Patients with **left temporal lobe epilepsy** showed greater **right lateralization of language** than right temporal lobe epilepsy patients as measured by hippocampal-language functional connectivity during **resting-state**

Hippocampal-Language Network Laterality in Temporal Lobe Epilepsy: A Novel Measure Using Resting-State Functional Connectivity

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INTRODUCTION

- Determining language lateralization is a crucial part of the epilepsy presurgical evaluation to inform the potential for language deficits, especially in patients with temporal lobe epilepsy. The most common method for measuring language lateralization uses fMRI language tasks.
- However, this measure is dependent upon the specific language task used (which varies widely across epilepsy centers), as well as the individual performance and compliance of the patient during the task. In addition, fMRI tasks often do not elicit activation of the hippocampus, which is where seizures originate for temporal lobe epilepsy patients. Thus, crucial information about how the hippocampus may be involved in the laterality of language functioning remains unknown. No measure of resting-state lateralization has yet used a hippocampal seed.
- In this study, we explored a novel resting-state functional connectivity measure of language lateralization in temporal lobe epilepsy patients by assessing laterality of the hippocampal-language network.

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)

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

Neuropsych Language Tests: Verbal Comprehension Index (WAIS), NAB Naming Test, Word Generation: Categories & Letters, Wechsler Memory Scales (WMS), California Verbal Learning Test (CVLT)

Segmentation of ROIs: Bilateral hippocampi were segmented into anterior and posterior sections using FreeSurfer, and 11 language regions in the frontal, temporal, and parietal lobes were segmented using MultiAtlas

Resting-State Language Lateralization Index (LI-Rest): LI-Rest was calculated using the Quantitative Intrinsic Laterality Index from Liue et al. (2009), where the seed was always the anterior or posterior hippocampus and the target was the frontal or temporo-parietal language regions. This resulted in four LI-Rest measures per subject, defined as values ≥ 0.20 indicating left lateralization and ≤ -0.20 indicating right lateralization.

$$LI - Rest = \frac{(LL-RL)-(RR-LR)}{|LL|+|LR|+|RR|+|RL|}$$

RESULTS

- The LI-Rest measures were found to produce **lateralized values in 68.1% of subjects**
- Repeated measures ANOVA revealed no significant differences in LI strength between Hippocampus Region (anterior, posterior), Language Region (frontal, temporo-parietal), or Group (control, right TLE, left TLE). However, there was a significant Language Region x Group interaction (p = .01), in which **the left TLE group showed significantly more right lateralization than right TLE in the temporo-parietal language region**s (LTLE M= -0.24 ± 0.43, RTLE M= 0.06 ± 0.52; p = .02; see Figure 1). This could suggest a compensatory mechanism of reorganization to the right hemisphere that has also been found in fMRI task lateralization studies for left TLE patients.
- In addition, within the left TLE group only, significant negative correlations were found between two LI-Rest measures and the CVLT Long Delay test of verbal memory, suggesting stronger right-sided LI to frontal and temporo-parietal regions is associated with better verbal memory abilities (see Figure 2; both p < .05).

CONCLUSIONS

- Our results suggest that a language lateralization measure acquired from resting-state functional connectivity between the hippocampus and language regions may be a useful tool to detect lateralization in cases where task LI is not suitable and warrants further investigation in a larger sample.
- Future work aims to compare our LI-Rest measure to the WADA and LI measured from fMRI tasks in the same patients.

This work was supported by NIH Health R01 NS075270, R01 NS108445, R01 NS110130, R00 NS097618, T32 EB001628.

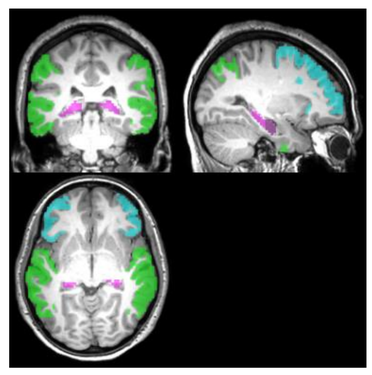
REGIONS OF INTEREST (ROIS)

- ***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
Planum temporale
Superior temporal gyrus
Transverse temporal gyrus
Angular gyrus
Supramarginal gyrus

Voxels included in Functional Connectivity LI-Rest Measures



Hippocampal-Language LI-Rest Measures Across Groups

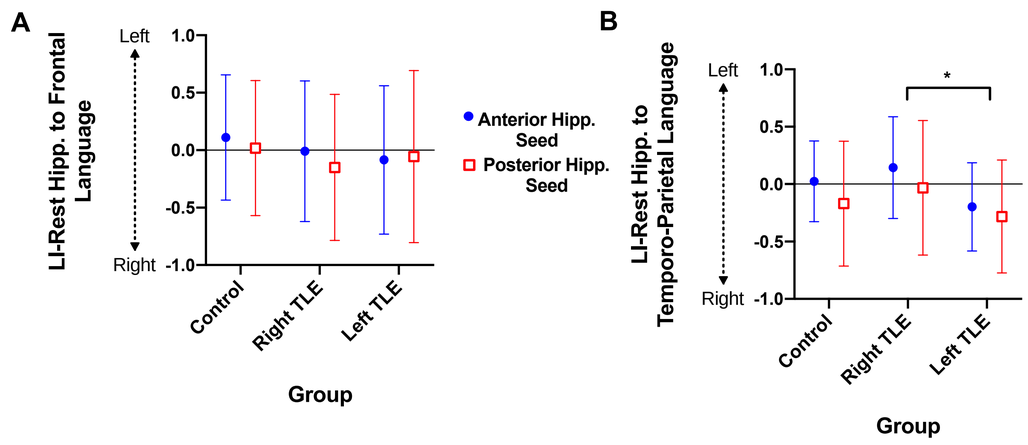


Figure 1. LI-Rest values calculated from both anterior and posterior hippocampal seeds to frontal and temporo-parietal language regions. The left TLE group showed significantly more right lateralization for temporo-parietal regions closest to the seizure focus than right TLE patients (LTLE M= -0.24 ± 0.43, RTLE M= 0.06 ± 0.52; $p = 0.02$).
Error bars represent standard deviations. *$p < .05$

Relation to Language and Verbal Memory Neuropsychological Measures

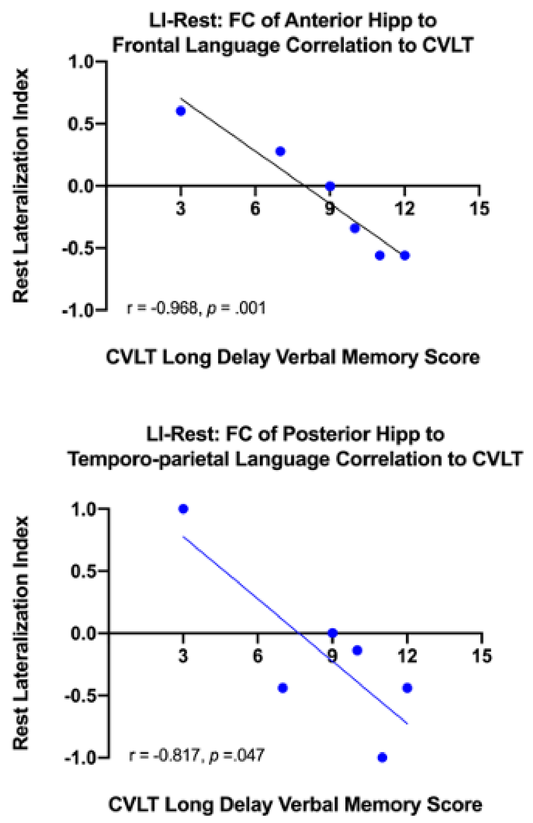


Figure 2. Left TLE Correlations between two LI-Rest measures and the California Verbal Learning Test (CVLT). Note that the full sample (n=13) was not able to be used because only a subset had CVLT scores. Top: LI-Rest measured as the lateralization of the functional connectivity between the anterior hippocampus and frontal language regions (r = -0.968, $p = .001$). Bottom: LI-Rest measured as the lateralization of the functional connectivity between the posterior hippocampus and temporo-parietal language regions (r = -0.817, $p = .047$). Both negative correlations signify that better verbal memory scores are associated with stronger right lateralization of hippocampal-language connectivity.

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