Imaging Blood Brain Barrier Dysfunction in Drug Resistance Epilepsy: A Multi-Center Feasibility Study

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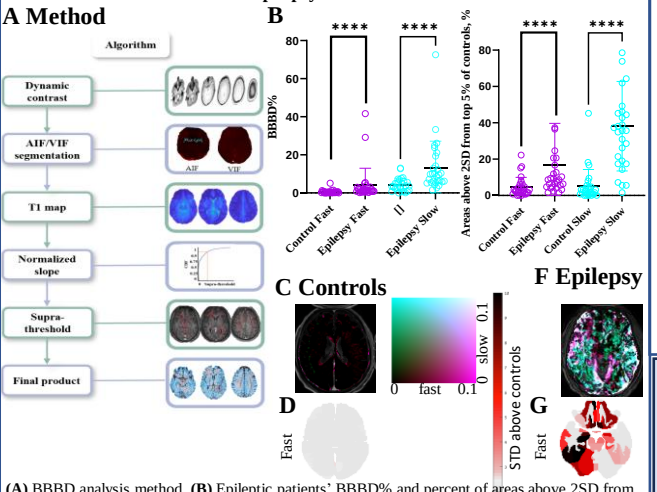
Introduction :

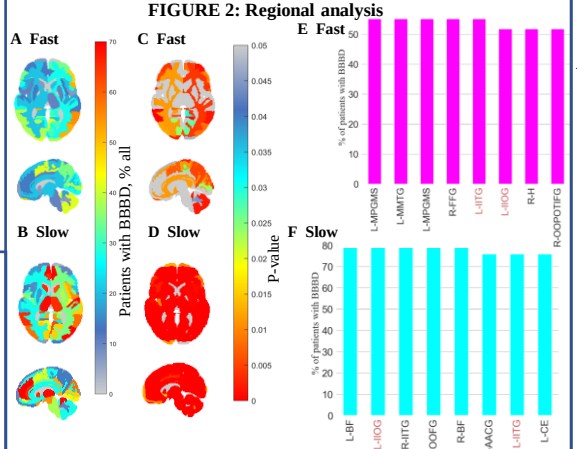
Epilepsy, a neurological disorder characterized by an increased risk of spontaneous seizures, Focal epilepsy is characterized by seizures that start in one part of the brain, while generalized epilepsy is characterized by seizures that start in both sides of the brain at the same time[1]. BBB dysfunction (BBBD) is common in many brain disorders and has been shown to have a critical role in epileptogenesis. Dynamic contrast-enhanced MRI (DCE-MRI) has become the most common approach to quantify the extent and localization of BBBD in human patients. Several models including the compartment *fast* model (~0-6 min after contrast injection)[2]. And the Veksler linear model has been shown to allow the detection of a *slow* (~6-20) BBB leakage [3].

FIGURE 1: Epilepsy vs controls



(A) BBBD analysis method. **(B)** Epileptic patients' BBBD% and percent of areas above 2SD from the top 5% of controls statistics compared to controls. **(C)** Example of controls without BBBD, with fast BBBD and slow BBBD. **(D)** Examples of controls fast regional maps. **(F)** Examples of patients with epilepsy without BBBD, with fast BBBD and slow BBBD and both fast and slow BBBD. **(G)** Examples of patients with epilepsy fast regional maps.

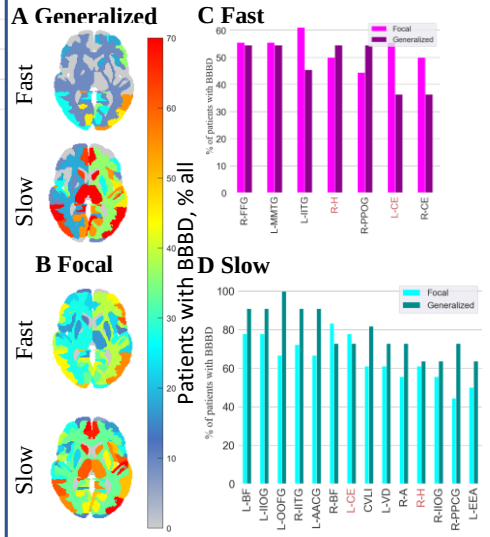
FIGURE 2: Regional analysis



(A) Percent of epileptic patients with BBBD of each region in fast model. **(B)** Significant regions of epileptic patients compared to controls in fast model. **(C)** Percent of epileptic patients with BBBD of each region in slow model. . **(D)** Significant regions of epileptic patients compared to controls in slow model. **(E)** Regions with most % of patients with BBBD in fast model (p value < 0.0001). **(F)** Regions with most % of patients with BBBD in slow model (p value < 1e-06). Areas in red are highly significant in both models. Regions legend: L-AACG: Left ACgG anterior cingulate gyrus, L-BF: Left Basal Forebrain, L-CE: Left Cerebellum Exterior, L-IIOG: Left IOG inferior occipital gyrus, L-IITG: Left ITG inferior temporal gyrus, L-MPGMS: Left MPrG precentral gyrus medial segment, L-MMTG: Left MTG middle temporal gyrus, L-OOFG: Left OFuG occipital fusiform gyrus, R-BF: Right Basal Forebrain, R-FFG: Right FuG fusiform gyrus, R-H: Right Hippocampus, R-IITG: Right ITG inferior temporal gyrus, R-OOPOTIFG: Right OrIFG orbital part of the inferior frontal gyrus

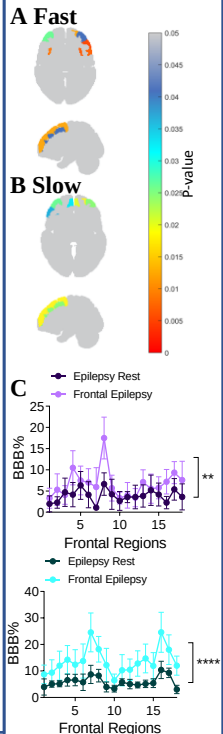
Conclusions: **1.** BBBD can serve as a reliable biomarker for epilepsy in human patients. **2.** Specific regions such as Left IOG (Inferior Occipital Gyrus) exhibits significant involvement in epilepsy. **3.** The Slow model effectively simulates epilepsy characteristics more than the fast model. **4.** Frontal focal epilepsy demonstrates higher sensitivity to BBBD compared to temporal focal epilepsy.

FIGURE 3: Focal vs Generalized



(A) Percent of focal epileptic patients with fast BBBD in each region. **(B)** Percent of generalized epileptic patients with fast BBBD in each region.**(C)** Regions with most % of patients with BBBD in fast model (p value < .01). **(D)** Regions with most % of patients with BBBD in slow model (p value < .0005). Areas in red are highly significant in both models. Regions legend; CVLI: Cerebellar Vermal Lobules I-V, L-AACG: Left ACgG anterior cingulate gyrus, L-BF: Left Basal Forebrain, L-CE: Left Cerebellum Exterior, L-EEA: Left Ent entorhinal area, L-IIOG: Left IOG inferior occipital gyrus, L-IITG: Left ITG inferior temporal gyrus, L-MMTG: Left MTG middle temporal gyrus, L-OOFG: Left OFuG occipital fusiform gyrus, L-VD: Left Ventral DC, R-A: Right Amygdala, R-BF: Right Basal Forebrain, R-CE: Right Cerebellum Exterior, R-FFG: Right FuG fusiform gyrus, R-H: Right Hippocampus, R-IIOG: Right IOG inferior occipital gyrus, R-IITG: Right ITG inferior temporal gyrus, R-PPCG: Right PCgG posterior cingulate gyrus, R-PPOG: Right POrG posterior orbital gyrus

FIGURE 4: Frontal focal epilepsy



(A) P value of frontal regions in frontal epileptic patients compared to rest of patients with epilepsy in fast. **(B)** in slow. **(C)** 2 way ANOVA frontal regions comparison.

References

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