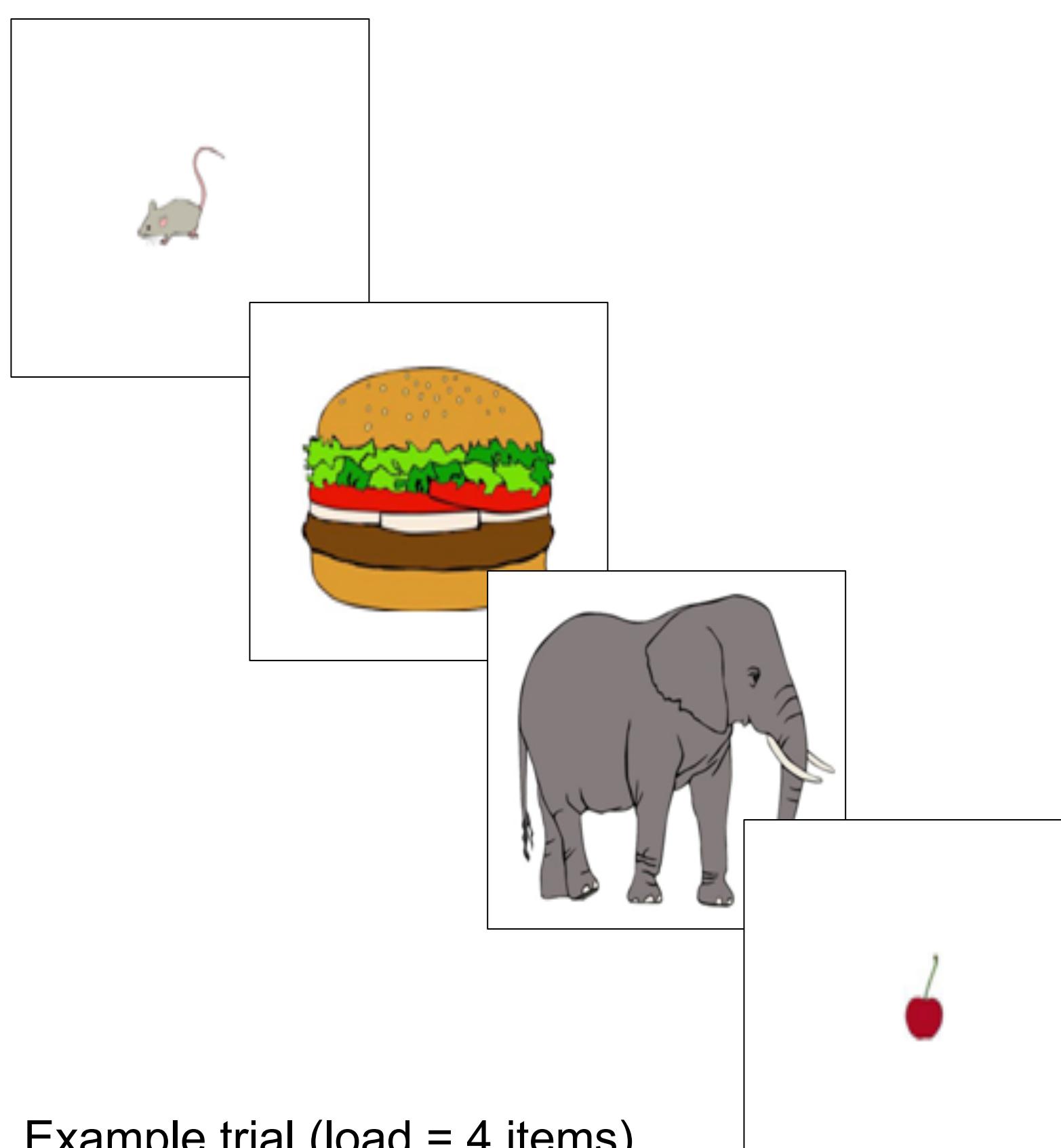


Introduction

- 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.¹⁻⁶
- 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*⁷ 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

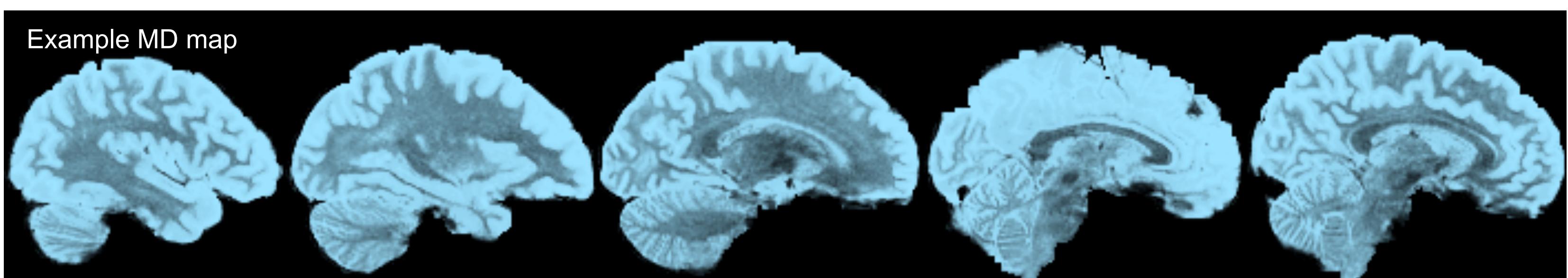


- 74 cognitively normal subjects (ages 22-35)
- Each trial featured a sequence of visual objects, which varied by both screen size and category.
- Subjects asked to recall the previously presented items in a specific order: Foods first (smallest to biggest) followed by Animals (smallest to biggest).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

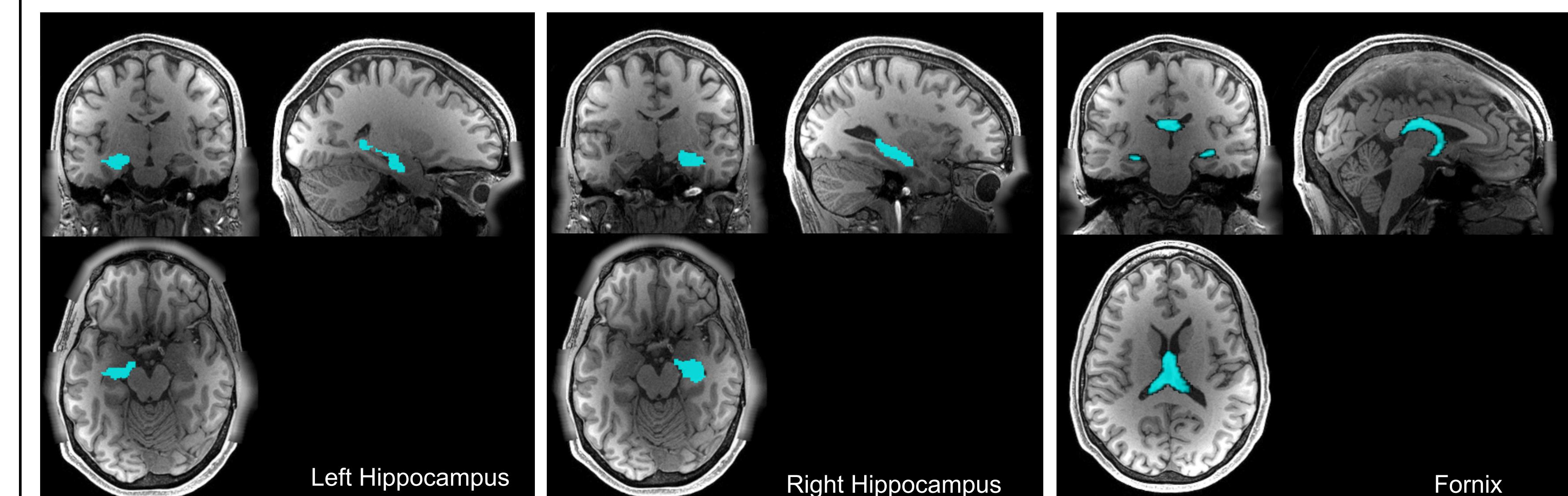
Example trial (load = 4 items)

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=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.⁸⁻¹⁰



- 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).

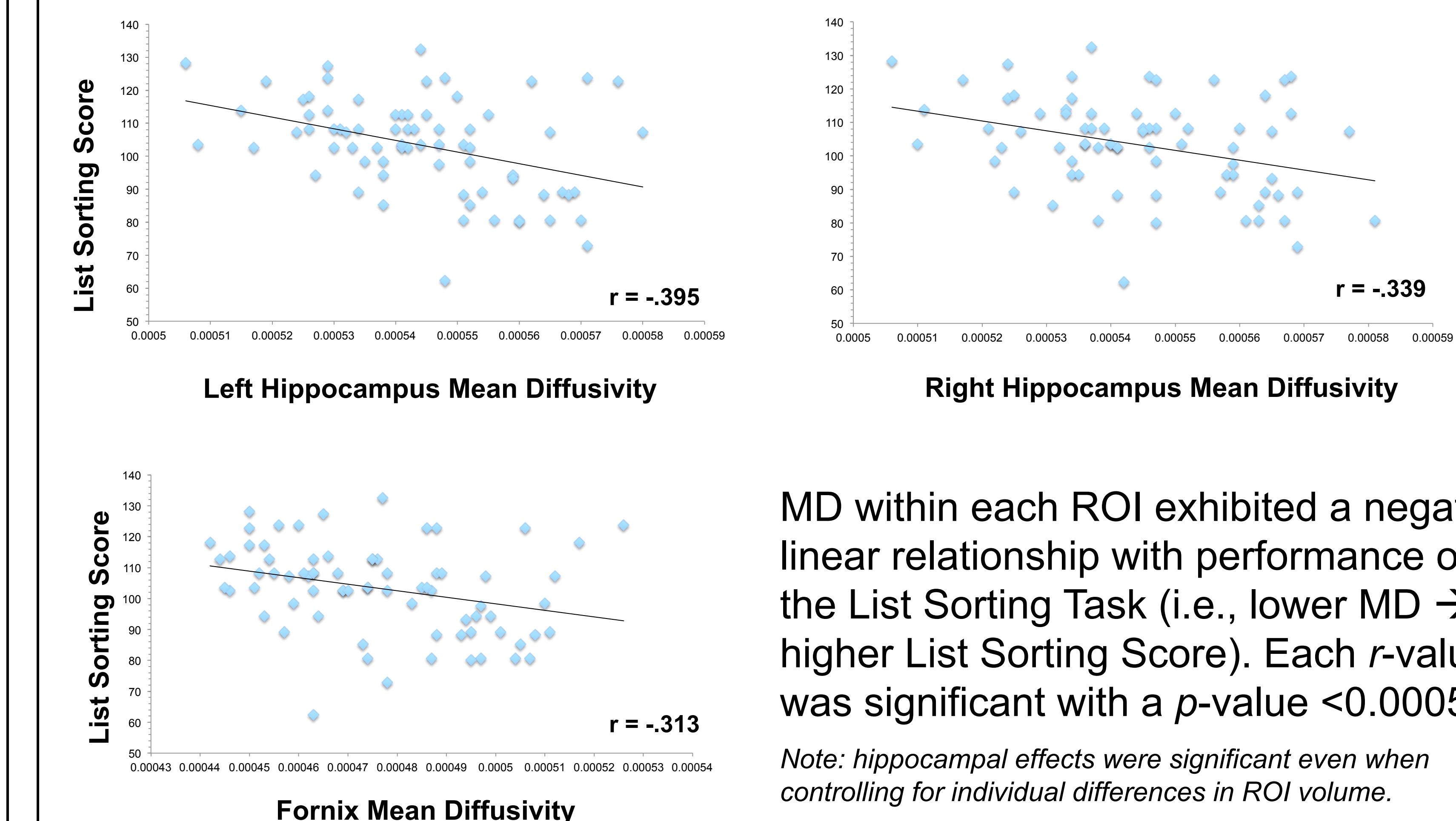


- Calculated average MD value across voxels within each ROI for each subject.
- We then examined whether individual differences in regional MD were correlated with individual differences in memory performance.

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.



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 .

Note: hippocampal effects were significant even when controlling for individual differences in ROI volume.

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.^{9,10} 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).

References

- Ranganath, C., & Blumenfeld, R.S. (2005). Doubts about double dissociations between short- and long-term memory. *Trends Cogn Sci*, 9(8), 374-380.
- Rissman, J., et al. (2008). Dynamic adjustments in prefrontal, hippocampal, and inferior temporal interactions with increasing visual working memory load. *Cereb Cortex*, 18(7), 1618-1629.
- van Vugt, M. K., Schulze-Bonhage, A., Litt, B., Brandt, A., & Kahana, M. J. (2010). Hippocampal gamma oscillations increase with memory load. *J Neurosci*, 30(7), 2694-2699.
- von Allmen, D.Y., et al. (2013). Neural activity in the hippocampus predicts individual visual short-term memory capacity. *Hippocampus*.
- Winston, G.P., et al. (2013). Structural correlates of impaired working memory in hippocampal sclerosis. *Epilepsia*, 54(7), 1143-1153.
- Yee, L.T.S., et al. (2014). Short-term retention of relational memory in amnesia revisited: accurate performance depends on hippocampal integrity. *Frontiers in human neuroscience* 8, 16.
- Van Essen, D.C., et al. (2013). The WU-Minn Human Connectome Project: An overview. *NeuroImage* 80(2013):62-79.
- Kim, H.J., et al. (2013) Alterations of mean diffusivity in brain white matter and deep gray matter in Parkinson's disease. *Neuroscience Letters* 550: 64-68.
- den Heijer, T., et al. (2012). Structural and diffusion MRI measures of the hippocampus and memory performance. *NeuroImage*, 63(4), 1782-1789.
- Carlesimo, G.A., et al. (2010). Hippocampal mean diffusivity and memory in healthy elderly individuals: a cross-sectional study. *Neurology*, 74(3), 194-200.

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