

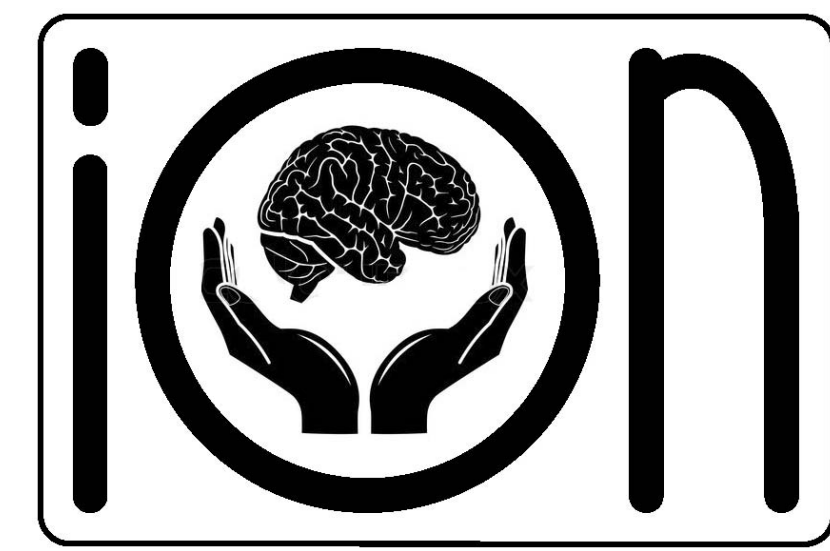


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The Relationship Between Cholinergic and Noradrenergic Activity and Behavioral State

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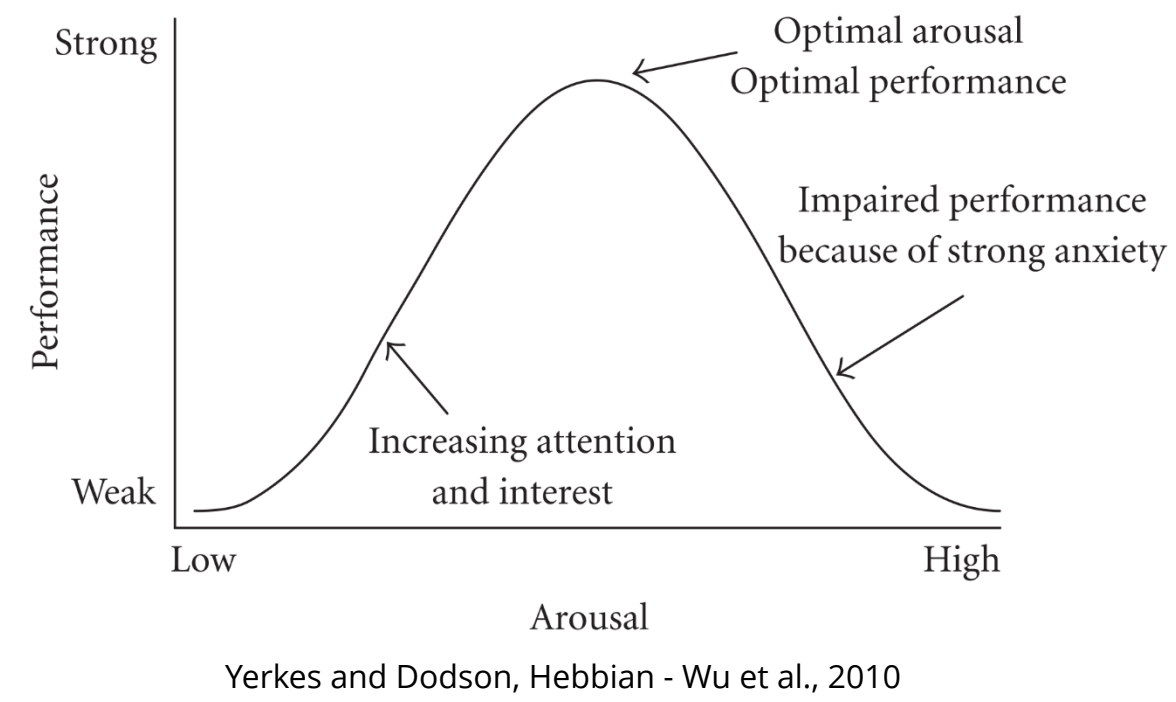
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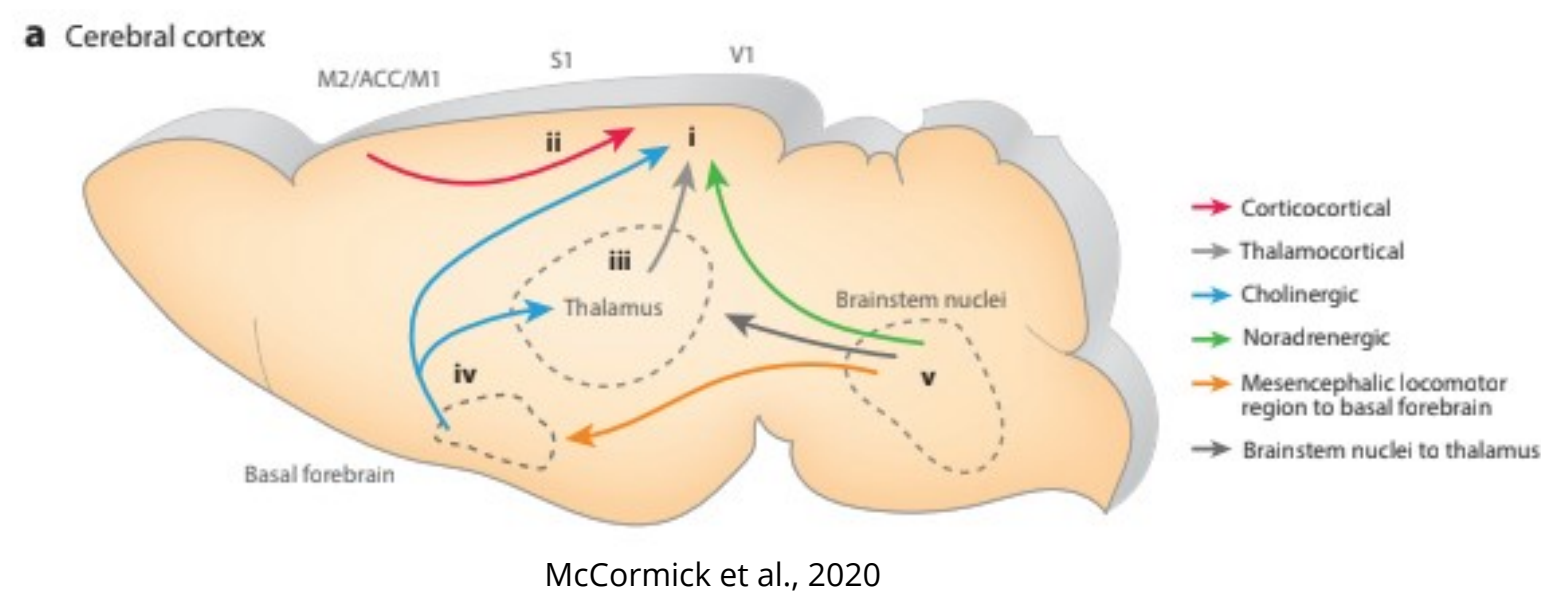
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Background

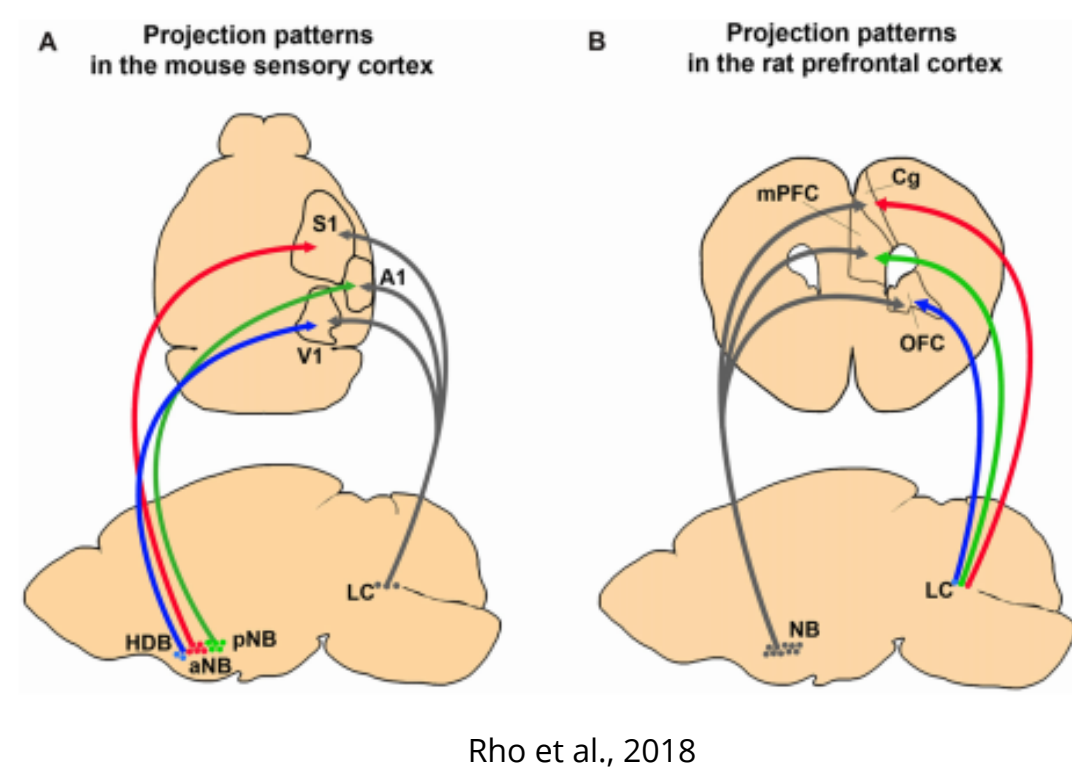
Moment-to-moment fluctuations in brain-state and arousal ultimately influence an animal's ability to perform and engage in different perceptual or cognitive behavioral tasks.



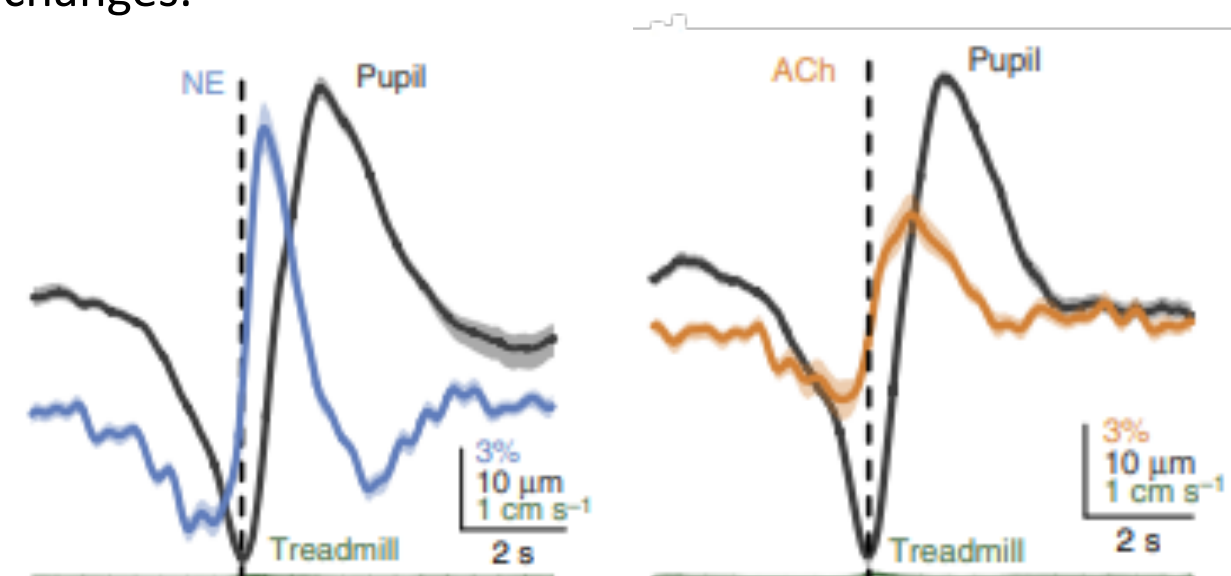
Rapid variation in behavioral state is, in part, influenced by various neuromodulatory systems within the brain.



Cholinergic projections from nuclei in the basal forebrain and noradrenergic projections from nuclei in the locus coeruleus innervate target regions within the cortex.



Neuromodulatory activity is linked to arousal state and behavioral state changes.



Reimer et al., 2016

Objectives

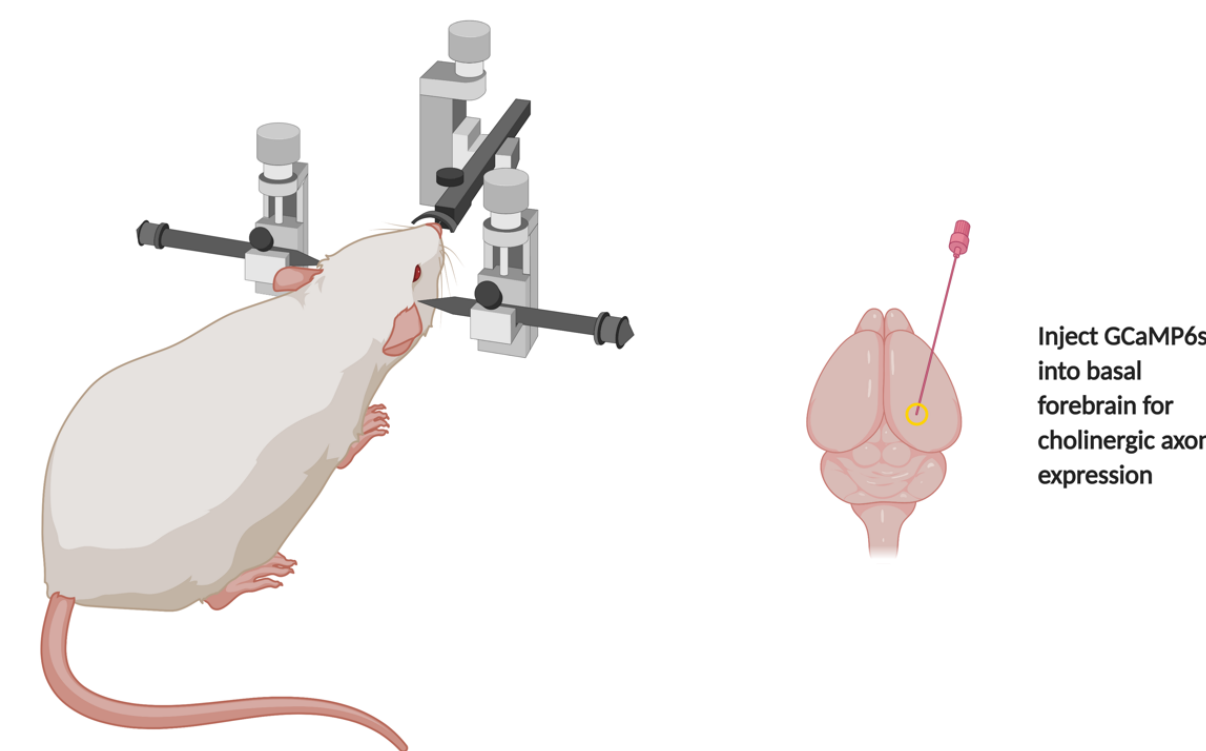
What is the relationship between cholinergic and noradrenergic neuromodulatory activity and behavioral state with respect to diverse arousal and behavior-dependent modes of neuromodulation?

- 1) Confirm the relationship between neuromodulatory activity and arousal previously demonstrated in the literature
- 2) Determine whether changes in neuromodulatory activity precede or follow the onset of behavioral events
- 3) Determine whether ACh and NA neuromodulation is specific to particular regions within the brain or if there is widespread synchrony of neuromodulatory systems across the brain during fluctuating arousal states

Methods

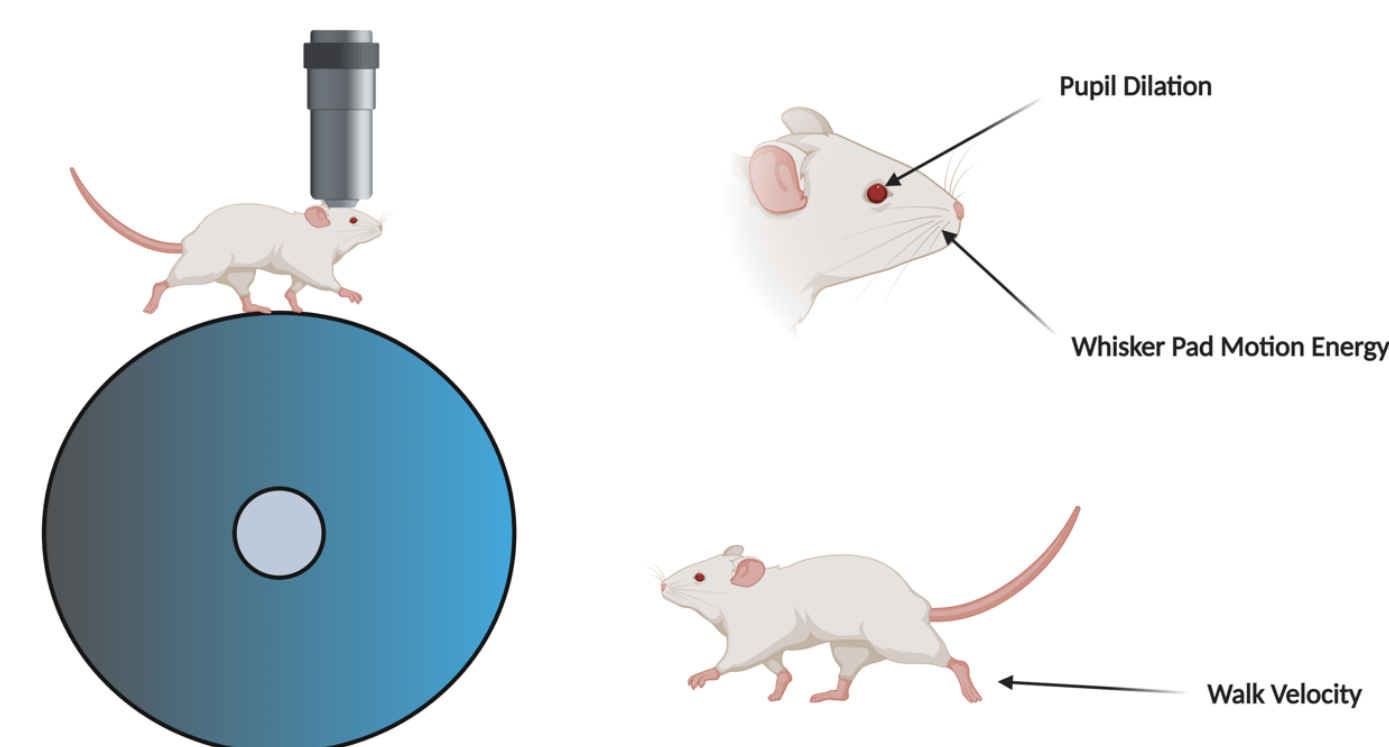
GCaMP6s was injected into the basal forebrain of ChAT mice to allow for cholinergic axon visualization.

- Viral injection of GCaMP6s into the locus coeruleus of DBH mice was not required for noradrenergic cortical activity visualization.



Simultaneous two-photon axon imaging and behavioral data acquisition allows us to directly compare axonal activity to behavioral state.

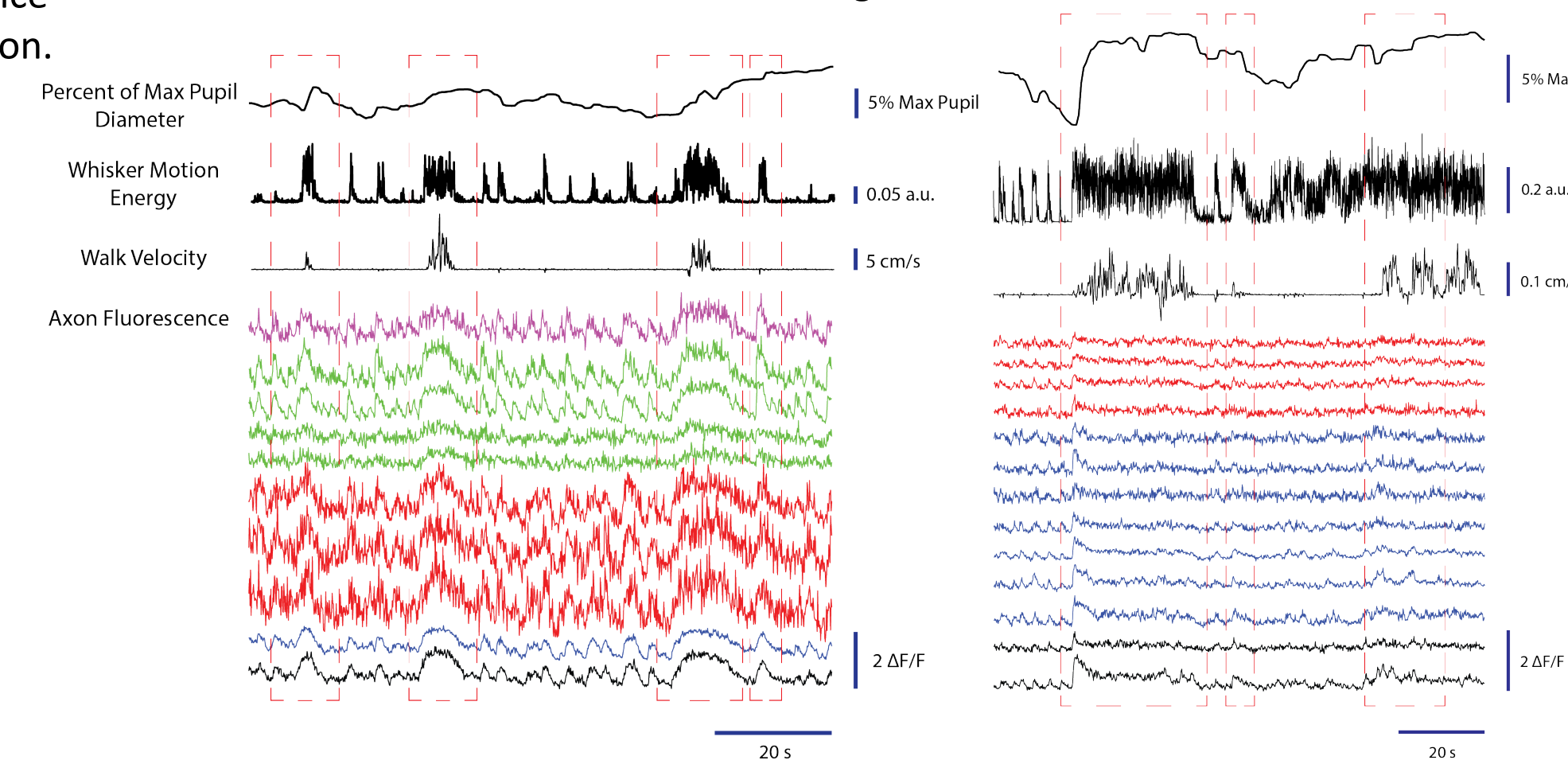
- From 2 ChAT mice, data were collected from 184 axons across 27 regions of interest (ROIs) from 6 recording sessions.
- From 3 DBH mice, data were collected from 94 axons from 24 ROIs across 7 recording sessions.



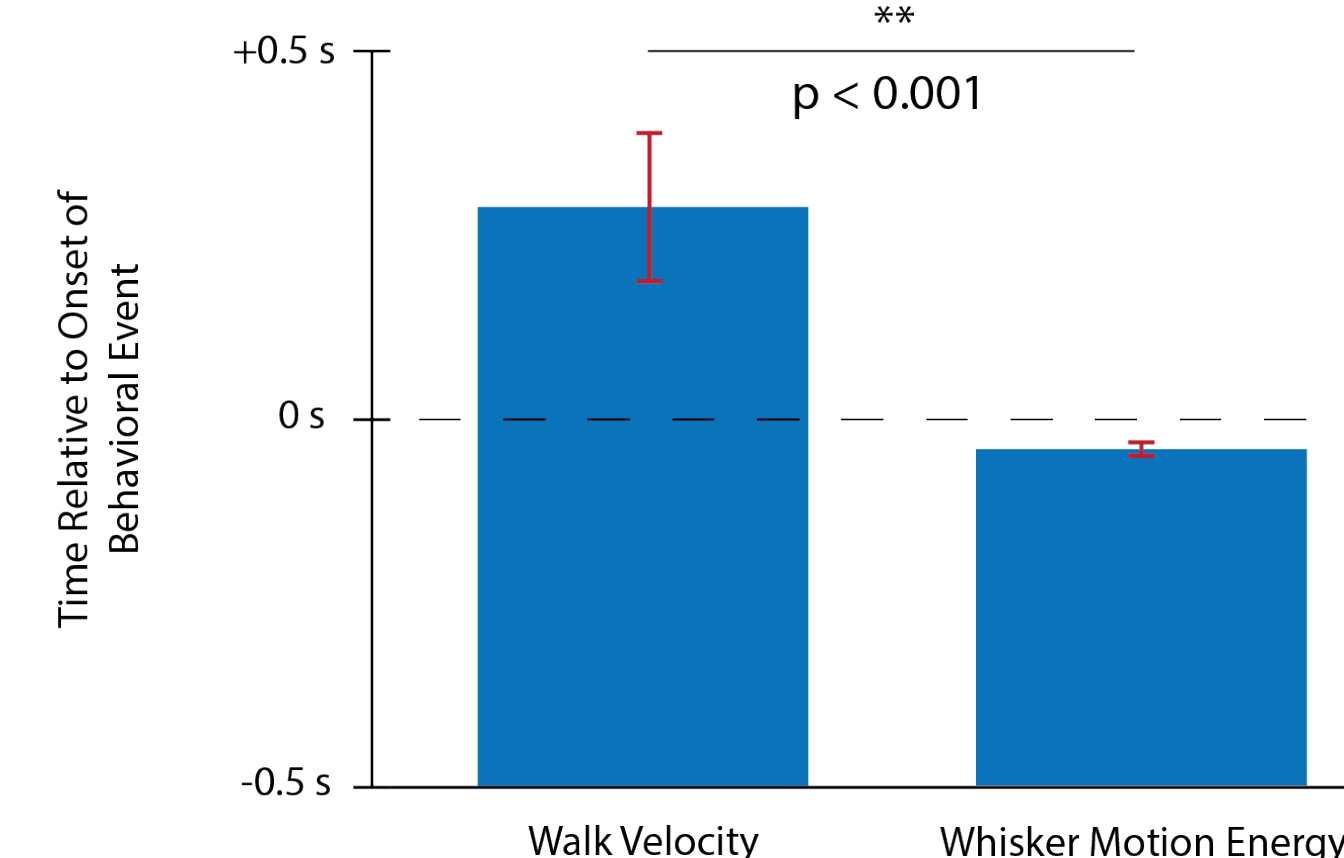
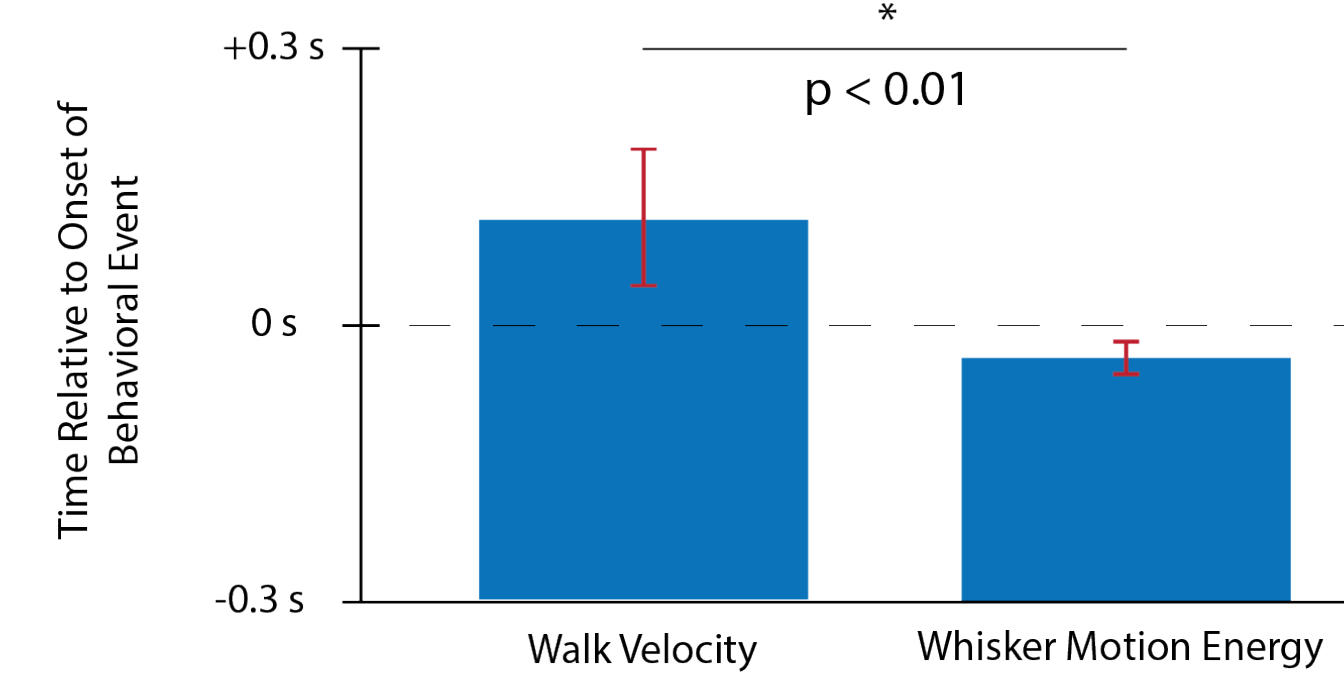
Histological verification of neuromodulatory nuclei was also performed to confirm that we were recording from either cholinergic or noradrenergic axons.

Results

Two-photon microscopy and behavioral recording show that ACh (left) and NA (right) neuromodulatory-related axonal fluorescence is closely related to moment-to-moment changes in behavioral state.

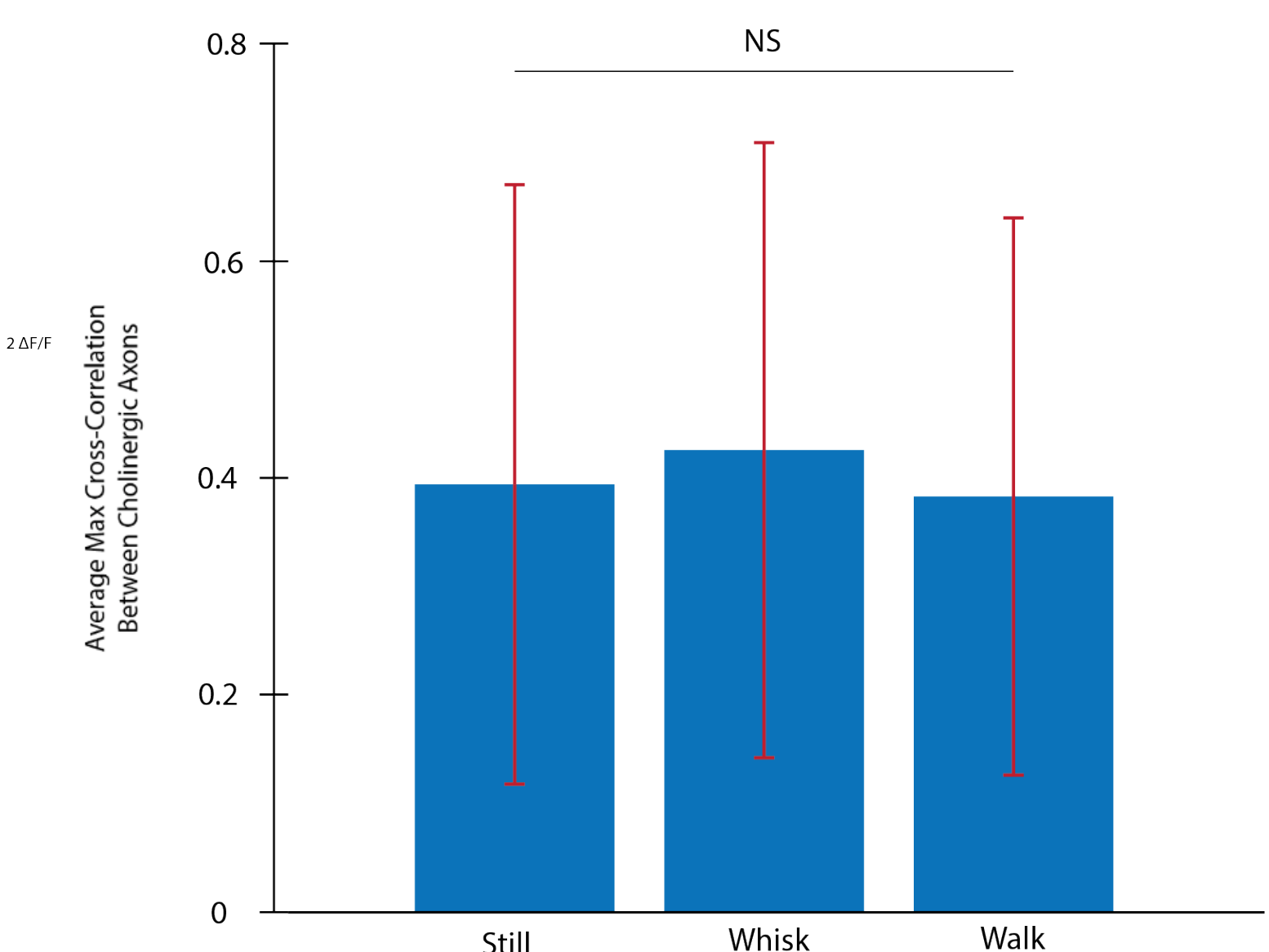
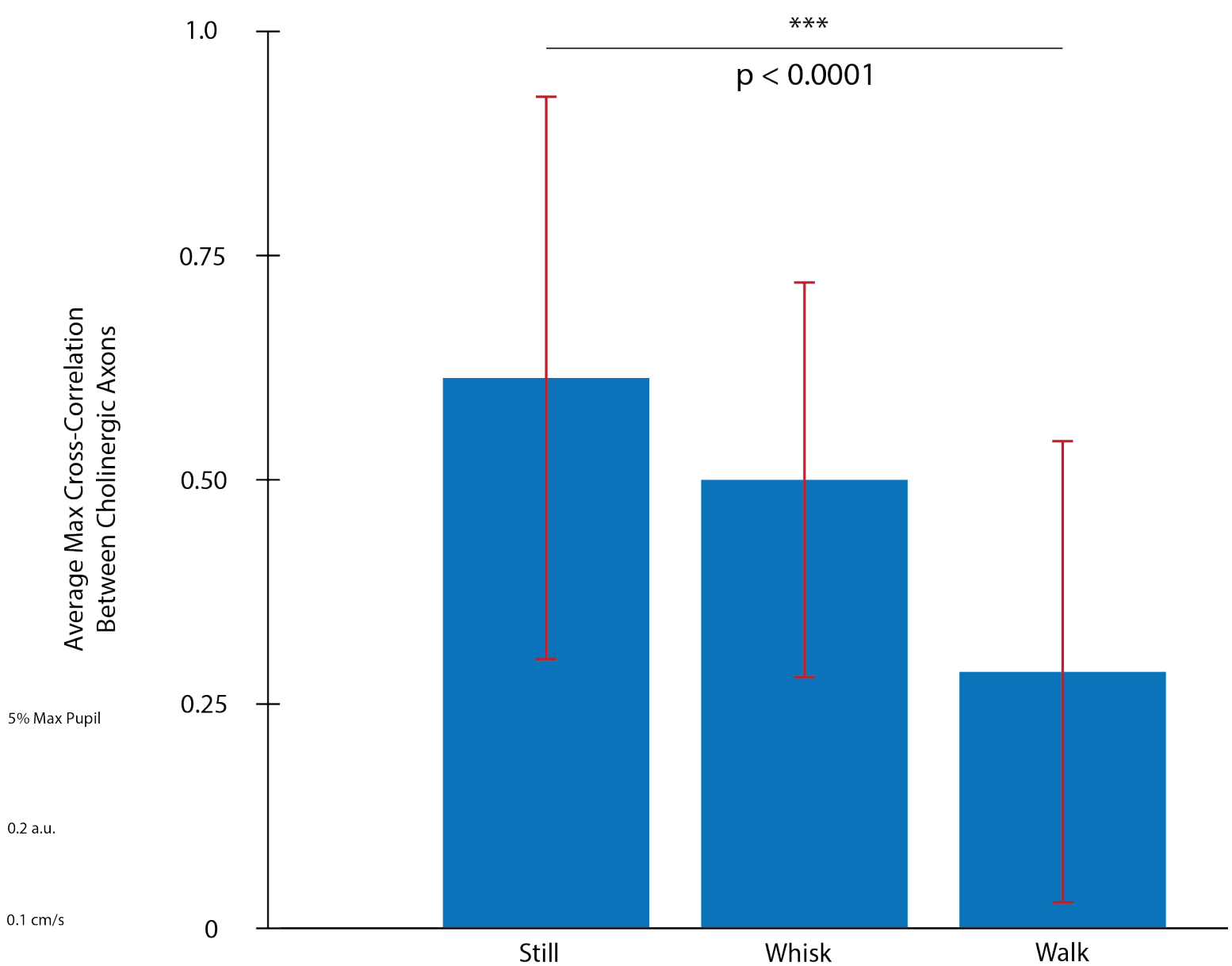


Increases in both ACh (top) and NA (bottom) neuromodulatory activity reliably precedes increases in whisking activity, but not walking behavior.



There exists more regional specificity with regard to localized, cholinergic neuromodulation of behavioral activity in a highly aroused animal (top).

- However, noradrenergic neuromodulation of these same behaviors exhibited more global synchrony (bottom).



Future Directions

Identify specific regions of the cortex from which ROIs were recorded.

- What are the relationships between cortical regions controlling distinct behaviors?

Implement other behavioral motifs into our behavioral analyses.

- Can we gain a more comprehensive understanding of neuromodulatory signaling with respect to more varied behavioral and arousal states?

References

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