Assessing Intrapartum Risk of Hypoxic Ischemic Encephalopathy Using Fetal Heart Rate with Long Short-Term Memory Networks

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Abstract

This study investigated the prediction of the risk of hypoxic ischemic encephalopathy using intrapartum cardiotocography records with a long short-term memory recurrent neural network. Across the 12 hours of labour, HIE sensitivity rose from 0.25 to 0.56 as delivery approached while specificity remained approximately constant with a mean of 0.71 and standard deviation of 0.04. The results show that classification improves as delivery approaches but that performance needs improvement. Future work will address the limitations of this preliminary study by investigating input signal transformations and the use of other network architectures to improve the model performance.

1. Introduction

Hypoxic ischemic encephalopathy (HIE) is a brain injury caused by the impaired delivery of oxygen to the brain [1]. The estimated incidence of neonatal HIE is around 1.5 per 1000 live births in developed countries and 10-20 per 1000 live births in low- and middle-income countries [1,2].

Neonatal HIE, a syndrome of disturbed neurologic function in the earliest days of life, is characterized by difficulty with initiating and maintaining respiration, depression of tone and reflexes, sub-normal levels of consciousness, and seizures [3]. Generally, over half of newborns diagnosed with neonatal HIE die or develop major impairment (such as cerebral palsy, hearing loss, visual impairment, cognitive problems) by age 3 years [4].

Clinicians monitor both fetal and maternal well-being during labour using cardiotocography (CTG) which measures fetal heart rate (FHR), uterine pressure (UP) and maternal heart rate (MHR). Clinicians use visual interpretation of these CTG signals to assess fetal condition and to determine when to intervene – by performing a Cesarian section (CS) – to prevent neonatal death or HIE [5]. Unfortunately, the visual assessment of CTG signals has significant inter- and intra-observer variability [5,6]. This inaccurate interpretation of CTG signals also contributed to an increased rate of CS and assisted deliveries [6,7]. Furthermore, clinical guidelines give no specific management recommendations for the great majority of FHR signals (over 80%) that are categorized as “indeterminate risk” [8,9].

Machine learning (ML) and deep learning (DL) methods may have the potential to improve the interpretation of CTG signals. The computation of engineered FHR features for use with classical ML methods is a difficult task that has yet to produce features sufficiently informative for FHR classification [10]. Some publications have reported approaches to fetal state detection using DL with CTG [11–14]. However, the majority of these have used datasets that were too small to fully support the development of DL models. Additionally, these datasets did not include HIE cases. Thus, there is a need to conduct DL experiments with a large cohort of births. Using the 250,000 CTG records in our database, our objective is to investigate DL models for the early assessment of the risk of developing HIE using raw and transformed CTG records. This paper presents early results using FHR and a long short-term memory (LSTM) network to assess the intrapartum risk of HIE.

2. Method

This section briefly discusses the clinical data and the data preprocessing carried out. Next, it describes the classification experiments conducted using these data.
2.1. Clinical data

The clinical data comprised 12 hours of de-identified CTG signals obtained from 246,973 births at the 15 hospitals of Kaiser Permanente Northern California between 2010 and 2019. We included singleton live births, with gestational age ≥ 35 weeks, without congenital or chromosomal abnormalities and with electronic fetal monitoring. Analysis was limited to vaginal births since CS pre-empts the observation of the normal labour time course.

HIE was defined as the presence of both acidosis and encephalopathy, where acidosis was defined as pH < 7 or base deficit ≥ 10 mmol/L from the umbilical cord blood gas measurements shortly after birth. The healthy group comprised newborns who exhibited no encephalopathy or seizures, had Apgar at 5 minutes ≥ 7, had no chest compression or intubation, and were discharged home alive.

The resulting data set comprised CTG signals from 173 HIE, 2,003 Acidosis and 24,620 healthy (without acidosis) cases. The number of HIE cases reflects its expected low incidence. This study focused on CTG signals from 145 HIE and 170 randomly under-sampled healthy fetuses.

2.2. Data preprocessing

We used PeriCALM Patterns, proprietary software from PeriGen Inc. [15], to identify artifacts, remove noise and repair the FHR signals. Figure 1 shows a repaired FHR signal. Each colored segment of FHR is separated by a gap, which occurs when sensors detach during acquisition. The repaired signals were decimated from 4 Hz to 1 Hz to reduce training time. The factor of 4 was selected after determining that this retained 96.9% of the FHR power for both HIE and healthy cases. The decimated FHR retained the low frequency (30–150 mHz) and movement frequency (150–500 mHz) bands [16]. Finally, we divided the recording into 20-minute non-overlapping segments, this generated 36 segments for the longest recordings of 12 hrs.

2.3. Classification

Train, test, and validation indexes were randomly permuted for each fold, generating 10 non-overlapping test sets for 10-fold cross validation. In each fold during training, the train and validation data for all segments were concatenated and used to train and validate a 3-layer LSTM model, with three hidden layers of 128, 256 and 128 cells. An early stopping value of 30 training epochs ensured that the trained model did not overfit the training dataset, while the maximum training epoch and batch size was set to 1000 and 32, respectively. For each fold, the LSTM model was trained 30 times and the model with the lowest validation loss retained. The Adam optimizer with learning rate of 0.0001 and binary cross entropy loss were selected for all classification experiments. This model was used to independently evaluate the fold’s test data for each labour epoch (i.e., we evaluated the classification performance for each segment separately) in terms of the average, across folds, of the sensitivity, specificity, and area under the receiver operating characteristic (AUROC) as functions of labour time.

3. Results

Figure 2 shows the AUROC, sensitivity, and specificity for the test data as functions of time. The AUROC rose steadily as delivery approached (from 0.51 to 0.67) as did HIE sensitivity (from 0.25 to 0.56); specificity remained approximately constant over the 12 hours with a mean of 0.71 and standard deviation of 0.04.
Figure 2. Classification performance metrics as a function of time before birth. (A) Area under the receiver operating characteristic (AUROC), (B) Sensitivity and (C) Specificity. The lines indicate the mean while the error bars represent the standard error of the mean.

4. Discussion

The current performance shows some promising results towards delivery but there is room to improve the prediction performance. Sensitivity captures the ability of a model to correctly recognize individuals with a medical condition while specificity captures the model’s ability to accurately identify patients without a medical condition. Due to the inherent challenge of class imbalance, the low sensitivity of HIE cases and the low specificity of normal cases will produce false negatives and false positives, respectively. However, the 0.56 sensitivity obtained near delivery correlates with clinical sensitivity of approximately 50% [16]. But an early prediction of the risk of HIE and a higher specificity is desirable within a clinical setting.

Our current approach is limited by class imbalance mitigation (through random under-sampling) that did not tap the potential of all our available data. In future works, we will explore other class imbalance approaches such as cost sensitive learning, where a higher cost (error weighting) will be assigned to the misclassification of samples from the minority class [17].

The separate classification of each 20-minute non-overlapping segment is not directly applicable in a clinical setting. This independent classification of each segment means there is no memory of past states in previous segments that could help predict the current state. We will resolve this limitation by using longer epochs or ensuring that the LSTM state is not reset at the end of the epoch.

The reliance on an LSTM- representation and a single-channel FHR input have not produced very good predictions by the trained models. Hence, we will explore the added benefits of adding MHR and UP to the DL model, which may also be beneficial.

The authors in [12] reported that convolutional neural networks models outperformed LSTM models, hence we will also assess these DL structures. Finally, we will assess the transformation of the raw preprocessed CTG using methods such as the spectrogram and scalogram.

5. Conclusion

The aim of this project is to improve the early detection of intrapartum risk of developing HIE using a large cohort of births. This current study focused on single channel FHR input to train an LSTM network. The preliminary studies show some promising results, but the model performance needs improvement and there are limitations to be addressed. Future work will work on improving the model performance and addressing the current limitations.
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References


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