CBF-ALFF Coupling as a Biomarker for Neurovascular Coupling in Epilepsy

Srikar Gudimella[1], Alfredo Lucas[2,3], **Kathryn A. Davis**[3,4]

University of Pennsylvania, School of Engineering and Applied Science, Class of 2025[1]; University of Pennsylvania, Perelman School of Medicine[2]; Department of Bioengineering[3]; Department of Neurology[4]

INTRODUCTION

- Temporal lobe epilepsy (TLE) is the most common type of focal epilepsy. It is often lateralized to one of the two hemispheres.
- Dysfunction in neurovascular coupling (NVC), which describes the coupling between neural activity and cerebral blood flow (CBF), is implicated in epilepsy and other neurological disorders.
- CBF-ALFF coupling is a noninvasive neuroimaging measure of NVC that could allow us to study NVC in the epileptic population.
- NVC coupling could help lateralize TLE. We hypothesized that coupling would be lower in the hemisphere that the TLE is lateralized in.

METHODS

Mapping CBF-ALFF coupling in Surface and Volumetric Space

- Cerebral blood flow (CBF) was measured using Arterial Spin Labelling (ASL) and Amplitude of Low Frequency Fluctuations (ALFF), derived from fMRI, was used as a measure for neural activity.
- ASL and ALFF data in a volumetric space was generated for 45 total patients: 21 with Left TLE, 17 with Right TLE, and 7 controls
- ASL and ALFF data was projected to subject's cortical surface using Freesurfer
- For each voxel/vertex in the brain volume/surface, a neighborhood of voxels/vertices was obtained. A weighted least square (WLS) regression was fitted for the neighborhood. The slope of the resulting line of best fit was assigned as the coupling value for the voxel/vertex. This was repeated across the entire brain.

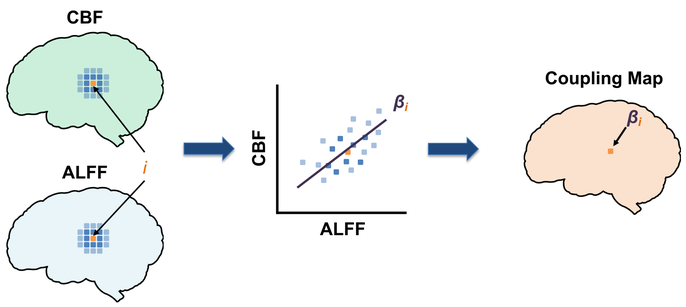

Figure 1 – Generating CBF-ALFF Coupling Maps

Assessing Lateralization of CBF-ALFF Coupling

- We created a metric called Asymmetry Index to assess if the CBF-ALFF coupling metric could help lateralize TLE.

$$AI = \frac{Mean\ LH\ Coupling - Mean\ RH\ Coupling}{Mean\ LH\ Coupling + Mean\ RH\ Coupling}$$

- Since we expect coupling to be lower in the hemisphere where TLE is lateralized, we expected the asymmetry index to be negative for Left TLE patients and positive for right TLE patients.

METHODS

Parameter Tuning

- Both the surface method and volumetric method use two parameters: radius and smoothness. Radius determine the size of the neighborhood used for the WLS regression and smoothness determines the weights that are assigned to neighbors of varying distances.
- Coupling maps for a single subject were generated with various combinations of parameters. These different maps were correlated with each other to create a correlation matrix.

RESULTS

Mapping CBF-ALFF Coupling in Volumetric Space Shows a Strong Effect Size for Lateralization of Neurovascular Coupling

- The asymmetric index values for the coupling maps that were generated in the volumetric space show a significant difference between the left TLE, right TLE and control groups. As hypothesized, the left TLE group had lower asymmetric index values than the right TLE group, with the control group in the middle.
- The effect size does not change significantly by varying the parameters.

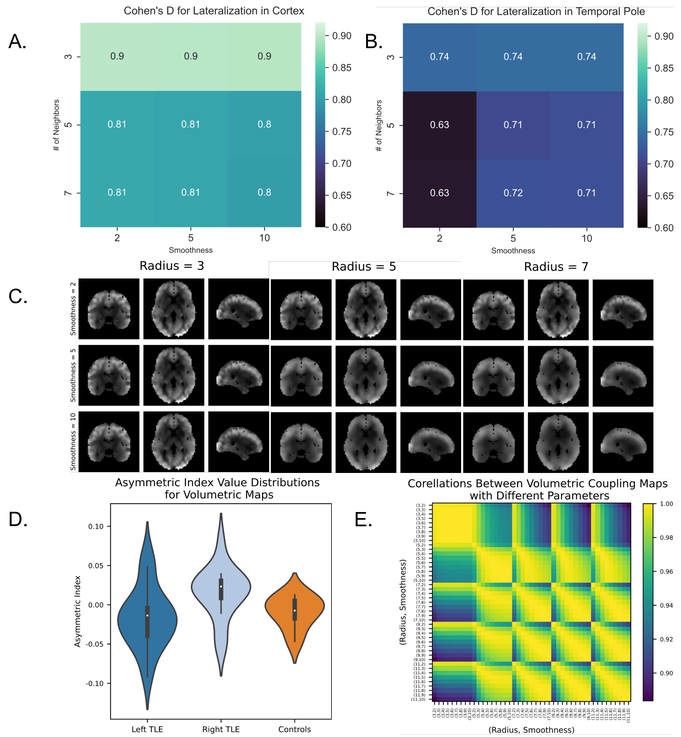

Figure 2 – CBF-ALFF Coupling in Volumetric Space: *A & B.* Cohen's D values for difference in asymmetry index values between LTLE and RTLE groups shows a large effect size that's consistent across different map generation parameters. *C.* Appearance of volumetric coupling maps generated under various smoothness and radius parameters. *D.* Violin plot generated from distribution of asymmetric index values of volumetric coupling maps for LTLE, RTLE, and control groups. *E.* Correlation matrix between volumetric coupling maps generated under 45 different combinations of parameters. All possible pairs of maps show high correlation of higher than 0.8. Parameter values increasing moving down and to the right.

RESULTS

Mapping CBF-ALFF Coupling in Surface Space Was Unable to Lateralize Temporal Lobe Epilepsy

- The asymmetric index values for the coupling maps that were generated in the surface space did not show any significant differences between the left TLE, right TLE and control groups.
- The surface coupling maps also had a roughly equal number of negative and positive coupling values. Negative coupling values conflict with the biology behind NVC. It's possible that errors in the registration and surface reconstruction process could have distorted the results.

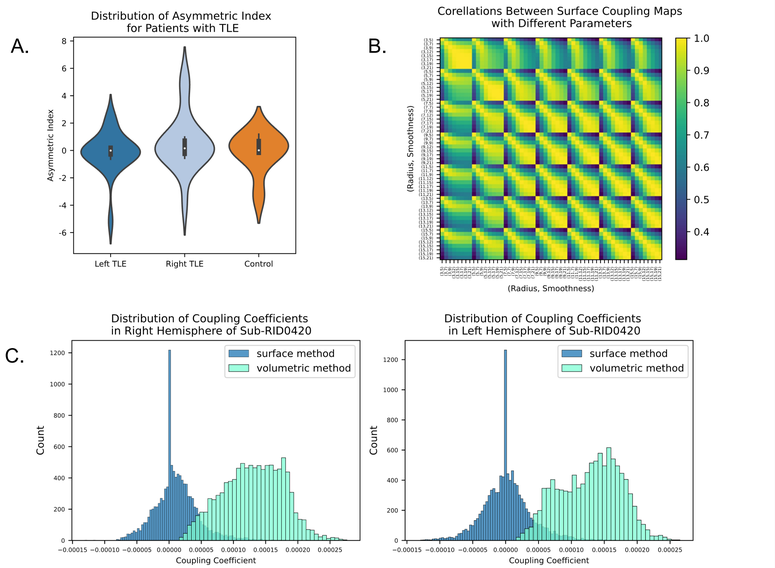

Figure 4 - Integration-segregation axis results: *A.* Violin plot generated from distribution of asymmetric index values of surface coupling maps for LTLE, RTLE, and control groups. *B.* Correlation matrix between volumetric coupling maps generated under 56 different combinations of parameters. *C.* Distribution of coupling values in surface and volumetric coupling maps of sub-RID0420. Parameter values increasing moving down and to the right.

CONCLUSIONS

- We found that mapping CBF-ALFF coupling across the volume of the brain was more robust and reliable than mapping CBF-ALFF coupling across the cortical surface.
- CBF-ALFF coupling in the volumetric space showed a large effect size in Asymmetric Index between patients with Left TLE and Right TLE groups. This aligns with the hypothesis that neurovascular coupling is decreased in the hemisphere affected by TLE.
- CBF-ALFF coupling could be a useful measure in lateralizing temporal lobe epilepsy.

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