Support Vector Machine for Early Prediction of Infants With Electrographic Seizures in Neonatal Hypoxic-Ischemic Encephalopathy

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***Abstract*—We propose a novel machine-learning method to predict seizure development in neonates with hypoxic-ischemic encephalopathy using a Support Vector Machines classifier. The method leverages a minimal feature set, comprising two features extracted from the first 12 hours of single-channel EEG recordings, spectral flatness and spectral entropy, and two early clinical parameters collected in the hospital condition. Validation was conducted on a dataset of 63 EEG recordings from neonates with HIE, all with a gestational age above 35 weeks. The model's performance was evaluated using the Matthews correlation coefficient (MCC) and the area under the receiver operating characteristic curve (AUC), achieving MCC 0.555 and AUC 0.83. These results demonstrate higher performance compared to the current state-of-the-art model, which utilizes clinical and quantitative EEG features.**

***Index Terms*—machine learning, EEG, neonatal seizures, prediction algorithm**

I. Introduction

Seizures occur in approximately 1 to 5 per 1000 live births [1], and represent one of the most common neurologic conditions in neonatology. These seizures can have various underlying causes, including hypoxic-ischemic encephalopathy (HIE), a severe neurological condition resulting from oxygen deprivation and reduced blood flow to the brain [2], [3]. It is a leading cause of neonatal morbidity and mortality, often resulting in long-term complications such as developmental delays, cerebral palsy, and epilepsy [4]. The incidence of HIE is estimated to range from 1.5 to 3 per 1,000 live births in developed countries, with significantly higher rates of 1.5 to 14.9 per 1,000 live births reported in low-income countries [4], [5]. Therapeutic hypothermia is currently the only recommended treatment for moderate to severe HIE. This intervention has been shown to reduce the overall seizure burden and improve long-term neurodevelopmental outcomes [6]–[8].

To enhance outcomes for neonates with HIE, early identification and effective management of seizures are critical. However, the gold standard for seizure diagnosis, continuous video-EEG monitoring, is not widely accessible because it requires expert personnel and specialized equipment [9]. To address these limitations, the goal is to develop a machine learning model capable of identifying infants at high risk of developing seizures, utilizing the EEG monitoring equipment already available in clinical environments. Early detection would enable timely initiation of treatment, minimizing delays and improving patient outcomes.

Over the years, significant efforts have been made to develop models for neonatal seizure prediction, utilizing a variety of clinical and physiological features. Early studies investigated correlations between biochemical parameters such as umbilical artery pH, bicarbonate, and PO_2, and neonatal outcomes like mortality, HIE, and respiratory distress syndrome [10]. Some models integrate clinical parameters like the 5 minute Apgar score, delivery room intubation, and biochemical measures such as pH, often in combination with EEG background analysis [11]. In recent years, machine learning (ML) techniques have enabled the creation of more advanced decision-support tools, offering significant potential in healthcare to assist professionals with early detection and intervention [12], [13]. The proposed ML models utilize quantitative and qualitative EEG features, either alone or in combination with clinical parameters [9]–[11], [14], [15], to predict neonates at a higher risk of developing seizures. The authors in [9], [16] have also explored replacing EEG with amplitude-integrated EEG (aEEG), a simplified trend-monitoring tool that displays one or two channels of processed, time-compressed EEG on a

semilogarithmic scale [17]. Despite potential benefits, there are still many unanswered questions prior to implementation of these techniques into routine clinical practice.

This study aims to develop a ML model for early prediction of neonates with HIE who later develop seizures, utilizing the first 12 h of EEG recordings alongside selected clinical parameters.

II. Dataset

In this study the dataset utilized consists of single-channel EEG signals recorded from neonates diagnosed with HIE. The recordings were obtained using the Olympic Medical CFM 6000 device (Natus Medical Incorporated, 5900 First Avenue South, Seattle, WA 98108, USA) between January 2021 and October 2024 in the Neonatal Intensive Care Unit of the Institute for Child and Youth Health Care of Vojvodina, Novi Sad, Serbia. EEG signals were acquired from parietal electrode locations P3 and P4, with a sampling rate of 200 Hz.

Neonates included in the study were diagnosed with moderate to severe HIE and eligible for therapeutic hypothermia. All neonates had a gestational age above 35 weeks, and only those with EEG recordings of a minimum duration of 12 hours, initiated within the first 6 hours of life, were selected.

The study population consisted of 63 neonates, divided into two groups based on the presence and frequency of neonatal seizures observed after the first 12 hours of EEG recordings. The first group included neonates who experienced no seizures or a single seizure episode, while the second group consisted of those with more than one seizure episode. The annotations were performed by two medical experts.

The clinical and biochemical data covered the mode of delivery, the neonate's gender, birth weight (BW), gestational age (GA), Apgar scores at first minute, Apgar score at fifth minute, assisted ventilation, pH, cardiopulmonary resuscitation in the delivery room (CPR), standard bicarbonate ($stHCO_3$), lactates, base excess, glycemia, and age at the time of onset of seizures.

For the analysis, 12 hours of single-channel EEG recordings were extracted for each neonate. These recordings underwent quantitative analysis to identify patterns associated with seizure activity.

III. Proposed Method

The study proposes a model designed to identify neonates with HIE who are at risk of developing more than one seizure episode after the first 12 hours of EEG recording. The objective is to detect this particularly vulnerable subgroup by combining clinical data with quantitative EEG features. From the available clinical variables in the dataset, two features were selected for inclusion: standard bicarbonate levels and the need for cardiopulmonary resuscitation in the delivery room. To enhance model performance and ensure comparability, these clinical features were standardized to have a mean of zero and a standard deviation of one. In addition to the clinical variables, the model also utilizes quantitative features derived from the EEG recordings, integrating them for a comprehensive analysis.

A. Quantitative-EEG Features Extraction

Quantitative-EEG analysis included extracting different features that describe time and frequency characteristics of EEG signal. Two features used for model development are spectral flatness and spectral entropy, both of which were calculated based on the Power Spectral Density (PSD). Prior to feature extraction, the EEG signal underwent preprocessing to prepare it for analysis. Firstly, the original signal, sampled at 200 Hz, was bandpass filtered to remove noise and irrelevant activity. As in [18], a bandpass filter with a range of 0.5 to 30 Hz was applied to eliminate the 50 Hz power-line interference and reduce frequencies below 0.5 Hz, which are typically associated with artifacts such as DC drift and sweat-related interference. This bandpass filtering step also served as an anti-aliasing filter, crucial for preventing aliasing during the subsequent downsampling to 64 Hz. After bandpass filtering, the signal was downsampled to 64 Hz, reducing computational complexity and storage requirements while preserving the essential characteristics for further analysis [19].

The PSD represents the distribution of signal power across different frequencies, and in this case, it was estimated using Welch's method, a widely used technique for spectral estimation. This method divides signal into overlapping segments, computes the periodogram for each segment, and averages these periodograms to obtain a more stable estimate of the power spectrum. The parameters for the Welch method used on EEG signals were as follows: a Hamming window was applied to minimize spectral leakage, the EEG signal segment length was $8 \times fs$ (sampling frequency), corresponding to 8 seconds of signal, and 75% overlap between segments was used to enhance the smoothness of the estimate. The equation for the PSD estimated using the Welch method is given by:

$$P_{\text{Welch}}(f) = \frac{1}{N} \sum_{k=0}^{N-1} \left| \frac{1}{M} \sum_{m=0}^{M-1} x_{k+m} w_m e^{-j2\pi fm} \right|^2 \quad (1)$$

where x_{k+m} is the segment of the signal for which the Fourier transform is calculated, w_m is the window function (in this case Hamming) applied to each segment, M is the length of the segment, N is the number of segments, and f is frequency.

Spectral entropy quantifies the degree of randomness or complexity in a signal and it was computed using the normalized PSD, denoted as $p_{\text{Welch}}(f)$, which represents the probability distribution of the energy across different frequencies. The method used calculates the Shannon entropy for the PSD, following the equation:

$$H(p) = -\sum_{i=0}^{N} p_{\text{Welch}}(f_i) \log p_{\text{Welch}}(f_i) \quad (2)$$

where $p_{\text{Welch}}(f_i)$ is the normalized value of the PSD at frequency f_i [20].

Spectral flatness, also known as Wiener entropy, measures how flat or noise-like a signal spectrum is [20]. It is calculated using the PSD, specifically through the geometric mean and

the arithmetic mean of the PSD. The arithmetic mean represents the average power level of the signal, while geometric provides a measure of central tendency. The spectral flatness S is then determined by the ratio of the geometric mean to the arithmetic mean, calculated as follows:

$$S = \frac{\exp\left(\frac{1}{K}\sum_{i=1}^{K}\log P_{\text{Welch}}(f_i)\right)}{\frac{1}{K}\sum_{i=1}^{K}P(f_i)} \tag{3}$$

where $P_{\text{Welch}}(f_i)$ is the PSD at frequency f_i, and K is the number of frequency bins.

B. Machine Learning (ML) Classifier

Developed ML model uses both clinical and quantitative-EEG features to predict neonates with HIE who experienced more than one seizure after the first 12 hours of EEG recording. Among the models evaluated, including Random Forest [21], Adaptive Boosting [22], and Logistic Regression [23], the Support Vector Machine (SVM) [24] demonstrated superior performance. Given the limited dataset, consisting of only 63 signals, a leave-one-out cross-validation approach was employed to maximize the use of available data. Model hyperparameters were optimized through a grid search within a nested 10-fold cross-validation.

C. Model Evaluation

In this study, the dataset is highly imbalanced, comprising a total of 63 EEG time series, of which 45 correspond to class 1 (neonates with HIE who develop a single seizure or no seizures), while 18 represent class 2 (neonates who experience more than one seizure). To address this class imbalance, the performance of the ML models was evaluated using the Matthews correlation coefficient (MCC) [25], which is well-suited for imbalanced datasets. In addition to MCC, other standard performance metrics were reported, including the area under the receiver operating characteristic curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Performance for binary classification is calculated by using the following expressions:

$$MCC = \frac{TP \cdot TN - FP \cdot FN}{\sqrt{(TP+FP)(TP+FN)(TN+FP)(TN+FN)}} \tag{4}$$

$$Sensitivity = \frac{TP}{TP + FN} \tag{5}$$

$$Specificity = \frac{TN}{FP + TN} \tag{6}$$

$$PPV = \frac{TP}{TP + FP} \tag{7}$$

$$NPV = \frac{TN}{FN + TN} \tag{8}$$

where TP represent true positives, TN true negatives, FP false positives and FN false negatives. TP corresponds to HIE infants who later develop seizures.

IV. Results

In this section, we evaluate the proposed method and compare its performance to the current state-of-the-art model, which utilizes continuous multichannel EEG data along with clinical features for prediction [9]. The reference study explored several models differing in the type of features employed. Among these, the highest performance was achieved by the model integrating clinical and quantitative EEG features, reporting a MCC of 0.513 and an AUC of 0.746. This model is selected as the benchmark because it uses clinical and quantitative-EEG features, aligning with the features used in the proposed model.

The performances of the proposed and benchmark model are shown in Table 1. The proposed model employs a total of 4 features, 2 clinical and 2 quantitative-EEG features. On the other hand, the benchmark model utilizes 41 features, 13 clinical and 28 quantitative-EEG features. Notably, the proposed approach outperforms the benchmark model across almost all evaluation metrics.

However, direct comparisons between the proposed model and the benchmark model are constrained by differences in dataset size and EEG configuration. While the benchmark model utilized multichannel EEG data, our approach is based on single-channel EEG recordings. To address this limitation, we conducted an additional comparison with our previous work [16], which employed the same dataset as the proposed method did, but used amplitude-integrated EEG (aEEG) instead of raw single-channel EEG. The transformation of single-channel EEG into aEEG involved filtering, rectification, smoothing, and amplitude integration, as described in [26]. Additionally, Table 1 includes the performance metrics of the approach presented in [16]. Once again, the proposed model demonstrates improvement in most of the evaluation metrics compared to this approach.

V. Conclusion

In summary, the proposed clinical and quantitative-EEG model for predicting neonates with HIE who are at risk of developing seizures demonstrates improvements compared to previously reported models [9], [16]. It achieved higher performance by using 4 features, 2 clinical and 2 quantitative EEG features. A key limitation of this study, similar to many others [9], [16], is the small dataset comprising only 63 neonates from the Institute for Child and Youth Health Care of Vojvodina, Novi Sad, Serbia. Despite this limitation, the proposed model represents a step forward in integrating machine learning support tools into clinical practice, aiding in the identification of vulnerable neonates with HIE.

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TABLE I
COMPARISON OF PERFORMANCES FOR DIFFERENT MODELS

ML model	Number of infants	MCC	AUC	Sensitivity	Specificity	PPV	NPV
Clinical and quantitative - EEG [a] [9]	159	0.513	0.746	75.5	78.0	62.5	86.7
Clinical and quantitative - aEEG [b] [16]	47	0.495	0.758	60.0	87.5	69.2	82.3
Proposed method (clinical and quantitative EEG model) [c]	63	0.55	0.83	55.6	93.3	76.9	84.0

[a] EEG=multichannel EEG
[b] aEEG=single channel EEG (P3-P4)
[c] EEG=single channel EEG

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