# Impaired Cerebrovascular Reactivity in Mesial Temporal Lobe Epilepsy

Kenda Alhadid HBSc. MD MSc(candidate); Julien Poublanc; Lashmi Venkatraghavan; Joseph A. Fisher MD; James Duffin; Olivia Sobczyk; David J. Mikulis MD; Taufik Valiante MD, PhD

Division of Neurosurgery, Toronto Western Hospital, University Health Network, University of Toronto

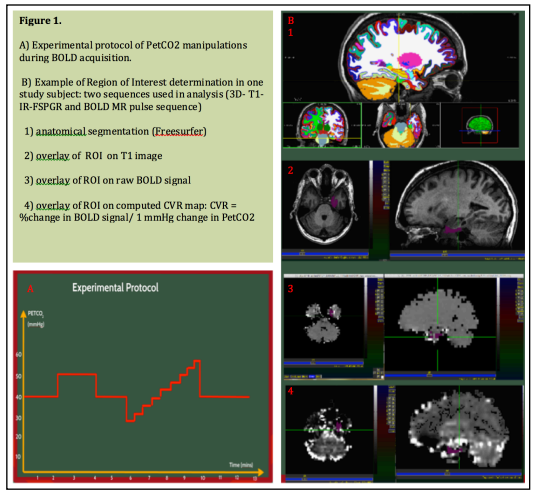
CNS 2015 ANNUAL MEETING NEW ORLEANS LOUISIANA SEPTEMBER 26-30, 2015

## Introduction

Epilepsy surgery is the best treatment for medically intractable epilepsy. Optimal pre-operative localization is essential to the success of epilepsy surgery with regards to achieving seizure freedom. Functional neuroimaging studies (PET, SPECT) in epilepsy patients are used to aid in pre-operative localization and have varying sensitivity and specificity. They are typically utilized when routine diagnostic tests provide discordant results. These tests have demonstrated the presence of inter-ictal perturbations in metabolism and perfusion to the epileptogenic zone. We hypothesized that the observed decreased inter-ictal perfusion and metabolism in the epileptogenic zone is due to an underlying vascular dysfunction. Cerebrovascular reacitivity is an aspect of cerebral autoregulation that is defined as the vasculature's response to a vasoactive stimulus, such as carbon dioxide. Our specific aim was to demonstrate impaired CVR in the epileptogenic zone and therefore, investigate the utility of CVR imaging in pre-operative localization.

## Methods

Unilateral mesial TLE patients (n=12) who had undergone standard pre-surgical investigations for seizure localization were studied. We utilized a novel technology that can precisely prospectively target arterial CO2 levels (Respiract™). Functional MRI images using the Blood Oxygen Level Dependent (BOLD) sequence as a surrogate for blood flow changes were obtained while iso-oxic changes in CO2 were induced. CVR imaging data for 12 healthy volunteers who had underwent the same study protocol was retrieved from an existing database at our institution.




## Results (1): Increased CVR in Epileptogenic PCC and Entorhinal Cortex

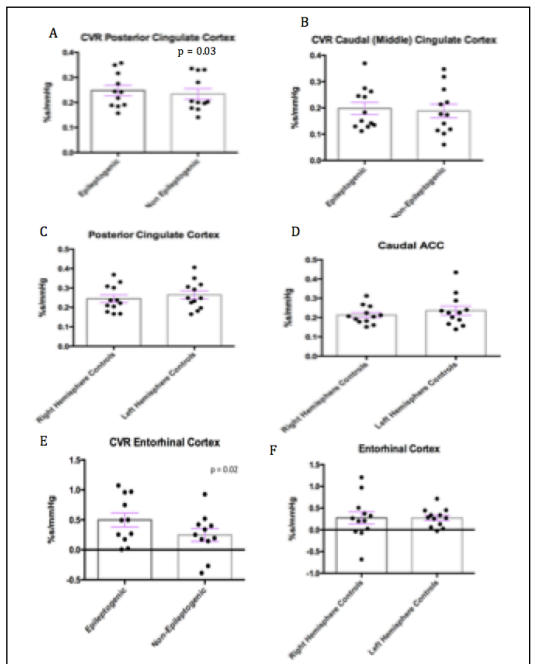



Fig. 2. A) CVR in epileptogenic posterior cingulate cortex compared to the contralateral hemisphere (0.247+/- 0.02 vs. 0.233 +/- 0.02) in the patient group: **paired T-Test p=0.03,** error bars represent standard error of the mean. B) CVR in anterior caudal (middle) cingulate cortex in epileptogenic hemisphere compared to contralateral hemisphere (0.197 +/- 0.23 vs. 0.188 +/- 0.025) p = 0.39). C) No significant difference in CVR between the right PCC vs. left PCC in control group (p =0.2) and between D) right and left middle cingulate in control group (p = 0.4). E) CVR is increased in epileptogenic entorinal cortex compared to contralateral hemisphere ((0.496 +/- 0.11 vs. 0.246 +/- 0.1) **p=0.02**. F) No significant difference in CVR between left and right entorhinal cortices in the control group.

## Results (2) No significant CVR impairments in epileptogenic mesial structures

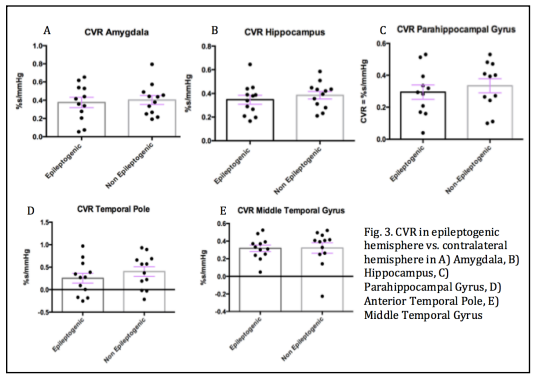



Fig. 3. CVR in epileptogenic hemisphere vs. contralateral hemisphere in A) Amygdala, B) Hippocampus, C) Parahippocampal Gyrus, D) Anterior Temporal Pole, E) Middle Temporal Gyrus

## Results (3) CVR not significantly Correlated with Cortical Thickness in epileptogenic PCC

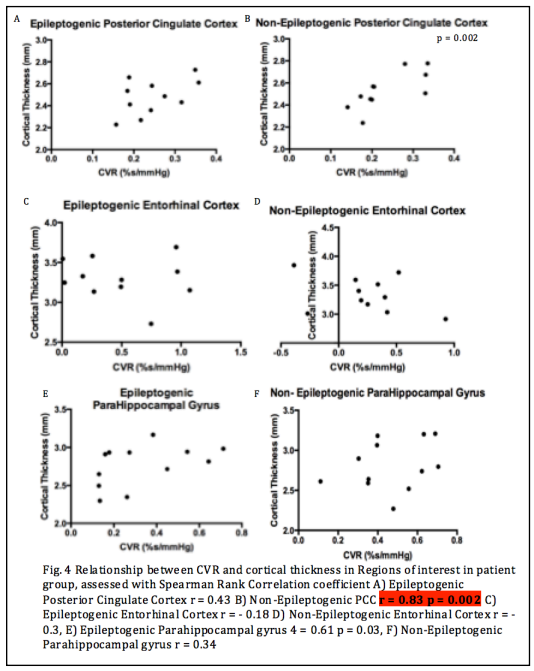



Fig. 4 Relationship between CVR and cortical thickness in Regions of interest in patient group, assessed with Spearman Rank Correlation coefficient A) Epileptogenic Posterior Cingulate Cortex r = 0.43 B) Non-Epileptogenic PCC **r = 0.83 p = 0.002** C) Epileptogenic Entorhinal Cortex r = - 0.18 D) Non-Epileptogenic Entorhinal Cortex r = - 0.3, E) Epileptogenic Parahippocampal gyrus 4 = 0.61 p = 0.03, F) Non-Epileptogenic Parahippocampal gyrus r = 0.34

## Results (4) CVR changes due to Amplitude vs. time delay of Vascular Response (*Tau*)

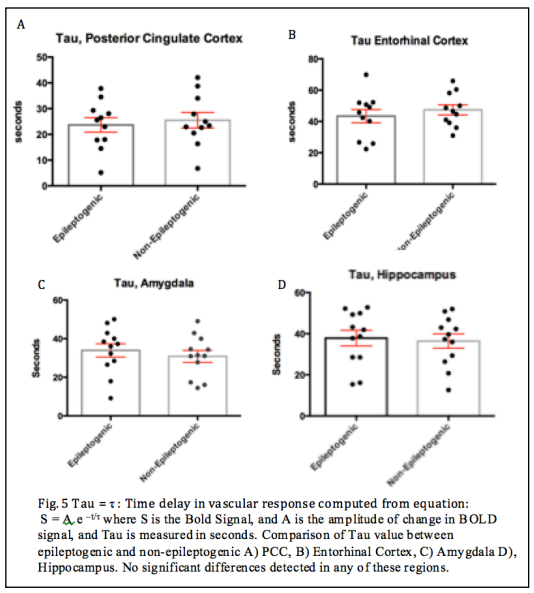



Fig. 5 Tau = τ: Time delay in vascular response computed from equation: $S = A_o e^{-t/\tau}$ where S is the Bold Signal, and A is the amplitude of change in BOLD signal, and Tau is measured in seconds. Comparison of Tau value between epileptogenic and non-epileptogenic A) PCC, B) Entorhinal Cortex, C) Amygdala D), Hippocampus. No significant differences detected in any of these regions.

## Learning Objectives

- Assessing vascular reserve can be achieved with a reproducible, accurate, non-invasive imaging technique
- Mesial temporal lobe epilepsy patients have impaired CVR in regions that lateralize with but are distal to the epileptogenic focus, suggesting that the underlying vascular pathology extends beyond the ictal-onset zone.

## Conclusions

Regional cerebral vasculature does not seem to display a homogenous repsonse to a global vasoactive stimulus in mTLE patients. Functional connectivity studies in patients with unilateral temporal lobe epilepsy frequently use seed-based analyses within which the PCC is chosen as the reference point. Our finding of increased CVR in the epileptogenic PCC compared to the contralateral hemisphere could affect the interpretation of connectivity findings as CVR encompasses the amplitude and time delay of the BOLD response. Further data is required to provide a higher statistical significance of preliminary findings.