Resting-state medial temporal lobe connectivity with reward centers predicts how motivation impacts learning

Lea E. Frank, Alison R. Preston & Dagmar Zeithamova

UNIVERSITY OF OREGON

Reward Motivates Learning

- Monetary rewards improve memory performance such that greater reward values lead to better memory (Adcock et al., 2006; Gruber et al., 2016; Wolosin et al., 2012)
- Motivated learning tasks activate reward-processing structures, like the midbrain, striatum and medial orbitofrontal cortex, as well as the medial temporal lobe (MTL), including the hippocampus and parahippocampal cortex (Adcock et al., 2006; Bialleck et al., 2006; Wolosin et al., 2012)
- Interactions between hippocampus and midbrain have been demonstrated during motivated learning and in a post-learning resting-state scan (Adcock et al., 2006; Gruber et al., 2016)
- Individual differences in sensitivity to reward correlate with task-related activation and post-learning resting-state connectivity (Gruber et al., 2016; Wolosin et al., 2012)
- Patterns of resting-state functional connectivity before the influence of a task may help identify individual differences (Finn et al., 2015)

- *Does connectivity between reward and memory structures increase as a function of learning?*
- *Does connectivity between reward and memory structures predict individual differences in reward-modulated learning?*

Methods

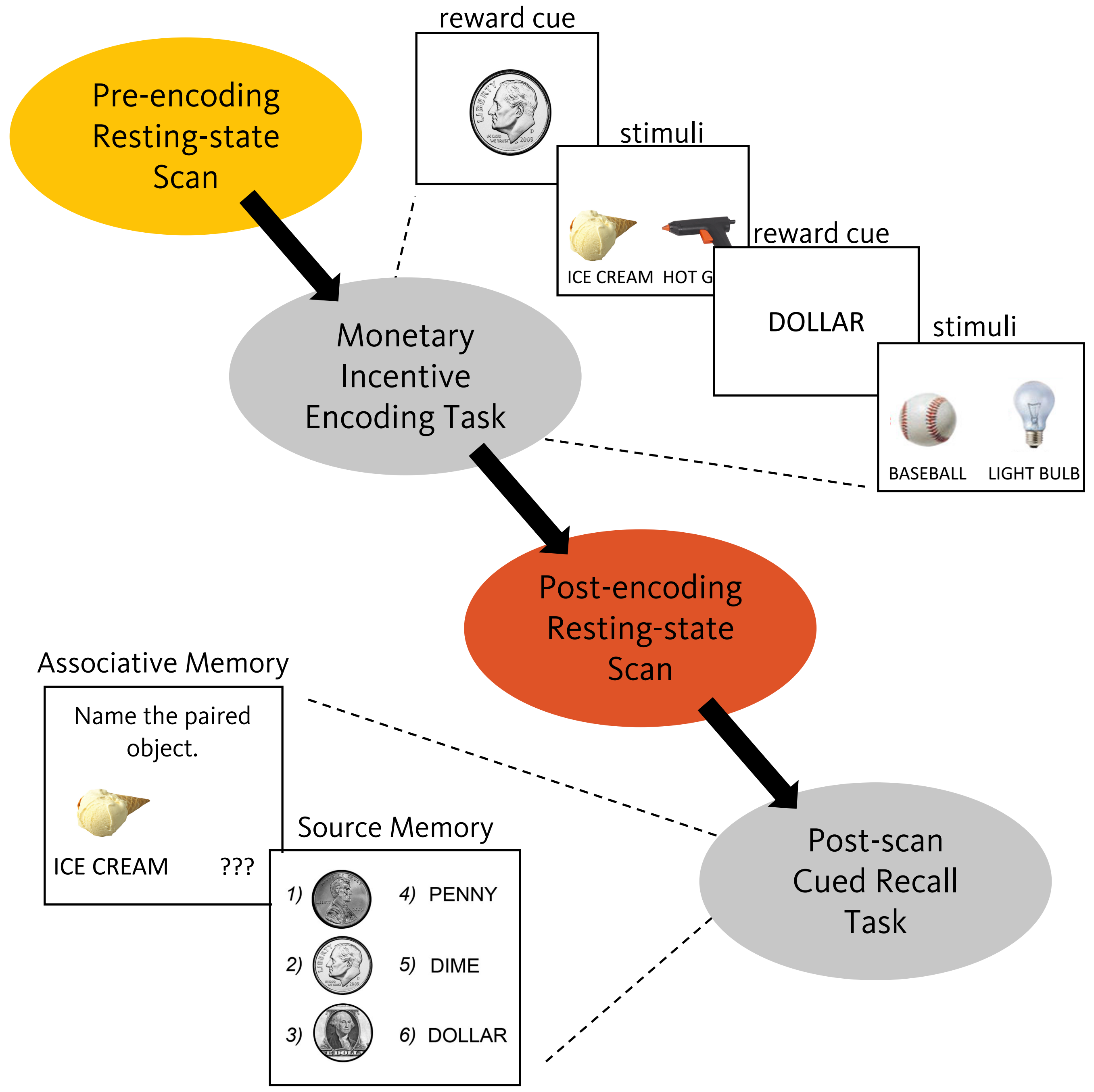
Participants
- N = 34, age 18-30, right handed
- 5 subject removed for excessive motion, 3 for interruptions during scanning, and 2 for missing data (final N = 24)

Scanning Parameters
- TR = 2s, 1.7 mm isotropic, multiband 3, grappa 2

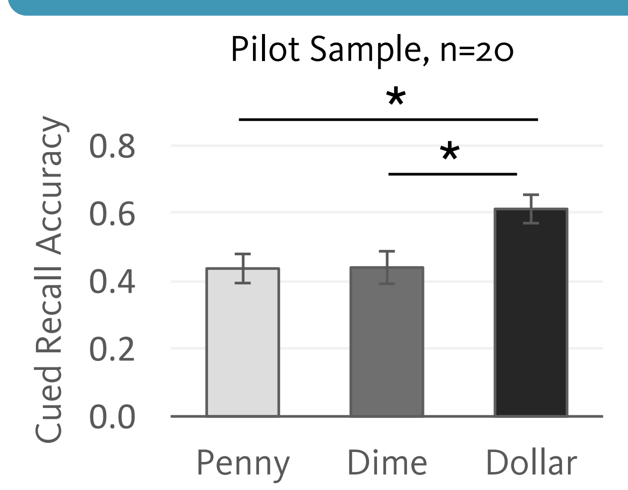
Scrubbing resting state scan:
- Scrubbing criteria: framewise displacement (FD) > .3, global signal (DVARS) > .4
- Thresholds were chosen as they removed all differences between groups on control measures (cerebrospinal fluid, white matter, FD, and DVARS)

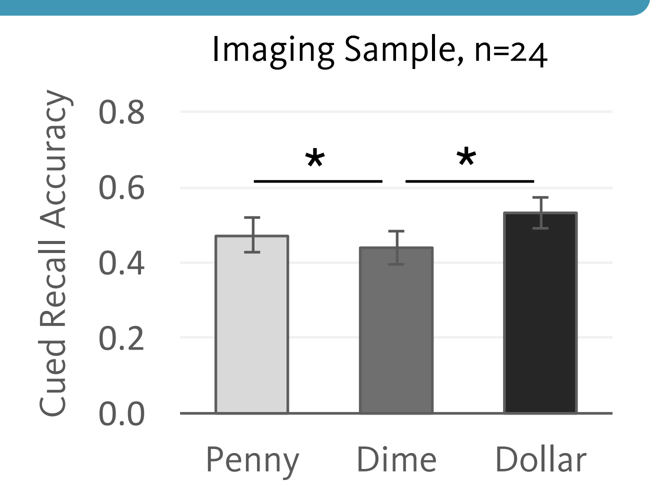
Connectivity Metric:
- Partial correlations controlling for white matter, cerebrospinal fluid, 6 motion parameters, and their derivatives. Fisher's z transformed

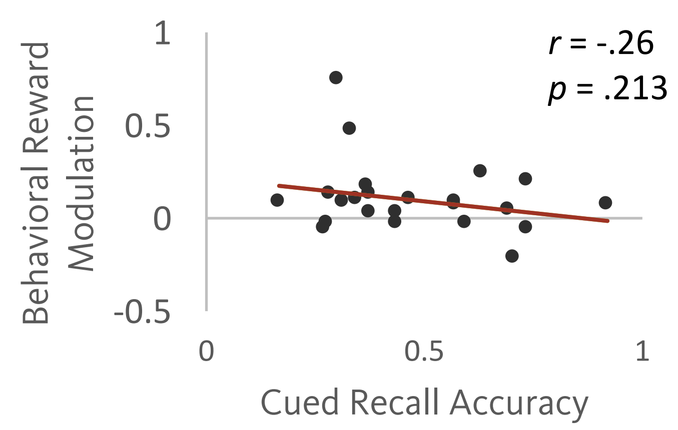
fMRI Paradigm



Behavioral Results







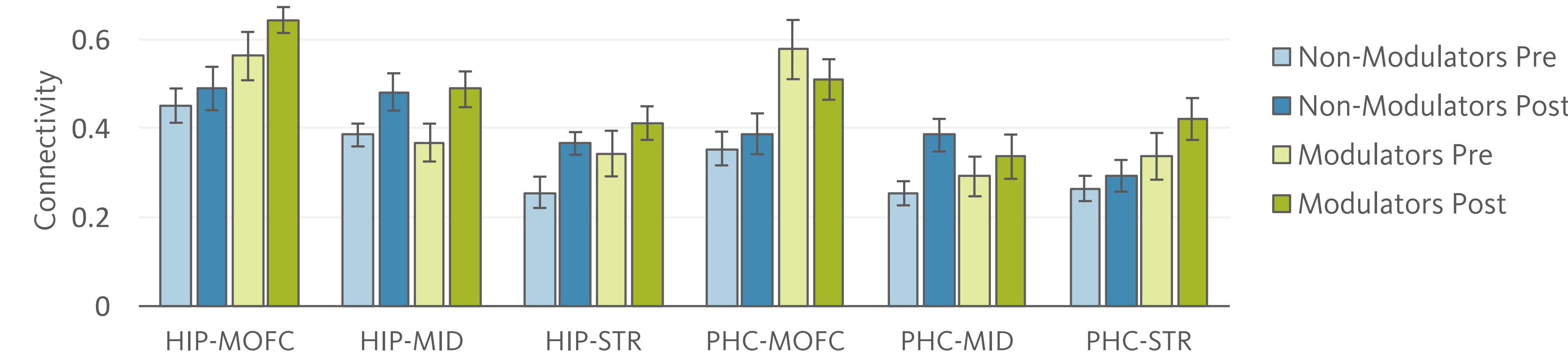
- Cued recall performance was better for high-value trials but behavioral sensitivity to reward varied among individuals
- Subjects split into 2 groups, reward **modulators** and **non-modulators**
- Overall recall accuracy and behavioral reward modulation not significantly correlated

Resting-state Functional Connectivity Results

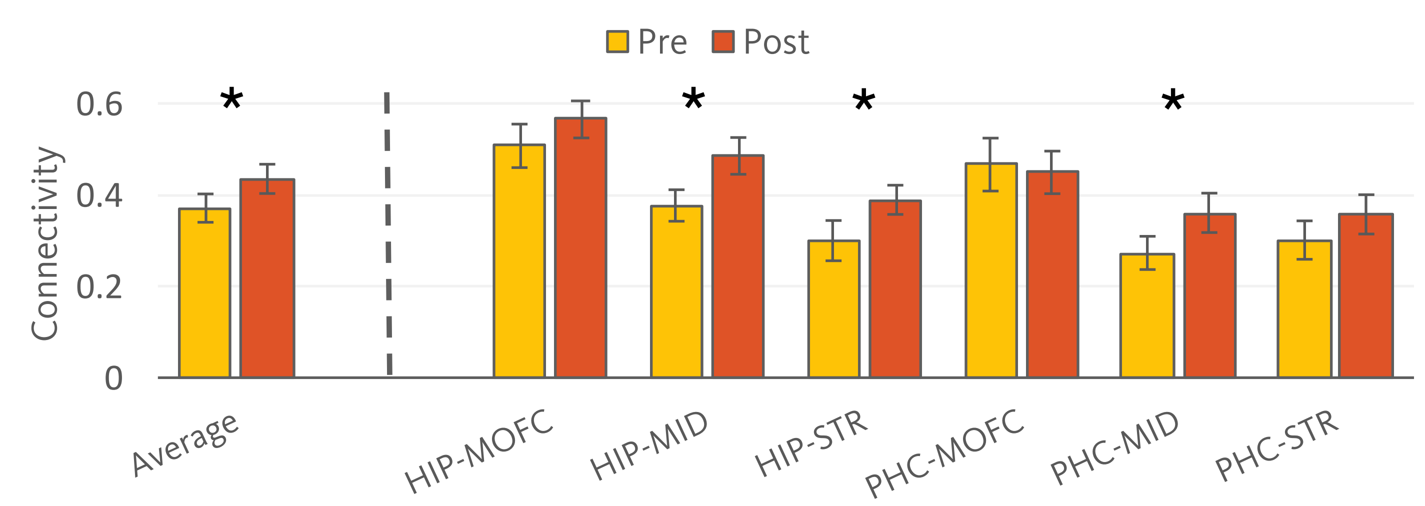
2x2x3 Repeated Measures ANOVA

Within Subjects:
- Pre vs. Post
- Memory Structures (HIP, PHC)
- Reward Structures (MOFC, VIDC, STR)

Between Subjects:
- Non-modulators vs. Modulators

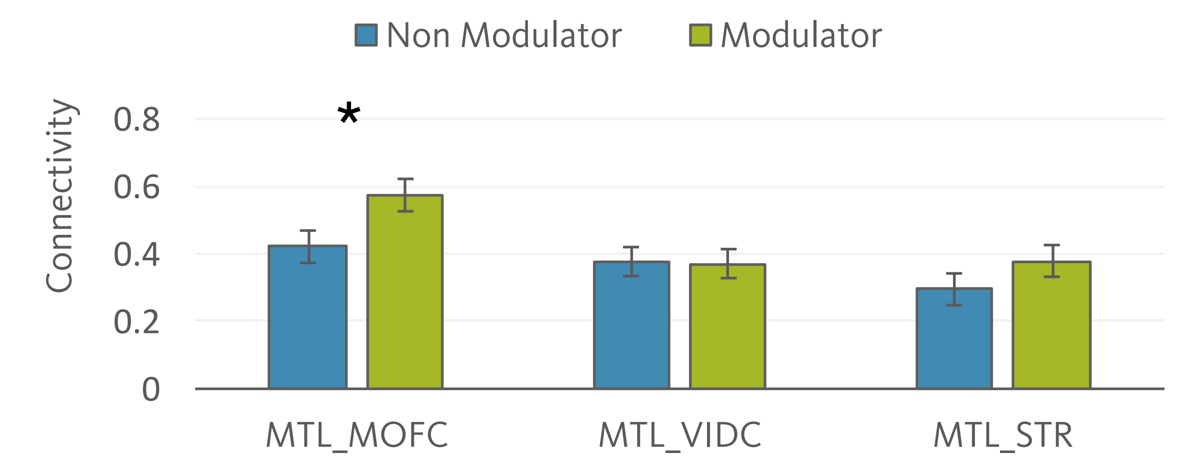


MTL Connectivity with Midbrain and Striatum Increases Pre to Post-Learning



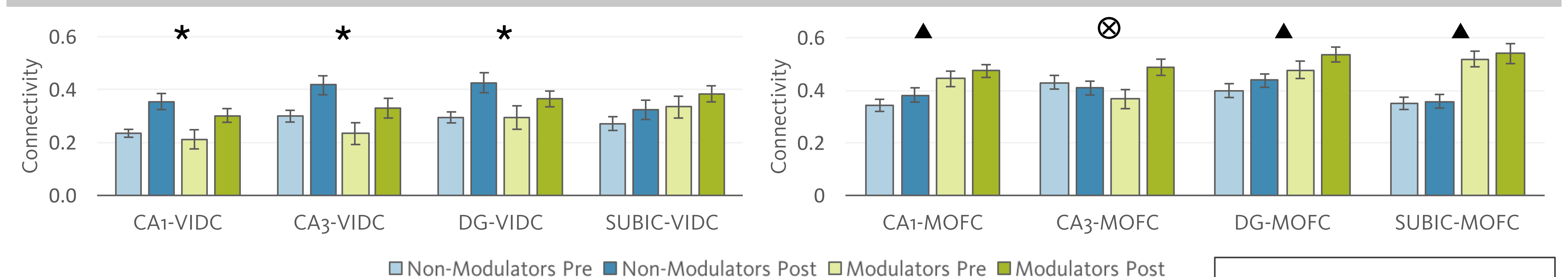
- MTL connectivity, specifically with the striatum and midbrain, significantly increased as a function of learning

MTL-MOFC Connectivity Predicts Behavioral Reward Modulation



- MTL-MOFC connectivity did not change pre to post, but rather tracked individual differences in reward modulation

Exploratory Analyses: Are hippocampal connectivity patterns driven by specific subfields?



- Greater connectivity with MOFC in modulators than in non-modulators was present in CA1, DG & subiculum
- CA3-MOFC connectivity increased pre-to-post in modulators only
- Pre-to-post increase in connectivity with midbrain was present in all subfields (n.s. in subiculum). Same pattern held for connectivity with striatum (data not shown)

★ = significant pre-to-post change
▲ = significant difference between modulators and non-modulators
⊗ = significant interaction

Conclusions

- Medial temporal lobe connectivity with the midbrain and striatum strengthened as a function of reward-motivated learning
- Medial orbitofrontal cortex connectivity with medial temporal lobe tracked individual differences in reward sensitivity
- Similar patterns were found for individual hippocampal-subfields, except for CA3 which showed significant pre-to-post increases for modulators but not non-modulators

References

Adcock, R.A., Thangavel, A., Whitfield-Gabrieli, S., Knutson, B., & Gabrieli, J.D.E. (2006). Reward-Motivated Learning: Mesolimbic Activation Precedes Memory Formation. *Neuron*, *50*(3), 507–517. https://doi.org/10.1016/j.neuron.2006.03.036

Bialleck, K.A., Schaal, H.P., Kranz, T.A., Fell, J., Elger, C.E., & Axmacher, N. (2011). Ventromedial prefrontal cortex activation is associated with memory formation for predictable rewards. *PloS One*, *6*(2), e16695. https://doi.org/10.1371/journal.pone.0016695

Gruber, M. J., Ritchey, M., Wang, S. F., Doss, M. K., & Ranganath, C. (2016). Post-learning Hippocampal Dynamics Promote Preferential Retention of Rewarding Events. *Neuron*, *89*(5), 1110–1120. https://doi.org/10.1016/j.neuron.2016.01.017

Finn, E.S., Shen, X., Scheinost, D., Rosenberg, M.D., Huang, J., Chun, M.M., Papademtris, X. & Constable, R. T. (2015). Functional connectome fingerprinting: Identifying individuals using patterns of brain connectivity. *Nature Publishing Group*, *18*(11), 1664–1671. https://doi.org/10.1038/nn.4135

Wolosin, S.M., Zeithamova, D., & Preston, A.R. (2012). Reward Modulation of Hippocampal Subfield Activation during Successful Associative Encoding and Retrieval. *Journal of Cognitive Neuroscience*, *24*(7), 1532–1547. https://doi.org/10.1162/jocn_a_00237