2023 5th International Conference on Bio-engineering for Smart Technologies (BioSMART) | 979-8-3503-3849-2/23/$31.00 ©2023 IEEE | DOI: 10.1109/BioSMART58455.2023.10162117

EEG-Based Classification of Stages of Alzheimer's Disease (AD) and Mild Cognitive Impairment (MCI)

Gabriel Ivan A. Calub, Erickson N. Elefante, Jose Colin A. Galisanao, Sofia Lyn Beatrice G. Iguid, Jeremae C. Salise, and Seigfred V. Prado, *Senior Member, IEEE*
Department of Electronics Engineering, University of Santo Tomas, Manila, Philippines, 1008

***Abstract*—Alzheimer's Disease (AD) accounts for 60-80% of dementia cases worldwide. According to the World Alzheimer Reports from Alzheimer's Disease International, dementia is now the 7th leading cause of mortality around the world while also being one of the highest costs to society. Diagnosing Alzheimer's Disease as early as possible is necessary to lessen the chances of the disease progressing to dementia and lessen the impacts - physical, physiological, social, and economic, on caregivers. No existing studies that use EEG as a modality for the analysis of changes in brain activity, have yet predicted the chances of patients with MCI symptoms eventually progressing to AD. Furthermore, none of these studies has characterized EEG signals of patients during the different stages of AD progression. In this study, we developed a machine learning model that can characterize electroencephalogram (EEG) signals and classify them accordingly for the detection and diagnosis of the different stages of AD. The proposed system was evaluated according to standard performance metrics. Upon performing cross-validation, our results show that the proposed system can accurately classify the stages of AD based on the patients' recorded EEG signals. Future work can focus on testing the proposed system on a larger and more diverse population with varying demographics, genetic backgrounds, and disease subtypes to validate its effectiveness in the early detection of mild cognitive impairment (MCI) and Alzheimer's disease (AD).**

***Index Terms*—Alzheimer's disease, severity, mild cognitive impairment, electroencephalography, artificial neural network**

I. Introduction

Alzheimer's Disease (AD) is a degenerative neurological condition that leads to functional disconnections in various cortical regions, resulting in permanent neuronal loss. [1]. It is the most common neurodegenerative disease among the elderly, which causes a gradual decline in cognitive function, significantly affecting their overall quality of life. Also, it is the most prevalent form of dementia, responsible for approximately 60–80% of all cases [2]. Currently, there are around 50 million people worldwide affected by dementia, and approximately 10 million new cases reported each year. Of these cases, about two-thirds reside in low- and middle-income countries. However, AD and dementia are not recognized as a major public health issue in low-income countries, such as the Philippines. It is seen as something that naturally comes with old age.

G.I.A. Calub[1], E.N. Elefante[2], J.C.A. Galisanao[3], S.L.B.G. Iguid[4], J.C. Salise[5], and S.V. Prado[6] are affiliated with the Department of Electronics Engineering, Faculty of Engineering, University of Santo Tomas, Manila, Philippines, 1008. The corresponding author is S.V. Prado (svprado@ust.edu.ph).

Patients diagnosed with these kinds of diseases are also seen as an economic burden because of the loss of productivity in the workplace and society. The symptoms of AD involve a gradual loss of brain cells over time, resulting in irreversible cognitive decline. These symptoms include memory loss, difficulty in learning new things and performing calculations, distorted perception of space, depression, delusions, and overall cognitive decline [3]. Hence, developing a biomarker for detecting and classifying AD will help patients get treatment as early as possible and help the people around them understand these kinds of diseases and provide appropriate assistance.

The evolution of the disease follows five stages: first, the "preclinical" stage, which is an asymptomatic stage, but the brain lesions of Alzheimer's disease are already present. Second, is Mild Cognitive Impairment (MCI) stage where patients have some memory impairments but maintain their functional capacities. Third, the "mild" AD stage where cognitive defect is notable. Fourth, "moderate" AD stage, and lastly, "severe" AD stage where almost all motor and cognitive functions are deteriorated [4]. The effects of AD include: (1) amyloid load deposition [5], wherein there is a relationship between greater amyloid burden and cognitive decline which suggests that as amyloid buildup progresses, subtle changes in cognitive abilities may accumulate over time; (2) neurodegeneration [5], which is a process that can result in permanent damage and death of neurons and a common final pathway present in aging and neurodegenerative diseases; and (3) lower synchronization between different brain regions [5]–[8], which hinders the communication and information integration between different regions, thus, affecting one's cognitive ability.

Mild cognitive impairment (MCI), on the other hand, is a syndrome characterized by cognitive decline that, although not interfering with daily life, is greater than expected given an individual's age. Roughly 60% of the individuals diagnosed with MCI progress to develop dementia within 5 years of MCI diagnosis [9]. Individuals with MCI are at high risk of developing dementia as it is regarded as the transitional stage between healthy aging and dementia, thus, a reliable and effective approach for early detection of MCI has become a critical challenge [10]; given the reliability and effectiveness, another factor to be considered is cost-effectiveness, to make testing inclusive and provide respective treatment to diagnosed individuals. Developing biomarkers that are evident with the early, preclinical phase of AD is crucial since patients are more

likely to benefit from disease-modifying treatments if given early in the disease process before significant brain damage occurs or even before the onset of MCI [2].

On the other hand, increasing evidence suggests that EEG biomarkers may help identify early-stage neuronal abnormalities before any detectable cortical tissue loss or cognitive decline occurs. Unlike other methods used to obtain candidate AD biomarkers, EEG is a noninvasive and cost-effective method for measuring brain activity, with established usefulness. [11]. Despite being available for several decades, using EEG as a cognitive biomarker for detecting and predicting MCI and AD in individuals is a relatively new undertaking. Scalp EEG has the potential to become a significant modality to extract biomarkers for the early stages of MCI and AD, enabling diagnosis before the clinical phase [12].

In this study, we developed a machine learning model that can characterize EEG signals and classify them accordingly for the detection and diagnosis of the different stages of AD.

II. Materials and Methods

This section discusses the materials and methodology of the study. The framework is summarized and visualized in Fig. 1a.

A. Description of the Dataset

The dataset used in this study was taken from [13]. The EEG signals were obtained with the approval of the local ethics committee of the Faculty Hospital Hradec Karlove. The EEG data were gathered from a cohort of 57 patients diagnosed with Alzheimer's disease, 7 patients with mild cognitive impairment (MCI), and 102 healthy participants who were matched for age and displayed no previous memory or cognitive deficits. The diagnosis of Alzheimer's disease in all patients was established using the National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) Alzheimer's Criteria. To assess cognitive function, the Mini-Mental State Examination (MMSE) Test was employed. The control group did not fulfill the NINCDS-ADRDA Alzheimer's criteria and was devoid of any indications of cognitive decline or other neurodegenerative disorders. The mean MMSE score of the Alzheimer's disease group was 14.9 (with a standard deviation of 2.3), while the mean ages of the three groups were 70.5 ± 4.9 years for the Alzheimer's disease group, 67 ± 7.6 years for the MCI group, and 72.2 ± 5.3 years for the normal subjects.

B. EEG Recording and Pre-processing

1) Recording of EEG Data: EEG signals were captured using a 21-channel digital EEG setup (Figure 1b) with a sampling frequency 256 Hz (Walter EEG PL-231, Germany) and a TruScan 32 with a sampling frequency of 128 Hz (Alien Technik Ltd., Czech Republic). The EEG electrodes were positioned in accordance with the 10-20 System during all recordings, which were conducted under similar standard conditions. The electrodes were named after the cerebral lobe they were positioned above, with pre-frontal electrodes (Fp) placed above the anterior part of the frontal lobe. Even numbers (2, 4, 6, 8) represented the right hemisphere, odd numbers (1, 3, 5, 7) represented the left hemisphere, and "z" represented an electrode on the midline. The resting state recording lasted 15 minutes, during which the participants were lying down in a comfortable position with their eyes closed [13].

2) Pre-processing of EEG Data: The EEG signals were filtered using a 10th order Butterworth bandpass filter with a low cut-off frequency of 0.5 and a high cut-off frequency 60Hz to eliminate out-of-band noise. A 10th order Butterworth filter was used since it would have a very sharp transition or a steep roll-off between the passband and stopband, resulting in a very steep attenuation of frequencies within the specified frequency range. Additionally, a notch filter was employed to eliminate the remaining line noise present in the initial signal at 50 Hz.

C. Feature Extraction

The next stage in the pipeline is feature extraction (see Fig. 1), which is used to derive a feature vector from the data vector. Feature extraction is used to uncover features or latent information that accurately discriminate the signals against other classes. Additionally, in this process, the features represent task-relevant information transforming raw EEG signals into a small number of relevant values [14].

1) Linear Univariate Features: Linear univariate features were extracted from EEG signals. They refer to a set of signal processing features that quantify the spectral properties of a signal. These features include the average band power in the delta, theta, alpha, beta, and gamma frequency ranges, which are commonly used to analyze brain signals such as EEG. In addition, the theta-to-beta ratio (TBR) is another feature used to assess the balance of activity between the theta and beta frequency bands. Delta average band power represents the average power of the EEG signal in the delta frequency range (0.5-4 Hz), while theta average band power is the average power in the theta frequency range (4-8 Hz). Alpha average band power quantifies the average power in the alpha frequency range (8-13 Hz), and beta average band power represents the average power in the beta frequency range (13-30 Hz). Gamma average band power is the average power in the gamma frequency range (30-100 Hz). TBR is the ratio of the theta power to the beta power. These features have been extensively utilized in studies related to brain activity, and they have been useful in various applications such as cognitive workload assessment, emotion recognition, and neurological disorder diagnosis [15].

2) Non-linear Univariate Features: Different non-linear univariate features were also extracted from the EEG signals such as sample entropy (SampEn) [16], Shannon entropy (SE) [17], [18], dispersion entropy (DE) [19], [20] and multiscale sample entropy (MSEnt) [21].

Sample entropy can be interpreted as the opposite of the logarithm of the likelihood that two sequences, which are alike at m points, will remain similar at the following point within a specific range of tolerance r, while excluding instances where

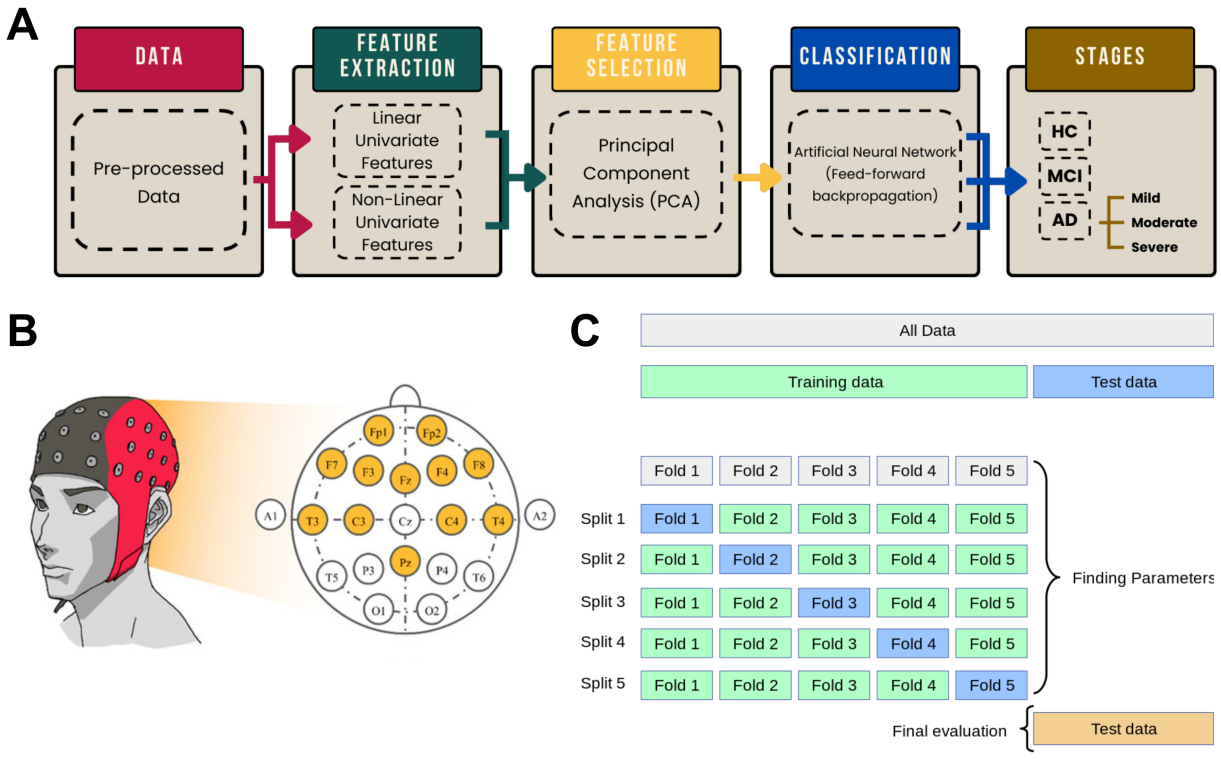


Fig. 1. **(a) Methods Framework.** First, the EEG data was processed; this process extracted both linear and non-linear univariate features, allowing us to obtain a numerical representation of the EEG signals. To ensure that we only use relevant features, Principal Component Analysis was employed as a feature selection technique. The resulting data was then classified using a trained Artificial Neural Network, which enabled us to categorize it into its appropriate groups. **(b) EEG Headset.** EEG signals were captured using a 21-channel digital EEG (Walter EEG PL-231). The EEG electrodes were positioned in accordance with the 10-20 System. **(c) *K*-fold cross-validation.** The data was divided into folds to form different sets of training and testing data. The machine learning model was trained and tested k times, and the average performance evaluation measures were averaged to compute the overall performance.

the sequences are identical. Shannon entropy was used to measure uncertainty of randomness in the observed time-series [17]. It quantifies the amount of information that is contained in a probability distribution. In other words, it measures the degree of randomness or unpredictability in a system [18]. Dispersion entropy is a complexity measure that incorporates amplitude information using the normal cumulative distribution function (NCDF). By capturing changes in both frequency and amplitude, it can effectively detect changes in signal dynamics [19], [20]. Lastly, multiscale sample entropy is a method for assessing the complexity of a signal across multiple time scales. The method involves calculating the sample entropy on coarsely grained sequences that capture the system's dynamics at different temporal resolutions.

D. Feature Selection: Principal Component Analysis

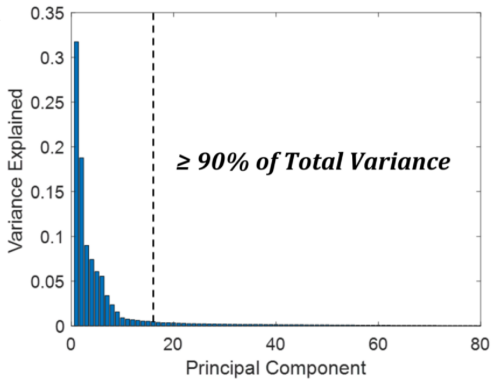
Principal Component Analysis (PCA) is a type of unsupervised learning technique that enables data compression by projecting high dimensional data into a lower dimensional space. This process significantly simplifies process monitoring procedures by reducing the dimensionality of the data [15], [22], [23]. PCA is a dimensionality reduction technique that produces a lower dimensional representation of the data while preserving the correlation structure between the variables. It is particularly effective at capturing the variability in the data, making it a valuable tool for exploratory data analysis. By projecting the data onto a lower dimensional space in a least square sense, PCA can identify and capture the most significant inconsistencies in the data while ignoring less important inconsistencies. Overall, PCA provides a powerful method for exploring and analyzing high dimensional data in a more manageable way [22].

E. Classification: Artificial Neural Network

In the process of classifying the feature vectors obtained in the previous step, an artificial neural network (ANN) was used. ANN is a type of information processing system that is modeled after the way the brain works. ANNs are composed of interconnected nodes or neurons, organized in layers, that process and transmit information using a set of mathematical operations. An optimization algorithm is employed to regulate the neurons in the network, minimizing the error between the predicted and actual output. This mechanism, referred to as backpropagation, involves transmitting the error backward through the network and modifying the weights and biases accordingly. ANNs are ideally suited for pattern classification problems, as they can learn from examples, reproduce any non-linear input function, and possess a highly parallel and regular structure [24]–[26].

Feed-Foward Back Propagation Network: The primary function of a Feed-Forward Back Propagation Network (FF-BPN) is to discover and map the connections between inputs

A



B

K-Fold	Accuracy			Sensitivity	Specificity	Precision	F1-Score
	Training	Validation	Testing				
1	100	88.9	100	100	100	100	100
2	100	94.4	100	100	100	100	100
3	100	94.4	94.4	98.33	98.75	93.33	95.13
4	100	88.9	94.4	97.78	98.82	90	92.16
5	100	100	88.9	89.33	97.29	86	85.33
6	98.8	94.4	88.9	92.5	97.5	90	89.14
7	100	100	88.9	88	97.42	88.33	85.42
8	100	100	94.4	93.33	98.67	95	93.14
Average	**99.85%**	**95.13%**	**93.74%**	**94.91%**	**98.56%**	**92.83%**	**92.54%**

Fig. 2. **Feature Selection, Classification, and Cross-Validation. (a) Variance explained by the principal components:** The variance explained by each of the principal components were plotted. As shown, taking only 16 out of the 190 principal components already capture more than 90% of the total variance. Hence, the rest of the principal components only present redundant and negligible contribution in the total information presented by the features, and can therefore be discarded before training the machine learning model. **(b) ANN Performance Evaluation and Cross-Validation.** An 8-fold cross-validation was performed to evaluate the performance of the trained ANN model, as well as to account for possible overfitting during training. Different performance metrics, such as accuracy, sensitivity, specificity, precision and F1-score, were computed for each fold.

and outputs. In order to attain the least amount of error, a system's weight values, and threshold values are also adjusted using the FFBPN learning rule [27]. FFBPN computes the gradient in a neural network very straightforwardly and effectively. The method's accuracy was improved by using back-propagation neural networks with the Levenberg-Marquardt algorithm, which has a faster convergence rate [28].

F. Evaluation of Classification Performance

1) Confusion Matrix: Confusion matrix is a square matrix of size N, where N represents the number of target classes utilized to evaluate the classification model's performance. It is employed to compare the actual target values with the predictions made by the machine learning model. The confusion matrix provides a comprehensive overview of the classification model's accuracy and the types of errors it is generating.

2) Accuracy: Accuracy is a metric that indicates how well a model performs over all classes. It is most effective when all classes are of equal importance. To determine the accuracy score, the total number of correct predictions is divided by the overall number of predictions that have been made.

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \tag{1}$$

True positive (TP) result signifies that the model correctly predicted the positive class. True negative (TN) result means that the model accurately predicted the negative class. False positive (FP) outcome arises when the model incorrectly predicts the positive class, whereas a false negative (FN) outcome occurs when the model inaccurately predicts the negative class.

3) Sensitivity: Sensitivity is a metric that assesses a machine learning model's ability to identify positive instances accurately. This performance evaluation measure provides insights into how many positive instances the model correctly classified. This metric is similar to *Recall* metric. If a model has high sensitivity, it will correctly identify most positive instances and have only a few false negatives. Sensitivity is essential because it determines a model's ability to detect all positive instances and make accurate predictions.

$$Sensitivity = \frac{TP}{TP + FN} \tag{2}$$

4) Specificity: Specificity is a metric that calculates the proportion of true negatives that the model correctly identifies. It means that there will be some actual negatives that the model may classify as positive, known as false positives.

$$Specificity = \frac{TN}{TN + FP} \tag{3}$$

5) Precision: Precision is the ratio of True Positives to all Positives. It is calculated by dividing the number of correctly classified positive samples (True Positive) by the total number of classified positive samples (either correctly or incorrectly).

$$Precision = \frac{TP}{TP + FP} \tag{4}$$

6) F1-Score: The F1 score is a metric used to compare the performance of two classifiers. It is defined as the harmonic mean of Precision (P) and Recall (R). When comparing two classifiers, F1 scores for both can be used to determine which produces better results. For example, if classifier A has a higher recall, and classifier B has a higher precision, the F1 scores of both classifiers can be used to determine which one is performing better.

$$F1 - score = \frac{2(P * R)}{P + R} \tag{5}$$

7) K-Fold Cross-Validation: K-fold Cross-Validation is a widely used technique employed in this study to assess the performance of a machine learning model. This is a popular method due to its simplicity and potential to provide a more impartial and reliable measure of the model's overall effectiveness and accuracy. It involves the random dividing of the dataset into k equal-sized folds.

III. Results and Discussion

A. Feature Extraction

Before extracting the features, the pre-processed signal was normalized and underwent band extraction to eliminate the out-of-band noise. The features extracted from the signals are their linear and non-linear univariate features. The extracted linear features include the delta, theta, alpha, beta, gamma, and theta to beta ratio, while the extracted non-linear features are sample entropy, Shannon entropy, dispersion entropy, and multi-scale entropy. Extracting the linear and nonlinear features of the signals resulted in a total of 190 features. Thus, each feature vector had a size of 1×190. Features that had NaN values were converted to 0.

B. Feature Selection

PCA was used for the feature selection process in order to identify the most significant features that contribute to the largest variance in the data, thereby reducing the dimensionality of the data before training the machine learning model. After PCA, the dimensionality of the feature vector was reduced from 190 to 16 dimensions, i.e., the 16 principal components that capture more than 90% of the total variance were only considered and the rest were discarded (see Fig. 2a). This is significant in reducing the computational complexity of the machine learning model that will be used for classification. Furthermore, the projection onto the first 16 principal components (or dimensions) were used as input in training the Artificial Neural Network (ANN) model.

C. Performance Evaluation

The confusion matrix serves as a tool for assessing the performance of a classifier by providing a concise summary of the number of accurate and inaccurate predictions made by the algorithm. Based on our results, the classifier correctly classified 12 instances of mild AD, 14 instances of moderate AD, 15 instances of severe AD, 7 instances of HC, and 50 instances of MCI.

In addition, an 8-fold cross-validation process is utilized to evaluate and assess the model's performance comprehensively. The ANN model yielded notable average classification rates of 99.85% for training, 95.13% for validation, and 93.74% for testing. These findings demonstrate the model's ability to accurately classify the data. A high average accuracy rate for the training implies that the model was able to learn the patterns in the training data accurately and generalize this learning to new data. On the other hand, the high average classification accuracy rate for validation means that the model is capable of generalizing to new data and is not overfitting to the training data. Finally, the relatively high average classification accuracy rate for testing indicates that the model can accurately classify new, unseen data.

The sensitivity, specificity, precision, and F1-score of the testing dataset were also obtained. The sensitivity of 94.91% indicates that the model was able to correctly identify a high proportion of positive cases, while the specificity of 98.56% suggests that the model was able to correctly identify a high proportion of negative cases. The precision of 92.83% indicates that when the model predicted a positive case, it was correct 92.83% of the time. Finally, the F1-score of 92.54% is a weighted average of the precision and recall (or sensitivity) of the model, indicating an overall balance between the two. These results are significant and demonstrate the effectiveness of the ANN model in accurately classifying the different stages of AD progression.

IV. Conclusion and Future Work

In this study, a machine learning model was created to classify the stages of AD and MCI using EEG data obtained from healthy (HC), MCI, and confirmed AD patients. More importantly, this study classified 3 stages of AD: Mild, Moderate, and Severe. Following the findings of this study, the authors conclude that the machine learning model has the potential to accurately classify different stages of Alzheimer's disease (AD) and mild cognitive impairment (MCI). The model achieved high accuracy rates for the training dataset, suggesting that the model has effectively learned the underlying patterns in the data. However, the accuracy of the model on the testing dataset was slightly lower, indicating that the model may have overfitted the training data.

Furthermore, this study presents a machine learning model that can detect the possibility of the progression of MCI to AD at an early stage. Identifying patients with MCI who are at high risk of progressing to AD can lead to early diagnosis and intervention. Early detection of AD can help patients and their families prepare for potential consequences. It can also help medical professionals to implement interventions that can slow down the progression of the disease.

To further validate the effectiveness of the proposed system in the early detection of mild cognitive impairment (MCI) and Alzheimer's disease (AD), future studies may focus on testing the model on a more extensive and diverse population, including individuals with varying demographics, genetic backgrounds, and disease subtypes. Furthermore, combining EEG analysis with other biomarkers and clinical measures may enhance the accuracy and reliability of the model, ultimately leading to earlier diagnosis and improved patient outcomes. Overall, the findings of this study present a promising step towards developing a reliable and non-invasive tool for the early detection and monitoring of AD.

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