



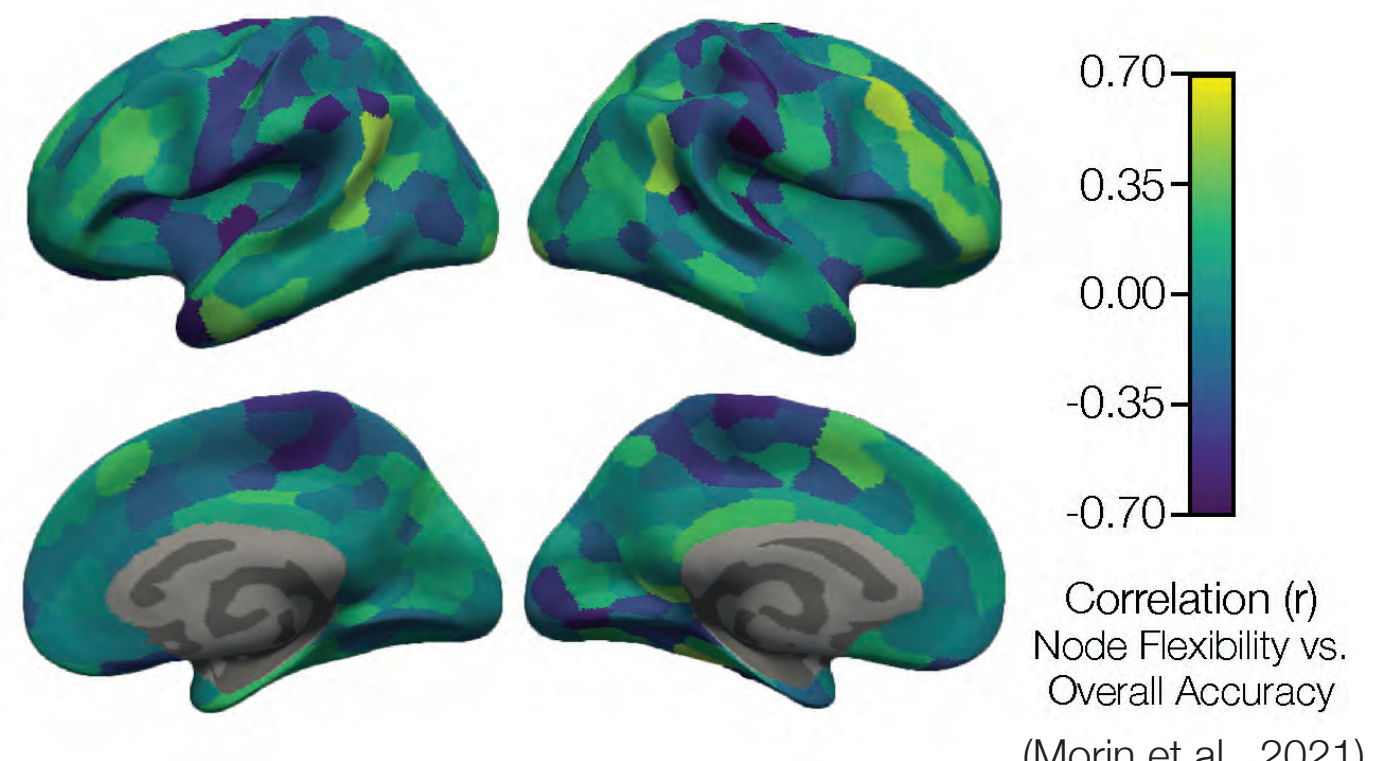
# Hierarchical gradients in prefrontal cortex and hippocampus support context-dependent rule learning

Thomas M. Morin,<sup>1,2,3</sup> Matthew F. Dunne,<sup>1,2,3</sup> Allen E. Chang,<sup>2,3</sup> and Chantal E. Stern<sup>1,2,3</sup>

<sup>1</sup> Graduate Program for Neuroscience, Boston University; <sup>2</sup> Center for Systems Neuroscience, Boston University; <sup>3</sup> Cognitive Neuroimaging Center, Boston University

## Background

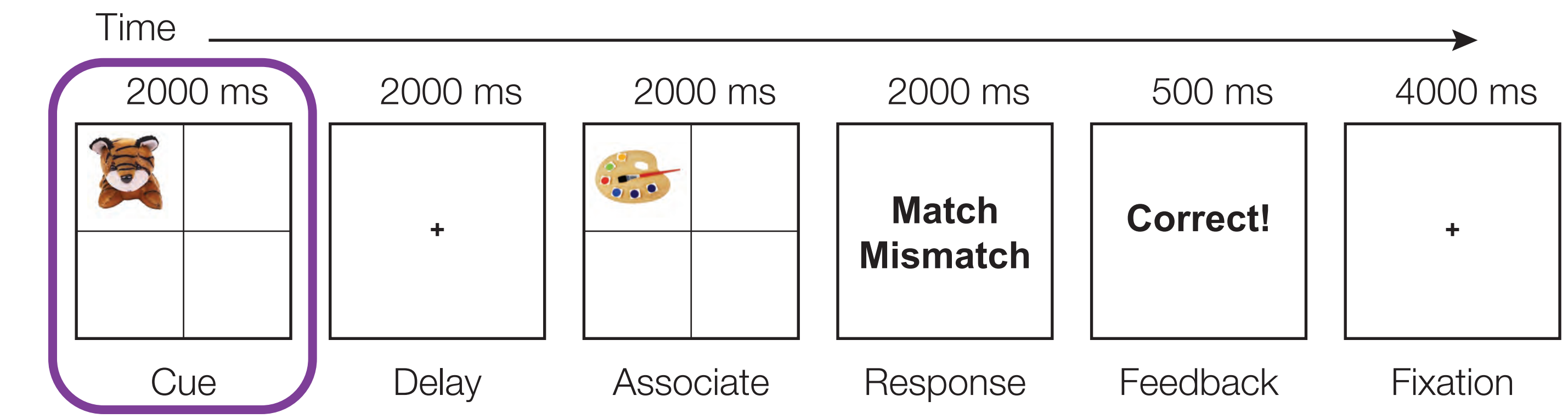
- The human hippocampus exhibits an anterior-posterior gradient organization when retrieving hierarchical rules (Brown et al., 2021).
- Prefrontal cortex is organized along a rostral-caudal axis with rostral regions important for incorporating abstract information and caudal regions implementing immediate motor actions (Badre & Nee, 2018).
- Previously, we showed that a more stable ventral attention network and more flexible cognitive control network support the formation of rule representations in successful learners (Morin et al., 2021).



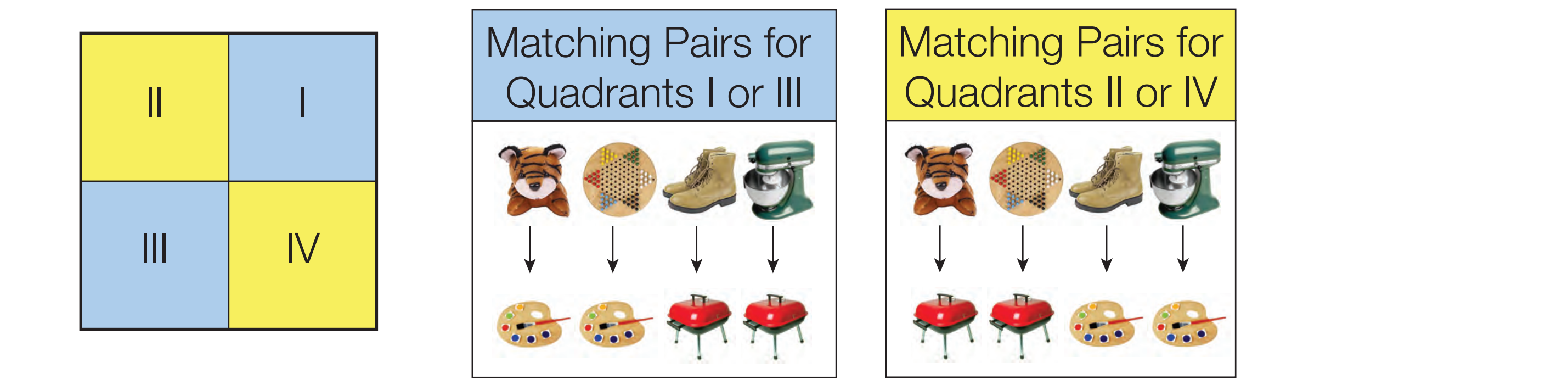
**We propose that a hierarchical functional connectivity gradient between the hippocampus and prefrontal cortex emerges as context-dependent rules are learned.**

## Methods

### A. Context-Dependent Rule Learning Task (Morin et al., 2021)

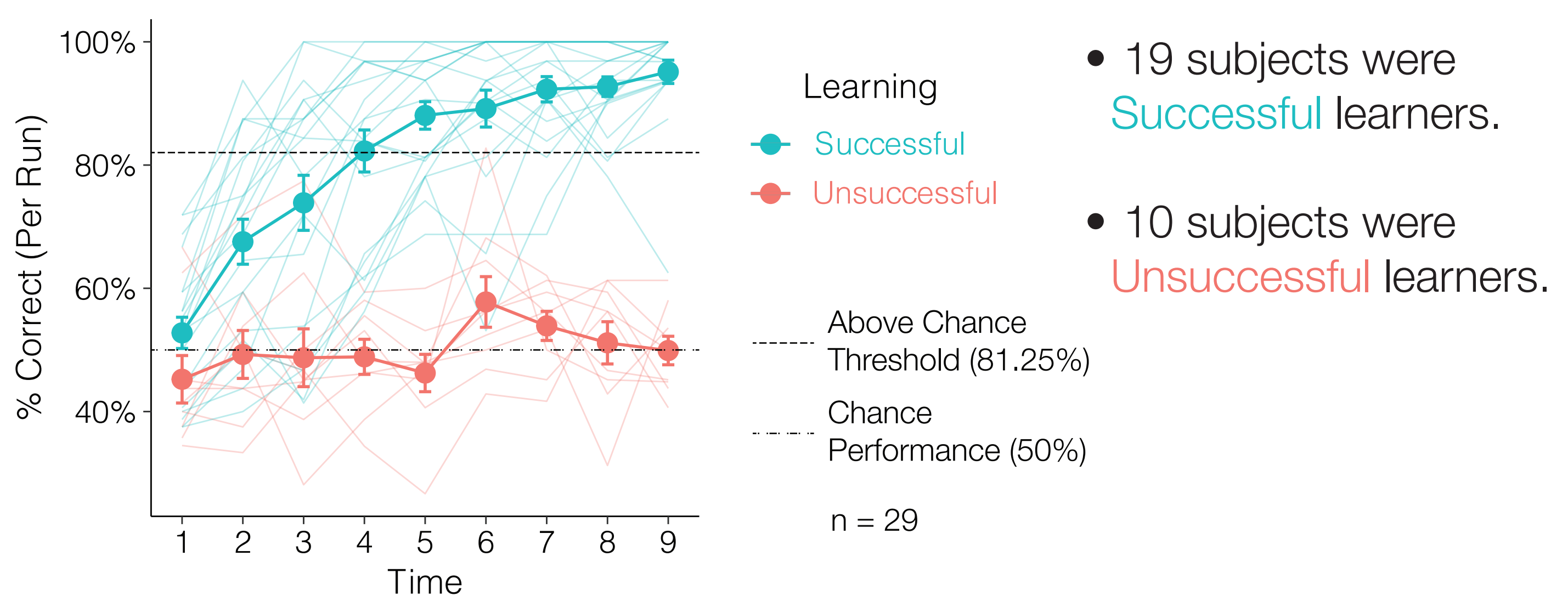


### B. Context-Dependent Rule Structure



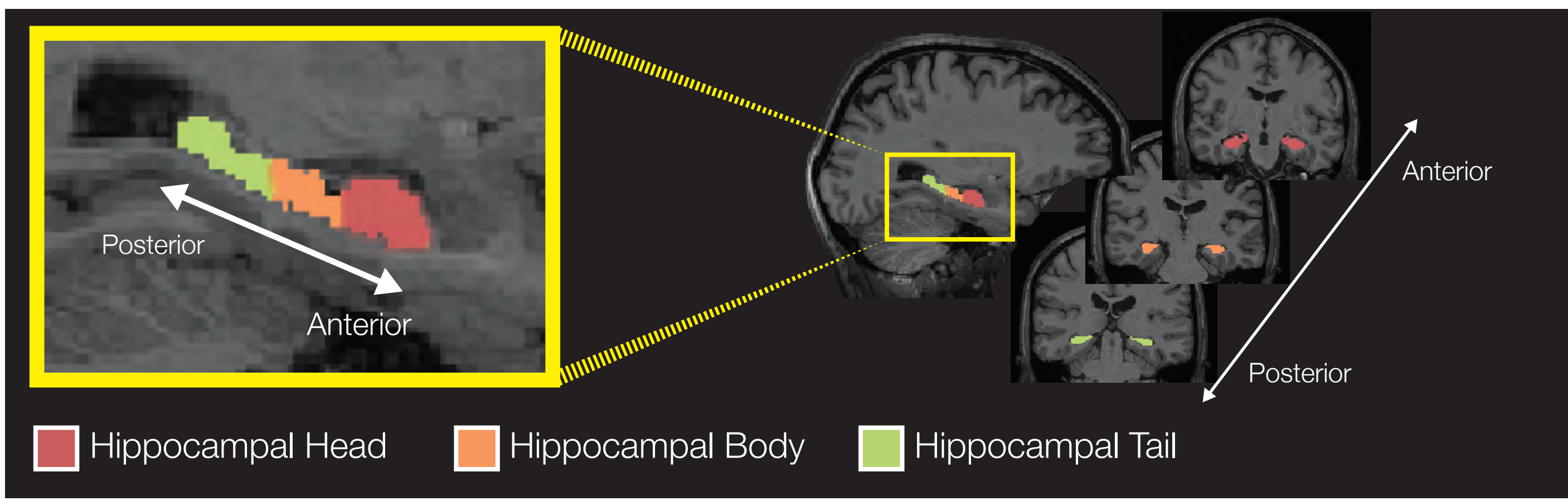
- Subjects attempted to learn the context-dependent rules across nine scanning runs.
- We used a beta-series correlation to calculate seed-based functional connectivity during each task period.
- Results shown on this poster are from the Cue Period.

## Behavioral Results

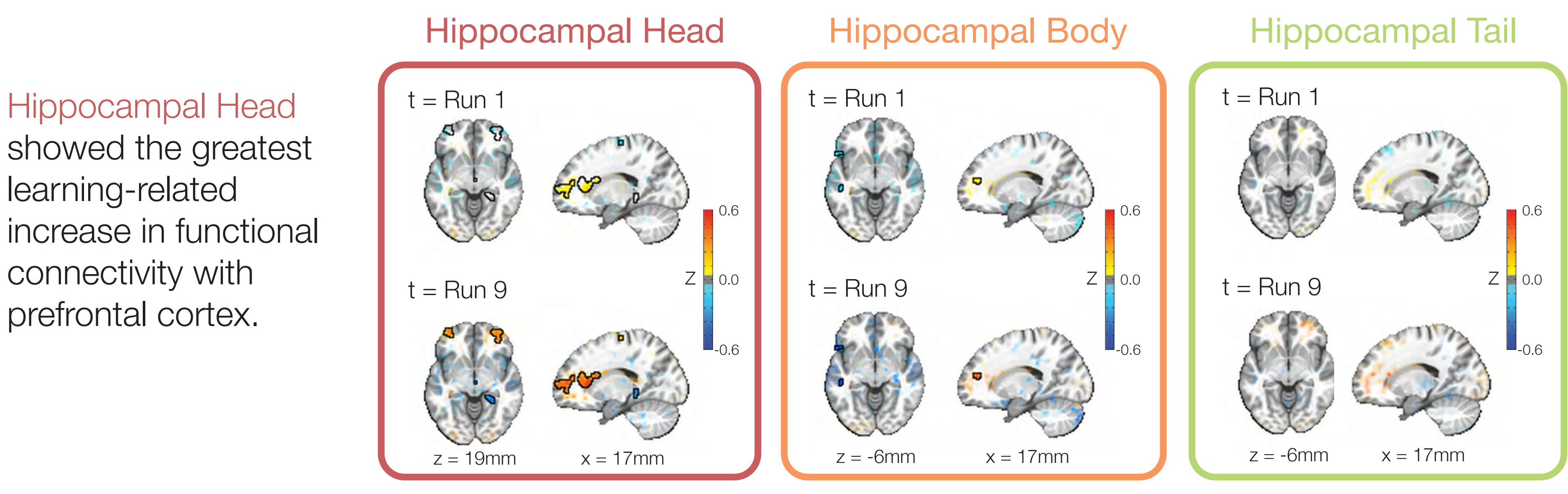


## Results

Hippocampal Head, Body, and Tail seed regions were traced for each subject (Pruessner et al., 2000; Daugherty et al., 2015).



### Seed-Based Functional Connectivity Successful > Unsuccessful Learners

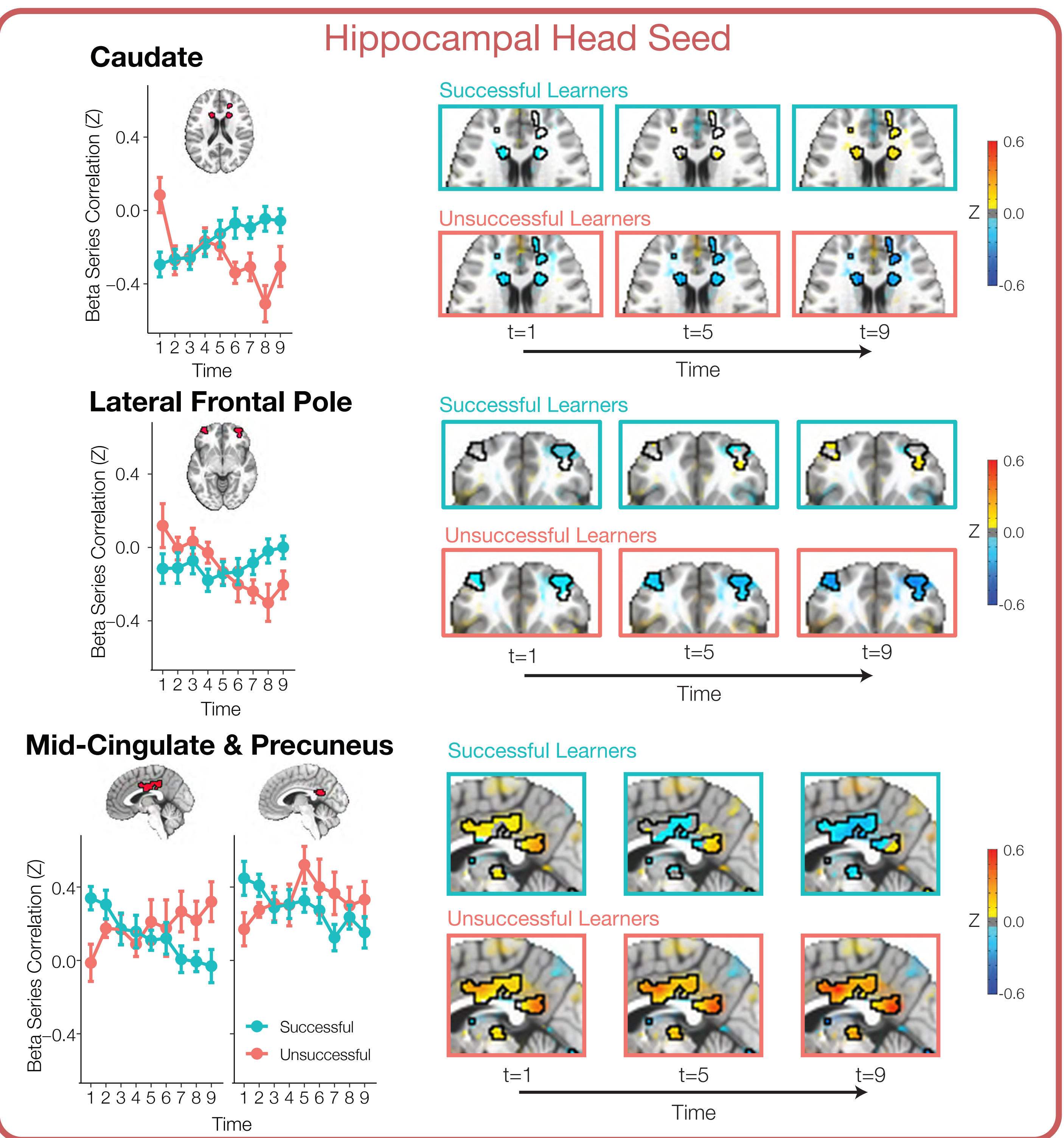


Hippocampal Head showed the greatest learning-related increase in functional connectivity with prefrontal cortex.

When examining functional connectivity with the Hippocampal Head over time...

Successful learners showed increasing hippocampal-head connectivity with caudate and lateral frontal pole throughout learning.

Successful learners showed decreasing hippocampal-head connectivity with the mid-cingulate and precuneus throughout learning.



## Summary & Conclusions

- Observed functional connectivity changes were strongest during the Cue period of the task, when subjects retrieved contextual information to determine which rule would apply.
- Increased functional connectivity between the hippocampal head and the frontal pole as well as the caudate supports the retrieval of successfully learned contexts when implementing context-dependent rules.
- This connectivity patterns emerges in successful learners as they learn, but not in a natural control group of unsuccessful learners.

**The results suggest that the hippocampal head is uniquely positioned to represent higher order rules and contexts through a gradient organization that mirrors the hierarchical organization of the prefrontal cortex.**

## References & Acknowledgements

### References

- Badre, D., & Nee, D.E. (2018). Frontal cortex and hierarchical control of behavior. *Trends in Cognitive Sciences*, 22(2), 170-188. <https://doi.org/10.1016/j.tics.2017.11.005>
- Brown, T.I., He, Q., Aselcioglu, I., & Stern, C.E. (2021). Evidence for a gradient within the medial temporal lobes for flexible retrieval under hierarchical task rules. *Hippocampus*, 31(9), 1003-1019. <https://doi.org/10.1002/HIPO.23365>
- Daugherty, A.M., Yu, Q., Flinn, R., & Ofen, N. (2015). A reliable and valid method for manual demarcation of hippocampal head, body, and tail. *International Journal of Developmental Neuroscience*, 41, 115-122. <https://doi.org/10.1016/J.IJDEVNEU.2015.02.001>
- Morin, T.M., Chang, A.E., Ma, W., McGuire, J.T., & Stern, C.E. (2021). Dynamic network analysis demonstrates the formation of stable functional networks during rule learning. *Cerebral Cortex*, 31(12), 5511-5525. <https://doi.org/10.1093/CERCOR/BHAB175>
- Pruessner, J.C., Li, L.M., Serles, W., Pruessner, M., Collins, D.L., Kabani, N., Lupien, S., & Evans, A.C. (2000). Volumetry of hippocampus and amygdala with high-resolution MRI and three-dimensional analysis software: Minimizing discrepancies between laboratories. *Cerebral Cortex*, 10(4), 443-442. <https://doi.org/10.1093/CERCOR/10.4.433>

### Funding

- Office of Naval Research MURI N00014-16-1-2832
- Office of Naval Research DURIP N00014-17-1-2304
- NSF Major Research Instrumentation 1625552



**Thomas Morin, Ph.D.**  
 tomorin@bu.edu  
 @ThomasMorin1  
 www.tmmorin.com