PREDICTING ALZHEIMER'S DISEASE PROGRESSION BY COMBINING MULTIPLE MEASURES

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ABSTRACT

Alzheimer's disease (AD) is a degenerative brain ailment that affects millions worldwide. It is the most common form of dementia. Patients with an early diagnosis of Alzheimer's disease have a strong chance of preventing additional brain damage by halting nerve cell death. At the same time, it begins to progress several years before any symptoms appear. The variety of data is the biggest problem encountered during diagnosis. Neurological examination, brain imaging, and often asked questions from his connected closed relatives are the three forms of data that a neurologist or geriatrics employs to diagnose patients. One of the biggest questions which need answering is the choice of a convenient feature.

The main objective of this paper is to help neurologists or geriatricians diagnose patient conditions. It proposes a new hybrid model for features extracted from medical data. It discusses AD's early diagnosis and progression for all features considered in the diagnosis and their complex interactions. It proves to have the best accuracy when compared with the state-of-the-art algorithm. Also, it proves to be more accurate against some recent research ideas. It got 95% in all cases, considering this work focused more on increasing the number of instances in comparison.

KEYWORDS

Alzheimer's disease, Diagnosis, Prediction, Classification, Feature Selection.

1. INTRODUCTION

Dementia is a general term used to describe symptoms that impact memory, the performance of daily activities, and communication abilities. Alzheimer's disease (AD) is the most common type of dementia. It gets worse with time and affects memory, language, and thought. As a result, it is a neurodegenerative disease described by progressive memory loss. It causes over 60% of dementia cases [1], [2]. Its patients usually have multiple symptoms. They range from a progressive loss of memory, language disorders, and disorientation. In general, there are several stages in AD. They are early, middle, and late (sometimes referred to as mild, moderate, and severe in a medical context) [3]. One of the main concerns facing specialists on the early detection of Mild Cognitive Impairment (MCI) is an intermediate stage between health and AD. It shows the potential of ongoing progression toward AD or other dementia. Although it does not

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interfere with daily activities, it is abnormal given their age and education level. That is why it does not meet the criteria for AD.

Recent research shows that only 20–40% of individual cases will change to AD within three years; This is a lower rate of exchange reported in medical samples than in clinical cases [2]. However, AD's progression starts several years before any symptoms become visible and progressive [3]. Many drugs are in development, as there is no available treatment for AD [4], [5]. Researchers were able to diagnose Alzheimer's disease using modern diagnostic methods and biomarker tests. By combining biomarkers, it achieves varying levels of accuracy [4]. Unfortunately, the present research focuses on using MRI to classify illness states at their current stage rather than combining various features. As a result, these studies function as proof of concept without being tested in the real world [6], [7].

In the current age of artificial intelligence and machine learning technologies, predicting AD conversion is considered an important research area. The institutional use of machine learning techniques and the shift toward a personalized medicine concept, particularly in medical fields, represents a chance to improve therapeutic results. It makes personalized predictions with a high level of certainty based on the subject's specific data, which could help researchers and physicians make better and more effective judgments[8].

In this article, we propose a novel AD diagnosis method by combining multiple measures. Our measures include tests and MRI. For each measure, we extract all features that are shown as feature sets, respectively. Therefore, each one within ranked by accuracy in descending order. The top-ranked features of each feature set are applied to the multi-layer perceptron rule to obtain the best classification accuracy. After achieving the best accuracy, we can get the optimal feature subset. Afterward, to investigate the performance with chosen features. We propose a combined classifier to achieve AD classification. The rest of the paper is arranged as follows: Section 2 discusses the previous work related to our objective. The proposed model is illustrated in section 3. Section 4 shows the experiments made to achieve an objective. Finally, the discussion is shown in section 5.

2. LITERATURE REVIEW

Most studies on Alzheimer's disease (AD) have focused on using medical imaging as the only factor. Martı-Juan et al. [9] is a survey concentrating on longitudinal imaging data. It focused on papers that have published between 2007 and2019. Hong et al. [10] introduce Long short-term memory (LSTM) to predict AD development. It carries out the future state prediction for the disease rather than the state of a current diagnosis. While Janghel develops and compares different methods to diagnose and predict AD using MRI scans only [11]. It implements one model, which is the convolution neural network (CNN). At the same time, it uses four different architectures of CNN. An embedded feature selection method based on the least-squares loss function and within-class scatter for selecting the optimal feature subset is proposed by Cai et al. [12]. The optimal subsets of features used for binary classification are based on a support vector machine (SVM). Also, deep learning technology was discussed by Bi et al.[13]. It focused on the problem of automatic prediction of AD based on MRI images. It applies two main steps: 1- implement the unsupervised CNN for feature extraction. 2- utilizes the unsupervised predictor to achieve the final diagnosis.

According to our knowledge, Grassi et al. [14] use a weighted rank average grouped by different supervised machine learning methods to predict three-year conversion. Only a limited set of diverse characteristics are used to make predictions. The employment of algorithmic decision-making tools is the critical benefit. Liu et al. [15] provide a new method for detecting AD

based on spectrogram characteristics collected from voice data. It can assist families in better understanding the progression of a patient's sickness at an early stage.

Guo et al. [16] forecast the conversion from MCI to AD efficiently. Researchers proposed a cerebral similarity network containing more progression information. The classifiers were trained and evaluated using leave-one-out cross-validation and support vector machine (SVM). With a high accuracy of 92.31%, the proposed methodology was shown to be effective.

The following studies serve as the foundation for our study. In ascending order, they are listed. The first, [17], explains how MRI data can improve the accuracy of diagnoses for the Mini-Mental State Examination (MMSE) and logical memory (LM)tests. It accesses model correctness via Multilayer Preceptor. The second, [14], shows how clinically translatable strategies for conversion can be predicted. It also detects high-risk people who are converted. It continues to work three years after the initial assessment. Then, Haaksma et al. [18] address the link between Alzheimer's disease and its predictors. It included some Alzheimer's disease cases that have had at least one examination following diagnosis. To determine whether there are latent classes of Mini-Mental State Examination (MMSE) and Clinical Dementia Rating sum of boxes (CDRsb) routes across time. It employs growth mixture models with parallel processes. To find baseline predictors of class membership, researchers utilized bias-corrected multinomial logistic regression. A multimodal data [19] classifier that employs a hybrid deep neural network classifier. It is based on a set of MRI pictures as well as EEG inputs. The goal is to improve the learning process by incorporating the weight component of DNN into CNN. Then it explains how the accuracy of hybrid classifiers is determined.

To find correlations between brain areas and genes, use the appropriate correlation analysis approach at the conclusion. [20] was proposed via a cluster evolutionary random forest (CERF). It adds the concept of clustering evolution to increase the random forest's generalization performance. Farouk and Rady [21] in 2020 investigated the use of unsupervised clustering methods for the early identification of Alzheimer's disease. Though classification techniques are used to identify medical disorders, the lack or inaccuracy of labeled data might be an issue. This study compares the k-means and k-medoids using Voxel-Based Morphometry (VBM) characteristics taken from MRI scans.

3. METHODOLOGY

The feature selection technique is a knowledge discovery tool that helps grasp a problem by analyzing the most critical aspects. It seeks to improve classifiers by listing essential features, which also helps to reduce computational load. Due to the high correlation between features, many equally ideal signatures are commonly produced, making standard feature selection methods unstable and reducing the confidence in selected features [18], [22]. This section describes the two-tier feature selection. The feature ranking stage employs information entropy (IE) that uses a filtering approach. The stage aims at ranking subsets of features based on high information gain entropy in decreasing order. Therefore, this stage aims to extend additional features that contribute to the relationship between alerts with better discriminative ability than the initially ranked features. [23].

This paper describes a method (IE-MLP) for disease diagnosis and prediction based on feature selection utilizing optimality criteria. The information entropy Multilayer Perceptron (IE-MLP) [23], [24], [25] method uses optimality criterion for feature selection. Its major objective is to make the doctor's assessment easier. Figure 1 shows the block diagram; it has two basic steps:

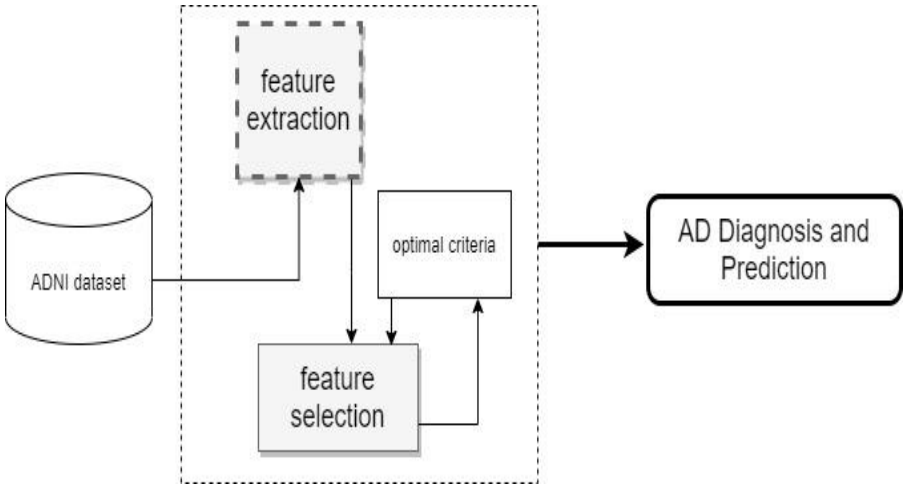

Figure 1: Block Digram of proposed Model

1) Feature extraction divides the data into three types in this phase (neurological test, MRI, diagnosis at baseline – the following section describes more details about the data). The doctor uses all three types of data at diagnosis. That is the reason behind selecting these various data sets kinds.

2) Feature selection reduces the number of features in a computation that uses many resources without losing important information. It makes the computer's task easier and faster; the importance of these steps is that it saves time and costs to increase diagnosis speed. It accepts the ADNI dataset's characteristics as input. Then, the Perceptron Learning Rule is applied to the smaller sets to determine the decision rule. It has a significant impact on disease diagnosis and prediction. The dataset goes through a pre-processing stage to alter data; the pre-processed data feds into the suggested model to extract relevant features. Perceptron rules are applied to the resultant feature vector to investigate the importance of various anatomical ROIs.

4. EXPERIMENTS

4.1. Dataset and Preprocessing

The Alzheimer's Disease Neuroimaging Initiative (ADNI) database was utilized to compile the data for this article (adni.loni.usc.edu). The ADNI began as a public-private partnership in 2003. The primary purpose of ADNI is to identify clinical, imaging, genetic, and biochemical indicators for Alzheimer's disease early identification and tracking (AD). It includes many cognitively normal, MCI, and AD patients recruited from over 50 different US and Canadian facilities, with six-month follow-up examinations. The proposed work uses ADNIMERGE (this subset is part of the official dataset released by ADNI). It includes Clinical and biomarker data from the Alzheimer's Disease Neuroimaging Initiative. It contains 90 attributes and 12612 instances. Although it has nine classes, we include only three in this paper (AD, MCI, and NL).

As previously stated, the ADNI collection contains a variety of data kinds. By setting the duration for test retakes, this effort intends to aid diagnosis utilizing other data. For these reasons, the categories of data used are as follows:

- Neurological Examination: For specialized examination of the brain and mental health issues (neuropsychologist). Tests included assessing memory and cognitive abilities in the evaluation.
- The patients' initial tests and diagnoses serve as a baseline.
- Image processing in the brain: Only two categories of technologies are available in the ADNI dataset (MRI used only)

4.2. Feature Selection

Table 1: Feature Selection Comparison

Original Datset	Attribute Number
Baseline (19 attributes)	1
MRI (7 attributes)	1
Neurological (9 attributes)	7

As mentioned in the previous subsection, data contains 87 attributes and 2700 instances. After data pre-processing, it includes 45 attributes and 2700 instances. In the beginning, 45 attributes are a significant number to analyze. So, the feature extraction and selection model chooses more convenient features. At the same time, the chosen features need to be acceptable by medication standards.

The IE-MLP works as follows: 1) Information entropies arranges the data in ascending order depending on their values 2) Multilayer perceptron got the arranged data, and the suitable feature is selected. Table 1 shows the number of attributes before and after the proposed model. The difference between each model and accuracy is discussed in more detail in section 5.

4.3. Classification Technique

A neural network (NN) is a type of machine learning which models itself after the human brain; While the basic unit of the brain is a neuron, the essential building block of NN is a perceptron connected to an extensive network. It can perform deep learning. An ANN and error function helps calculate the gradient of a loss function for all the weights in the network. In this paper, a multi-layer perceptron (MLP) chose for the training model. The following are some of the reasons for choosing this model:

1. It is fast, simple, and easy to program
2. It is flexible as it does not require prior knowledge
3. It does not need any special mention of the features of the function to be learned.

The NN uses no hidden layer, and it contains seven input and three output units. With a Learning rate equal to 0.3. The activation function used is Approximate Sigmoid, and the loss function is squared error.

5. DISCUSSION

A confusion matrix describes the performance of a classification model (or "classifier"). Equations1:4 contains a set of rates lists that computes from a confusion matrix. Lets now define the most basic terms, which are whole numbers (not rates):

- True positives (TP): These are cases in which we predicted yes (they have the disease), and they do have the disease.
- True negatives (TN): We predicted no, and they do not have the disease.
- False positives (FP): We predicted yes, but they do not have the disease.
- False negatives (FN): We predicted no, but they do have the disease.

Table 2: Confusion Matrix for 800 attributes

Measure	Value (%)
Accuracy	95.8
Error Rate	4.5
Specifity	95.5
Sensitivity	95.6
Roc-Curve	99

Table 3: Varying data size vs. Time

Data Size	Time (Sec)
800	2.28
700	2.04
600	1.71
500	1.43

The following criteria are the chosen ones from the confusion matrix. The reason behind selecting them is that they will have real meaning to our objective. According to equation1, accuracy is one metric for evaluating classification models. It is the ratio of the number of correct predictions to the total number of input samples.

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \qquad (1)$$

$$Error\ Rate = \frac{FP + FN}{TP + TN + FP + FN} \qquad (2)$$

Equation 2 illustrates the Error Rate, which is the number of all incorrect predictions divided by the total number of the dataset. The best error rate is 0.0, whereas the worst is 1.0. As the error rate increases, the model reliability decreases.

Specificity (SP) is the number of correct pessimistic predictions divided by the total number of negatives. It showed in equation 3. It is also called actual negative rate (TNR)

$$Specifity = \frac{TN}{N} \qquad (3)$$

Precision discussed in equation 4; tries to answer what proportion of identifications was correct. Our model got 0,95. It means a high number of instances that were correctly classified.

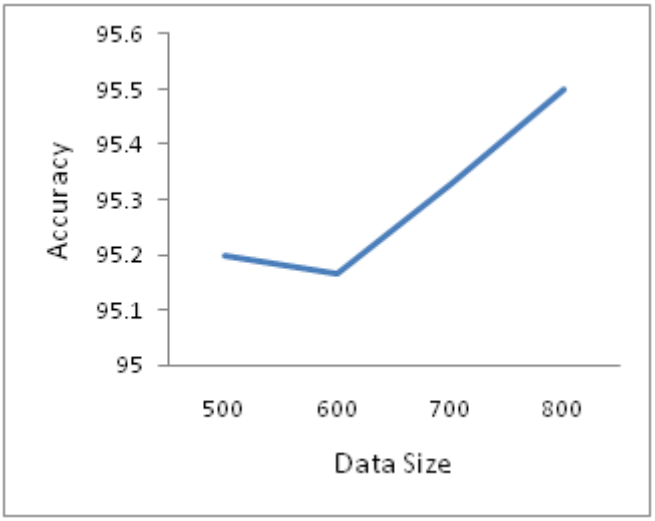

Figure 2. Varying Datasize Vs. Time

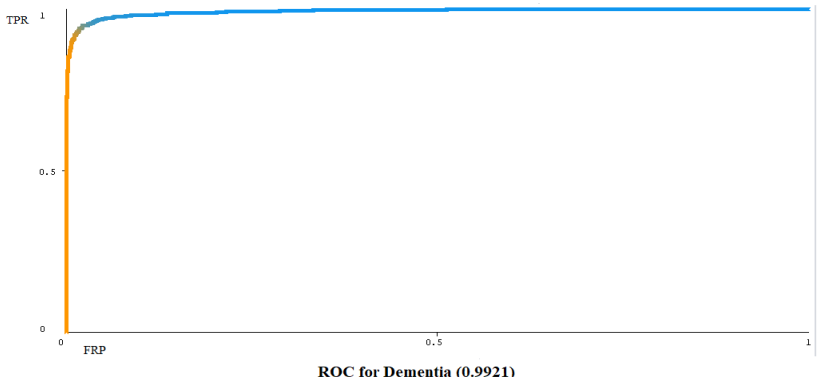

Figure 3. Area Under Curve-AUC for dementia

$$Sensitivity = \frac{TP}{TP + FN} \qquad (4)$$

ROC curves are a valuable tool for evaluating a diagnostic test's performance over a wide range of possible values for a predictor variable. The area under a ROC curve is a measure of discrimination that researchers can use to compare the results of two or more diagnostic tests. A ROC curve shows the relationship between clinical sensitivity and specificity for every possible cut-off. The ROC curve is a graph with:

- The x-axis shows 1 – specificity
- The y-axis shows sensitivity

In Order to view the difference based on varying data sizes, including data sizes from 500 to 800, the confusion matrix (equation 1:4) comparison with different feature types is taken in Table 2. The results show that our algorithm achieves the best performance with a chosen feature. Table 3 and figure 2 show that our model is stable in most of the features.

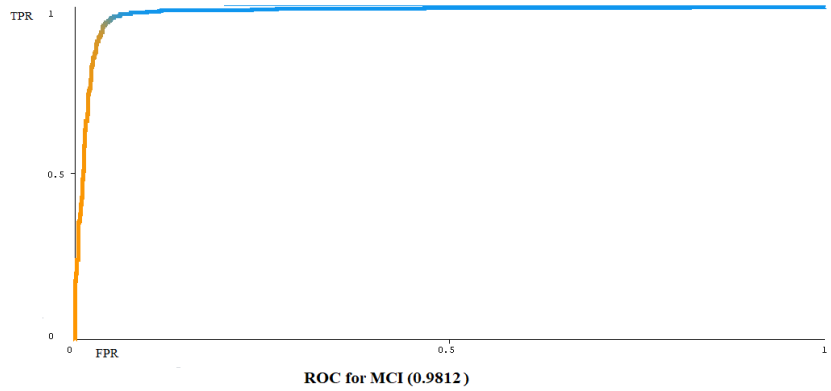

Figure 4. Area Under Curve-AUC for MCI

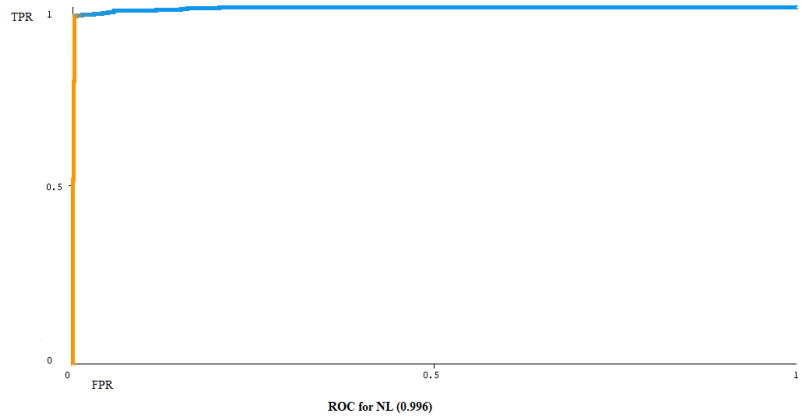

Figure 5. Area Under Curve-AUC for NL

ROC curves depict the relationship/trade-off between clinical sensitivity and specificity for each conceivable cut-off for a test or a set of tests in a graphical format. Furthermore, the area under the ROC curve provides insight into the value of using the test(s) in question. Figure 3, 4,5 shows the ROC area for three classes (Dementia, MCI, NL). The proposed model got a 0.99 average value for 800 class attributes. To indicate better performance by curves that are closer to the top-left corner [26]. It means that the model has a good measure of separability, which means there is a 99% chance that the model will distinguish between different cases. The next step in the proposed work is to apply the results in actual experiments to evaluate the model performance.

6. CONCLUSIONS

This study introduced a proposed framework for Alzheimer's disease diagnosis by combining multiple measures. It explores the effect of features extraction from MRI and neurological tests. Diagnosis of AD depends on multiple features that facilitate the process. The main objective of this study is to improve time and save time on specialties' needs. Experimental results on the ADNI database have shown that our proposed method is efficient and can achieve better classification performance. The proposed approach managed successfully to obtain an early AD diagnosis with an accuracy of 97%. The clustering techniques used in the proposed approach provided an automated preliminary insight discovering vital early patterns in the data with reliable accuracy. Our results further demonstrate that clinical AD diagnosis could benefit from calculating multiple measures from diagnostic data and incorporating these all in automated analysis.

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