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Classification of Scalp EEG States Prior to Clinical Seizure Onset

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ABSTRACT Objective: To investigate the feasibility of improving the performance of an EEG-based multistate classifier (MSC) previously proposed by our group. Results: Using the random forest (RF) classifiers on the previously reported dataset of patients, but with three improvements to classification logic, the specificity of our alarm algorithm improves from 82.4% to 92.0%, and sensitivity from 87.9% to 95.2%. Discussion: The MSC could be a useful approach for seizure-monitoring both in the clinic and at home. Methods: Three improvements to the MSC are described. Firstly, an additional check using RF outputs is made prior to alarm to confirm increasing probability of a seizure onset state. Secondly, a post-alarm detection horizon that accounts for the seizure state duration is implemented. Thirdly, the alarm decision window is kept constant.

INDEX TERMS Epilepsy, clinical seizure onset, early detection, cross-frequency coupling features, patient trial.

I. INTRODUCTION AND CLINICAL NEED

Features that could reliably identify a state prior to clinical seizure from scalp EEG are desirable for home-monitoring applications, as the engulfing fear of unpredictability of seizures has a major impact on quality of life for subjects living with epilepsy [1]. A recent paper from our group [2] described a multistage state classifier (MSC) using cross frequency coupling (CFC) features in human scalp EEG. CFC markers in intracranial EEG (iEEG) have localized epileptogenic tissue (ET) [3], [4] and distinguished ictal and interictal states [5]. In scalp EEG, source imaging assisted by CFC measures localized the ET [6]. In animal work, CFC from iEEG predicted drug treatment outcomes in mice [7] and forecast canine seizures [8].

In the previous work, three states were identified to train the MSC: I_I, interictal baseline; and S_1, S_2, 10s immediately prior and subsequent to electrographic (EG) seizure onset respectively. The MSC is based on three RF classifiers: I_IS_1 (outputs probability of S_1 over I_I), I_IS_2, and S_1S_2. In practice, these classifiers detected CFC changes in advance of a clinical seizure onset, not necessarily at the EG onset. This suggested that state transitions similar to those occurring at EG could also occur before EG onset.

In this paper, using the trained RF classifiers, we propose three improvements to the logical framework of the MSC. Firstly, an additional state check reduces false positives. Secondly, a detection horizon prevents duplicate alarms. Thirdly, the algorithm is restructured to use two consecutive 2s windows only. Using the same set of patient recordings as previously published, we show that these modifications significantly improve sensitivity and specificity of pre-clinical seizure state classification.

II. RESULTS

An example alarm from the MSC is shown in Fig. 1 (A), where an alarm is indicated 57s prior to clinical onset. The improved structure of the MSC is shown in Fig. 1 (B). Receiver-operator characteristic (ROC) curves are shown in Fig. 1 (C) for two patient groups and three EEG electrode configurations. Performance metrics across are summarized in Table I. For Patient Group 1 (on which the classifiers were trained), there is an improvement in all metrics. For Patient Group 2 (on which the classifiers were *not* trained), improvements in all metrics are seen, notably specificity which rises from 79.9% to 89.5%. Across the entire patient set, improvements across all metrics are seen. Performance is

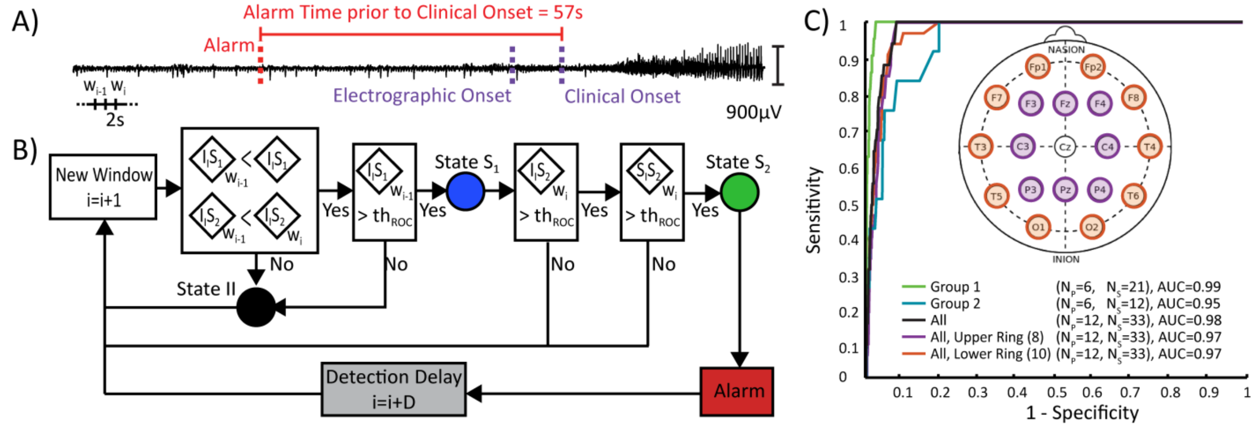

FIGURE 1. (A) Example of MSC operation on Patient 1, Seizure 2. The MSC operates using features from 19 10-20 scalp EEG electrodes; 1 electrode shown for brevity. The MSC signals an alarm prior to clinical seizure onset by detecting changes in cross-frequency coupling features. (B) New MSC algorithm structure. The trained random forest (RF) classifiers (individual diamond boxes) are unchanged from the original work, but the surrounding logic structure is modified in 3 ways. Firstly, a new check is introduced which tests that the RF outputs for early-onset seizure states S1 and S2 states are both increasing vs interictal baseline II. This is intended to improve specificity of the alarm to true seizure events. Secondly, the MSC now operates with a detection delay. Post-alarm, the algorithm skips a number of windows D to avoid duplicate alarms for the same event. Thirdly, the MSC consistently operates on two consecutive 2s windows. (C) MSC receiver-operator characteristic (ROC) performance across testing subsets. Green ROC = Group 1, on which the system received training. Turquoise ROC = Group 2, on which the system received no training. Black ROC = All patient testing data. Purple / Orange ROCs = All patients, 8 or 10 electrode rings respectively. Np = # of patients, Ns = # of seizure events, AUC = area-under-the-curve.

TABLE 1. Performance metrics of MSC across patient groups and electrode subsets.

Patient Group	(# of channels)	Alarm Time (s)* Old	Alarm Time (s)* New	AUC (%) Old	AUC (%) New	Accuracy (%) Old	Accuracy (%) New	Sensitivity (%) Old	Sensitivity (%) New	Specificity (%) Old	Specificity (%) New
Group 1	(19)	48 ± 16	52 ± 15	98.8	99.3	95.0	97.0	97.5	99.1	95.0	97.0
Group 2	(19)	47 ± 15	47 ± 11	91.6	94.7	79.0	89.5	85.2	93.8	79.9	89.4
All	(19)	45 ± 16	50 ± 14	93.4	97.5	82.4	92.1	87.9	95.2	82.4	92.0
All Upper Ring	(8)	41 ± 11	50 ± 13	93.9	97.4	83.9	92.1	89.8	95.1	83.9	92.0
All Lower Ring	(10)	54 ± 7	59 ± 5	93.3	97.1	82.9	92.1	87.8	95.4	82.9	92.0

* mean ± standard deviation

TABLE 2. Sensitivity analysis on modifications using performance metrics across all patients.

Modifications		Change in Performance Metrics (*(New-Old)/Old x 100%*) Mean Alarm Time	AUC	Accuracy	Sensitivity	Specificity
1:	State Check	-6.6	2.4	3.2	2.5	3.2
1 + 2:	State Check, Detection Delay	-6.6	8.9	18.8	14.2	18.8
1 + 2 + 3:	State Check, Detection Delay, Fixed Window	7.7	8.8	18.9	14.2	18.8

also assessed using recordings from reduced electrode subsets (8 or 10 electrode circumferential rings) appropriate for headband-type home-monitoring devices. Performance on these ring subsets is comparable to all electrodes.

III. DISCUSSION

Table 2 summarizes the impact of each change on the MSC performance metrics. The additional logical state checks and the detection delay lead to improved sensitivity and specificity of the MSC. Switching to a fixed window approach improves alarm times. The MSC can identify a state prior to clinical seizure from scalp EEG, making it suitable for clinical and home monitoring of seizures.

IV. METHODS

A. NUMBER OF SUBJECTS AND RECRUITMENT

Patient EEG recordings were collected from 12 subjects with temporal or extratemporal lobe epilepsy who underwent pre-surgical evaluation at the Toronto Western Hospital Epilepsy Monitoring Unit. The dataset is divided into two: Group 1 (N = 6, patients 1-6) with recordings split between both training and testing, and Group 2 (N = 6, patients 7-12) reserved exclusively for testing purposes. Electrographic and clinical seizure onsets were defined by an expert neurologist. About 3 hours of seizure epochs (56 events) and 10 hours of interictal recordings were collected. All available seizure onset epochs were used, and all interictal data that was free from large-scale movement artifacts was included in this study. Seizure onset epochs were defined as the complete clinical seizure plus 66s leading up to the clinical seizure onset. 66s was selected because it was the greatest duration observed between EG and clinical onset, and should include seizure transition states.

B. INCLUSION AND EXCLUSION CRITERIA

Subjects were selected based on availability of video-EEG recordings with at least one seizure, and interictal separated from seizure by hours. Additionally, patients in Group 1 were selected for availability of simultaneous scalp and iEEG recordings. All patients meeting these criteria were included in this study.

C. CONFIDENTIALITY AND SAFETY PROTOCOLS

Informed consent was obtained from each patient. Patient recordings were used with Research Ethics Board approval.

D. FEATURE EXTRACTION AND CLASSIFICATION DEFINITIONS

Spectrograms in two ranges are generated for each 2s window for a given channel using a complex Morlet wavelet transform. The low range is $f_L \epsilon$ (1, 1.1, ..., 10) Hz and the high range is $f_H \epsilon$ (20, 21, ..., 150) Hz. Using the low-frequency phase $\varphi(t, f_L)$ and high-frequency amplitude $A(t, f_H)$ from the complex wavelet coefficients, a measure for phase-amplitude is computed. In this case, we use Tort's modulation index [8], referred to as I_{cfc}, which is averaged across channels to produce the global spatial average $\bar{I}_{cfc}$. This feature is used for classification once a binary threshold is applied. The threshold level was determined by a 5-fold cross validation process during training. A complete mathematical description of this pipeline is described in previous work [2].

For the interictal data, every tested window is counted toward the total of actual negative events N. An alarm at any point is a False Positive (*FP*), and the lack of alarm is a True Negative (*TN*). For the seizure onset epochs, the entire epoch constitutes a positive event, so the number of seizure onset epochs equals to the number of actual positive events P. An alarm at any individual window during the seizure onset epoch counts that epoch as a True Positive (*TP*) event. Conversely, every window during a seizure onset epoch must lack an alarm to constitute that epoch as a False Negative (*FN*). Sensitivity, specificity and accuracy can then be assessed as in the previous work. The detection threshold th_{ROC} ϵ *[0,1]* is then varied to produce ROC curves, as shown in Fig. 1.

E. MODIFIED CLASSIFICATION ALGORITHM

1) An additional state check implemented to reduce false positives, on the premise that there should be an increasing probability of leaving the baseline interictal state before an alarm. As such, the outputs from $\mathrm{I_IS_1}$ and $\mathrm{I_IS_2}$ are assessed on consecutive windows $\mathrm{w_i}$ and $\mathrm{w_{i-1}}$. Only if $\mathrm{I_IS_1(w_i)} > \mathrm{I_IS_1(w_{i-1})}$ and $\mathrm{I_IS_2(w_i)} > \mathrm{I_IS_2(w_{i-1})}$ does the MSC proceed to the subsequent test stages.

2) A detection horizon of D duration following an alarm is included to prevent duplicate alarms for a single event. Accordingly, D = 200s was selected because it is equal to the duration of a convulsive human seizure state including the duration of post-ictal generalized electrographic suppression (PGES) [9] during which another seizure onset will not occur.

3) The alarm decision is based on using two consecutive 2s windows. The version proposed here has a fixed decision window that is applied uniformly across every window of the tested data, in contrast to the variable decision window in the previous approach.

V. FUTURE DIRECTIONS AND POTENTIAL CLINICAL IMPACT

The three modifications proposed above improve the performance of the MSC algorithm. Across all patient testing data, the specificity of the MSC algorithm is improved from 82.4% to 92.0%, with a corresponding improvement in sensitivity from 87.9% to 95.2%. The alarm times prior to clinical seizure onset are slightly improved from 45±16s to 50±14s, and the classifier performance is not deteriorated by the choice of a reduced electrode ring configuration These improvements make the approach more suitable for implementation in a headband-type wearable device, such as those reported in [11] for home-monitoring applications that would enhance the quality of life for epileptic patients.

A limitation of the current work is the relative scarcity of interictal data used; the ratio of seizure to interictal recording in this dataset is 0.17, higher than would be experienced by most patients. Future work involving unabridged, uninspected, long-term EEG would help prove the clinical utility of this approach. Furthermore, the algorithm needs to be optimized for computational efficiency before it can be translated to a wearable device. The current pipeline, implemented in Matlab, running on a Core i5 CPU with 8GB RAM, takes approximately 0.6s to process a single window, most of which is used for feature extraction. Future work should attempt to minimize this time.

We speculate that additional classifiers, each trained to recognize the CFC signature of a given EEG artifact, could further increase the specificity of this approach. If the dataset can be increased, then replacing the RF classifiers with deep neural nets may further improve specificity.

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