Whole brain ultrahigh resolution functional magnetic resonance imaging analysis of associative mnemonic processes

Stephanie Langella[1], Wei-Tang Chang, Ph.D.[2], Weili Lin, Ph.D.[2], Kelly S. Giovanello, Ph.D.[1,2]

[1]University of North Carolina at Chapel Hill, Department of Psychology and Neuroscience; [2]Biomedical Research Imaging Center at UNC-Chapel Hill

Background

- The hippocampus includes distinct anatomical subfields (e.g., CA1, CA3, DG), each contributing differentially to learning and memory processes.
- Prior high-resolution imaging studies have been limited in FOV to the hippocampus and surrounding MTL.
- Discrimination, generalization, and match detection are processes supported differentially by the hippocampal subfields; however, these processes have not been studied using a whole-brain FOV.
- Further, previous studies in humans have been unable to differentiate CA3 from DG, although the subfields are known to contribute differentially to mnemonic processes.
- Examining hippocampal subfield and cortical activity in tandem is integral to developing a more complete understanding of mnemonic processing.
- Multiband-3D (MB3D) imaging allows a whole-brain concurrent examination of hippocampal subfield and cortical activity, as well as the ability to functionally and structurally distinguish between CA3 and DG.

Methods

Participants

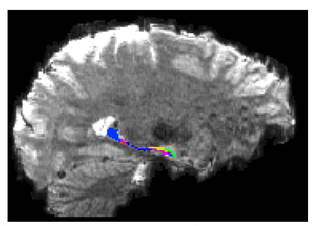
- 19 young adults (*M* = 21.2 years, 12 female) from UNC and the surrounding community

Imaging Protocol

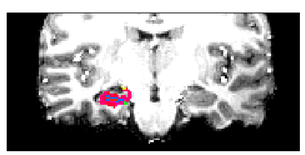
- Siemens Magnetom 7T scanner
- Two 6-min resting-state scans
- Six blocks alternating encoding & retrieval phases
  - MB3D imaging (partition encoding = 5, multiband factor = 35, in-plane acceleration =2, TR = 2s, TE = 23ms)
  - 1.0mm isotropic, 120x152x175mm^3 field of view
- MP-RAGE
- T2-weighted anatomical (0.6mm isotropic)

Preprocessing and Analysis

- Preprocessing and analysis steps were implemented using FSL and ANTS, including EPI distortion correction, motion correction, and co-registration
- Subfield segmentation completed through FreeSurfer v6[3] and manually checked for accuracy

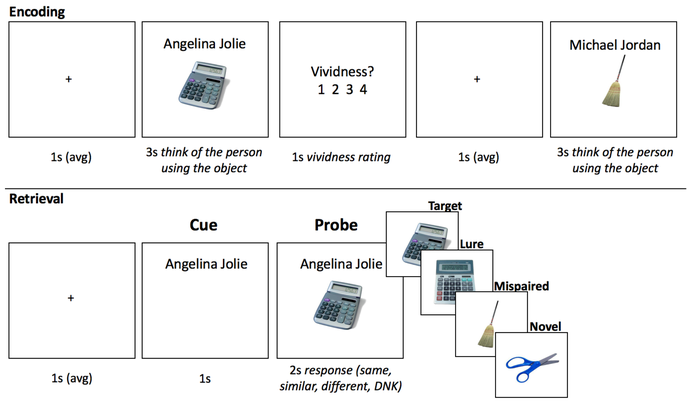


Segmentation overlay on functional scan



Segmentation overlay on structural scan

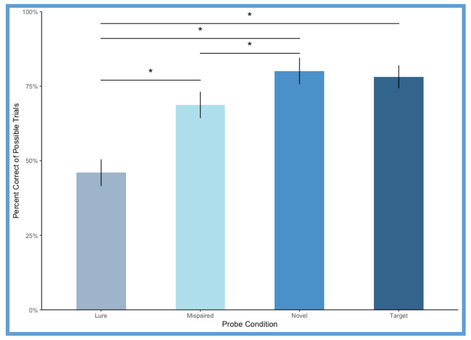
Associative memory paradigm



adapted from De Shetler & Rissman (2017)[4]

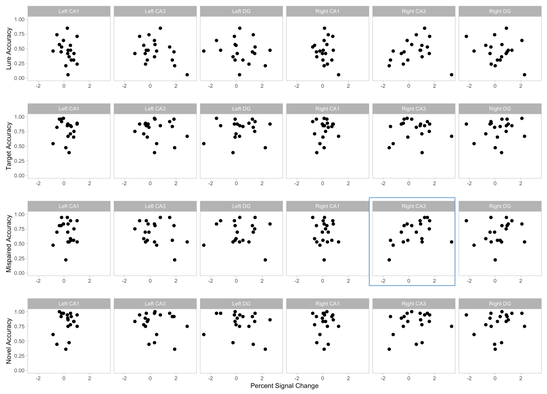
Behavioral performance

- Accuracy was lowest in the lure condition and highest in the target and novel conditions.
- Due to a high degree of accuracy, only correct trials were modeled in retrieval fMRI analyses.

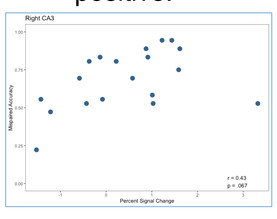


Activity-behavior correlation results

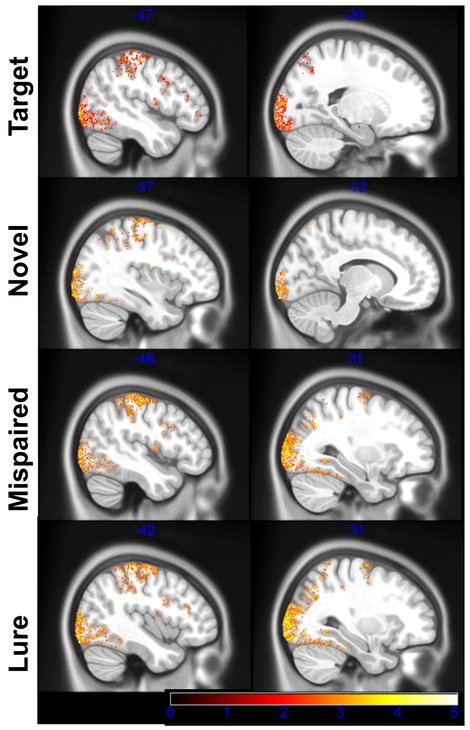
How does hippocampal subfield activity at encoding relate to retrieval performance?



- No comparisons reached statistical significance (*p* < .05), but several comparisons were trending.
- In general, left hemisphere correlations were negative, whereas right hemisphere correlations were positive.
- CA3 was positively related to accuracy in the mispaired condition (*p* = .067).



Whole-brain retrieval results



Common activity

-<u>All conditions</u>: lateral PFC, superior parietal cortex, superior frontal gyrus, middle frontal gyrus

-<u>Lure & Mispaired</u>: inferior parietal cortex

-<u>Mispaired & Novel</u>: fusiform gyrus

Condition-specific activity

-<u>Lure</u>: subiculum, pars orbitalis

-<u>Mispaired</u>: Precuneus, Insula

Discussion

- Lure trials were uniquely characterized by activity in the subiculum and orbital part of the ventrolateral prefrontal cortex, whereas mispaired trials were uniquely characterized by activity in precuneus and insula.
- There was a high degree of overlap in cortical activity across task conditions.
- Preliminary results indicate that CA3 activity at encoding may relate to better memory performance.
- Future studies will employ connectivity methods to probe how hippocampal subfields and cortical regions interact during various mnemonic processes.

References Cited

[1]Rolls, ET. (2013). The mechanisms for pattern completion and pattern separation in the hippocampus. *Frontiers in Systems Neuroscience, 7*, 1-21.

[2]Lacy J.W., Yassa, M.A., Stark, S.M., Muftuler, L.T., & Stark, C.E.L. (2011). Distinct pattern separation related transfer functions in human CA3/dentate and CA1 revealed using high-resolution fMRI and variable mnemonic similarity. *Learning & Memory, 18*, 15-18.

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[4]De Shetler, N. G., & Rissman, J. (2017). Dissociable profiles of generalization/discrimination in the human hippocampus during associative retrieval. *Hippocampus, 27*(2), 115–121.