Title: Behavioral and arousal states control neurovascular-coupling

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Abstract:

Hemodynamic signals in the brain are used to infer neural activity, and bilateral correlations in

hemodynamic signals have been observed in the absence of any overt stimulus or task.

However, recent studies have suggested that the nature and strength hemodynamic signals

depend on arousal state. Here, we monitored neural activity and hemodynamic signals in

un-anesthetized, headfixed mice to understand how sleep and wake states impact cerebral

hemodynamics. In parallel with electrophysiological recordings, we used intrinsic optical

signal imaging to measure bilateral changes in cerebral blood volume (CBV). We concurrently

monitored body motion, whisker movement, muscle EMG, and cortical LFP to classify the

arousal state of the mouse into awake, NREM sleep, or REM sleep. We found that mice

regularly fell asleep for a few minutes at time during imaging. During both NREM and REM

sleep, mice showed large increases in CBV relative to the awake state. During NREM sleep,

the amplitude of bilateral low-frequency oscillations in CBV increased markedly. Bilateral

correlations in neural activity and CBV were highest during NREM sleep, and lowest in the

awake state. Our results show that hemodynamic signals in the cortex are strongly modulated

by arousal state and emphasize the importance of behavioral monitoring during studies of

spontaneous activity.

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**Figure outline**

Panels 1-3 data setup, sleep scoring information, and phenomena of increased blood flow during sleep

Panel 4 – Ravi’s simulations showing how the increased diameter during sleep shows extracellular clearance/flow

Panels 5,6 – bilateral hemisphere correlations and how they change during sleep

Panels 6/7 – transition to single hemisphere and neurovascular coupling

Panel 8 - summary

**Figure panel 1**

* IOS schematic – with single hemisphere window
* Single trial example – Awake/NREM/REM sleep with all parameters. Show pupil images
* Example Hypnogram – some sort of sleep duration statistics

**Figure panel 2**

* 2P schematic – with single hemisphere window
* Single trial example – Awake/NREM/REM sleep with all parameters
* Example Hypnogram – some sort of sleep duration statistics

**Figure Panel 3**

* Behavioral transitions (IOS)
* Average CBV/Flow/Vessel Dilations during each behavior (Whisk,Rest,NREM,REM,Iso)
* Average Heart rate per behavior - IOS only (Whisk,Rest,NREM,REM,Iso)

**Figure panel 4**

* Ravi’s simulation showing how individual vessels (ideally the one from the example figure) drives solute clearance

**Figure panel 5**

* Bilateral IOS Coherence
* Power Spectra

Figure panel 6

* Bilateral Pearson’s correlation’s
* Single hemisphere cross-correlation

Figure panel 7

* HRF kernels, predictions, single trial example

Figure panel 8

* Summary figure for bilateral correlations (“U” curves”)
* Summary figure for NVC - ?