Varying patterns of brain-wide neuronal activity underlie correlation structure of low-frequency spontaneous hemodynamic signals

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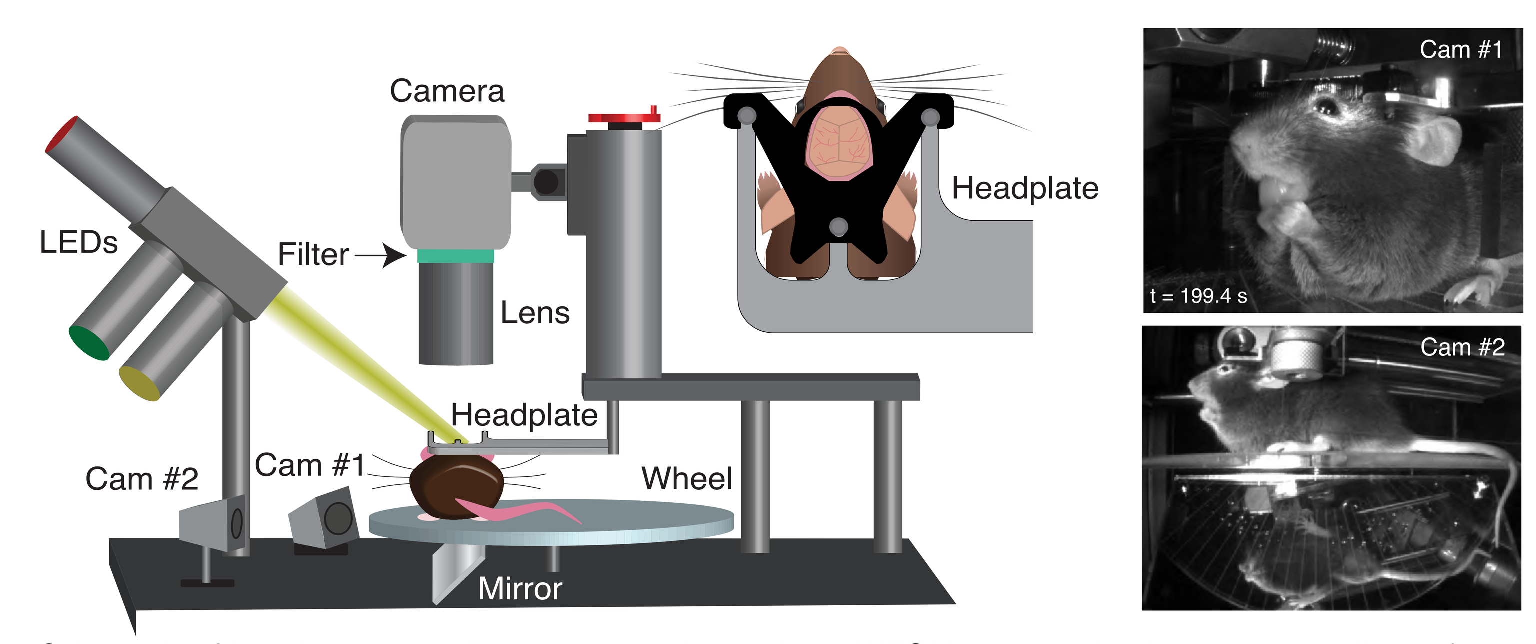
Introduction

Resting-state functional magnetic resonance imaging (fMRI) studies have extensively investigated the correlation structure of 'baseline' hemodynamic fluctuations. These studies have revealed resting-state neural networks whose dynamic changes may be related to shifts in brain states during rest. The findings, however, have been inconsistent and difficult to interpret. The primary reason for this is the lack of a thorough understanding of the neural basis that underlies hemodynamic correlations.

Goal of Study

Here, wide-field optical mapping (WFOM) provided us with a unique opportunity to simultaneously record neuronal calcium and hemodynamic signals in awake, spontaneously behaving mice. We aimed to characteriz dynamic changes in cortex-wide neuronal correlation patterns and their relationship to mouse behavior and brain hemodynamics.

Methods and Materials

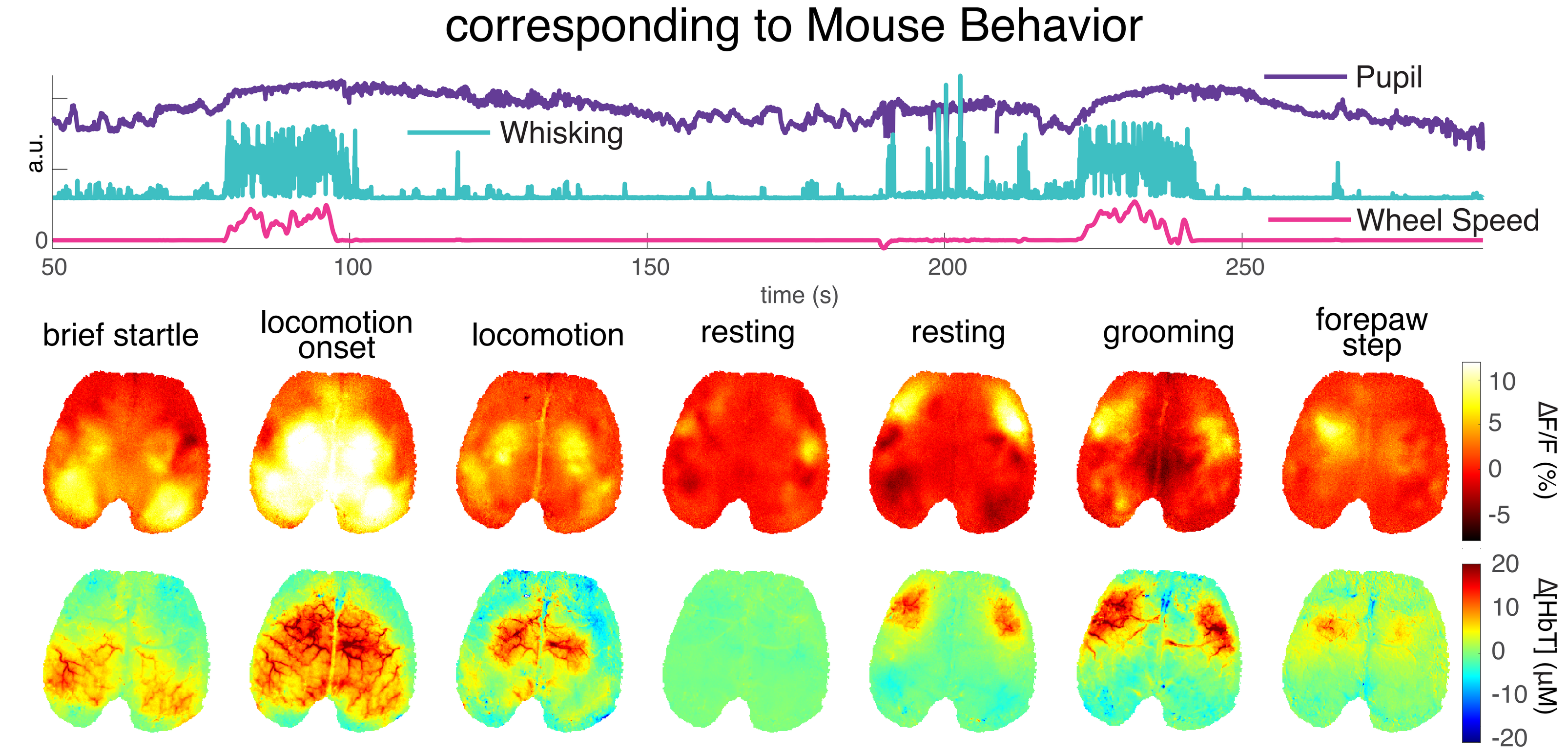


Schematic of imaging system. Data were acquired using a WFOM system, simultaneous recordings of the jRGECO1a fluorescence (neural, lime LED) and reflectance (hemodynamic, Red and Green LEDs) data. Two cameras were used to monitor mouse behavior.

- Five transgenic thinned-skull male adult Thy1-jRGECO1a mice expressing red-shifted calcium indicators were used in this study.
- Each recording session was 10 minutes. Mice were head-fixed but allowed to move freely on a transparent acrylic wheel that rotated.
- Variables such as whisking, pupil diameter, and locomotion were used to measure changes in mouse behavior.

Neuronal and Hemodynamic Images

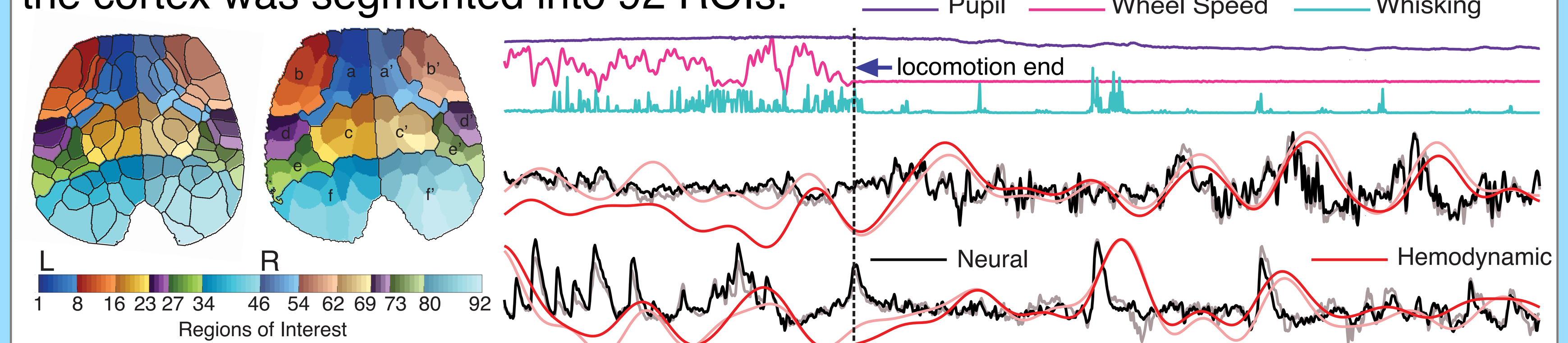
Neuronal and Hemodynamic Activity presenting Sensory and Motor Function corresponding to Mouse Behavior



- Several patterns are observed, corresponding to a variety of behaviors.

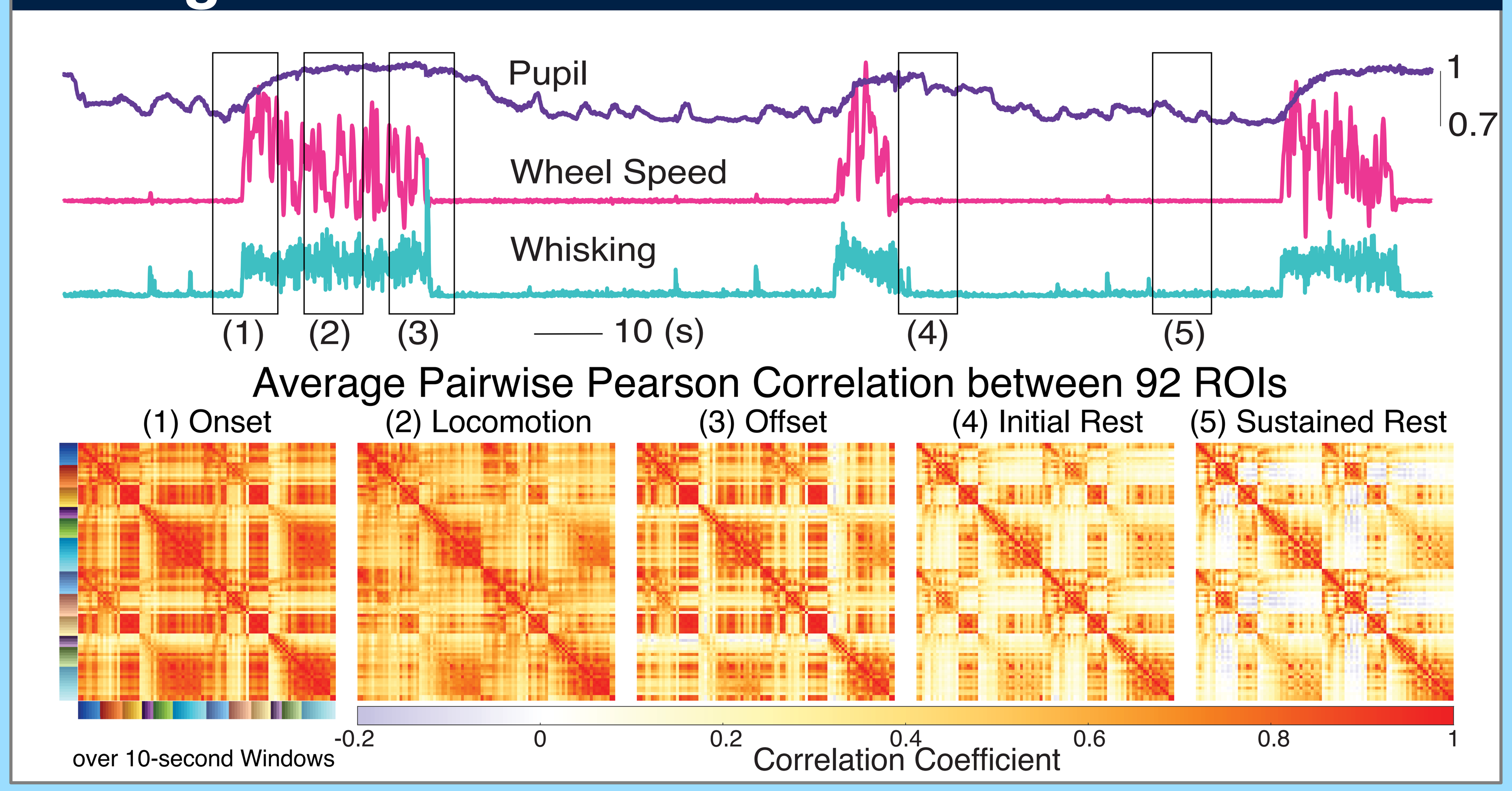
Regions of Interest

Applying k-means clustering on neuronal activity during rest for each mouse, the cortex was segmented into 92 ROIs.



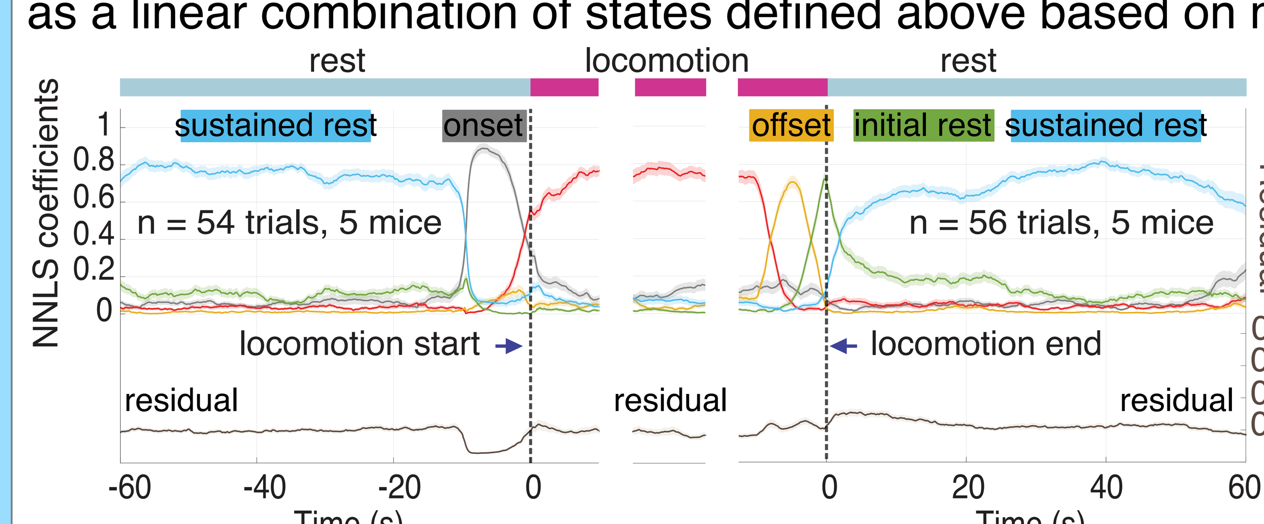
Neural and hemodynamic activity were extracted from two example bilateral ROIs within the anterior lateral frontal cortex (upper time series) and visual cortex (lower time series). The hemodynamic signals were low-pass filtered with the cutoff frequency of 0.25 Hz.

Changes in Neuronal Correlation Patterns



Dynamic Changes of Correlation Structure predicting Mouse Behaviour

- Using a non-negative least squares fit to reconstruct every correlation map as a linear combination of states defined above based on mouse behavior.

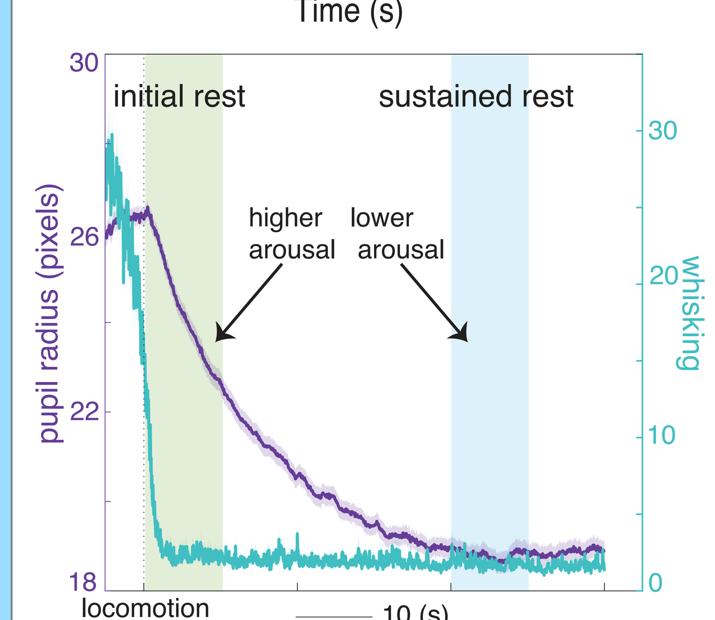


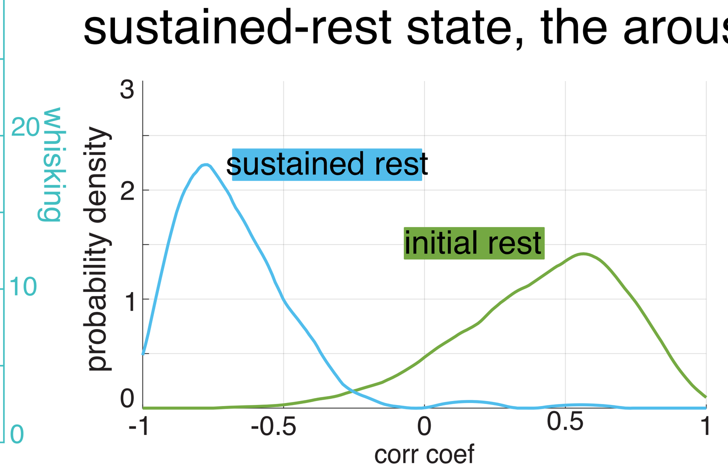
$$d(92,92,t) = \sum_{n=1}^{5} x(92,92)_n c(t)_n$$

$$\varepsilon = \frac{\|(d - cx)^2\|_1}{\|d^2\|_1}$$

d = actual correlation map
c = brain state coefficients
x = brain states

- During the initial-rest state, the arousal level is higher, while during the sustained-rest state, the arousal level is lower.

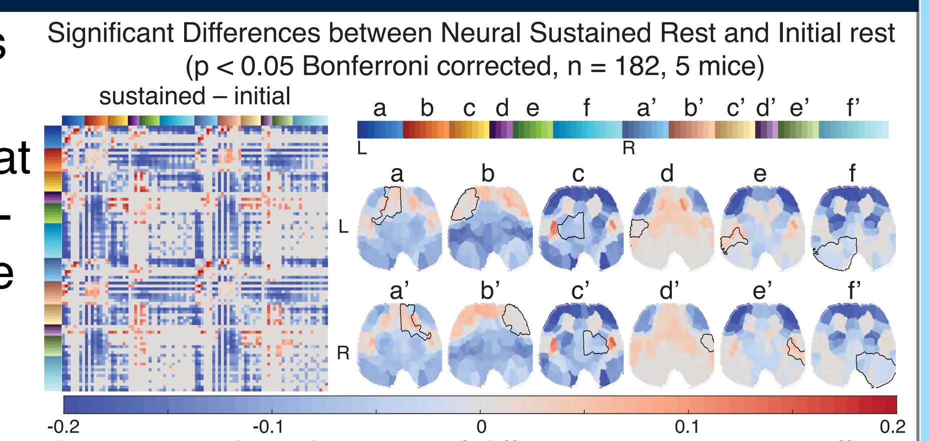




Distributions of correlation values between NNLS resting-state coefficients and pupil size. Using the Kolmogorov-Smirnov test, the initial-rest distribution was significantly different than the sustained-rest one ($p < 0.00001$, n = 182, 5 mice).

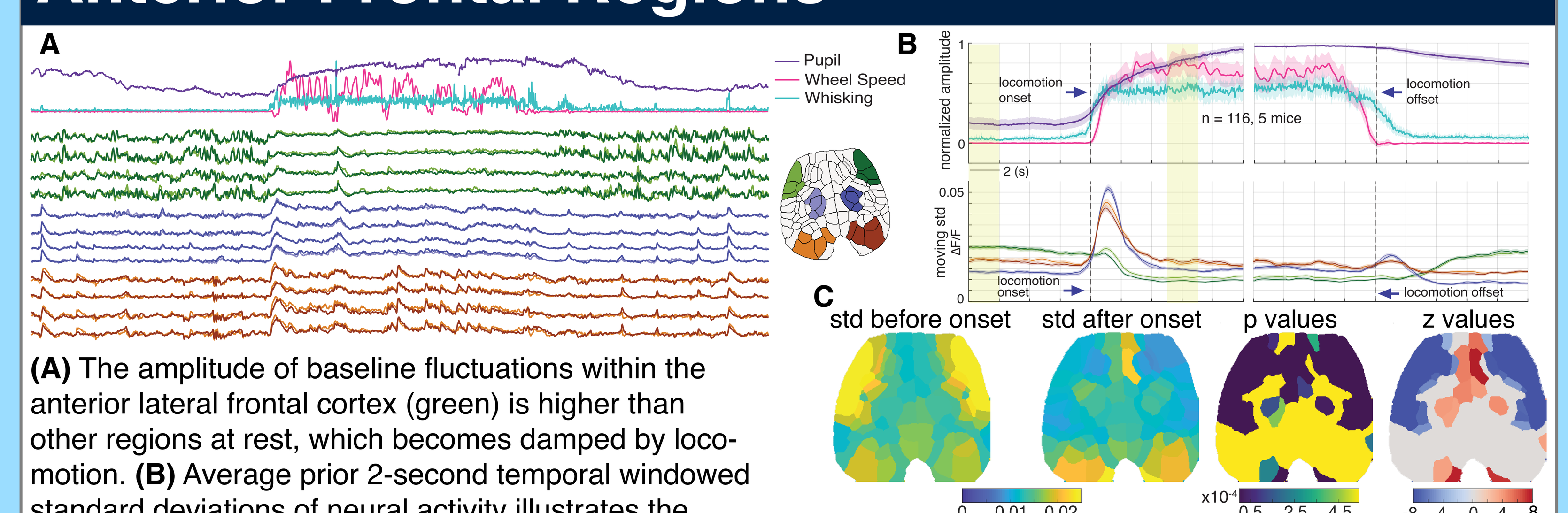
Anterior-Posterior Desynchronization associated with Lower Arousal Level

A comparison of correlation maps over sustained-rest periods with those over initial rest indicates that the correlation between frontal regions, particularly those within the anterior lateral frontal cortex, and posterior regions, including the visual cortex and somatosensory areas, significantly decreased.



Brain maps show the mean of differential correlation coefficients between each subgroup and all ROIs. The red and blue colors indicate increased and decreased correlations.

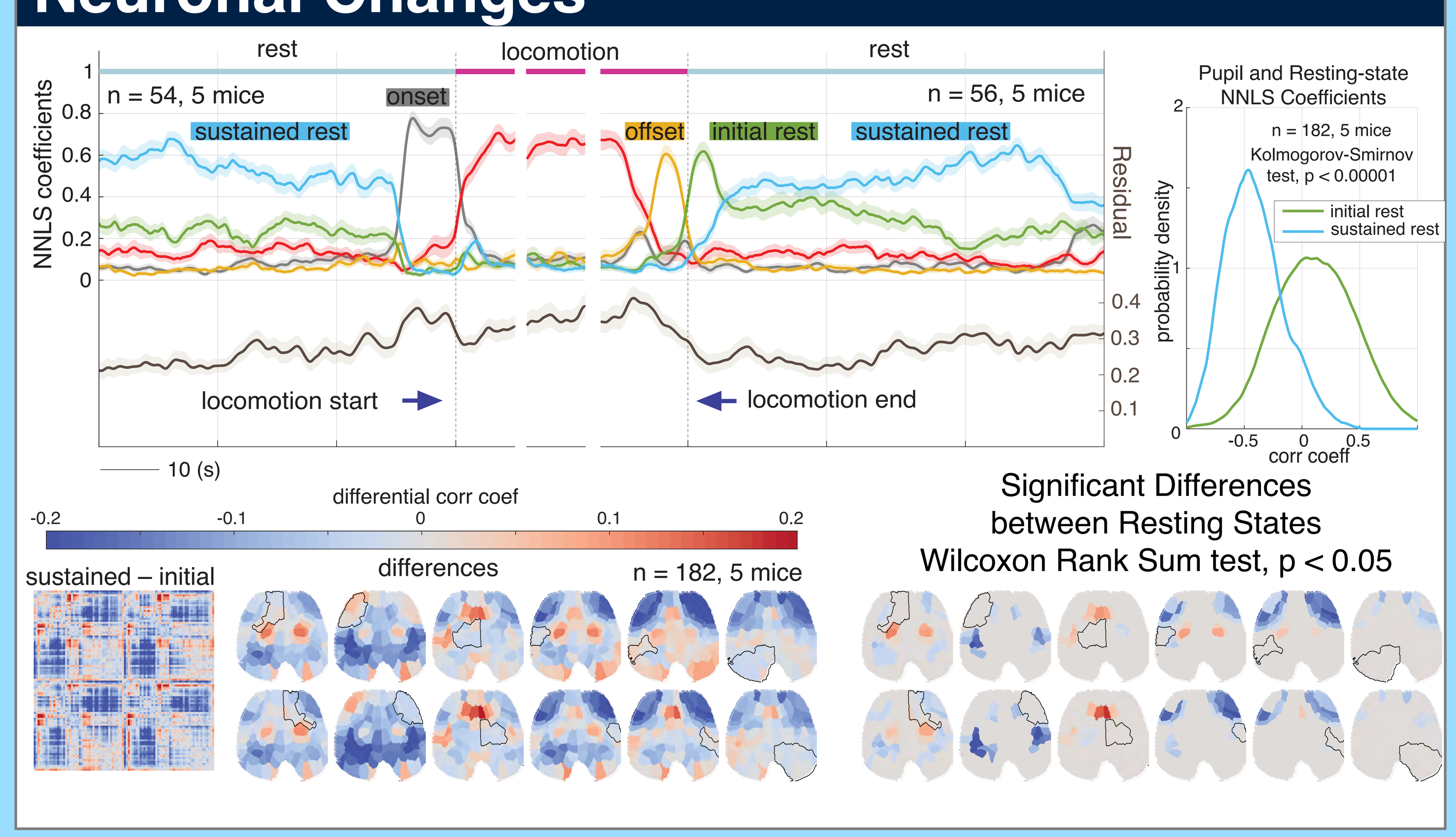
Antereior-Posterior Desynchronization driven by Increased Fluctuations in the Lateral Anterior Frontal Regions



(A) The amplitude of baseline fluctuations within the anterior lateral frontal cortex (green) is higher than other regions at rest, which becomes damped by locomotion. **(B)** Average prior 2-second temporal windowed standard deviations of neural activity illustrates the larger variation in the anterior lateral frontal cortex before locomotion onset and after locomotion offset.

(C) Comparing standard deviations (std) between after and before locomotion onset shows the significant differences, using Wilcoxon Rank Sum test, $p < 0.05$.

Brain Hemodynamics represnts underlying Neuronal Changes



Significant Differences between Resting States
Wilcoxon Rank Sum test, $p < 0.05$

Conclusions

- Cortex-wide neuronal correlation structure can be explained by both over and covert behavior
- Lower arousal levels are characterized by lower anterior-posterior correlations
- Baseline fluctuations of the anterior lateral frontal cortex may play a critical role in regulating arousal level
- A neural basis for hemodynamic correlation structure has been introduced

Acknowledgment

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