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Cracking the Seizure Code: Leveraging Bi-LSTM Models for Neonatal EEG Interpretation and Seizure Classification

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ABSTRACT: This research investigates how Bidirectional Long Short-Term Memory (Bi-LSTM) networks can be used to identify neonatal seizures from EEG data, with an emphasis on mirroring expert neurologist annotations rather than independently predicting seizures themselves. Timely detection of seizures in infants is crucial in Neonatal Intensive Care Units (NICUs); however, traditional methods often delay critical intervention and treatment. Machine learning offers a promising alternative solution. For this study, EEG data from 79 neonates within a publicly available dataset were cleaned, filtered, split into appropriate segments, and processed so the model could learn most effectively. The Bi-LSTM model, trained over eight epochs, achieved an overall accuracy of 83%. A key limitation of this study is the absence of "ground truth," as even expert annotations are subjective, which introduces variation within the training data. Additionally, the overlap between seizure and normal brain activity in the EEG signals contributes to lower model accuracy in certain patient cases. Nevertheless, this study highlights the potential of Bi-LSTM models in enhancing neonatal seizure detection and improving long-term outcomes for vulnerable neonates, offering an essential step toward faster, more effective diagnosis in NICUs.

KEYWORDS: Computational Biology and Bioinformatics, Computational Neuroscience, EEG Pattern Recognition, Neonatal Seizure Detection, and Machine Learning in Neurology.

Introduction

The neonatal period is a critical stage in which the infant's brain is particularly vulnerable. During this period, the brain undergoes rapid changes, characterizing it as a time of high risk for various neurological conditions. One of the most common neurological conditions is seizures, described by Huff & Murr as changes in the degree of "consciousness, behavior, memory, or feelings." Seizures are often caused by atypical, unconstrained electrical activity in the brain.[1] The prevalence of neonatal seizures in the general population is roughly 1.5%, with the overall occurrence being three per every 1000 live births. However, given the chance, a newborn is born prematurely, prevalence increases to around 57–132 per 1000 live births.[2] The most common cause of neonatal seizures is hypoxic-ischemic encephalopathy (HIE), a type of brain damage resulting from the lack of oxygen to the brain soon after delivery. Although they can also be caused by a variety of other factors, such as stroke, cranial blood clots, and other brain defects.[3] Not all seizures tend to have long-lasting effects since many are brief and only momentary. Regardless, prolonged neonatal seizures can lead to permanent brain damage, especially if they are not detected early enough.[4]

Currently, expert neurologists diagnose seizures in neonates by analyzing the patients' electroencephalogram (EEG) data, which measures the general electrical activity in various regions of the brain. Most often, however, they require specialized experts like pediatric neurologists to be able to diagnose neonates with higher efficacy. This results from the unique pathophysiology and electrographic findings of infants' EEG data, causing it to be more difficult to identify their seizures specifically. Most frequently, newborns do not show similar visual signs of seizures to adult patients, such as full-body convulsions. Their "symptoms" often appear to look like normal baby behavior, for instance, thrashing legs or random eye movements, along with a sucking tongue. Additionally, newborns may even have symptoms, such as jitteriness or sleep myoclonus, that tend to mimic seizure activity, even in the absence of genuine seizures.[5] Due to the lack of clear observable clinical manifestations, physicians must rely on more advanced brain monitoring techniques to accurately diagnose the presence of seizure activity in newborns. The most preferred method is continuous video EEG monitoring, allowing clinicians to determine if unusual features are seizures.[6] Once a seizure is detected or simply suspected, physicians may perform laboratory testing and other imaging modalities such as head ultrasonography and magnetic resonance imaging (MRI) to confirm potential causes before treatment. If continuous video EEG monitoring is inaccessible, practitioners may turn to amplitude-integrated EEG (aEEG). Amplitude-integrated EEG, described as being able to "present time-compressed and filtered EEG data," offers an alternative method for areas lacking the support that continuous video EEG monitoring requires.[5] However, aEEG does have a low sensitivity, which can lead to false negatives in the diagnosis, potentially allowing seizure activity to go undetected. Unfortunately, the entire process of traditional detection is costly, time-consuming, and does not guarantee full accuracy as annotations vary from professional to professional. Moreover, if a neonate is not diagnosed and treated in a timely fashion, the damage to the developing brain could cause "cognitive disorders, developmental delay, epilepsy, or cerebral palsy," displaying the crucial need for rapid diagnosis.[7] A faster, reliable

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diagnostic method would significantly benefit the medical specialty of neonatology.

A rising consideration in medicine is the use of Machine Learning (ML). Machine Learning allows for diagnosis beyond what the naked eye can detect and is anticipated to improve many areas of medicine, including accuracy, prediction methods, and quality of patient care.[8] At the moment, ML positions itself in a more supportive role in healthcare, easing the workload of physicians. In large facilities, machine learning techniques have been implemented in a multitude of ways, such as in record organization, medical imaging, and robot-assisted surgeries.[8] Countless studies have worked with EEG for seizure detection, leading to the possibility of earlier and more accurate seizure detection. However, implementing those computational methods on patients in real clinical settings will require further development as ML continues to evolve. Nevertheless, once it does, patients with neurological conditions, such as epilepsy, will receive significantly improved outcomes.

Neural networks, a subset of ML, have been well-studied for their use in the medical field.[9] Recently, with the increasing availability of public EEG data, many types of Neural Networks have been used, particularly to detect seizures. Recurrent Neural Networks (RNNs) deal with sequential, time-evolving data, which makes them well-suited for analyzing time-series data such as EEG signals, in which the order of information is essential. However, there is a lack of research on investigating RNNs' effectiveness in neonatal seizure detection. Additionally, this research solely relies on the key assumption that by treating annotations from human expert neurologists as the "ground truth", we are accurately detecting seizures within all of these infants. Building on the strengths of RNNs, the model essentially functions as a universal classifier, designed to generalize across multiple patients rather than being specialized for a specific neonate. This approach allows the model to learn and understand patterns that apply to a wider range of EEG data, making it useful for diverse clinical settings. This universal classification approach ensures that the model is accurate across varying cases and not limited to a single patient's data.

In this study, Recurrent Neural Networks (RNNs) were proposed for their ability to process sequential data and capture temporal dependencies, such as those of EEG data, specifically Bidirectional Long Short-Term Memory Networks (Bi-LSTMs), a certain type of RNN. Although traditional RNNs function as a valuable model in ML, they frequently experience a certain challenge known as the vanishing gradient problem. This occurs during backpropagation when the gradient becomes increasingly small until it ultimately "vanishes." Normal LSTMs overcome this issue by their additive update mechanism, with the use of gates. Specifically, the LSTM architecture is constructed of the following parts: a cell, an input gate, a forget gate, and an output gate. The forget gate is what allows the model to reset its state.[10] And the Bidirectional portion allows the LSTM to view data from both forward and backward time standpoints. Thus, this study intends to address the following research question: To what degree can a Bi-LSTM model accurately capture and interpret complex associations between neonatal EEG data and clinician-labeled annotations, and how accurately can it classify seizure events across diverse patient data?

Methods

Dataset:

The dataset chosen required high-quality data, corresponding annotations, and a large diversity. This was found in a publicly available dataset labeled "A Dataset of Neonatal EEG Recordings with Seizure Annotations."[11] The dataset has EDF files available for multi-channel EEG recordings for seventy-nine term neonates, a MAT file for the visual interpretations of the data, and a CSV file with the corresponding clinical information for each patient. The data was recorded from the Neonatal Intensive Care Unit at the Helsinki University Hospital, Finland, one of Europe's largest healthcare providers. Out of the seventy-nine neonates, seizure consensus variability was visible with 39 infants labeled as seizure-prone and 22 labeled as seizure-free. The interquartile range for the EEG recordings was broad, from 64 to 96 minutes, with a median recording duration of 74 minutes, and the signals themselves were sampled at 256 Hz. The EEG recordings' visual interpretations were annotated independently by three expert neurologists and stored in a MAT file for further use. The specialists defined seizure activity as visible on the EEG recordings when there was an "emergence of abnormal discharges in bursts, termed ictal epileptiform discharges… Escalate in frequency, evolving into rapid, continuous spikes and waves, and ultimately peak with numerous spikes accompanied by buried waves."[12] Annotations from the three experts, however, are also accessible in individual CSV files, categorized as 'A', 'B', and 'C'.

Data Preprocessing:

Several preprocessing steps were carried out to prepare data for input into the model, including bad signal removal, band-pass filtering, segmentation in fixed-length epochs, feature selection, and standardization. The EEG recording dataset has 21 total channels, with the bipolar montage displayed in Figure 1; however, two of those channels are Electrocardiogram (ECG) and Respiratory Effort Channels. Unnecessary noise, spike waves, and artifacts caused by the extra channels may corrupt training, so to prevent contamination of the pure EEG data, removal of the ECG and Resp-Effort Channels was required. The raw continuous EEG data is then band-pass filtered from 0.1 to 15 Hz due to the range capturing the relevant brainwave frequencies associated with neonatal seizures while minimizing noise. Afterward, the neonatal EEG data is segmented into epochs of one second each, corresponding with the annotations per patient.

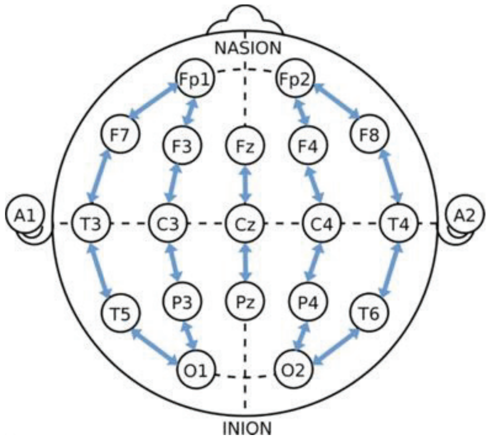

Figure 1: The bipolar montage represents the 21 EEG electrodes used in collecting the neonatal data used in the model. This montage follows the standard 10-20 system used globally for electrode placement, certifying comprehensive data collection. The recorded data was later processed and analyzed to train the Bi-LSTM efficiently for neonatal seizure detection.

$$\textit{Mean}: E(x) = \frac{1}{n}\sum_{i=1}^{n} x_i$$

$$\textit{Variance}: Var(x) = \frac{1}{n-1}\sum_{i=1}^{n}(x_i - E(x))^2$$

$$\textit{Skewness}: S(x) = E\left[\left(\frac{x - E(x)}{\sqrt{Var(x)}}\right)\right]^3$$

$$\textit{Kurtosis}: K(x) = E\left[\left(\frac{x - E(x)}{\sqrt{Var(x)}}\right)\right]^4$$

Figure 2: The statistical features breakdown displays the mean, E(x), which refers to the average of all n data points collected, and the variance, Var(x), describing the average squared distance from the mean, or in simpler terms, the standard deviation of the data, squared. Skewness, S(x), indicates the measure of the asymmetry of the expected value (E) in the classic distribution of the data, and kurtosis, K(x), measures the "tailedness" or the sharpness of the peak in the data distribution, indicating how much of the variance in the data is due to extreme values.[13]

Statistical features regarding mean, variance, skewness, and kurtosis were extracted from the data (Figure 2). In addition to statistical features, time-domain features (TDF) and frequency-domain features (FDF) were also extracted. Within the TDF, zero crossing and peak-to-peak features were combined into a vector for each epoch. Zero Crossing calculates the number of times the EEG signal waves' amplitude values cross the zero-amplitude level.[14] Peak-to-peak measures the difference between the maximum and minimum value of the EEG signals, showcasing the range or variation within the signals. Referring to the frequency domain, Power Spectral Density (PSD) was calculated. PSD measures the "signal's power content versus frequency," applied through Welch's method.[14] The following three feature vectors, statistical features, time-domain features, and frequency-domain features, were combined, leading to one large feature matrix, used as the input for the model. The data was then split at 70:30; 70% of the data was used for training (74,276 training samples), while the other 30% was used for testing and validation (31,833 testing samples), as seen in the input shapes for the training and testing datasets. Lastly, the complete feature set data was standardized post-split for further accuracy. Standardization is where each data value is scaled to be centered around the mean with a standard deviation of one. This allows for increased model reliability by allowing it to learn necessary patterns in the data more effectively.

Since the EEG data was annotated by three separate neurologists, to improve results, the 3 CSV files were first imported as arrays and then combined into a matrix based on majority voting. Hence, a value is only added as '1' if two or more annotators marked that epoch as seizure activity. Otherwise, the value is added as '0' or normal brain activity. This allows for more consistency by considering consensus between multiple neurologists. Neonates that did not contain any positive '1' values were then removed from the training set.

Model Architecture:

The model was built using the Keras Sequential Model, which is beneficial for efficiently stacking multiple layers.[15] The architecture of this model was adapted from a study by Zeedan et al., with significant adaptations to better suit the feature selection requirements of this research.[16] Two Bidirectional Long Short-Term Memory (Bi-LSTM) layers were included with 64 units each to capture the necessary temporal dependencies. A Bi-LSTM creates an additional layer of the reverse structure to produce more efficient information than traditional LSTM-based models or even basic RNNs.[17] The Bi-LSTM layers used activation functions of hyperbolic tangent or TanH, which are commonly implemented for RNNs. Afterwards, two Dense layers were added with 32 and one unit(s) respectively for binary classification, each with Rectified Linear or ReLu activation functions. Several regularization techniques were used to prevent overfitting, including Dropout, implemented at a rate of 0.1, allowing the network to be readjusted with an alternate group of neurons discarded for every training sample. Aside from Dropout, Batch Normalization, and L2 Regularization were also implemented to prevent overfitting (Figure 3).

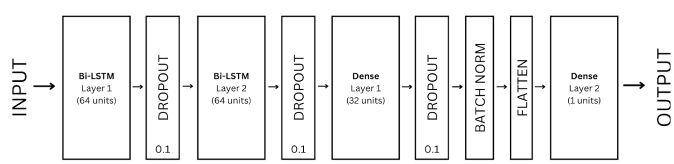

Figure 3: The following visual represents the architecture that the model utilized. The first layer depicts a Bi-LSTM layer of 64 units, in which the neural network receives its input matrix of (74276, 1, 2489), applies its transformations, and releases its output to the next layer, which in this case is a Dropout Layer. This layer effectively releases 10% of its neurons to increase variability within the model's training, before inputting it into another Bi-LSTM layer, where this cycle repeats once more. The data then enters a Dense layer with 32 units for further data processing before reaching the respective Dropout Layer. In the final stretch, Batch Normalization increases the stability of the activation functions by normalizing the data, and the following Flatten Layer converts the multi-dimensional output into a single vector. Lastly, the data is input into a Dense Layer with one sole unit, allowing the model to binarily classify the output as seizure or non-seizure data.

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The ADAM (Adaptive Moment Estimation) optimizer was used because of its fast convergence and is widely accepted as the best choice for optimizers in similar problems. The ADAM optimizer is set with a learning rate of 0.01. Most often, ADAM is used with a learning rate of either 0.01 or 0.001; however, a learning rate of 0.001 is better suited for image classification tasks rather than temporal features in our case.[18] The model was then trained with 8 epochs using the Binary Cross-Entropy loss function, most widely accepted for binary classification tasks. To handle the clear class imbalance present in the data, with most epochs having an output of 0, or normal brain activity, in all the neonates present in the data, the Synthetic Minority Oversampling Technique (SMOTE) was implemented to create synthetic data points for the minority class. In this case, positive '1' values indicating seizure activity were boosted through SMOTE to help balance the distribution of the data across the training sets, allowing the model to learn the patterns of both classes equally.

Evaluation Metrics:

The model's overall performance was evaluated using a variety of metrics. A confusion matrix calculates the False Negative, True Negative, False Positive, and False Negative values, along with a traditional classification report with the performance measurement tools displayed for the F1-Score, Recall, Precision, and Accuracy. Lastly, the Area Under the Receiver Operating Characteristic Curve (AUC-ROC) was calculated to understand the correlation between the True Positive Rate and False Positive Rate.

Results and Discussion

The resulting Bi-LSTM model was able to achieve accuracy rates of individual patients in a range from as low as 56% to as high as 93%. Overall, the model obtained an accuracy of 83% across the testing dataset of all 79 individuals. Although it was able to accurately classify 91% of neonates with a lack of seizure activity as negative, it was only able to diagnose 53% of neonates having a seizure as positive. These results are shown in the Confusion Matrix presented in Figure 4. As indicated, the Bi-LSTM tended to perform better with negative cases. The model had a Precision rate of 88%, a Recall of 90%, and an F1-score of 89% for predicting lack of seizure activity. However, the model only had a Precision rate of 58%, a Recall of 53%, and an F1-score of 55% for predicting the presence of seizure activity in neonates. This explains that the model has a high specificity but a low sensitivity.

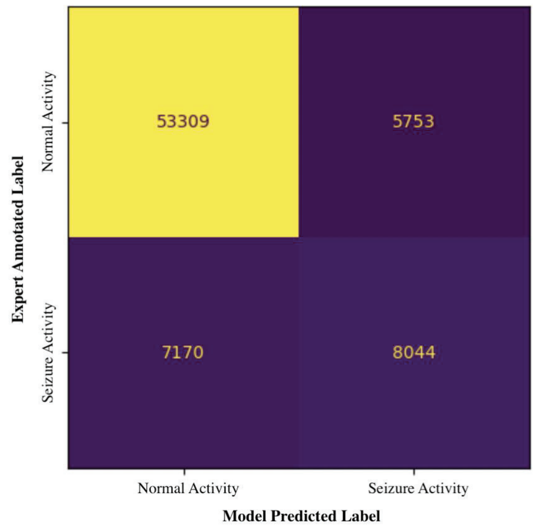

Figure 4: Each quarter of the confusion matrix displays a different outcome. The bottom left corner shows the false negative rate, or when the model misinterprets seizure activity as normal brain activity. The bottom right corner shows the true positive rate when the model accurately predicts seizure activity. The top left corner shows the true negative rate when the model accurately predicts normal brain activity. Lastly, the top right corner shows the false positive rate, or when the model misinterprets normal brain activity as seizure activity.

During the model's training process, the loss and accuracy graphs (Figures 5 and 6) suggest strong overfitting. In Figure 5, the validation loss is shown not to decrease significantly after running through the epochs, while the training loss continues to drop. Figure 6 supports this by showing oscillations in validation accuracy while training accuracy is increasing steadily throughout the entire training process. This gap between training and testing performance suggests that the Bi-LSTM was becoming overly specialized to the training data, even with techniques set in place attempting to reduce overfitting, such as Dropout, Batch Normalization, and L2 regularization. Thus, this reduced its ability to generalize to new, unseen cases. These observations align with the model's habit of performing well on negative cases while struggling with positive cases.

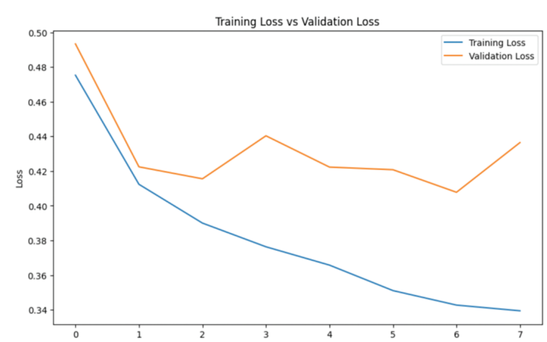

Figure 5: Displays the training vs. validation loss across multiple epochs. Training loss is depicted as consistently decreasing toward zero. Validation loss, on the other hand, plateaus around 0.42 to 0.44, indicating clear overfitting within the Bi-LSTM model.

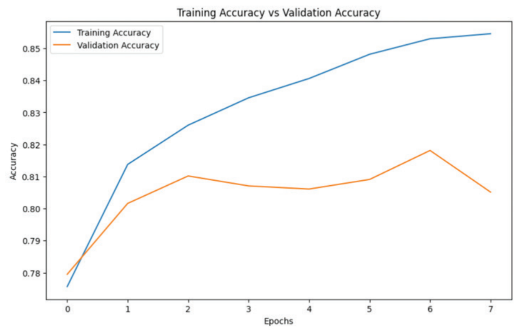

Figure 6: Displays the training vs. validation accuracy across multiple epochs. Training loss is depicted as consistently increasing toward one, while validation accuracy fluctuates near 0.81, indicating the model is becoming overly specialized to the training data itself.

Lastly, both the Confusion Matrix (Figure 4) and ROC curve (Figure 7) highlight the model's ability to reduce False Negatives while emphasizing the need for clearer detection of True Positive events. The Area Under the Curve (AUC) score is 0.808, which, although it is a significant jump from random prediction at 0.5 AUC, still requires large model improvement necessary in determining differences between seizure versus non-seizure EEG data.

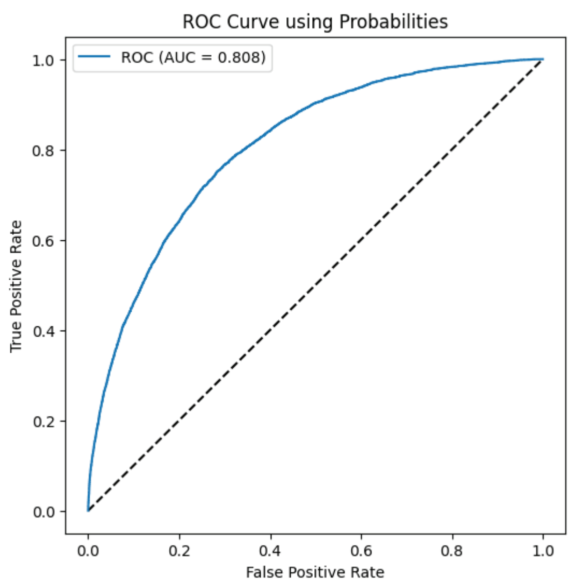

Figure 7: Represents the correlation between the false positive and true positive rate of the Bi-LSTM model through the receiver operating characteristic (ROC) curve.

Seizure vs. Non-Seizure Epochs:

By comparing EEG data examples from both groups, we can better see how the model decides to make its choices. Figures 7 and 8 display a side-by-side comparison of correctly classified seizure and non-seizure events, revealing the brain wave features that the Bi-LSTM was able to accurately understand.

In Figure 7, the non-seizure epochs display consistent brain wave patterns with limited spikes or sudden shifts. On the other hand, Figure 8, which shows seizure epochs, has chaotic activity, sharp peaks, and large amplitude changes that aren't seen often in non-seizure states. These differences likely influenced how the model made its predictions. However, as observed, the distinction between these two classes isn't as clear throughout all the infants, explaining why the accuracy varied considerably. Some cases had overlapping patterns, which could have led to the model missing certain seizures. To improve detection, further improvements to the model are needed, especially for less clear seizure cases.

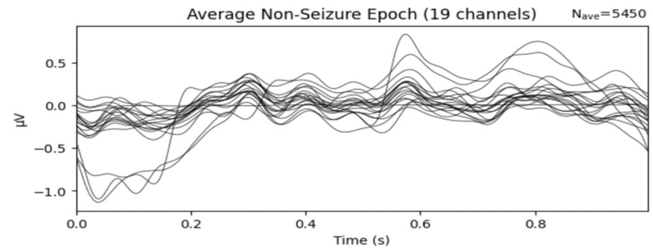

Figure 8: Illustrates the average EEG epoch across nineteen channels that were identified as normal brain activity for a single patient. Brain waves are characterized by minimal spikes or abrupt shifts, indicating the absence of seizures within the segment of data.

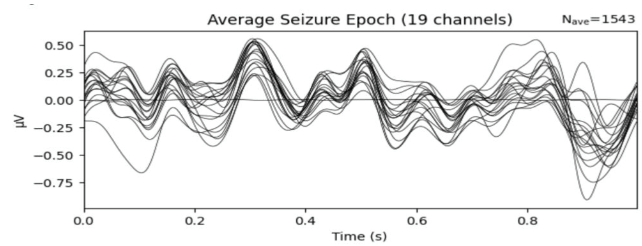

Figure 9 : Showcases the average EEG epoch across nineteen channels that were identified as seizure activity for a single patient. Visually depicts key features that distinguish the data from a normal EEG segment to both the Bi-LSTM model and neurologists.

Discussion:

The Bi-LSTM achieved an overall accuracy of 83%, demonstrating the model's ability to distinguish between normal and seizure epochs. The model's sensitivity refers to the number of correctly diagnosed True Positive events, or accurately diagnosed seizure events, over the total amount of seizure events in the EEG data. The specificity of this model refers to the number of correctly diagnosed True Negative events, or accurately classified non-seizure events, over the total amount of regular events in the EEG data. One of the key strengths of this model was its high specificity. The model was able to accurately diagnose 90% of non-seizure epochs, demonstrating the model's reliability in classifying normal cases without the presence of any seizure activity. However, the model did lack sensitivity. The Bi-LSTM model was only able to accurately diagnose 53% of seizure epochs, as reflected in the confusion matrix (Figure 4). This distinction indicates that, while the model performs well in detecting normal brain activity in neonatal patients, it may overlook more subtle seizure patterns, resulting in the lower sensitivity rates presented. The resulting false negatives are particularly concerning with infants, however, since missed seizures could result in delayed treatment options. This issue emphasizes the need for increased sensitivity, even if it comes at the cost of a lower specificity.

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Limitations:

These complications can be caused by the various limitations present in the data. First of all, even the medical professionals who annotated the dataset struggled with determining a positive case. The three annotators all had varying annotations with each patient within the dataset. Some would consider one epoch a sign of key seizure activity, while others would label the same epoch as a negative case. Attempts to combat this issue were made by combining the three neurologists' annotations and using the majority rule to determine the information used in the model. However, this did not guarantee that the model was tested on true information, as although the majority rule relies upon consensus, one cannot state that the consensus was 100% valid. The accuracy of the model depends on the accuracy of the expert's annotations, which will always remain uncertain. Some results that were analyzed as False Positives could indeed mean the patient has symptoms of seizure activity, and the experts had just overlooked it in the analysis. Nonetheless, there is no certain way to fully know whether these cases were truly accurate or not. Thus, this model does not predict the onset of neonatal seizures but showcases how close artificial intelligence can come to predicting the methods behind human neurologists' annotation of neonatal seizures through the visual analysis of EEG data. Each percentage of accuracy indicates how similar the model came to predicting seizures in the way human experts can.

Second, visual comparisons of the classified positive and negative epochs (Figures 7 and 8) reveal key characteristics that may have guided the model's predictions. Commonly, non-seizure epochs exhibited regular-appearing EEG activity, with no apparent erratic spikes and fluctuations seen in the seizure epochs.

However, the overlap between normal and seizure-like activity in certain patient cases very likely contributed to the Bi-LSTM's lower sensitivity. This is shown in the performance of the model, which varies significantly across individuals, with accuracy having an overall range of 56% to 93% across all 79 patients. Differences in EEG signal quality could have also caused this variation, although the distinctiveness of seizure patterns across patients in the lower range of accuracy certainly impacted the model's apparent performance. Neonates with clearer seizure patterns were more easily classified, while those with larger, ambiguous activity led to a lower sensitivity of the model.

Third, analysis of the training process revealed strong signs of overfitting, as indicated by the loss graph in Figure 5. The validation loss oscillated frequently, never truly declining the way the training loss was able to. This could have been averted by running a larger number of epochs; however, the size of the data led to numerous epochs becoming computationally prohibitive. This caused the model to be overly specialized to the training data and struggle with unseen cases in the testing data.

Future Work:

Significant improvements are required to improve the model's sensitivity to neonatal seizure data. To enhance the model's performance and increase its clinical applicability, several key areas for future study can be explored. First of all, using advanced feature extraction techniques may provide more detailed signals for seizure detection. Additionally, optimizing the model architecture, possibly by using a more complex hybrid-based (Conv-LSTM) model, may provide more accurate results. Lastly, during preprocessing, it may be beneficial to analyze patient data separately and feed it through the model individually, rather than combining multiple patients' data as done in this study. These improvements could allow for increased model accuracy and more personalized neonatal seizure classification, resulting in better clinical outcomes.

Conclusion

A Bidirectional Long Short-Term Memory (Bi-LSTM) model was utilized in this study to analyze its usefulness in predicting neonatal seizures relative to human experts. The Bi-LSTM model was selected because of its effectiveness in working with time series data, capturing both past and future information simultaneously, without running into challenges often seen with basic Recurrent Neural Networks. Three feature sets were extracted from the Helsinki dataset, involving EEG data from 79 term infants, including statistical features, time-domain features, and frequency-domain features. The corresponding seizure annotations from three expert neurologists were combined based on majority rule and fed into the model. The Bi-LSTM model achieved an overall accuracy as a universal classifier for all 79 neonates of 83%.

Although the model was unable to predict the majority of seizure-activity instances, this research still represents a valuable step toward improving neonatal care worldwide. Enhancing early seizure detection, even with its valid limitations, could facilitate earlier interventions in many critical cases, considering the model does indeed have a higher True Positive rate than a False Positive Rate. Even now, it is difficult for less-equipped healthcare facilities to attain the proper assistance and tools required for suitable infant care, having to travel large distances to larger hospitals during critical times. With the use of AI, these hospitals may have an opportunity for rapid detection before they can receive appropriate care from medical professionals. That, in turn, has the potential to reduce the severity and long-term neurological effects commonly associated with neonatal seizures. Further improvements in this model could enhance its sensitivity, offering even greater benefits to the developmental outcomes and quality of life of the affected newborns.

Thus, this study contributes to the ever-growing body of knowledge on neonatal care and seizure detection by leveraging advanced recurrent neural network techniques. These findings demonstrate the potential to enhance the timeliness and accuracy of neonatal seizure detection. With further refinement and validation, this research approach holds promise for future clinical applications, potentially improving outcomes for newborns at risk of seizures. Combining artificial intelligence's rapid computational power with clinicians' empathy and observational expertise projects a revolution in the future of neonatal patient care.

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