Quantifying Water Exchange through the Blood Brain Barrier in Focal Temporal Lobe Epilepsy

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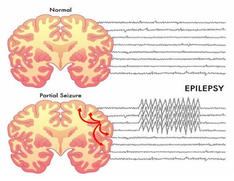
Background

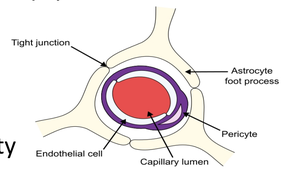
Epilepsy

- Abnormal synchronous electrical activity in the brain, causing seizures
- Epilepsy affects around 65 million individuals globally
- Can be focal or generalized
- Patients with drug-resistant epilepsy (DRE) face increased trauma and mortality



Blood Brain Barrier

- Maintains the brain's chemical balance, and protects against harmful substances
- A "leaky" blood brain barrier may be implicated in epilepsy
- Proteins and cells infiltrate into the brain, and disrupt electrical activity

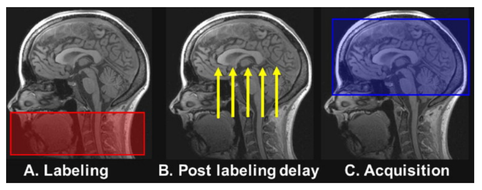


Goals

Magnetic Resonance Imaging (MRI) is an important tool to image soft tissue, like the brain. We aim to use MRI images to characterize blood brain barrier permeability in people with epilepsy.

Methods

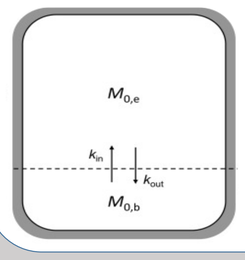
TRUST MRI



- T2 relaxation underspin tagging (TRUST) MRI using arterial spin labeling (ASL) MRI to label water molecules
- pCASL uses a narrow labeling plane and a series of short RF pulses
- Non-invasive and a more accurate measure of water exchange

Water is magnetically labeled. Difference between "labelled" and control measures brain perfusion

T_{EX} Calculation



- The ratio of the water diffusing in and out of the blood vessels is calculated as time of exchange (T_{EX})
- T_{EX} is a measure of the blood brain barrier water exchange

Analysis

- Statistical analysis performed using R
- Shapiro-Wilk test for normality
- Mann-Whitney for 2 groups
- Kruskal-Wallis test for 3+ groups, with post-hoc Dunn's test

Results

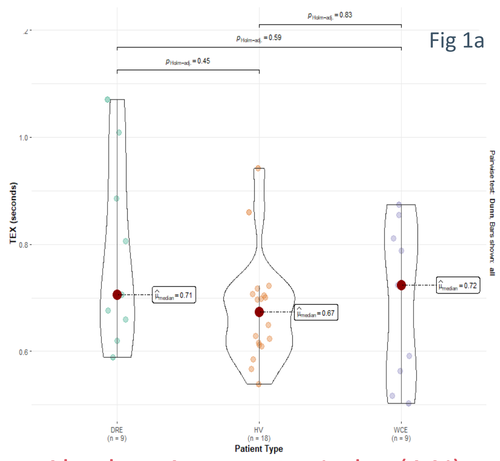
Clinical Characteristics

	Drug Resistant Epilepsy (WCE)	Well Controlled Epilepsy (WCE)	Healthy Volunteers
Number of Participants	13	11	15
Age, median (range)	40, 25-61	37, 32-59	34, 23.7-50.61
Sex, Female n (%)	5, 38%	7, 63%	7, 47%
Epilepsy Duration, median years (range)	17	24	-
Seizure Type			
FA	1	3	-
FIAS	12	10	-
FM	1	0	
MRI Result			
Mesial Temporal Sclerosis (MTS)*	3	4	-
Focal Cortical Dysplasia (FCD) †	2	0	-
Heterotopia‡	1	0	-
Medications			
Phenobarbital	2	0	-
Clonazepam	0	0	-
Diazepam	0	0	-
Topiramate	2	0	-

*Mesial Temporal Sclerosis is scarring and loss of neurons in of the deep temporal lobe, can be caused by epilepsy
†Focal Cortical Dysplasia is abnormal neural organization and development
‡Heterotopia is when neurons have not migrated to the cortex correctly

Exchange Time (TEX) in Epilepsy and Controls

Fig 1a



Absolute Asymmetry Index (AAI)

Fig 1b

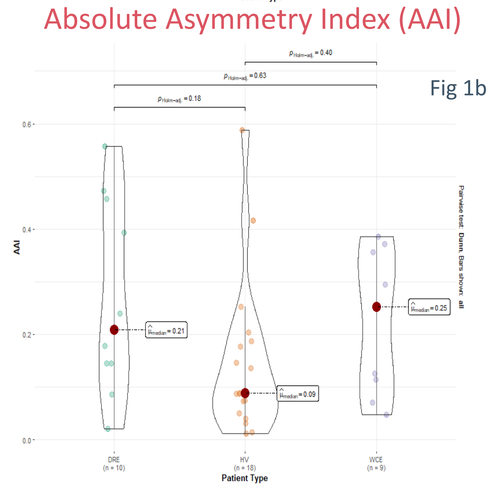
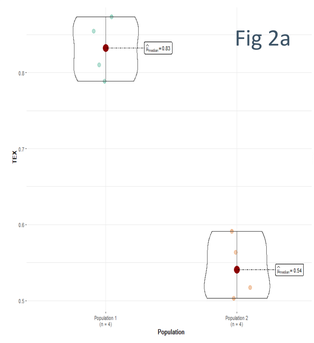


Fig1a: TEX values between DRE, WCE, HV (X^2=0.34, p = 0.34)
Fig1b: AAI values between DRE, WCE, HV (X^2=4.01, p = 0.13)

Controlled Epilepsy

Fig 2a



Drug-Resistant Epilepsy

Fig 2b

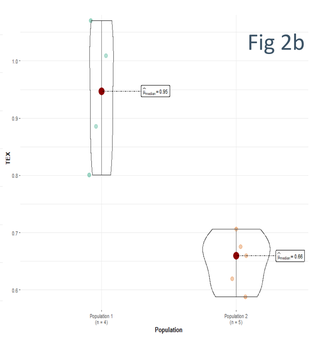
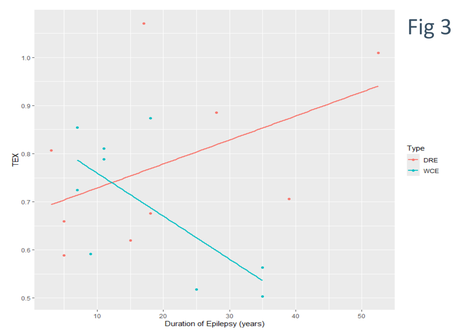


Fig2a: WCE Mann-Whitney W= 16.00, p = 0.03*
Fig 2b: DRE Mann-Whitney W= 20.00, p = 0.02*

Duration of Epilepsy and TEX

Fig 3



WCE: Adjusted r-squared = 0.3989, p = 0.04*
DRE: Adjusted r-squared = 0.1219, p = 0.190

Ipsilateral vs Contralateral TEX

Fig 4a

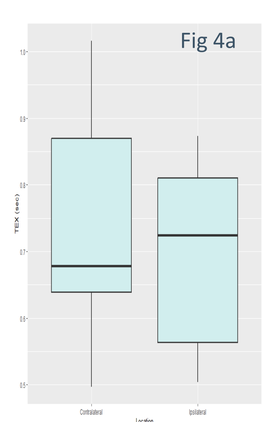


Fig 4b

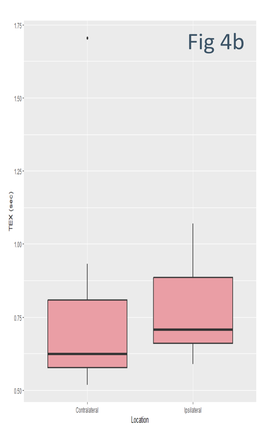


Fig4a: WCE Ipsilateral vs Contralateral TEX
Fig4b: DRE Ipsilateral vs Contralateral TEX

MRI Images

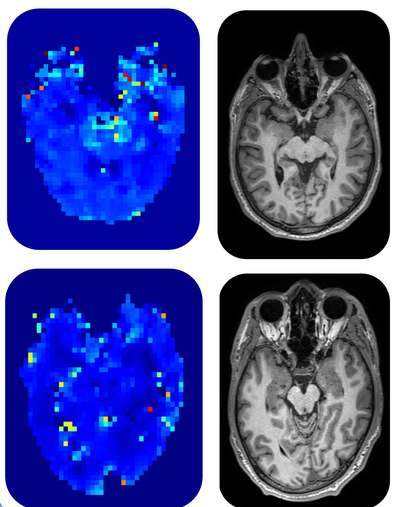


Fig5a
Patient with drug-resistant epilepsy

Fig5b
Healthy Volunteer

Discussion

Results

- Trend for higher asymmetry index at seizure foci compared to healthy controls
- Group T_{EX} did not significantly differ between 3 groups
- Broad range of TEX values in patients
- Heterogeneous Epilepsy population: location, MRI lesion
- Duration of epilepsy is correlated with TEX in WCE and anti-correlated in DRE

TRUST MRI

- TRUST MRI allows non-invasive quantification of water permeability
- TRUST is utilized to differentiate between intravascular and extravascular T2 relaxation times
- Two-compartment model allows for accurate quantification of water exchange

Future Directions

- Analysis with a larger group to clarify the trend observed in this study to test for significant difference
- Possible effect on permeability from certain medications: benzodiazepine and barbiturates
- Further MRI processing to improve SNR
- Separate lesional and non-lesional MRI in analysis

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