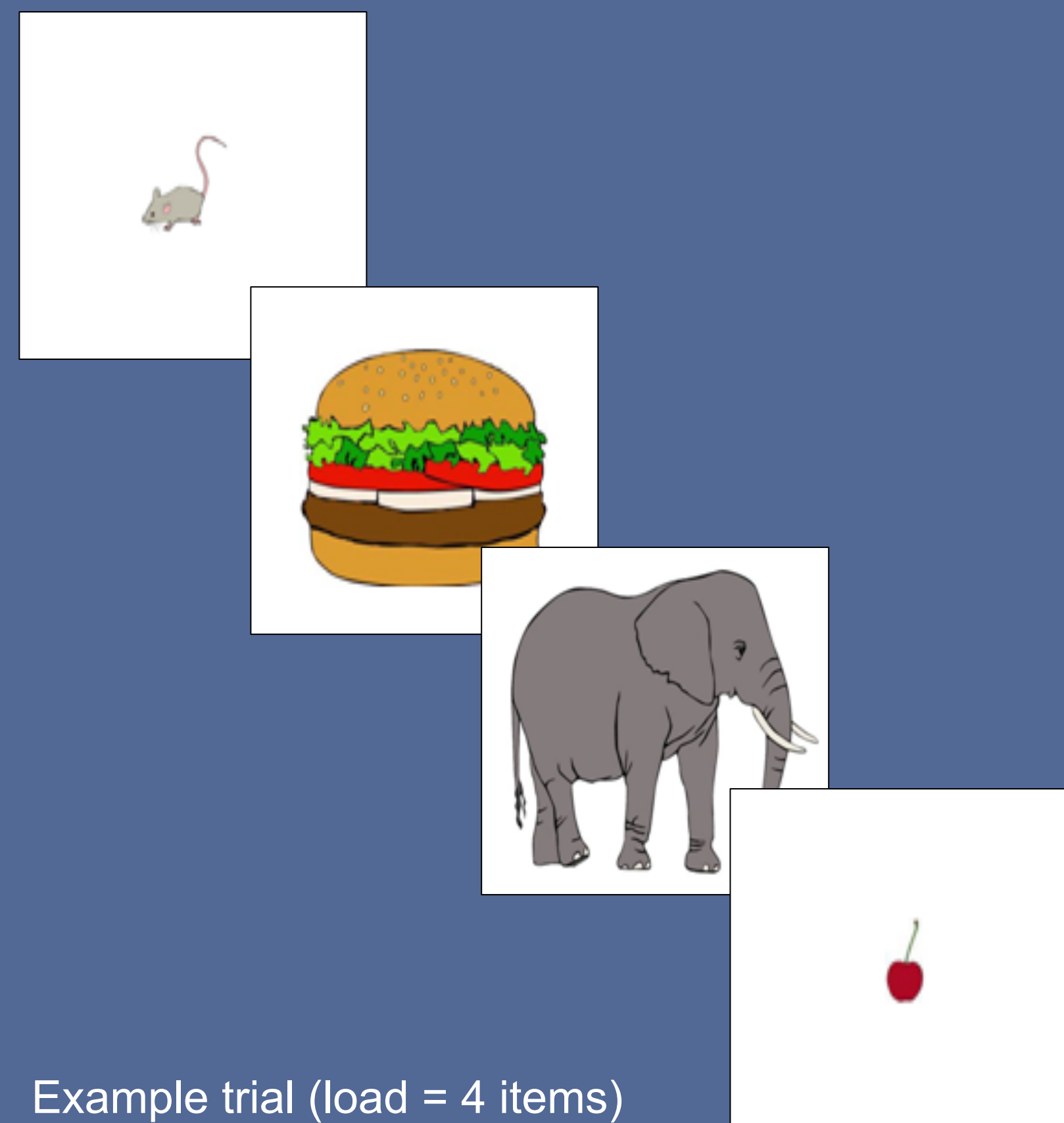


Introduction

- 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.
- 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. In other words, 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 to evaluate the degree to which the structural integrity of individuals' hippocampal circuitry might account for variance in working memory performance.

Cognitive Task Paradigm

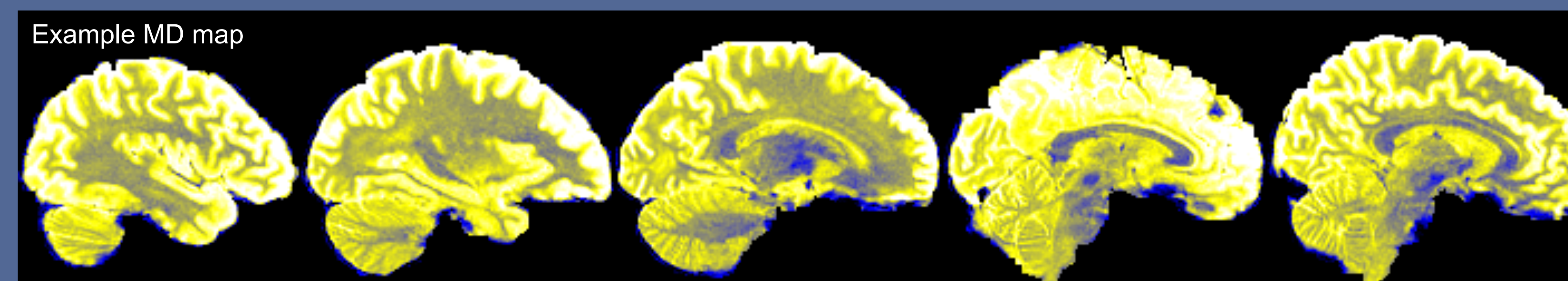
NIH List Sorting Task



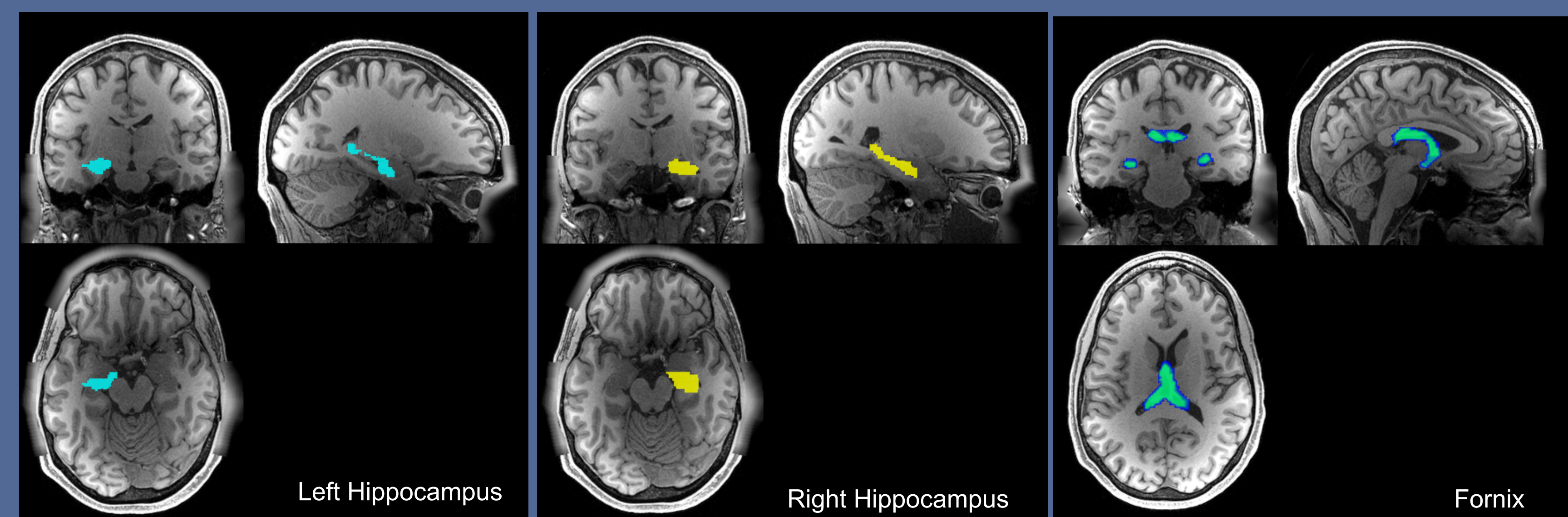
- 74 cognitively normal subjects (ages 22-35)
- Each trial featured a sequence of visual objects, which varied by both size and category.
- Subjects asked to recall the previously presented items in a specific order: Foods first (smallest to biggest) followed by Animals (smallest to biggest).
- Memory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

Methods

- Diffusion-weighted images (288 directions; $b_0=0$; $b=\{1000,2000,300$ s/mm² interspersed}; TR=5520ms; TE=89.5ms; 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.^{1,2,3}



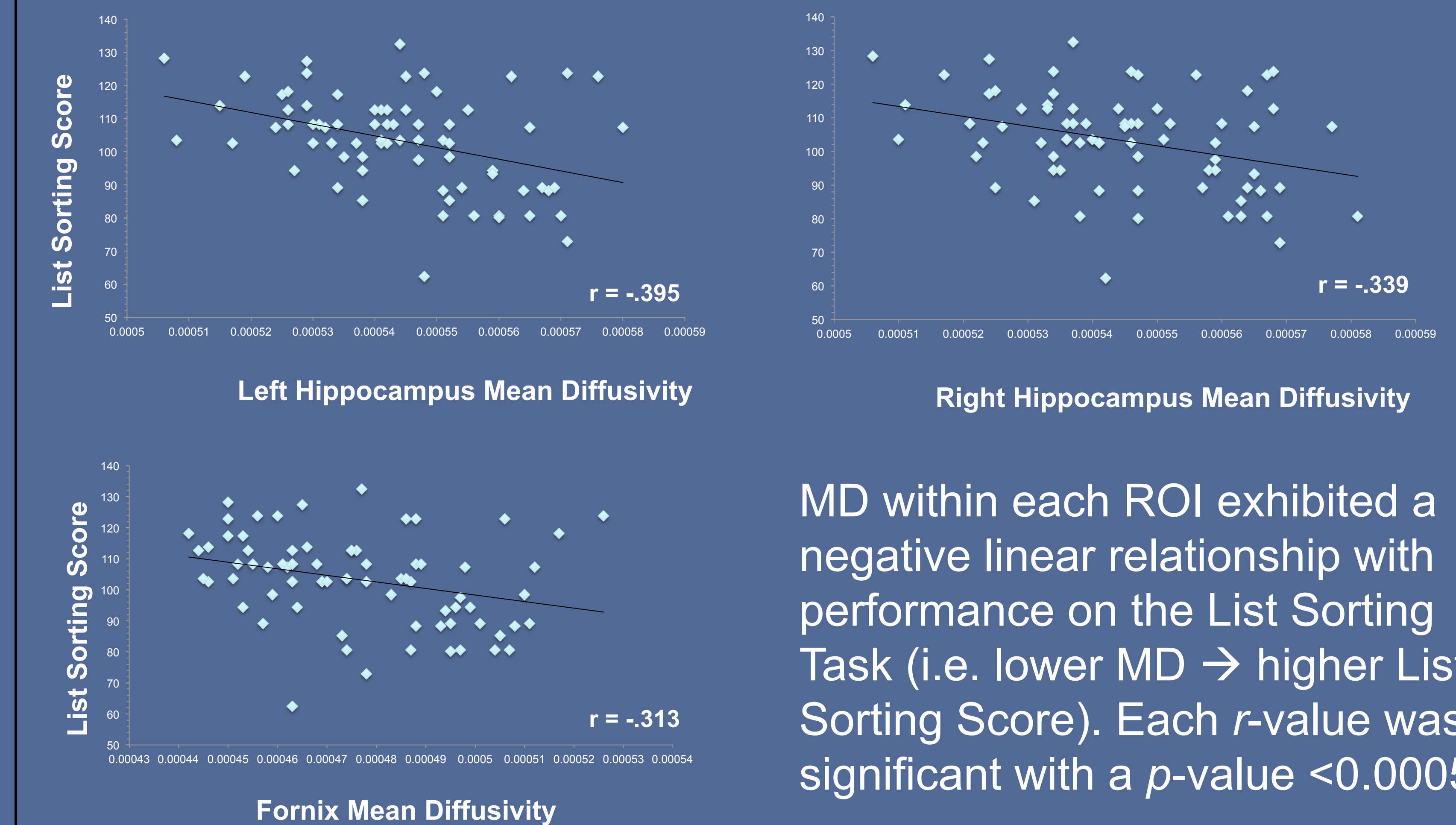
- Our analysis focused on three regions-of-interest (ROIs):
 - Left Hippocampus, Right Hippocampus, and Bilateral Fornix**
 - We used Freesurfer's Automated Segmentation Algorithm on structural MRI images (MPRAGE; 0.7mm³; TR=2400ms; TE=2.14ms) to identify each subject's Left and Right Hippocampus.
 - 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).



- Using FSL Stats, we calculated the average MD value for all for all voxels within each ROI for each subject.
- We then looked to see whether individual differences in MD were correlated with individual differences in memory performance.

Results

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



MD within each ROI exhibited a negative linear relationship with performance on the List Sorting Task (i.e. lower MD → higher List Sorting Score). Each r -value was significant with a p -value <0.0005.

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.
- 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).
- Hippocampal MD may prove to be an informative biomarker of the health of this critical memory circuit, even in young adult brains.

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