Differences Between Left and Right Mesial Temporal Lobe Epilepsy Using Resting-State Network fMRI and SEEG Connectivity

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1 Introduction

- About 51.7 million people globally have epilepsy.[1]
- 40% of people continue having seizures, despite medications.[2]
- Drug-resistant patients may experience seizure reduction/elimination from epilepsy surgery.[3]
- Mesial temporal lobe epilepsy (mTLE) is the most common type of surgically treatable epilepsy.[4]
- Lateralizing mTLE is problematic due to rapid contralateral spread.[5]
- Resting-state functional MRI (fMRI) has been used to identify abnormal connectivity in mTLE, involving mesial temporal structures and resting-state networks, but rarely investigated for lateralization.[6]
- Noninvasive epileptogenic lateralization in mTLE has proven challening with fMRI.[7]

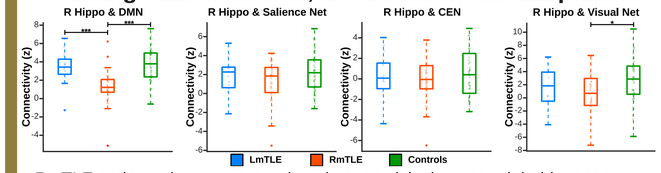
Questions:

- Would directed and nondirected functional connectivity (FC) between mesial temporal structures and resting-state networks facilitate mTLE lateralization?
- Does directionality of hippocampal connectivity alterations using fMRI resemble those measured using stereo-electroencephalography (SEEG) in mTLE patients?

2 Methods

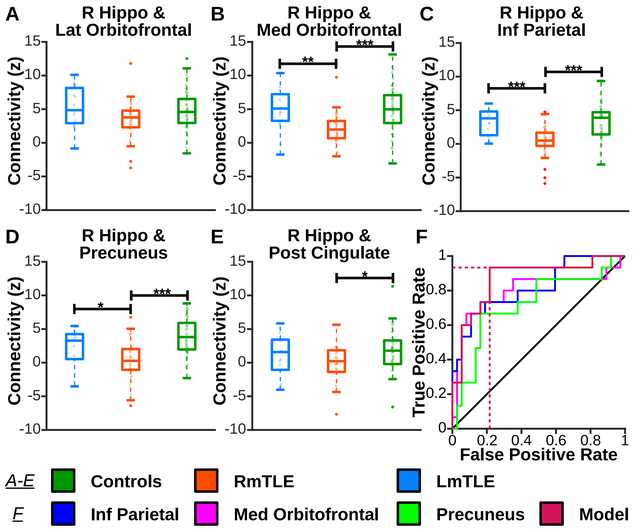
- For 52 left (LmTLE) or right (RmTLE) patients and matched control subjects.
- We acquired 20 minutes of resting-state fMRI.
- Using nondirected Pearson correlation, receiver-operating characteristic (ROC) curves, and network-based statistic (NBS), we compared the ability to distinguish between LmTLE and RmTLE patients using mesial structure and resting-state network connectivity.
- We evaluated fMRI with directed dynamic causal modeling.
- We acquired two minutes of resting-state SEEG in 17 mTLE patients.
- We calculated hippocampal versus extrahippocampal inward partial directed coherence (PDC) strength.
- We compared the PDC results calculated with SEEG to the directed dynamic causal modeling results calculated with fMRI.

3 FC between right hippocampus and DMN, but not other resting-state networks, is reduced in RmTLE patients



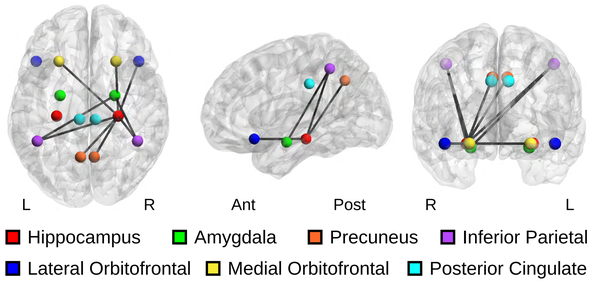
RmTLE patients demonstrate reduced connectivity between right hippocampus and DMN structures compared to LmTLE patients and control subjects. ***p<0.001, **p<0.01, *p<0.05, one-way ANOVA with Tukey's honest signficant difference criterion post hoc and with Bonferroni-Holm correction. N=15 LmTLE patients, N=37 RmTLE patients, and N=52 control subjects. CEN=central executive netowrk, DMN=default mode network, hippo=hippocampus.

4 Connectivity between right hippocampus and certain individual DMN structures is reduced in RmTLE patients



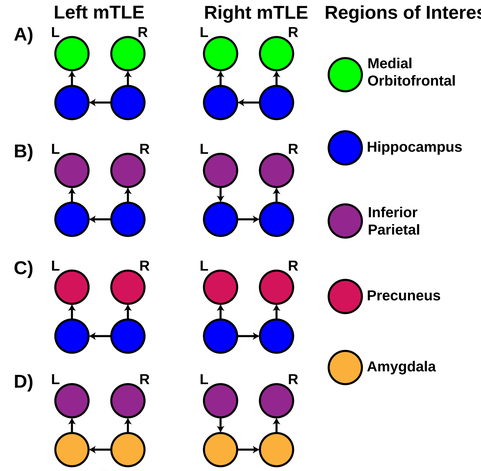
No differences in FC between right hippocampus and lateral orbitofrontal cortex were noted (A). Compared to LmTLE patients and control subjects, RmTLE patients demonstrated reduced FC between right hippocampus and medial orbitofrontal cortex (B), inferior parietal lobule (C), and precuneus (D). RmTLE patients also showed reduced FC between right hippocampus and posterior cingulate cortex compared to LmTLE patients but not controls (E). ROC curves demonstrate true and false positive rates in predicting LmTLE vs RmTLE patients. ***p<0.001, **p<0.01, *p<0.05, one-way ANOVA with Tukey's honest significant difference criterion post hoc and with Bonferroni-Holm correction. N=15 LmTLE patients, N=37 RmTLE patients, and N=52 control subjects. AUC =area under the curve, hippo=hippocampus, inf=inferior, lat=lateral, med=medial, post=posterior, R=right, ROC=receiver-operating characteristic.

5 Network most clearly distinguishing LmTLE vs RmTLE patients includes right medial temporal and bilateral DMN structures



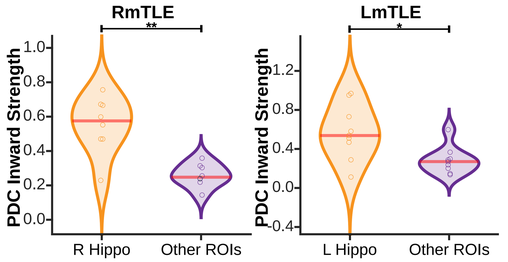
Using network-based statistic, performed at P=0.006 with family wise error correction, to evaluate bilateral DMN and mesial temporal nodes and edges, the network where connectivity differences most clearly distinguished LmTLE from RmTLE patients contains the right hippocampus and amygdala, bilateral inferior parietal lobules, precuneus, and medial orbital frontal cortex, and right lateral orbital frontal cortex. N=15 LmTLE patients and N=37 RmTLE patients. Ant=anterior, L=left, Post=posterior, R=right.

6 DCM analyses suggest mostly inward cross hippocampal/amygdalar connectivity at epileptogenic hippocampi



Analyses from four DCMs are shown with nodes including bilateral hippocampi and medial orbitofrontal cortices (A), hippocampi and inferior parietal cortices (B), hippocampi and precuneus (C), and amygdalae and inferior parietal lobules (D). Models selected, except for right (A), demonstrate inward connectivity from non-epileptogenic mesial regions to epileptoggenic mesial structure. N=15 LmTLE patients and N=37 RmTLE patients. DCM=dynamic causal modeling, L=left, R=right.

7 Inward SEEG connectivity is higher at epileptogenic hippocampi vs other structures sampled



PDC inward strength was higher in the epileptogenic hippocampus vs other brain regions sampled with SEEG. *p<0.05, **p<0.01, paired-sample t-tests, Bonferroni-Holm correction. N=9 LmTLE patients, N=8 RmTLE patients. hippo=hippocampus, L=left, R=right, ROIs= regions of interest.

8 Conclusions

- Nondirected connectivity patterns between mTLE structures and default mode network structures may aid in mTLE lateralization for surgery.
- Dynamic causal modeling revealed general inward connectivity from non-epileptogenic mesial temporal structures to epileptogenic mesial temporal structures.
- If improved, this may aid surgical planning and reduce the need for intracranial monitoring in mTLE patients.

9 References

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