Wavelet Spectral Deep-training of Convolutional Neural Networks for Accurate Identification of High-Frequency Micro-Scale Spike Transients in the Post-Hypoxic-Ischemic EEG of Preterm Sheep

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Abstract—**Early diagnosis and prognosis of babies with signs of hypoxic-ischemic encephalopathy (HIE) is currently limited and requires reliable prognostic biomarkers to identify at risk infants. Using our pre-clinical fetal sheep models, we have demonstrated that micro-scale patterns evolve over a profoundly suppressed EEG background within the first 6 hours of recovery, post HI insult. In particular, we have shown that high-frequency micro-scale spike transients (in the gamma frequency band, 80-120Hz) emerge immediately after an HI event, with much higher numbers around 2-2.5 h of the insult, with numbers gradually declining thereafter. We have also shown that the automatically quantified sharp waves in this phase are predictive of neural outcome. Initiation of some neuroprotective treatments within this limited window of opportunity, such as therapeutic hypothermia, optimally reduces neural injury. In clinical practice, it is hard to determine the exact timing of the injury, therefore, reliable automatic identification of EEG transients could be beneficial to help specify the phases of injury. Our team has previously developed successful machine- and deep-learning strategies for the identification of post-HI EEG patterns in an HI preterm fetal sheep model.**

This paper introduces, for the first time, a novel online fusion approach to train an 11-layers deep convolutional neural network (CNN) classifier using Wavelet-Fourier (WF) spectral features of EEG segments for accurate identification of high-frequency micro-scale spike transients in 1024Hz EEG recordings in our preterm fetal sheep. Sets of robust features were extracted using reverse biorthogonal wavelet (rbio2.8 at scale 7) and considering an 80-120Hz spectral frequency range. The WF-CNN classifier was able to accurately identify spike transients with a reliable high-performance of 99.03±0.86%.

Clinical relevance—**Results confirm the expertise of the method for the identification of similar patterns in the EEG of neonates in the early hours after birth.**

I. Introduction

Perinatal brain injury after a hypoxia-ischemic insult occurs primarily after then end of the insult, evolving substantially over time and leads to significant grey and white matter injury causing life-long impaired neurodevelopment [1, 2]. Our pre-clinical data from fetal sheep HI models show that evolving micro-scale epileptiform patterns in the form of high-frequency spike transients (Fig.1) and sharp waves (see Fig.2 of [3]), develop over a suppressed EEG background during a 6-8 hours cerebral oxidative metabolism recovery phase after a hypoxic insult (called the latent phase), before high-amplitude EEG seizures [2, 4, 5]. Our studies have shown that the number and timing of these patterns are predictive of neural outcome [6]. Further, available therapeutic protocols such as hypothermia are shown to be optimally neuroprotective if initiated in early hours of the latent phase and before the start of the seizures [1, 7]. Unlike the pre-clinical experiments, clinical HIE and the phases of injury are not necessarily aligned with the time of birth as the insult could have happened before birth [1, 7]. Prognostic and diagnostic biomarkers could help to reveal timing information of the injury and ultimately help to improve utilization of treatments. Our team has been actively focused on developing machine- and deep-learning approaches for the identification of spikes [3, 8-10] and sharp waves [6, 11-13]. Our experimental preterm sheep data demonstrate that the number of automatically quantified high-frequency spike transients (in 80-120Hz gamma-band) peaks at around 2-2.5 hours from insult [3], decreasing thereafter before high-amplitude seizures appear at ~6-7 h post-insult [3]. Epileptsy studies have also shown that the bursts of clinical high-frequency oscillations with >80Hz frequency are the early indicators of later epileptic seizures [14].

We recently developed a novel, high-performance, two dimensional deep CNN classifier for EEG sharp wave identification using Gaussian wavelet scalogram images of EEG segments in post-HI data from preterm sheep models [15]. However, the previous WS-CNN sharp wave classifier [15] requires high-performance facilities (i.e. clusters) for the analysis of computationally-intensive scalogram images, in large scale. This paper proposes, for the first time, a complementary approach to our previous work [15] by introducing a robust 2D-CNN spike transient classifier trained over an alternatively much simpler set of features. The paper examines how only the major spectral envelopes of an arbitrary EEG epoch, through reverse biorthogonal wavelet transform along with the corresponding gamma-range frequency filtered spectrums, can be extracted to create computationally-efficient feature maps for a 11-layers deep 2D-CNN classifier to accurately identify spike transients from noise and background activity. The proposed strategy is generic and has the potential to be used for the identification of EEG patterns in clinical data.

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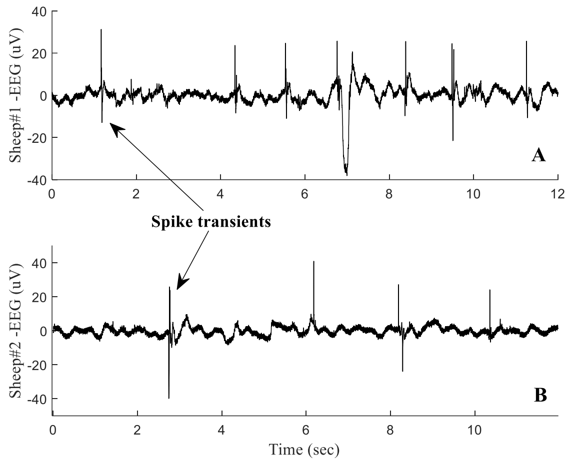

Figure 1. Examples of post HI-insult 1024Hz EEG intervals containing high-freq micro-scale spike transients, during the first 2 hours of HI from A: asphyxicated preterm fetal sheep (#1) and B: sheep (#2).

II. METHODS

A. Data collection

The dataset used in this research was approved by the Animal Ethics Committee of the University of Auckland. Raw HI data was recorded at 104 days of gestational age (human brain maturation equivalent to 28-30 weeks) at 1024Hz using one pair of EEG electrodes on the left and right sides of the preterm fetal brain (n=2). Probes (made of Cooner wire, Chatsworth, CA, USA) were symmetrically situated over dura matter over the parasagittal parietal lobe while a reference electrode was sewn on the occiput. Data from the dural placement of electrodes is referred to as the electrocorticogram (ECoG), and therefore from here we refer to data as ECoG. An inflatable silicone occluder was placed around the cord during surgery for post-surgical occlusion of the umbilical cord for 25 min [16]. Complete asphyxia was assured by analysis of blood gas analysis and cardiovascular changes [16]. Data was initially annotated by an expert (HA), manually. For consistency with clinical and experimental definitions, pointed peak EEG/ECoG events with less than 70ms duration (namely less than 12.5ms, equal to >80Hz frequency range) and amplitudes >20μV were labeled as HI gamma spikes.

B. Feature extraction

Machine and deep-learning approaches are often perform much better when accompanied by a robust feature extraction strategy that optimally provides the appropriate features from the data. Non-complex reverse biorthogonal wavelets offer desirable properties (i.e. symmetry) that match well with inherent features of an ideal high-frequency spike transient [3, 8, 17]. We previously detailed the superior compatibility of rbio2.8 reverse biorthogonal wavelet of scale 7 for the optimal time-localization of high-frequency spike transients in HI ECoG [3]. Unlike the full-range spectrums (scalogram images) in our previous work [15], here, only two spectrally-dominant set of features are directly extracted from an arbitrary raw ECoG segment to create an input set. Data was initially zero-meaned, and the continuous wavelet transform (CWT) coefficients of ECoG segments were calculated using Rbio2.8 at scale 7. The Fourier transform (FFT/IFFT) time-series of the data were also evaluated, and the spectral components within 80-120Hz were preserved. The CWT and IFFT time series as well as the original raw ECoG segments (length: 72×1), were combined to shape the input-matrices (size 72×1×3) to be fed into the deep 2D-CNN classifier. Examples of the actual post HI spike transients from the original ECoG recordings are shown in Fig 2A-B. The rbio2.8 CWT of the spike transients (at scale 7) along with the spectrally band-pass-filtered patterns from IFFT of the spike transients are shown in Fig 2C-D and Fig 2E-F, respectively. Similarly, examples of the non-spike events, as well as their corresponding CWTs and IFFTs, are shown in Fig 3. The data in Fig 2 and 3 suggest that the strategy of obtaining only the main spectrally-dominant features of an arbitrary segment can provide rich-enough inputs for the 2D-CNN to create feature maps for acute classification between a spike and a non-spike event. The classifier was trained and tested using the original noisy data to generalize the outcomes.

C. The proposed deep 2D-CNN classifier

Enhanced deep CNN structures hold strong classification capability and have been recently used for neonatal seizure detection in HI recordings [5, 18-20]. We have also recently developed a robust 11-layer deep CNN sharp wave classifier, trained using high-resolution scalogram images of the ECoG segments, with 95.34% accuracy [15]. This work introduces an updated version of the robust WS-CNN classifier from the previous work, while here the classifier was trained using a much simpler, but computationally much more efficient, input feature-matrices, instead of the computationally-intensive scalogram input-images. The proposed WF-CNN classifier is detailed in Table I and Fig. 4. Initially, input features-matrices (72×1×3, each) were fed into the WF-CNN classifier to generate feature maps through four convolutional (with rectified linear activation units (ReLU) after each convolutional layer), four max-pool and three fully connected layers (total of 11 layers). The output was finally passed through a softmax and a classification layer for final decision making on an ECoG epoch. The training parameters of the WF-CNN (weights and bias) were updated using a stochastic gradient descent with momentum (SGDM) strategy. To minimize the loss function, α (learning rate) and γ (momentum) were initially set to 0.01 and 0.9, respectively. α and γ were not further tuned due to the satisfactory performance of the classifier. Initially, a random 90 min (75% of the first 2 hrs of the latent phase recordings) and the remaining 30 min (25% of the 2 h) from the post-HI data of the 1st fetal sheep (#1) were respectively used to train and validate the classifier. This was chosen due to the much higher number of spike transients in the dataset from sheep #1. The entire first 2 h of data of the 2nd fetal sheep (#2) were allocated to test the net. The data sets from sheep #1 and #2 were then swapped around to briefly cross validate the classifier's performance across two sets of subjects. The classifier was trained over a total of 120 epochs. A total of 4314 ECoG segments, including 1266 gamma spikes and 3048 non-spikes, were manually labeled to evaluate the performance of the net.

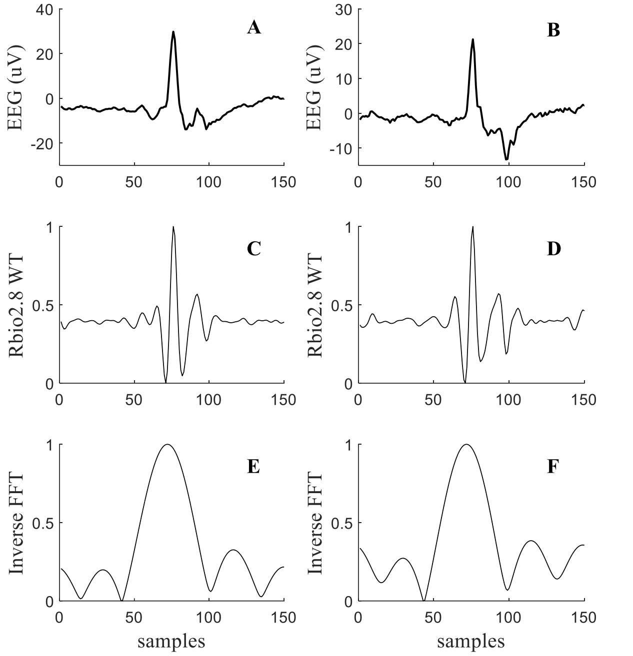

Figure 2. (A-B): Examples of post-HI micro-scale ECoG spike transients. (C-D): The corresponding Rbio2.8 wavelet transforms of the spikes in A and B at scale 7. (E-F): The corresponding inverse Fourier transforms of the spikes in A and B using band-pass filter 80-120Hz.

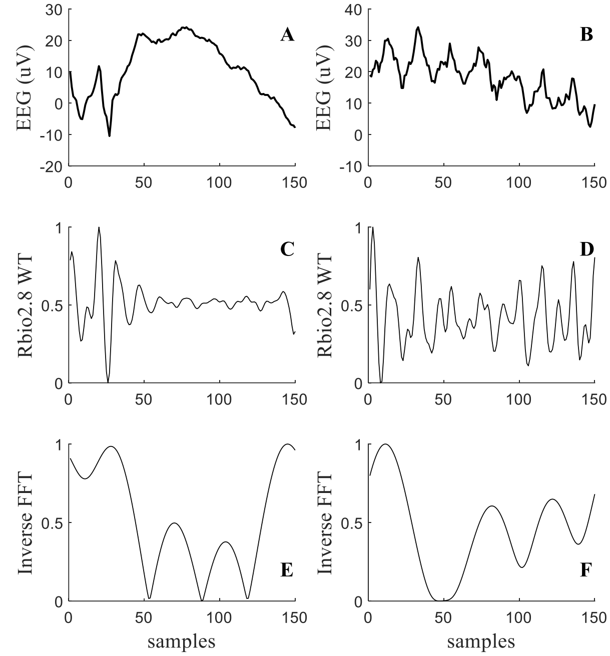

Figure 3. (A-B): Examples of non-spike ECoG background events. (C-D): The corresponding Rbio2.8 wavelet transforms of the ECoG segments in A and B at scale 7. (E-F): The corresponding inverse Fourier transforms of the ECoG segments in A and B using band-pass filter 80-120Hz.

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. Table II demonstrates the confusion matrix results of the WF-CNN classifier. Initially, the trained WF-CNN classifier (using 2h of data from the 1st sheep) was able to accurately identify spike transients in the test-set from the 2nd sheep (unseen data) with an overall high-accuracy of 99.89% (AUC: 0.999). An overall high-performance of 98.17% (AUC: 0.985) was achieved when the classifier was trained on data from the 2nd sheep and tested on the entire 2hrs data of the 1st sheep. Fig. 5 illustrates the ROC plots of the results. Data distribution for training, validation and test of the classifier as well as the cross validated performance of the proposed classifier are represented in Table II. The high-performance of the classifier were obtained through its very low number of false negative (missed) and false positive (wrong) detections. The achieved high-accuracies of the WF-CNN classifier, that employs a much simpler, and computationally-efficient, feature extraction strategy compared to our WS-CNN method [15], confirm the robustness of the technique for the identification of high frequency ECoG events, although a more detailed further analysis will be required using a larger dataset. As a result, the spectrally-sufficient extracted features from an ECoG epoch also allowed classification of inverse polarity spikes in the data.

TABLE I. The Arcituchure of the Proposed 2D-CNN

Layers	Type	No. of Neurons	Kernel size	Stride	No. of Filters
0-1	Conv.	72×3	3	1	32
1-2	Max_pool	36×2	[2 1]	2	
2-3	Conv.	36×2	3	1	64
3-4	Max_pool	18×1	2	2	
4-5	Conv.	18×1	3	1	128
5-6	Max_pool	9×1	[2 1]	2	
6-7	Conv.	9×1	3	1	256
7-8	Max_pool	4×1	[3 1]	2	
9-11	Fully_connected	1280			
	Fully_connected	20			
	Fully_connected	2			

IV. Conclusion

This paper introduced a novel extension to our 2D-CNN sharp-wave classifier by presenting a computationally more efficient feature-extraction approach that robustly provides the dominant spectral feature-sets of an arbitrary EEG/ECoG pattern for training of a 2D 11-layers deep CNN classifier. The method we utilized was able to accurately identify high-frequency spike transients in a noisy background of 1024Hz sampled ECoG, in real-time, with a high-accuracy of 99.03±0.86%, tested over a total of 4 hours post HI ECoG recordings. Results emphasize the correct choice of the proposed spectral feature extraction strategy to efficiently obtain minimal, but dominant, features that result in optimal classification performance of the suggested deep WF-CNN architecture for spike transient identification. Overall, the exceptionally accurate results of the WF-CNN classifier, using a much simpler but computationally much faster feature extraction approach suggest that this method could be used for automated analysis of 256Hz neonatal EEG for the early detection of EEG biomarkers which may provide valuable diagnostic & prognostic information for clinicians.

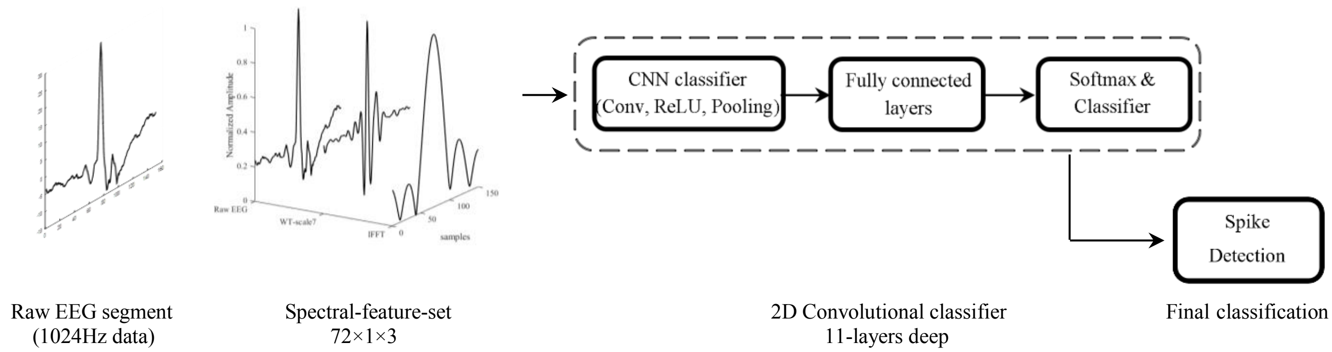

Figure 4. The schematic of our proposed WF-CNN classifier.

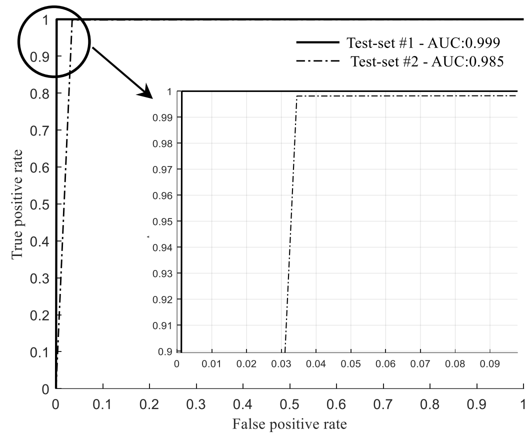

Figure 5. ROC curve and the corresponding AUC for the 11-layers WF-CNN gamma spike classifier

TABLE II. PERFORMANCE MEASURES OF THE WF-CNN CLASSIFIER

	Data	TP hits	TN hits	FP hits	FN hits	Sensitivity (%)	Selectivity (%)	Precision (%)	Accuracy (%)
Train-set: Sheep #1 Test-set: Sheep #2	Train	856	1858	0	0	100	100	100	100
	Val	214	464	0	0	100	100	100	100
	Test	196	725	1	0	100	99.86	99.49	99.89
Train-set: Sheep #2 Test-set: Sheep #1	Train	157	581	0	0	100	100	100	100
	Val	39	145	0	0	100	100	100	100
	Test	1068	2262	2	60	94.68	99.91	99.81	98.17

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