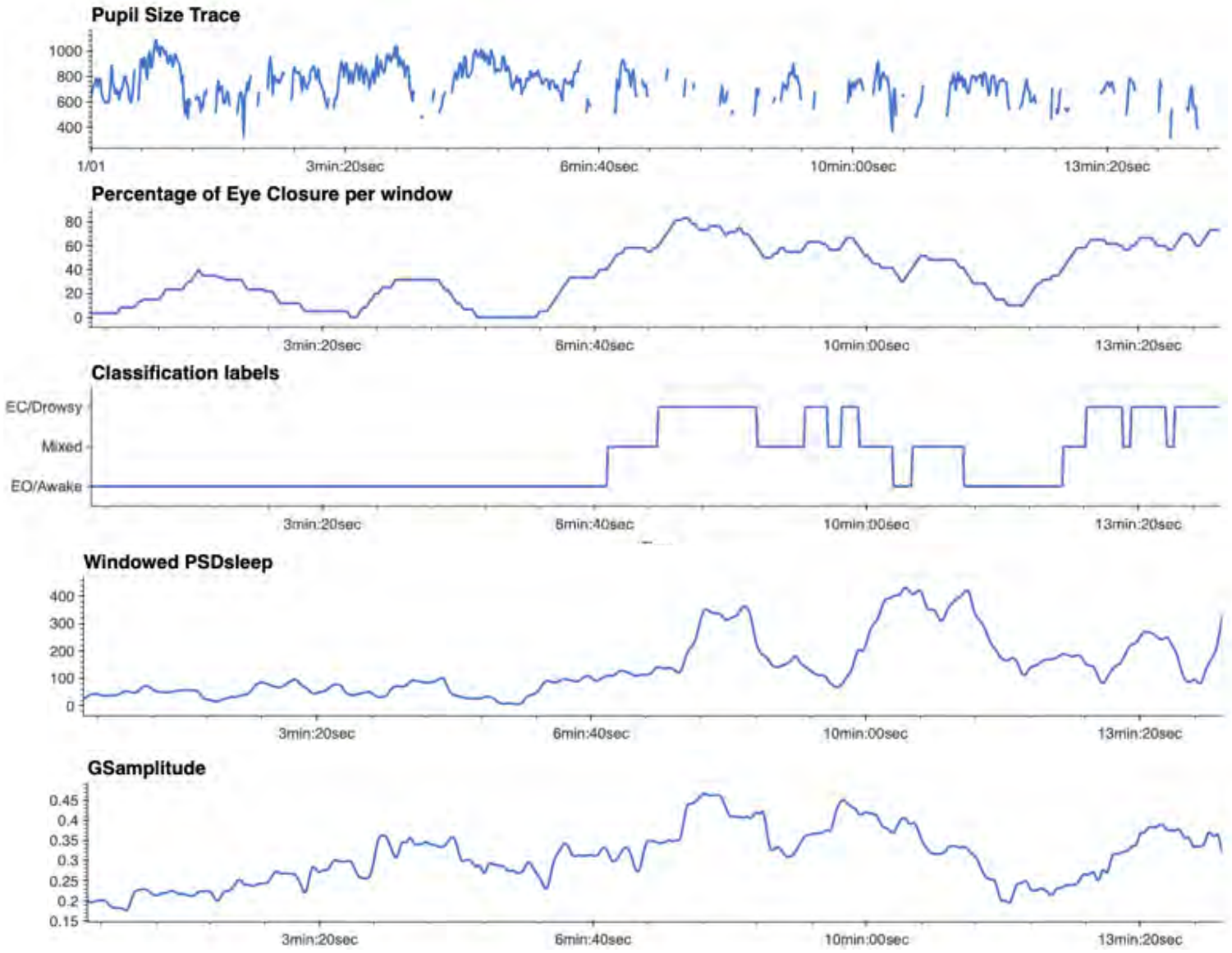
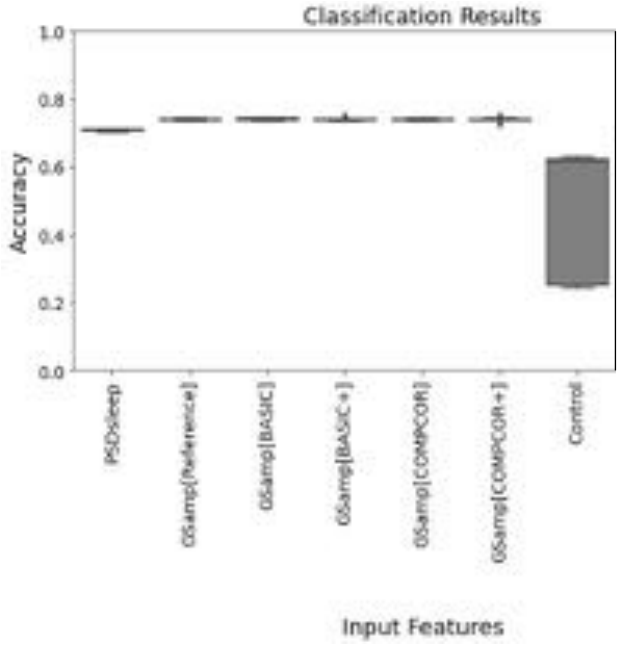
Avg. PSD_{sleep} as a marker of drowsiness [Time-resolved]

Label Generation

Input Features





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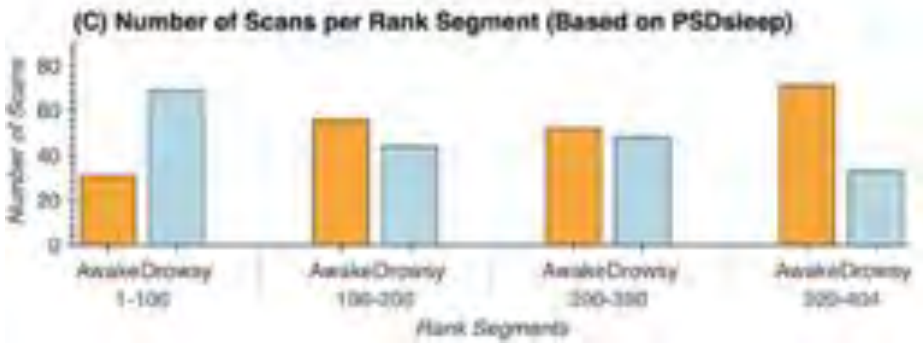
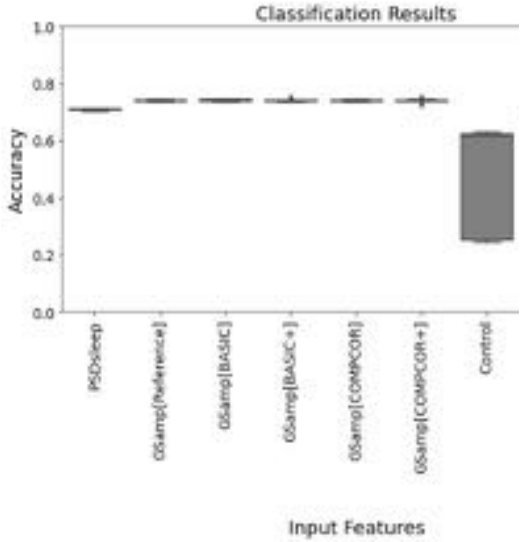
Our Particular Questions

Q2. If so, can this signal be used as a simple marker of wakefulness in existing fMRI datasets that lack concurrent EEG and/or eye tracker measurements?





Limited Value, similar to that of the Global Signal

Our Particular Questions

Q1. Can this 0.05Hz fluctuation be found on other datasets not necessarily optimized for detecting in-flow?

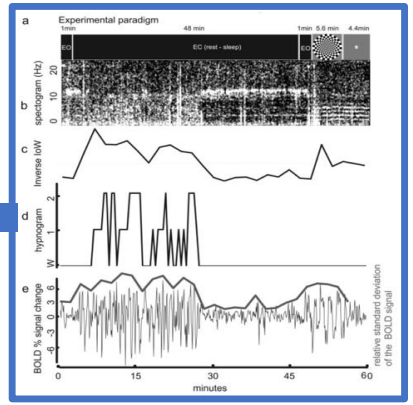
YES

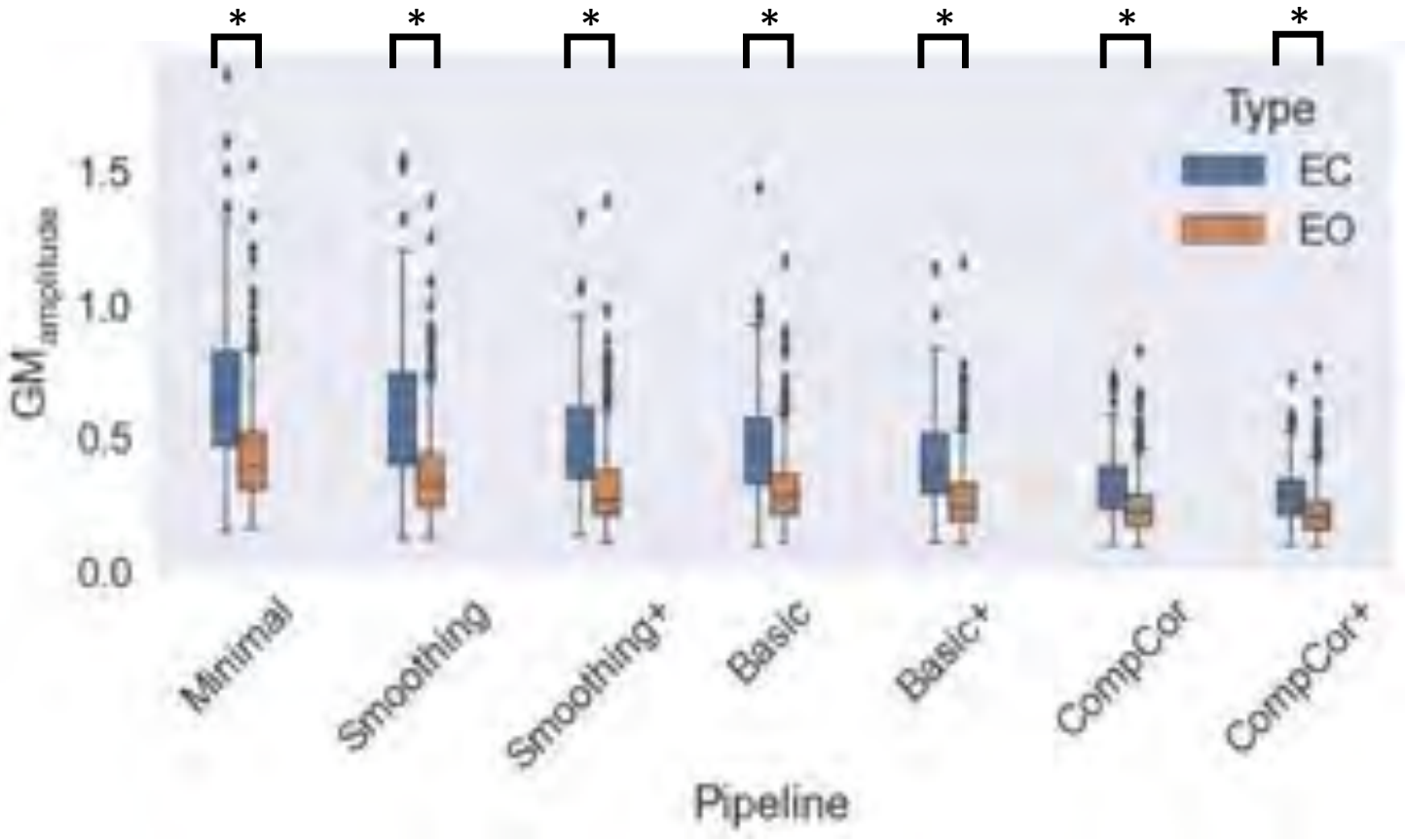
Q2. If so, can this signal be used as a simple marker of wakefulness in existing fMRI datasets that lack concurrent EEG and/or eye tracker measurements?

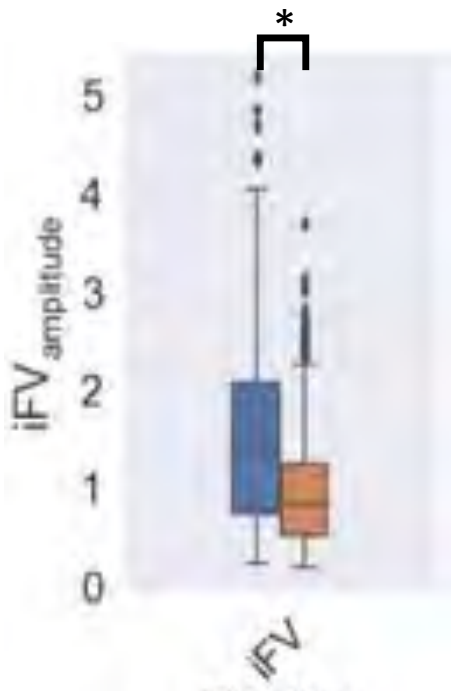
Limited Value, similar to that of the Global Signal

Q3. Do these fluctuations appear anywhere else in the brain (e.g., contribution to GS) and, if so, how do they affect FC estimates?

Relationship to the Global Signal







Minimal | HCP Minimal Preprocessing Pipeline (spatial steps)

Smoothing | Minimal + Blur (FWHM=4mm) + Band Pass Filtering (0.01 – 0.1 Hz)

Basic | Smoothing + Regress Motion & 1st Derivative

CompCorr | Basic + CompCorr Regressors

\+ | Shifted version of the FV signal that best correlates with each voxel as extra regressor

Gonzalez-Castillo et al. NeuroImage (2022)

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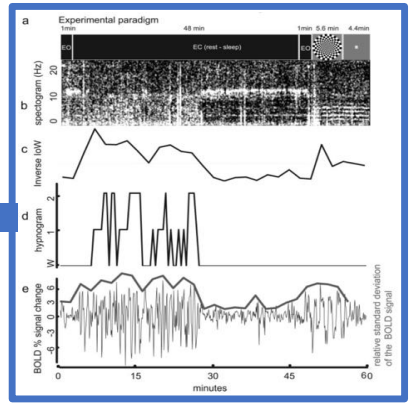
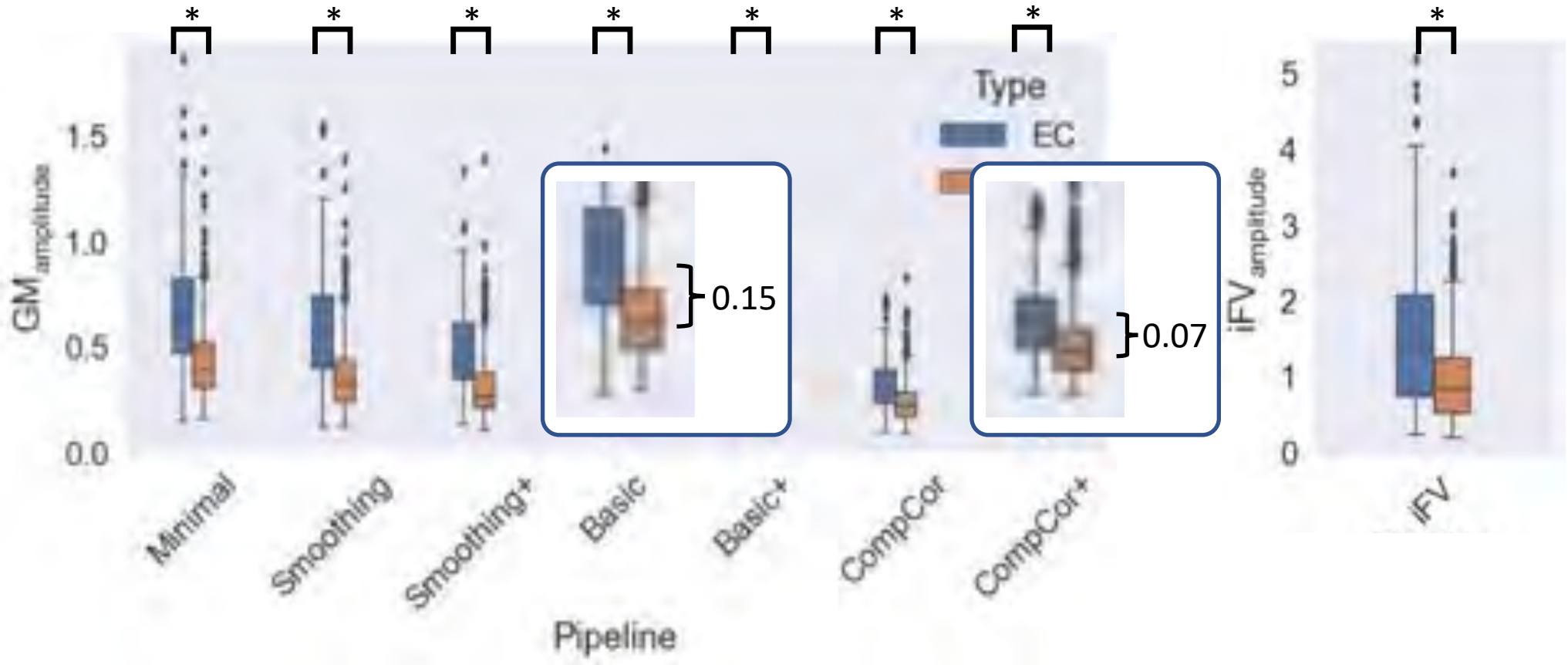
Relationship to the Global Signal





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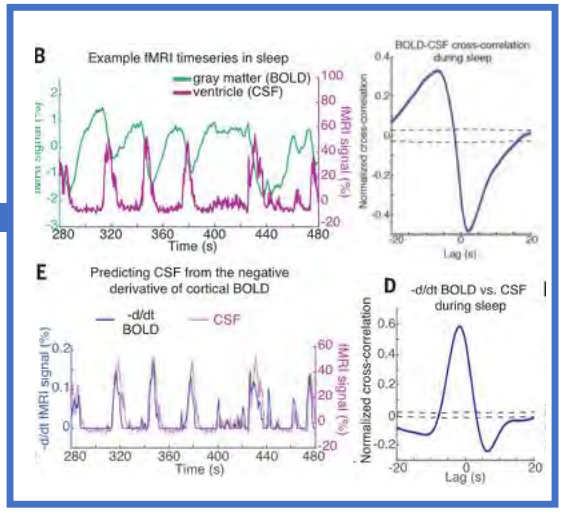
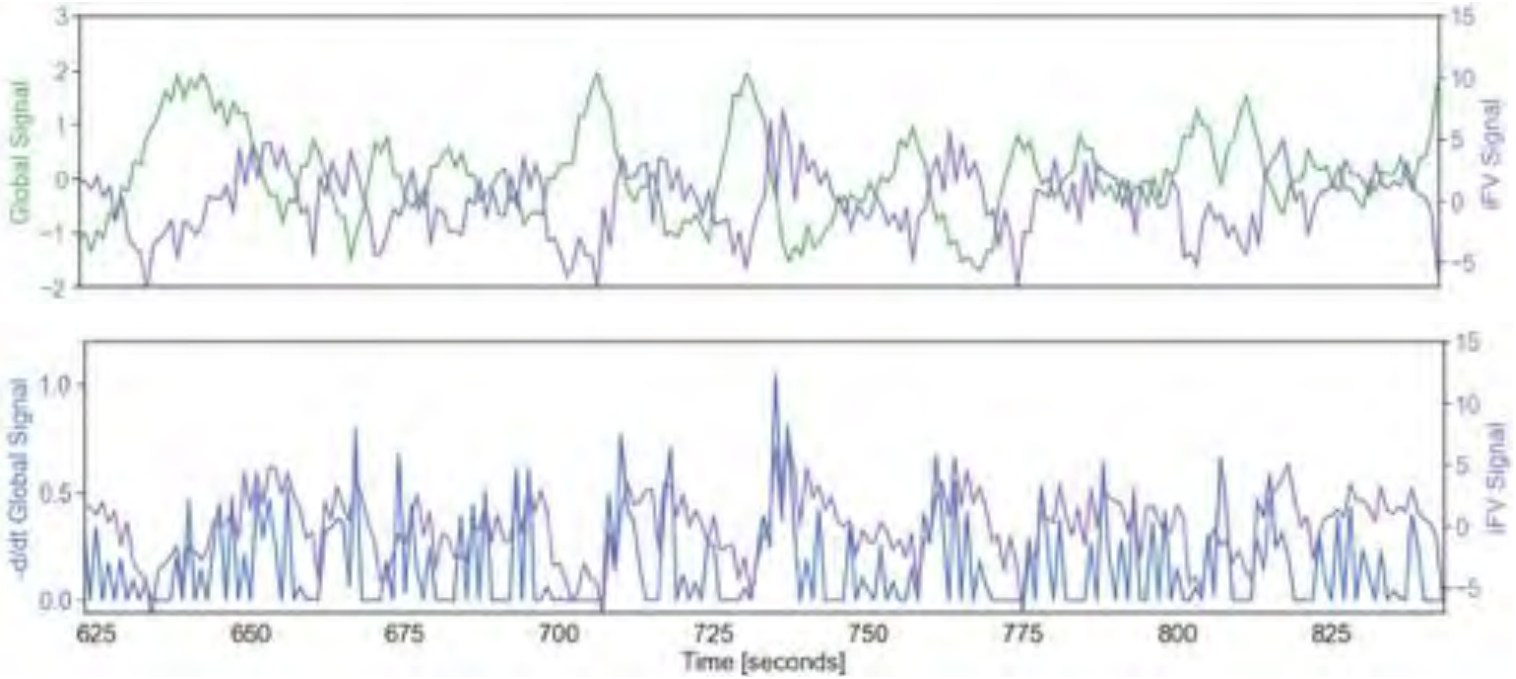
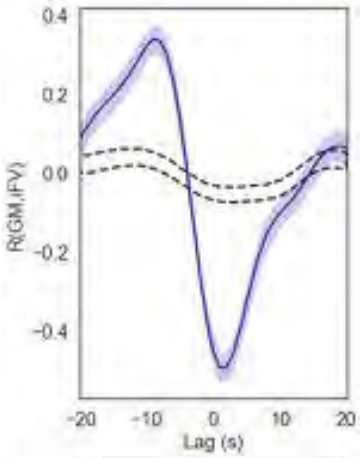
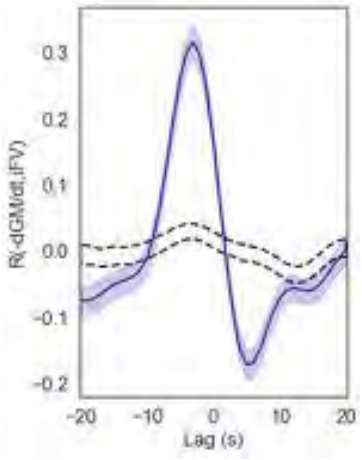
Relationship to the Global Signal



Representative Eyes Closed Segment







GM Global Signal 4th Ventricle Signal d/dt GM Global Signal

Gonzalez-Castillo et al. NeuroImage (2022)

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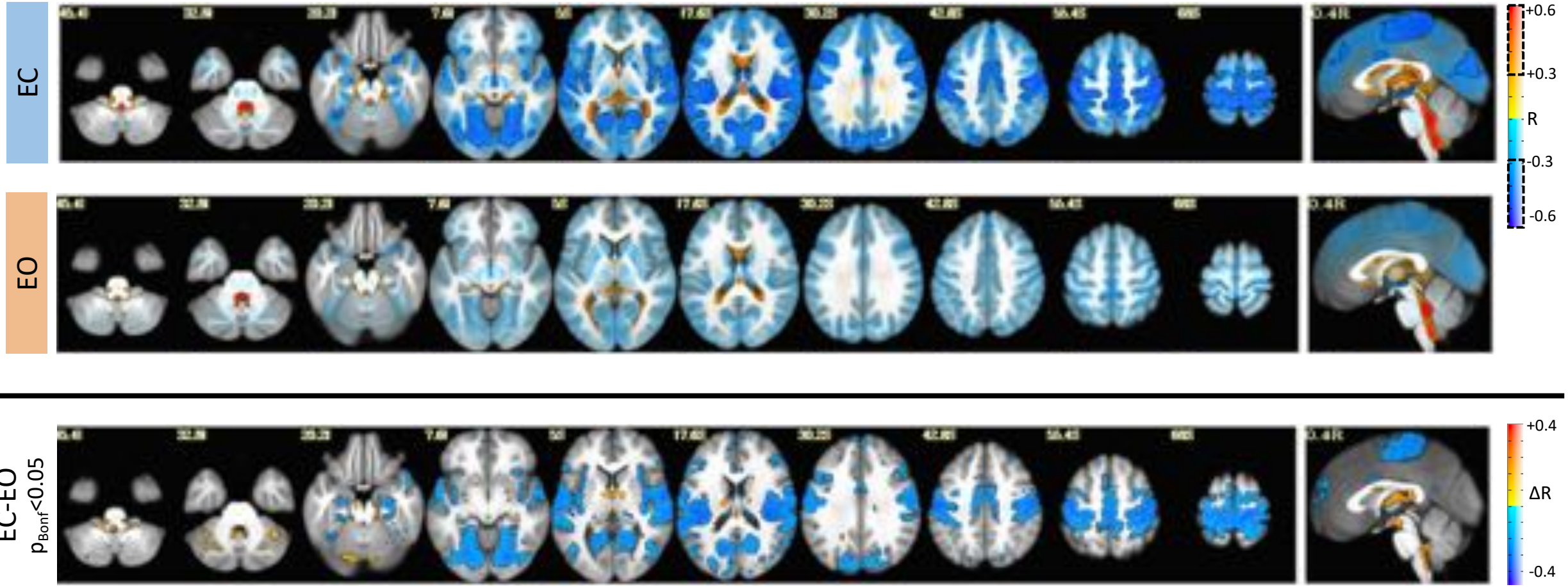
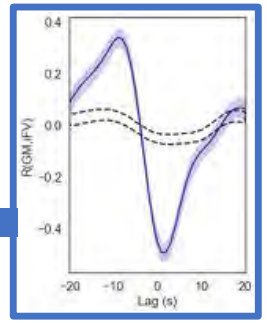
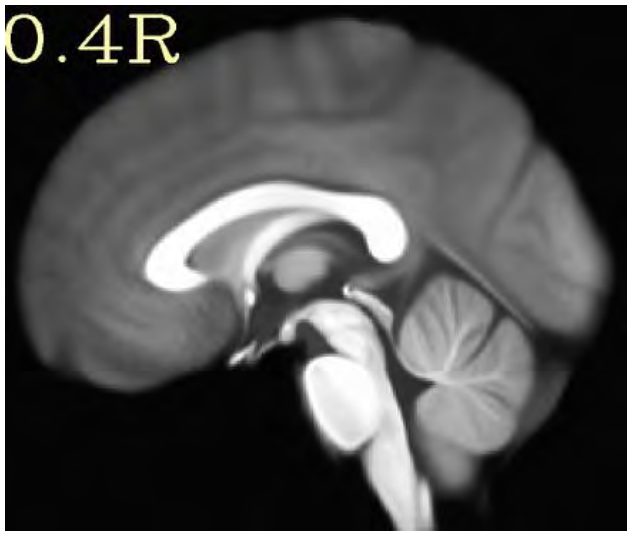
Where exactly? | Zero-Lag Correlation

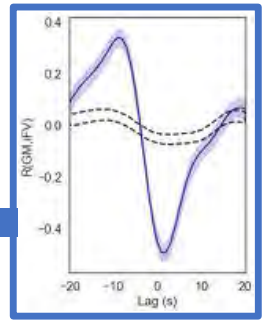


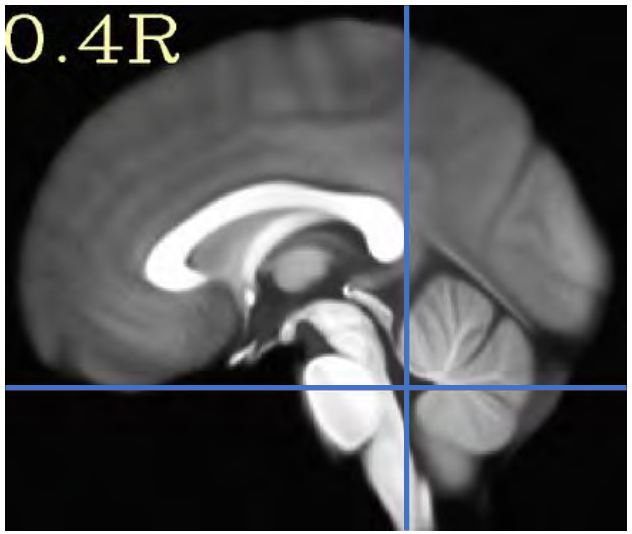
Spatial Profile of Delays

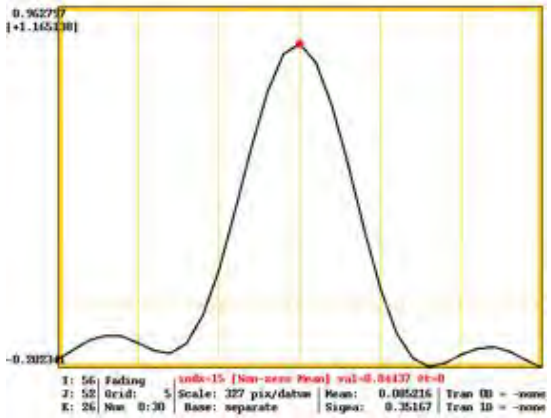




Spatial Profile of Delays

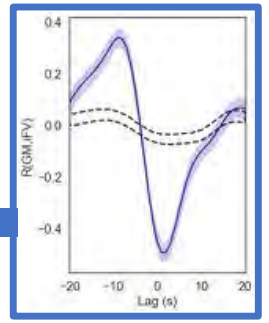


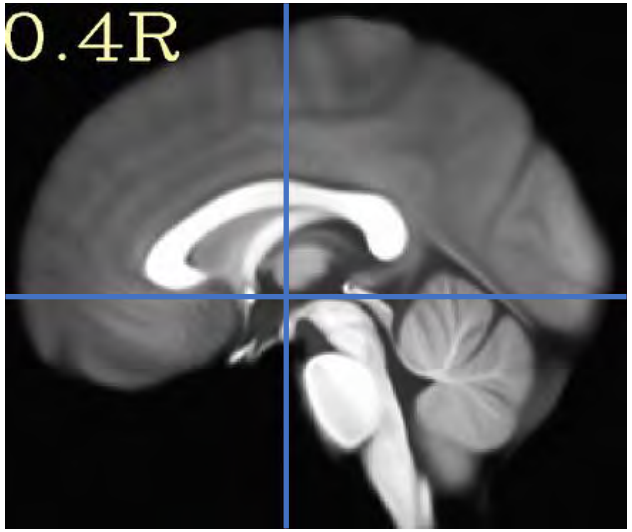


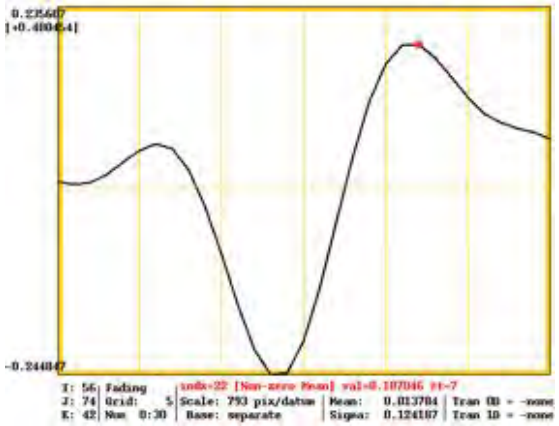


Lag = 0s

Spatial Profile of Delays







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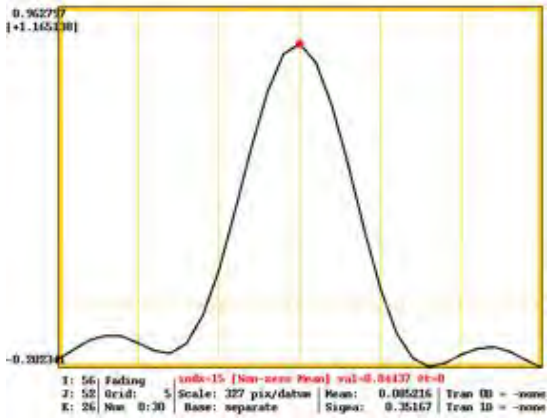

Lag = 0s

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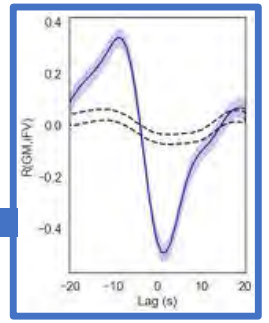
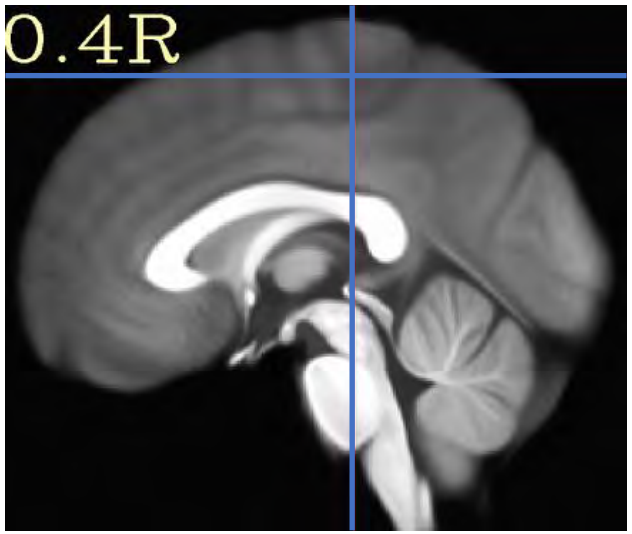
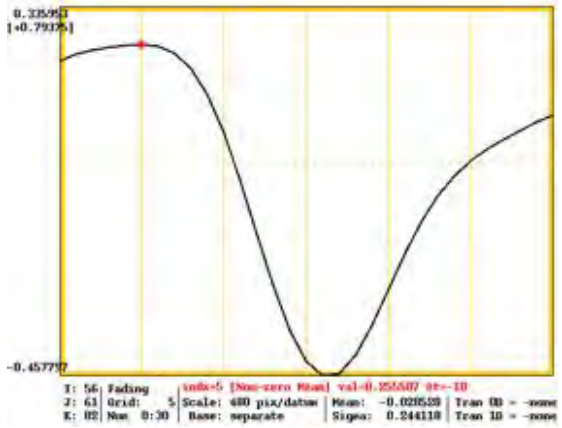
Spatial Profile of Delays







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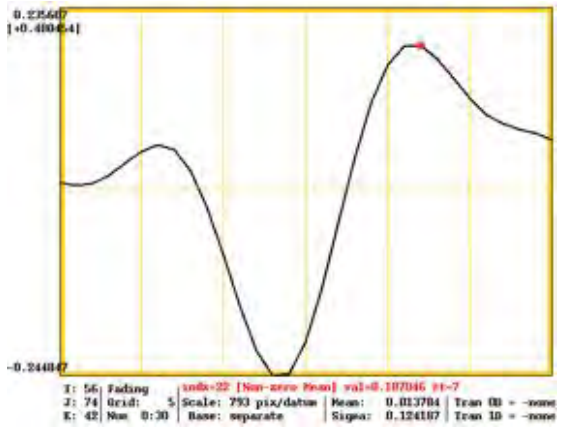

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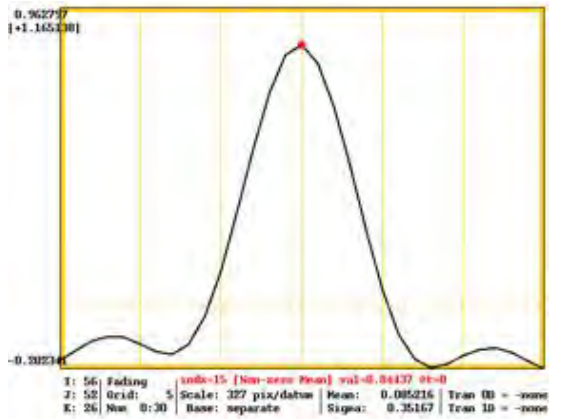

Lag = 0s

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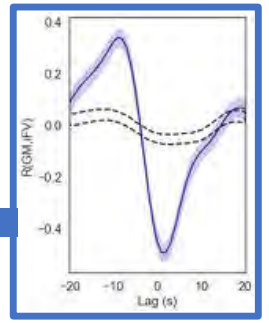
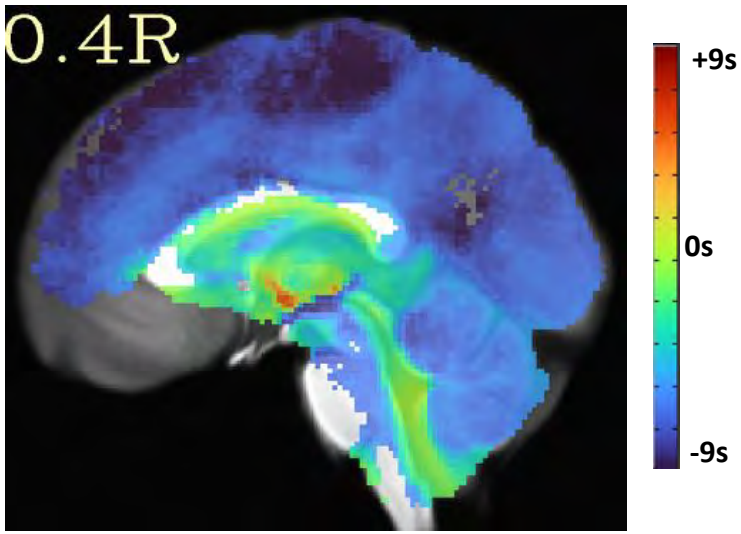
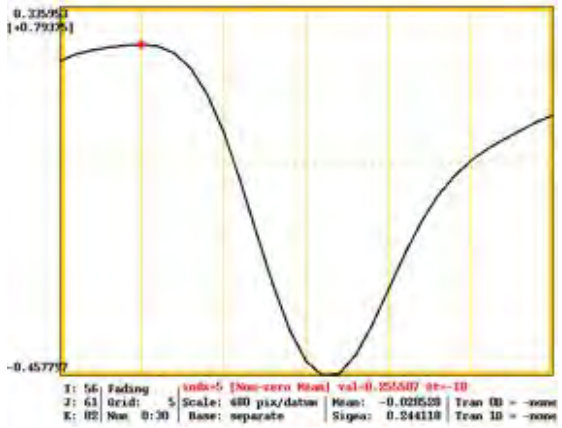
Spatial Profile of Delays







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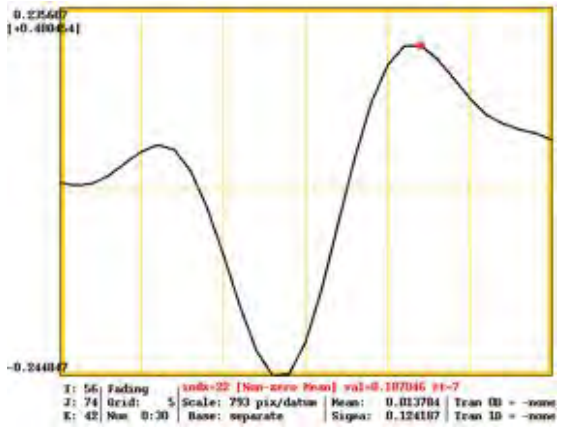
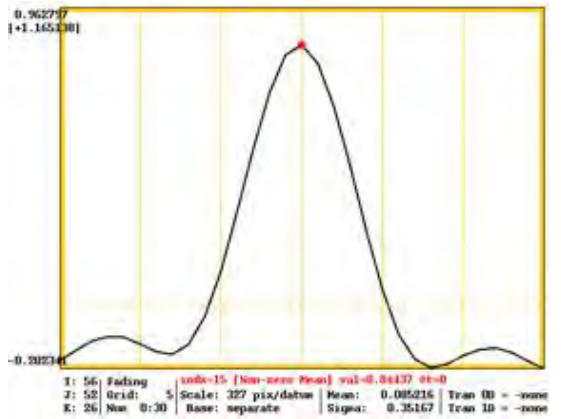


Lag = 7s



Lag = 0s

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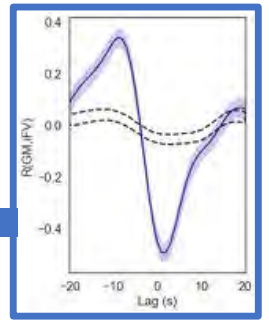
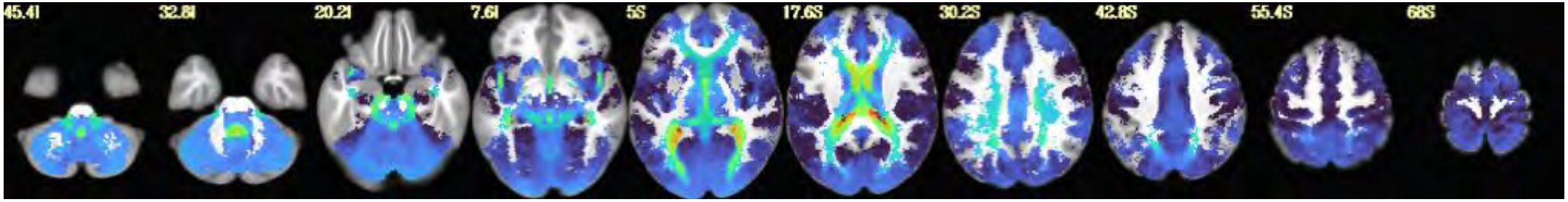
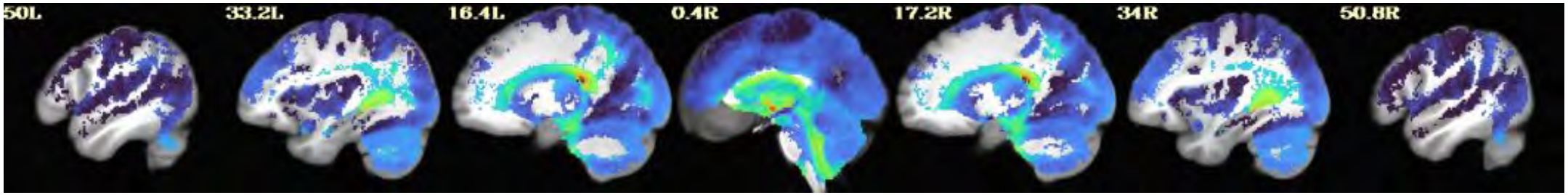
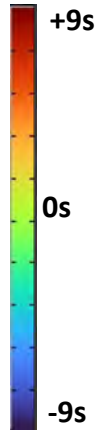
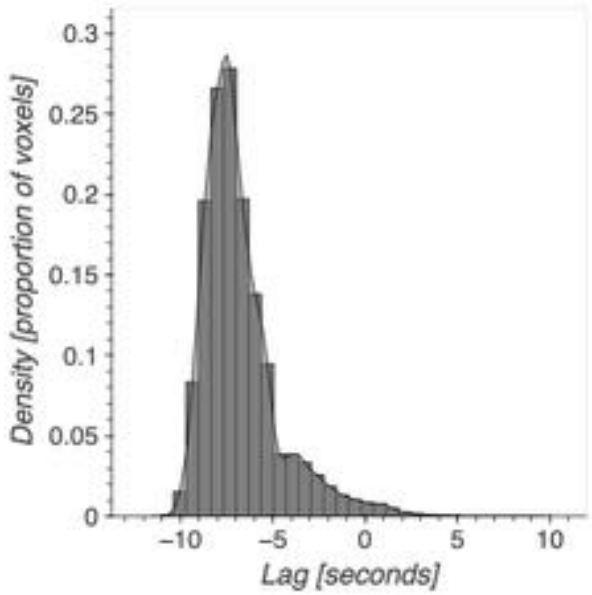
Spatial Profile of Delays

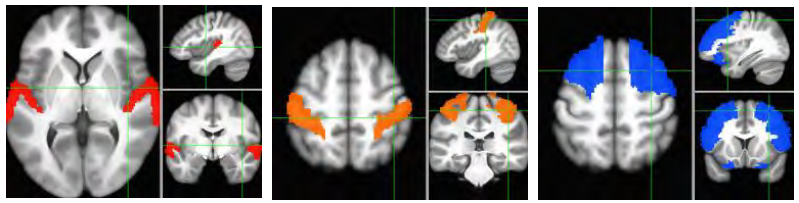


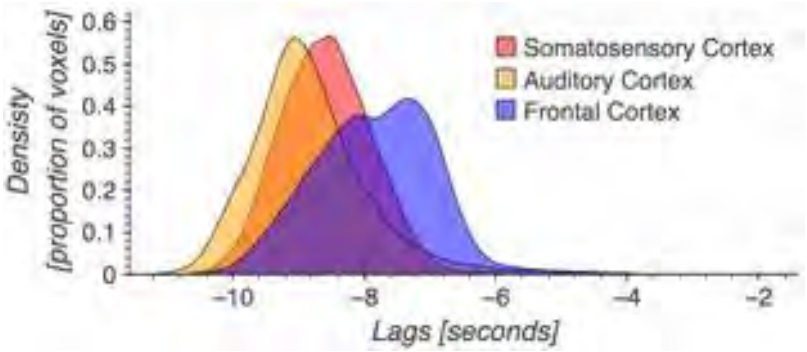












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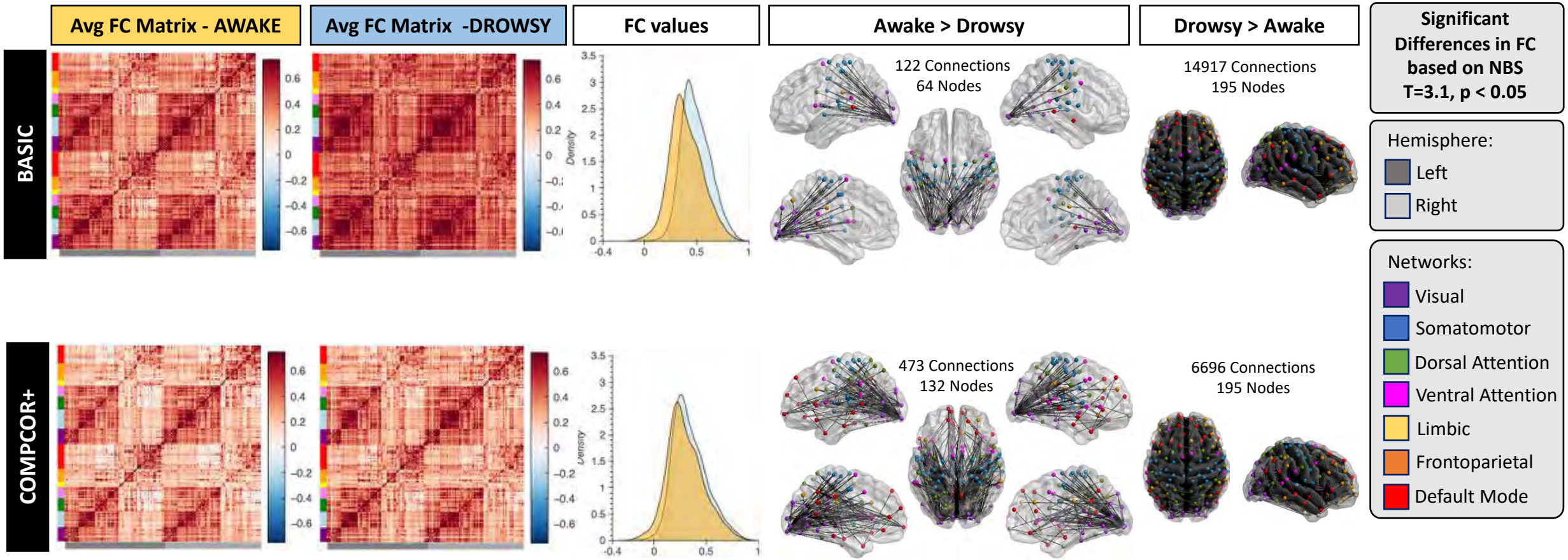
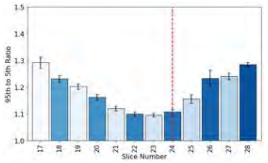
Modulatory Effects in FC

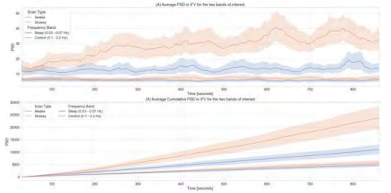


Conclusions

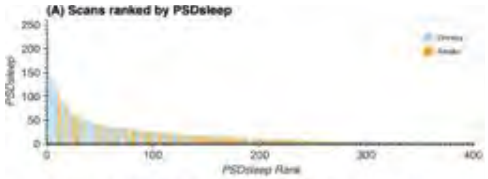
- Fourth ventricle ultra-slow fluctuations (~0.05Hz) with inflow characteristics were observed during long periods of eye closure in this larger sample.



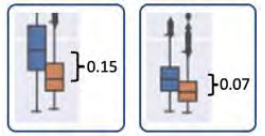
- The temporal evolution of these fluctuations can uncover previously reported sample-level patterns of sleep (i.e., propensity of subjects to fall asleep after 3 minutes of scanning)



- Has equivalent predictive value to that of the GS as a marker of drowsiness



- Important contributor to the GS during periods of drowsiness: account for 50% of the increase in $GS_{amplitude}$ that accompanies sleep.



- Using ventricular signals are nuisance regressors change FC patterns across the brain in a substantial way.

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Thank you

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