Functional networks of hippocampal subfields are altered by associative encoding and retrieval

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Background

- The hippocampus includes distinct subfields (e.g., CA1, CA3, DG), each contributing to learning and memory processes.
- The brain-wide functional network of hippocampal subfields may be altered under different experimental conditions.
- fMRI with 1-mm isotropic resolution is beneficial to reduce false-positive correlations. However, ultrahigh-resolution fMRI with brain-wide coverage is technically challenging.
- We developed Multiband-3D (MB3D) functional imaging which allows for a whole-brain examination of hippocampal subfield and cortical activity.
- The Mnemonic Similarity Task (MST) was used to elicit memory encoding and retrieval processes.
- Targeted questions: 1) How do anatomically-defined hippocampal subfields connect within hippocampus under different experimental conditions? 2) How do anatomically-defined hippocampal subfields connect with the cortical surface under different experimental conditions?

Methods

Participants

- Adults from UNC-CH and the surrounding community completed resting-state, memory encoding, and memory retrieval scans (n = 18). Participants were 18 to 30 years (M = 21.2 years, 7 male)

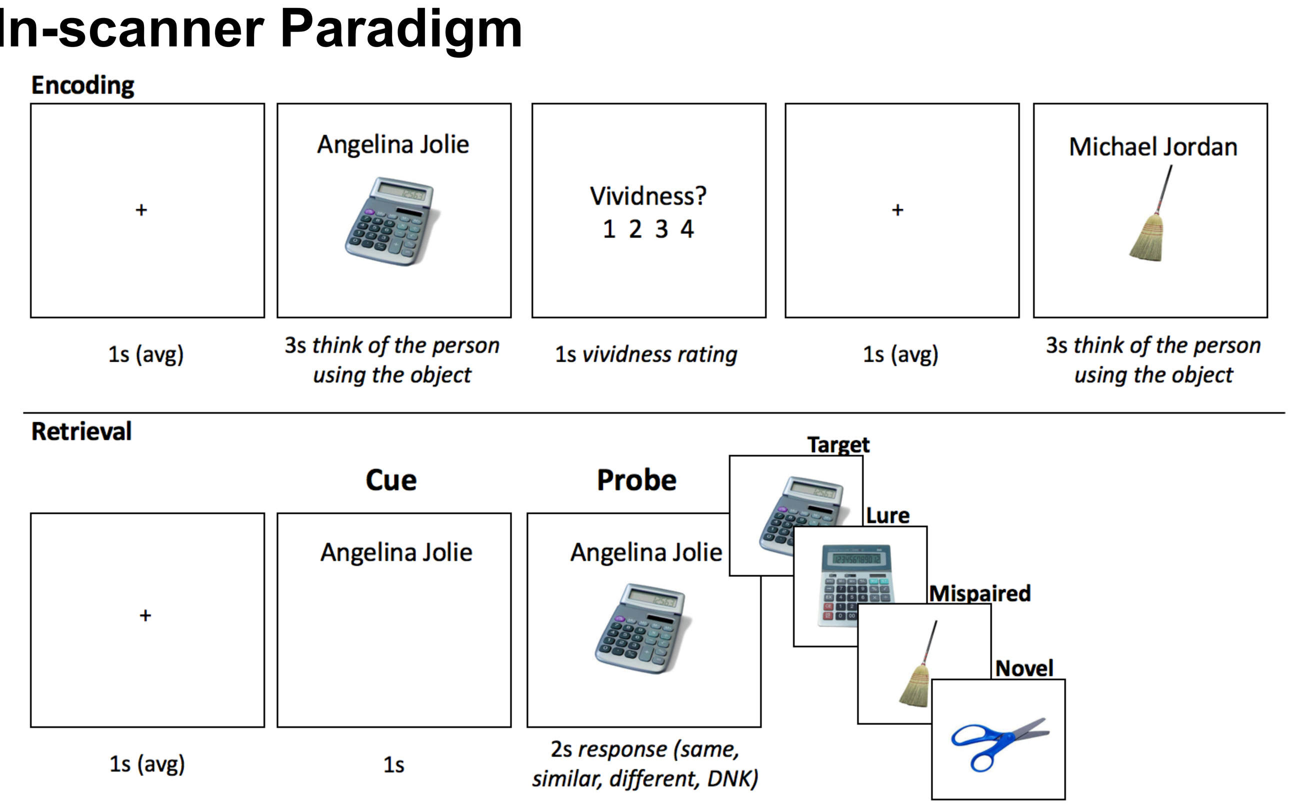
Imaging Protocol

- Siemens Magnetom 7T scanner
- Forward & reverse phase encoding
- Two 6-min resting-state scans
- Six blocks alternating encoding & retrieval phases
  - MB3D imaging (number of partition encoding = 5, multiband factor = 35, in-plane acceleration =2, TR = 2s, TE = 23ms)
  - 1.0mm isotropic, 120x152x175mm^3 field of view (SI-LR-AP)
- MP-RAGE sequence with 1-mm isotropic resolution
- T2-weighted anatomical image with 0.6-mm isotropic solution

Preprocessing and Analysis

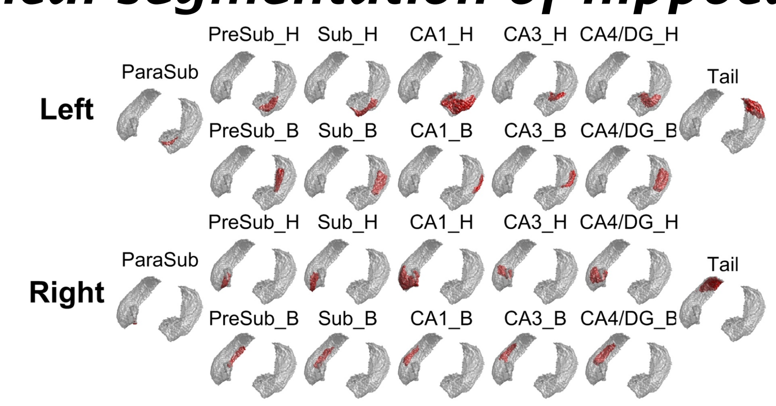
- Preprocessing and analysis steps were implemented using in-house MATLAB code, FSL and ANTS, including motion correction, and spatial coregistration
- Subfield segmentation completed through FreeSurfer v6[3] and manually checked for accuracy

In-scanner Paradigm



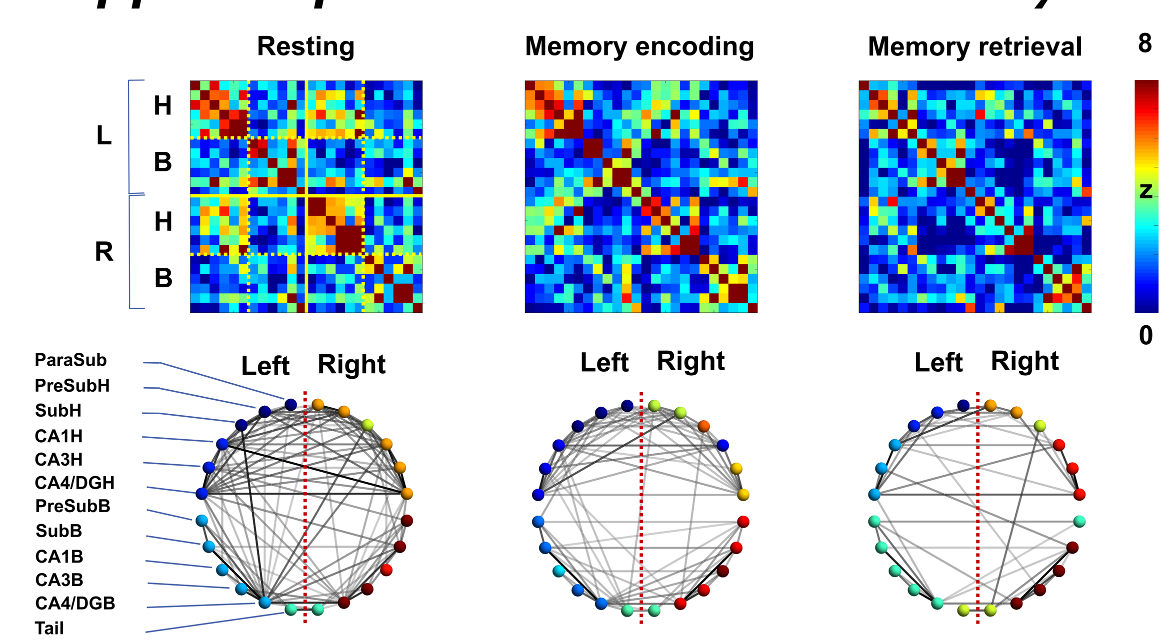
Results

Anatomical segmentation of hippocampus



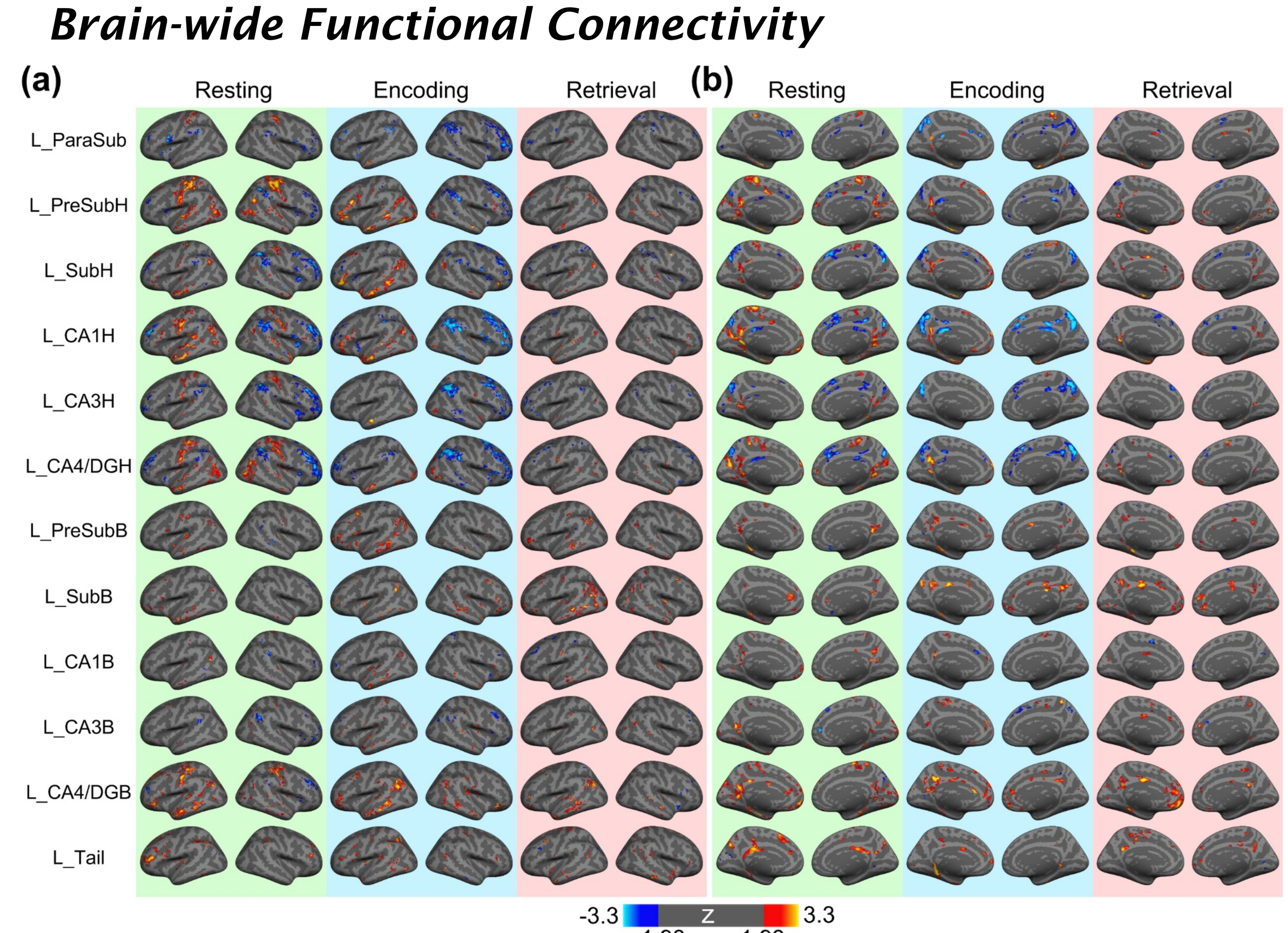
- Surface reconstruction of the hippocampal subfields. Presubiculum, subiculum, CA1, CA3, CA4/DF are subdivided into head and body portions.

Intrahippocampal Functional Connectivity

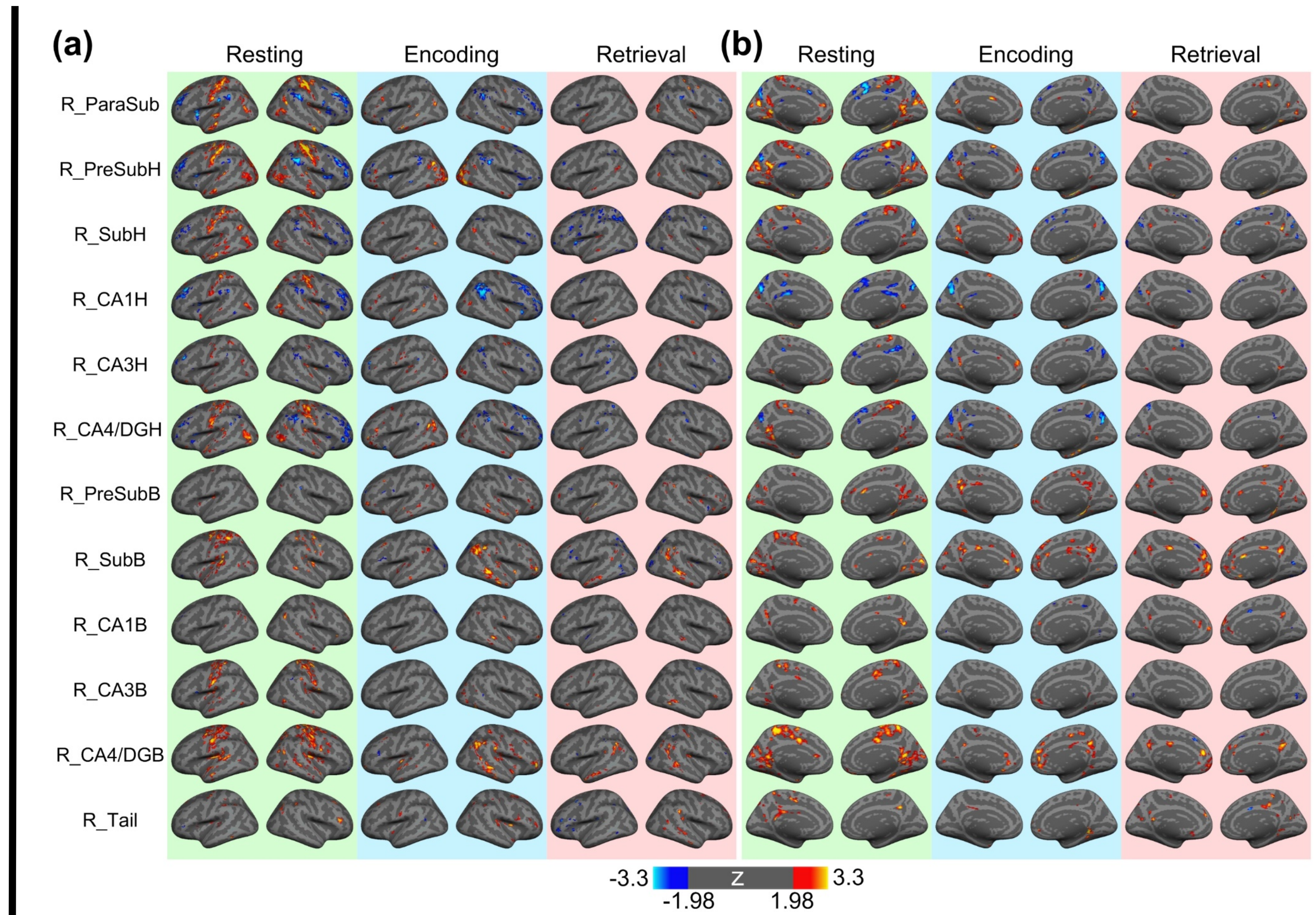


- The upper row shows the matrices of intrahippocampal correlation under different experimental conditions. The bottom row shows the thresholded functional connectivity.
- The functional connectivity (FC) was significantly decreased from resting to encoding, and even fewer functional connections during retrieval.

Brain-wide Functional Connectivity



- This figure shows the functional connectivity maps associated with right hippocampal subfields. The lateral views are shown in panel (a) and medial views in panel (b).



- This figure shows the functional connectivity maps associated with right hippocampal subfields. The lateral views are shown in panel (a) and medial views in panel (b).
- Primary sensory cortices, such as visual and sensorimotor cortex, are significantly connected with subiculum, CA1, CA3 and CA4/DG, but become dissociated with hippocampus during encoding and retrieval.
- The frontoparietal network is anti-correlated with the head portions of CA1, CA3 and CA4/DG during resting and encoding, but not during retrieval.
- The head portion of hippocampus shows less functional connectivity during retrieval.

Discussion

- The current study addressed two specific questions. First, how do hippocampal subfields connect within the hippocampus under different experimental conditions? Second, how does functional connectivity between cortex and hippocampal subfields change under different conditions?
- We found that intrahippocampal FC is stronger during resting and weaker during encoding and retrieval.
- We observed functional connectivity with primary sensory cortices primarily at rest, not during encoding/retrieval.
- Additionally, anti-correlations between frontoparietal network and hippocampal head were observed during encoding.
- The hippocampal head showed weaker FC with the cortical surface during retrieval.

References Cited

[1]Dale, A.M., Fischl, B., Sereno, M.I. (1999). Cortical surface-based analysis. I. Segmentation and surface reconstruction. *Neuroimage, 9*, 179-194.