Guy Bar-Klein et al., J Neurol Disord 2015, 3:4
http://dx.doi.org/10.4172/2329-6895.C1.005

OMICS International
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International Conference on
Epilepsy & Treatment
September 21-22, 2015 Baltimore, USA

Magnetic resonance imaging of blood-brain barrier dysfunction as a biomarker for Epileptogenesis

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Acquired epilepsy is frequently followed brain insults. Interestingly, these insults are frequently associated with dysfunctional Blood-Brain Barrier (BBB). We recently showed that BBB injury lead to albumin-mediated activation of Transforming Growth Factor β (TGF-β) signaling in astrocytes, astrogliosis, local inflammatory response followed by epileptiform discharges and delayed seizures. Importantly, the FDA-approved AT1 antagonist, losartan, blocked albumin-induced TGF-β signaling and prevents epileptogenesis. Here we performed a longitudinal study in rats exposed to paraoxon to induce Status Epilepticus (SE) and epileptogenesis and executed repeated Magnetic Resonance Imaging (MRI) to quantitatively monitor BBB integrity. Continuous video Electrocorticographic (ECoG) recordings were acquired to monitor for seizures. Analysis of the ECoG signals revealed that 13 out of 22 of the rats presented ≥2 spontaneous seizures and therefore were defined as epileptic. Signal analysis in 13 defined brain regions using logistic regression and forward selection suggested that focal BBB breakdown in olfactory structures increases the likelihood of a rat to become epileptic while diffuse damage decreases this likelihood. We, thus, were able to predict epilepsy with high sensitivity and specificity (92.3% and 77.8%, respectively) with 12 out of 13 epileptic rats classified correctly and only 2 out of 9 non-epileptics falsely classified as epileptic. Our results demonstrate that increased BBB permeability in specific brain regions may serve as a reliable biomarker for SE-induced epileptogenesis and together with our findings showing losartan as anti-epileptogenic drug, highlight the potential of specific anti-epileptogenic treatment for patients identified with high risk to develop epilepsy.

Biography

Guy Bar-Klein has completed his PhD from Ben-Gurion University of the Negev and is currently a Postdoctoral Associate at the Howard Hughes Medical Institute. He has a BSc in biophysics and MMedSc in neurophysiology. In his research, main focus is on in vivo electrophysiological recordings and molecular assays of epileptogenic processes and pathologies associated with Blood-Brain Barrier (BBB) dysfunction. Studying the mechanisms regulating BBB permeability and the following effects, will hopefully lead to potential therapeutic treatments for BBB-related processes, emphasizing on post-traumatic epilepsy and other epileptogenic syndromes.

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