Diagnosing Alzheimer’s Disease and Frontotemporal Dementia Using Machine Learning and EEG

ABSTRACT

Alzheimer’s disease (AD) and frontotemporal dementia (FTD) are types of neurodegenerative dementias characterized by progressive cognitive decline. Electroencephalography (EEG) signal analysis is becoming a promising, inexpensive method to early diagnose AD and FTD. Prior research has applied machine learning to classify AD and healthy patients (HC) based on EEG readings, but not distinguishing between AD, FTD, and healthy patients. In the present paper, power spectral features will be extracted from raw EEG recordings for random forest classifiers and artificial neural networks to differentiate among AD, FTD, and HC patients. The first two minutes of 88 EEG recordings were used from the 2nd Department of Neurology in Thessaloniki. The models achieved 96%, 92%, and 95% accuracy when dealing with binary classification problems (AD and HC, AD and FTD, HC and FTD) and 90.4% for all three classes. The accuracies improve upon the results of previous literature.

Introduction

Dementia is a “general term for loss of memory, language, problem-solving, and other thinking abilities that are severe enough to interfere with daily life” (*What is,* 2023). The most common form of dementia, Alzheimer’s disease (AD) is a neurodegenerative disease affecting more than six million Americans as of 2023 (“2023 Alzheimer's”, 2023). AD, more common in older individuals, is caused when beta-amyloid proteins accumulate outside neurons and tau proteins accumulate inside neurons, resulting in neuronal cell death and brain tissue damage (“2023 Alzheimer’s”, 2023). The neurons that are affected first control memory, language, and thinking, which may lead to cognitive decline in affected individuals.

Frontotemporal dementia (FTD) is another type of dementia caused by the degeneration of nerve cells in the frontal and temporal lobes of the brain, resulting in an abnormal buildup of tau or TDP-43 protein (“2023 Alzheimer’s”, 2023). According to the Alzheimer’s Association, there are currently 50,000 – 60,000 Americans with FTD, primarily between 45 – 65 (*Frontotemporal,* 2023). Unlike Alzheimer's, however, FTD has no treatment to stop the disease's degenerative progression.

While there is no cure for AD and FTD, early diagnosis of these diseases benefits patients and caregivers by allowing time to adapt to changes in behavior. Additionally, in the case of Alzheimer’s, treatment options can be explored to help lessen symptoms (Leifer, 2003). Conventional techniques, such as clinical-pathologic diagnosis, to early diagnose Alzheimer’s disease are expensive (Petersen, 2018). However, electroencephalography (EEG) is an inexpensive, promising method used to evaluate and diagnose different types of brain disorders, including Alzheimer’s disease and other forms of dementia

(*Electroencephalogram,* 2023). EEG measures electrical activity in the brain through electrodes, or small, metal discs, non-surgically attached to the scalp. To cleanse the raw data collected by electrodes attached to the scalp, preprocessing methods are used to denoise and remove artifacts (Sharma et al. 2019). Afterward, power spectral density features, or the signal's frequency content, are extracted to help detect abnormalities in EEG recordings (Dressler et al., 2004). Supervised machine learning (ML) models are trained using the cleansed data, or training set, before making predictions on new data, or the validation set (Schrider & Kern, 2018).

In the present paper, the researcher will evaluate the accuracy of random forest classifiers and neural networks to differentiate between Alzheimer's disease and frontotemporal dementia. A random forest classifier is a popular ML algorithm that classifies a subject from the outputs of multiple decision trees (DT) (Belgiu & Dragut, 2016). An artificial neural network (ANN) is also a commonly used classification tool that uses processing elements, or nodes, to replicate the structure of the brain (Subasi & Ercelebi, 2005). While there is existing literature surrounding the early diagnosis of Alzheimer's using EEG and ML, little research focuses on ML's applications to differentiate between different types of dementias. The preprocessed dataset used for the present study, consisting of EEG data for patients with AD, FTD, and healthy individuals (HC), was collected by neurologists at the 2nd Department of Neurology of AHEPA General Hospital of Thessaloniki (Miltiadous et al., 2023). After extracting power spectral density features, an experimental design methodology will be used by creating random forest classifiers and artificial neural network models with varying layers and applying them to four classifications, namely (AD and HC), (AD and FTD), (HC and FTD), and (AD and HC and FTD). From there, accuracy, recall, precision, and error on the validation set will be evaluated and compared to existing literature.

Literature Review

Historically, differentiating between AD and FTD has been challenging. Due to the difficulty of associating symptoms with AD and FTD, clinicians tend to misdiagnose FTD patients with Alzheimer's disease or leave them undiagnosed (Beber & Chaves, 2013; Yener et al., 1996). Misdiagnosing or not diagnosing does have serious implications as early diagnosis of FTD and AD is critical for clinicians to begin developing treatment plans. This is especially concerning, however, as medications found to help treat AD have been known to have no benefit and may even worsen symptoms for those with FTD (Neylan & Miller, 2023).

Researchers have turned to electroencephalogram (EEG) to help aid with AD and FTD diagnosis. Due to the complexity of EEG signals, they can be divided into five frequency bands for analysis: delta (0.5 – 4.5 Hz), theta (4.5 – 8.5 Hz), alpha (8.5 – 11.5 Hz), sigma (11.5 – 15.5 Hz), beta (15.5 – 30 Hz), and gamma (30 – 45 Hz). According to a 2010 paper published by the Massachusetts Institute of Technology, slower and reduced complexity of EEG readings has been characteristic of patients with Alzheimer's disease (Dauwels et al., 2010). On the other hand, FTD generally has different frequency band readings in widespread areas of the frontal lobe and parietal lobe compared to AD (Nishida et al., 2011). The differences in EEG frequency bands allow researchers to create ML models that are able to differentiate between diseases.

Much of the existing literature surrounding differential diagnosis by ML models solely focuses on Alzheimer's disease. In a 2014 article published by Tongji University, researchers Yilu Zhao and Lianghua He received 92% accuracy after training support vector machines (SVM) to diagnose Alzheimer's disease (Zhao & He, 2015). Similarly, researchers from the Computing and Cognition Center (CMCC) in Sao Paulo received similar results when they created SVMs to early diagnose AD patients (Trambaiolli et al., 2011). Recall, a support vector machine attempts to identify a hyperplane that is able to distinguish between different groups (Noble, 2006). However, due to the hyperplane dividing the N-dimensional space into two distinct regions, SVMs are more suited for binary classification problems rather than multi-classification. In a paper published by Uninettuno University, Daniele Pirrone utilized DTs, SVMs, and k-nearest neighbor (KNN) algorithms to differentiate between healthy patients, patients with Alzheimer's, and patients with Mild Cognitive Impairment (MCI), for the early stages of dementia (Pirrone et al., 2022). By extracting and algebraically manipulating PSD features, the researchers were able to reach 83% – 97% accuracy when performing binary classifications and 75% accuracy when dealing with all three classes. Much of the AD detection literature using machine learning has been very similar. Increases in model accuracy are a result of different methods for feature extraction. Due to the abundant existing research surrounding AD classification using machine learning algorithms, exploring ML's capabilities to differentiate between types of dementia is more appropriate.

Currently, there are few publications that examine AD, FTD, and healthy differential diagnosis using machine learning and EEG data. Andreas Miltiadous and other researchers at the University of Ioannina obtained 78.5% accuracy for AD detection and 86.3% for FTD detection using DTs and random forest models with mean, variance, IQR, and frequency band power metrics (Miltiadous et al., 2021). These results were fairly similar to previous literature, generally in the range of 80% to 90% accuracy when dealing with binary classification problems (Lindau et al., 2003; Nishida et al., 2011; Caso et al., 2012; Fiscon et al., 2018; Safi & Safi, 2021). However, it is important to note that all of these researchers performed binary classifications when evaluating the accuracy of their models.

Much of the existing literature surrounding machine learning's applications for disease diagnosis focuses on being able to differentiate healthy individuals from patients with dementia. However, little research focuses on being able to differentiate between types of dementia (Dauwels et al., 2010). Of all of the studies that focus on the differential diagnosis of AD, FTD, and healthy patients, none of the researchers chose to evaluate the accuracy of a model to distinguish between all three classes. Due to similar symptoms and different treatment plans, it is imperative that correct early diagnosis is made to ensure that patients are appropriately treated. This gap in knowledge led to the central question of the research: To what extent are ML algorithms able to distinguish between different types of dementia, specifically Alzheimer's disease and frontotemporal dementia, based on EEG data? After exploring the characteristics of EEG readings with respect to AD and FTD, the researcher hypothesizes that supervised learning algorithms will have moderate to high accuracy in differentiating AD and FTD from healthy individuals. To answer the research question, the researcher will use an experimental design methodology to create and tune random forest classifiers and neural networks with multiple layers, which will be used for three binary classification problems (AD and FTD, AD and HC, FTD and HC) and one multi-classification problem (AD and FTD and HC). Using power spectral density (PSD) feature extraction, the researcher hopes to improve the accuracy of the models. Afterward, the accuracy and validation set error will be evaluated and the researcher will provide their recommendation on an optimal model to classify Alzheimer's and FTD.

Methods

This research aims to assess the ability of ML algorithms to differentiate between AD, FTD, and healthy patients. To answer the central question of research, an experiment design methodology similar to past literature will be used in order to create and tune different machine learning models to obtain the highest accuracy and lowest error on the validation set. An experimental methodology was chosen as many researchers who had previously researched differential diagnosis had developed and tuned models of their own. Additionally, the researcher could compare the accuracy of the new model with existing supervised learning models. Similar to other papers in the field, the methodology will be split into four parts: data acquisition, preprocessing, feature extraction, and classification.

Data Acquisition

The publicly available dataset used for this study was composed of 88 EEG recordings (36 AD, 23 FTD, 29, CN) collected in a resting, eyes-closed state by neurologists at the 2nd Department of Neurology in Thessaloniki (Miltiadous et al., 2023). The EEG readings were sampled from 19 scalp electrodes using the international 10-20 system at a rate of 500 Hz for a time period ranging from 5-16 minutes. Due to the significant memory allocation used when analyzing 5-16 minutes of raw EEG data at 500 Hz, the first two minutes (120 seconds) of EEG readings, normalized to 128 Hz, will be used for analysis.

Preprocessing

In the preprocessing step, the MNE-Python library was used to filter the EEG data. To remove artifacts and other noise, the low and high cutoff frequencies used were 0.1 Hz and 45 Hz, respectively. Epochs of five seconds with one-second overlap were then created using the filtered EEG data, and bad epochs were dropped from further analysis.

Feature Extraction

In the feature extraction step, features to help assist with classification are extracted from the preprocessed EEG data. Generally, when analyzing EEG data, power spectral density, or the distribution of power of different frequency components, is a feature extracted from the time-frequency domains (Perez-valero et al., 2021). Patients with Alzheimer's disease tend to have decreased alpha and beta power and higher theta power in the power spectrum compared to patients with FTD (Nardone et al., 2018). To extract PSD features, the epochs for the Alzheimer's subjects were concatenated to create a continuous dataset. Similarly, the EEG signals for the healthy and FTD classes were also concatenated. The power spectral density of the EEG data was then computed using the Welch method, a standard method used to estimate the power spectrum (Xiong et al., 2020) (estimating the power spectral density using the fast Fourier transform is another appropriate method). The PSDs were then normalized, and the mean PSD was computed for each frequency band. Finally, the mean PSD values were concatenated into a feature vector.

Classification

Random forest classifiers and ANNs were used to conduct three binary classifications (AD and HC, AD and FTD, HC and FTD) and one multi-classification (AD and HC and FTD). The signal classification will be run on Python using the sci-kit-learn and tensorflow libraries.

A random forest classifier combines the output of n different DTs and selects the majority output as the result (Belgiu & Dragut, 2016). A diagram of a random forest classifier created by Janosh Riebesell depicts the process of training and evaluating data using the random forest classifier model (Riebesell, n.d.). Five-fold cross-validation, an unbiased method to evaluate the skill of a model, was performed for the random forest classifiers using n = 100 DTs, and the accuracies were averaged.

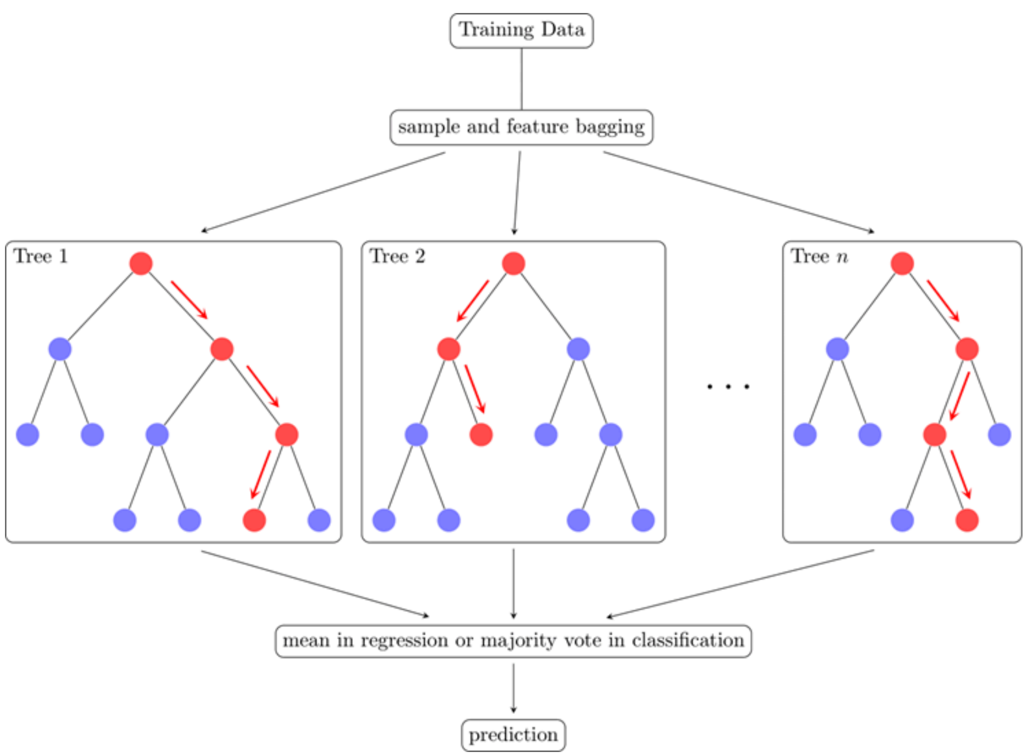

Figure 1. Illustrative diagram of a random forest classifier model containing *n* DTs

On the other hand, an ANN is composed of an input layer, an output layer, and possibly hidden layers (Subasi & Ercelebi, 2005). The nodes in the layers, excluding the input layer, contain a bias. In a fully connected neural network, each node connects to one another and contains a certain weight or threshold. A neuron, or node, is considered activated if the output of the node is above the threshold value. A diagram of an ANN with one input layer, three hidden layers, and one output layer created by Izaak Neutelings is depicted in the figure below (Neutelings, n.d.). Note that the values are the input values, denote the activation value of the m^{th} node in the l^{th} layer, and are the output values of the output layer.

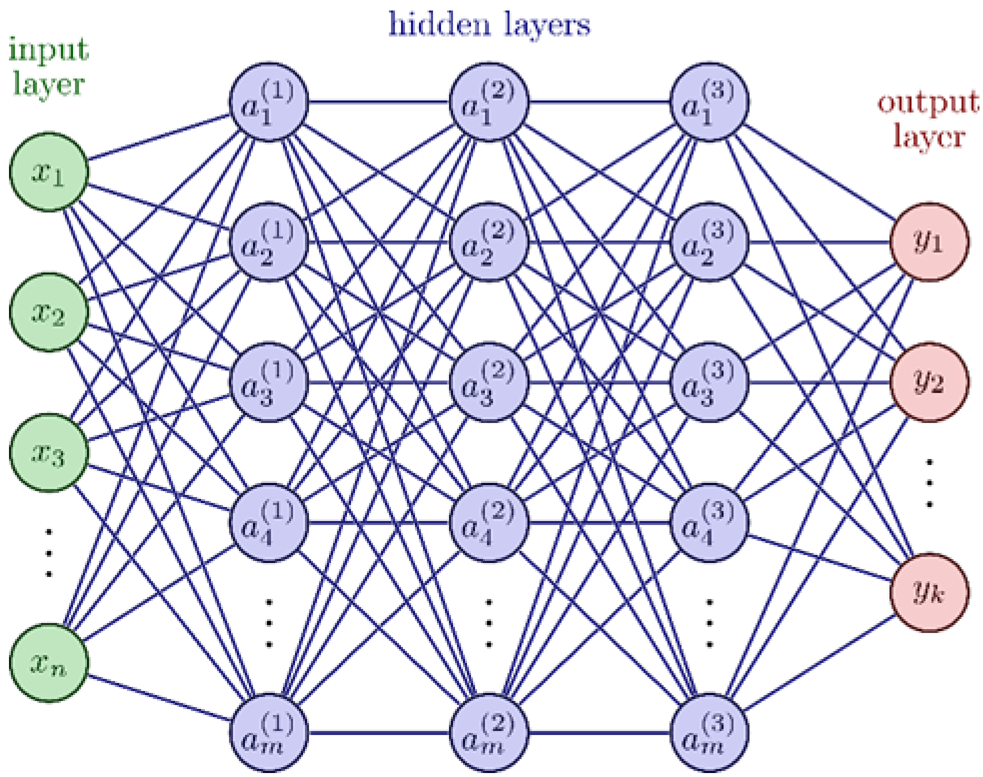

Figure 2. Illustrative diagram of an ANN with one input layer, three hidden layers, and one output layer

For the artificial neural networks, 75% of the data were randomly selected to train the model, and the remaining 25% of the data was used to evaluate the accuracy and validation error. The features were then scaled. For the binary classification problems, binary cross entropy was used to evaluate the validation set error. Initially, only one layer was created with a sigmoid activation function. However, in the end, three layers with 20, 3, and 1 nodes and the relu, relu, and sigmoid activation functions were used. To prevent the model from overfitting, l2 regularization was performed with lambda values ranging from 0 to 0.0012. The model with the highest accuracy and lowest validation set error was chosen as the optimal model for the classification problem.

For the multi-classification problem, categorical cross-entropy was used as the error and three layers with 20, 3, and 3 nodes and the relu, relu, and softmax activation functions were created. l2 regularization was also performed.

For each classification problem, the accuracy, precision, recall, and validation set error were calculated are the results are displayed in the tables below.

Results

Although the random forest classifier accuracies were not high, the artificial neural networks achieved high accuracy and low validation set error when performing signal classification. Tables 1 – 4 display the accuracy, precision, recall, and validation set error for random forest classifiers and ANN.

Table 1. Accuracy of four classification algorithms using random forest classifiers and ANN.

Accuracy of Classification Problem	Random Forest	Artificial Neural Network (ANN)
AD/HC	76.6%	96%
AD/FTD	61.3%	92%
HC/FTD	67.4%	95%
AD/HC/FTD	55.6%	90.4%

Table 2. Precision of four classification problems using ANN.

Precision of Classification Problem	Artificial Neural Network (ANN)
AD/HC	96%
AD/FTD	92%
HC/FTD	95%
AD/HC/FTD	90%

Table 3. Recall of four classification problems using ANN.

Recall of Classification Problem	Artificial Neural Network (ANN)
AD/HC	96%
AD/FTD	92%
HC/FTD	95%
AD/HC/FTD	90%

Table 4. Validation set error of four classification problems using ANN.

Validation Set Error of Classification Problem	Artificial Neural Network (ANN)
AD/HC	10.6%
AD/FTD	24.9%
HC/FTD	15.4%
AD/HC/FTD	31.3%

Discussion

The development of machine learning models to perform four signal classification problems aimed to answer the central question of research: To what extent are machine learning algorithms able to distinguish between different types of dementia, specifically Alzheimer's disease and frontotemporal dementia, based on EEG data? Random forest classifiers and ANN were trained using EEG signal data and extracted power spectrum features with the aid of the MNE Python library. While the random forest classifiers may not have reached promising results with accuracies ranging from 55.6% – 76.6%, deep learning ANN obtained accuracies ranging from 90.4% – 96%. Here, the ranges of deep learning accuracies achieved similar, if not more accurate, predictions than previous literature surrounding the differential diagnosis of AD (Pirrone et al., 2022; Miltiadous et al., 2021).

By extracting power spectral features and applying an FIR filter, Pirrone et al. obtained 97% accuracy using 5-fold cross-validation when differentiating between AD and healthy patients (Pirrone et al., 2022). The researchers also achieved accuracies of 95%, 83%, and 75% when performing classifications on healthy patients and patients with mild cognitive impairment (MCI), patients with MCI and AD, and healthy, AD, and MCI patients, respectively. Initially, the researcher of the present paper refrained from conducting feature extraction on the dataset and instead created models using raw EEG signals. The accuracies achieved by ANNs were much lower, around 60%, which reaffirms the findings of previous studies that AD and FTD affect the power spectrum of patients (Kulkarni & Bairagi, 2018; Elgandelwar & Bairagi, 2021).

Miltiadous et al. achieved 78.5% accuracy for AD detection using DTs and 86.3% accuracy for FTD detection using random forest classifiers using leave-one-patient-out cross-validation (Miltiadous et al., 2021). While the researchers did perform 10-fold cross-validation and reached accuracies in the ranges 97.7% – 99.1% for random forest classifiers and 90% – 98% for ANN, they claimed that the accuracy values were inflated. While 5-fold cross-validation was used for the random forest classifiers in this study, the algorithms achieved much lower accuracies, which may be affected by the power spectral features that were extracted. Future research should analyze the implications of performing k-fold cross-validation and leave-one-patient-out cross-validation on AD, FTD, and healthy patient signal classification.

The absence of research on the multi-classification of AD, FTD, and healthy patients hinders a foundational basis for comparison.

Conclusion

The primary objective of the present paper was to answer the research question, “To what extent are machine learning algorithms able to distinguish between different types of dementia, specifically Alzheimer’s disease and frontotemporal dementia, based on EEG data?” Through the creation and implementation of random forest classifiers and ANN, high accuracies and low validation loss were obtained, affirming the results of past literature.

From the results reached in the present study, random forest classifiers and ANN are capable of differentiating between AD, FTD, and healthy patients solely based on EEG data. Future research should examine the implications of different models and features on EEG data.

Limitations

Although high accuracy ranges were obtained for the signal classifications, several limitations may have impacted the present study and should be addressed in future research. Firstly, the first two minutes of EEG signal recording were chosen for analysis due to a RAM overload when concatenating epochs. The remainder of the EEG recordings may have contained characteristic changes in the power spectrum, which may have improved the accuracy of the machine learning model. Additionally, although the models obtained high accuracies, several had higher validation set loss, which may be due to overfitting. Performing l2 regularization, changing the size of the training and validation set, and referencing a larger dataset may prove helpful to overcome overfitting. Past research regarding AD signal classification also extracted frequency band energy frequency-domain features and mean, variance, and IQR time-domain features (Miltiadous et al., 2021). Another paper extracted average power spectral density features but calculated the square of the absolute difference when constructing a double digital filter (Pirrone et al., 2022). Future research should examine the implications of extracting different features from raw EEG data when performing signal classification. Finally, random forest classifiers and ANN were created and trained using the dataset. Past research also focused on the implementation of SVMs for signal classification, which may be an algorithm to examine further, despite not natively being used for multi-classification problems.

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