



# Characterizing common and dissociable involvement of medial temporal lobe regions during episodic source memory retrieval and analogical reasoning



Andrew J. Westphal<sup>1</sup>, Nicco Reggente<sup>1</sup>, Kaori Ito<sup>1</sup>, W. Harry Fortuna<sup>1</sup>, Yama Nawabi<sup>1</sup>, Edward R. Owens<sup>1</sup>, Jesse Rissman<sup>1,2</sup>

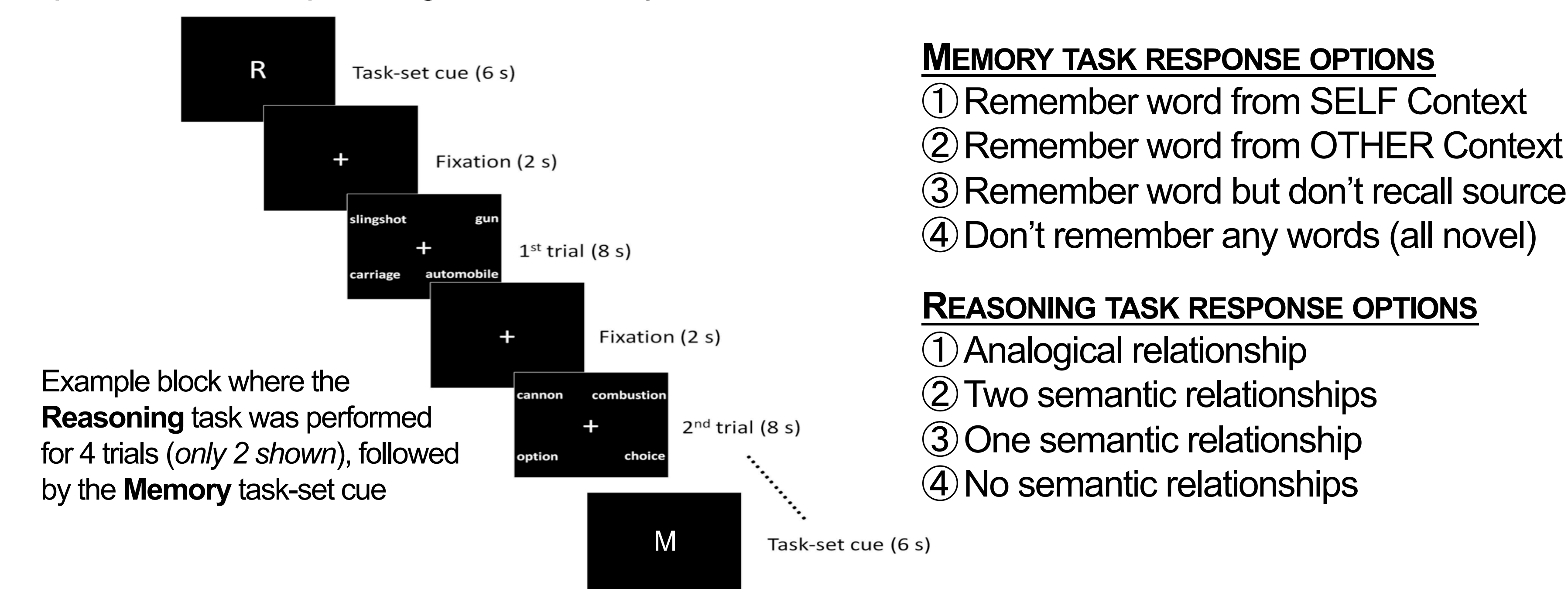
<sup>1</sup>Department of Psychology, <sup>2</sup>Department of Psychiatry & Biobehavioral Sciences, University of California, Los Angeles

## Background

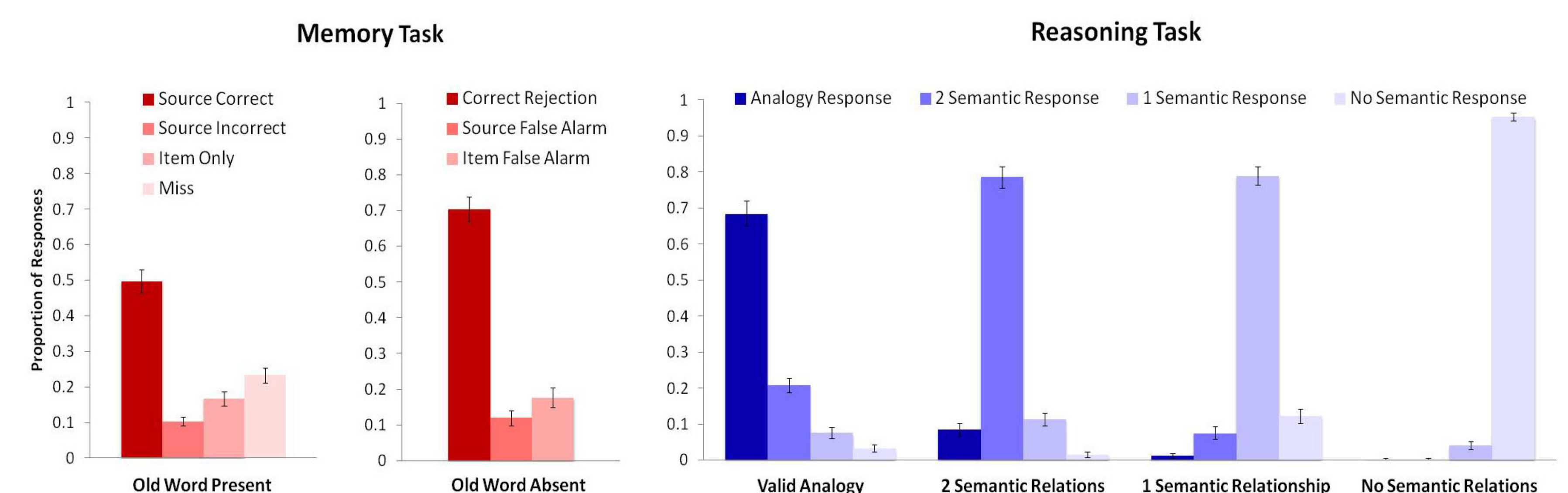
- Medial temporal lobe (MTL) structures are well-known to contribute to the encoding and retrieval of episodic memory<sup>1</sup>. However, emerging data have also showcased a potential role for MTL regions in the online representation of task-relevant information<sup>2</sup>, especially when working memory capacity is heavily taxed or exceeded<sup>3</sup>.
- This begs the question of what role MTL structures might play in cognitively demanding tasks, such as analogical reasoning, involving the integrative processing of multiple stimuli and the active representation of their conceptual relationships.
- While transitive inference tasks have been shown to engage the hippocampus<sup>4</sup>, its involvement in more abstract analogical reasoning tasks has received less study.
- The present fMRI study seeks to compare the degree to which MTL regions are recruited during analogical reasoning and episodic retrieval in a novel task paradigm that holds bottom-up stimulus processing and response demands constant.
- Importantly, recent studies have shown that the long-axis of the hippocampus has distinct functional specialization, potentially mediated through differential patterns of structural connectivity<sup>5</sup>. We aimed to explore how regions of anterior and posterior hippocampus modulate their functional connectivity with cortical networks depending on task demands for memory vs. reasoning.

## Experimental Design

- 20 subjects underwent fMRI scanning (3.0T Siemens, TR=2s, TE=30ms; Voxel size=3x3x3.7mm) as they alternated between performing cognitive tasks that each involved viewing 4-word stimulus arrays and selecting between four response options. There were 96 trials per task.
- Memory (M):** *Day 1:* subjects were given 80 words to encode and were instructed to visualize themselves interacting with the word (SELF context) or somebody else interacting with the word (OTHER context). *Day 2:* In the MRI scanner, subjects performed a memory retrieval task, in which the goal was to identify which, if any, of the 4 words had been previously encountered during the first day of the study and indicate the contextual source of the memory, if possible.
- Reasoning (R):** Judge whether the top and bottom word pairs shared the same abstract relationship or specify whether any non-analogous semantic relationships were present.
- Before each 4-trial block, a task-set cue (R or M) informed the subject of the cognitive operations to perform on the upcoming stimulus arrays.



## Behavioral Results



## MTL Region of Interest Processing

- Using Freesurfer, the high resolution T1 scan from each subject was parcellated into left and right hippocampus, parahippocampal cortex and perirhinal cortex.
- The hippocampus was further split into anterior (35%) and posterior (65%) components, using percentile-based axis segmentation<sup>6</sup>, that correspond to the head and body/tail of the hippocampus, respectively.
- These regions of interest (ROIs) were normalized into MNI-space with the same transformation that was performed on the functional images.

## Univariate fMRI Analysis

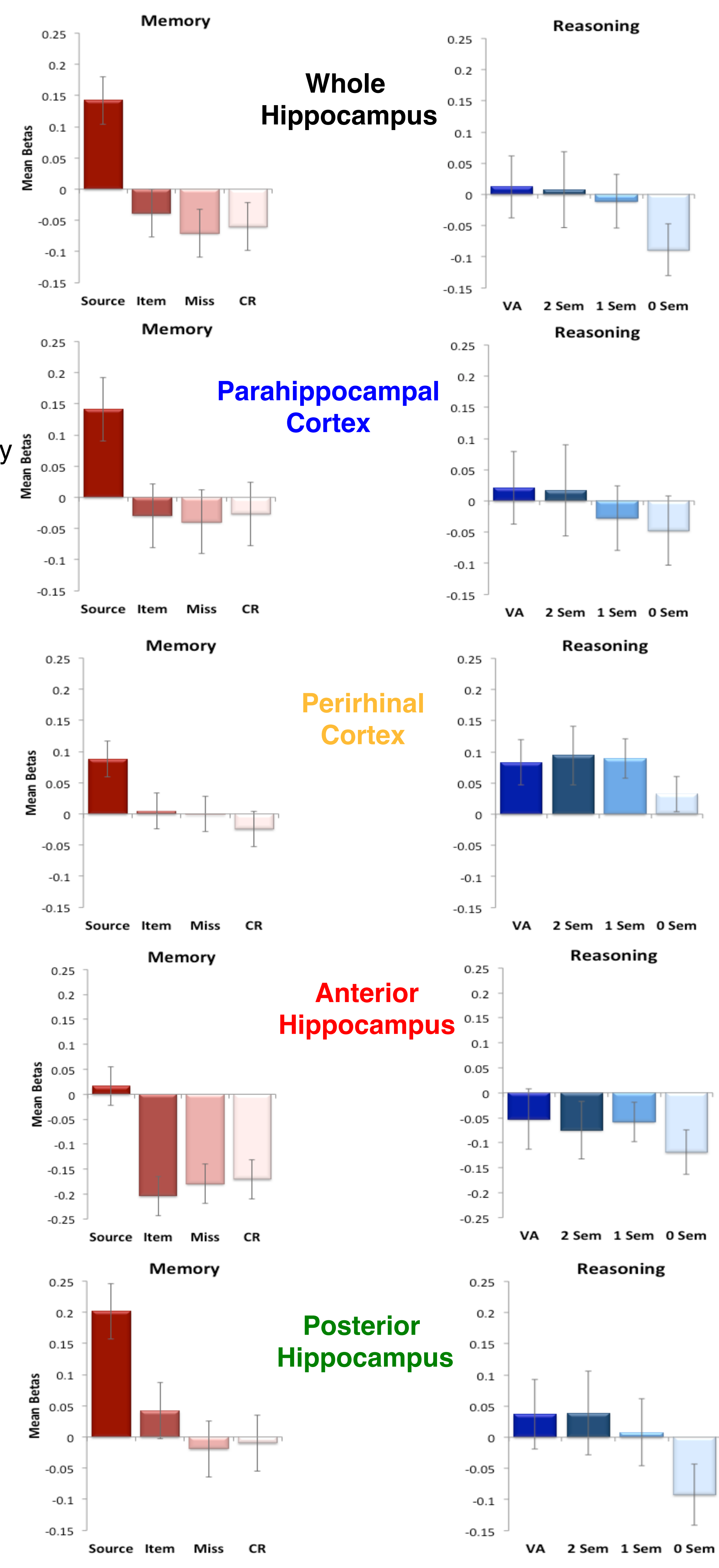
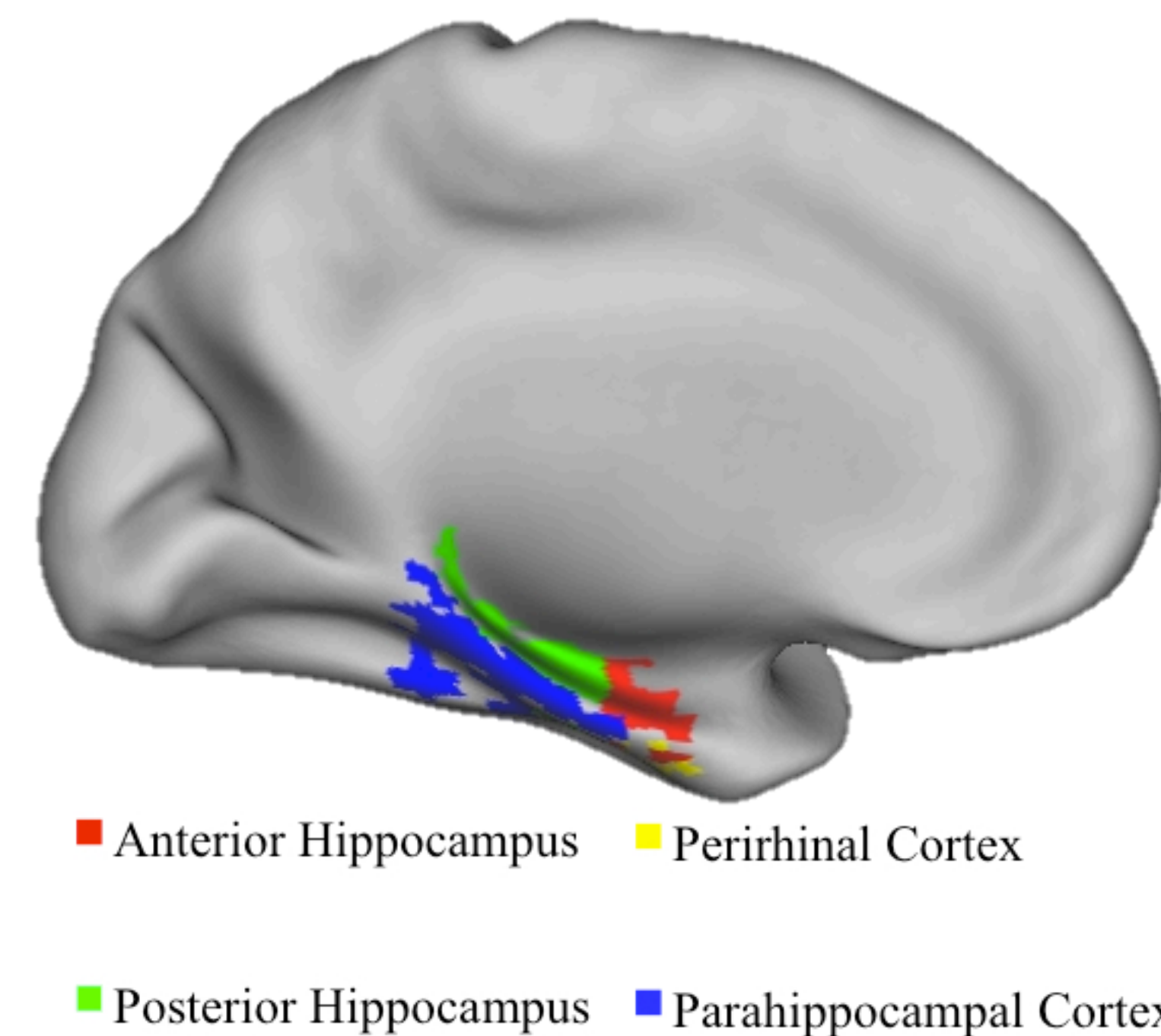
- A mixed block / event-related design modeled sustained and transient hemodynamic effects
- 17 subjects had 5 or more trials of each condition of interest and their parameter estimates were extracted
- ROIs were extracted from the left hemisphere, which generally showed more involvement in this verbal task.

- The **hippocampus** and the **parahippocampal cortex** :
  - Both ROIs show a source memory effect, but not a familiarity effect (i.e., activity during "Item Only" memory was equivalent with Correctly Rejected novel items).

- The **perirhinal cortex** :
  - Shows a source memory effect comparable in magnitude to its activation during reasoning trials that had at least one semantic relationship.

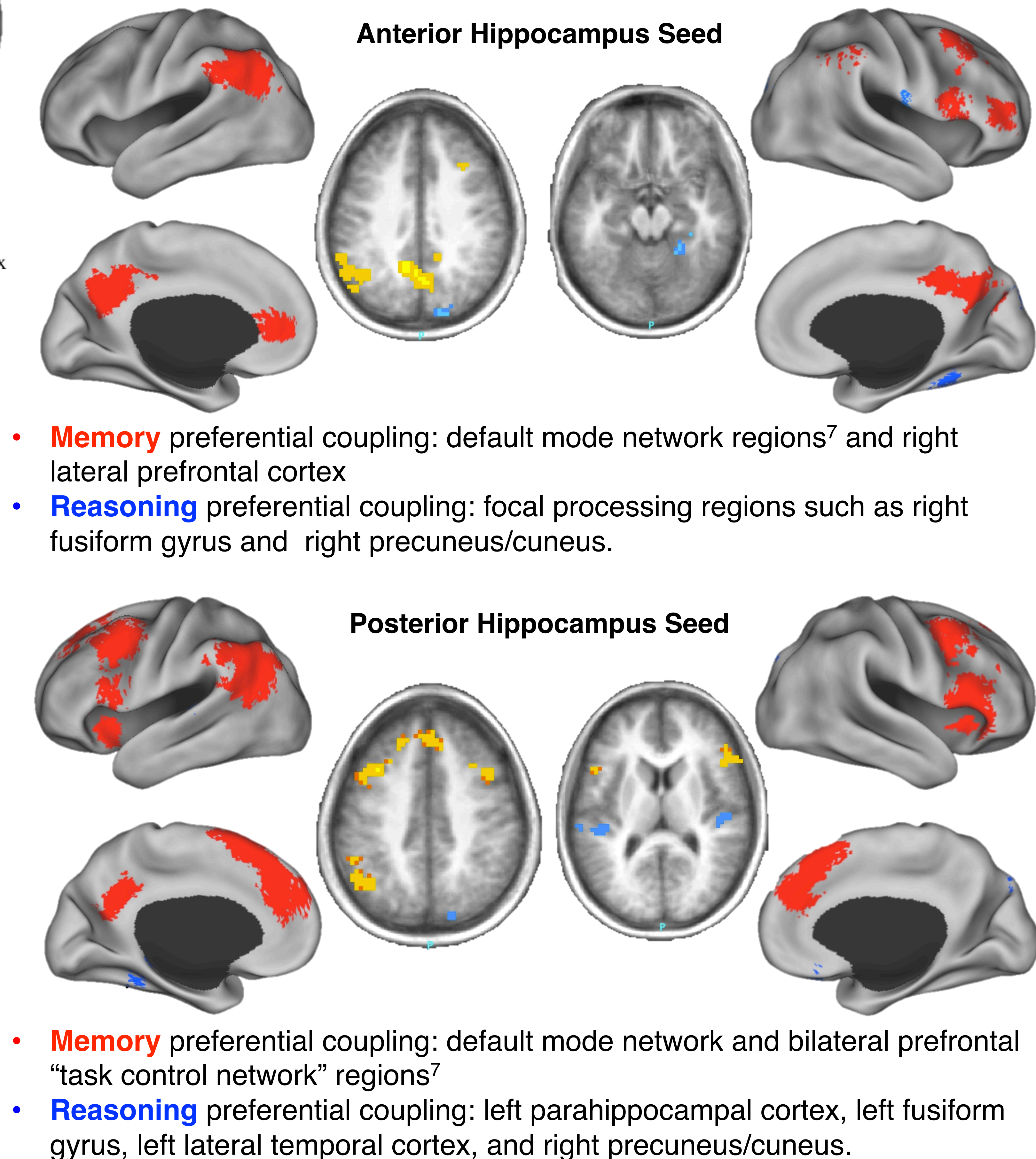
- The **anterior hippocampus** :
  - Shows a source memory effect manifested by deactivation in all non-source memory and reasoning conditions.

- The **posterior hippocampus** :
  - Shows a strong source memory effect and a semantic processing effect during reasoning (i.e., all conditions greater than 0 Sem)



## Psychophysiological Interactions Analysis

- Generalized form of context-dependent psychophysiological interactions (gPPI) analysis was performed using the left anterior and posterior hippocampal seeds to examine how their functional connectivity changes across task contexts (**Memory** vs. **Reasoning**). Regions favoring one task-context over and above the other are shown. Each tail was thresholded at  $p < .005$  using AlphaSim, resulting in a cluster threshold of 21 voxels.



## Summary and Conclusions

- All MTL regions queried preferentially responded during episodic source retrieval relative to other memory conditions.
- Only the perirhinal cortex showed comparable activity during analogical reasoning and episodic retrieval.
- Only the posterior hippocampus showed sensitivity to the semantic processing demands posed by the analogical reasoning task.
- Our functional connectivity results provide novel evidence that anterior and posterior hippocampal regions show divergent coupling depending on whether task goals require analogical/semantic analysis or episodic retrieval.
  - Most regions showed stronger hippocampal connectivity during memory, but some focal areas showed stronger connectivity during reasoning. More work will be needed to characterize the functional contribution, if any, of these areas to reasoning.

- References:**
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