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Relating Resting-State Functional Connectivity of the Hippocampus and Language Cortex to Language Abilities in Temporal Lobe Epilepsy

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INTRODUCTION

- The vital role of the hippocampus in memory function has been well-established, but recent studies have also highlighted the direct contributions of the hippocampus to language processing in healthy adults.
- These novel findings suggest that the hippocampus and its connections to language regions may be related to language abilities in patients with hippocampal damage or impairment, like temporal lobe epilepsy (TLE).
- Previous studies assessing the relationship between functional connectivity of the hippocampus and neurocognitive abilities in TLE have primarily focused on memory abilities, and brain regions involved in memory.
- The purpose of the present work was to:
 - 1) Determine whether patterns of functional connectivity between the bilateral hippocampi and fronto-temporo-parietal language regions differ between healthy adults and patients with right or left TLE
 - 2) Measure the relationship between hippocampal-language functional connectivity and scores on neuropsychological language measures in patients with TLE

METHODS

SUBJECTS

- 54 healthy controls (age: M: 37.00 years, SD: 13.78)
- 40 unilateral presurgical TLE patients with seizures identified using standard clinical assessments by neurosurgery team (video-EEG, MRI, PET)
 - 27 right TLE patients (age: M: 39.44 years, SD: 10.52)
 - 13 left TLE patients (age: M: 37.62 years, SD: 15.23)

NEUROPSYCH LANGUAGE TESTS

- Verbal IQ Score, Boston Naming Test, Word Generation Task

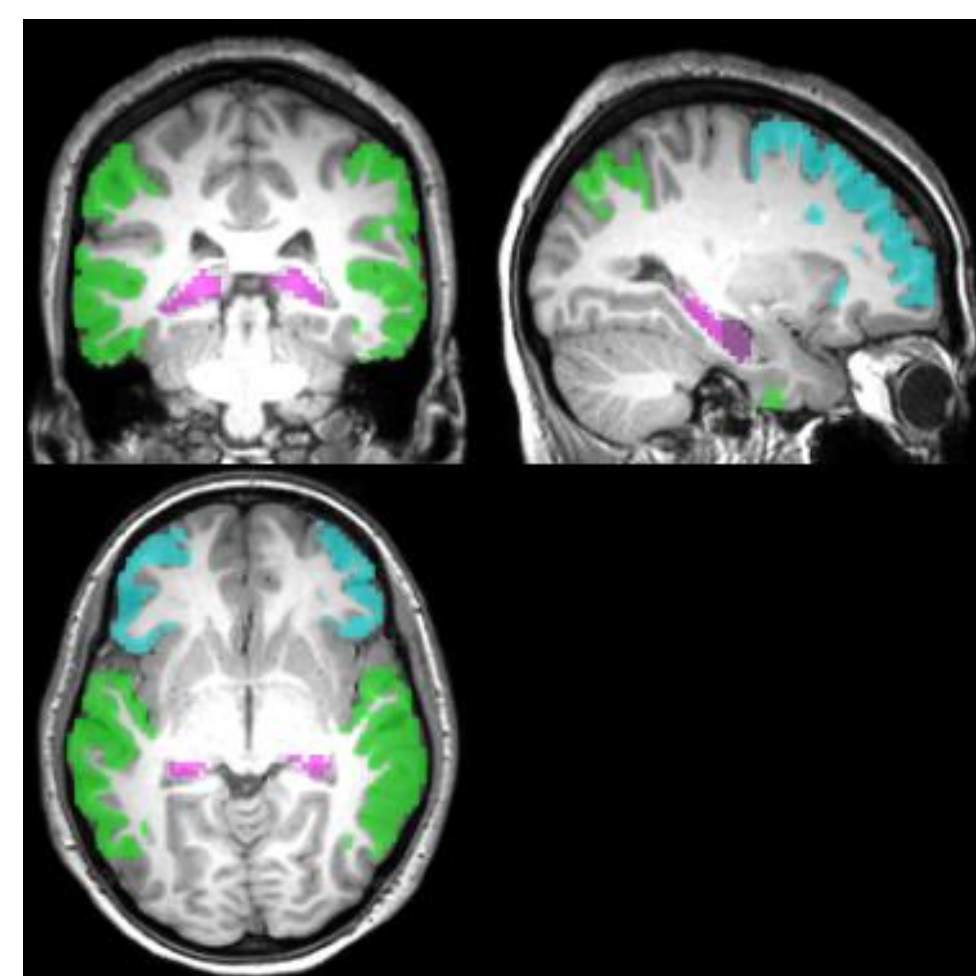
IMAGING

- 3T MRI resting state T2* weighted BOLD fMRI [TR: 2 s, total duration: 10 mins, voxel size: 3 x 3 x 4 mm³]

REGIONS OF INTEREST (ROIS)

- Bilateral Hippocampi**
 - Segmented into **anterior** and **posterior** sections using FreeSurfer
- Language Regions**
 - Segmented using MultiAtlas
 - Frontal Regions:**
 - Middle frontal gyrus
 - Orbital inferior frontal gyrus
 - Triangular inferior frontal gyrus
 - Temporo-Parietal Regions:**
 - Inferior temporal gyrus
 - Middle temporal gyrus
 - Planum polare
 - Superior temporal gyrus
 - Transverse temporal gyrus
 - Angular gyrus
 - Supramarginal gyrus

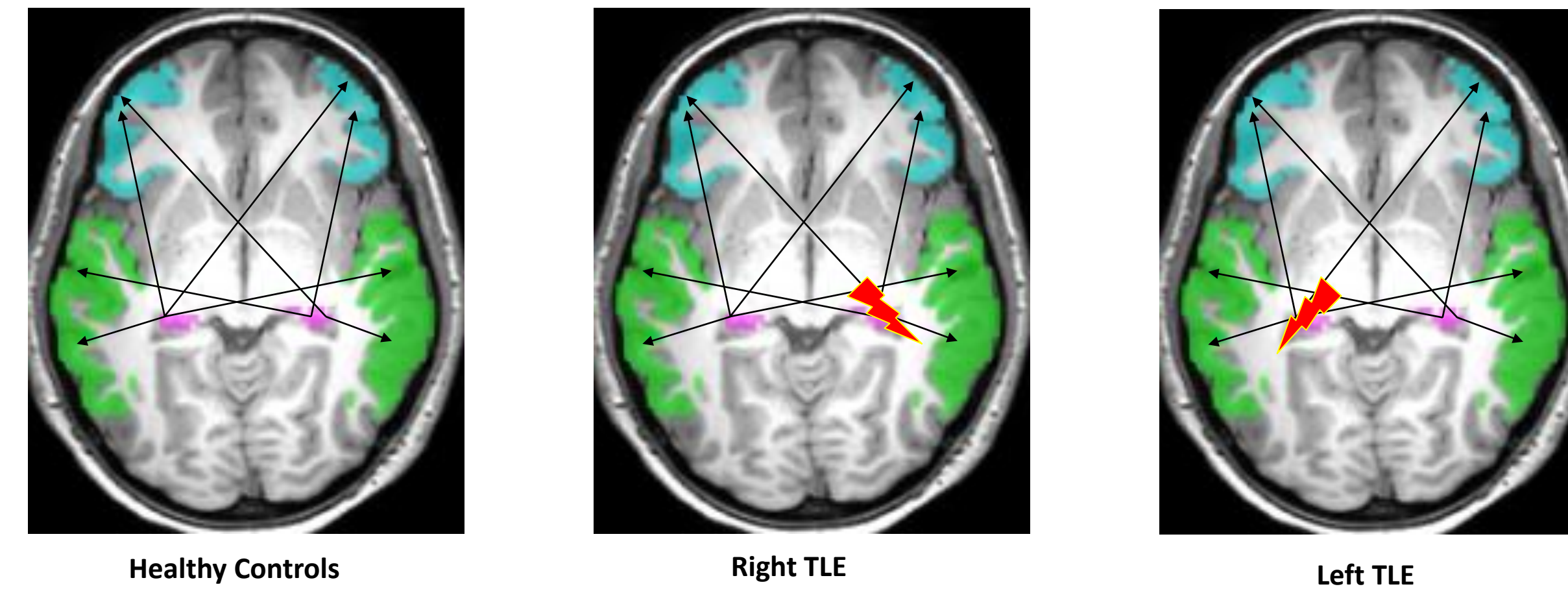
Voxels included in Functional Connectivity Analysis



FUNCTIONAL CONNECTIVITY (FC) ANALYSIS

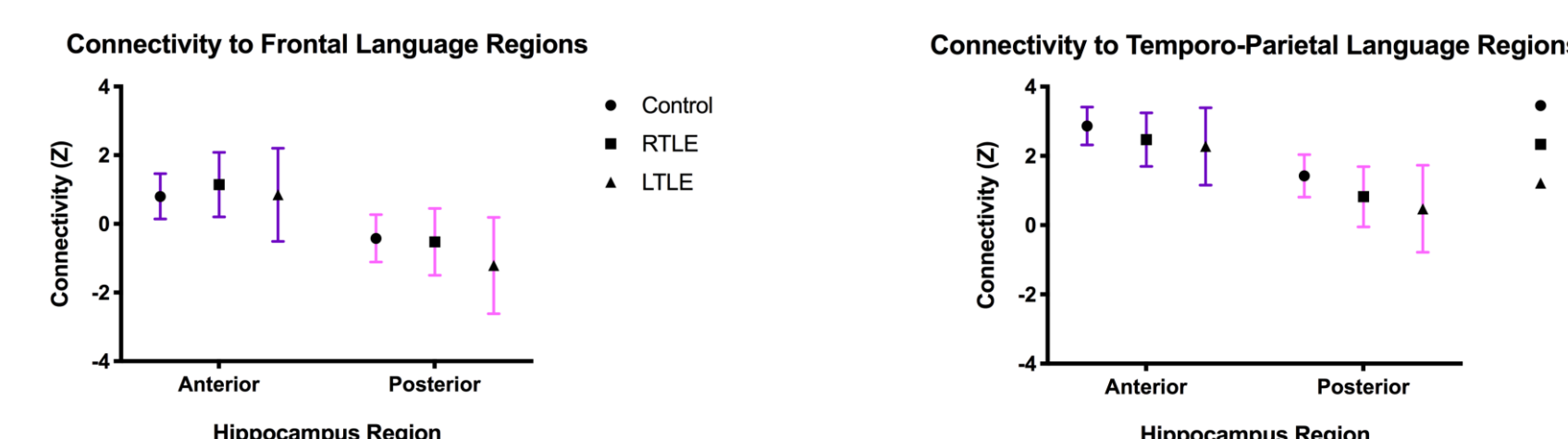
- FC was measured as the pairwise partial correlation between the time series of the hippocampus sections to each language region, and then averaged into single FC values for anterior and posterior hippocampus to Frontal and Temporo-Parietal regions

METHODS CONT.



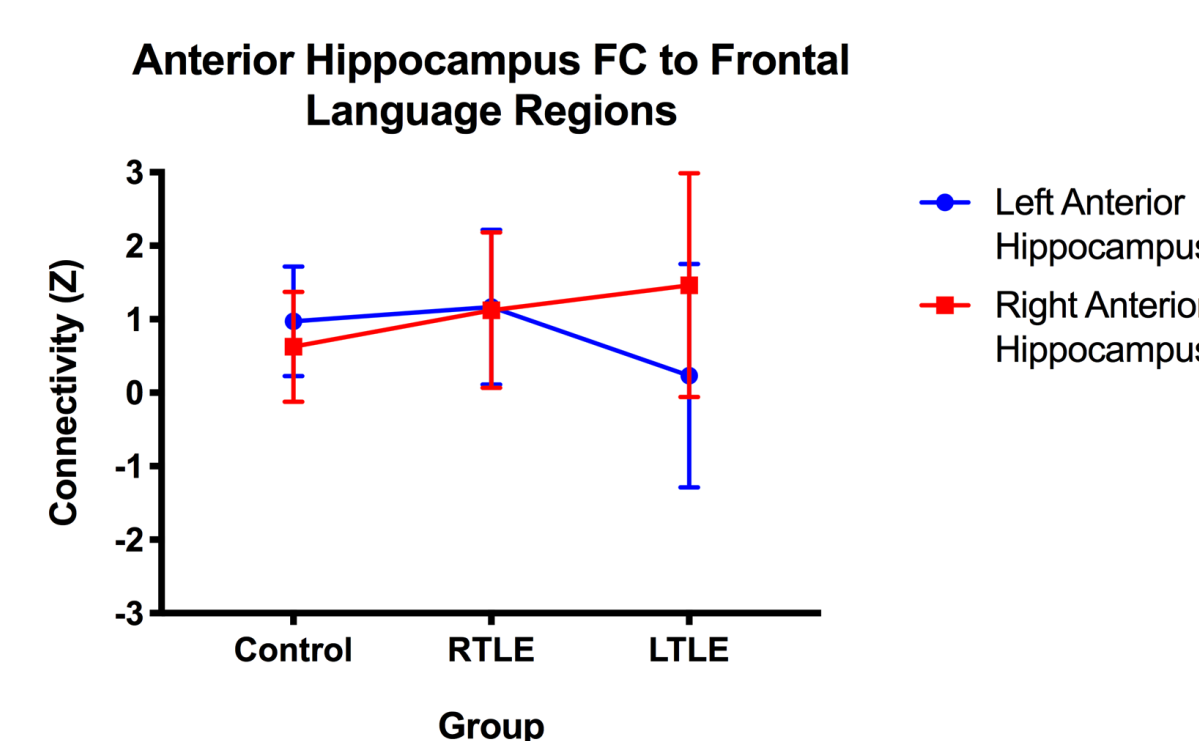
RESULTS: FUNCTIONAL CONNECTIVITY PATTERNS

FC of Anterior vs. Posterior Hippocampi to Language Regions



Significantly stronger connectivity from both frontal and temporo-parietal language regions to the bilateral anterior hippocampus compared to bilateral posterior hippocampus ($p < 0.001$)

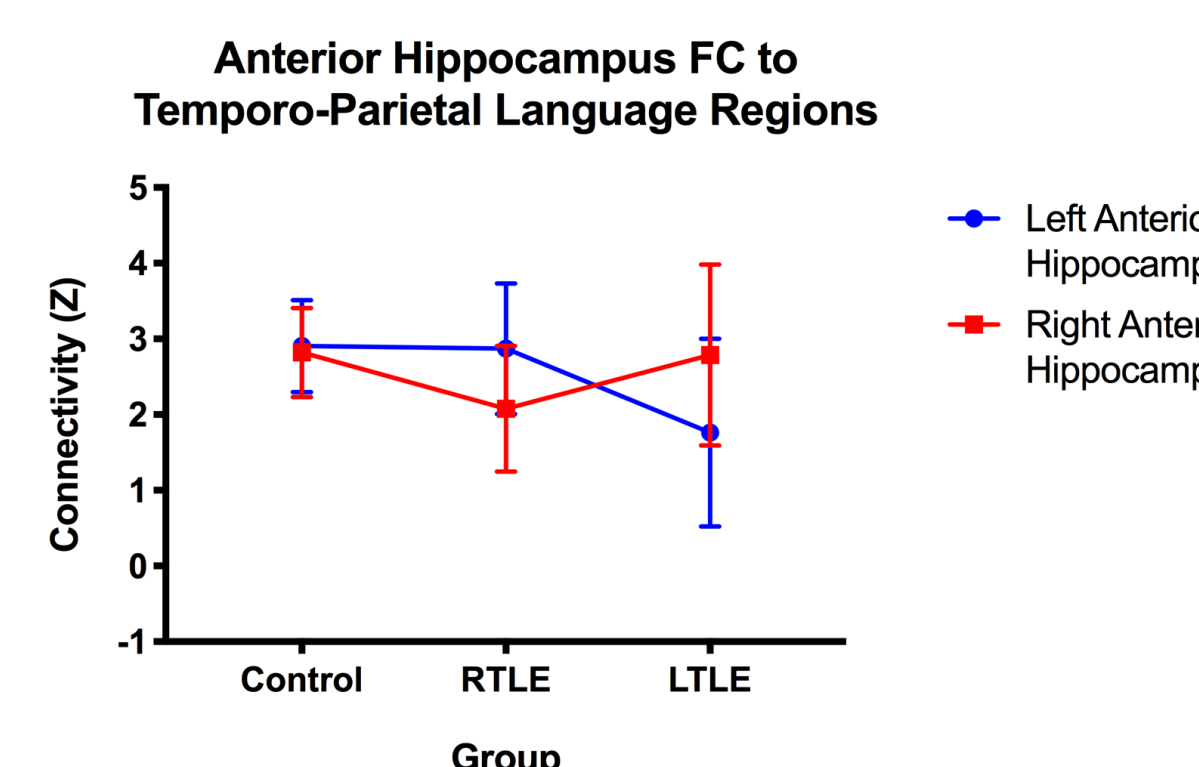
FC of Anterior Hippocampi to Frontal Language Regions



Across groups: No significant differences between anterior hippocampal-frontal language connectivity

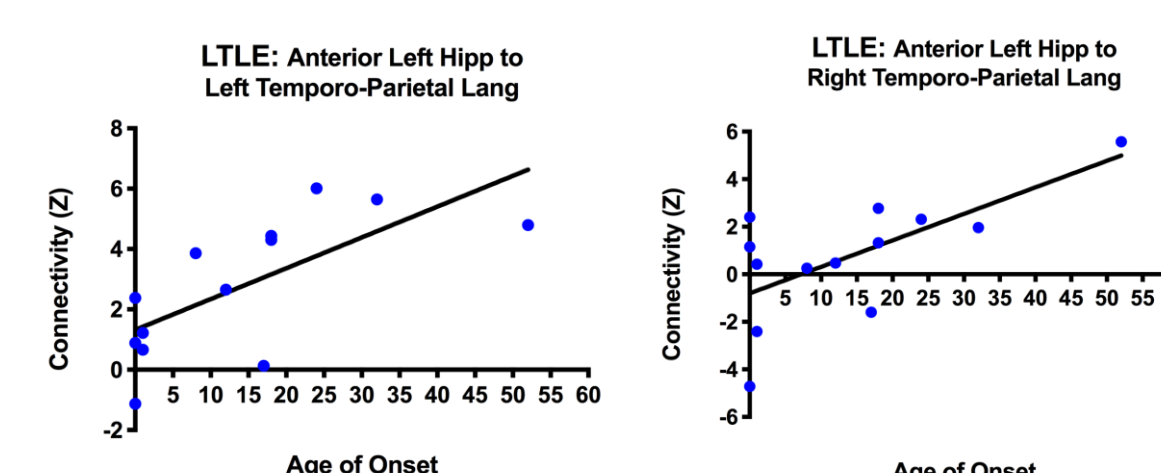
Within groups: no significant differences between right vs. left anterior hippocampus FC

FC of Anterior Hippocampi to Temporo-Parietal Language Regions



Across groups: Significant interaction ($p = 0.01$) between groups and left vs. right anterior hippocampal FC

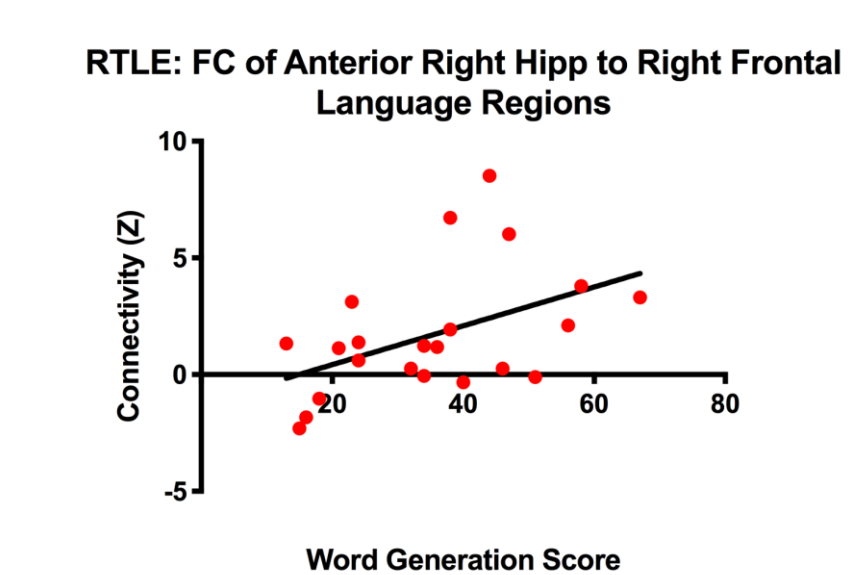
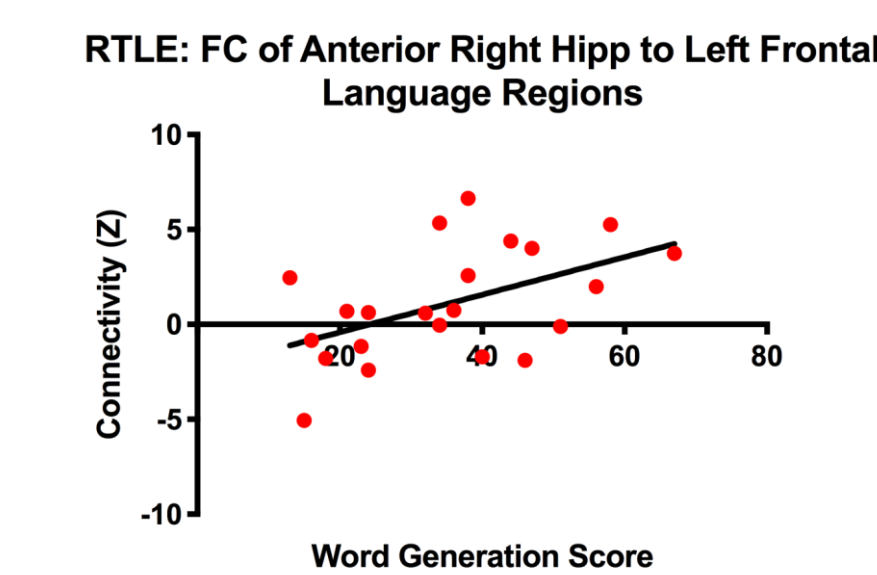
Within groups:
Control = no significant differences ($p = 0.73$)
RTLE = significantly stronger FC to left anterior hippocampus ($p = 0.02$)
LTLE = significantly stronger FC to right anterior hippocampus ($p = 0.04$)



Within LTLE group only, significant correlations found between Age of Onset of epilepsy and connectivity of the left anterior hippocampus temporo-parietal language regions of both left and right hemisphere

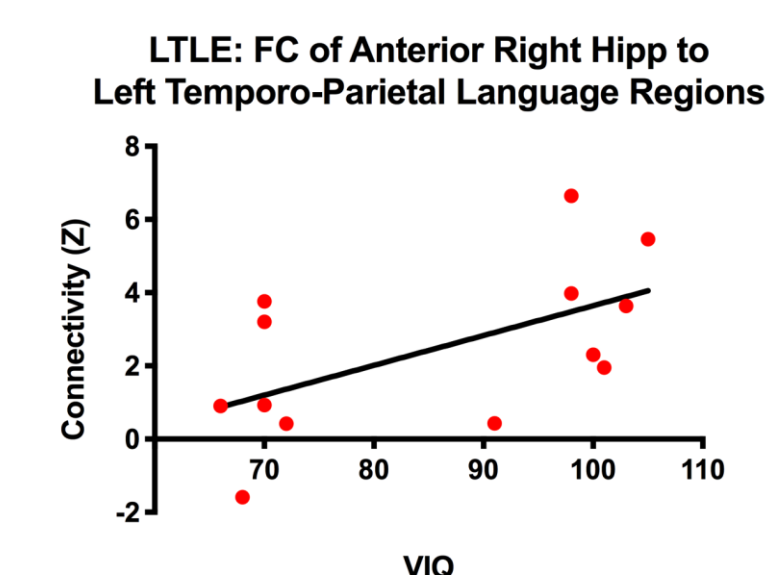
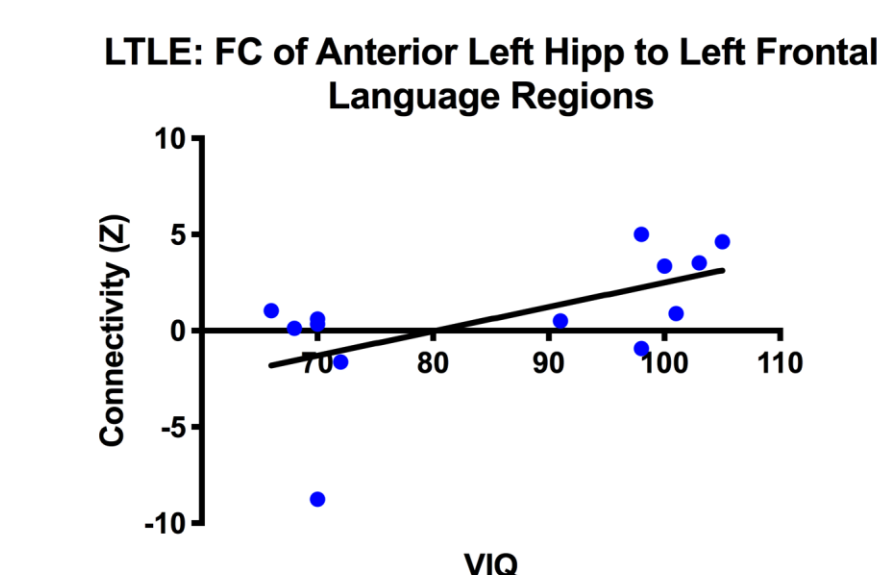
RESULTS: RELATION TO LANGUAGE ABILITIES

Right TLE



Significant positive correlations between the Word Generation Score and the right anterior hippocampus to left frontal language regions ($r = 0.47$) and right frontal language regions ($r = 0.50$; both $p < 0.05$)

Left TLE



Significant positive correlations between VIQ and the left anterior hippocampus to left frontal language regions ($r = 0.58$) and the right anterior hippocampus to left temporo-parietal language regions ($r = 0.57$; both $p < 0.05$)

CONCLUSIONS & FUTURE DIRECTIONS

Conclusions:

- Across all groups, functional connectivity was strongest between frontal and temporo-parietal language regions and the anterior portion of the bilateral hippocampi
- Functional connectivity between the anterior hippocampi to the more distal frontal language regions did not reveal different patterns across groups
- Functional connectivity between the anterior hippocampi to the temporo-parietal language regions closer to the seizure foci did suggest differences between RTLE and LTLE groups – each patient group showed stronger connectivity to their unimpaired hippocampus
- Significant associations were found between anterior hippocampal-language functional connectivity and neuropsychological measures of language that may inform novel mechanistic models of language impairment in patients with TLE

Future analyses on this dataset will:

- 1) Investigate hippocampus-language FC in an fMRI language task to determine whether connectivity patterns differ in controls and epilepsy patients during active language processing compared to resting-state
- 2) Investigate hippocampus-language FC in postsurgical fMRI data in the same patients to determine whether reorganization of functional connectivity patterns is related to language outcomes after surgery

ACKNOWLEDGEMENTS

This work was supported by NIH NS075270, NIH NS108445, NIH NS110130 (Morgan) and NIH NS097618 (Englot)