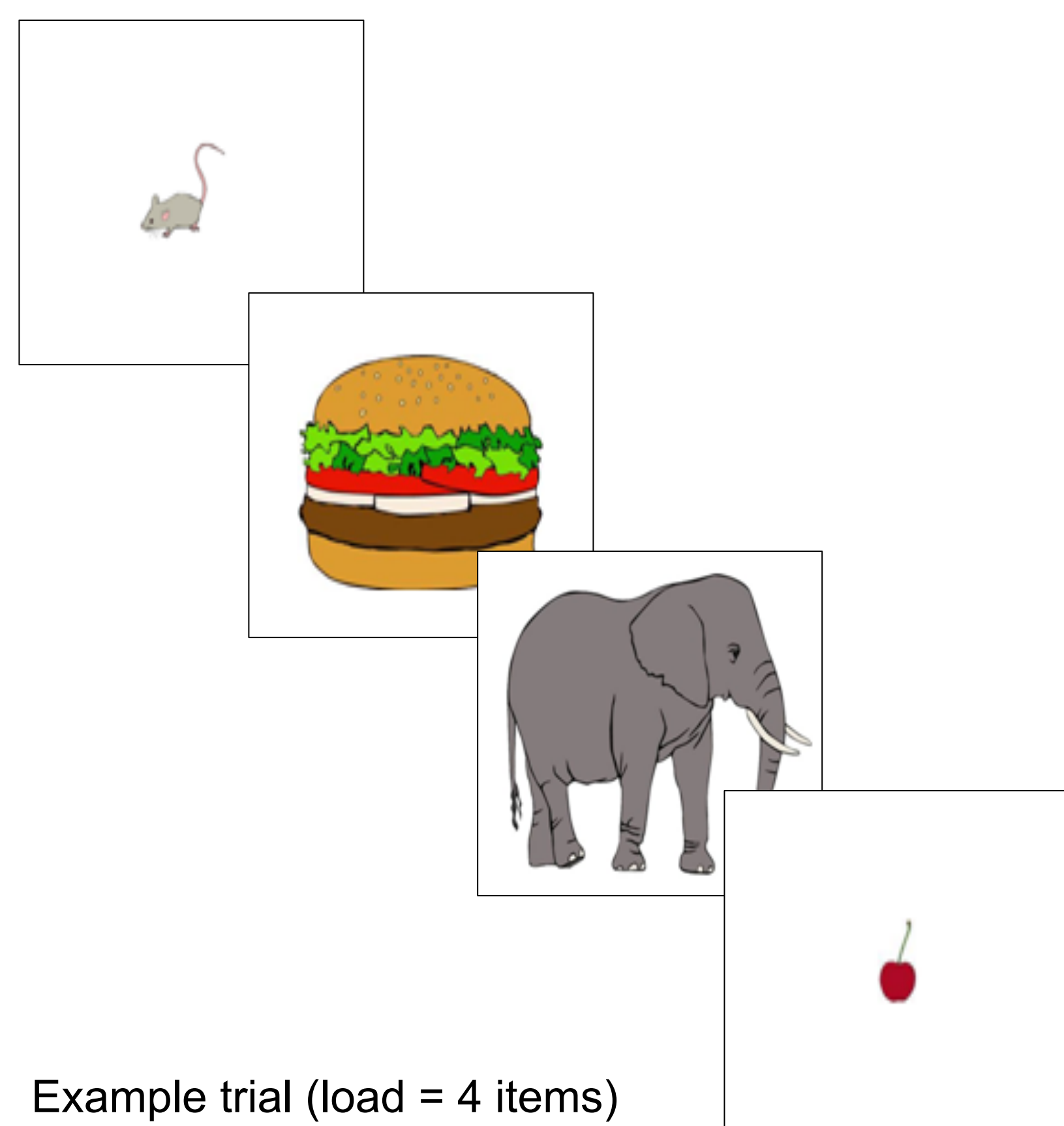


## Introduction

- Although the hippocampus is well known to contribute to the storage and retrieval of long-term memories, emerging data suggest that the hippocampus may also contribute to the online maintenance of task-relevant representations in some tests of working memory.<sup>1-6</sup>
- We hypothesize that a well-functioning hippocampus may facilitate performance on working memory tasks when the to-be-maintained items are novel and multi-featural, memory load is high, and opportunities for rehearsal are transiently disrupted by demands for manipulation.
  - Under these circumstances, hippocampal processing may supplement a capacity-limited frontoparietal circuit.
- In the present investigation, we used diffusion tensor imaging (DTI) data provided by the *Human Connectome Project*<sup>7</sup> to evaluate the degree to which the structural integrity of individuals' hippocampal circuitry might account for variance in working memory performance.

## Cognitive Task Paradigm

## NIH List Sorting Task

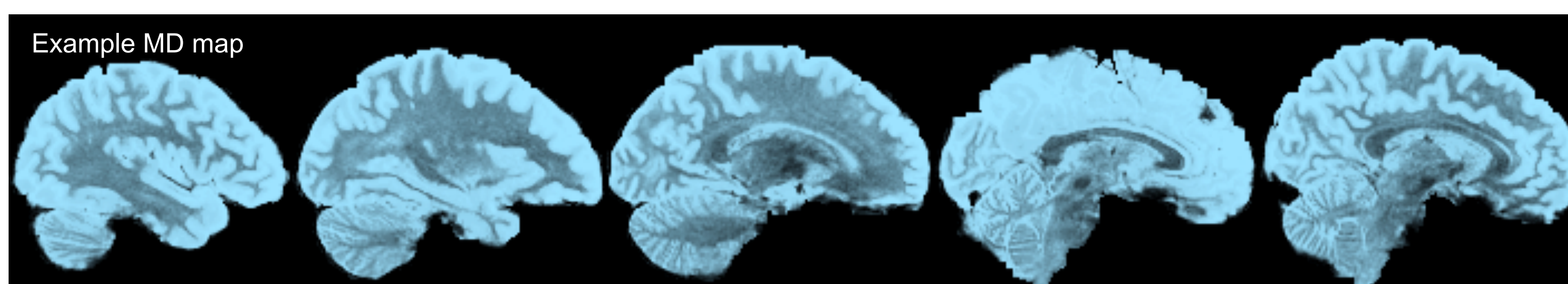


Example trial (load = 4 items)

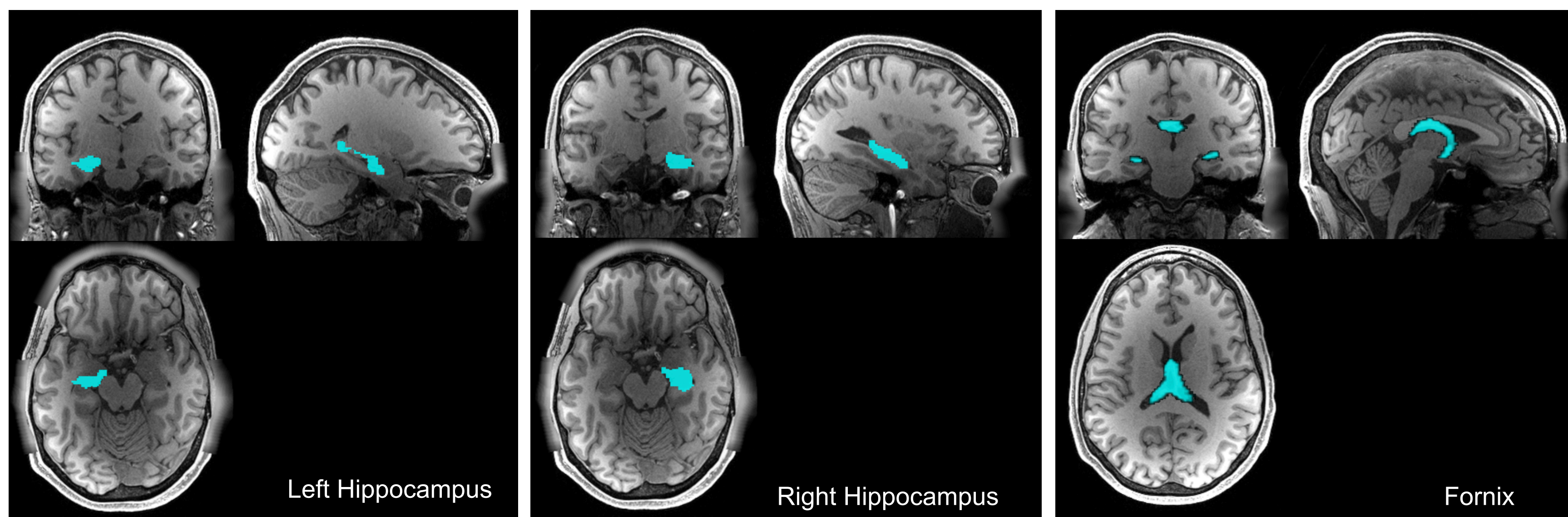
- 74 cognitively normal subjects (ages 22-35)
- Each trial featured a sequence of visual objects, which varied by both screen size and category.
- Subjects asked to recall the previously presented items in a specific order: Foods first (smallest to biggest) followed by Animals (smallest to biggest).
- Memory load increases progressively up to 7 items; test takes 10 min to administer.

## Methods

- Behavioral and MRI data obtained from Human Connectome Project
- Diffusion-weighted images (288 directions;  $b_0=0$ ;  $b=\{1000,2000,300 \text{ s/mm}^2$  interspersed};  $TR=5520\text{ms}$ ;  $TE=89.5\text{ms}$ ; Slices=111) were eddy-corrected and processed with FMRIB's Diffusion Toolkit to yield diffusion tensor maps.
- Whole-brain **Mean Diffusivity (MD)** maps were created for each subject.
  - This measure, which quantifies the overall degree of diffusion of water molecules, has been shown to index the microstructural integrity of brain tissue, including in grey matter.<sup>8-10</sup>



- Our analysis focused on three regions-of-interest (ROIs):
  - Left Hippocampus, Right Hippocampus, and Bilateral Fornix**
    - We used FreeSurfer's Automated Segmentation Algorithm on structural MRI images (MPRAGE;  $0.7\text{mm}^3$ ;  $TR=2400\text{ms}$ ;  $TE=2.14\text{ms}$ ) to identify each subject's Left and Right Hippocampus.
      - ROIs were then re-sliced into subject-specific diffusion space using SPM 8.
    - We extracted our Fornix ROI from the JHU-White Matter Atlas.
      - ROIs were reverse normalized to subject-specific diffusion space using Advanced Normalization Tools (ANTS).

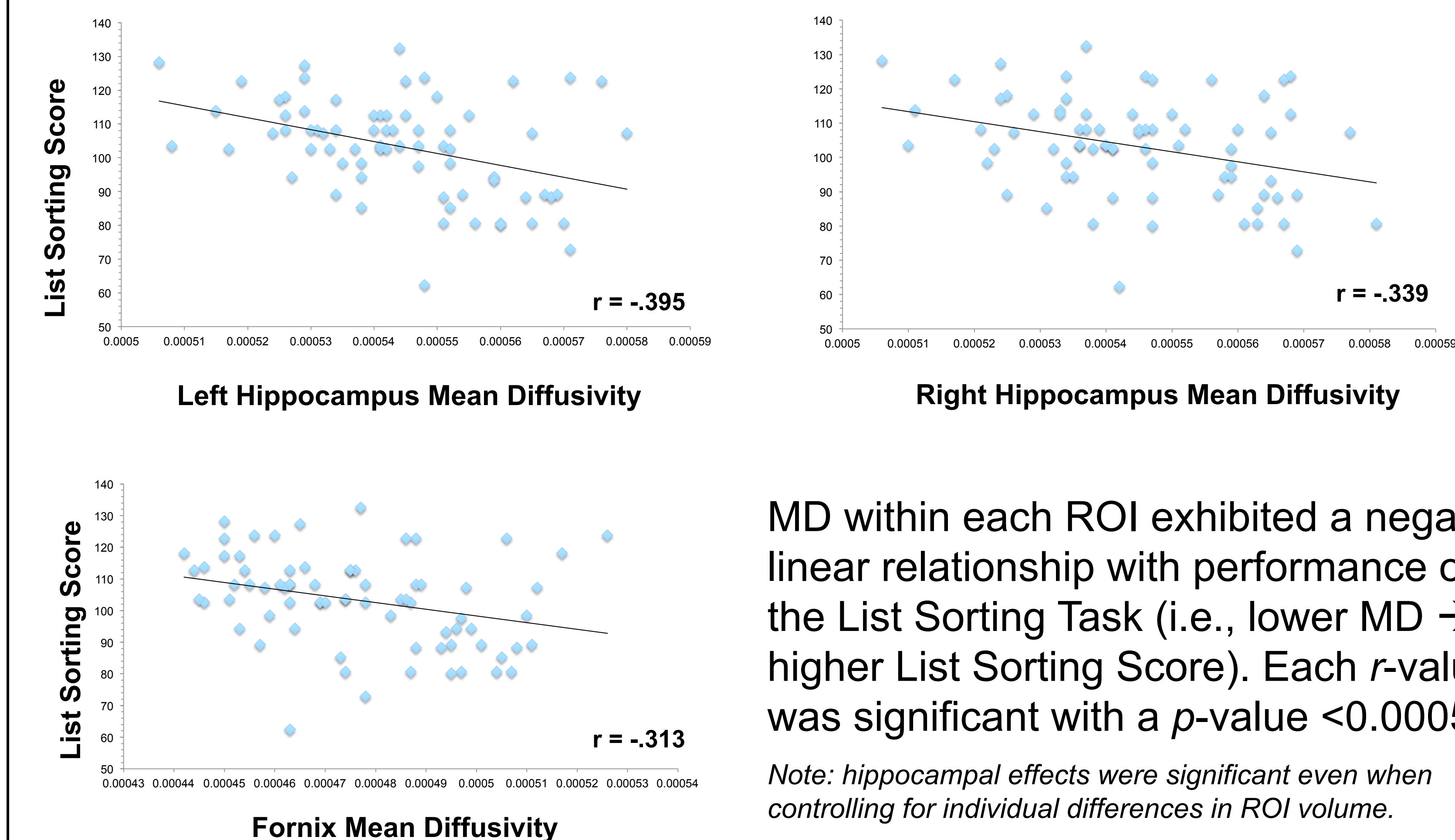


- Calculated average MD value across voxels within each ROI for each subject.
- We then examined whether individual differences in regional MD were correlated with individual differences in memory performance.

Data were generously provided by the Human Connectome Project (Q3 release), WU-Minn Consortium (PIs: David Van Essen & Kamil Ugurbil; 1U54MH091657) funded by the 16 NIH Institutes and Centers that support the NIH Blueprint for Neuroscience Research; and by the McDonnell Center for Systems Neuroscience at Washington University.

## Results

- MD within all three ROIs accounted for a significant portion of the variance in working memory performance scores.



## Conclusions

- These results suggest that the underlying integrity of hippocampal circuitry, as measured with DTI, can at least partially explain an individual's ability to perform a challenging visual working task such as the NIH List Sorting Task.
- These results expand on previous research that shows high hippocampal MD (over and above hippocampal volume) predicts memory decline in healthy elderly individuals.<sup>9,10</sup> Our results illustrate that hippocampal MD may prove to be an informative biomarker of the health of this critical memory circuit, even in young adult brains.
- Our structural imaging findings add to a growing body of functional neuroimaging work suggesting that the hippocampus can contribute to memory performance even when recall is tested after a very brief delay (i.e., seconds rather than hours or days).

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