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Multiple Sensor Integration for Seizure Onset Detection in Human Patients Comparing Conventional Disc versus Novel Tripolar Concentric Ring Electrodes

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***Abstract*— As epilepsy affects approximately one percent of the world population, electrical stimulation of the brain has recently shown potential for additive seizure control therapy. Closed-loop systems that apply electrical stimulation when seizure onset is automatically detected require high accuracy of automatic seizure detection based on electrographic brain activity. To improve this accuracy we propose to use noninvasive tripolar concentric ring electrodes that have been shown to have significantly better signal-to-noise ratio, spatial selectivity, and mutual information compared to conventional disc electrodes. The proposed detection methodology is based on integration of multiple sensors using exponentially embedded family (EEF). In this preliminary study it is validated on over 26.3 hours of data collected using both tripolar concentric ring and conventional disc electrodes concurrently each from 7 human patients with epilepsy including five seizures. For a cross-validation based group model EEF correctly detected 100% and 80% of seizures respectively with <0.76 and <1.56 false positive detections per hour respectively for the two electrode modalities. These results clearly suggest the potential of seizure onset detection based on data from tripolar concentric ring electrodes.**

I. Introduction

Epilepsy is a neurological disorder that affects approximately one percent of the world population [1]. Anti-epileptic drugs are ineffective in up to 30% of persons with epilepsy and can cause side effects [2]. Recently, electrical brain stimulation has shown promise to reduce seizure frequency [3]. Several closed-loop seizure control systems were proposed based on different brain stimulation modalities being triggered by automatic real-time seizure onset detectors and validated in both animals [4], [5] and humans [6]. While a great number of algorithms have been proposed for automatic seizure onset detection, in this study we concentrate on the non patient-specific group models applied to scalp electroencephalogram (EEG) recordings [7]-[9]. Automatic noninvasive scalp EEG seizure detection is hindered by a higher number of false detections due to global artifacts compared to the invasive EEG but it does not incur the surgical risks and represents a strong preference of epilepsy patients and caregivers [10]. The group model can be used on data from a patient that the detector has not been previously trained on and therefore is advantageous for practical applications.

Some of the challenges of noninvasive seizure detection stem from the drawbacks of using scalp EEG via conventional disc electrodes. In particular, EEG has poor signal-to-noise ratio resulting mainly from strong attenuation and blurring of brain signals from the skull [11], [12]. Rather than relying on signal processing techniques to alleviate shortcomings of EEG we propose to use noninvasive tripolar concentric ring electrodes (TCREs) [13], [14]. TCRE has been shown to have significantly better spatial selectivity (approx. 2.5 times higher), signal-to-noise ratio (approx. 3.7 times higher), and mutual information (approx. 12 times less) than conventional disc electrodes [15] and is resistant to motion/muscle artifacts that regularly contaminate EEG due to very high common mode noise rejection [14]. Because of such unique capabilities TCREs have found numerous applications in a wide range of areas including brain-computer interface [16], seizure attenuation using transcranial focal stimulation applied via TCREs [17]-[20], and, recently, seizure onset detection in acute pentylenetetrazole-induced seizure model in rats [5], [21]-[23].

While the detection methodologies proposed in [5] and [21] are based on data from a single TCRE in [22] we proposed to integrate data from three TCREs using the exponentially embedded family (EEF) approach that has been recently proposed for multi-sensor detection [24], [25]. Applied to hypothesis testing EEF has been shown to have superior performance compared to existing methods for cases where the sensor outputs are not independent [24], [25]. Further, with EEF the weights for each sensor are estimated from the samples making it a robust method. As shown in [22] the contribution of each sensor is proportional to the amount of useful information it contains. The proposed seizure onset detection approach has been validated on a subset of the dataset used in [5] and EEF outperformed our previously proposed methodology with more than twice the sensitivity (69.4% vs 29.1%), comparable specificity (95.9% vs 98.3%), higher percentage of rats with seizure onset

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detected in advance of the early behavioral seizure activity (100% vs 80%), and smaller delay from seizure induction to detection (18.2 s vs 26.6 s) [22].

Based on promising results in the animal model, in this preliminary study we take the next fundamental step validating EEF based seizure onset detection on data from human patients with epilepsy. EEG using conventional disc electrodes and Laplacian EEG using TCREs (tEEG) were collected simultaneously to allow a direct comparison of detection results for two sensor modalities. Our results are also compared indirectly to the results from the recent group model seizure onset detection studies on scalp EEG [7]-[9].

II. METHODS

A. EEG and tEEG Data

We collected electrographic seizure data from patients with epilepsy at the Epilepsy Center of the Rhode Island Hospital (Providence, RI, US) and at the Neurophysiology Department of the National Institute of Neurology and Neurosurgery (Mexico City, Mexico) after Institutional Review Board approval. EEG and tEEG data were recorded simultaneously in each of seven patients by placing a set of TCREs directly behind the conventional disc electrodes that were in the standard 10-20 system locations used in the institutions. Grass Technologies™ (West Warwick, RI, US) Comet AS40 and Aura LTM64 systems were used to acquire the EEG and tEEG signals correspondingly. Our TCREs were interfaced to the Aura via our custom preamplifier. For all the patients EEG data was band pass filtered 1-70 Hz with 60 Hz notch filter and digitized at 200 S/s. For tEEG data was preamplified with gain equal to either 6 (for four patients) or 100 (for three patients) and 0.3 Hz high pass filter and band pass filtered and digitized at different sampling frequencies for different patients. For three patients the data were filtered 1-100 Hz and digitized at 200 S/s, another three were filtered 1-200 Hz and digitized at 400 S/s and for the remaining patient the data was filtered 1-500Hz and digitized at 1600 S/s. The 60 Hz notch filter was active for all the patients. A total of almost 29 hours of data were used in this study including a total of five seizures from four of the patients. The data from three other epilepsy patients, who did not have seizures during the recordings, were added to confirm the false positive detection rate. While the data from these last three patients did not contain seizures it did contain epileptic activity. The data were reviewed by certified neurologists and seizure onset time and duration were determined for each seizure. Seizure onset time was defined as the beginning of the first observable seizure pattern in either EEG or tEEG. Collection of data was non-selective in terms of seizure characteristics such as duration, frequency composition, morphology and topography. No data were excluded because of the presence of artifacts (e.g. movement related) or poor data quality (e.g. due to technical problems).

B. Data Preprocessing

For tEEG derivation, two differential signals from each TCRE were combined with an algorithm to provide a Laplacian derivation of the signal as reported previously in [14]. Finally, all the data were adjusted for the preamplifier gain and down-sampled to 200 S/s for consistency. No gain adjustment was needed since EEF test statistic is invariant to data scaling [22]. All the signal processing for this study was performed using Matlab (Mathworks, Natick, MA).

C. Seizure Onset Detection Using EEF

We have implemented the EEF for 3 TCREs in [22]. We expanded it from three to 19 TCREs and 16 conventional disc electrodes (any number is possible) for this preliminary study. While this expansion is mathematically trivial one important change has been made to the EEF methodology. In our previous study [22] we derived the EEF detection threshold based on the theoretical distribution under the null hypothesis H_0 assumed to be chi-squared distribution with a number of degrees of freedom equal to the number of channels (TCREs) to integrate. This is an asymptotic result that holds for large sample sizes and, more importantly, it depends on data following the white Gaussian noise distribution assumption. Human baseline EEG has been shown to resemble colored pink noise rather than white Gaussian noise [26]. With this assumption being invalid the EEF test statistic can still be used for real-time detection if the detection threshold is set and updated based on the empirical test statistics similar to the way it was done in [27] and not the theoretical distribution under H_0. The detection threshold for data from a certain patient has to be set with a given probability of false alarm (P_{FA}) equal to, for example, 3% or 0.03. To set the threshold the first M test statistic values for this patient are sorted in ascending order and the threshold is set equal to the value of the test statistic whose index after sorting is equal to the $0.03*M$ rounded to the closest integer. If this integer is equal to zero or is larger than the total number of test statistics M then the index is set equal to 1 or to M respectively.

The first 10 minutes of artifact free baseline data were used to calculate the EEF test statistic values for the rest of the recording for each patient in the increments of the data window (hereafter referred to as detection epoch) size equal to 5 s in the same way as in [22]. Out of those detection epochs the test statistic values for the first M were used to set the initial detection threshold using the given P_{FA}. Once the initial threshold was established it was compared with the test statistic value for the next detection epoch number $M + 1$ to determine whether it belongs to seizure or not and the detection threshold was recalculated for the first $M + 1$ detection epochs. With such an adaptive learning scheme each subsequent detection epoch number $M + i + 1$ is compared to the detection threshold updated based on the $M + i$ previous detection epochs [27]. Analogous to an addition of a smoothing algorithm in this study the threshold based on $M + i$ detection epochs was compared not just to the epoch $M + i + 1$ but to an average of three consecutive detection epochs: $M + i - 1$, $M + i$, and $M + i + 1$ to increase the likelihood of discriminating seizure from movement artifact. The use of this adaptive learning scheme with updated threshold is justified because both background brain activity and the changes introduced by seizures are nonstationary. In our experiments M was equal to 132 detection epochs (11 min) of data. Adding the M detection epochs to the first 10 minutes of data for each patient that were used to calculate the EEF test statistic and subtracting it from the total duration of the dataset leaves a little over 26.3 hours of data on which seizure onset detection was performed and all the reported results are based on that data duration.

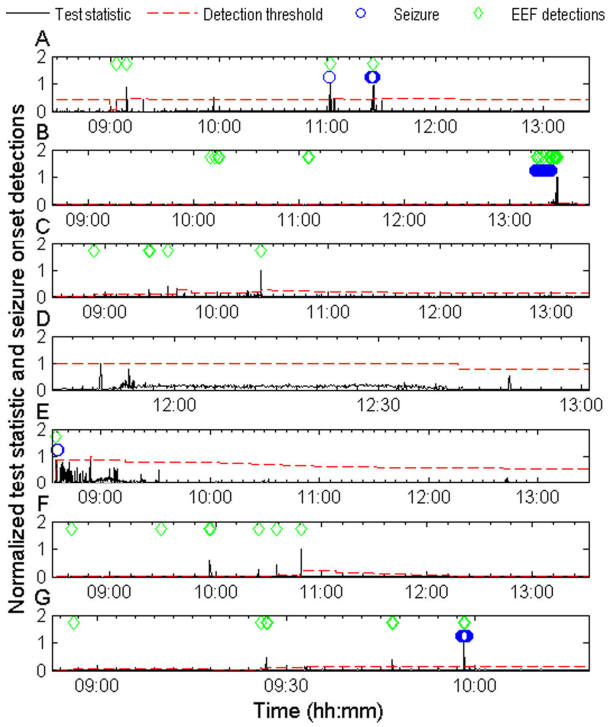

Figure 1. tEEG: test statistics, detection thresholds and automatic EEF detections (n = 7; letters A-G denote individual patients).

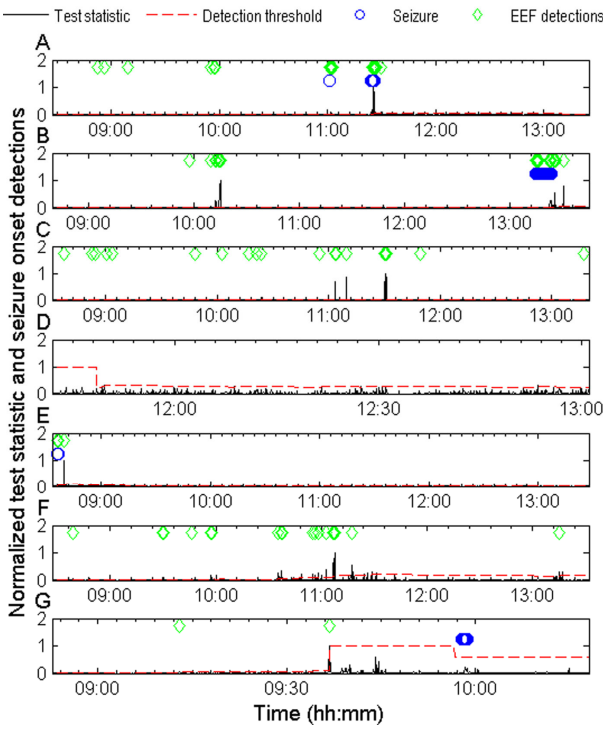

Figure 2. EEG: test statistics, detection thresholds and automatic EEF detections (n = 7; letters A-G denote individual patients).

III. Results

A group detection model was used through k-fold cross-validation with each fold representing all the available data from a single patient. Sensitivity (correct detection rate), selectivity (false positive detections per hour, FPH), and detection delay were analyzed to allow comparison with the results of others [7]-[9]. As in [22] training was performed using grid search minimizing the FPH while maintaining the sensitivity of at least 0.85 for a range of P_{FA} values. A suboptimal P_{FA} value was obtained from 6 training patients during the training phase of the cross-validation and used during the validation phase on the data from the remaining test patient.

Accuracy of detection was interpreted in terms of events rather than detection epochs. Continuous automatic detections or detections separated by less than 30s (6 detection epochs) were grouped and counted as a single detection (either true positive or false positive) as in [9]. Since the duration of some of the seizures we recorded were only a few seconds long the automatic detections that occurred within 1 min (12 detection epochs) after the start of a seizure were still counted as true positive detections independent of seizure duration. Any detections occurring later than one minute after the seizure were counted as false positives. Moreover, when a single automatic detection immediately preceded, i.e. occurred within 1 epoch from the start of the seizure, it was also counted as a true positive detection since it could have happened due to a rounding error in the epoch calculation. Finally, since some strong seizures may be followed by a large number of postictal artifacts related to patient treatment and checking the integrity of the recording equipment the automatic detections falling within 5 minutes (60 detection epochs) after the end of a seizure were discarded while any detected later were counted as false positives.

For the tEEG group model EEF achieved sensitivity of 100% with selectivity of <0.76 FPH and detection delay of 31 ± 23 s (Fig. 1). For the EEG group model EEF achieved sensitivity of 80% with selectivity of <1.56 FPH and detection delay of 10 ± 4.1 s (Fig. 2).

IV. Discussion

In this preliminary study we, for the first time, compared seizure onset detection in humans on data collected using conventional disc electrodes and novel TCREs. Using the same detection methodology EEF showed better performance on tEEG compared to conventional EEG with higher sensitivity and less than half the FPH suggesting the potential of using tEEG for seizure onset detection. Even though the detection delay was lower for EEG the delays for the two sensor modalities cannot be compared directly unlike sensitivity and selectivity. First, lower detection delays that are due to the higher overall EEG FPH decrease the practical value of the detector. Second, one seizure detected with tEEG was not even detected with EEG (patient G in Figs. 1 and 2) resulting in absence of detection delay. This seizure may be challenging to detect and therefore result in a longer detection delay.

Better EEF performance on tEEG data compared to EEG is likely due to the fact that tEEG via TCRE decreases mutual information increasing the level of independency between electrodes compared to EEG via conventional disc electrodes [15]. Due to the lower mutual information multiple TCRE sensors collect more independent local data. Therefore, integration of multiple TCREs increases the total information possibly improving seizure detection.

EEF results for tEEG are comparable to the recent results of others obtained on large scalp EEG datasets: in [7] sensitivity of 90.9%, selectivity of 0.29 FPH, and delays of 10-44 s were reported. In [8] sensitivity of >96%, selectivity of <0.5 FPH, and average delay of 1.6 s were obtained. Finally, in [9] sensitivity of 76%, selectivity of 0.34 FPH, and a median delay of 10 s were achieved. The potential advantage of EEF applied to tEEG is the 100% sensitivity obtained in this preliminary study. Further investigation on a larger dataset is needed to allow a more accurate comparison.

An analysis of false positive detections in this study revealed that the vast majority of them were caused by major movements (standing up, going to the bathroom, etc) and touching and adjusting the electrodes. Movement data, such as from an accelerometer, and input from the user/patient should decrease these types of false positives.

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