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Research Article

Automated Detection of Alzheimer's Disease using raw EEG time series via. DWT-CNN model

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ABSTRACT

Dementia is an age-related neurological disease and gives rise to profound cognitive decline in patients' life. Alzheimer's Disease (AD) is the progression of dementia and AD patients generally have memory loss and behavioral disorders. It is possible to determine the stage of dementia by developing automated systems via. signals obtained from patients. EEG is a popular brain monitoring system due to its cost effective, non-invasive implementation, and higher time resolution. In current study, we include participants of 24 HC (12 eyes open (EO), 12 eyes closed (EC)), and 24 AD (HC (12 eyes open (EO), 12 eyes closed (EC)). The aim of current study is to design a practical AD detection tool for AD/HC participants with a model called DWT-CNN. We performed Discrete Wavelet Transform (DWT) to extract EEG sub-bands. A Conv2D architecture is applied to raw samples of related EEG sub-bands. According to obtained performance metrics calculated from confusion matrices, all AD and HC time series are correctly classified for alpha band and full band range under both EO and EC. Classification rate of AD vs. HC increases under EO state in all cases even if EC is commonly preferred in other studies. We will add MCI patients with equal size and similar demographics and repeat the experimental steps to develop early alert system in future studies. Adding more participants will also increase generalization ability of method. It is also promising study to combine EEG with different modalities (2D TF image conversion, or MRI) in a multimodal approach.

Introduction

Dementia is an age-related neurological disease and gives rise to profound cognitive decline in daily routine. It ultimately causes death owing to inadequate health care service and symptom attenuating medications [1]. It has been reported that 47 million patients are suffering from dementia in worldwide and number of patients is approximated as 131.3 million by 2050.Moreover, the global healthcare expenses of dementia accounts for 818 billion USD per year, and this cost is continuously increasing [2]. Early diagnosis may decrease this treatment cost. Alzheimer's Disease (AD) is the progression of dementia and AD patients generally have memory loss, behavioral disorders and even there is noticeably change in their shape and size of brain compared to controls [3].

Neurofibrillary tangles and amyloid plaques in the cerebral cortex are some of anatomical reasons behind AD. It is possible to determine the stage of dementia by evaluating biomarkers obtained from patients, but this process is expensive, invasive and requires more expertise and specialized centers [4]. Electroencephalography (EEG) has gained popularity for brain monitoring system due to its cost effective, non-invasive implementation, and higher time resolution [5]. The distinctive effects of dementia of human brain are assumed as follows: decreased complexity, slowing EEG fluctuation, and reduced synchronization in EEG dynamics [6]. In other words, dementia causes less neurons interacting each other, lower cortical connection, and higher linearity in EEG behaviors. In addition, EEG shows lower amplitude in fast frequencies, and higher amplitude in slow frequencies [7]. It can be deduced that EEG's amplitude itself gives clues for content of data. It is crucial to develop an automated detection system learning from data samples without any feature engineering, and non-linear analysis.

We can collect feature engineering under 4 sub-sections in terms of EEG: time domain features, frequency domain features (obtained from Fourier and Wavelet analysis), spatial features (2D topographical maps), and connectivity values calculated between different electrodes. EEG serves high time resolution, and we can directly utilize raw time series records as input vectors of machine learning methods. Deep architectures have become the frontiers approach for establishing diagnostic models based on neurological data. Data from different participant groups feed networks as input sets to train an automated deep architecture.

Many studies have performed binary, and multi-way classification to develop a diagnostic tool for dementia. Bi and Wang (2019) extracted 2D colored spectral topographical maps including 4 Healthy Conditions (HC), 4 Mild Cognitive Impairment (MCI), and 4 AD [8]. MCI is conversion stage from HC to AD, and it is crucial to include MCI patients in experiments. They proposed Spike Convolutional Deep Boltzmann Machine as machine learning architecture and obtained 95% acc. for 3-way classification. Kim and Kim (2018) calculated Relative Power features from 10 MCI patients with 10 HC and implemented Deep Neural Network with 4 hidden layer [9]. They achieved 75% acc. for MCI vs. HC classification task. Ieracitano et al.(2019) used 2D grayscale Periodogram images as input sets for CNN with 1 hidden layer [10]. They collected dataset from 63 AD, 63 MCI with same number of HCs. They performed 2-way (AD vs. HC: 91% , AD vs. MCI: 84% , MCI vs. HC : 92%), and multi-class method (AD vs. MCI vs. HC: 80%) in acc. Morabito et al. (2016) carried out an experiment including 23 HC, 23 MCI, and 23 AD patients and calculated 2D RGB images of Mexican Hat Continuous Wavelet Transform (CWT). They implemented CNN with 2 hidden layers and obtained 82% acc. for 3-way classification. Zhao and He (2015) used raw data of 15 HC and 15 AD participants via. Restricted Boltzmann Machine with 3 hidden layers and achieved 92% acc. for AD vs. HC [11]. J Huggins et al. (2021) calculated 2D RGB Scalogram images of 52 HC, 37 MCI and 52 AD patients with Alex-Net architecture [12]. They yielded 95.51% acc. for 3-way classification. Alvi et al. also used raw EEG data directly to the input of Long-Short Term Memory (LSTM), Gated Recurrent Units (GRU), k-Nearest Neighbors (k-NN), and Support Vector Machines (SVM) classifier, and obtained highest acc. of 95.51% with GRU [13]. In recent study, we include participants of 24 HC (12 eyes open (EO), 12 eyes closed (EC)), and 24 AD (HC (12 eyes open (EO), 12 eyes closed (EC)). We implemented Discrete Wavelet Transform (DWT) to extract EEG Sub-bands. A Conv2D architecture is applied to raw samples of related EEG sub-bands. We also consider the effects of eye states on discrimination of AD from HC samples. The aim of current study is to design a practical AD detection tool for AD/HC participants with a model called DWT-CNN. We combined both eyes' states to consider the effects on performance metrics within a binary classification task.

The rest of the paper is organized as follows: In material and methods section, we describe dataset, pre-processing protocol, and DWT-CNN architecture. We describe parameters in proposed network. In Results and Discussion section, all related outcomes are given based on illustrations. Study is concluded with conclusion and future work section.

Materials and Methods

In this section, dataset description, pre-processed steps to construct input tensors, evaluation of method, proposed deep learning architecture, and calculated performance metrics are given. The overall steps followed in proposed study is given in Fig. 1. Input tensors of time series data are created in MATLAB R2021a and stored. The rest of implementation is performed in Spyder (Python 3.9.) with a workstation including 32 GB RAM and 12 GB VRAM NVIDIA GeForce RTX 3060 GPU.

Dataset

The dataset was acquired by researcher at Florida state University from 19 electrodes ($F_{p1}, F_{p2}, F_z, F_3, F_4, F_7, F_8, C_z, C_3, C_4, T_3, T_4, P_z, P_3, P_4, T_5, T_6,$ $O_1,\ and\ O_2$) using international 10-20 replacement. Dataset divides into 4 sub-groups: A (HC, EO), B (HC, EC), C (AD, EO), and D (AD, EC). Groups A, and B include 24 HC participants (average age 72, range 61-83) and groups C and D have 24 AD patients (average age 69, range 53-85). Each participant has 8 s length of EEG segment, band range of record is 1-30 Hz, and sampling frequency f_s = 128 Hz. Detailed explanation of dataset can be found in [14].

Discrete Wavelet Transform

Wavelet Transform (WT) is widely used for time-frequency analysis of biomedical signals and serves practical solutions especially due to EEGs non-stationary, and non-linear behaviors. WT used narrow window functions for high frequencies and wider windows for lower frequencies. Discrete Wavelet Transform uses low pass (h(n)) and high pass (g(n)) filter pairs for down-sampling process of time series. Approximate (A) and detail (D) are obtained after each down-sampling to obtain low and high frequency components respectively. Same process continues until reaching out desired frequency level. Low pass, and high pass filtering process is given as follows:

$$\varphi j, k(n) = 2^{j/2} h(2^j n - k) \quad (1)$$

$$\varphi j, k(n) = 2^{j/2} h(2^j n - k) \quad (2)$$

,in which $n = 0, 1, 2, \dots, M-1$; $j = 0, 1, 2, \dots, J-1$; $k = 0, 1, 2, \dots, 2j-1$; $J = log_2^M$, and M is length of the signal. Approximate A_i and detail D_i coefficients can be expressed as follows:

$$\mathrm{Ai} = \frac{1}{\sqrt{M}} \sum_n x(n) \times \varphi\mathrm{j}, \mathrm{k(n)} \quad (3)$$

$$\mathrm{Di} = \frac{1}{\sqrt{M}} \sum_n x(n) \times \psi\mathrm{j}, \mathrm{k(n)} \quad (4)$$

, in which $k = 0, 1, 2, \dots, 2j-1$,and M is length of discrete EEG time series. In current study, 4^{th} level DWT with 'db2' is used to obtain delta (< 4 Hz), theta (4-8 Hz), alpha (8-13 Hz), and beta (13-30 Hz).

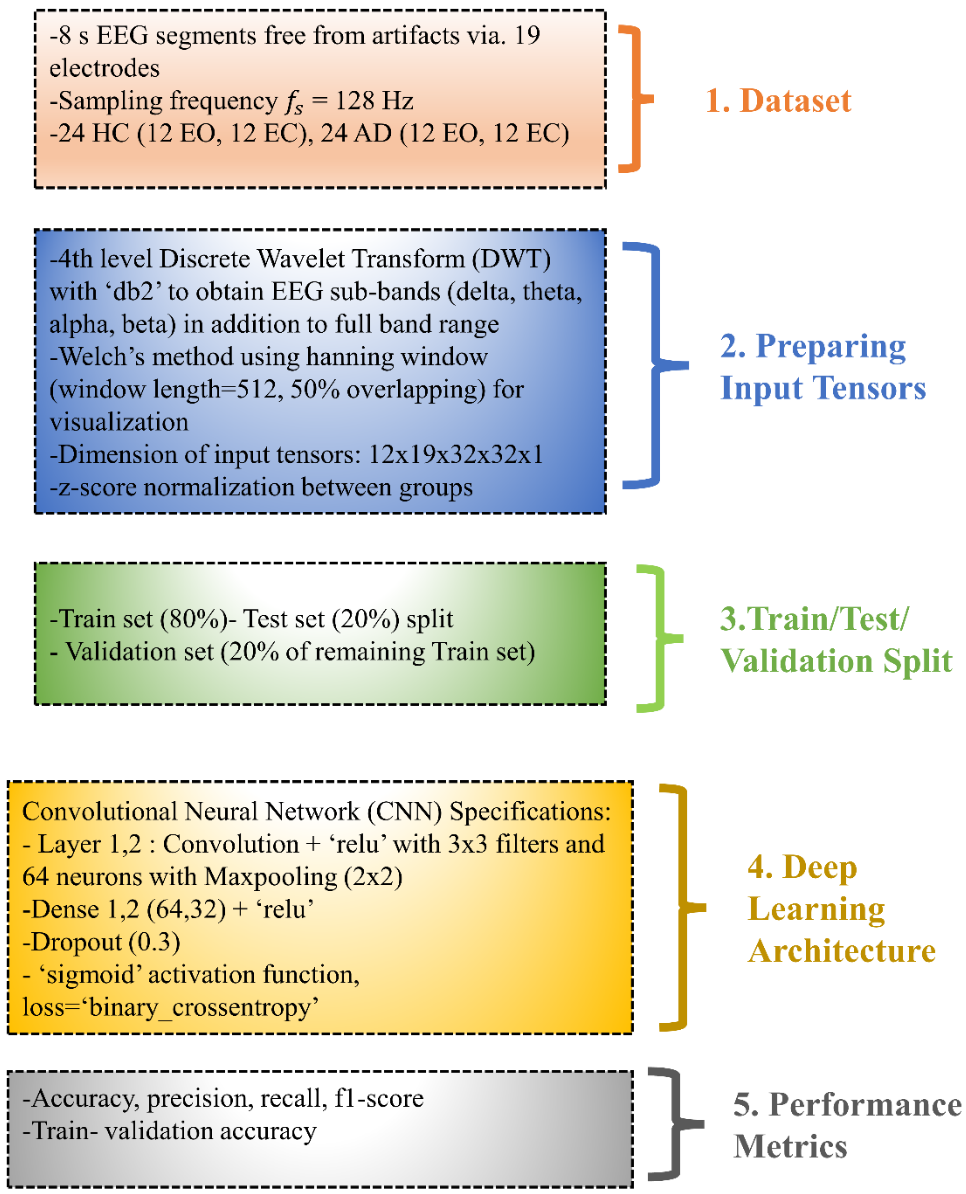


Figure 1. Steps followed in proposed methodology

Welch's Method for Power Spectrum Density Visualization

Welch's method estimates the power spectrum density (PSD) of a given signal using overlapped segment averaging estimator. Every segments are windowed with window function. PSD estimation is achieved by averaging modified periodograms[15] . ith periodogram of a given x(n) is express as:

$$S_{xx}^{(i)}(f) = \frac{T_s}{K.M}\left|\sum_{n=0}^{M-1} x_i(n)w(n)e^{-j2\pi f_n}\right|^2 \quad (5)$$

, in which f is normalized frequency, w(n) is window function,T_s is sampling coefficient. Normalization constant K is defined as:

$$= \frac{1}{M}\sum_{n=0}^{M-1} w^2(n) \quad (6)$$

To sum up, we calculated ith PSD of a signal x(n) as:

$$P_{welch}(f) = \frac{1}{L}\sum_{i=0}^{L-1} S_{xx}^{(i)}(f) \quad (7)$$

, where L refers to lenght of time signal.

In this study, we estimate PSD of EEG sub-bands using 'Hann' window with 50% overlapping. Length of window function is selected as 512. We picked up and combined central, temporal, parietal, and occipital electrodes from a randomly selected participant from each class. We excluded frontal electrodes to avoid redundant noises due to eye movements.

Preparing Input Tensors, and train-test split

In each class of A, B, C, and D, we equally have 12 participants. Each participants have 8 s record for each of 19 channel. We totally have 12x1024x19 data samples for each class. 1024 length of sample are converted into squared matrices 32x32. Afterwards, each class has 12x19x32x32x1 input tensors. Z-score transform is finally applied to combination of 2 class for data normalization (i.e. data distribution of each column has mean 0 and standard deviation 1). For the validation and evaluation step, we initially divide input data as 80% training and 20% test set. Then, 20% of remaining training set is determined as validation set.

Conv2D as Deep Learning Architecture

CNN performs for both feature extraction and classification task simultaneously. Features extracted from raw data automatically using convolution stage, activation function and pooling layers, and classification task is performed via. a fully connected multi-layer neural network. Convolution operation uses the kernels (i.e. filters) and expressed as:

$$Y_j = \sum X_i * K_j + B_j \quad (8)$$

, in which B_j refers to bias and * corresponds for convolution operation. Local region X_i convolves with jth filter and it shifts over all input tensor with stride s. We obtain a feature map Y_j with size of y_1 and y_2,expressed as:

$$y_{1,2} = \frac{h - k_{1,2} + 2\,x\,p}{s} + 1 \quad (9)$$

, where p is zero padding parameter. An activation function, generally sigmoid or hyperbolic tangent preferred, is used for nonlinear transfer function. 'ReLu' has gained popularity due to its better performance for generalization and learning time in CNN architecture. In order to reduce the resolution of input feature vectors, pooling layers haven been utilized. It is important to capture invariant features by using pooling layer. Max-pooling is an effective sub-sampling operator to increase generalization performance and capture important features. Fully connected layer has neurons connected to every unit of previous layers and size of last layer is equal to number of current classes [16].

The proposed architecture of Conv2D is given in Fig. 3. In current study, we implemented 2 convolutional layer + 'relu' with 3x3 filters and number of 64 neurons. 2x2 max pooling is used to capture distinct feature and reduce dimension of feature maps. 2 dense layer (64,32) is coming after feature extractor layer and drop out (0.3) is added after dense layers. 'binary_crossentropy' is selected as loss function. We have trained the Conv2D architecture along 100 epochs for classification of AD and HC EEGs.

Evaluation of Performance Metrics

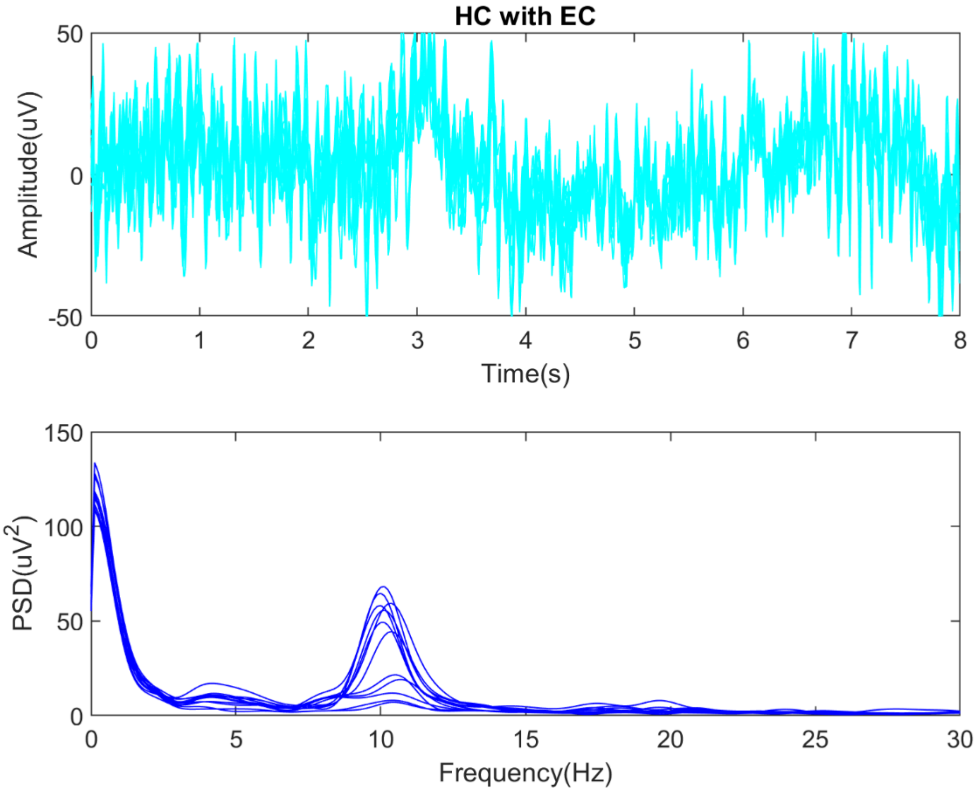
We evaluated many performance metrics estimated from confusion matrices. Accuracy, sensitivity (recall), specificity, precision, and f1-score are calculated for classification purpose. In an ideal classifier, FP and FN should be zero. Moreover, precision and recall values needs to be one. F1-score is a metric that takes precision and recall into account and show trustworthy results. Formulas of performance metrics are given as given below:

$$Accuracy = \frac{TP+TN}{TP+FP+FN+TN} \quad (10)$$

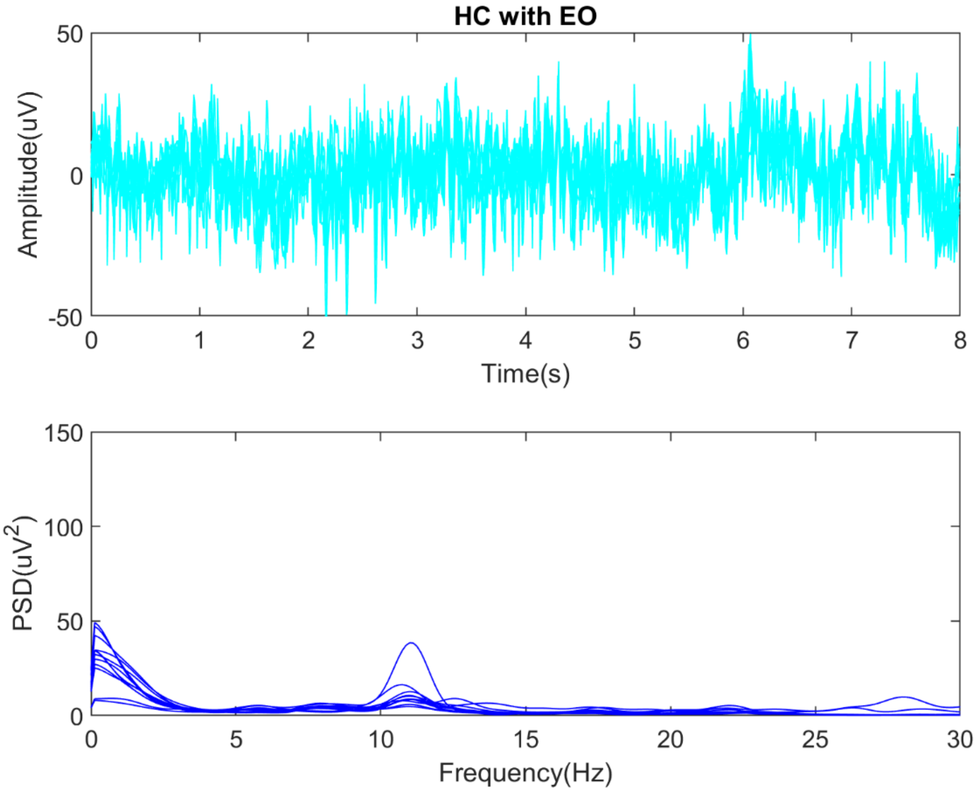
$$Sensitivity\ (Recall) = \frac{TP}{TP+FN} \quad (11)$$

$$Precision = \frac{TP}{TP+FP} \quad (12)$$

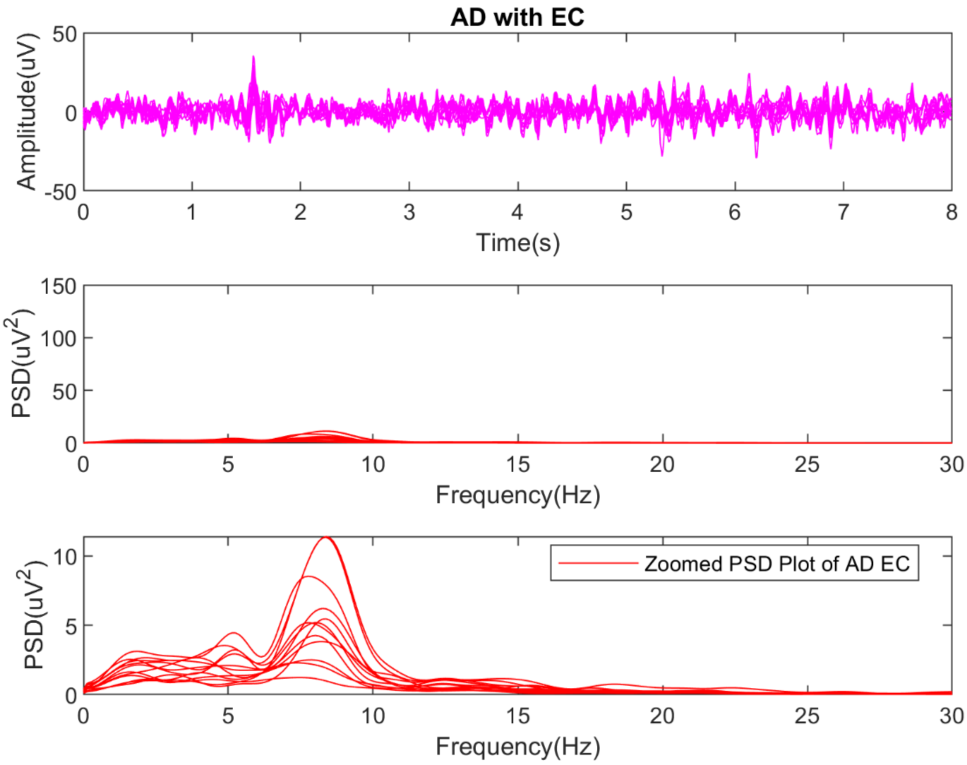
$$F1 - core = 2 * \frac{Precision*Recall}{Precision+Recall} \quad (13)$$


HC with EC
Amplitude(uV)
Time(s)
PSD(uV^2)
Frequency(Hz)

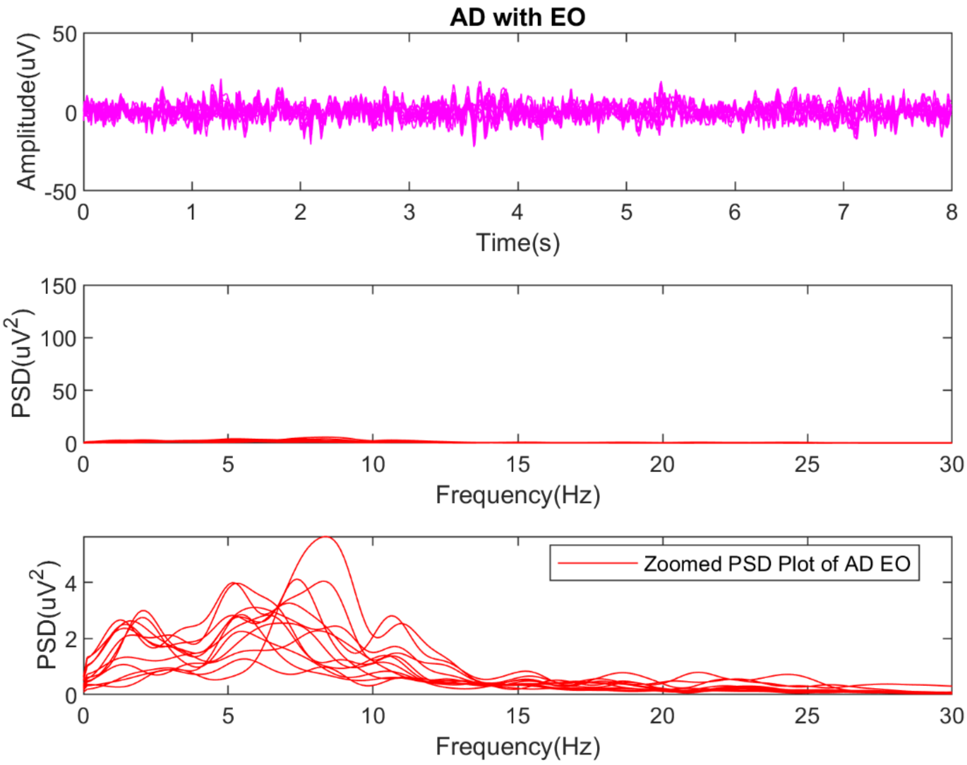
(a)


HC with EO
Amplitude(uV)
Time(s)
PSD(uV^2)
Frequency(Hz)

(b)



(c)



(d)

Figure 2. Samples of 8 s EEG records and their (0-30 Hz) PSDs belong to randomly selected participants from (a) HC with EC (b) HC with EO (c) AD with EC and (d) AD with EO classes

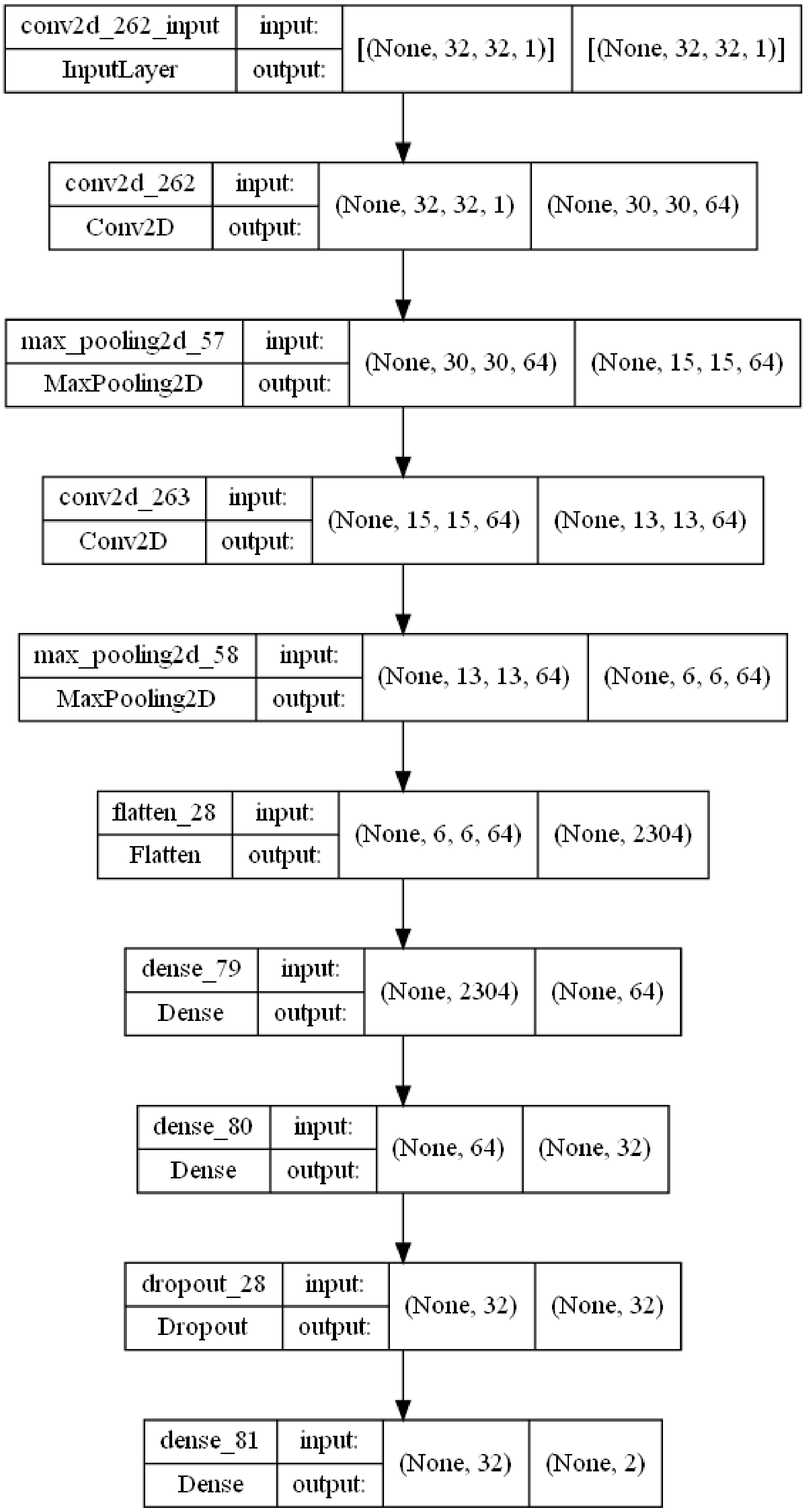
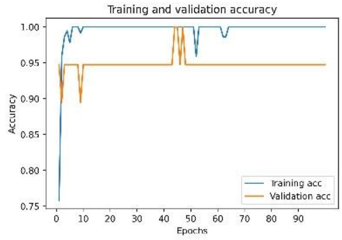
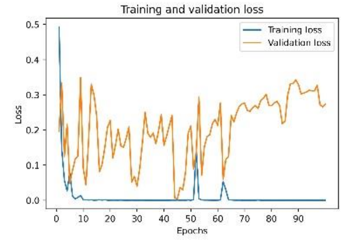
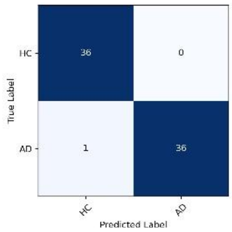
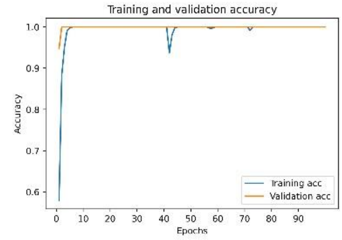
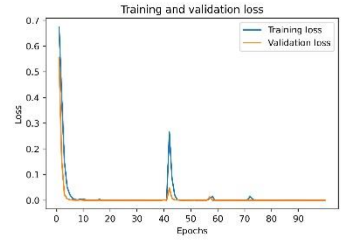
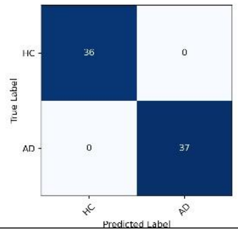
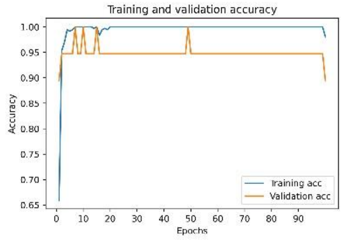
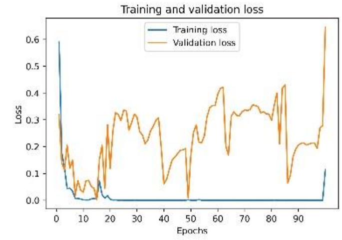
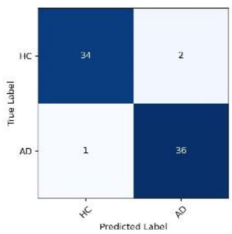
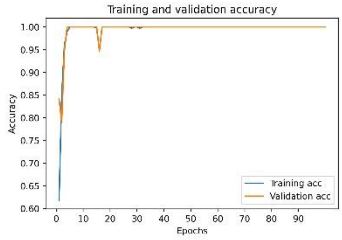
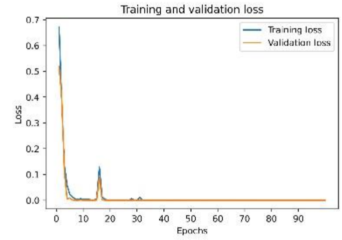
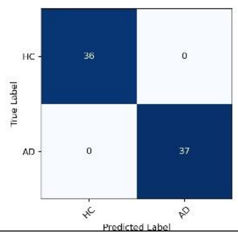
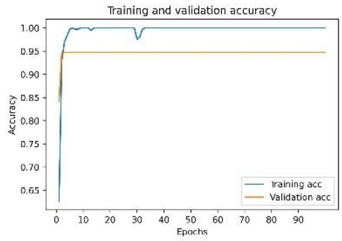
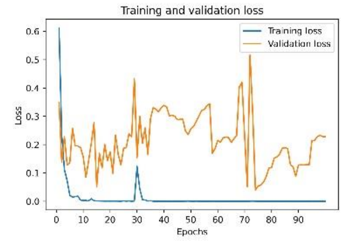
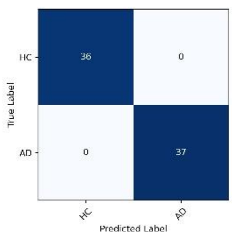
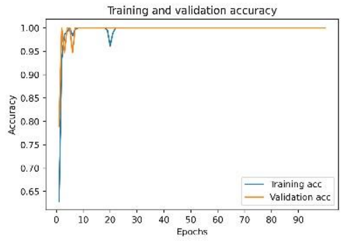
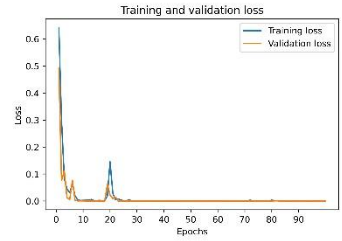
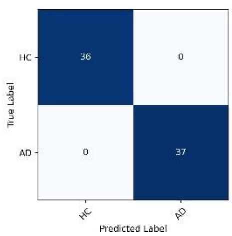


Figure 3. Architectural summary of proposed Conv2D model

Table 1. Train/validation accuracy, loss plots along 100 epochs and related confusion matrices for EEG sub-bands and full band range under different eyes states

		Train/validation accuracy	Train/validation loss	Confusion matrices
Delta Band (<4 Hz)	Eyes Closed			
	Eyes Open			
Theta Band (4-8 Hz)	Eyes Closed			
	Eyes Open			
Alpha Band (8-13 Hz)	Eyes Closed			
	Eyes Open			

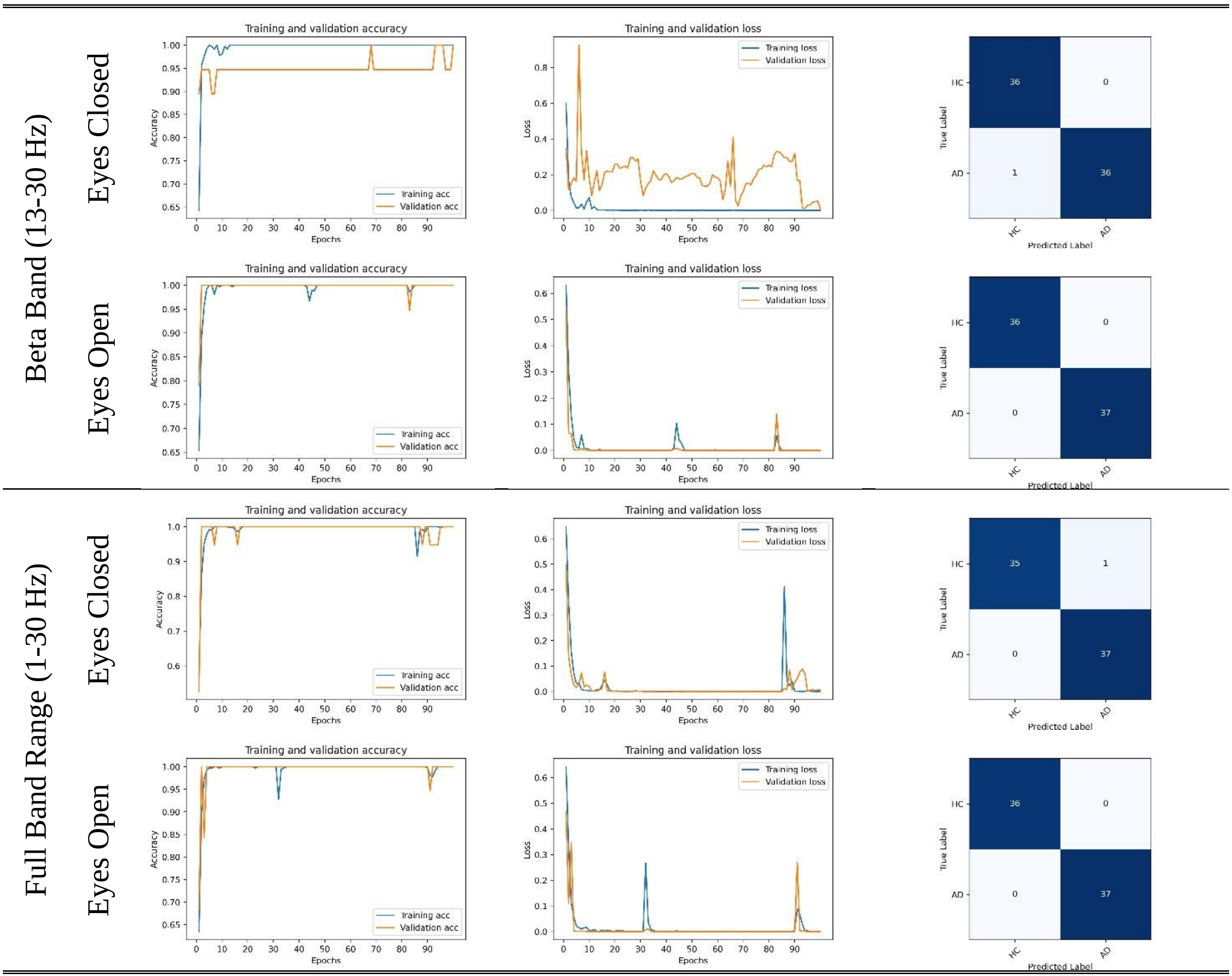


Table 2. Performance metrics for classification of AD vs. HC participants for EEG sub-bands and full band range under different eyes states

EEG Sub-bands	Eye Conditions	Participants	Accuracy	Precision	Recall	F1-score
	EC	HC	0.99	0.97	1	0.99
Delta		AD	0.99	1	0.97	0.99
	EO	HC	1	1	1	1
		AD	1	1	1	1
	EC	HC	0.96	0.97	0.94	0.96
Theta		AD	0.96	0.95	0.97	0.96
	EO	HC	1	1	1	1
		AD	1	1	1	1
	EC	HC	1	1	1	1
Alpha		AD	1	1	1	1
	EO	HC	1	1	1	1
		AD	1	1	1	1
	EC	HC	0.99	0.97	1	0.99
Beta		AD	0.99	1	0.97	0.99
	EO	HC	1	1	1	1
		AD	1	1	1	1
	EC	HC	0.99	1	0.97	0.99
Full Band		AD	0.99	0.97	1	0.99
Range	EO	HC	1	1	1	1
		AD	1	1	1	1

Table 3. Literature studies for AD detection based on deep learning architectures

Authors	**Dataset**	**Extracted features**	**Machine Learning Architecture**	**Achieved Results (accuracy%)**
Bi and Wang (2019) [8]	4 HC, 4 MCI, and 4 AD	2 D RGB spectral topographical maps	Spike Convolutional Deep Boltzmann machine	AD vs. MCI vs. HC: 95%
Kim and Kim (2018) [9]	10 HC, 10 MCI	Features from Relative Power	Deep Neural Network With 4 hidden layer	MCI vs. HC: 75%
Ieracitano et a. (2019) [10]	63 HC, 63 MCI, And 63 AD	2D grayscale Periodogram images	CNN with 1 Hidden layer	AD vs. HC: 91% AD vs. MCI: 84% MCI vs. HC: 92% AD vs. MCI vs. HC: 80%
Morabito et al. (2016)	23 HC, 23 MCI, And 23 AD	2D RGB images of Mexican Hat CWT	CNN with 2 hidden layer	AD vs. HC: 85% AD vs. MCI: 78% MCI vs. HC: 85% AD vs. MCI vs. HC: 82%
Zhao and He (2015) [11]	15 HC, 15 AD	Raw Data	Restricted Boltzmann Machine with 3 hidden layers	AD vs. HC: 92%
J Huggins et al. (2021) [12]	52 HC, 37 MCI, and 52 AD	2 D RGB of Scalogram images	AlexNet	AD vs. MCI vs. HC: 98.9%
Alvi et al. 2022 [13]	16 HC, 11 MCI	Raw EEG Data	LSTM, GRU, k-NN SVM	MCI vs. HC: 95.51%
Current study	24 HC (12 EO, 12 EC); 24 AD (12 EO, 1 EC)	Raw EEG Sub-bands	2D CNN	AD vs. HC: 100% for both EO and EC in alpha band

Results and Discussion

In Fig. 2., amplitudes of 8s EEG samples and their PSDs with respect to time and frequency are given. These are the samples of randomly selected subjects from class of A (HC with EO), B (HC with EC), C (AD with EO), and D (AD with EC). Amplitudes of EEGs are set in range of [-50, 50] μV and Amplitudes of PSDs are between [0-150] μV^2. It is very difficult to differentiate ADs and HCs by only observing time series samples. It can be clearly seen that there is an increased alpha band effect during EC. This finding is compatible with previous findings [17]. Amplitude range of HC condition under EC and EO is wider in comparison with ADs. EEG patterns are so repetitive and changed in a narrowed in for AD patients. Amplitude of PSDs belong to EC is higher regarding EO. It is easily deduced that linearity is distinctively increased for AD patients. Amplitude of EEG has potential to classify ADs and HCs without any conversion stage and feature engineering. We only apply DWT to EEGs to investigate frequency specific observations.

Train/validation accuracies and train/validation losses are given with confusion matrices in Table 1 for all EEG sub-bands, and full band range under EC and EO conditions. Validation losses are so stable along 100 epoch for EO condition. Losses are suddenly increases and more fluctuations are observed for EC. Validation accuracy is lower in comparison with training accuracy in most cases of EC. Discrimination rate of AD vs. HC increases under EO state in all cases. Most of the studies based on AD detection are included subjects with EC because EC states prevents possible eyes blinks and ocular noises. In addition to this advantageous case, alpha activity is increased during EC and authors in [17] stated that epoch with less alpha effect increases the discrimination of mild Alzheimer's. In current study, according to obtained performance metrics calculated from confusion matrices, all AD and HC time series are correctly classified for Alpha band and full band range under both eyes' state.

Table 3 summarizes binary and 3-way deep learning-based studies for detection of AD via. different perspective. All studies include equal size of participant class to balance sample size. Some of the studies have MCI, a conversion stage between HC and progression of dementia AD, for early detection purpose. Most of the studies proposed a 2D conversion method from 1D EEG time series to colored, or grayscale spectral maps for feature extraction. Very few studies processed with extracting direct features or using raw EEG itself. CNN, spike convolutional networks, pre-defined deep architectures (i.e. AlexNet) for 2D input arrays, and CNN is considered as most popular deep learning-based approaches with different architectural structures. For binary approach using AD and HC participant, highest accuracy of 92% is obtained via. applying Restricted Bolzman Machine to raw EEG data [11]. We correctly discriminate all AD and HC instances with 100% accuracy by applying raw EEG inputs to 2 layered- CNN network. 8 s records are converted 32x32x1 squared input tensors to feed deep architecture. None of the literature studies in Table 3. reported any deduction and results to observe effects of different eyes states on AD detection. We put forward that EO state increases classification rate of AD vs. HC. Miraglia et al. (2016) suggest that eyes open state may reflect better the cortical impairment as well as information processing rather than eyes closed [18]. Authors in suggest eyes-closed EEG state with epochs including less alpha activity works better for diagnosis of AD [19].

There have been many methods for pre-processing step such as notch filtering, band pass filter, value normalization to [0-1], and artifact removal methods such as independent component analysis, visual inspection , blind source separation, baseline correction, and so on [20]. We believe that z-normalization is also a crucial pre-processing step before classification stage. z-normalization eliminates outliers coming from different classes and make an alignment in data distribution. Moreover, DWT maintains user an effective artifact handling using its low pass, and high pass filter pairs.

Conclusion

In current study, DWT-CNN approach is applied for classification of AD and HC EEG records. 4th level DWT with ‘db2’ is applied to obtain EEG sub-bands. We have processed 8 s artifact free raw EEG segments via. 19 electrodes and constructed 12x19x32x32x1 input tensors for each of HC with EO, HC with EC, AD with EO and AD with EC states. Z-core normalization is applied to eliminate outliers coming from AD and HC classes and set data distribution with mean 0 and standard deviation 1. 2-layered CNN is used as machine learning architecture. According to performance metrics, all AD and HC time series are correctly classified for alpha band and full band range for both EO and EC state. Classification rate of AD vs. HC increases under EO state in all cases.

Drawbacks of current study are assumed as follows: including MCI patients may help to develop an early detection of dementia with handling MCI vs. AD, or MCI vs. all classification task. We will add MCI patients with equal size and similar demographics and repeat the experimental steps in future studies. Generalization ability of current approach may also increase within increasing number of participants. Combining 2D TF RGB images with raw EEG time series tensors in a multimodal learning approach is also potential work for further research. In a similar point of view, it is also promising study to combine EEG and MRI images as input sets for classifier. Moreover, a hyperparameter optimization task can be carried out via. alternative deep networks (transfer learning with pre-trained networks, CNN-LSTM hybrid architectures, etc.) in upcoming studies.

Ethics committee approval and conflict of interest statement

"There is no need to obtain permission from the ethics committee for the article prepared"

"There is no conflict of interest with any person / institution in the article prepared"

Authors’ Contributions

Seker M: Study conception and design, visualization, analysis, and interpretation of data, drafting of manuscript

Ozerdem MS: supervised the project, critical revision

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