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Detection of High Frequency Oscillations with Teager Energy in an Animal Model of Limbic Epilepsy

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***Abstract*—High Frequency Oscillations (HFO) in limbic epilepsy represent a marked difference between abnormal and normal brain activity. Faced with the difficult of visually detecting HFOs in large amounts of intracranial EEG data, it is necessary to develop an automated process. This paper presents Teager Energy as a method of finding HFOs. Teager energy is an ideal measure because unlike conventional energy it takes into account the frequency component of the signal as well as signal amplitude. This greatly aids in the dissection of HFOs out of the noise and other signals contained in the EEG. Therein, Teager energy analysis is able to detect high-frequency, low-amplitude components that conventional energy measurements would miss.**

Keywords—**limbic epilepsy, latent period, High Frequency Oscillation, Teager Energy**

I. INTRODUCTION

Epilepsy is a widespread affliction, affecting over 60 million people worldwide. Stroke is the only neurological disorder that occurs more frequently than epilepsy [1]. Typically, the condition arises due to damage to medial temporal structures anywhere from months to years prior to seizure onset. While the true mechanism for epileptogenesis is not known it is thought that during the ictogenic period changes in the neural network occur. Seizures are identified as a large amplitude wave propagated over the neural network, disrupting normal brain activity. While the end result of epilepsy is seizure activity, investigators have found a strong correlations between high frequency oscillations (HFO) and epileptogenesis [2]. It is believed HFOs are the activity of hypersynchronous neurons that play a role in the formation of the epileptic brain [3, 4].

Many changes happen to the brain during the latent period before the first seizure; of particular interest are the HFO that establish a marked difference in the normal and abnormal brain. HFOs are sometimes termed fast ripples [3, 5, 6] or high frequency epileptiform oscillations [2, 7]. Recent studies have shown that HFOs in the range of 100 to 200 Hz are apparent in the normal hippocampus and entorhinal cortex [8, 9]; however, it is HFOs in the range of 200 Hz and above that are deemed abnormal [10]. These HFOs are thought to relate to physical changes which occur during epileptogenesis [5]. These HFO have long gone unnoticed because the clinical instrumentation, commonly used to record EEG, signals records at or below 200 Hz. Advancements in computers, DSP technology and ever increasing storage capacity now allow the high-frequency activity to be investigated. Spectral analysis of highly sampled data shows events that could not be seen with lower sampled data. A spectrogram showing normal, seizure and HFO activity [Fig 1], illustrates the difference between "normal" activity, HFO and seizure activity predominantly occurs in the 100 Hz - 2 kHz band.

The current favored method of detecting HFOs is to band-pass filter the time series, leaving only the frequency ranges of interest. The HFOs are then detected as the signal that passes a standard deviation threshold above the noise[5, 11-13]. One study was found that used Teager energy and curve length to detect oscillations of about 100 Hz [7]. Of the papers that reported the accuracy of HFO detection, their success rates were in the 80% range for detecting HFOs found by [7, 14].

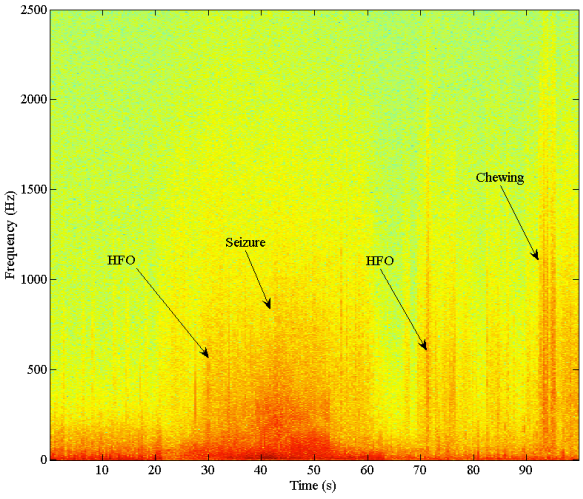

Fig 1: Spectrogram plot showing 100 seconds around a seizure; High Frequency Oscillations (HFOs) and chewing artifacts are labeled. The power strength is indicated with color, with red being highest power.

II. METHODS

A. Experimental Epilepsy Animal Model

The Chronic Limbic epilepsy model was used for these experiments[15]. In this model, the animal displays an epileptogenic period similar to that of human patients in which there is an initial insult to the brain, quiescent period then seizures later in life. To induce eventual spontaneous

seizures, the rat is stimulated into status epilepticus for roughly 1 hour. After the initial insult the rat exhibits "normal" behavior for up to 6 weeks, then develops recurrent, spontaneous seizures for the rest of its life. It is not understood exactly how these seizures come about, but it is thought to be due to structural changes in the brain, as in the loss of inhibitory neurons, the strengthening of excitatory networks, or the suppression of GABA receptors [16].

B. Electrode Placement and Data Acquisition

A total of 32 tungsten microwire electrodes were implanted in the CA1 and Dentate Gyrus areas of the hippocampus bilaterally, with ~8 microwires implanted into each area. The electrodes are implanted in two rows, which are spaced 420 µm apart, and each electrode in the row spaced 210 µm apart. The exact electrode location is then determined with high resolution MR imaging. The data was digitized at 16 bits, and recorded continuously at 12207 Hz using custom written acquisition software and a Tucker-Davis Pentusa DSP (hardware band pass filter set from 0.5 Hz to 6 kHz).

After sufficient recovery time from surgery, 1-2 weeks of baseline data was recorded. The animal was then stimulated in the manner prescribed for the Chronic Limbic Epilepsy Animal Model [15, 17]. Recording began again within 1 day of stimulation and continued until after the animal spontaneously seized. The experimental controls were implanted with the same electrode configuration and recorded for roughly the same amount of time as the experimental rats. Seizure screening was done via continuous video recordings.

After several seizure episodes were recorded the animal was euthanized and the brain removed and perfused for MR Imaging with a 17.6 Tesla MRI machine. [18]

C. Data Analysis Methodology

The resulting data was then analyzed using Teager and conventional energy measures:

Teager energy is defined in equation (1):

$$E_T = A^2 \sin(\Omega)^2, \qquad \Omega = 2\pi \frac{f}{f_s} \tag{1}$$

and is implemented as delineated by Kaiser [19] in equation(2):

$$E_T = x_n^{\,2} - x_{n+1}x_{n-1} \tag{2}$$

While a baseline conventional energy is calculated as amplitude squared as shown in equation (3):

$$E_C = A^2 \tag{3}$$

it is implemented in discrete time series as in equation (4):

$$E_C = x_n^{\,2} \tag{4}$$

A routine was prototyped to compute the Teager energy and conventional energy over a 1-minute block with a 1 second window overlap.

The Teager algorithm (2)[19] requires that the frequency for calculation be 1/8 of the sampled frequency so that the relative error is below 11%. The data is therefore filtered. A Butterworth was chosen because of its stable pass band, ease of implementation and previous work done using the same filter [20].

Conventional energy is implemented in much the same way, using the formula in (4). The values are then averaged over a data window.

III. RESULTS

Based on analysis of time series with known seizure, HFO, and artifact activity, the Teager algorithm detected HFOs reliably. HFOs show up on the Teager graphs as sharp peaks with relatively medium sized amplitudes on the time series; seizures have larger, broader features (see Fig 2). Artifacts from chewing also were present in the analysis due to the sensitivity of the algorithm. These results are easily picked out when looking at the spectrogram (see Fig 1) and time series; however, spectrograms are computationally intensive. Teager analysis allows one to pick out the HFO as well as providing a resolution high enough to make out individual features of the HFO and seizures present.

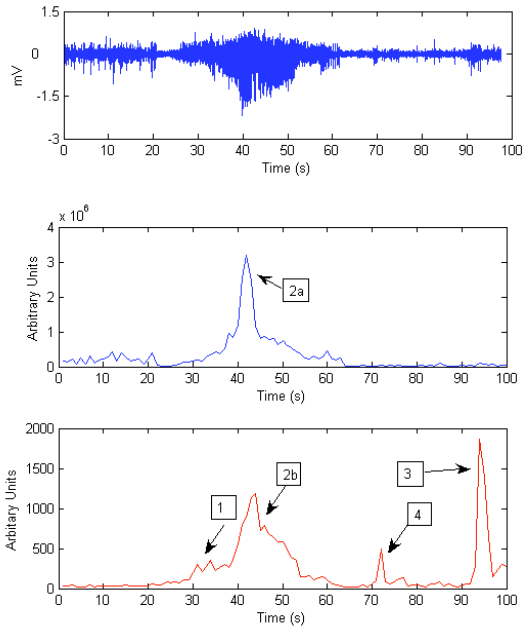

Fig 2: (A) Time series containing seizure; (B) Conventional energy: 2a energy signature of the seizure; (C) Teager energy: 1 and 4 show HFOs, 2b is the seizure, and 3 is chewing artifact.

IV. CONCLUSIONS AND FUTURE WORKS

Teager energy is a robust method for detecting HFOs in EEG time series, and can be also used to identify seizures while suppressing extraneous features of the time series. With the benefits of being fast and easy to implement Teager shows great promise as a means of rapidly detecting and marking HFOs for more in depth study.

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VI. WORK CITED

[1] H. Witte and L. D. Iasemidis, "Special issues on epileptic seizure prediction," *IEEE Transactions on Biomedical Engineering*, vol. 50, pp. 537-539, 2003.

[2] G. A. Worrell, L. Parish, S. D. Cranstoun, R. Jonas, G. Baltuch, and B. Litt, "High-frequency oscillations and seizure generation in neocortical epilepsy," *Brain*, vol. 127, pp. 1496 - 1506, 2004.

[3] A. Bragin, I. Mody, C. L. Wilson, and J. E. Jr., "Local Generation of Fast Ripples in Epileptic Brain," *The Journal of Neuroscience*, vol. 22, pp. 2012-2021, 2002.

[4] A. Bragin, C. Wilson, and J. Engel, "Chronic Epileptogenesis Requires Development of a Network of Pathologically Interconnected Neuron Clusters: A Hypothesis," *Epilepsia*, vol. 41, pp. S144-S152, 2000.

[5] A. Bragin, C. Wilson, R. Staba, M. Reddick, I. Fried, and J. Jerome Engel, "Interictal High-Frequency oscillations (80-500Hz) in the Human Epileptic Brain: Entorhinal Cortex," *Annals of Neurology*, vol. 52, pp. 407-415, 2002.

[6] A. Bargin, J. Engel, C. Wilson, E. Vizentin, and G. Mathern, "Electrophysiological analysis of a chronic seizure model after unilateral hippocampal KA injection," *Epilepsia*, vol. 40, pp. 1210-1221, 1999.

[7] O. L. Smart, G. A. Worrell, G. J. Vachtsevanos, and B.Litt, "Automatic Detection of High Frequency Epileptiform Oscillations from Interracial EEG Recordings of Patients with Neocortical Epilepsy," Georgia Institiute of Techonology, Mayo Clinic, University of Pennsylcania.

[8] G. Buzsaki, Z. Horvath, R. Urioste, J. Hetke, and K. Wise, "High-Frequency Network Oscillation in the Hippocampus," *Science*, vol. 256, pp. 1025-1027, 1992.

[9] J. Csicsvari, H. Hirase, A. Czurko, A. Mamiya, and G. Buzsaki, "Fast Network Oscillations in the hippocampal CA1 Region of the Behaving Rat," *The Journal of Neuroscience*, vol. 19, pp. 1-4, 1999.

[10] A. Bragin, J. Engel, C. L. Wilson, I. Fried, and G. W. Mathern, "Hippocampal and Entorhinal Cortex High-Frequency Oscillations (100–500 Hz) in Human Epileptic Brain and in Kainic Acid-Treated Rats with Chronic Seizures," *Epilepsia*, vol. 40, pp. 127-137, 1999.

[11] N. Maier, M. Guldenagel, G. Sohl, H. Siegmund, K. Willecke, and A. Draguhn, "Reduction of high-frequency network oscillations (ripples) and pathological network discharges in hippocampal slices from connexin 36-defficient mice," *Journal of Physiology*, vol. 541, pp. 521-528, 2002.

[12] A. Bragin, C. Wilson, J. Almajano, I. Mody, and J. Engel, "High Frequency Oscillations after Status Epilepticus: Epileptogenesis and Seizure Genesis," *Epilepsia*, vol. 45, pp. 1017-1023, 2004.

[13] R. Staba, C. Wilson, A. Bragin, D. Jhung, I. Fried, and J. Engel, "High-Frequency Oscillations Recorded in Human Medial Temporal Lobe during Sleep," *Annals of Neurology*, vol. 56, pp. 108-115, 2004.

[14] R. Staba, C. Wilson, A. Bragin, I. Fried, and J. Engel, "Quantitative Analysis of High-Frequency Oscllations (80-500 Hz) Recorded in Human Epileptic Hippocampus end Entorhinal Cortex," *Journal of Neurophysiology*, vol. 88, pp. 1743-1752, 2002.

[15] E. W. Lothman, E. H. Bertram, J. Kapur, and J. L. Stringer, "Reccurrent spontaneous hippocampal seizures in the rat as a chronic sequela to limbi status epilepticus," *Epilepsy Research*, vol. 6, pp. 110-118, 1990.

[16] I. Khalilov, M. L. V. Quyen, H. Gozlan, and Y. Ben-Ari, "Epileptogenic Actions of GABA and Fast Oscillations in the Developing Hippocampus," *Neuron*, vol. 48, pp. 787-796, 2005.

[17] E. W. Lothman, E. H. Bertram, J. W. Bekenstein, and J. B. Perlin, "Self-sustaining limbic status epilepticus induced by 'continous' hippocampal stimulation: electrographic and behavorial characteristics," *Epilepsy Research*, vol. 3, pp. 107-119, 1989.

[18] J. Sanchez, T. Mareci, W. Norman, J. Principe, W. Ditto, and P. Carney, "Evolving into epilepsy: Multiscale electrophysiological analysis and imaging in an animal model.," *Exp Neurol*, vol. 198, pp. 31-47, 2006.

[19] J. F. Kaiser, "On a simple algorithm to calculate the 'energy' of a signal," *Acoustics, Speech, and Signal Processing, 1990. ICASSP-90., 1990 International Conference on*, vol. 1, pp. 381-384, 1990.

[20] A. Roongta, "Using Energy Measure to Study Epilepsy Evolution," 2004.