Individual Differences in Memory Functions and Their Relation to Hippocampal Connectivity

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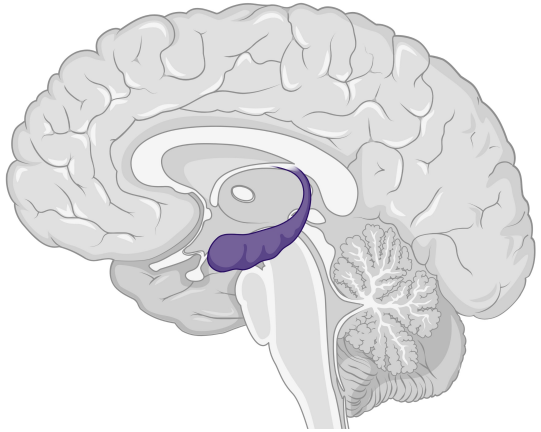
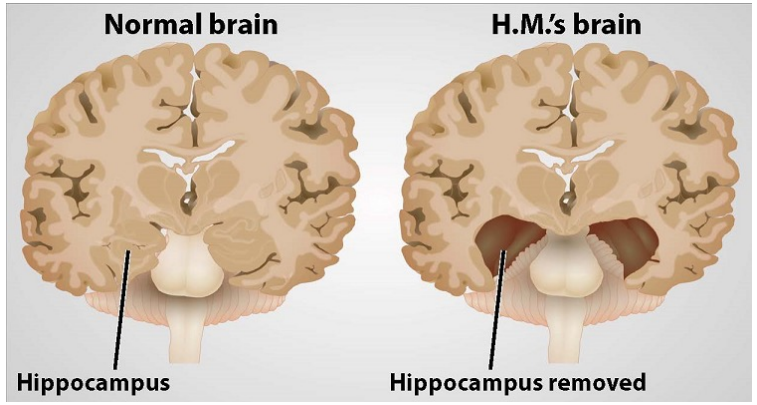
Chapter Outline

1. Introduction
2. Functional connectivity between memory and reward centers across task and rest track memory sensitivity to reward
3. Differential functional connectivity along the long axis of the hippocampus aligns with differential role in memory specificity and generalization
4. Hippocampal connectivity predicting individual differences in memory specificity and generalization
5. Discussion

Hippocampus supports multiple memory functions



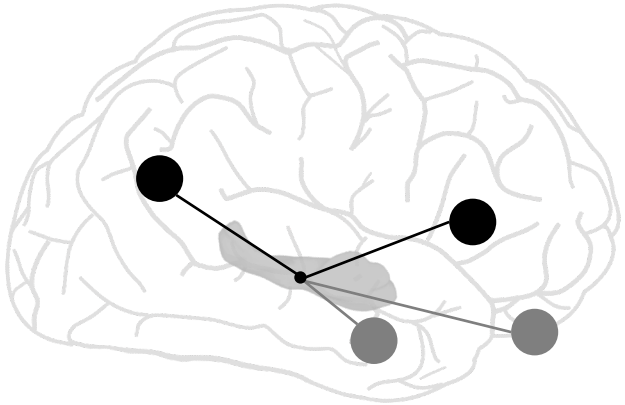


- Forming and storing new episodic memories[1-2]
- Other functions:
  - Spatial navigation[3]
  - Prioritizing memory for salient events[4-5]
  - Linking related memories to form generalized knowledge[6-7]

How does a single structure support different types of learning?

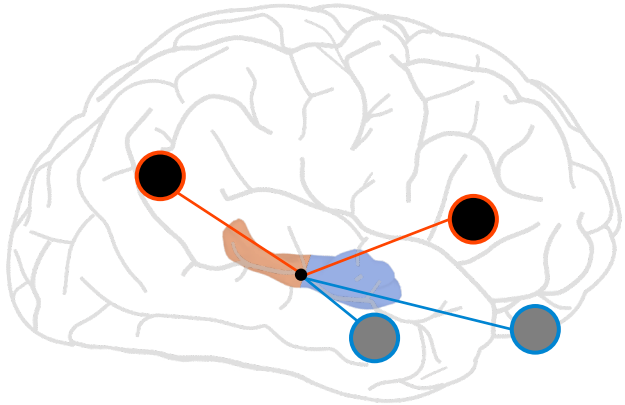
1. Scovil & Millner (1957); 2. Squire (1992); 3. Ekstrom et al. (2003); 4. Adcock et al. (2006); 5. Phelps (2004); 6. Preston et al. (2004); 7. Bowman & Zeithamova (2018)

How does the hippocampus support multiple forms of learning?



Function 1 Function 2

Hippocampus interacts with distinct brain regions to support different types of memory[1-3]

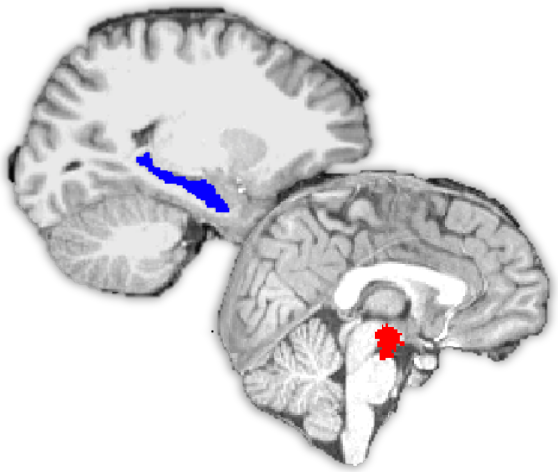


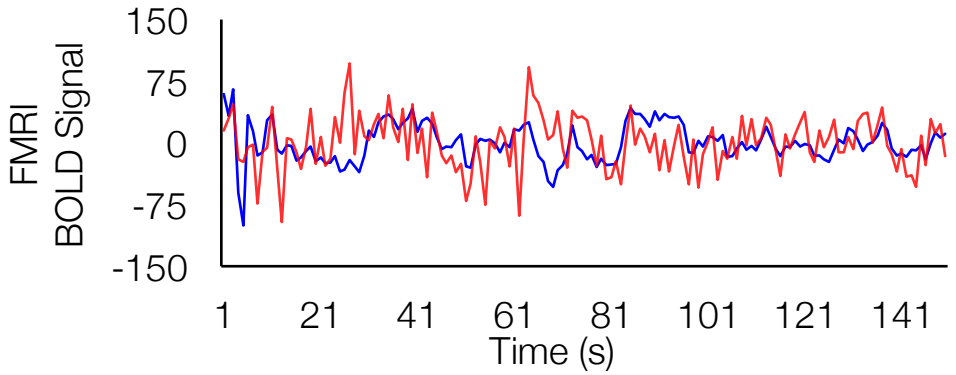
Posterior fine-grained ⟷ **Anterior** coarse-grained

Functional differences between anterior and posterior hippocampus contribute to different types of memory[4]

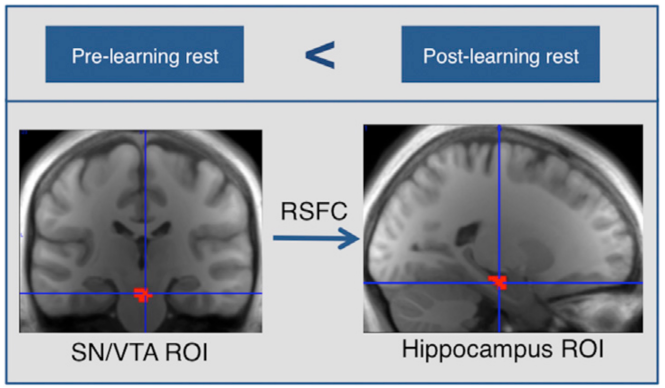
1. Schlichting, Mumford & Preston (2015); 2. Zeithamova, Dominick & Preston (2012); 3. Wittman et al. (2005); 4. Poppenk et al. (2013)

Functional connectivity measures coordinated activity between distant brain regions

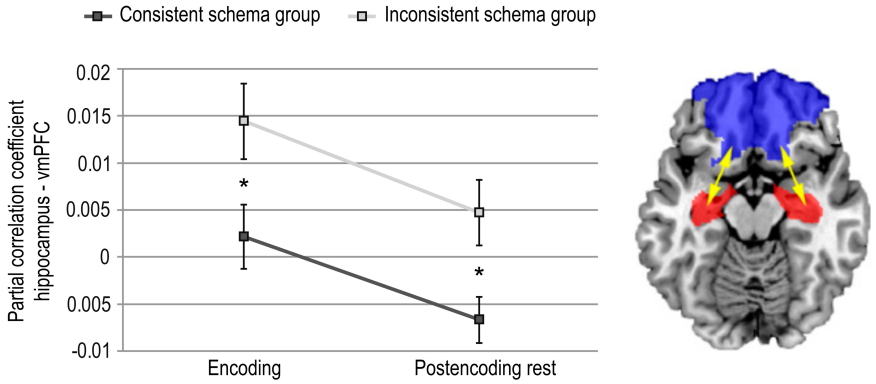




stronger correlations = greater functional relatedness[1]



Gruber et al. (2016). *Neuron*

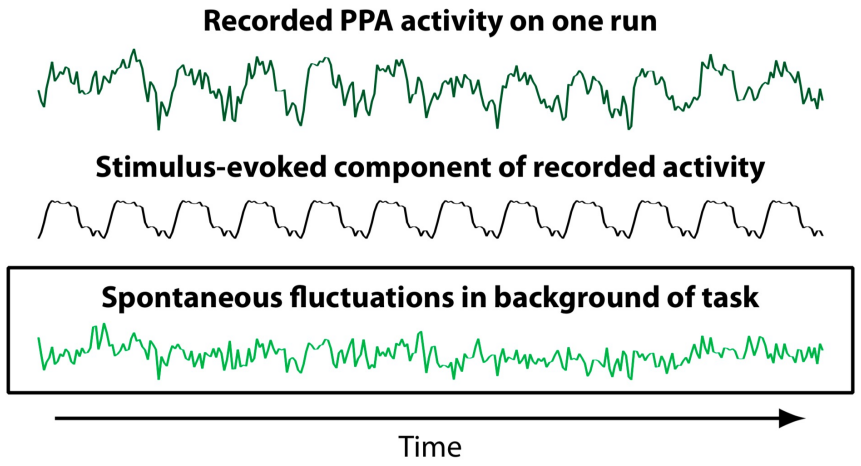


van Kesteren et al. (2010). *PNAS*

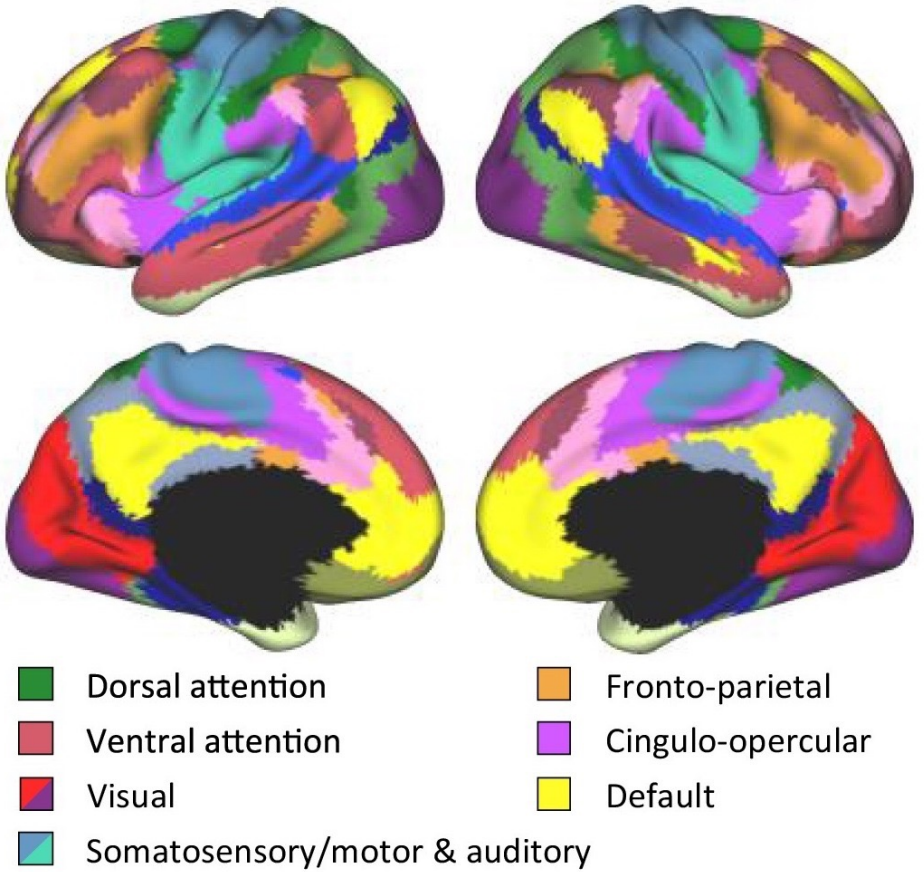
1. Friston (1994)

Intrinsic functional connections predict individual behavior

- Intrinsic connectivity measured independent of an external task
  - resting-state functional connectivity[1-2]
  - background connectivity[3]



Al-Aidroos, Said & Turke-Browne (2012). *PNAS*



Wig (2018). *Trends in Cognitive Sciences*

1. Buckner, Krienen & Yeo (2013); 2. Finn et al. (2015); 3. Fox et al. (2006)

Goals of Dissertation

1. Understand how different hippocampal connections relate to different memory processes

2. Test whether intrinsic hippocampal connections can predict individual memory abilities

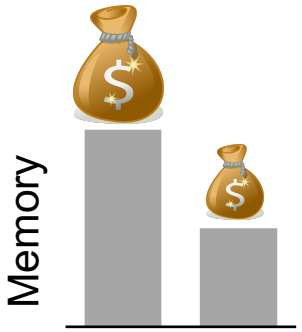
Chapter 2

Functional connectivity between memory and reward centers across task and rest track memory sensitivity to reward

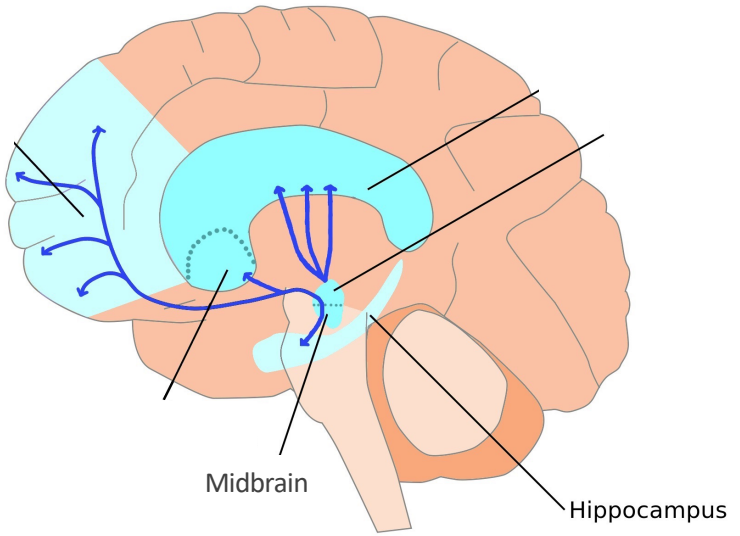
Frank, Preston & Zeithamova (2019). *Cognitive, Affective & Behavioral Neuroscience*

Prioritization of motivationally salient information

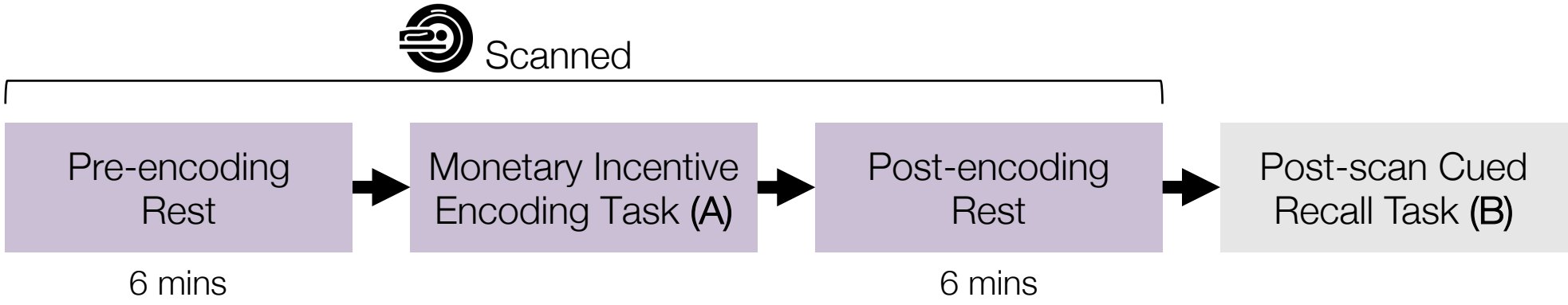
- Individual differences in how reward influences memory[1-2]
- Focus on midbrain and task-driven interactions[1-3]



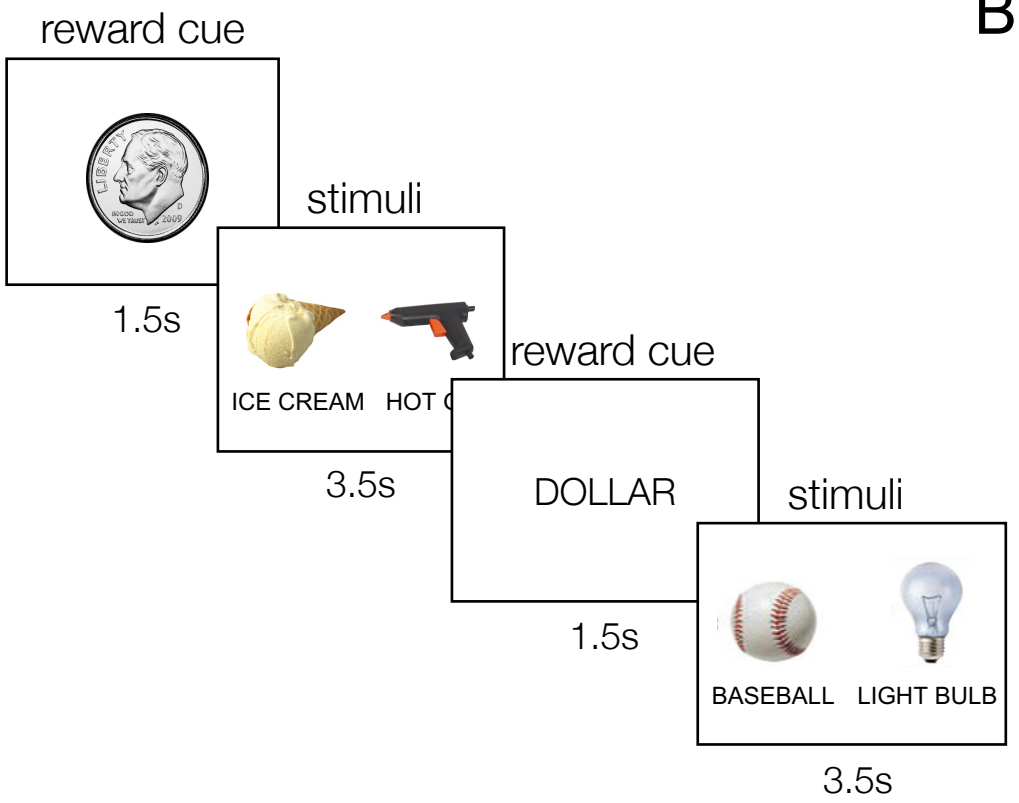
1. *Do hippocampal connections to additional reward processing regions also support reward-motivated learning?*
2. *Do intrinsic hippocampal connections predict individual effects of reward on memory?*



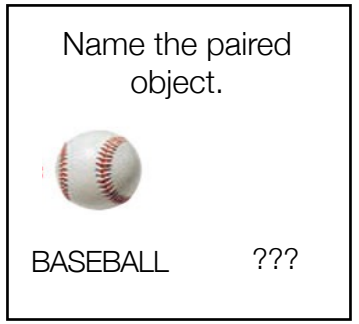
1. Wolosin, Zeithamova & Preston (2012); 2. Gruber et al. (2016); 3. Lisman & Grace (2005)

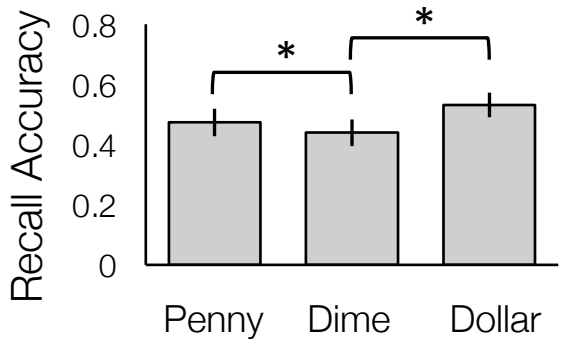


A



B



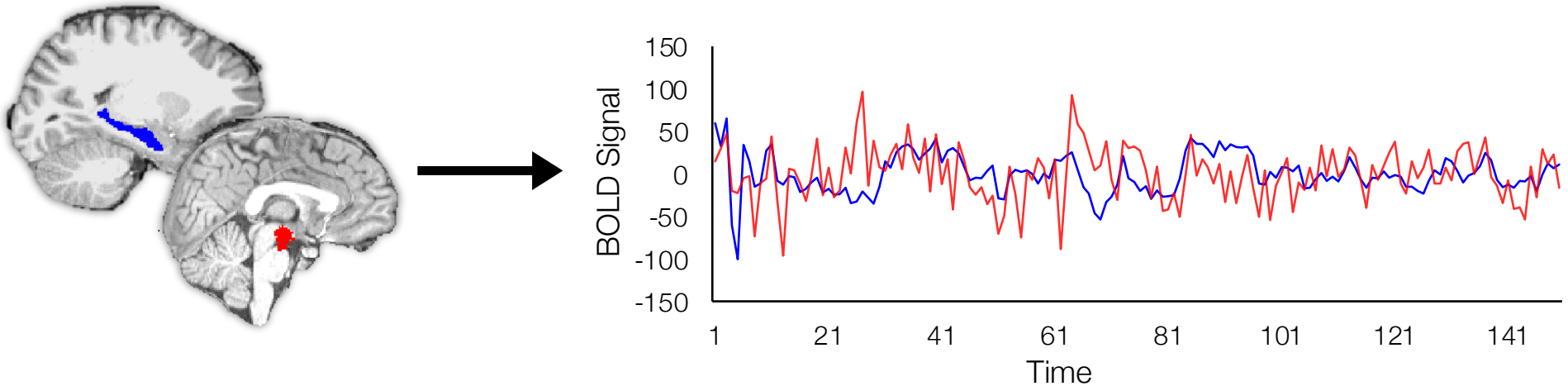


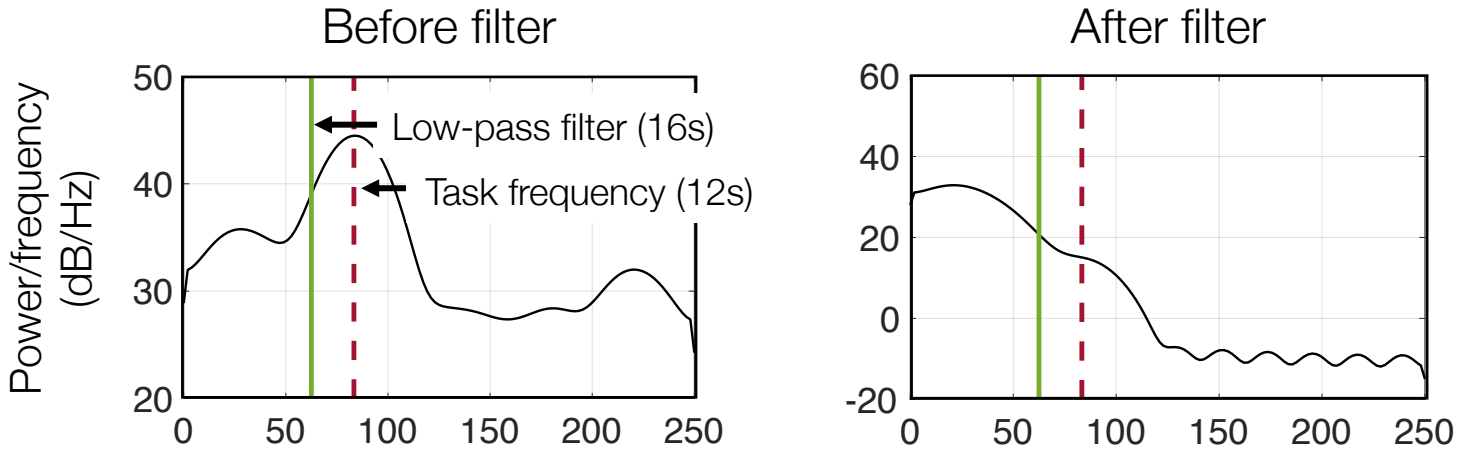
Behavioral reward modulation (BRM) = dollar – dime

Modulators Non-Modulators

N = 24

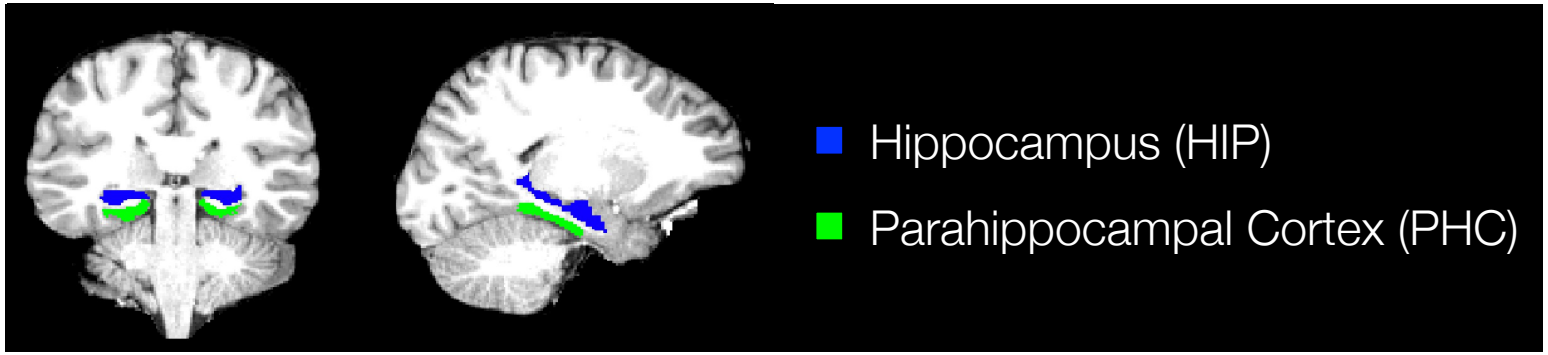
Measuring resting-state and background connectivity



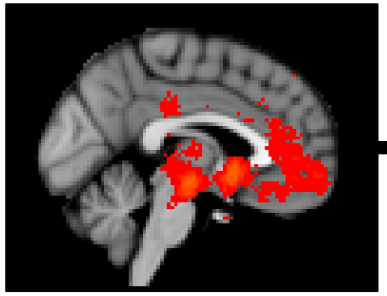


*LOC signal in example subject

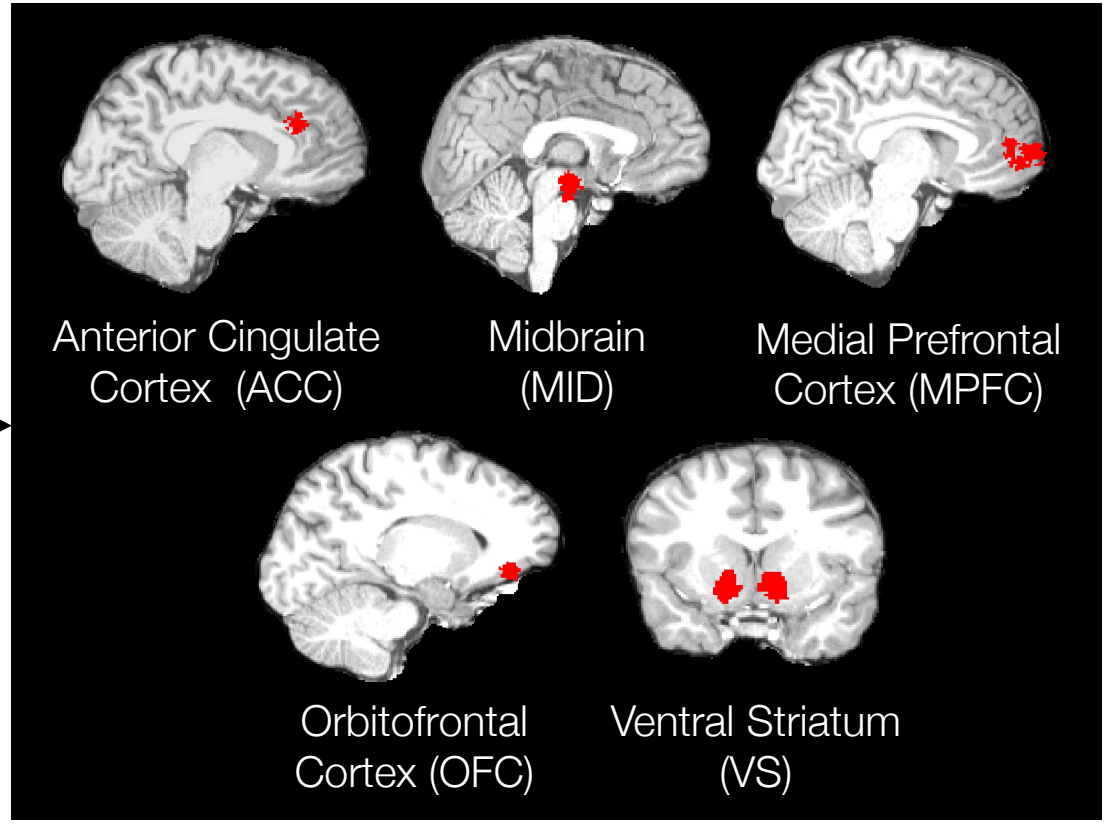
Memory Regions of Interest (ROIs)



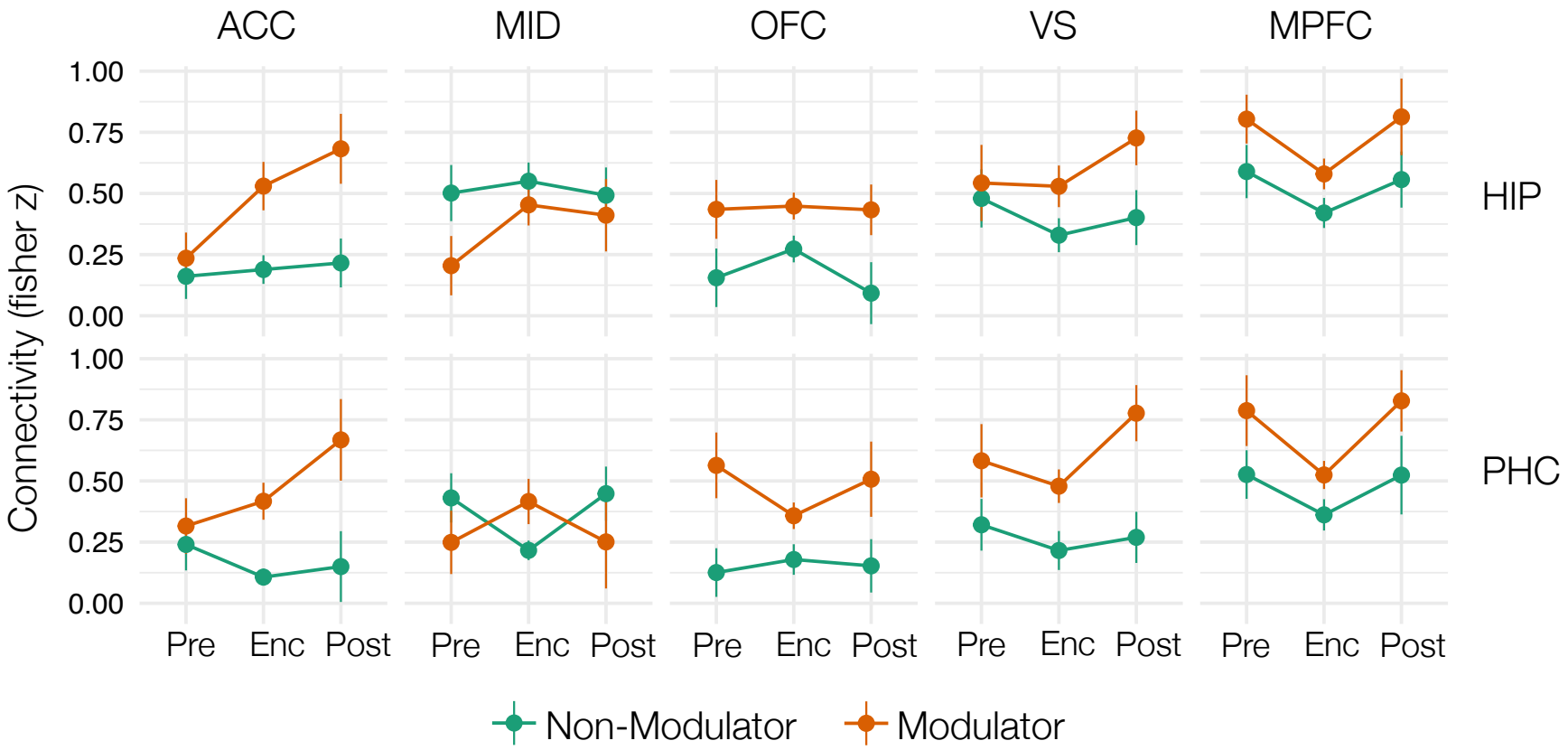
Reward ROIs



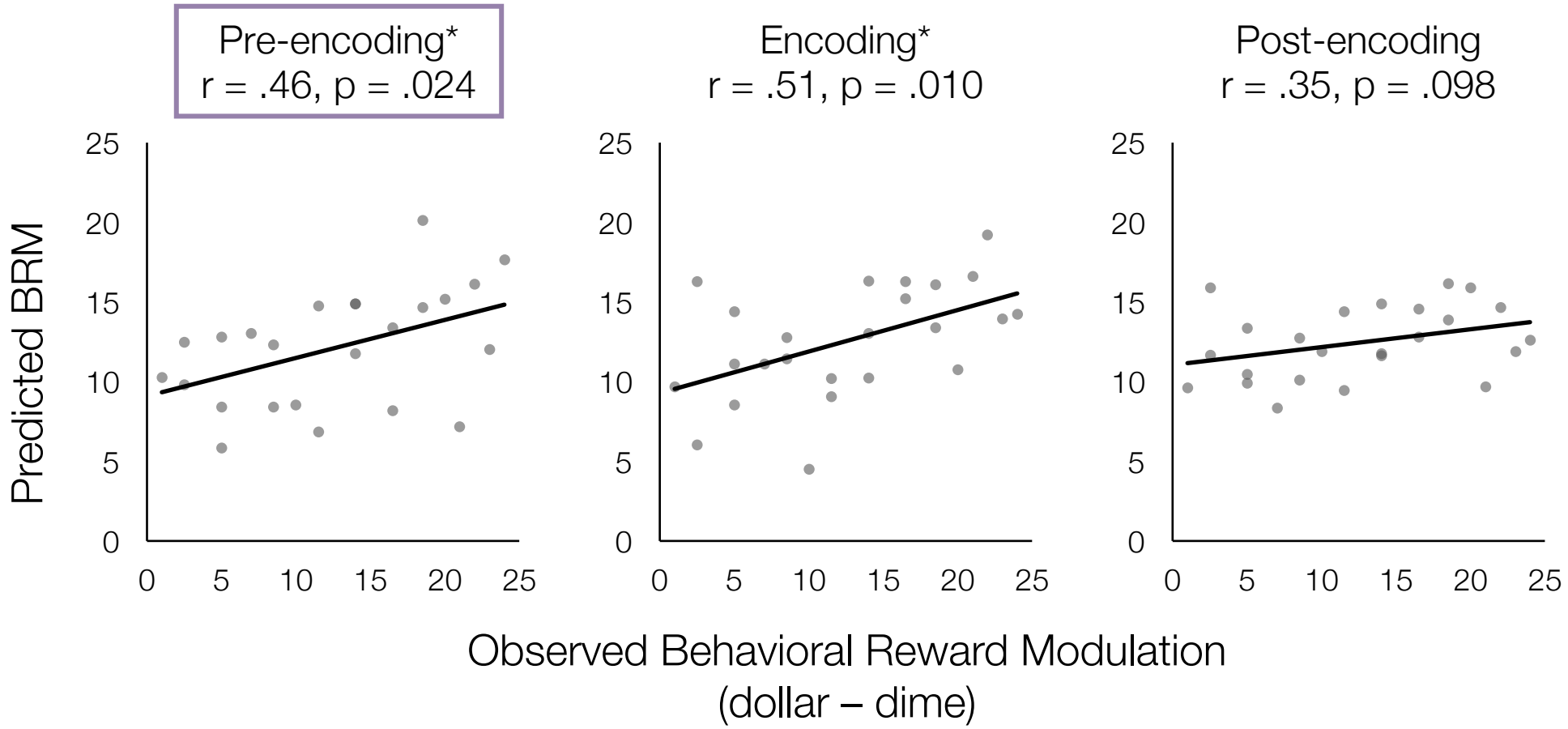
Meta-analysis of "reward" studies



2 Memory ROIs
x
5 Reward ROIs
= 10 connections



- Modulators show greater connectivity than non-modulates
- Relationship to behavior apparent *before learning* and relatively stable
- No reliable differences between rest and task

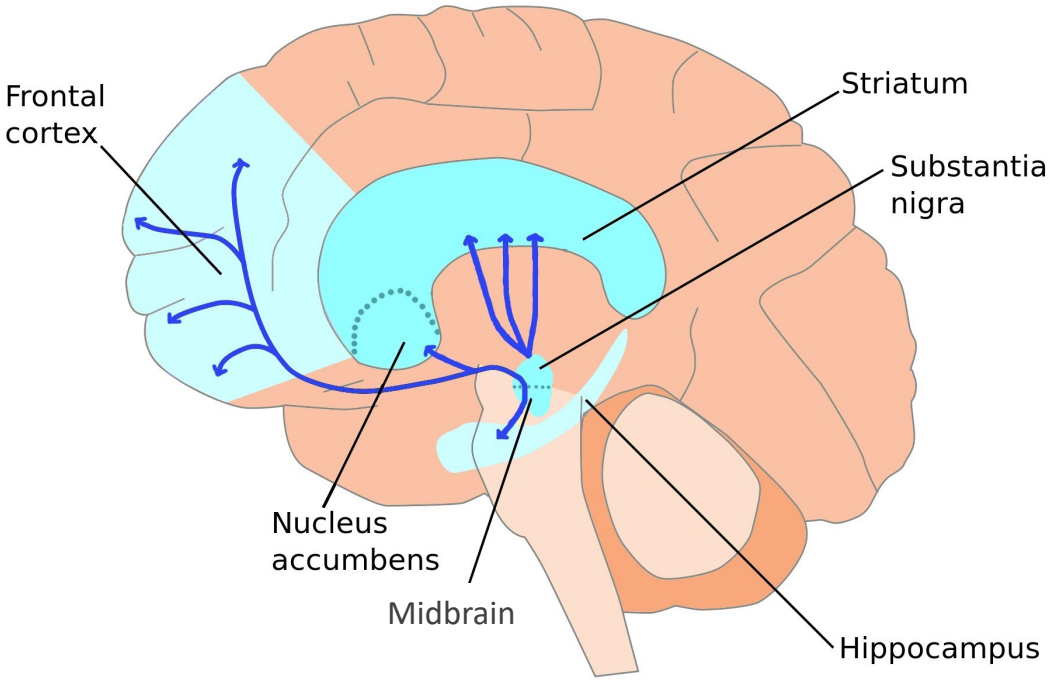


↳ Connectivity *prior to* learning predicts individual BRM scores

Chapter Summary

- Hippocampal interactions with a broader network of reward-processing regions track individual effects of reward on memory

- Relationship between connectivity and behavior was present prior to learning



Chapter 3

Differential functional connectivity along the long axis of the hippocampus aligns with differential role in memory specificity and generalization

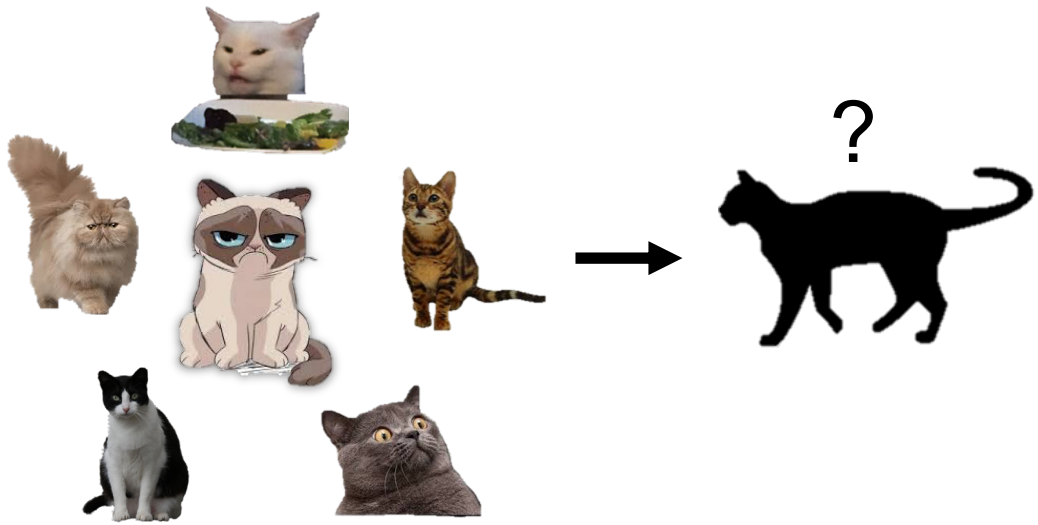
Frank*, Bowman* & Zeithamova (2019). *Journal of Cognitive Neuroscience*

*these authors contributed equally to this work

Generalization = link related experiences to generate new knowledge

- Retrieving memories of individual experiences[1-2] (memory specificity)
- Recalling generalized knowledge, like concepts[3-4]

How do intrinsic hippocampal interactions contribute to category generalization?



1. Kumaran & McClelland (2012); 2. Medin & Schaffer (1978). 3. Posner & Keele (1968); 4. Bowman & Zeithamova (2018)

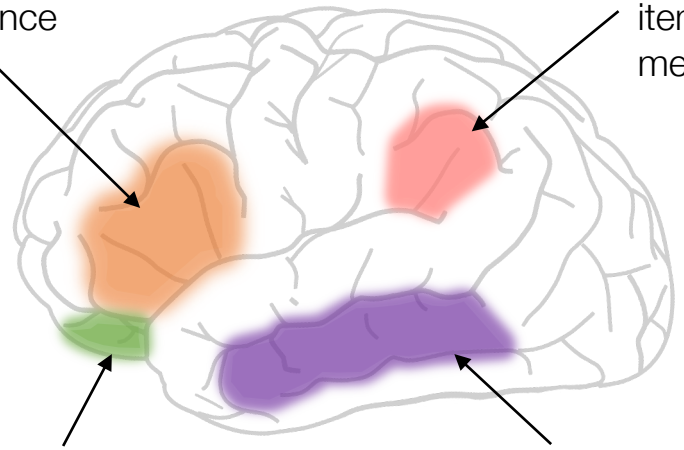
Putative Specificity Regions

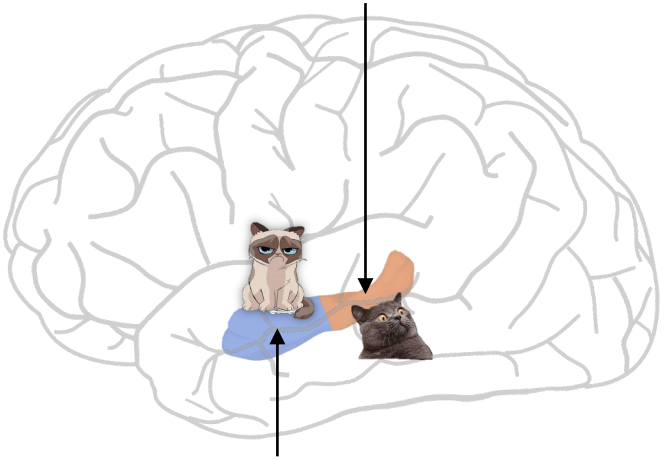
fine-grained/specific

Posterior Hippocampus

Inferior frontal gyrus[5-6]
resolving interference

Angular gyrus[7-8]
item representation
memory fidelity





Ventromedial prefrontal cortex[1-2]
memory integration
schemas

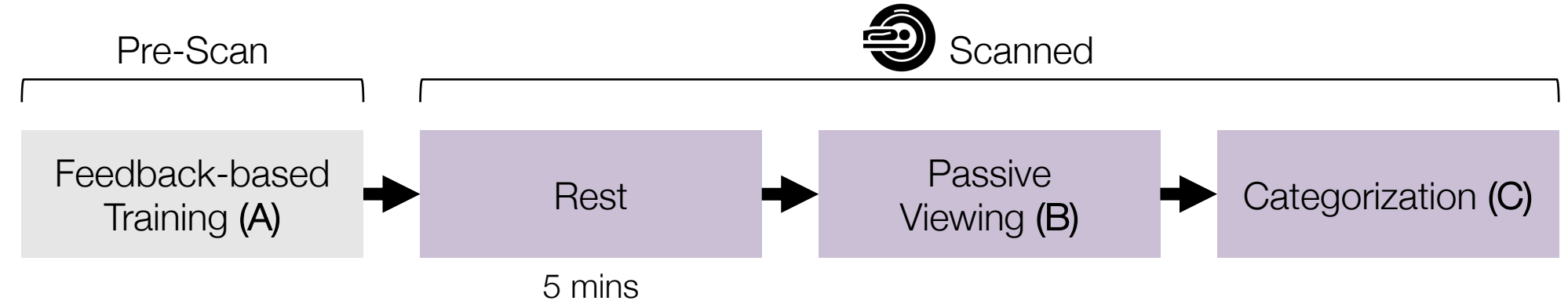
Middle temporal gyrus[3-4]
concepts
semantic memory
"gist" representations

Anterior Hippocampus

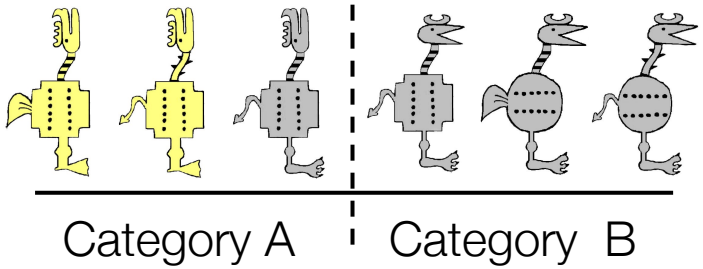
coarse-grained/generalized

Putative Generalization Regions

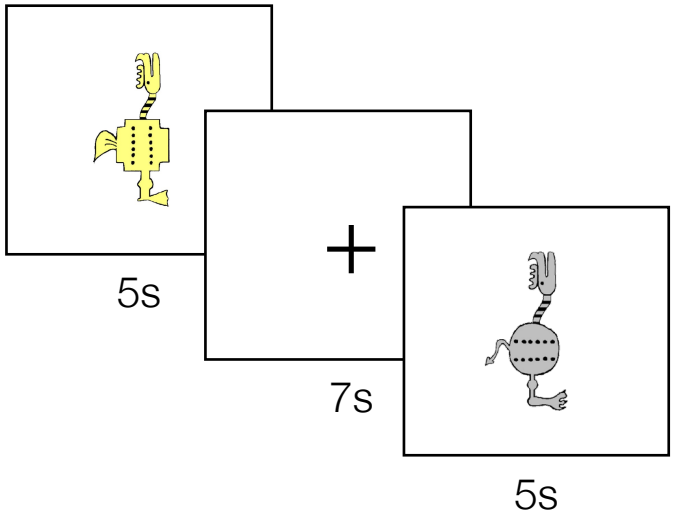
1. Schlichting, Mumford & Preston (2015); 2. van Kesteren et al. (2012); 3. Mummery et al. (2000); 4. Dennis, Kim & Cabeza (2008); 5. Kuhl et al. 2007; 6. Bowman & Dennis (2016). 7. Kuhl & Chun (2014); 8. Xiao et al. (2017) Poppenk et al. (2013).


Pre-Scan
Scanned
Feedback-based Training (A)
Rest
Passive Viewing (B)
Categorization (C)
5 mins

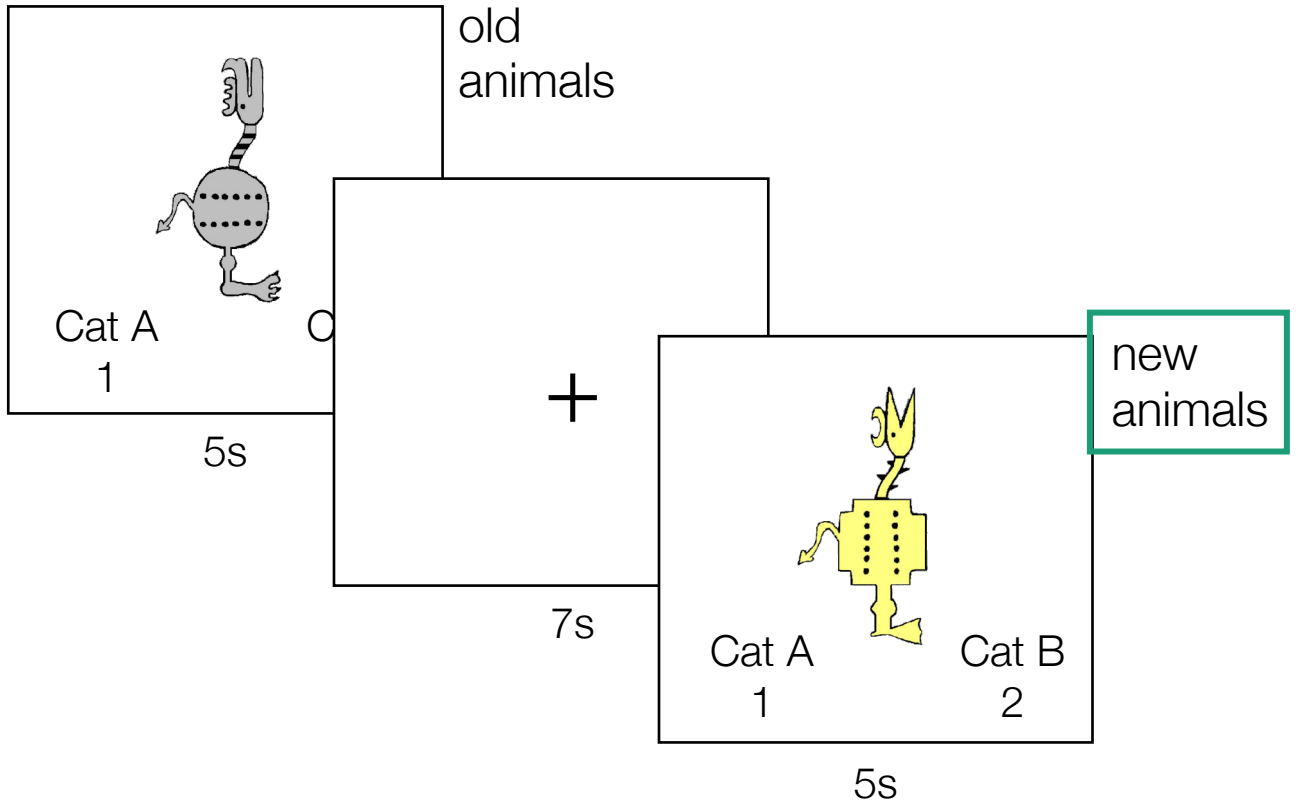
A


Category A
Category B

B

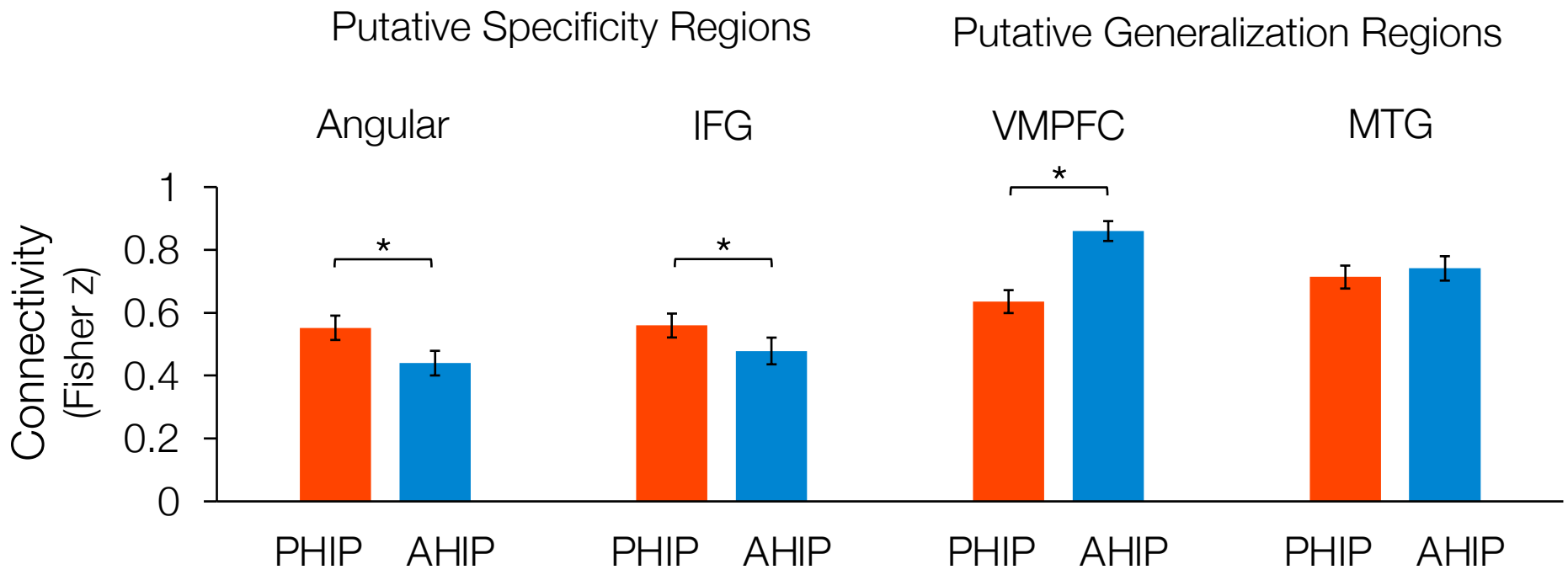

5s
7s
5s

C

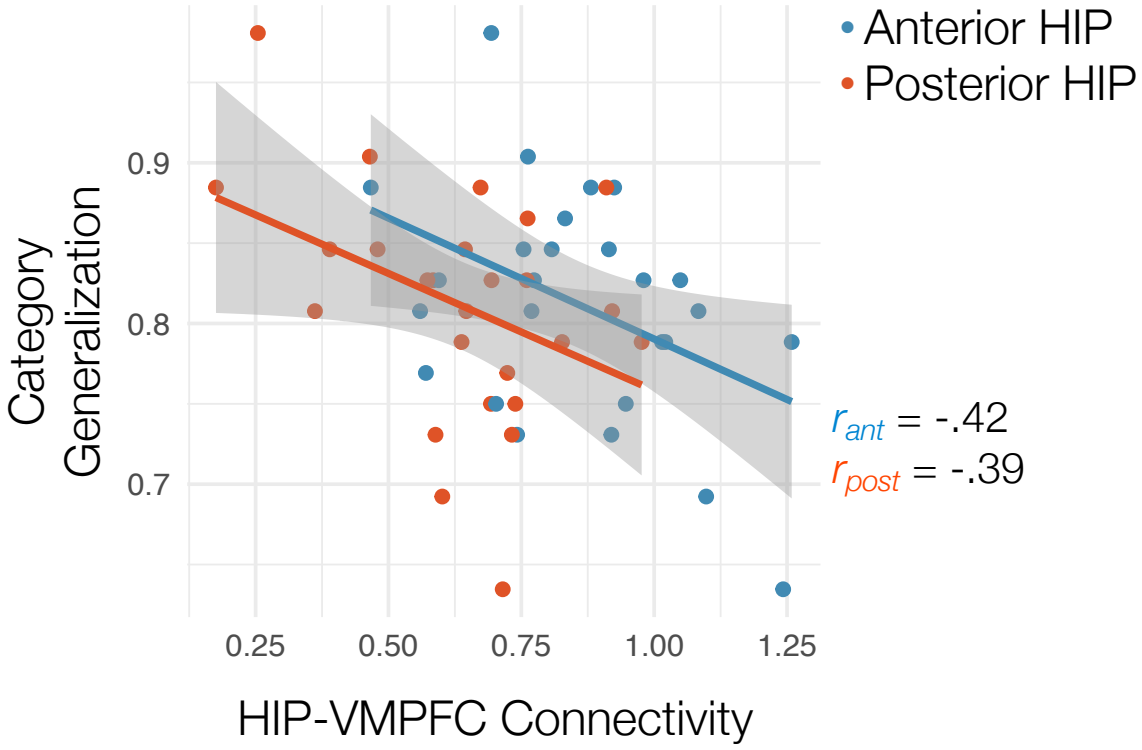

old animals
Cat A
1
5s
7s
new animals
Cat A
1
Cat B
2
5s

N = 26

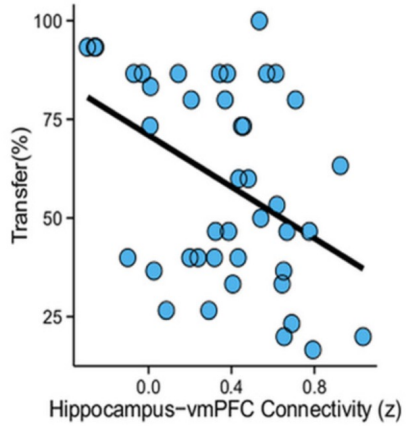
Posterior and anterior hippocampal connectivity align with proposed role in specificity and generalization



- Posterior hippocampus more connected to "specificity" regions, anterior hippocampus more connected to VMPFC
- Connectivity relatively stable from rest to task (except for IFG)



van Kesteren et al. (2010). *PNAS*
Gerraty et al. (2014). *J Neuro (see below)*

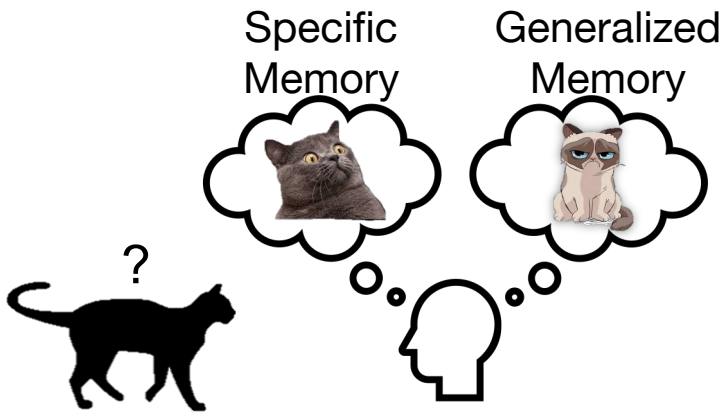


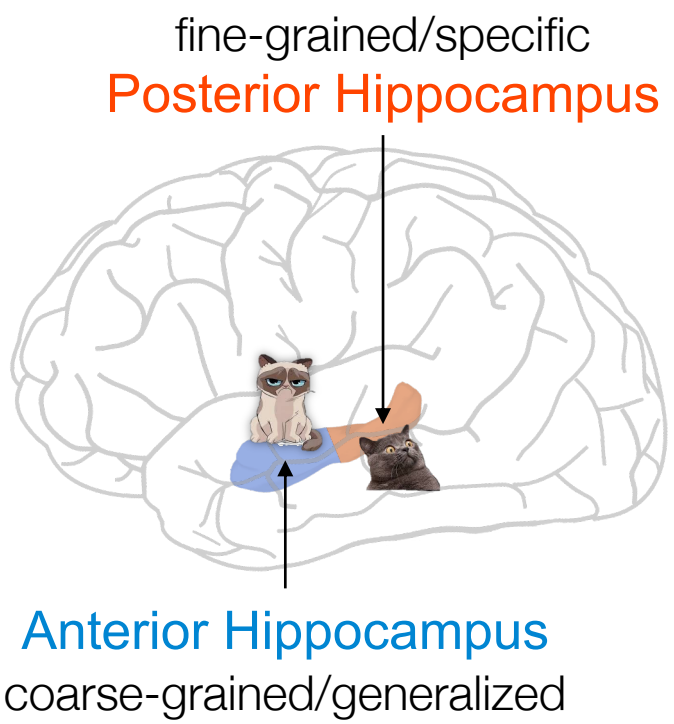
- ↳ Significant during passive viewing & categorization
- ↳ Both anterior and posterior hippocampal connectivity with VMPFC predicted behavior
- ↳ Relationship to behavior was negative
- ↳ No other significant connections

Chapter Summary

- Posterior and anterior hippocampus form connections consistent with predicted roles in specificity & generalization

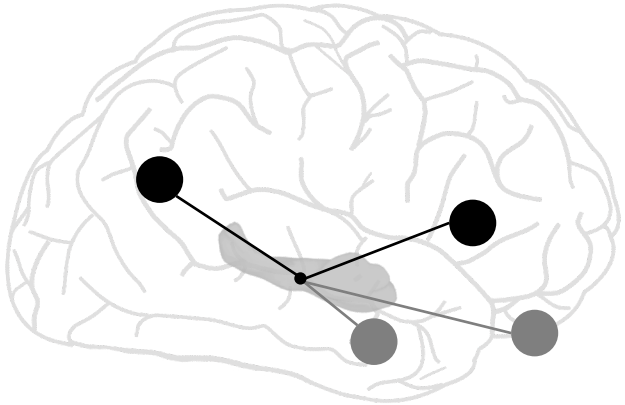
- Hippocampal-VMPFC interactions may contribute to individual differences in category generalization





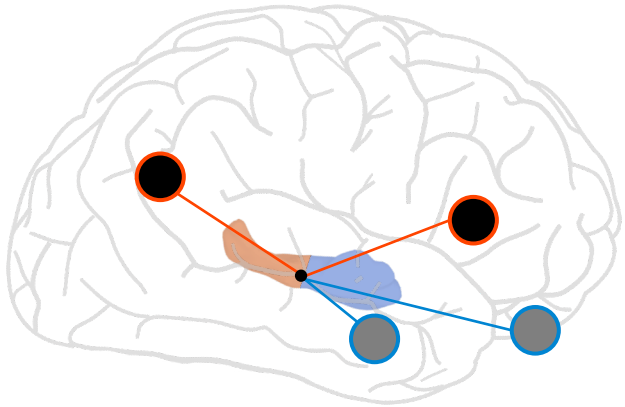
Chapter 4

Hippocampal connectivity predicting individual differences in memory specificity and generalization



Specificity **Generalization**

Do distinct hippocampal connections predict specificity and generalization?



Posterior **Anterior**

fine-grained /specificity

coarse-grained /generalization

Do anterior/posterior hippocampus differentially predict specificity and generalization?

Days 1 & 2: Behavioral Testing

N = 151

Generalization Measures

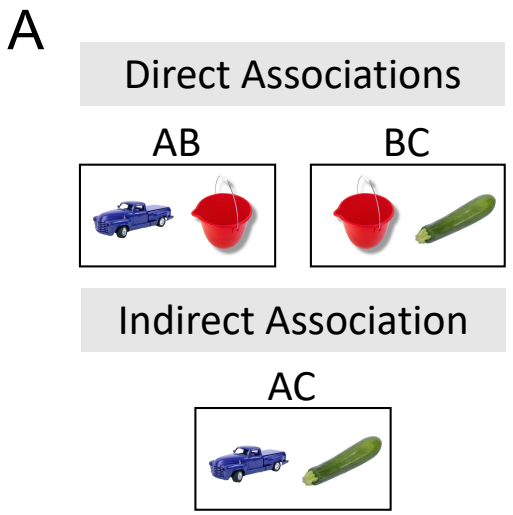
- Associative inference (A)
- Acquired equivalence (B)
- Category learning (faces) (C)
- Category learning (animals) (D)
- Transitive inference
- DRM false memory

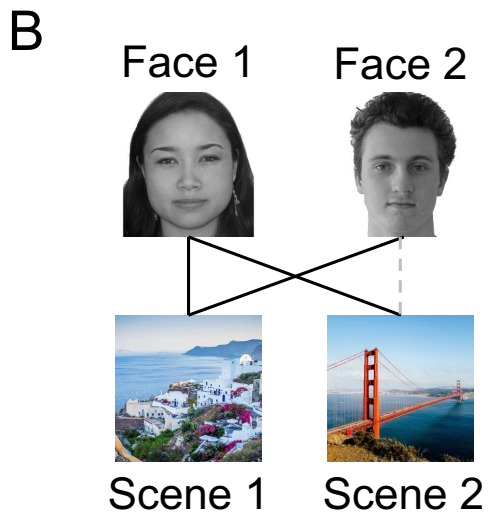
Specificity Measures

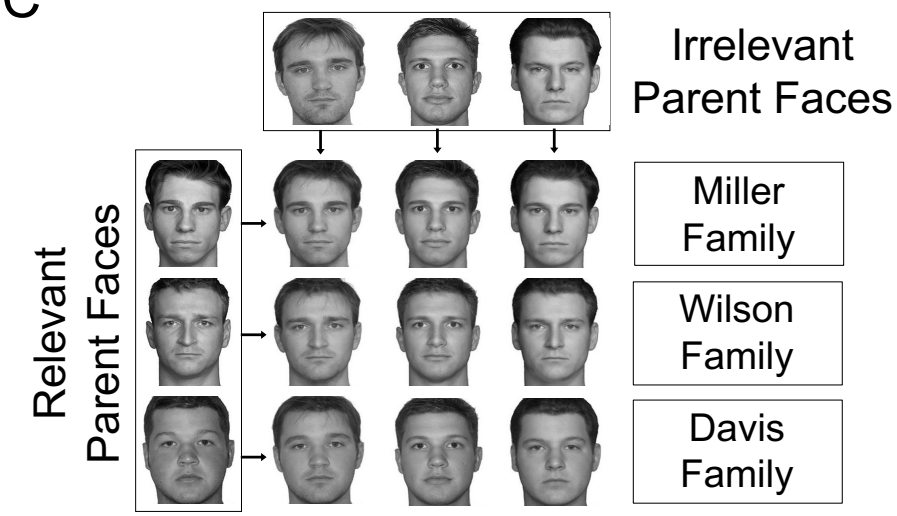
- Source memory
- Face/object recognition
- Paired associates
- Pattern separation
- Word recall

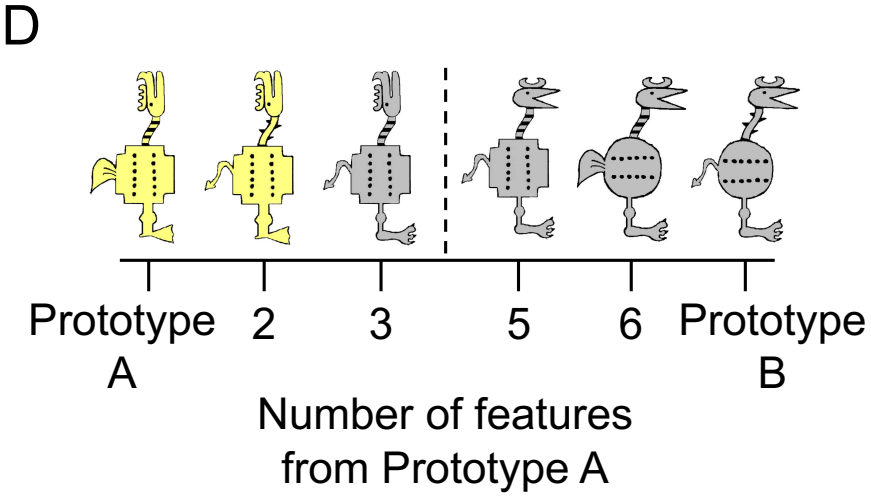
Principal Component Analysis

➥ individual composite scores of **generalization** & **specificity** abilities









Days 1 & 2: Behavioral Testing

N = 151

Generalization Measures

- Associative inference (A)
- Acquired equivalence (B)
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- Category learning (animals) (D)
- Transitive inference
- DRM false memory

Specificity Measures

- Source memory
- Face/object recognition
- Paired associates
- Pattern separation
- Word recall

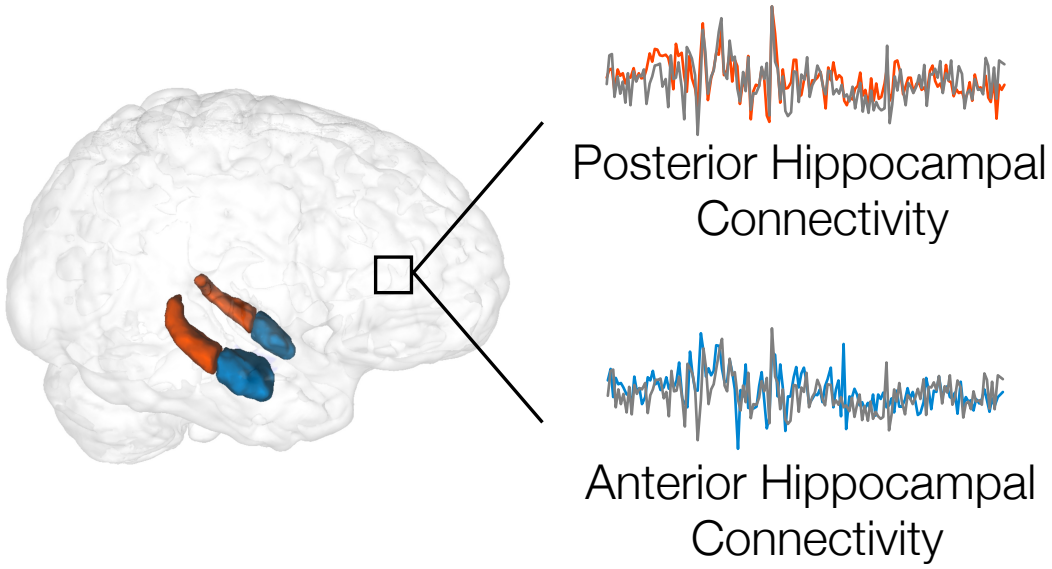
Principal Component Analysis

➥ individual composite scores of **generalization** & **specificity** abilities

Day 3: MRI Scan

N = 58

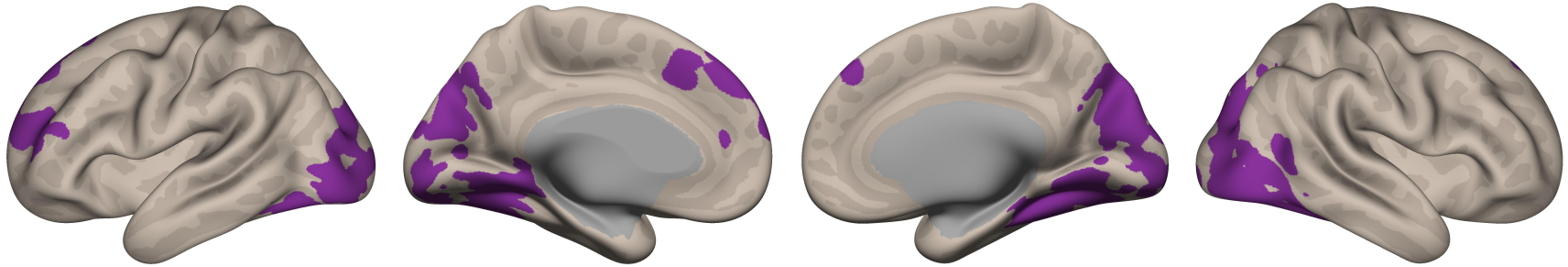
Resting-state fMRI



➥ Connectivity ↔ Memory Abilities

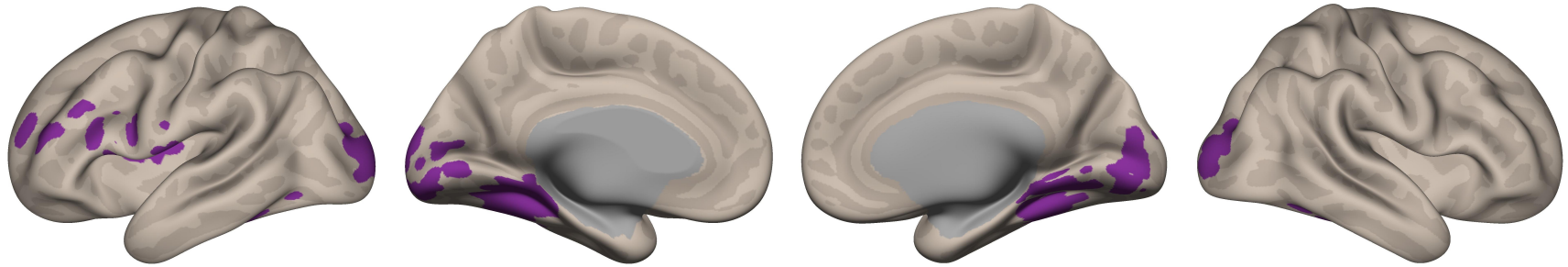
Do distinct hippocampal connections predict specificity v. generalization?

Hippocampal connections predicting **generalization**



L R

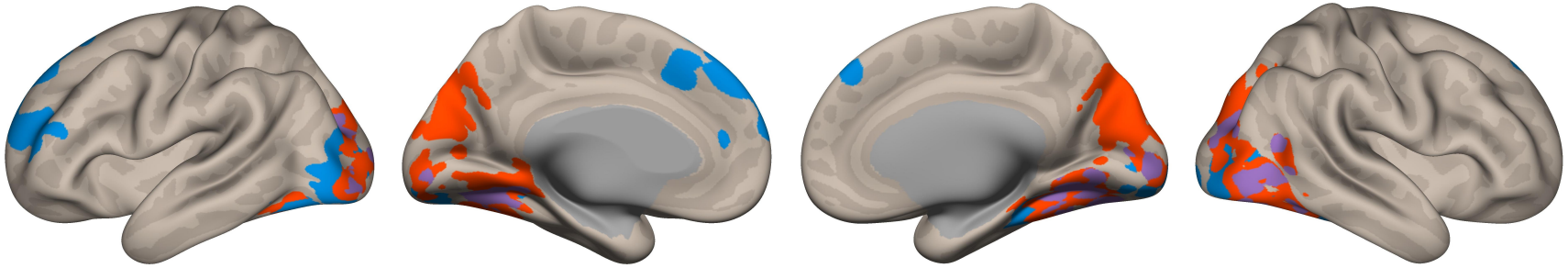
Hippocampal connections predicting **specificity**



↳ Distinct hippocampal-PFC connections relate to the different types of learning
↳ Connectivity to visual regions relate to both memory specificity and generalization

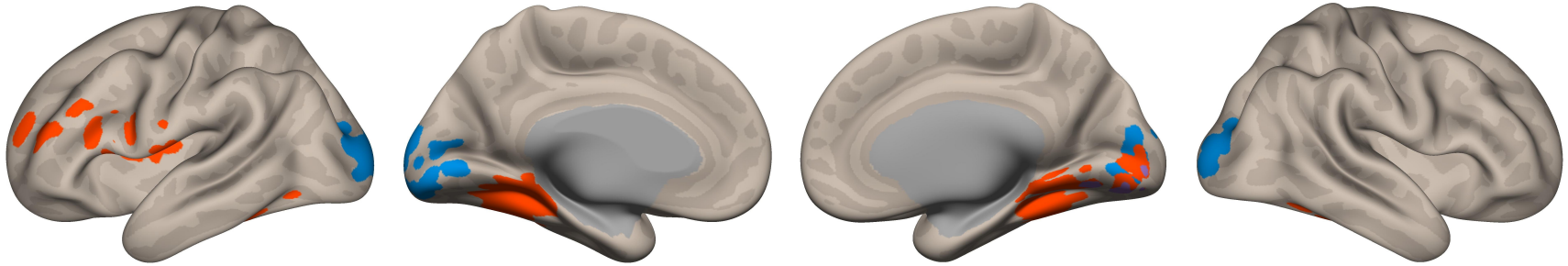
Are anterior and posterior hippocampal connections differentially important to each memory ability?

Hippocampal connections predicting **generalization**



L R

Hippocampal connections predicting **specificity**



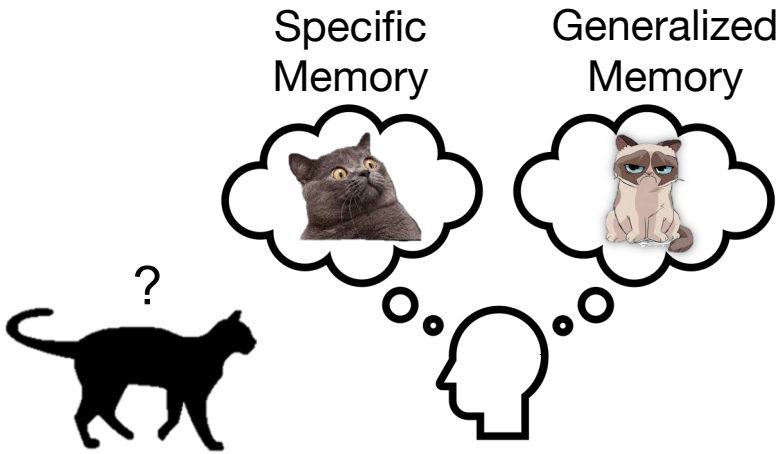
● Posterior Hip ● Overlap ● Anterior Hip

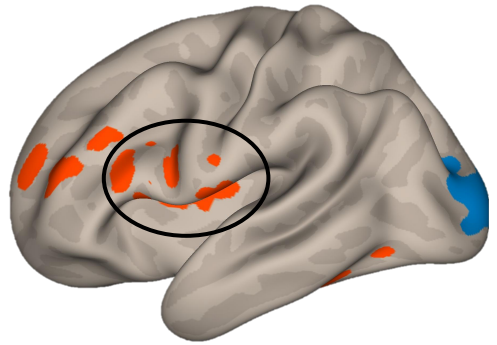
➥ Some evidence for anterior/posterior hippocampal differences, but only in PFC

Chapter Summary

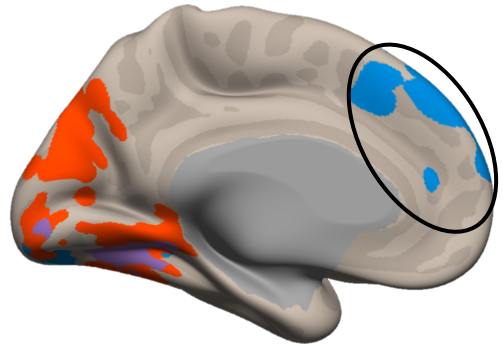
- Distinct hippocampal-prefrontal connections contribute to specificity & generalization

- Hippocampal connectivity to visual processing regions associated with both specificity & generalization





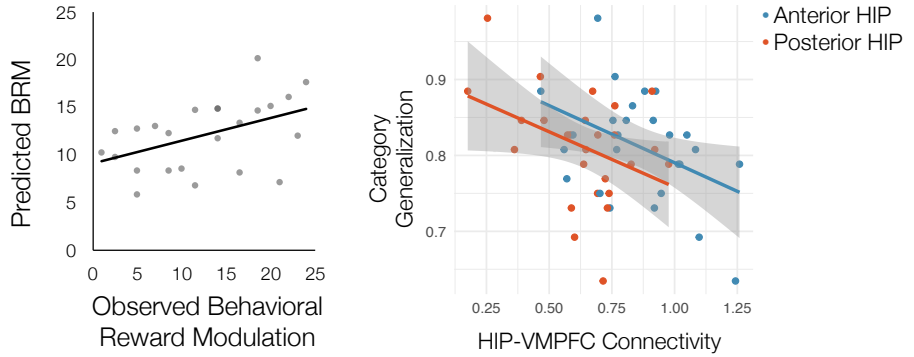
PHIP → Specificity



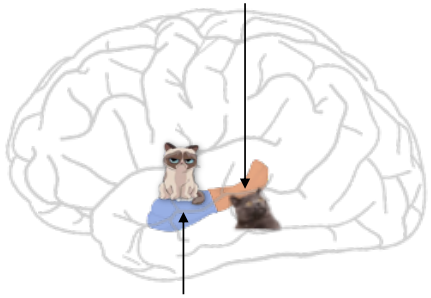
AHIP → Generalization

General Discussion

- Hippocampus supports multiple memory processes through interactions with different regions



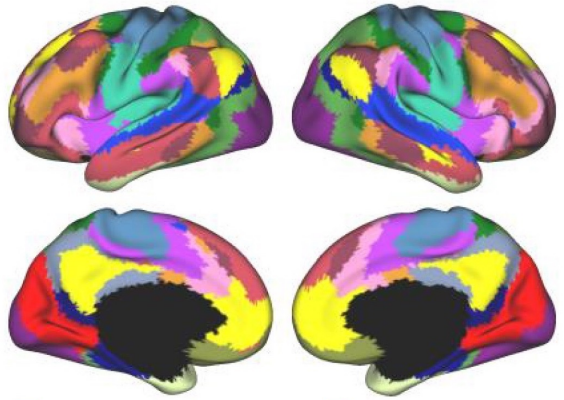
fine-grained/specific
Posterior Hippocampus



Anterior Hippocampus
coarse-grained/generalized

- Some evidence for functional differences between anterior and posterior hippocampal connectivity

- Individual memory abilities may be supported by stable, trait-like hippocampal connections



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