Task Induced Modulation of Intrinsic Functional Connectivity in Medial Temporal Lobe Subregions

Mark Hollenbeck[1,3], Alyson Negreira[1,3], Michael Brickhouse[1,3], Brad Dickerson[2,3,4]

MGH Frontotemporal Dementia Unit, Departments of and Psychiatry[1] and Neurology[2]; Martinos Center for Biomedical Imaging[3]; Massachusetts General Hospital and Harvard Medical School[4], Boston, MA

BACKGROUND

- Two major parallel visual pathways, often characterized as pathways for object and spatial sensory information, converge on distinct medial temporal lobe (MTL) subregions, enabling the associative binding of object and context.

- The perirhinal cortex (PrC) receives afferent input from ventral visual association areas, including the fusiform gyrus. The PrC sends efferent projections via the lateral entorhinal cortex (lErC) to the hippocampal formation.

- The parahippocampal gyrus receives input from the dorsal visual association areas, and sends efferent projections via the medial entorhinal cortex to the hippocampal formation, where objects and locations are thought to be bound together.

OBJECTIVES

- To further investigate both the specificity of functional-anatomic connectivity between MTL subregions and visual cortical areas, and whether the strength of functional connectivity between these regions can be modulated in a content-specific fashion in visual encoding tasks.

- We hypothesize that the strength of functional connectivity between fusiform and both PrC and anterior hippocampal formation (aHip) will be increased after an object-based encoding paradigm.

- We also hypothesize that the strength of functional connectivity between the parahippocampal gyrus and the posterior hippocampus (pHip) will increase after a spatial-based encoding paradigm.

DATA ACQUISITION

Dataset 1: Resting-state fMRI (rs-fMRI) was acquired for 89 healthy young adults (mean age=22.24; 44 male)

Dataset 2: rs-fMRI data was acquired prior to, and following, face, place, and object recognition encoding fMRI tasks for 17 healthy young adults (mean age=23.11; 5 male). Each task consisted of an encoding task (30 image/name pairs; 15 famous, 15 non-famous) followed by a post-scan retrieval memory task (60 image/name pairs; 30 famous, 30 non-famous).

Rs-fMRI → Task (Places, Faces, or Objects) → Rs-fMRI

DATA ANALYSIS

DEFINING THE ROIs OF THESE CIRCUITS

Dataset 1 was used to define the ROIs for these circuits in a presumably generalizable fashion from a large sample of subjects who were scanned during the "resting state."

To explore the connectivity between the object-sensitive ventral visual association areas and the MTL, we localized a region in the right fusiform gyrus that is specific to faces, the fusiform face area (FFA). Similarly, the parahippocampal place area (PPA) was used to explore the functional connectivity between the spatially-sensitive dorsal visual association areas and the MTL.

Timecourse of spontaneous activity was extracted from the FFA and PPA ROIs and used for intrinsic functional connectivity MRI analysis (fcMRI) in dataset 1. Group-level Fisher's *r*-to-*z* maps were generated to determine connectivity with two MTL sub-regions, the PrC and the posterior parahippocampal cortex (PPHC). The PrC was identified from FFA connectivity, and the PPHC from PPA connectivity.

The PrC and PPHC regions were then used as seeds in a subsequent fcMRI analysis to locate hippocampal and entorhinal ROIs. The lErC and aHip were defined from PrC connectivity, and pHip from PPHC connectivity.

MODULATION EFFECTS

Dataset 2 was used to examine the modulation of functional connectivity between the regions defined above. FcMRI Fisher's *r*-to-*z* maps were generated separately for the pre- and post-objects task and pre- and post-places task.

Statistical maps of modulation by each task were generated by computing a 2-class general linear model (GLM) analysis testing for the effect of task on connectivity at each voxel. These maps were used for visual exploration of connectivity modulation within the MTL.

To quantitatively assess the modulation within the object-sensitive circuit, the mean correlation values between FFA, PrC, lErC, and aHip were extracted from the modulation map of each task. The spatially-sensitive circuit was assessed in the same manner for PPA, PPHC, and pHip.

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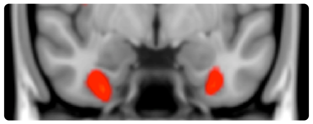
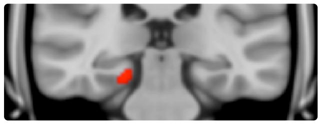
RESULTS

FFA Functional Connectivity Map



FFA functional connectivity map showing the PrC , $Z(r) > 0.05$

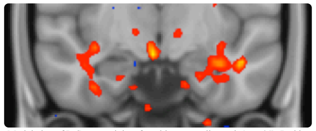
PPA Functional Connectivity Map



PPA functional connectivity map showing the PPHC, $Z(r) > 0.3$

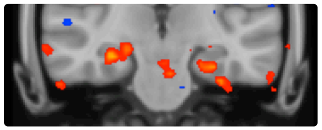
MODULATION OF FUNCTIONAL CONNECTIVITY

PrC Modulation (After Objects Encoding)

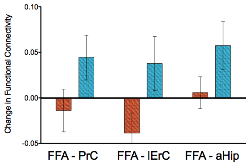


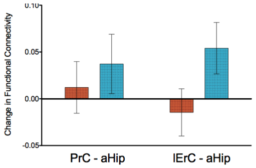
Modulation of PrC connectivity after objects encoding task ($p < .05$). Red is increased connectivity after task, blue is decreased.

PPHC Modulation (After Places Encoding)



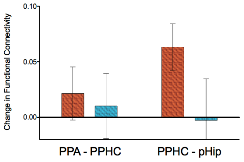
Modulation of PPHC connectivity after places encoding task ($p < .05$). Red is increased connectivity after task, blue is decreased.





OBJECTS
PLACES

Mean correlation values of ROI-to-ROI connectivity modulation. Positive is increased connectivity after task, negative is decreased connectivity after task.



CONCLUSIONS

Our results support the hypothesis that 1) resting state functional connectivity reflects both anatomic connectivity as well as the dynamic history of the circuit; and 2) the specific pathways hypothesized to bring visual information into the hippocampal formation, based on animal studies, function in a similar content-specific fashion in humans during the encoding of new information. The encoding of objects increases functional connectivity between the ventral temporal association regions in the fusiform gyrus and the PrC, as well as PrC/ErC and anterior hippocampus, while the encoding of spatial information does not. In contrast, the connectivity between PPHC and posterior hippocampal regions is increased after encoding of spatial information but not after object encoding.

REFERENCES: Dickerson and Eichenbaum, Neuropsychopharmacology, 2009; Grill-Spector et. al, Nature Neuroscience, 2004.