Amplitude of Low Frequency Fluctuations (ALFF) in Epileptic White Matter Using fMRI

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Abstract

Amplitude of low frequency fluctuations (ALFF) can be used to detect epileptic grey matter regions using resting-state fMRI. In order to investigate ALFF differences in white matter, fMRI and diffusion weighted imaging (DWI) data were combined for 45 mesial temporal lobe epilepsy (mTLE) patients and 93 controls. Results indicate higher ALFF values in white matter tracts connecting epileptic grey matter regions (which also display higher ALFF values), suggesting a direct 'spread' of ALFF and thus, spread of the epileptic zone (EZ).

Introduction

Mesial temporal lobe epilepsy (mTLE) is the most common form of epilepsy and is characterized by seizures that originate from a focus in the temporal lobe. Surgical resection of the focus leads to seizure-freedom in 60-70% of patients[1]. Failures in this procedure are often attributed to the spread of the epileptic zone beyond the area of resection.

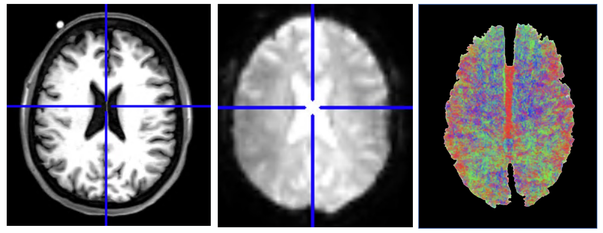
Using resting-state fMRI (rsfMRI), it has been demonstrated that changes in the amplitude of low frequency fluctuations (ALFF) can identify epileptic regions[2]. The aim of this project was to analyze white matter ALFF differences in tracts connecting epileptic grey matter regions. Results could impact surgical treatment and outcomes for mTLE patients by providing a non-invasive method of measuring epileptic spread and severity.

Data Collection

Subjects
- 45 unilateral mTLE patients (20 female, 39.6±12.8yrs, 14 left mTLE)
- 93 controls (46 female, 37.6±13.1yrs)

3T MRI imaging (SPM12)
- T1-weighted MRI (1x1x1mm^3) for tissue and regions of interest (ROIs) segmentation (MultiAtlas[6])
- Two 10-minute resting state fMRI (rsfMRI) scans (TR = 2s, 3x3x4mm^3)
- Standard preprocessing with RETROICOR for slice time correction, motion correction, and physiological noise correction

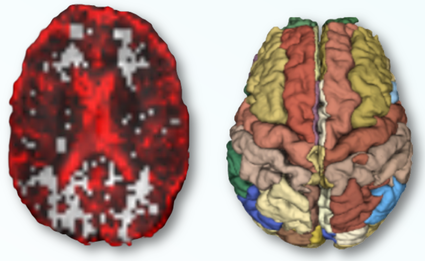
3T Diffusion Weighted Imaging (DWI)
- 2.5x2.5z2.5 mm^3, 92 directions, b-value = 1600 s/mm^2
- Whole brain anatomically constrained tractography using MRtrix3



T1W2D scan | fMRI scan | Brain tractography

Methods

ALFF calculation and connectome generation
- Motion and csf signals were regressed out of the rsfMRI data
- rsfMRI time course at each voxel were transformed to frequency domain with Welch's method
- ALFF: summed amplitudes across 0.0083-0.1 Hz frequency band, normalization across white matter
- Resulting ALFF maps were coregistered to diffusion space
- Whole brain tractography and multi-atlas segmentation of 117 total brain regions were combined with the individual ALFF maps. The ALFF values were averaged across white matter tracts connecting every pair of grey matter regions
- ALFF connectome was reduced to display 24 ROIs in the right and left temporal regions, along with the default mode network

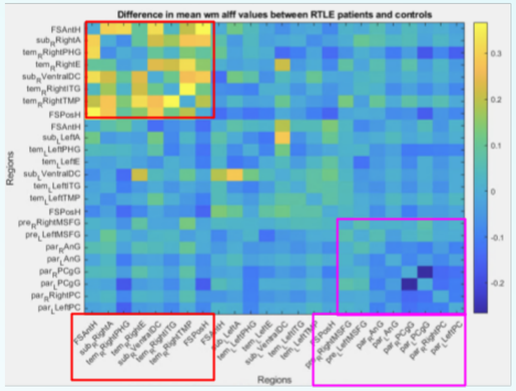


ALFF map | Multi-atlas ROIS

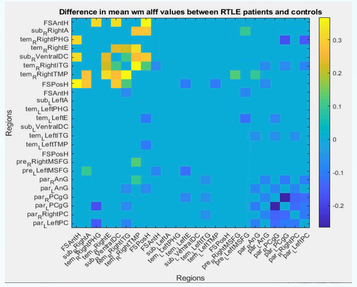
Statistical analysis
- ALFF connectome was compared between patients and controls using two-sample t-tests (without Bonferroni correction)
  - Results were compared to ROIs that demonstrate higher grey matter ALFF values
- ALFF values were compared to functional connectivity values, epilepsy duration, seizure frequency, and other clinical outcomes using Spearman correlation
- ALFF values were compared to surgical outcome metrics using two-sample t-tests between successful and unsuccessful patients

Results

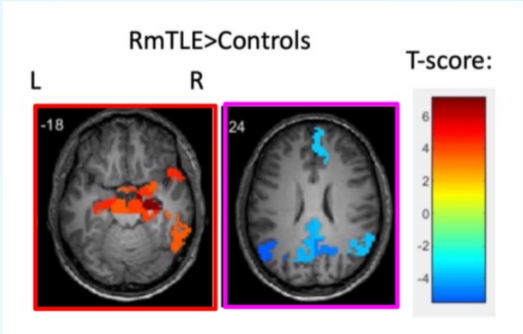
RTLE > Controls: White matter



Right temporal regions | Default mode network



RTLE > Controls: Grey matter



Left: Difference in white matter ALFF values in RTLE patients versus controls. Higher ALFF values were observed in the white matter tracts connecting right temporal regions, while lower ALFF values were observed within the default mode network. Significant differences (without correction) are shown below the figure.

Right: Difference in grey matter ALFF values in RTLE patients versus controls. Higher ALFF values are observed in temporal regions, while lower ALFF values are observed in the default mode network.

No correlations were detected between white matter ALFF values and functional connectivity or other clinical measurements. ALFF values were not predictive of successful vs unsuccessful surgical outcome (p = 0.44).

Conclusions, Acknowledgments, and References

Increased ALFF values were detected in white matter tracts connecting epileptic temporal regions, which themselves have higher grey matter ALFF values in patients compared to controls. This suggests that the ALFF signal is 'spread' directly from one region to another, rather than an associative relationship. Future studies could incorporate additional regions of interest and other clinical metrics, such as EEG or network studies. A temporal study could be conducted to infer directionality.

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