Talk 4.3, Poster: 45
Evolution into Epilepsy
(NIBIB R01-EB004752 FY 04)
William L. Ditto, Ph.D.
University of Florida

Paul R. Carney, M.D.
University of Florida

Thomas Mareci, Ph.D.
University of Florida

To better understand the functions of complex neurological changes during epileptogenesis, we have proposed to elucidate the mechanisms of pathological evolution of epilepsy by comparing different levels of temporal and spatial development via histology, multi-electrode array recording, and MR imaging, along with linear and nonlinear analysis of data in a validated rat model of temporal lobe epilepsy. By characterizing the latent development of epilepsy from status epilpeticus to onset in the chronic limbic epilepsy rat model, essential relationships between the onset pathology and the remodeling of the neural tissue are being described and correlated. Over the past year, we have been able to track and quantify hippocampus signal unit activity and bursting neurons during the epileptogenesis. Nonlinear and linear time series analysis has revealed specific spatial and temporal changes. Concomitantly, we have focused our MRI efforts in two areas: 1) we began a longitudinal characterization of the rat brain *in vivo*, with MR imaging, as the animal develops epilepsy. In this longitudinal study, we started with 5 rats where each is image *in vivo* prior to the implantation of simulating electrodes in the brain, post-implantation of simulating electrodes, and during the evolution of the injured brain, following stimulation, through the period of status epilepticus until the animal was sacrificed (~ 60 days following stimulation). 2) Also we have examined the excised rat brain with high-resolution MR imaging in order to define detailed structural changes in the epileptic brain. To support this work, we have optimized our data acquisition protocols and post-processing methodologies to allow us to characterize normal tissue and pathological changes, such as edema, hemorrhages and cavitations, in specific brain regions. Using our unique 11.1 Tesla magnet system in the Advanced Magnetic Resonance Imaging and Spectroscopy Facility of the McKnight Brain Institute at UF, and with a custom MR coil built in our lab, we have obtained very high resolution, high quality images of the rat brain *in vivo*. During each imaging session, we acquire a series of high-resolution T2-weighted images in orthogonal planes, a series of T1 and T2 weighted images (from which we quantify relaxation times), and high-angular resolution diffusion-weighted imaging to characterize the nervous tissue structure. We have found that structural changes in hippocampus and entorhinal cortex coincide with changes in neuronal activity, and precede the onset of epilepsy. We plan to further evaluate these changes with tissue molecular techniques, computational analysis, and modeling during the upcoming year.

Project (or PI) Website

http://www.bme.ufl.edu/epilepsy

Publications

1. Iasemidis LD, Shiau DS, Pardalos PM, Chaovalitwongse W, Narayanan K, Prasad A, Tsakalis K, , Sackellares JC, Carney PR. Long-term prospective on-line real-time seizure prediction. Clinical Neurophysiol. 2005; 116 (3): 532-544.

2. Chaovalitwongse W, Pardalos PM, Iasemidis LD, Shiau D-S, Suharitdamrong W, Carney PR, Sackellares JC. A robust method for studying the dynamics of the intracranial EEG: Application to epilepsy. Epilepsy Res 2005; 64: 93-113.

3. Iasemidis LD, Shiau DS, Pardalos PM, Chaovalitwongse W, Narayanan K, Prasad A, Tsakalis K, Carney PR, Sackellares JC. Long-term prospective on-line real-time seizure prediction. Clin Neurophysiol. 2005 Mar;116(3):532-44.

4. Chaovalitwongse W, Iasemidis LD, Pardalos PM, , Shiau DS, Carney PR, Sackellares JC. Performance of a seizure warning algorithm based on the dynamics of intracranial EEG. Epilepsy Res. 2005 May; 64(3):93-113.

5. Neill JC, Liu Z, Mikati M. Holmes GL., Pilocarpine seizures cause age-dependent impairment in auditory location discrimination. J Exp Anal Behav 2005; 84 (11): 357-370.

6. Pardalos PM, Boginski VL, Prokopyev OA, Suharitdamrong W, Carney PR, Chaovalitwongse W, Vazacopoulos A. Optimization techniques in medicine. In: Eds. Audet C, Hansen P, Savard G. Essays and Surveys in Global Optimization. Springer, 2005.

7. Ozarslan E, Vemuri BC and Mareci TH. Generalized Scalar Measures for Diffusion MRI Using Trace, Variance and Entropy. Magn. Reson. Med. 2005;53;866-876.

8. Sanchez JC, Principe JC, and Carney PR. Is neuron discrimination preprocessing necessary for linear and nonlinear brain machine interface models? 11th International Conference on Human-Computer Interaction, 2005.

9. Shiau DS, Nair SP, Iasemidis LD, Carney PR , Norman W, Principe JC, Pardalos PM, Suharitdamrong W, Cho J, Sackellares JC. Seizure warning and dynamic response to electrical stimulation in a rodent model of chronic limbic epilepsy. EMBEC 2005.

10. Sanchez JC, Mareci T, Norman W, Principe J, Ditto W, and Carney PR. Evolving into epilepsy: multiscale electrophysiological analysis and imaging in an animal model. Exp Neurol. 2006 Mar; 198(1):31-47.

11. Sanchez JC, Alba N, Nishida T, Batich C, and Carney PR. Structural modifications in chronic microwire electrodes for cortical neuroprosthetics: A Case Study. IEEE TNSRE 2006 June; 14(2).

12. Geyer JD, Carney PR, and Gilliam F. Focal dyshormia: focal epileptiform spikes in conjunction with k-complexes. Clinical Neurophysiol, In press.

13. Nair SP, Shiau DS, Iasemidis LD, Norman WM, Pardalos PM, Sackellares CS, and Carney PR. Seizure predictability in an experimental model of epilepsy. Proceedings, Quantitative Neurosci Conf; In press.

14. Ozarslan E, Shepherd TM, Vemuri BC, Blackband SJ, Mareci TH. Resolution of Complex Tissue Microarchitecture using diffusion Orientation Transform. NeuroImage 2006, in press.

15. Shepard TM, Ozarslan E, King MA, Mareci TH, Blackband SJ. Structural Insights from High-Resolution Diffusion Tensor Imaging and Tractography of the Isolated Rat Hippocampus. NeuroImage 2006, in press.

16. Holmes GL. Khazipov R, Liu Z, Sarkisian MR, Stafstrom CE. Behavioral consequences of status epilepticus in the immature brain, Book chapter, in press