Machine Learning for Detection of Cognitive Impairment

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Abstract: The detection of cognitive problems, especially in the early stages, is critical and the method by which it is diagnosed is manual and depends on one or more specialist doctors, to diagnose it as the cognitive decline escalates into the early stage of dementia, e.g., Alzheimer's disease (AD). The early stages of AD are very similar to Mild Cognitive Impairment (MCI); it is essential to identify the possible factors associated with the disease. This research aims to demonstrate that automated models can differentiate and classify MCI and AD in the early stages. The present research used a combination of Machine Learning (ML) algorithms to identify AD, using gene expressions. The algorithms used for the classification of cognitive problems and healthy people (control) were: Linear Regression, Decision Trees (DT), Naîve Bayes (NB) and Deep Learning (DP). The result of this research shows ML algorithms can identify AD, in early stages, with an 80% accuracy, using a Deep Learning (DL) algorithm.

Keywords: Machine Learning; Alzheimer disease; Mild Cognitive Impairmen; Deep Learning

1 Introduction

In the normal process of aging, we start to degrade various functions of our brain, which prevents us from performing daily tasks, because they affect our motor and cognitive functions. Alzheimer's disease (AD) is the most common type of

dementia in the elderly. Alzheimer's disease usually affects people over the age of 65, which is where aging changes are most notable. To identify the factors that differentiate the normal aging process and cognitive disorders, a set of neurological tests and analyses are carried out for the confirmation of cognitive impairment, which as they progress towards becoming. AD is currently the sixth cause of death in the United States of America, and 65-year-olds with AD are expected to increment to 13.8 billion by 2050. Over the next 20 years, the number of people with dementia is projected to increase 40% in Europe, 63% in North America, 77% in the southern cone of Latin America (for example, in Argentina and Chile), and 89% in developed Asia-Pacific countries. There is no reliable diagnosis of AD because the symptoms of Alzheimer's in the early stages are very similar to cognitive impairment and aging and when it is possible to establish an idea of the diagnosis the disease is very advanced. Alzheimer's disease is currently diagnosed based on the results of a set of tests the patient has been evaluated for. There are few semi-automated mechanisms to diagnose cognitive disorders. This is because physicians lack systematic assessments to help identify these diseases under the dementia category. The manual diagnosis of cognitive impairment requires several tests such as the neuropsychological test score Mini-Mental State Examination (MMSE), laboratory tests, reports of other medical specialists, interview with family members, among other tests.

All of these data create a consistent picture of the disability of each person where efficiency and pressure depend on the level of experience of the medical professional. Mild Cognitive Impairment (MCI) is an intermediate state between normal aging and the most severe deterioration of dementia. This impairment may increase the risk of dementia in the future caused by Alzheimer's disease, but it can be the case where MCI does not get worse and becomes dementia. The MCI effects: memory, thinking, guidance, understanding, calculation, learning ability, language, and judgment. When these effects get worse, the domains of thought get worsened; the MCI process goes into Alzheimer's disease. These people have one of the biomarkers of Alzheimer's disease, which is determined by high levels of amyloid-beta. This is one of the characteristics of the disease that helps differentiate MCI from Alzheimer's. These particular variables are remarkable for family and friends but not for people who are not in a close circle. The symptoms presented in the early stages of AD do not interfere with routine activities. The ability to think get worst when the brain can no longer compensate for the number of neuron deaths caused by Alzheimer's disease.

Advances in technologies such as Machine Learning algorithms have found that Artificial Intelligence can identify patterns to differentiate cognitive diseases. These Machine Learning algorithms offer an alternative method of detection that can provide an automated process and valuable knowledge for the diagnosis and classification of cognitive disorders. The diagnosis of cognitive diseases has always been a challenge, and nowadays considerable research has pointed to technology as a facilitator to diagnose [1]. The challenge in this research, is to

establish questions that can be answered through a Machine Learning analysis. The knowledge of Big Data and the accessibility of Machine Learning have further increased the desire to build better learning models.

Several tools are currently used to perform manual diagnostic tests. By performing these tests, the patient's results are retrieved, and this data collection is what the specialist uses to diagnose the patient. Based on the findings of the literature review, a dependency has been found on which only a trained person can read, perform the analysis of test results to provide diagnostics. This diagnostic process can be automated using a combination of Machine Learning (ML) methods. The amount of data that comes out as a result of the different tests that are done to the patient is what makes a dataset excellent for research, the more information that is needed can become. In this work, we aim to see whether gene expression in the blood can be used as a biomarker for AD diagnosis by using Machine Learning techniques. Results obtained are promising and reveal the feasibility of our approach.

In the next section, a brief of methods of ML applied in cognitive impairment diagnosis in the medical field. Section 3 reports the related work. Section 4 shows an overview of how Machine Learning and Deep Learning algorithms can identify Alzheimer's diseases in the early stages using gene expressions. In the last section, the conclusion and further work are outlined.

2 Machine Learning in the Medical Field

Numerous researchers have put an effort to delay and cure the progression of Alzheimer's disease. These efforts have generated a lot of data, including brain neuroimaging, that offers opportunities to investigate Alzheimer's behavior and other kinds of dementia. This research has used the advances of technologies such as Machine Learning (ML) and Artificial Intelligence (AI) as tools to answer questions about the ability of automated diagnostics for patients with cognitive problems and dementia. The most commonly used parameters are the combination of Alzheimer's data from multiple sources, the identification of biomarkers, and the analysis of brain connectivity. Recent studies show that brain imaging parameters are the most consistent measures for Alzheimer's diagnosis. Neuroimaging techniques such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and Computerized Tomography (CT) offer great potential to determine specific biomarkers that can identify people with dementia in their early stages [2]. Machine Learning algorithms offer an alternative method of detection that can provide an automated process and valuable knowledge for diagnosis and classification [3]. These ML algorithms assist many Alzheimer-related research by enabling the fusion of multiple source data and the identification of biomarkers, as well as, the analysis of brain connectivity.

Numerous authors define the term algorithm as a series of statement lists to resolve a calculation or abstract problem. An algorithm is considered some steps that convert data from a problem, which is considered an input, into a solution, which is considered an output, not all algorithms end up solving a particular problem.

Another source used by researchers to study the classification between people with Alzheimer's and healthy people is Amyloid, β- Amyloid. It is a molecule derived from the Amyloid Precursor Protein (APP) and forms the amyloid plaques that are the markers of Alzheimer's disease [4]. These ML algorithms assist many Alzheimer-related research by enabling the fusion of multiple source data and the identification of biomarkers, as well as the analysis of brain connectivity. Numerous authors define the term algorithm as a series of statement lists to resolve a calculation or abstract problem. An algorithm is considered some steps that convert data from a problem, which is considered an input, into a solution, which is considered an output, not all algorithms end up solving a particular problem. Another source used by researchers to study the classification between people with Alzheimer's and healthy people is Amyloid, β-Amyloid. It is a molecule derived from the Amyloid Precursor Protein (APP) and forms the amyloid plaques that are the markers of Alzheimer's disease [5]. Machine Learning's clustering algorithms have helped to identify patterns among Alzheimer's patients, which has been difficult for medical specialists [1]. The grouping method is a powerful Machine Learning tool for detecting structures in datasets. In the field of medicine with the clustering method, patterns have been discovered in labeled data and unlabeled data that contribute to diagnostic research.

There are two types of commonly used clustering methods: supervised and unsupervised:

- Monitored grouping is the learning process with a mapping function of a set of input variables of an object variable. This method refers to the algorithm training process being monitored and obtaining the correct answers. In other words, this method works by a label. The target result is already known in advance with this method because the data has been labeled.
- When you have only one set of variables and there are no output variables, that is, when the data is not labeled, the learning process is known as unsupervised grouping. In unsupervised learning, there are no correct answers to learning training, but they discover the structures in the datasets.

The objective of the clustering method is to discover subgroups within heterogeneous data so that each group has a greater homogeneity than the set [6]. Labeled data collection is more difficult to collect in various applications than data without tags.

In these cases, they result in a data set consisting of a large number of unlabeled variables and a small set of labeled variables, this method of knowledge is known as semi-supervised learning. Semi- supervised learning uses labeled and unlabeled data to improve the accuracy of the learning model.

Alzheimer's disease leads to structural and functional loss of neurons in the regions of the cortex, hippocampus, and other areas in the brain. Several studies over the past 20 years have pointed to possible biomarkers for diagnosis including brain atrophy revealed by magnetic resonance imaging [7]. The MRI is one of the tools they use today to look for biomarkers for Alzheimer's disease. Diagnosis currently depends on revisions through MRI techniques or cerebrospinal fluid analysis. One of the limitations of diagnosis is that in the early stages of dementia a robust diagnosis is not provided and this represents arrears in medical benefits. By not diagnosed early, treatment delays are provided. It's because of this the discovery of effective biomarkers and the efficiency with which correct correlations and relationships to symptoms can be established has become a high-demand application [8]. More recent studies have proposed ML models to identify biomarkers for gene expression-based diagnosis. The analysis of gene expression data generates a metric of the abundance of RNA throughout the genome in parallel which provides possible materials to bridge the gap between the genotype and the phenotype that is based on the evaluation of biomarkers.

Genotype is the genes that humans charge from generation to generation; these are genetic characteristics of humans. Phenotypes are physical characteristics that can be observed such as human behavior. The physical properties of the organism directly determine its chances of survival and reproductive production, but the inheritance of physical properties depends on the inheritance of the genes. The gap between genotype and phenotype is considered the basis for the evaluation of biomarkers for Alzheimer's diagnosis because in this case the APOE genotype and the e4 allele of the Apolipoprotein is the main genetic risk factor of Alzheimer's disease (AD), but the APOE genotype can modulate the disease's phenotype. It has been reported that allele 4 carriers have more pathology of the temporal medial lobe (MTL) and less memory than non-carriers [9]. In other words, carriers show a greater deterioration in memory retention measures. By analyzing the genetic network that is responsible for modeling its interactive activities, it is possible to detect genes that play a crucial role in the development of AD. The incidence of disease in brain regions is sequential as the disease progresses; that is why it is necessary to identify molecular biomarkers using gene data in different brain regions. Based on related studies some genes influence the development of Alzheimer's disease as the amyloid precursor protein gene (APP, chromosome 21) and two Presenilin genes (PS1 and PS2) in chromosomes 14 and 1. People with either of these two genes tend to develop AD at a young age between 30 and 40 years, however, carriers of the genetic variant ApoE4 have a better chance of developing Alzheimer's. Late-onset AD occurs around 65 years of age. This protein has also been implicated as one of the causes of AD, especially including

abnormal production of Beta-amyloid, hyperphosphorylation of TAU and Neurofibrilar Ovillos (NFT), synaptic pathology, oxidative stress, inflammation, protein processing, among others, and yet the pathogenic factors that initiate these processes remain obvious [10].

There are several reasons for the substantial resistance of AD to the analysis. One of these is the great extent and complexity of the disease, which affects many molecules, cells, and systems and prevents attempts to determine which alterations are specifically associated with early pathology. This is one of the fundamental reasons why the initiative is taken to implement an automatic learning model that contributes to the diagnosis and classification of cognitive problems in its beginnings.

3 Related Work

In the last decade, machine learning approaches have been discovered to be quite beneficial in the identification of Alzheimer's disease [17-19]. Support vector machine (SVM), artificial neural network (ANN), and deep learning are the most extensively used classification approaches. The nature of the optimization issue is the major difference between SVM and ANN. SVM [20] provides a globally optimal solution, whereas ANN provides a locally optimal solution. Feature extraction is a key stage in both SVM and ANN. Shi et al. [21] proposed that medical image processing could benefit from a combination of neural networks and intelligent agents. As our work, there are some research works focused on seeing whether gene expression in the blood can be used as a biomarker for AD diagnosis. Mestizo Gutierrez et al. have proposed the use of decision tree to classify different stages of Alzheimer's disease [14]. Deep learning, on the other hand, includes the feature extraction procedure directly into the learning model [22][23]. Deep learning has been found to be effective for huge datasets, particularly picture data [22]. Some researchers employed ensemble approaches to increase Alzheimer's disease classification accuracy [24-26]. Most biomarker research focuses on case-control studies, comparing healthy people to Alzheimer's patients regardless of disease severity; however, in this work our goal is to create a model for distinct stages of Alzheimer's disease severity: incipient, moderate, and severe. Furthermore, we compare machine and deep learning algorithms using the same dataset.

4 Detection of Alzheimer's Diseases using Machine Learning Algorithms

Our work aims to see whether gene expression in the blood can be used as a biomarker for AD diagnosis. To do this, machine and deep learning algorithms were utilized.

The micro-array genes provide new tools to abound complexity because they allow general views of simultaneous multi-cellular activity. However, the interpretation of micro-array data is often disrupted by low statistical power, high false positives or false negatives and the uncertain relevance for functional endpoints. This paper exposes supervised machine learning algorithms for the classification and early detection of AD, Naîve Bayes NB, Decision Trees, and Logistic Regression. Moreover, a Deep Learning model is implemented. One of the most common types of dementia is Alzheimer's disease, which has been studied intensively over the past few decades because understanding the disease has been a challenge. Early AD has been resistant to analysis due to the complexity of the disease and the overlap of its markers at the early stage with the normal aging process. The overall objective of this research is developing an artificial intelligence model to identify cognitive disorders at an early stage.

Early detection of AD is strictly related to the detection of Mild Cognitive Impairment (MCI) that manifests as progressive loss of memory and other thinking skills. When a person suffers from MCI they eventually face dementia. In other words, the primary deficiency of the MCI is memory and it is very likely that these symptoms will escalate to dementia due to AD.

To carry out our approach, we applied a research method comprising three phases: Phase #1: approach definition, which refers to an ad hoc literature review on machine learning applied to automatic detection of biomarkers related to Alzheimer's disease, as well as, the identification of related work; Phase #2: solution proposal, which refers to the design and implementation of machine and deep learning algorithms; and Phase #3: evaluation, which refers to the use of a public dataset to evaluate the algorithms (GDS810 [12]).

In this research two models were developed:

- A simple classifier using algorithms: Naîve Bayes, Decision Trees and Logistic Regression;
- A slightly more complex classifier: Deep Learning.

4.1 Machine and Deep Learning algorithms

Next, we present brief description about different machine learning and deep learning techniques.

4.1.1 Naîve Bayes

The most likely class for a particular case described by its feature vector is assigned by Bayesian classifiers. By assuming that characteristics are independent of class, learning such classifiers can be considerably simplified.

Despite this implausible assumption, the resulting classifier, known as Naive Bayes, is very effective in practice, often outperforming far more complicated algorithms. Many practical applications of Naive Bayes have been demonstrated, including text classification, medical diagnosis, and system performance management [13].

4.1.2 Decision Trees

The decision trees are nested decisions that are used to categorize the data. When we run the data through a decision tree, we get rules that allow us to classify it. A set of nodes, leaves, and branches make up a tree. The internal nodes correspond to each of the inquiries regarding the particular property of the problem, whereas the root node is the attribute from which to begin the classification process.

The attribute's possible values are labeled on the branches that branch out of each of these nodes. End nodes or leaf nodes are associated with a decision that corresponds to one of the problem's class variables. The induction of the tree and the categorization of the tree are the first and second stages of a decision tree creation process [14]. In this work, two implementations of decision trees were implemented: j48 and Random Forest.

4.1.3 Logistic Regression

The logistic regression model uses a univariate score of multiple predictive variables to model the likelihood of an interest event, indicated by p_i, as $p_i = \exp(s_i)/1 + \exp(s_i)$, where si is a weighted linear sum of predictive variables.

The well-known, s-shaped curve, represents the relationship between s_i and p_i. Si is frequently employed as a classifier in the sense that if si 0, which is equivalent to p_i 1/2, we categorize the *i-th* subject into the positive class (the class of an event of interest). The subject is placed in the normal group if everything else is normal [15].

4.1.4 Deep Learning

Despite the fact that numerous studies have lately used machine learning approaches to diagnose Alzheimer's disease, most existing studies have found a bottleneck in diagnosis performance, owing to the congenital constraints of the chosen learning models. Moreover, the performance of machine learning models depends heavily on the representation quality of the original training samples.

To overcome those issues, we construct a deep learning architecture with stacked auto-encoders and a sigmoid output layer in this study. As demonstrated in Figure 1, the deep learning technique described in this paper uses a neural network with numerous hidden layers. The original input vector is represented by input layer neurons. Each concealed layer can be thought of as a higher-level representation of the one before it, though defining the exact meaning of each layer is frequently a challenge. With the same dimensionality as the input layer, the output layer is a sparse representation of the input layer [16].

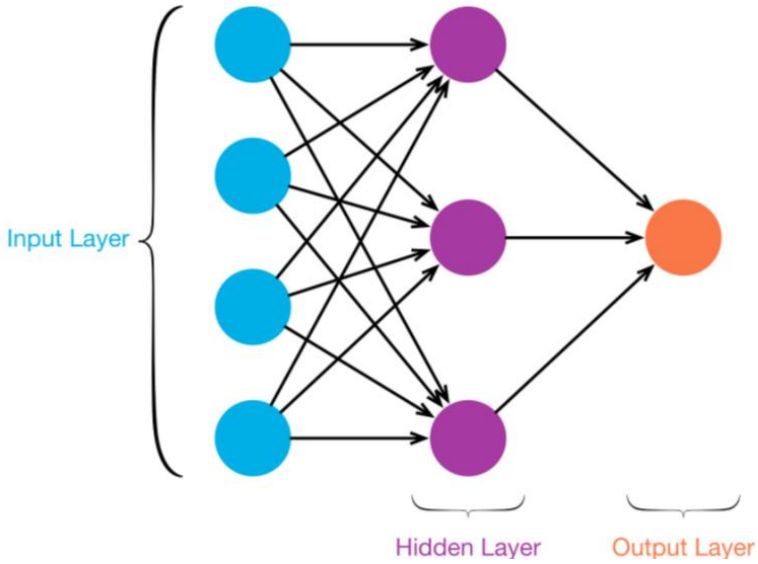

Figure 1
Illustration of the deep learning structure with a multilayered

4.2 Implementation Details

This section describes the pre-processing steps for the data, and the implementation of machine learning algorithms along with the assessment scenarios.

4.2.1 Data Pre-Processing

We used the public human GDS810 array dataset obtained from the National Center for Biotechnology Information (NCBI) Gene Expression Omnibus (GEO) database (Affymetrix Gene Chip (HG-U133A). The GDS810 microarray published by [12] assessed gene expression changes in the hippocampal CA1 subfield from a total of 31subjects 9 controls and 22 AD subjects of varying AD severity (7 incipient, 8 moderate and 7 severe) with a total of 22,283 genes.

This dataset includes Mini-Mental State Examination (MMSE) and neurofibrillary tangle (NFT).

Using the dataset, we worked with 69 genes from which we took a set of 15 attributes of 31 patients that includes some of the main genes with their different allelic expressions that encode proteins that are directly involved with the distinctive marker of AD that are: APP, APOE (alleles: 212884, 203381 and 203382) BACE1, NCSTN, PSEN1 (alleles: 203460 and 207782) PSEN2 (alleles: 211373, 204261 and 204262) MAPT (alleles: 203928, 203930, 203929 and 206402). One of the main objectives of this research was to use machine learning algorithms for the classification of cognitive problems using biomarkers data from Alzheimer's disease. With the aim to obtain outperforming classifiers we decided to "binary-ize" the output variable of the dataset taking the values {healthy, incipient, moderate, severe}. As a result, the output variable takes the {healthy, ill}.Our dataset is available[1].

For the performance evaluation of classifiers, the percentage of correctly classified instances was considered. Taking concepts of the Information Retrieval field, given a test set of N documents expressing patients, a contingency table is constructed for each binary classification problem containing the count of true positives (TP) or number of correctly classified patients, false positives (FP) or number of patients incorrectly classified in the category in question, true negatives (TN) or number of patients correctly not classified in the category in question and false negatives (FN) or number of patients incorrectly not classified in the category in question. Using these values, the metrics for binary-decisions are defined as follows:

- **Precision:** Chance that a randomly selected patient will have Alzheimer's.

$$P=TP/(TP+FP)$$

- **Recall:** Probability that a patient with AD will be selected at random.

$$R=TP/(TP+FN)$$

- **F-measure:** Measure evaluation of the model implemented. It is calculated from the precision and recall of the model.

$$F=2*P*R/(P+R)$$

[1] shorturl.at/ceyVW

4.2.2 Machine Learning Methods Implementations

In this section, the results for conducting the research of the approach were defined 4 scenarios. For all scenarios, we used Weka [2]to implement the algorithms.

Scenario 1: shows the results obtained in a first stage test with the 15 attributes. The highest percentage of correctly classified instances was obtained with Logistic Regression with 64.5%, as shown in Figure 2.

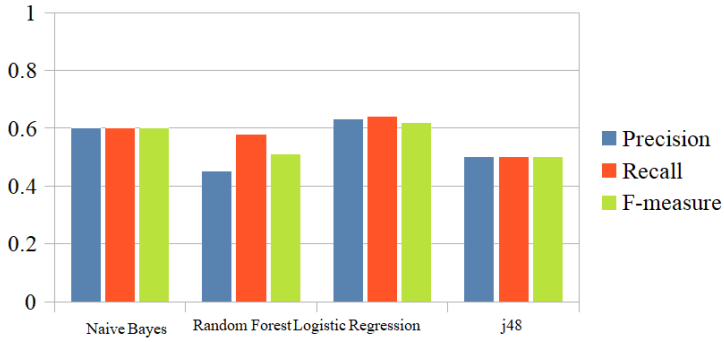

Figure 2
Results of Scenario 1

Scenario 2: APOE, NCSTN, PSEN1, PSEN2, and MAPT (203930- 206401) were considered. We obtained 67.74% correctly classified instances with Logistic Regression, as shown in Figure 3.

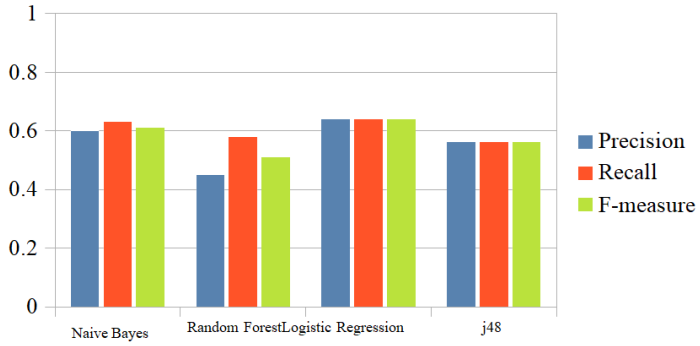

Figure 3
Results of Scenario 2

[2] https://www.cs.waikato.ac.nz/ml/weka/

Scenario 3: APOE, NCSTN, and BACE1 were considered: using the same algorithm, and 77.41% of correctly classified instances were obtained, as shown in Figure 4.

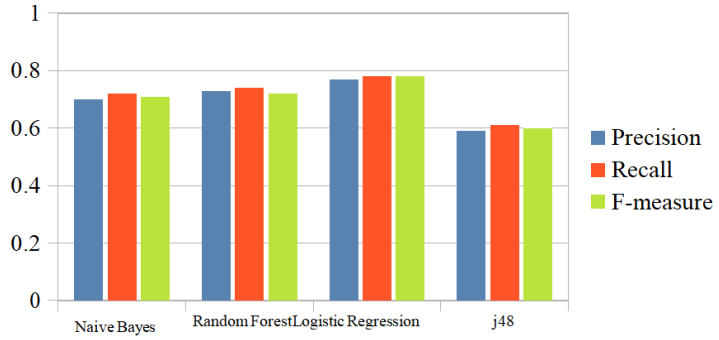

Figure 4
Results of Scenario 3

Scenario 4: APOE (203381) was considered with 70.96% of instances correctly classified using Random Forest, as shown in Figure 5.

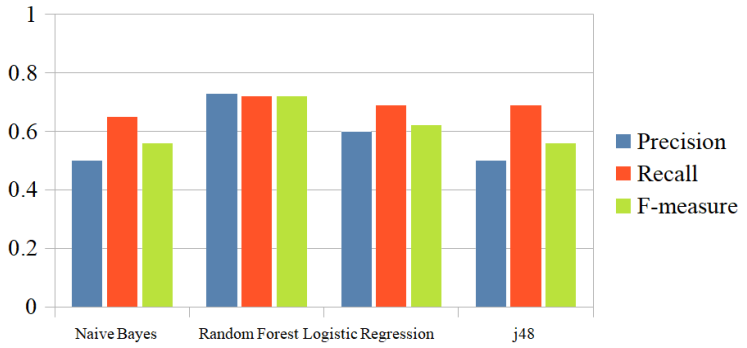

Figure 5
Results of Scenario 4

In summary of the findings, an average general accuracy of 70% was obtained for the Logistic Regression and 72% for Random Forest. One of the limitations found was the data sample used for the research. On the other hand, it was shown that the APOE, NCSTN, and BACE1 expressions have the potential to detect patients with Alzheimer's disease even early.

For all the scenarios, we have used 10-cross-fold validation. The initial set of independent variables were 15 (Scenario 1), and we obtained from [14]. Then, we have selected features with the aim of improving the algorithms' performance. In each selection, we have created the following scenarios: 2, 3, and 4. In all the cases the algorithms worked with the same parameters with default values.

4.3 Deep Learning for Classification

For this research, it was decided to use Deep Learning (DL) as a fifth classification method. The objective of this model is to achieve differentiation between healthy (control) persons and patients with Alzheimer's (sick), using the binary class (control: 0, sick: 1). A model was developed using Deep Learning algorithms. Batch size is the number of sub-samples given to the network after which parameter update occurs. The model presented had an accuracy of 80%. Likewise, machine learning algorithms, we have defined the following metrics:

Precision_score: This function can obtain the accuracy of each predicted class (control, disease) to achieve this, obtained the number of correct predictions for a class divided by the total number of predictions to this class.

Recall_score: This function obtains the number of classifications for each successful class divided by the number of instances (times) that belong to that class in the input set. The number of times was 20 in this case the batch was 2048 of the attributes.

The Keras [3]tool was used to make this model. It is a Neural Networks (NN) library, which is specially designed to enable the short-time experimentation with deep learning networks known by its English acronyms Deep Learning (DL). Keras follows the best practices for reducing cognitive burden, offers consistent and simple APIs, minimizes the number of user actions for common causes, and offers decipherable messages. Keras was chosen as it is an easy tool to use and implement. This tool allows you to port Keras models to JavaScript to run directly in any browser. We chose to implement this model in Tensorflow[4]. This tool was developed by Google and can train neural networks to detect, decrypt patterns and correlations analogous to human learning and reasoning.

The objective of this model is to differentiate between healthy and patients with Alzheimer's (ill), using the binary class (healthy: 0, ill: 1). For this, a model is developed using Deep Learning algorithms. For this, the Anaconda container was used, this is a platform developed by data scientists to solve more serious problems in the science industry. This tool can solve non-existent problems. It was decided to use this tool because it allows access to more advanced learning resources, can compile Python for fast execution and is the most complete container for data science with Python Jupyter Notebook was used for real-time data visualization on the web. Using the model created in Keras, a sequential model of Neural Networks (NN) was developed which contains 4 hidden layers, using the binary target (healthy: 0, ill: 1).

[3] https://keras.io/

[4] https://www.tensorflow.org/?hl=es-419

The training vector consists of 21 subjects and the test vector of 10 subjects. As mentioned above, NN attempt to imitate human-like behavior, the network is composed of interconnected neurons. Each of these neurons is characterized by its weight, bides, and activation function.

The following activation functions were used to construct the four-layer sequential model:

Sigmoid: Is a type of function that is used for the output layer when making binary predictions, which is the research case. This is one of the most commonly used non-linear activation functions since it transforms values between range 0 and 1.

Rectified Linear Unit (ReLU): This is another non-linear activation function in the Deep Learning domain, this function was used as it has the benefit that it does not activate all neurons at the same time.

In the first layer, it is of type Embedding and processes input data by modifying it in the elements of the matrix which will allow calculation to obtain weights for each layer. The second layer makes it easy to get the best weights. The third layer of Dropout will be used to reduce the likelihood of overfitting occurrence during the training model. The fourth and last layer is from Dense which will allow classification from data generated by the previous layers. Once the algorithm was trained, the model validation process was passed for this case, 21 subjects were used for training and the remaining (10) for the validation process (holdout method). Using the Keras model allows us to separate a part of the data to train together validation data sets and to evaluate the performance of your model in that validation data set at each epoch (epoch). Every time is the number of times that all training data is shown to the network. This process consists of increasing the number of times since the accuracy of validation begins to decrease even when the accuracy of training increases.

4.4 Results and Discussions

In this research, we present an approach based on supervised automatic learning for the early detection of Alzheimer's disease. The GDS810 data set was used, consisting of patients with AD and controls (healthy). The first classification model is implemented using the analysis of the selection of characteristics, we obtained the most informative genes, and a classification model is developed using Naîve Bayes, Decision Tree (Random Forest and j48), and Logistic Regression.

For the second model, deep learning algorithms were implemented in which data from people with Alzheimer's Disease and Normal Control were successfully classified with an accuracy of 80% using the 4-layer Sequential RN architecture that was trained and tested with a large number of attributes. This deep learning

solution and the research objective not only open new avenues for analysis and study of genes attributed to AD. This deep learning solution allowed us to select and classify features with a unique architecture.

The precision achieved with this method was high, confirming that the network architecture was selected correctly and that the DL and ML models bring great value to the classification of cognitive diseases. As research into the diagnosis of Alzheimer's disease progresses, theories are being established about incorporating tests that deal with biomarkers.

The ideal biological marker that should detect a fundamental characteristic of the neuropathology of the disease and should have been validated in cases confirmed by neuropathological studies, have a specificity greater than 80% to distinguish from other dementias, and be reliable [11]. The research found that the implementation of Machine Learning (ML) and Artificial Intelligence methods to the type of diagnosis of people with cognitive disorders, dementia, Alzheimer's, and other related dementia has yielded positive results with great efficiency that encourages further research and knowledge about the pathology of the disease. We found that the most popular ML found methods applied to the classification of people with cognitive disorders, people with Alzheimer's, and healthy people are Naïve Bayes (NB), Linear Regression, and Decision Trees. All of them obtained an acceptable performance reaching 70% of the accuracy average. Remarkably, Artificial Neural Networks reached an 80% accuracy.

From a comparative perspective, Table 1 shows the results of the scenarios in terms of precision. In the Scenario 1, the work of Gutiérrez et al. outperforms ours considering the same set of proteins. However, our work outperforms Gutiérrez's with a reduced set of proteins. Furthermore, our work outperforms Gutiérrez's with the same set of proteins and using a Deep Learning model (80%).

Table 1
Comparison with Gutiérrez et al. 2004

	Scenario 1 (ML/DL) APP, APOE, BACE1, NCSTN, PSEN1, PSEN2, MAPT		Scenario 2 (ML) APOE, NCSTN, PSEN1, PSEN2, MAPT	Scenario 3 (ML) APOE, NCSTN, BACE1	Scenario 4 (ML) APOE
Our approach (precision)	64.5%	**80%**	67.4%	**77.41%**	70.96%
Gutiérrez et al. [14] (precision)	**77%**	-	-	-	-

Conclusions

In this research, an average general accuracy of 70% was obtained for RL and 72% for Random Forest. Even when the data were limited, it was shown that the APOE, NCSTN, and BACE1 expressions have considerable potential to detect

early-stage patients with Alzheimer's disease. On the other hand, using the same data set, it was decided to implement a model using artificial intelligence to evaluate which of the two algorithms was most accurate in being able to identify people with Alzheimer's early stage. For this implementation, a neural network library was used using the Anaconda container, this platform developed by data scientists to solve specific problems.

This classifier managed to identify with 80% pressure using a 4-layer Sequential RN architecture. The implementation of these methods proved the hypothesis that supervised learning algorithms can identify people who have Alzheimer's at an early stage, which has been a great challenge for decades. The second method was aimed at identifying efficiency among the methods implemented. Based on the results, it was shown that deep learning algorithms manage to identify with more accuracy with 80% more than deep learning algorithms vs. 72%, with Random Forest in the implementation of supervised learning algorithms.

Each study that has applied Machine Learning (ML) or other algorithm methods is unique, as it depends on the complexity of the target dataset. The rise of research in this field of diagnosis continues to grow over the years, but they are still in "future" research. Implementing these new methods requires studies with larger populations and over time. This research needs to be evaluated before it can be implemented. One of the limitations found in the research and which has been one of the most encountered limitations in all the studies studied is the amount of data that exists under the theme of attributes that contribute to the classification of cognitive problems.

The limitations are associated with the large amount of good quality data required, provided by image techniques and other variables entered to achieve optimal algorithms. Artificial intelligence and Machine Learning algorithms are statistical and pattern recognition systems for analyzing, identifying, and understanding data patterns. The efficiency of an algorithm is the amount of data available for analysis. The more raw data the algorithm has, the more accurate the result. The goal of this algorithm is that you can automatically perform tasks that humans will have to accomplish or reduce workloads by automating certain aspects of tasks. Machine learning algorithms are trained with experience and analysis. The Machine Learning model is given an entry, a given task to complete and can make decisions, then sets a course, to accomplish this task with minimal human intervention. The more times the model resolves the task and produces an output the result will be more efficient.

As future work, it has been considered to include other databases that include sources of information about patients with Alzheimer's disease to identify levels of exposure of candidate genes at the onset of the disease. Because the data set used for research was made up of people who were healthy and who had the disease. An interesting topic to research and to know a little more about the behavior of pathology once it's in stage three, which is the most difficult and

longest. At this particular stage, personality changes begin and people become more violent. Conversely, another research line would be to continue to explore the implementation of deep neural network algorithms to improve the values obtained.

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