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Research paper

Alzheimer Disease Classification Model Using Machine Learning Techniques

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Abstract

Technological advances have allowed the machine learning area of the field of artificial intelligence to emerge and provide new solutions to different problems. Medicine is one of the sciences driving these advanced solutions. Using real-time data, a model has been developed for the classification of brain images taken through neuroimaging techniques to assist in the diagnosis of Alzheimer's disease (AD). Alzheimer's is a very important condition as it affects cognitive functions and daily living activities. For the development of this work, convolutional neural networks were used with a total of 5,600 images for training and testing; the images were extracted from medical reports. In the end, an accuracy level of 70% was reached in all cases during training and evaluation. This percentage was considered acceptable by the medical specialist.

Keywords: *Machine Learning; Convolutional Neural Networks; MRI Brain Images; Image Classification.*

1. Introduction

According to the World Health Organization (WHO), cases of dementia will triple and reach 152 million people by 2050 [1]. With the increase in life expectancy, thanks to advances in medical technology that have come to offer good technological achievements in disease prevention, treatment, drugs and greater access to health services, the growth rate of dementia cases has become one of the main challenges of public health, with 40-50 million people currently living with this condition [2]. The care of such patients has wide-ranging consequences for families, health systems, and society. Dementia encompasses a series of progressive diseases that affect attention, memory, and other cognitive and behavioral skills [3]. There are more than 100 forms of dementia, and the most common is Alzheimer's disease (AD), which accounts for 60% to 80% of all cases [4]. In Figure 1, we can see the percentage of cases of other forms of dementia, such as Lewy body, vascular, and frontotemporal [5].

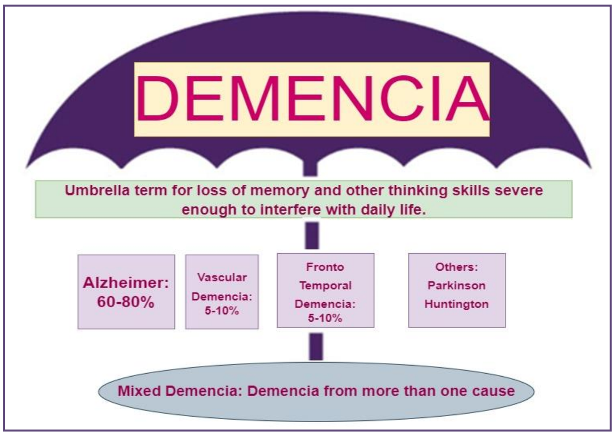


Fig. 1: Percentage of Dementia Cases.

Dementia is a neurodegenerative disease whose development structurally modifies the brain, especially in the regions responsible for cognitive functions. The human brain grows gradually until the age of 21, after which a progressive but discreet decline begins. Brain volume only declines after the age of 60, which becomes more pronounced between the ages of 70 and 90. The annual brain atrophy of a patient with neurodegenerative disease is between 2 and 3%, while healthy individuals have 0.2 to 0.5% atrophy [5]. Figure 2 illustrates the difference between a normal brain and an affected brain.

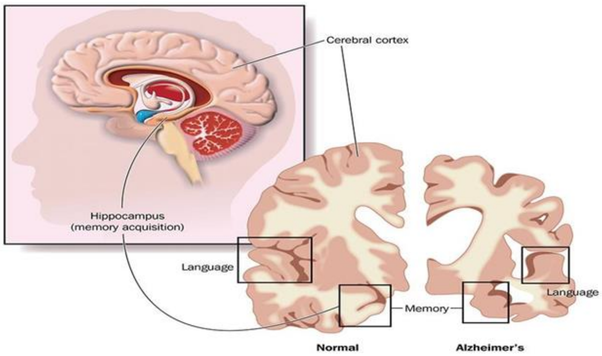


Fig. 2: Example Of Cerebral Shrinkage for Two Subjects: Normal Brain on the Left and Brain with AD on the Right.

Currently, there is no cure for dementia; thus, early diagnosis is crucial for managing symptoms and slowing disease progression. MRI scans enable doctors to detect early signs or assess severity in advanced cases. Early diagnosis is essential for proper treatment, and Machine Learning (ML) techniques can aid in monitoring patient progression from mild cognitive impairment to dementia.

Therefore, this article aims to verify the performance of ML models that can be used to help doctors in the early detection of dementia, based on basic characteristics of the patient. To this end, we will use the dataset made available by the Open Access Series of Imaging Studies (OASIS) [7], a project that aims to make brain datasets freely available to facilitate future discoveries in basic and clinical neuro-science. The chosen dataset is OASIS-1, which contains magnetic resonance imaging data.

2. Literature review

In the literature, there are numerous studies on dementia, whether to discover its cause, relationship with other diseases, possible reversal of symptoms, or early diagnosis. Below are some related studies that can add to our knowledge about the evolution of science on the subject, whether using data science.

2.1. Artificial intelligence predicts Alzheimer's years before diagnosis

A study published in Radiology demonstrates the use of artificial intelligence (AI) to predict Alzheimer's disease (AD) by analyzing brain images. Researchers found that changes in glucose metabolism in the brain, detectable through 18-F-fluorodeoxyglucose PET (FDG-PET) scans, can indicate the disease process. These subtle metabolic changes are challenging to identify manually.

Using data from the AD Neuroimaging Initiative (ADNI), scientists trained a deep learning (DL) algorithm with over 2,100 FDG-PET brain scans from 1,002 patients, reserving 10% of the data for testing. The algorithm achieved 100% sensitivity in detecting disease features on an independent set of 40 scans, potentially predicting AD up to six years before symptom onset.

2.2. Scientists find link between anemia and increased risk of dementia

According to a study published in Neurology [9], scientists concluded that there is a direct relationship between the increased risk of developing dementia as an adult ages and their hemoglobin levels being above or below normal.

Hemoglobin is a protein present in red blood cells and is responsible for the red color of blood. Its function is to transport oxygen throughout the body, and when the concentration in the blood drops below normal levels, it causes anemia [10].

The study was conducted on approximately twelve thousand participants, with an average age of 64, over a period of 12 years. At the end of the proposed period, it was found that 1,520 individuals had developed dementia. They observed a U-shaped association between hemoglobin levels and dementia, so that both low and high levels were associated with an increased risk of dementia.

The scientists explained that, since hemoglobin transports oxygen throughout the body, if there is too little, some parts of the brain may be left without it, which can cause inflammation and damage the brain. As for high hemoglobin levels, the theory is that it would make the blood more viscous, making it difficult for it to enter smaller blood vessels and potentially reducing the supply of oxygen to the brain.

2.3. Reversing symptoms

A study published in ScienceDaily suggests it may be possible to reverse early-stage Alzheimer's using the Affirmative Health Personal Therapeutic Program (PTPr). Researchers tested a personalized program on 35 individuals with subjective and mild cognitive impairment. Participants attended a four-day immersion program with personal therapy plans, physician consultations, and follow-up telemonitoring. Results showed improved blood glucose, insulin, and vitamin B12, D3, and E levels. Montreal Cognitive Assessment (MoCA) scores stabilized for the group and improved significantly for those with a baseline score of 24 or less. The study indicates that a personalized approach can improve cognitive and metabolic functions, supporting the need for larger, placebo-controlled clinical trials.

2.4. Related works

Literature [12] applied rules in conjunction with pattern recognition methods in SPECT (Single Positron Emission Computer Tomography) images to distinguish patients with AD from normal individuals.

Literature [13] applied a set of rules and data obtained from fMRI images (Functional Magnetic Resonance Images) to classify patients with dementia from normal individuals. Unlike SPECT acquisitions, fMRI images are considered non-invasive imaging techniques due to the absence of radioactive contrast, and yet, they have high spatial resolution and response speed. Despite the promising results shown by the analysis techniques of medical images and other biological signs, in this thesis, we did not use data from these images, as these data were not available for most patients in the two databases of clinical cases used in the development of this work.

Literature [14] combined information extracted from the patient's electronic medical record, such as radiological reports, clinical attributes, and sociodemographic information. Feature extraction was performed with Stacked Denoising AutoEncoders (sDAE), and the classification layer was implemented with random forests to predict 72 diseases. The prediction of liver cancer achieved an accuracy of 92.5%, which is the disease for which a computerized diagnostic aid obtained the highest performance in this work.

Literature [15] combined features extracted from computed tomography images, such as size, perimeter, and degree of deformation of nodules, and the report of radiological findings to classify focal liver lesions as benign or malignant. The classification of these features was tested in different ML algorithms such as Bayesian Networks and Support Vector Machines, obtaining a maximum accuracy of 91.71% when using the approach proposed by the authors called Three-way Decision.

Literature [16] combined features extracted by Wavelet transform from computed tomography images and clinical attributes to aid in the diagnosis of hepatocellular carcinoma. The ML algorithm used for classification was the Support Vector Machine, and the maximum accuracy obtained in this work was 88.46%.

Literature [17] combined clinical attributes and behavioral information to aid computerized diagnosis of hepatocellular carcinoma using Bayesian networks. The accuracy obtained for the set of 23 test patients was 100%.

Literature [18] combined clinical, sociodemographic, and magnetic resonance imaging attributes for the prognosis of chemoembolization treatment in patients with hepatocellular carcinoma, obtaining a mean accuracy of 78.00% using random forests.

Literature [19] combined clinical attributes and cancer biomarkers found in urine to aid computerized diagnosis of hepatocellular carcinoma. Both information were processed using different ML approaches, and the Random Forest was the technique that achieved the highest performance in this work, reaching a maximum accuracy of 94.70%.

It is possible to see from the studies cited that scientists are looking for ways to predict, correlate, or even reverse symptoms of this neurodegenerative disease, using techniques or data that they did not previously have. This work has the same goal, although ML is not a current method, we were able to prove that using the right algorithm and metrics, we can diagnose or even detect the possibility of an individual having the disease at some point in their life [20-21].

3. Procedure for diagnosis of Alzheimer’s disease (AD)

This section focuses on implementing a deep learning (DL) system for detecting and classifying Alzheimer's disease (AD). Using an image database with four classes representing dementia stages, a CNN model is developed for classification. Test results and details of the architecture will also be presented.

3.1 Database used

The model classifies MRI brain images into four Alzheimer's stages: No dementia (ND), Very mild dementia (VMD), Mild dementia (MD), and Moderate to Severe AD (MAD and SAD). Using a database of 382 images, divided based on Clinical Dementia Rating (CDR) scores, the model targets patients aged 20 to 88. Data augmentation is applied to expand and balance the dataset, enhancing the model's learning rate. Preprocessing involves scaling images from 256 × 256 to 224 × 224 to suit the CNN model's requirements.

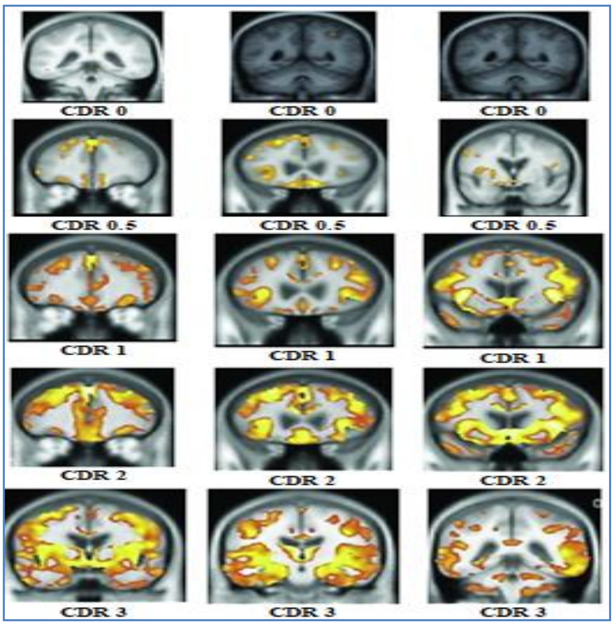


Fig. 3: Sample Data Set.

Table 1: The Classification of the Database Used According to CDR

Clinical dementia rate (CDR)	Number of samples
ND	1670
VMD	870
MD	1050
MAD	230
SAD	126

4. Development of a classification model

To develop the model, the methodology is composed of 4 main processes:

- Pre-processing, extraction of information (images) to train and validate the model.
- Learning, start of training, to be able to select the algorithm that allows classification with the greatest precision.
- Evaluation, selection of metrics to evaluate model performance.
- Prediction, tests are carried out to verify the prediction.

After having carried out all these data preparation activities, the group shown in Table 2 was obtained, and as a percentage, we can see it in Figure 4.

Table 2: Number of Images Used

Type	Number of images
ND	151
VMD	644
MD	1,209
MAD	841
SAD	2,853
Total:	5,698

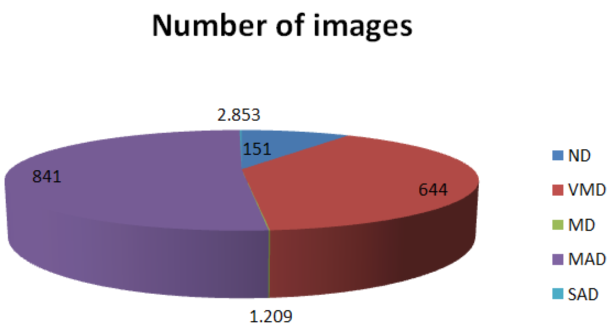


Fig. 4: Number of Images Processed.

4.1. Prototype development

Once the image organization phase was finished, the ML algorithm began to be tested for the development of the prototype. Convolutional neural networks (CNN) are a DL model that is designed to work with images, as it enables the computer to 'see' and interpret image features. The support vector machine (SVM) algorithm was tested; this method has also been adapted for image classification tasks.

In the comparison between the algorithms (Table 3), CNN was the best option to perform training for image classification because it presented the highest levels of precision with test data.

Table 3: CNN vs SVM Comparison

Comparison	CNN	SVM
Accuracy without data cleaning	29 %	22 %
Initial precision with data cleaning	60 %	50 %
Processing time per iteration without GPU	60 seconds	75 seconds
Processing time per iteration with GPU	2.5 seconds	3.5 seconds
Accuracy without data cleaning	29 %	22 %
Initial precision with data cleaning	60 %	50 %

The convolutional neural network was worked on with Python, TensorFlow, Keras, and scikit-learn.
To construct the convolutional network, we proceeded as follows:

- The Train_test_split method from the scikit-learn library was used to create arrays with the images loaded in memory.
- The arrays were normalized so that the values are in the range of 0 and 1, through the to_categorical method of scikit-learn, converting the labels into outputs with binary values to better classify the neural network, in the present investigation we have 5 labels of AD images: ND, VMD, MD, MAD and SAD; The output will be a vector with 5 elements, where each position represents the label in the aforementioned order, this indicates that the image has been classified as Very Mild Dementia (VMD).
- For training and testing, the values 80-20 were used, that is, 80% of the images for training and 20% for testing.
- The following constants were defined:
- Learning rate for error tolerance of 0.001.
- Number of iterations (epochs), starting from 50 to 3000 epochs, to obtain the highest precision in the model.
- Batch size of the images to be processed in memory: a value of 64 was used.
- A layer of 2-dimensional convolutional neurons of 120x120x3 was created
- 32 filters (kernel) of size 3x3 were applied, which detect image characteristics.
- The LeakyReLU function was used to activate the neurons, this function behaves well with images, it performs well in convolutional networks and is similar to the ReLU function, it transforms the entered values by multiplying the negative ones by a rectified coefficient (which in this case case was alpha = 0.1), alpha is a constant for numbers below zero, so that only positive values are entered.
- To avoid overfitting, the technique called Dropout was added. This technique allows neurons to be randomly selected and others to be ignored during training. According to the information reviewed on the application of the function, it is recommended to use dropout rate values that are between 20% to 50%, a probability that is too low has a minimal effect, and a value that is too high results in underlearning of the network (Geron, 2017; Brownlee, 2019). When a probability of 20% was used, a precision of 64% was achieved and with 50% a precision of 70% was obtained.
- The images were subsequently flattened with 32 filters, equivalent to 32 Dense neurons.
- The last output layer was established with 5 neurons, and the Softmax activation function was used to normalize the output layer because it handles multiple classes; in this case, there are 5 labels to be classified.
- And finally, the neural network is compiled with the Adam algorithm optimizer, which adapts the learning rate to the established parameters.

4.2. Prototype training

During the training process and for the correct functioning of the prototype and the convolutional neural network, images of 120 x 120 pixels were used, because a larger dimension caused memory overflow, limiting us to carrying out a few iterations or epochs.
The keras library during training uses different neural networks and for each epoch it generates 4 metrics, which improve with each iteration (figure 5), the metrics are: precision, loss percentage, precision validation (val_accuracy) and loss validation (val_loss). All this data generates a history that can be presented through a graph.

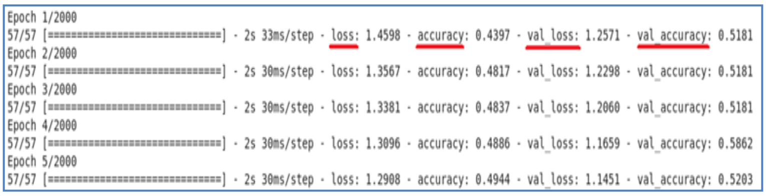


Fig. 5: Training Results by Epoch.

Different iterations were carried out to obtain the highest precision value: 50, 80, 150, 250, 500, 1000, 2000 and 3000 epochs. The iterations carried out are detailed below (Table 4):

Table 4: Accuracy Calculated by Scikit-Learn

No. of epochs	Precision Micro Average	Macro Average	Weighted Average
50	64	68	64
80	67	64	66
150	67	66	67
250	66	68	68
500	67	68	67
1000	69	69	69
2000	67	69	67
3000	67	69	66

According to the data in Table 4, it was decided to use the model trained for 1000 epochs, because it has the highest precision values, that is, the precision at the level of each class was the highest (macro average), the precision with contribution from other classes was also the highest (micro average) and the precision according to the number of instances per label was also the highest (weighted average). The details of the precision values obtained for each class are shown in Table 5.

Table 5: Metric Calculation with Scikit-Learn

	Precision	Number of images
Class 0 (ND)	0.95	33
Class 1 (VMD)	0.99	136
Class 2 (MD)	0.90	261
Class 3 (MAD)	0.99	164
Class 4 (SAD)	0.91	546
Micro average	0.99	1140
Average Macro	0.99	1140
Weighted average	0.99	1140

4.3. Image classification model with CNN

After the training process, the most representative model that was obtained was with a thousand epochs and with a precision value of 90%, where the maximum precision value achieved during training was close to 95%. With greater iterations, it was not possible to improve the precision. Once the cleaning process was completed, the images were loaded, categorized, and the data converted into matrices for the respective operations.

In the first convolution, 32 3x3 filters were used with the LeakyRelu activation function because it has better performance with CNNs, where basic information is obtained from an image with edges and shadows. It is worth mentioning that the extraction of these characteristics is typical of the form of the image and the edges extracted in the cleaning process.

The second convolution worked with 32 3x3 filters with the LeakyRelu activation function, seeking to obtain more specific features such as textures and contrasts. Due to the quality of the images, adding more convolution layers did not help extract new features for the training process.

Subsequently, the flattening of the images was carried out with 32 filters equivalent to 32 dense neurons to be able to use it as a feature vector in this layer and as the last layer the softmax activation function was used with 5 dense neurons for the 5 labels that we have, To normalize the output and this according to the "hot encoding" that was carried out in the configuration, we can graphically represent the model as seen in figure 6.

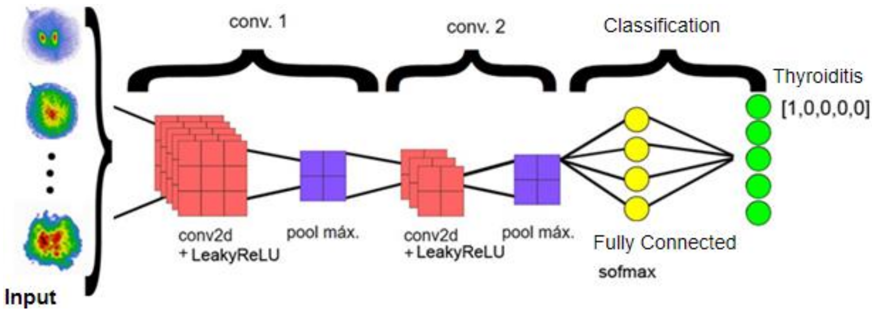


Fig. 6: Image Classification Model with CNN.

This model was used for the evaluation stage with the confusion matrix through its respective indicators: precision, accuracy, sensitivity, and specificity. This model was also used for prediction tests, comparing against other images that were not considered during the training and testing phase.

5. Results

Once the model with the highest precision value has been obtained, the model is evaluated through the calculation of the indicators that have been defined: precision, accuracy, specificity, and sensitivity. Subsequently, its behavior is verified when making predictions with new images.

5.1. Model evaluation

Once the model was built with the prototype that obtained the best average precision, it was decided to use the confusion matrix to see the performance of the algorithm used in supervised learning.

During the training phase, the images were organized into 5 groups following the 80 – 20 rule. Of the 5,698 images, 20% were used for the evaluation, that is, 1,140 images. The number of elements for each class was determined by Keras as shown in Table 6:

Table 6: Labels with Quantities of Elements

Label	Tag or class name	Number of images
0	ND	33
1	VMD	136
2	MD	261
3	MAD	164
4	SAD	546

Using scikit-learn, the calculation of the respective values for the confusion matrix has been carried out, and the result obtained can be seen in Table 7:

Table 7: Confusion Matrix Obtained from Scikit-Learn

	ND	VMD	MD	MAD	SAD
ND	14	0	2	2	15
VMD	0	59	6	7	64
MD	0	2	194	19	46
MAD	1	3	30	81	49
SAD	2	17	44	28	455

In this matrix (Table 7), the diagonal represents the cases effectively classified by each label or class (ND, VMD, MD, MAD and SAD); these values represent the real positives (TP).

On the other hand, to identify the other values (real negatives, false positives, and false negatives), calculations must be carried out for each of the labels or classes created.

False positive (FP) values, where cases belong to a class, but the model predicted they do not; They are represented by the sum of the columns without counting the values of the diagonals (Table 8).

Table 8: Calculation of False Positives

	ND	VMD	MD	MAD	SAD
ND	14	0	2	2	15
VMD	0	59	6	7	64
MD	0	2	194	19	46
MAD	1	3	30	81	49
SAD	2	17	44	28	455
False positives	3	22	82	56	174

The calculation of the real negative values of all classes is seen in Table 9.

Table 9: True Negative Results by Class

Class or label	TN
ND	1104
VMD	982
MD	797
MAD	920
SAD	420

The model accuracy indicator is calculated by the sum of the correctly identified values (TP) between the sum of the total elements of the matrix (Accuracy = 90.43)

To calculate the sensitivity (also called recall), specificity, and precision indicators of the model, it had to be calculated for each label and the average values (table 10):

Table 10: Sensitivity, Specificity, and Precision Values Per Label

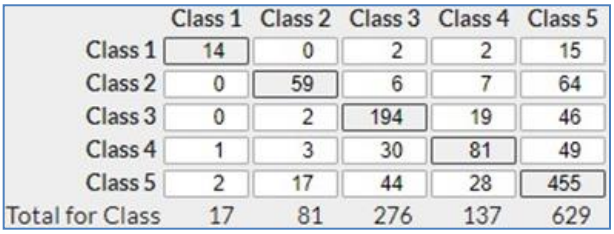
Class or label	Sensitivity (TP / (TP + FN))	Specificity (TN / (TN + FP))	Precision (TP / (TP + FP))
ND	0.9242	0.9830	0.9335
VMD	0.9338	0.9897	0.9283
MD	0.9432	0.9224	0.9028
MAD	0.9939	0.9172	0.9912
SAD	0.9333	0.9709	0.9233

The previously achieved indicators cannot be averaged commonly: add all the values and divide it by the number of elements, because different quantities of images were taken per class (table 6) that are not proportional in quantity per class, for this In this case, the weighted average (PP) is used, which takes each value obtained by the number of instances of the class.

Then, through the confusion matrix, the indicators mentioned in the operationalization of variables were obtained:

- The accuracy of the model reached 90.31%.
- Sensitivity: 90.43% of cases were correctly identified.
- Specificity: 95.14% of negative cases were correctly classified.

To compare the data obtained with the confusion matrix, some online resources were searched, where 2 websites were found, which allow entering the values of the confusion matrix and determining the precision. In the first site, the precision obtained is 90.44% (Matrix, 2018); in this case, the precision value is the same as that calculated with the confusion matrix (Figure 7).



	Class 1	Class 2	Class 3	Class 4	Class 5
Class 1	14	0	2	2	15
Class 2	0	59	6	7	64
Class 3	0	2	194	19	46
Class 4	1	3	30	81	49
Class 5	2	17	44	28	455
Total for Class	17	81	276	137	629

Fig. 7: Precision Calculation with the Confusion Matrix.

Another page was found from the AI researcher named Marco Vanetti, who developed a confusion matrix calculator, where the precision value obtained was 70.44% (figure 8), as well as the previous page and the precision calculated using the confusion matrix, the value is the same [22].

		Class 1	Class 2	Class 3	Class 4	Class 5	Classification overall
Classifier results	Class 1	14	0	2	2	15	33
	Class 2	0	59	6	7	64	136
	Class 3	0	2	194	19	46	261
	Class 4	1	3	30	81	49	164
	Class 5	2	17	44	28	455	546
	Truth overall	17	81	276	137	629	1140

Fig. 8: Precision Calculation with the Confusion Matrix.

Using scikit-learn, the accuracy of the model on the test set was 90.31%. In addition, we used two online calculators for validation: one calculator gave a similar result (90.44%, probably due to performance), and the other calculator gave a 70.44% result, possibly due to different interpretations of the metric or observation class imbalance. Therefore, the calculation results based on the confusion matrix are considered authoritative.

5.2. Prediction

Once the neural network model was trained and adjusted, the model generated during the training phase was used, which, through an application developed with Python, different images were provided to the model so that make a prediction to which of the labels it belongs. The locations of the output array are the same as the labels that were used during the training phase: ND (0), VMD (1), MD(2), MAD (3), and SAD (4):

In the model prediction, it was identified 100% as MAD, in small percentages, it was found like the other labels. This prediction was incorrect, as shown in Figure 9.

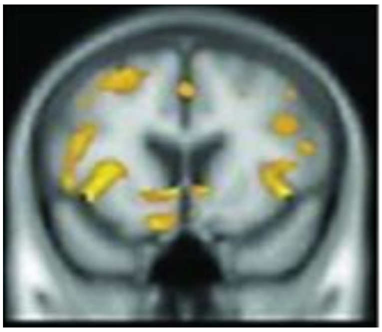


Fig. 9: No Dementia.

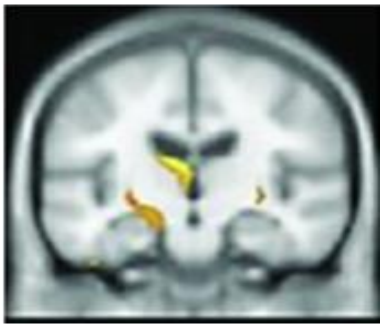


Fig. 10: Mild Dementia.

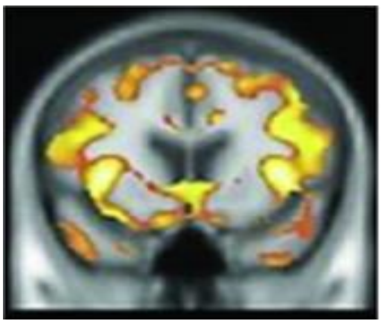


Fig. 11: Very Mild Dementia.

Fig 10 was also not correctly predicted because the gland had ND, but the model indicated that it was a SAD.

Fig 11, the prediction was correct because the AD did have a VMD.

In addition to the 5,698 used in training and testing, 50 images were used for prediction tests (Table 11), where the following results were obtained:

- In the case of images labeled as ND, only 5 out of 10 were correctly predicted; the remaining 5 were misclassified as SAD.
- In the case of a normal AD, 8 images were correct predictions, and in the other 2 predictions, the model indicated that it was a SAD.
- In the case of MAD, due to the characteristics of the images, 2 predictions indicated that it was a ND, 2 predictions were correct and the other 6 predictions indicated a SAD.
- In the case of SADs, 15 of the predictions were correct, and 3 indicated that it was a ND.
- For ND, no prediction was accurate.

Table 11: Comparison of Predictions Using Images

Diagnosis	Total Cases	ND	VMD	MD	MAD	SAD
ND	10	5			5	
VMD	10		8		2	
MD	10	2		2		6
MAD	18		3			15
SAD	2			1	1	

Of the 50 prediction cases, 30 were correct predictions, which is equivalent to saying that 60% were correct predictions.
From the information provided, it could be seen that:

- 50% of patients have SADs and need further investigation to rule out that the images are not AD.
- 21% are patients with VMD
- 11% of patients have MD
- 15% of patients have MAD.
- 3% of patients have ND.

5.3. Hypothesis testing

The null hypothesis was used, where H0:

- H0: The ML-based model diagnoses the type of Alzheimer's disease with an accuracy of less than 70% using MRI brain images.

In the case of ML, instead of the equation for calculating the critical value, the keras and scipy libraries have been used with the Anderson-Darling method. With the model obtained through the keras prediction method, an arrangement was obtained with the normalized values as shown in Figure 12.

```
Predictions= AD_Model.Predict(Valid_X, verbose=0), flatten()
Print (predictions.shape)
Print (predictions)

(4555, )
[0.11970718 0.27637592 0.00384649....0.00201238 0.3306+14656 0.01712583]
```

Fig. 12: Prediction with Normalized Values.

6. Conclusions

Regarding the objectives set in this work, the following is concluded:

- It was possible to describe the procedure carried out to obtain images with MRI brain images so that the specialist doctor can analyze the image and prepare the respective report with the respective diagnosis. There are images with a clear pattern that allow the diagnosis of the AD; however, some images present a poorly defined shape, which is why the expert's experience is required for an accurate diagnosis.
- The prototype was developed with the ML algorithm so that the model can classify the images. Many tests were carried out until a stable prototype was achieved with a neural network of the CNN type.
- The image classification model was developed, seeking the highest precision value. This was evaluated, and an overall accuracy value of 70% was obtained. It should be noted that because the number of images of SADs is greater, the model has a greater capacity to identify a SAD. During the training phase, the precision value reached 85% in these cases.
- Regarding the hypothesis raised in this research, we can indicate that the level of precision reached with the diagnostic model for the identification of types of ADs using ML was 70% considering all the study images.
- MRI brain images are an imaging technique that does not provide good quality images for training the model with ML, which represents a limitation when trying to improve the level of precision in the image classification model. Although it is a limitation, in our environment, it is one of the diagnostic techniques frequently used in state hospital centers.
- From the information collected and processed, it was observed that several patients have SADs, around 50%, who tend to have AD, which would have to be reviewed in more depth and prevent invasion into other organs. which would seriously complicate the patient's health status.

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