Wavelet Spectral Time-Frequency Training of Deep Convolutional Neural Networks for Accurate Identification of Micro-Scale Sharp Wave Biomarkers in the Post-Hypoxic-Ischemic EEG of Preterm Sheep

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***Abstract*—Neonatal hypoxic-ischemic encephalopathy (HIE) evolves over different phases of time during recovery. Some neuroprotection treatments are only effective for specific, short windows of time during this evolution of injury. Clinically, we often do not know when an insult may have started, and thus which phase of injury the brain may be experiencing. To improve diagnosis, prognosis and treatment efficacy, we need to establish biomarkers which denote phases of injury. Our pre-clinical research, using preterm fetal sheep, show that micro-scale EEG patterns (e.g. spikes and sharp waves), superimposed on suppressed EEG background, primarily occur during the early recovery from an HI insult (0-6 h), and that numbers of events within the first 2 h are strongly predictive of neural survival. Thus, real-time automated algorithms that could reliably identify EEG patterns in this phase will help clinicians to determine the phases of injury, to help guide treatment options. We have previously developed successful automated machine learning approaches for accurate identification and quantification of HI micro-scale EEG patterns in preterm fetal sheep post-HI. This paper introduces, for the first time, a novel online fusion strategy that employs a high-level wavelet-Fourier (WF) spectral feature extraction method in conjunction with a deep convolutional neural network (CNN) classifier for accurate identification of micro-scale preterm fetal sheep post-HI sharp waves in 1024Hz EEG recordings, along with 256Hz down-sampled data. The classifier was trained and tested over 4120 EEG segments within the first 2 hours latent phase recordings. The WF-CNN classifier can robustly identify sharp waves with considerable high-performance of 99.86% in 1024Hz and 99.5% in 256Hz data. The method is an alternative deep-structure approach with competitive high-accuracy compared to our computationally-intensive WS-CNN sharp wave classifier.**

Clinical relevance—**The suggested classifier could robustly identify EEG patterns of a similar morphology in preterm newborns during recovery from an HI insult.**

I. Introduction

Perinatal difficulties during labor may cause a significant HI insult leading to HIE. [1, 2]. Therapeutic hypothermia is now standard of care for providing neuroprotection for HIE in term newborns [3]. This treatment derived from pre-clinical studies in a variety of term fetal and neonatal animal species, which showed that therapeutic hypothermia is neuroprotective, but only when started within ~6 hours after the end of an HI insult, with efficacy greater the earlier the treatment is started [3]. Other treatments are being developed and may have similar limited windows of opportunity, and thus it is important that we establish biomarkers to determine phases of injury [1].

Our HI studies in preterm fetal sheep have demonstrated that there is shown that there is a significant increase in gamma spikes and sharp waves superimposed on a suppressed EEG background during the first 6 hours post-HI [2, 4-6]. Further, we have demonstrated the timing of changes in numbers of sharp waves (Fig. 1) and how they correlate to subcortical neuronal injury [6, 7]. The micro-scale EEG activities evolve over time until the beginning of the secondary phase which is generally characterized by the appearance of high-amplitude stereotypic evolving seizures [8, 9]. Given the potential for micro-scale epileptiform events to be an early predictive biomarker for later neural injury, there is a need to develop automated strategies for the precise identification and characterization of such early micro-scale signatures of HIE to help improve our management of neonates with HIE.

We have previously developed various successful automated strategies for accurate identification of spikes [4, 10-13] and sharp waves [6, 14, 15]. Last year, we presented a novel deep 2D-CNN classifier, trained over Gaussian wavelet scalogram images of EEG segments, which was very accurate in identifying sharp waves in the EEG of preterm fetal sheep during early post-HI recovery [16]. This paper presents, for the first time, a complementary approach to our previous work by demonstrating an exceptionally robust 2D-CNN classifier trained over much simpler feature-sets, instead of using the computationally-heavy high-resolution scalogram images. The paper describes how the new feature extraction strategy of extraction of only the major spectral envelopes of an arbitrary EEG epoch, is a successful alternative strategy for detection of sharp waves. The current approach creates a simpler, but more robust, spectral feature map input for a 17-layers deep 2D-CNN classifier to accurately identify sharp waves from background activity and noise compared to our previous computationally-intensive WS-CNN approach. Results are reported using both 1024Hz high-frequency data and their 256Hz down-sampled versions, which is more typically used in clinical recordings.

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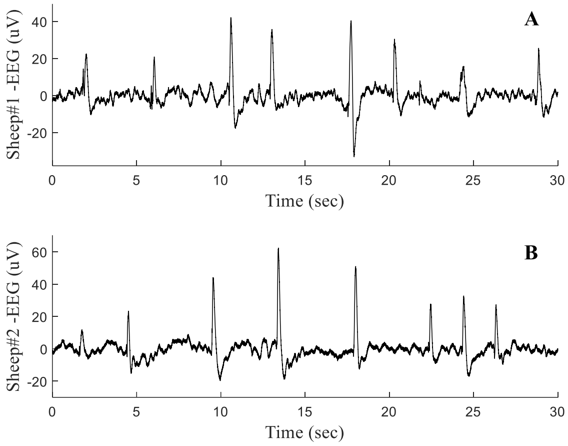

Figure 1. Examples of post HI-insult EEG intervals containing micro-scale sharp waves, during the first 2 hours of HI from asphyxicated preterm fetal sheep used in: A: traning set (sheep#1). B: test set (sheep#2).

II. Methods

A. Data collection

The animal procedures in this study were approved by the Animal Ethics Committee of the University of Auckland. HI signals were collected from two preterm fetal sheep at around 0.7 gestational age (~104 days, where term is 147 days gestation). Fetal sheep brain maturation at this age is equal to a preterm human brain of age 27-30 weeks gestation [17]. The animal management and surgical procedures have been described previously [8]. 7 hours of raw data were recorded at 1024Hz using one pair of left/right electrodes (made from Cooner wire, Cooner Wire, Chatsworth, CA, USA). Probes were symmetrically located on the dura of the fetal parasagittal cortex and covered and secured in place [8]. A reference electrode was placed over the occiput. Technically, this placement provides an electrocorticogram recording (ECoG) and therefore we will refer to signal as an ECoG. An inflatable silicone occluder was placed around the umbilical cord for inflation (25 minutes) to produce and acute HI insult. Complete asphyxia was assured by the analysis of blood compositions, before and after occlusion and cardiovascular changes [8]. The first two hours of post-HI ECoG recordings from fetal sheep #1 was used for training and validation of the 2D-CNN, while the first hour post-HI ECoG of fetal sheep #2 was used to test the classifier. Data were initially annotated by an expert (HA) and provided a sufficient number of sharp waves for training, validation, and testing of the classifier. For consistency with clinical and experimental definitions, pointed peak ECoG events with 70-250ms duration (equal to 4-12.5Hz) and amplitudes >20µV were labeled as sharps [7].

B. Feature extraction

Our previous studies detailed the superior compatibility of Gaussian 2 basis function for sharp wave analysis in comparison to other wavelet basis functions [15, 18]. Gaussian 2 (or Mexican hat wavelet) provides desirable properties that are well-matched with inherent characteristics of an ideal sharp that could allow optimal time-localization of an HI sharp wave [15, 18]. A well-designed feature extraction approach plays a key role in a machine-learning strategy to achieve ideal accuracies. Despite the full-range spectral feature extraction (wavelet scalograms) in our previous work [16], here, only two spectrally-dominant features of an arbitrary ECoG epoch were directly extracted from the raw recordings to form an input set, detailed below. Data were initially zero-meaned, and the continuous wavelet transform (CWT) coefficients of each ECoG segment were calculated using Gaussian 2 of scale 32. Moreover, the Fourier transform (FFT/IFFT) time-series of the data were obtained, and the spectral components within 4-12.5Hz were preserved. The 400×1 time series from the CWT and IFFT, as well as the original raw ECoG segment, were combined to create the input-matrix of size 400×1×3 to be fed into the deep 2D-CNN classifier. Examples of the actual post insult sharp waves from the original HI ECoG are shown in Fig 2A-B. The Gaus2 CWT of the sharp waves (scale 32) along with the spectrally band-pass filtered patterns from IFFT of the sharp waves are demonstrated in Fig 2C-D and Fig2E-F, respectively. Similarly, examples of the non-sharp events, as well as their corresponding CWTs and IFFTs, are shown in Fig 3. Comparing the illustrations in Fig 2 and 3, it is inferred that the introduced strategy, through obtaining only the main spectrally-dominant features of an arbitrary ECoG epoch, can provide rich-enough features for the 2D-CNN to build feature maps for acute classification between a sharp and a non-sharp event. The classifier was trained and tested using the original noisy data to generalize the outcomes.

C. The proposed deep 2D-CNN classifier

Deep learning structures, and in particular, convolutional neural networks (CNN), are the enhanced ANNs with significant demonstrated ability in image processing of epilepsy data [19, 20] and seizure recognition in neonatal HI EEG [21, 22]. Recently, we developed an accurate 17-layer deep CNN sharp wave classifier, trained over high-resolution wavelet scalograms of the ECoG segments using Gaussian 2 CWT at scale-range of 1-40, with 95.34% accuracy [16]. Due to the effective performance of the WS-CNN classifier, this study used an updated version of the 2D-CNN architecture from that previously used. However, here the classifier was fed with a much simpler input-matrix of features, instead of the computationally-intensive scalogram images, to accelerate the analysis. The proposed 2D-CNN classifier is detailed in Table I. A graphical demonstration of the proposed WF-CNN classifier is represented in Fig 4. The WF-CNN takes the input matrix of features (400×1×3), and analyses the extracted feature maps through seven convolutional (with rectified linear activation units (ReLU) after each convolutional layer), seven max-pool and three fully connected layers (total of 17 layers). It then passes the output through a softmax and a classification layer for final reasoning. A stochastic gradient descent with momentum (SGDM) strategy was employed to update the parameters of the WF-CNN (weights and bias). Learning rate, α, and momentum, γ, parameters were initially set to 0.01 and 0.9, respectively, to minimize the loss function. Due to the satisfactory performance results of the classifier, α and γ were not further tuned. The classifier was trained and validated on the first 2hrs post-HI data from the 1st fetal

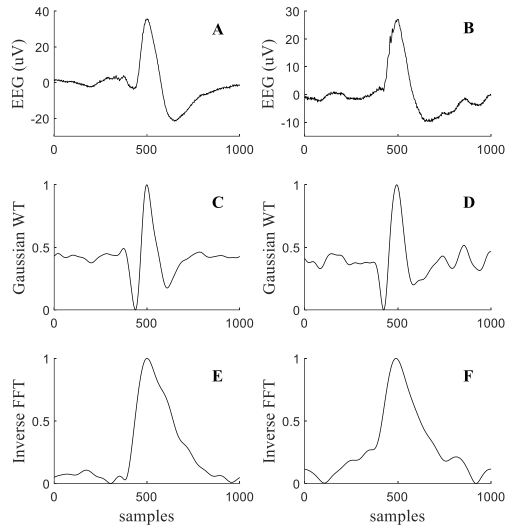

Figure 2. (A-B): Examples of post-HI micro-scale ECoG sharp waves. (C-D): The corresponding Gassian 2 wavelet transforms of the sharps in A and B at scale 32. (E-F): The corresponding inverse Fourier transforms of the sharps in A and B using band-pass filter 4-12.5Hz.

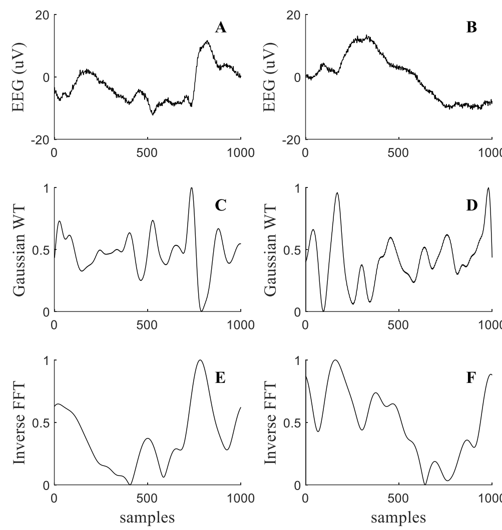

Figure 3. (A-B): Examples of non-sharp ECoG background events. (C-D): The corresponding Gaus2 wavelet transforms of the ECoG segments in A and B using scale 32. (E-F): The corresponding inverse Fourier transforms of the ECoG segments in A and B using band-pass filter 4-12.5Hz.

sheep (#1). A random 90 min (75% of the 2 hrs) and the remaining 30 min (25% of the 2 hrs) were used, respectively, to initially train and validate the classifier. This was chosen due to the much higher number of sharp waves in the data from sheep #1. One hour data from the 2nd fetal sheep (#2) was used for testing the net. The training process was executed using a total of 120 epochs. We then down-sampled the original1024Hz data to 256Hz frequency to assess the performance ability of the WF-CNN classifier at frequency more commonly used for clinical data sampling. A total of 4120 ECoG segments, including 824 sharp waves and 3290 non-sharp waves, were manually annotated for training, validation, and testing of the classifier.

III. Results

The algorithm was developed, trained, and tested in Matlab® software on a single workstation computer: Intel® Core™ i7-7700 CPU 3.60GHz, 4 cores processor with 16GB RAM memory. The confusion matrix results of the WF- CNN classifier are displayed in Table II. The trained WF-CNN

TABLE I. The arcituchure of the proposed 2D-CNN

Layers	Type	No. of Neurons	Kernel size	Stride	No. of Filters
0-1	Conv.	400×3	3	1	16
1-2	Max_pool	400×3	[2 1]	2	
2-3	Conv.	200×2	3	1	32
3-4	Max_pool	200×2	2	2	
4-5	Conv.	100×1	3	1	48
5-6	Max_pool	100×1	[2 1]	2	
6-7	Conv.	50×1	3	1	72
7-8	Max_pool	50×1	[2 1]	2	
8-9	Conv.	25×1	3	1	96
9-10	Max_pool	25×1	[3 1]	2	
10-11	Conv.	12×1	3	1	128
11-12	Max_pool	12×1	[2 1]	2	
12-13	Conv.	6×1	3	1	256
13-14	Max_pool	6×1	[2 1]	2	
14-17	Fully_connected	1536			
	Fully_connected	24			
	Fully_connected	2			

classifier accurately identified sharp-waves with an overall accuracy of 99.86% for the 1024Hz sampled ECoG (AUC: 0.999). This was closely followed by 99.50% accuracy for the 256Hz down-sampled data (AUC: 0.993 - Fig. 5). This was the result of the training of the net over 2720 segments within the first 2 h data from sheep #1 and testing the classifier over 1 hour ECoG from the 2nd sheep, including 1400 segments. This is validated through obtaining the very minimal number of missed detections (False Negative (FN)) and wrong detections (False Positive (FP)). Results suggest the correct choice of spectral features for an ECoG epoch is a key for obtaining optimal results from a deep neural network, where in this case, the WF-CNN demonstrated considerable accuracy to correctly classify sharp waves. The correct choice of spectral-features also allowed to classify upside-down sharps (inverse polarity) within the data.

IV. Conclusion

This paper is a novel extension to our 2D-CNN sharp-wave classifier by introducing a much more computationally-efficient feature extraction strategy that provides the major time-frequency features of an ECoG pattern as the inputs to a deep Convolutional Neural Network. The high degree of accuracy of the WF-CNN verified the reliability of the classifier for the identification of micro-scale sharp wave biomarkers from noise and other background activity in high-frequency sampled HI ECoG, post HI-insult. The proposed strategy is a big step forward towards real-time identification of EEG biomarkers by demonstrating considerably high-accuracies of 99.86% and 99.50% for the 1024Hz and 256Hz down-sampled data, respectively. Overall, the preliminary, but reliable, results of the this paper, using a much simpler but computationally much faster feature extraction approach, address the promising capability of the introduced WF-CNN classifier for early diagnosis of EEG biomarkers in the current 256Hz clinical recordings, in real-time. Further data is needed to investigate the capabilities of the net on a bigger dataset.

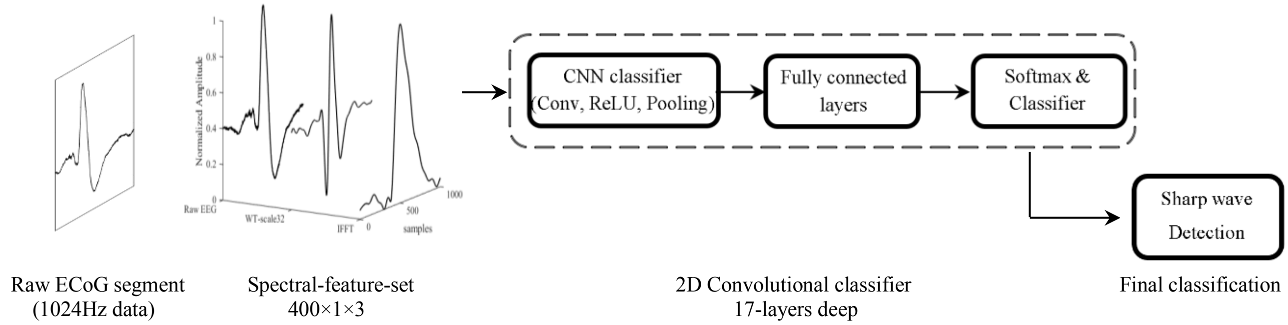

Figure 4. The schematic of our proposed WF-CNN classifier.

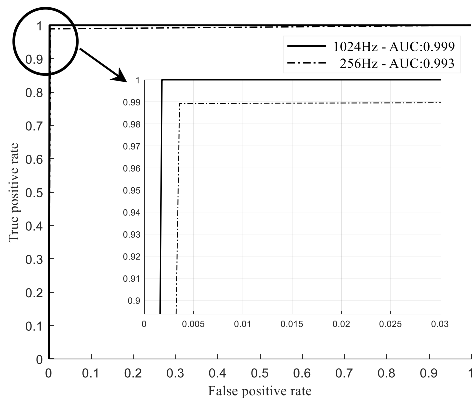

Figure 5. ROCs and the corresponding AUCs for the 1024/256Hz data

TABLE II. PERFORMANCE MEASURES OF THE WF-CNN CLASSIFIER ON 1024HZ AND 256HZ DOWN-SAMPLED DATA

	Data	TP hits	TN hits	FP hits	FN hits	Sensitivity (%)	Selectivity (%)	Precision (%)	Accuracy (%)
1024Hz data	Train	435	1632	0	0	100	100	100	100
	Val	108	543	1	1	99.08	99.82	99.08	99.69
	Test	280	1118	0	2	99.29	100	100	99.86
256Hz data	Train	435	1632	0	0	100	100	100	100
	Val	107	540	1	3	97.27	99.82	99.07	99.39
	Test	277	1116	3	4	98.58	99.73	98.93	99.50

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