**THE EFFECTS OF ANTICONVULSANTS ON THE MORPHOLOGY AND DETECTION OF SEIZURES**

*D. Ochal, T. Ahsan, M. Refford, V. Tchiong, J. Picone and I. Obeid*

***Abstract* -- Although anticonvulsants are primarily used to deliver clinical relief to patients experiencing seizures, they have also been found to impact the electrographic activity of the brain, which can be detected using electroencephalographic (EEG) recording. Feature analysis of EEG records of multiple epileptic patients from the Temple University Hospital EEG Corpus suggests that this class of medications can cause a significant decrease in energy, frequency, spatial confinement, and duration of seizure events. The resulting analysis showed a maximum \*\*average and standard deviation of percent difference from control\*\* reduction in energy, and a maximum \*\* avg std %\*\* decrease in frequency between patients. The medicated seizures then become less morphologically distinct from patient baseline and neurological slowing, an event characterized by a transient decrease in frequency. As anticonvulsants blur the lines between baseline, non-seizure slowing events, and seizures, automated seizure detection system performance has been found to drop in subsets of medicated patients versus that of non-medicated patients. Automated seizure detection showed \*\*% sensitivity, #false alarms\*\* for a medicated patient set and \*\*% sensitivity, #false alarms\*\* for the non-medicated control.**

Introduction

Electroencephalographic (EEG) monitoring has been the primary tool in the diagnosis and observation of both clinical and neurological seizures in patients across the world. The measurement of scalp electric potentials gives insight to the underlying brain signals that fluctuate distinctively in both normal and “abnormal” epileptic patients. These measurements result in the characteristic waveforms that are the EEG record. The morphology of these waves can be broken down into discreet, mathematically defined features.

Among these features is energy, a feature that is a function of both frequency and amplitude. Basal frequency information may also be gathered in addition to event duration and spatial confinement. Spatial information can be obtained through channel data from EEG records. These channels correspond with the specific placement of electrodes on the scalp.

Automated seizure detection is a rapidly expanding field of signal interpretation that aims to improve treatment and monitoring of epileptic patients in both the hospital and home settings. Systems analyze EEG features to make decisions on whether a patient is likely seizing or not during a given timeframe.

Anticonvulsant and epilepsy medications have been shown through previous research and clinical data to suppress the motor effects of many seizures as well as to decrease the neurological severity and frequency of seizures in many patients. When it comes to hospital reports and medical procedures, these medications are cited as causes behind EEG patterns such as burst-suppression, slowing, and synchronization which involve significant changes in frequency, amplitude, and other features. They are also known to heavily impact seizure morphology.

As such, automated seizure detection is likely impacted by the use or lack thereof of anti-epilepsy medications (AEDs). The research detailed by this paper aims to quantify this impact and provide a direction for system development with regards to medication effects.

Methods

Patient EEG record files were selected from the TUSZ training set based on the presence of general, focal, complex-partial, or simple partial seizures as well as the recorded administration of the five most common anticonvulsant medications.

TUSZ is an annotated subset of the TUH EEG Corpus (TUH-EEG) [8], the world’s largest publicly available database of clinical EEG data. It currently includes over 30,000 sessions, over 16,000 patients and 29 years of signal data. Other types of seizures (such as absence seizures) were not considered as they make up a very small and separate portion of patient seizures and do not respond to medications. For simplicity, only five specific but common medications were studied in this investigation. Patients were then separated into the following medicated groups: Dilantin, Keppra, Phenobarbital, Depakote, and Ativan, with a non-medicated control. Multiple-medication groups were also created (i.e, Dilantin and Keppra). The EEG records of the patients were then evaluated, both by individual record and by patient as a whole, on the following criteria: duration, spatial spread, energy, and frequency. Each patient was then given equal statistical weight and used to determine average feature values for each category.

**Figure here: most likely a comparison between high energy and low energy seizures.**



Figure 1. This table shows the breakdown of information size in each category of patients according to medication. (\*\*we need to get categorization of multiple-medicated patients\*\*). While seizure counts are high, there are relatively low numbers of patients in the single-medicated and control (none) categories.

The prototypical automated seizure detection system based on (\*\*insert system information\*\*) was then run on the experimental and control groups, and then compared to reference seizure annotations. These annotations were created and inter-rater reviewed by undergraduate students at Temple University and demonstrate high accuracy even compared to board-certified neurologists (\*\*reference IRA paper?\*\*). Statistical analysis of maximum system performance of sensitivity, specificity, and false alarm rate on each group was then completed to reveal any potential effects of medications on seizure detection. To do so, again each patient was given equal statistical weight in comparison so as to avoid the skewing of high-seizure file patients.

Results

Table 1 - Feature analysis

As can be seen above, there appears to be a significant difference in multiple features across the experimental and control groups. The control non-medicated group had the highest average frequency and spatial confinement, while increasing numbers of medications resulted in higher energies and lower frequencies. Although the patient sample size was low, chi-squared analysis shows that the differences in features are strong enough to reject the null hypothesis (\*\*This is a placeholder and we need to understand real statistical analysis to confirm or deny that medications actually caused the expected differences in feature values\*\*).

Table 2 - Detection rates

The seizure detection system was found to perform statistically better on less medicated patients, with the highest sensitivity rates and lowest false alarms found on the control group. (\*\*Again, we need to know how to analyze any results we get statistically\*\*)

Conclusion

Based on feature analysis, it can be determined that anticonvulsant medications have a significant impact on the morphologies of seizure events, which coincides with a decreased difference between baseline, slowing, and seizures in heavily medicated patients. In addition, automated seizure detection performance worsened considerably with increased use of anticonvulsant medication. This suggests that these medications are strongly implicated in barriers facing the development of accurate automated seizure detection systems.

Information regarding medication may be integrated by machine learning pre-processing in order to obtain both higher sensitivity and lower false alarm rates.

We hope this paper provides vital information for the progression of seizure detection systems as we continue to improve the technology.

Acknowledgments

Research reported in this publication was most recently supported by the National Human Genome Research Institute of the National Institutes of Health under award  
number U01HG008468. The content is solely the  
responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. This material is also based in part upon work supported by the National Science Foundation under Grant No. IIP-1622765. Any opinions, findings, and  
conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the National Science Foundation. The TUH EEG Corpus work was funded by (1) the Defense Advanced Research Projects Agency (DARPA) MTO  
under the auspices of Dr. Doug Weber through the Contract No. D13AP00065, (2) Temple University’s College of Engineering and (3) Temple University’s Office of the Senior Vice-Provost for Research.

**Figure here: histogram**