

Welch Spectral Analysis and Deep Learning Approach for Diagnosing Alzheimer's Disease from Resting-State EEG Recordings



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ABSTRACT

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Alzheimer's disease (AD) is a serious and progressive neuronal disease that damages brain cells, resulting in loss of cognitive function and memory. Early diagnosis is crucial for medical intervention to prevent brain damage and preserve daily functioning for longer. In this study, a deep learning approach was proposed for early diagnosis of AD from electroencephalography (EEG) recordings at resting-state. The dataset contains EEG recordings of 24 healthy individuals and 24 Alzheimer's patients. To extract the features from the EEG recordings, the power spectral densities of the frequencies between 1-49 Hz were calculated using the Welch spectral analysis method. Using extracted features, the performances of random forest (RF), k-nearest neighbor (kNN), support vector machine (SVM), and bidirectional long-short term memory algorithms were compared. In addition, under different resting state conditions (open eyes; closed eyes; open eyes and closed eyes), the effectiveness of EEG signals was analyzed. As a result of the experiments, the bidirectional long-short term memory algorithm had the highest performance. The algorithm achieved promising performance with 98.85% accuracy, 0.986 recall, 0.990 precision, 0.990 specificity, 0.988 f1-score, and 0.977 Matthews correlation coefficient. The combination of the Welch spectral analysis and the bidirectional long-short term memory deep learning approach can be used to accurately and effectively distinguish AD and HC groups from resting-state EEG recordings. More accuracy was achieved in this study compared to investigations using cutting-edge technology.

1. INTRODUCTION

Alzheimer's disease (AD), a neurodegenerative condition manifested by cognitive dysfunction and progressive memory loss, has serious social, financial, and medical implications. It is the most common type of dementia [1]. There are more than 55 million people with dementia in the world, and according to the estimations of the World Health Organization, AD contributes to 60-70% of cases [2]. This figure is expected to increase to approximately 82 million in 2030 and to 52 million in 2050. Besides its prevalence, the economic burden of AD management is also quite high. AD patients use significantly more medical services each year until their diagnosis [3]. For example, the global cost of AD treatment to the healthcare system was \$305 billion in 2020. Given the growing number of people suffering from AD and the costs of care, this economic burden is expected to increase by more than \$1 trillion. Moreover, AD is the fifth leading cause of death among people over the age of 65 [4]. AD is manifested only by simple forgetfulness. As the disease progresses, the patient forgets recent events and the disease causes problems in all areas of life, including family, educational, social, personal, physical and professional [5]. These patients are often stigmatized, their human rights are likely to be violated and they are likely to be discriminated against. People suffering from AD become unable to recognize their family and close environment and become in need of care in the last stage. Therefore, this disease not only affects people suffering from

AD, but also has devastating effects for their families, caregivers, and society in general [6]. Early detection of AD is critical in predicting prognosis, managing disease or optimizing medical intervention, and delayed diagnosis can cause permanent damage to the body.

In most cases, it is too late to confirm because it is unclear what causes AD. Early diagnosis is at least a better strategy to prevent disease or rapid deterioration, even if timely treatment won't have much of an impact [7]. The first step in treating diseases is to make an accurate diagnosis. Diagnosis of AD is based on qualitative interviews and assessment of behavior, including psychiatric history and present symptoms. These observations can be subjective, imprecise, and incomplete [8, 9]. In addition, traditional techniques for diagnosing AD are costly and tedious [10]. Insidious onset, increasing memory impairment, and other cognitive functions are all necessary for the diagnosis of AD. However, in the early stages of the disease, there aren't any noticeable symptoms. A significant challenge for clinicians and researchers is the early diagnosis of AD [11]. To overcome these limitations, EEG recordings are an effective candidate to support the diagnosis of AD [12]. AD-related neurodegeneration causes changes in neural and synaptic activity. The information content of the EEG recordings can reflect these changes. Therefore, EEG recordings offer useful information about changes in electrophysiological brain dynamics, and it can be used to diagnose AD [13]. Among modern neuroimaging techniques, EEG has advantages such as inexpensive, non-invasive,

portability, relative simplicity, less recording [1]. Because of these advantages, automated methods based on EEG signal analysis combined with deep learning and machine learning have become an important research topic to support clinicians in the difficult process of early AD diagnosis [14]. Reduced complexity in EEG signals has been described as a hallmark of AD progression. This is thought to be connected to neuronal loss and potential connection brought on by the pathological aging process [1]. Therefore, it plays an important role in medical intervention that aim to lessen brain damage and prolong daily functioning. Early diagnosis of AD from EEG recordings provides an opportunity for early treatment. Therefore, it is particularly promising.

There are limited studies investigating the connection between EEG recordings and AD diagnosis. During the resting-state, EEG slowing in general has been noticed in various studies. Visually, this slowing can be seen as a reduction in the speed of the dominant basic rhythm or as an amplification of the spectrally slower rhythms at the expense of the faster ones [15]. Bi and Wang [7] proposed a multitasking learning framework for the purpose of making an early diagnosis of AD. They used Boltzmann Machine with hybrid feature maps model. This framework for multi-task learning aims to accurately classify an EEG spectral image into one of three classes (AD, MCI: mild cognitive impairment, and HC: healthy controls). The EEG dataset contains EEG spectral images recorded from 4 HC, 4 MCI and 4 AD at resting-state with closed eyes. The model, which used Fast Fourier Transform (FFT) and Deep Boltzmann Machine achieved 95.04% success [7]. Amini et al. used the time-dependent power spectrum descriptor and CNN approach in the task of classifying AD, MCI and HC groups and achieved an accuracy of 82.3% [16]. Similarly, Ruiz-Gómez et al. classified AD, MCI and HC groups. Spectral analyzes, non-linear analyzes and Multi-Layer Perceptron approach were used and 78.43% accuracy was achieved [17]. Bairagi focused on wavelet and spectral features for Alzheimer diagnosis using EEG recordings in early stage diagnosis. SVM and kNN classifiers were used to distinguish between AD and HC groups. In their study, they obtained the highest classification performance as 94% by classifying the spectral-based features with the SVM algorithm [18]. The limited number of related studies reveals that studies on the classification of AD and HC groups should be repeated and their results compared. Considering that early diagnosis can slow down the progression of the disease, an objective, timely, and effective diagnosis of AD is critical. Therefore, there is a need to develop easy and applicable methods and enhance performance.

In the paper, we proposed a deep learning model for EEG-based diagnosis of AD. This study was one of the rare attempts to compare the effectiveness of EEG signals under different resting state conditions (open eyes; closed eyes; open eyes and closed eyes). Welch spectral analysis and Bi-LSTM approach framework for classification of AD was presented for the first time. Reducing the prediction bias by using welch spectral analysis, and providing higher performance compared to known related studies are the advantages of the proposed deep learning model. The main contributions of the study can be summarized as follows:

a) An automatic deep learning model, which efficiently combines welch spectral analysis method and the BiLSTM deep learning classifier, was used for early diagnosing of AD from resting-state EEG recordings.

b) The welch spectral analysis method reduced the prediction bias, because of the average of the periodograms reduces the variance of all data compared to a single periodogram estimate. In addition, it had advantages such as less processing load, smoother spectrum, no assumptions about the input data, being applicable to all kinds of signals and providing high performance.

c) The best classification performance was determined by comparing the deep learning and machine learning approaches. Also, the effectiveness of EEG signals was compared at different resting-state conditions.

d) Early, accurate and effective diagnosis of AD offers opportunities for early intervention.

This paper is organized as follows: Section 2 includes material and methods, in which the main theoretical background of the proposed method is introduced. The experimental results are given and performance evaluations discussed in Section 3. Finally, a brief conclusion is presented in Section 4.

2. MATERIAL AND METHODS

2.1 Proposed model

In this study, a deep learning approach was proposed for early diagnosis of AD from EEG recordings at resting-state. The implementation steps of the proposed model are given in Figure 1:

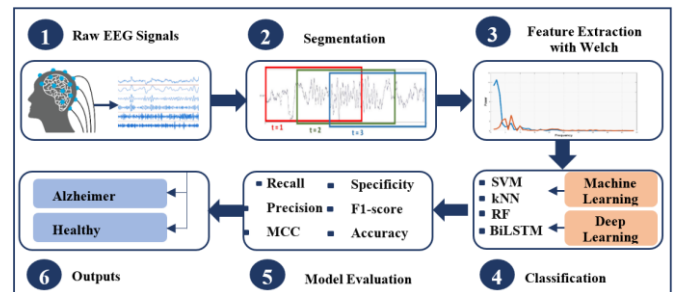


Figure 1. Implementation steps of the proposed model

The proposed deep learning model includes the following implementation steps: i) In the first stage, the segmentation process was performed on the raw EEG recordings. EEG recordings were divided into two 4-second segments, ii) In the second stage, the power spectral density (PSD) values of the frequencies between 1-49 hertz of the EEG recordings were calculated using the welch spectral analysis method, and 49 features were extracted, iii) Then, the EEG dataset was divided into test dataset and training dataset to evaluate the classification performance using the holdout method, iv) Finally, the performances of deep learning and machine learning approaches were compared for EEG-based AD classification.

2.2 Dataset

The Alzheimer's EEG dataset, which was publicly available and newly presented, was used in the study. The dataset consists of EEG signals by Florida State University researchers from 48 subjects, 24 AD patients and 24 HC. EEG recordings were performed in two resting conditions: open eyes and closed eyes. EEG signals were recorded in groups A

and C with their eyes open, and groups B and D with their eyes closed. Groups A and B contain 24 HC subjects, who do not have any neurological disorder. Groups C and D each contain 24 AD patients, diagnosed according to the “National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association”, and “Diagnostic and Statistical Manual of Mental Disorders” criteria [19]. Dataset characteristics are given in Table 1.

Table 1. Dataset characteristics

Groups	Number	Resting-state	Labels	Duration
A	12	open eyes	HC	8 seconds
B	12	closed eyes	HC	8 seconds
C	12	open eyes	AD	8 seconds
D	12	closed eyes	AD	8 seconds

EEG signals were recorded using 19 electrodes: Fp1, Fp2, Fz, F3, F4, F7, F8, Cz, C3, C4, T3, T4, Pz, P3, P4, T5, T6, O1, and O2. EEG recordings were performed in four groups (A, B, C, and D) under the resting-state using Biologic Systems Brain Atlas III Plus workstation labelled in accordance with an international 10–20 system at 128 Hz sampling rate, 8 seconds duration [19]. Figure 2 shows the 10-20 electrode layout.

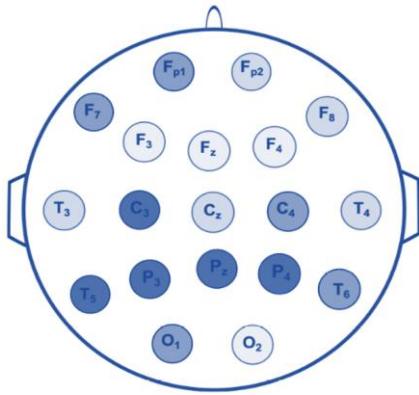


Figure 2. Electrodes positioning for the international 10-20 system

2.3 Signal processing

In the signal processing stage, segmentation and feature extraction were performed. The dataset consisted of 8-second EEG recordings. In the segmentation stage, the EEG signals were divided into two 4-second segments to increase the number of data. Welch spectral analysis method was used in the feature extraction stage.

Feature extraction is a derived sub-attribute set that fully and accurately describes the original dataset [20]. Feature extraction effectively reduces the amount of data that needs to be processed, facilitates subsequent learning and generalization steps, improves classification performance, and reduces processing complexity. In this study, the PSD values of the EEG signals’ frequencies between 1-49 Hz were calculated using the Welch spectral analysis method. The mathematical foundations of the method are presented in 2.3.1.

2.3.1 Estimation of PSD values with the Welch method

Spectral analysis methods are applied to determine the PSD values of signals and to interpret their properties. A signal’s

power distribution over a frequency range is described by the PSD, of which the periodogram is the most basic form [21]. The Welch spectral analysis method is an improved version of the periodogram. In the Welch method, the data is first divided into overlapping segments. Then, the specified windows are added to each segment. Fast Fourier Transform (FFT) is applied to windowed segments and the periodogram of each windowed segment is computed. Finally, all periodograms are averaged to obtain the PSD values [22]. The average of the periodograms reduces the variance of all data relative to a single periodogram estimation [23]. It is calculated as in Eq. (1) [24]:

$$\hat{f}_{xx}^W(\omega) = \frac{1}{P} \sum_{p=0}^{p-1} \hat{f}_{xx}^p(\omega) \quad (1)$$

where, P is the total number of windowed segments, $\hat{f}_{xx}^p(\omega)$ is the calculated periodogram for each windowed segment, and $\hat{f}_{xx}^W(\omega)$ is the average of the periodograms in Eq. (1). Welch spectral analysis method is very popular because of the advantages of having less variance than other methods, bringing less processing load, creating a softer spectrum, making no assumptions about the input data, being applicable to all kinds of signals and providing high performance.

2.4 Training and test datasets

Using the holdout method, the EEG dataset was split into two groups: test dataset and training dataset. The training dataset was used to train the suggested model, and the test data was used to assess the model’s performance. Three different experiments were carried out in the study. In all three experiments, EEG signals from 19 electrodes were divided into two segments at four-second intervals.

a) In Experiment 1, EEG signals from groups A and C recorded at resting-state with open eyes, were used. The total number of datasets in Experiment 1 was 912 (24 subject x 19 channel x 2 segment).

b) In Experiment 2, EEG signals from groups B and D recorded at resting-state with closed eyes, were used. The total number of datasets in Experiment 2 was 912 (24 subject x 19 channel x 2 segment).

c) In Experiment 3, EEG signals from groups A, B, C and D recorded at resting-state with open eyes and at resting-state with closed eyes, were used. The total number of datasets in Experiment 3 was 1824 (48 subject x 19 channel x 2 segment).

Table 2. The distribution of training and test datasets

Experiments	Dataset	Labels	Distribution of datasets	Number of datasets
Experiment 1	Training	AD	313	608
		HC	295	
Experiment 2	Test	AD	154	304
		HC	150	
Experiment 2	Training	AD	302	608
		HC	306	
Experiment 3	Test	AD	138	304
		HC	166	
Experiment 3	Training	AD	601	1216
		HC	615	
Experiment 3	Test	AD	301	608
		HC	307	

In each experiment, 2/3 of the dataset was allocated as the training dataset and 1/3 of the dataset was allocated as the test dataset. Table 2 lists the distribution of the training and test datasets for each experiment.

The success of the model was checked by using deep learning and machine learning algorithms with 1/3 of the dataset.

2.5 Classification algorithms

The performances of BiLSTM, SVM, RF, and kNN algorithms were compared by using feature vectors extracted with calculating the PSD values. The BiLSTM algorithm provided the best performance. Therefore, the BiLSTM algorithm was introduced in 2.5.1.

2.5.1 BiLSTM deep learning algorithm

BiLSTM deep learning networks are extensions of the Long Short Term Memory (LSTM) networks [25]. LSTM training involves computing the output value of the LSTM unit in accordance with forward propagation, the LSTM unit's error value in accordance with back propagation, and the weight gradient in accordance with the error value. The optimization algorithm is used to carry out the gradient descent, and real-time recursive weight updates are made [26]. However, while the LSTM can only learn the information of the one-way sequence, the BiLSTM evaluates forward and backward computations simultaneously. Therefore, processing information in both directions provides an advantage in EEG signal processing.

The LSTM has an input x_t which can be the input sequence directly. h_{t-1} and c_{t-1} are the inputs from the previous time-step LSTM. o_t is the output of the LSTM for this time-step. The LSTM also generates the c_t and h_t for the consumption of the next time-step LSTM. The LSTM cell are calculated as follows [27]:

$$f_t = \sigma(w_f \cdot [h_{t-1}, x_t] + b_f) \quad (2)$$

$$i_t = \sigma(w_i \cdot [h_{t-1}, x_t] + b_i) \quad (3)$$

$$o_t = \sigma(w_o \cdot [h_{t-1}, x_t] + b_o) \quad (4)$$

$$\tilde{c}_t = \tanh(w_c \cdot [h_{t-1}, x_t] + b_c) \quad (5)$$

$$C_t = \sigma(f_t \cdot C_{t-1} + i_t \cdot \tilde{c}_t) \quad (6)$$

$$h_t = \tanh(C_t) \cdot o_t \quad (7)$$

$$y_t = h_t \quad (8)$$

In the equations, f_t is forget gate, i_t is input gate, o_t is output gate, c_t is cell state, and h_t is hidden state. The term b denotes the bias vector and the w denotes the self-updating weights of the hidden layer. The $\tanh(\cdot)$ and $\sigma(\cdot)$ are hyperbolic tangent function and sigmoid respectively. The LSTM block and the BiLSTM block are given in Figure 3.

The BiLSTM architecture consists of forward and backward LSTM where data can be processed in forward and reverse directions. Therefore, BiLSTM better captures the hidden features and pattern of data ignored by LSTM [28]. In experiments, the model evaluation criteria were used to compare the performances of classification algorithms.

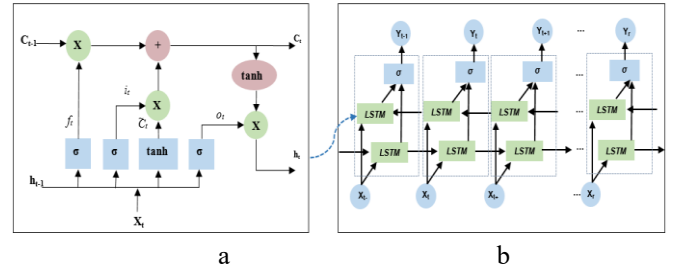


Figure 3. a. LSTM block; b. BiLSTM block

2.6 Evaluating model performance

Model performance evaluation metrics are recall, precision, specificity, Matthews correlation coefficient (MCC), f1-score, and accuracy. These metrics are calculated with the parameters True Positive (TP), True Negative (TN), False Negative (FN), and False Positive (FP) in the confusion matrix. The formulas of model performance metrics are given below [29, 30]:

$$\text{Recall} = \text{TP} / (\text{TP} + \text{FN}) \quad (9)$$

$$\text{Precision} = \text{TP} / (\text{TP} + \text{FP}) \quad (10)$$

$$\text{Specificity} = \text{TN} / (\text{TN} + \text{FP}) \quad (11)$$

$$\text{F1-score} = 2 \times \text{Recall} \times \text{Precision} / (\text{Recall} + \text{Precision}) \quad (12)$$

$$\text{MCC} = \frac{\text{TP} \times \text{TN} - \text{FN} \times \text{FP}}{\sqrt{(\text{TN} + \text{FN}) \times (\text{FP} + \text{TP}) \times (\text{TN} + \text{FP}) \times (\text{FN} + \text{TP})}} \quad (13)$$

$$\text{Accuracy} = (\text{TP} + \text{TN}) / (\text{TP} + \text{FN} + \text{TN} + \text{FP}) \quad (14)$$

3. RESULTS AND DISCUSSION

This study compared the performances of deep learning and machine learning approaches for classifying AD using EEG signals, and it was also investigated whether there was a significant difference in EEG signals between open eyes and closed eyes at resting-state. The raw 4-second EEG signals of AD and HC groups from the Fp1 channel at resting-state with open eyes and closed eyes are given in Figure 4.

The raw EEG signals from other channels have similar characteristics. When plots of the raw EEG signals were examined, EEG signals between HC and AD groups were different. The EEG signals of AD group was lower than HC group. In addition, EEG signals recorded at resting-states with open eyes and closed eyes were also different from each other.

In the study, three different experiments were conducted: a) EEG signals recorded from 48 subjects at resting-state with open eyes and closed eyes, were used b) EEG signals recorded from 24 subjects at resting-state with their open eyes, were used, and c) EEG signals recorded from 24 subjects at resting-state with their closed eyes were used. In all experiments, the k value of the kNN algorithm was chosen as 5 and the "KernelFunction" value of the SVM algorithm was chosen as "rbf". BiLSTM hyper-parameters were used as "MaxEpochs" value 3000, "InitialLearnRate" value 0.001, "MiniBatchSize" value 384, "SequenceLength" value 1000, "GradientThreshold" value 1, and "optimization method" value Adam, respectively. The confusion matrix parameters of the experiments are given in Table 3.

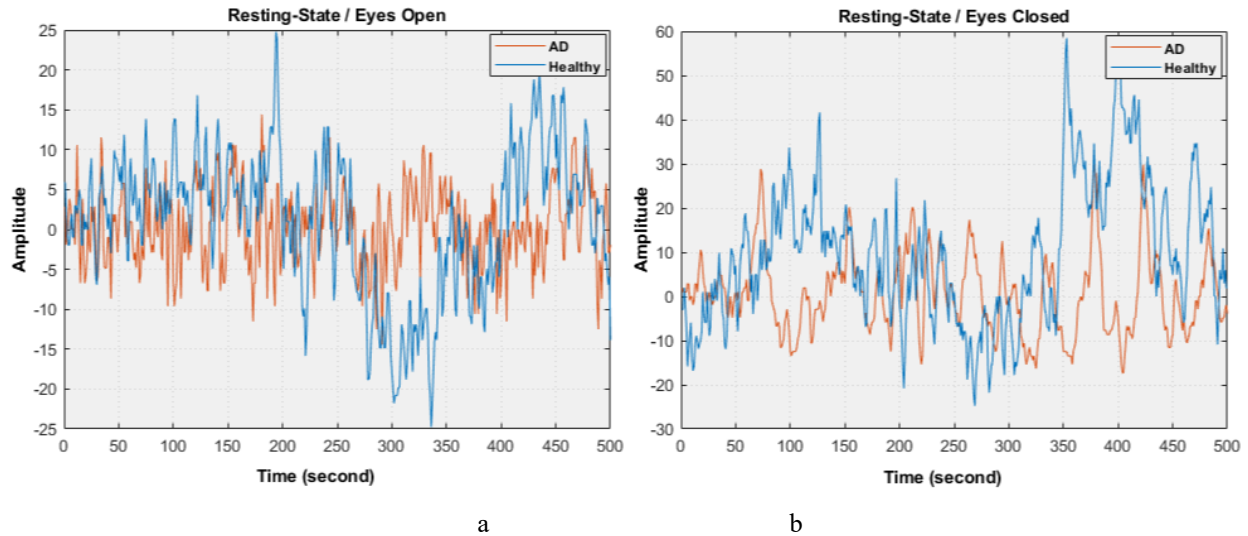


Figure 4. a. Raw EEG signal – open eyes; b. Raw EEG signal – closed eyes

In all experiments, the BiLSTM deep learning algorithm has the highest number of correctly classified data. When the confusion matrix of the BiLSTM algorithm was examined, the total number of correctly classified samples (TP+TN) in Experiment 1 was 296, the total number of correctly classified samples in Experiment 2 was 293, and the total number of correctly classified samples in Experiment 3 was 601. Experiment 3 results, in which EEG signals from 48 subjects at resting-state with open eyes and closed eyes were used, had the highest number of correctly classified samples. In the confusion matrix parameters of Experiment 3, TP was 298, FP was 3, FN was 4, and TN was 303. The performance of deep learning and machine learning algorithms evaluated using the recall, specificity, precision, f1-score, MCC and accuracy values. These values were calculated from the confusion matrix parameters. The performance results of deep learning and machine learning algorithms are given in Table 4.

When the results of the experiments in Table 4 are examined, the BiLSTM algorithm had the highest performance in all experiments. The performance of the BiLSTM deep learning algorithm was followed by RF (95.39%), kNN (93.09%), and SVM (87.50%) algorithms in all experiments, respectively. The accuracy values of the BiLSTM algorithm were 97.37% in Experiment 1 (open eyes), 97.70% in Experiment 2 (closed eyes) and 98.85% in Experiment 3 (open eyes, closed eyes). In the data analysis, deep learning algorithms generally achieve higher performance compared to machine learning algorithms. Machine learning algorithms (RF, kNN, or SVM etc.) are insufficient in the analysis of data in case of a large number of data. Therefore, one of the main reasons for the success in performance analysis was the use of the BiLSTM deep learning algorithm. Experiment 1 and Experiment 2 performance results showed that on this EEG dataset, EEG

recordings resting-state with closed eyes were more effective than EEG recordings resting-state with open eyes. Among the experiments, BiLSTM algorithm had the highest performance in Experiment 3, where there was a higher number of subjects. Performance analysis results of Welch spectral analysis and BiLSTM algorithm in Experiment 3 were calculated as 0.986 recall, 0.990 precision, 0.990 specificity, 0.977 MCC, 0.988 f1-score, and 98.85% accuracy. If these values of the model performance criteria are close to 1, it indicates that there is no random success of the model. While evaluating the performance of the model, the other model evaluation criteria, especially the f1-score should be examined as well as accuracy. Accuracy is the number of correctly predicted data divided by the total number of data. The f1-score is the harmonic mean of precision and sensitivity. If the distribution between groups in the data set is not balanced, only the examination of accuracy may not give reliable results, f1-score gives accurate results even if the distribution between groups is not balanced. Therefore, it is more appropriate to examine the f1-measure as well as accuracy in the analysis of models. When Table 4 is examined, besides the high accuracy of the classification algorithms, the f1-scores were close to 1. In Figure 5, the accuracy values of the deep learning and machine learning algorithms in the experiments are given.

In all experiments, BiLSTM deep learning algorithm achieved higher success than machine learning algorithms. The fact that deep learning models achieve higher success than machine learning models is an expected result, especially in the analysis of non-linear and non-stationary signals such as EEG recordings where the number of data is sufficient. Comparative analysis of the results of the proposed model and related studies in the literature including EEG-based Alzheimer's diagnosis are given in Table 5.

Table 3. Confusion matrix parameters

Experiments	Labels	SVM			RF			KNN			BiLSTM		
		AD	HC	TP+TN	AD	HC	TP+TN	AD	HC	TP+TN	AD	HC	TP+TN
Experiment 1	AD	150	4	266	143	11	290	150	4	283	149	5	296
	HC	34	116		3	147		17	133		3	147	
Experiment 2	AD	88	50	249	129	9	293	135	3	271	136	2	297
	HC	5	161		2	164		30	136		5	161	
Experiment 3	AD	294	7	548	288	13	590	261	40	561	298	3	601
	HC	53	254		5	302		7	300		4	303	

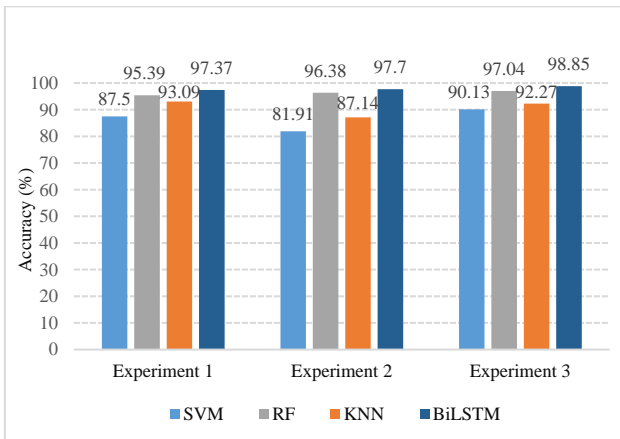
Table 4. Performance results of machine learning and deep learning algorithms

Experiments	Algorithms	Labels	Recall	Precision	Specificity	F1- score	MCC	Accuracy
Experiment 1	SVM	AD	0.815	0.974	0.966	0.887	0.764	87.50%
	RF	HC	0.979	0.928	0.930	0.953	0.909	95.39%
	kNN	AD	0.898	0.974	0.970	0.934	0.864	93.09%
	BiLSTM	HC	0.980	0.967	0.967	0.973	0.947	97.37%
Experiment 2	SVM	AD	0.946	0.637	0.763	0.761	0.656	81.91%
	RF	HC	0.984	0.934	0.948	0.959	0.927	96.38%
	kNN	AD	0.818	0.978	0.978	0.891	0.797	87.14%
	BiLSTM	HC	0.964	0.985	0.987	0.974	0.953	97.70%
Experiment 3	SVM	AD	0.847	0.976	0.973	0.907	0.812	90.13%
	RF	HC	0.982	0.956	0.958	0.969	0.941	97.04%
	kNN	AD	0.973	0.867	0.882	0.917	0.850	92.27%
	BiLSTM	HC	0.986	0.990	0.990	0.988	0.977	98.85%

Table 5. A comparison of studies on EEG-based Alzheimer's diagnosis

Researchers	Signal Processing	Dataset	Best Classifier	Resting-State	Accuracy
Pirrone et al. [10]	SSTL	68 (48 AD, 20 HC)	DT	closed eyes	97%
Yu et al. [11]	PSI	60 (30 AD, 30 HC)	N-TSK	open eyes closed eyes	94.78% 97.3%
Kulkarni and Bairagi [31]	Complexity-based features	100 (50 AD, 50 HC)	SVM	closed eyes	96%
Fiscon et al. [32]	WT	72 (49 AD, 23 HC)	DT	closed eyes	83.3%
Aslan [33]	WT	48 (24 AD, 24 HC)	kNN	closed eyes & open eyes	91.12%
Gómez et al. [34]	Bispectral features	36 (17 AD, 19 HC)	LR	-	86.11%
The proposed deep learning model	Welch spectral analysis	24 (12 AD, 12 HC)	BiLSTM	open eyes	97.37%
		48 (24 AD, 24 HC)		closed eyes	97.70%
				closed eyes & open eyes	98.85%

SSTL: Finite response filter, shift-to-the-left; PSI: Phase synchronization index; N-TSK: Network-based Takagi-Sugeno-Kang fuzzy classifier; WT: Wavelet Transform; DT: Decision Trees; LR: Logistic regression

**Figure 5.** Accuracy performance results of classification algorithms

The proposed model is discussed with the studies in the relevant literature presented in Table 5, according to signal preprocessing methods, dataset, resting-state condition, classification methods and accuracy values. In this study, a deep learning approach was proposed to automatic diagnosis of AD from resting-state EEG recordings using welch spectral analysis. In the signal preprocessing stage, the features were extracted by welch spectral analysis. When we examined the relevant literature, methods such as SSTL [10], PSI [11], complexity-based features [31], WT [32, 33] and bispectral features [34] were used in the signal preprocessing stage. In this study, welch spectral analysis was preferred for feature extraction. Because of its advantages such as having less bias, less processing load, creating a softer spectrum, not making

any assumptions about the input data, applicability to all kinds of signals and providing high performance compared to other methods [23]. When the datasets are examined in the relevant literature, the datasets used in the studies are private datasets [31-32], except for the Aslan [33] study. The dataset used in this study is an accessible and public dataset. The use of the public version reduces bias and increases transparency and accountability. Public datasets are important in terms of producing innovative solutions, creating new models, increasing the quality of data and creating a basis for uses in the data field. Aslan used the same public dataset and using the WT and kNN algorithm, it achieved 91.12% accuracy [33]. When different resting-state conditions are examined; The effectiveness of EEG recordings recorded in the resting-state with closed eyes state is higher than in the resting-state with open eyes state [11]. Similarly, in this study, the effectiveness of EEG recordings recorded in the resting-state with closed eyes condition was higher than in the resting-state with open eyes condition. However, the highest success (98.85%) was achieved by using both the recordings in the eyes-open resting state and the recordings recorded in the eyes-closed resting state in this study. In Table 4, the algorithms used in the relevant literature were DT [10, 32], N-TSK [11], SVM [31], kNN [33], and LR [34]. In this study, the performances of BiLSTM algorithm and machine learning algorithms were compared. In more recent studies, deep learning approach is preferred because deep learning algorithms are more successful than machine learning algorithms in classification tasks [35]. To the best of our knowledge, this study had the most success in diagnosing AD. The main reason for this success is the use of deep learning approach and welch spectral analysis. Because the proposed model was effective in

reducing high variance compared to many machine learning algorithms such as RF, SVM or kNN, and also provided performance increase by reducing bias.

This study has some limitations. Firstly, the study was focused to classify AD and HC groups from EEG signals. A multi-classification study can be investigated to determine stages of AD from EEG signals. Secondly, EEG signals were recorded from 48 subjects, by Florida State University researchers. Therefore, the external validity and generalizability of the results of the study is limited to 48 subjects. Despite these limitations, the proposed deep learning model offers significant strengths. The strengths of the deep learning models were a) providing high performance compared to the known related studies in the task of classification of EEG-based AD, using the BiLSTM deep learning algorithm, b) comparing the effectiveness of EEG signals at different resting-states, and c) reducing the prediction bias with the Welch spectral analysis method.

4. CONCLUSIONS

In conclusion, we proposed a deep learning approach for early AD diagnosis from resting-state EEG recordings that successfully combines the Welch spectral analysis method and BiLSTM algorithm. Three different experiments were carried out in the study. Experiment 1 was performed using EEG recordings at resting-state with open eyes. Experiment 2 was performed using EEG recordings at resting-state with closed eyes. Experiment 3 was performed using both the recordings at resting state with open eyes and the recordings at resting state with closed eyes. In all experiments, the performances of RF, kNN, SVM, and BiLSTM algorithms were compared using Welch spectral analysis method. The highest performance was achieved using the BiLSTM algorithm in Experiment 3. The BiLSTM algorithm achieved promising performance with 98.85% accuracy, 0.986 recall, 0.990 precision, 0.990 specificity, 0.988 f1-score, and 0.977 MCC in Experiment 3. However, the performance of Experiment 2 was higher than that of Experiment 1. The values of the model performance evaluation criteria are quite high. These results indicate that the model does not have a random performance [36]. The accuracy of the diagnosis is greatly influenced by the experience and situation of the experts, so the diagnostic process is complex and uncertain, subjective. The proposed deep learning model can assist expert in the diagnosis of AD. Although there is no definitive cure for AD, early diagnosis of the disease can slow down the process and improve the quality of life. Therefore, early diagnosis of AD offers important opportunities for early intervention. Moreover, these experts need long-term training. Deep learning models have a great capacity to process data automatically. The practical benefits of automated methods based on the analysis of EEG signals using deep learning are to support experts and decrease the workload, and to clarify the diagnostic process. In the future, the authors aim to determine which channels are more sensitive in the diagnosis of AD and to use the proposed deep learning model with a dataset of different races and countries. Moreover, these techniques can be applied to different biomedical signals. Also, it may be suggested to investigate multiple classification tasks including different neurodegenerative diseases, such as spinal muscular atrophy, Huntington's disease, and amyotrophic lateral sclerosis. Multiple classification studies involving different

neurodegenerative diseases may provide important contributions to the relevant literature.

AVAILABILITY OF DATA AND MATERIAL

The EEG recordings are publicly accessible datasets: Pineda, A. M., Ramos, F. M., Betting, L. E., Campanharo, A. S. (2020). Quantile graphs for EEG-based diagnosis of Alzheimer's disease. *Plos One*, 15(6): e0231169. Data from: "https://osf.io/s74qf".

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