Hippocampal Pathology Affects Local and Global Network Controllability in Temporal Lobe Epilepsy

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PURPOSE

Drug-resistant temporal lobe epilepsy (TLE) in adults commonly includes a pathology of hippocampal sclerosis (HS), neuronal loss and gliosis that can extend into the amygdala. However, TLE involves impairment of brain regions and networks beyond the seizure focus.

The purpose of this study was to investigate the impact of pathology on network-wide brain dynamics in presurgical TLE patients, using networks derived from diffusion-weighted imaging (DWI) and average regional controllability (ARC) which is a measure to determine a region's influence on brain state dynamics.

METHODS

Subjects
- 52 unilateral TLE patients (16 left TLE, 42 HS)
- 95 healthy controls

3T MRI imaging
- T1-weighted MRI (1x1x1mm^3)
- 117 cortical and subcortical regions of interest using automated parcellated
- DWI: 2.5x2.5x2.5 mm^3, 92 directions, and b-value = 1600 s/mm^2

ARC
- Structural connectomes (SC) were generated using whole-brain tractography with strength defined as the weighted number of streamlines between each region pair
- ARC: a measure of the ability for each brain region to steer the network into different states with little effort [1]
- ARC computed for each region in every subject

Statistical analysis
- TLE patients were separated into two groups: (1) Pathology confirmed HS, and (2) either partial gliosis or normal pathology
- Unpaired t-tests were performed with ARC for each region between each group of patients and controls
- A total z-score of absolute distance from controls was computed in each hemisphere for each group of patients and was compared between hemispheres

RESULTS

Structural connectome generation

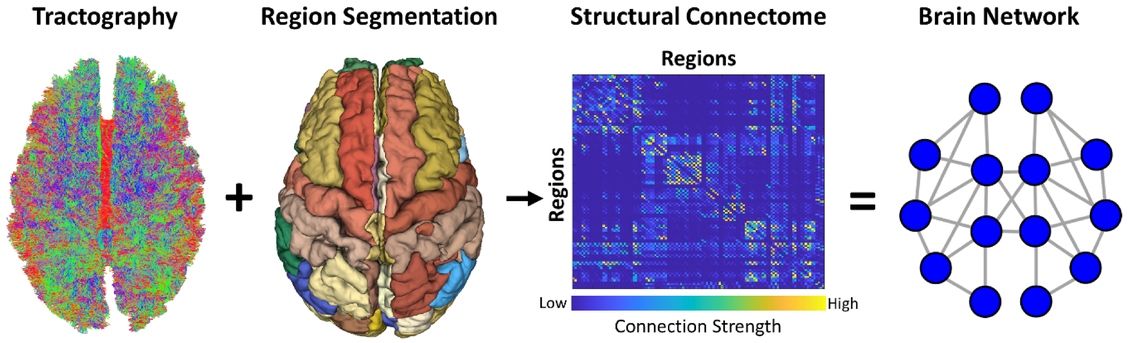


Figure 1. Structural brain network generation from diffusion weighted imaging. Whole brain anatomically constrained tractography is combined with a 117 brain region parcellation to generate a structural connectome defining the strength of connection between every pair of regions. The connectome is treated as a graph network and dynamic measures of controllability are computed for each region in the network.

ARC differences in TLE and across hemispheres

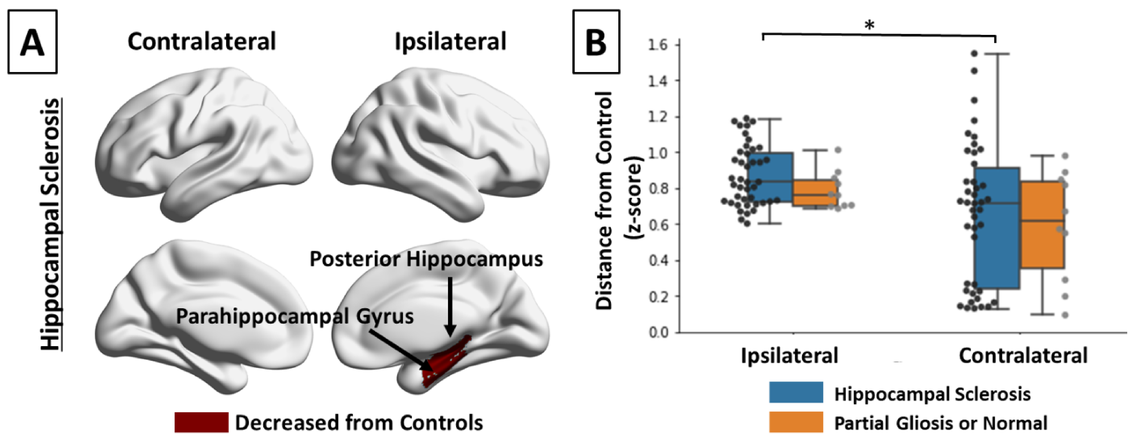


Figure 2. Average regional controllability (ARC) differences in TLE patients separated by hippocampal pathology. (A) Reductions in ARC in TLE with hippocampal sclerosis (HS) compared to healthy controls within the posterior hippocampus and parahippocampal gyrus ($p<0.05$, adjusted $\alpha=0.05/117$). (B) Total absolute distance (z-score) from healthy controls, across each hemisphere, in TLE with HS and TLE with partial gliosis or normal pathology. For TLE-HS, the ipsilateral hemisphere demonstrated higher distance from controls compared to the contralateral hemisphere (*$p=0.002$). No other comparisons were significant.

CONCLUSIONS

ARC is decreased around the seizure focus.

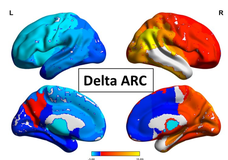
ARC distance from controls is increased in TLE-HS in the ipsilateral vs. contralateral hemisphere

ARC is not changed in patients without HS

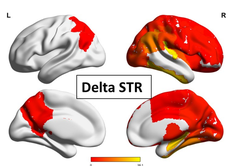
This study suggests that hippocampal pathology in the seizure focus has both local and global effects on how brain regions coordinate brain state dynamics.

FUTURE WORK

Future work will investigate the effect of node removal on ARC and node strength (STR) across the brain.



Simulated mesial temporal resection in controls



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1. Gu et al., *Nat Comm* 2015; 6(1): 8414

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