Implementación de un modelo predictive basado en redes neuronales convolucionales 3D en el paso de deterioro cognitivo leve a Alzheimer sobre imágenes por resonancia magnética

Implementation of a 3D Convolutional Neural Network Predictive Model for the Transition from Mild Cognitive Impairment to Alzheimer's Disease using Magnetic Resonance Imaging (MRI) Images

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Resumen

La enfermedad del Alzheimer es un trastorno neurológico que causa la pérdida de autonomía y memoria en las personas que la padecen. Debido al aumento de casos de este padecimiento y la falta de precisión de las herramientas de diagnóstico se da paso al desarrollo de nuevas herramientas capaces de disminuir esta problemática. El objetivo principal de este trabajo investigativo es implementar un modelo de red neuronal convolucional tridimensional con estructura base tipo AlexNet3D para obtener la predicción de un posible diagnóstico de la enfermedad Alzheimer (AD) a partir del análisis de imágenes por resonancia magnética, utilizando como etapa temprana el síndrome de deterioro cognitivo leve (MCI). Este proyecto brindará la explicación de cada fase planteada, las cuales fueron dividas en selección de las bases de datos, elección de características, procesamiento de los datos, desarrollo del modelo para su entrenamiento y validación, y por último, resultados obtenidos a partir de las pruebas de predicción. Con las cuales pudo obtenerse un porcentaje del 72,222 %, permitiendo catalogar al modelo K-Net95 como una red estable y eficiente, a pesar de las limitaciones computacionales a las que se vio limitado el proyecto.

Palabras clave: *Alzheimer, Clasificación, Deterioro Cognitivo Leve, Imágenes por Resonancia Magnética, Predicción, Red Neuronal Convolucional Tridimensional.*

Abstract

Alzheimer's disease is a neurological disorder that causes loss of autonomy and memory in people who suffer from it. Due to the increase in cases of this disease and the lack of accuracy of diagnostic tools, new tools capable of addressing this issue are being developed. The main objective of this research work is to implement a three-dimensional convolutional neural network model with AlexNet3D type base structure to predict the possible diagnosis of Alzheimer's disease (AD). from the analysis of magnetic resonance images, using as an early stage mild cognitive impairment syndrome (MCI). The construction phases of the project will be explained, divided into database selection, feature selection, data processing, model development for training and validation, and finally, results obtained from prediction tests. With this it was possible to obtain a

percentage of 72,222 %, allowing the K-Net95 model to be cataloged as a stable and efficient network, despite the computational limitations to which the project was limited.

Key Words: *Alzheimer's Disease, Classification, Magnetic Resonance Imaging, Mild Cognitive Impairment, Prediction, Three-Dimensional Convolutional Neural Network.*

1. Introduction

Recognized as one of the foremost research domains, the medical sector grapples with challenges to enhance non-invasive and diagnostic techniques, thereby improving the quality of life for patients. Early detection of terminal illnesses remains a significant focus. Consequently, the medical field has spearheaded numerous investigations, intertwining with the realms of automatic computing and engineering. These collaborations aim to optimize treatments and diagnoses for various diseases [1, 2]. The pressing need has led to the development of novel diagnostic techniques that amalgamate the use of emerging technologies with non-invasive clinical studies. Consequently, there has been a recent surge in the adoption of artificial intelligence models, representing the science of automation striving to create intelligent systems capable of extracting information from their environment, learning from it, and utilizing it to make informed decisions [3]. These models find diverse applications, ranging from voice recognition, sentiment analysis in text, and feature recognition in textual images to the automatic segmentation of elements in images and the analysis of medical imagery [4]. Notably, in the context of image analysis, an architecture belonging to the subset of Deep Learning known as Convolutional Neural Network (CNN) is employed [5].

Various factors are associated with the onset and progression of this disease, including environmental changes experienced over the years, family genetics or mutations, and lifestyle choices. However, the understanding of this question has primarily emerged from the study of individuals in the middle and advanced stages of life, as they are most vulnerable to developing Alzheimer's disease. This perspective has paved the way for a novel approach aimed at enabling early detection of the disease, known as Mild Cognitive Impairment (MCI) syndrome. In this project, MCI has been regarded as a potential precursor to Alzheimer's disease, as indicated by several studies [6, 7]. These studies have explored the use of deep learning techniques to differentiate this stage from the definitive neurodegenerative disease (AD).

This current project endeavours to provide a supportive tool for identifying features associated with the development of neuro-diseases, with the goal of predicting the progression from cognitive impairment to a potential diagnosis of Alzheimer's disease. To achieve this, a convolutional neural network is trained using magnetic resonance images to detect anomalies that may not be readily discernible to the human eye. The implementation of this novel tool is anticipated to provide diagnosed patients with various treatment options to potentially slow down the advancement of the disease [8].

2. Methodology

2.1. Databases

For this project, magnetic resonance images (MRI) obtained from two different repositories were used, and these will be presented throughout this section. The data were divided into 3 study groups known as training, validation, and test data. Both databases contain clinical information and neuroimages of healthy patients (Cognitive Normal), those affected by Alzheimer's (AD), and Mild Cognitive Impairment (MCI).

The first two groups consist of individuals in the stages of Alzheimer's (AD) and Mild Cognitive Impairment (MCI). The data for these groups were sourced from the free repository offered by the Alzheimer's Disease Neuroimaging Initiative (ADNI) [9]. An example of a raw MRI image of a healthy 85-year-old male patient can be seen in Figure 2-1. These groups are for training and validation of the model.

Regarding the test group, the image datasets were extracted from the database provided by the Comfamiliar Clinic in the city of Pereira. Since the test phase will involve the MCI disorder, a specific selection of patients with this characteristic was made. Consequently, the images selected for the test group encompass the three study groups as proposed. Further details regarding this data will be outlined in the subsequent section.

The datasets from both repositories primarily contain structural information and brain textures captured through volumetric pixels or voxels, which can be viewed as sets of two-dimensional images across the brain's three axes (axial, coronal, and sagittal).

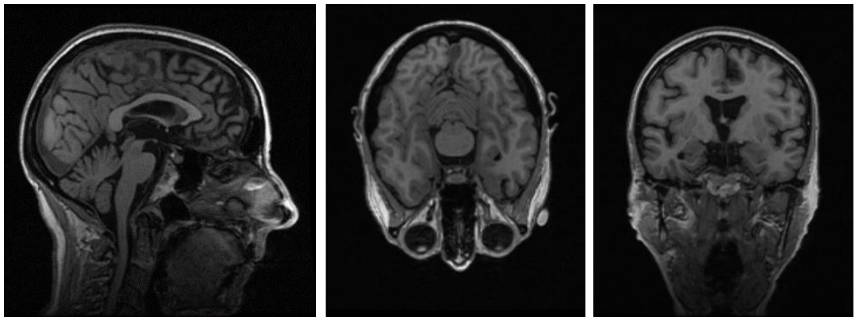

Figure 2-1. Axial, sagittal, and coronal slices of a healthy unprocessed male brain.

2.2. Feature selection

For the images within the training and validation groups, the ADNI-1 and ADNI-2 phases were selected, primarily due to the substantial volume of data available in these groups, which facilitates the establishment of a standardized quality benchmark. To optimize computational capacity and streamline analysis, a limit of 500 images per patient was set for the formation of these 3D arrays. Additionally, an age range of 50 to 80 years was chosen to enable effective comparison between the brains of healthy individuals and those affected by

the disease within the middle-aged and older age groups. Furthermore, T1 weighting was selected as the final filter, ensuring enhanced contrast for the brain structure. Here´s an example of the images selected.

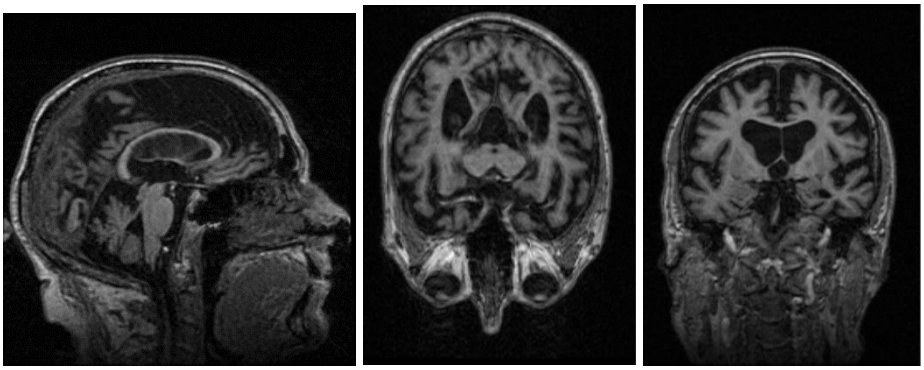

Figure 2-2. Axial, sagittal, and coronal slices of a 77-year-old male patient with AD.

From the Comfamiliar clinic repository, three patients aged 79 years at the time of their initial MRI were selected. These MRI scans were conducted between 2007 and 2012, with multiple image captures taken at approximately one-year intervals to monitor any changes. These images were acquired using T1-weighted imaging. Here´s an example of the images selected.

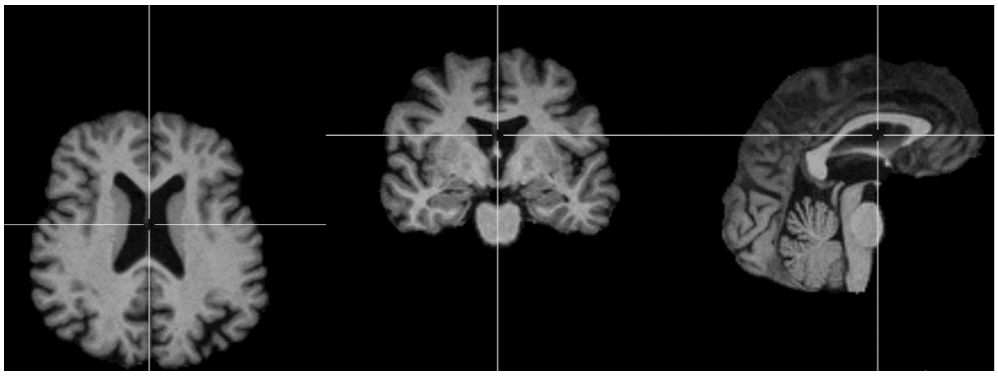

Figure 2-3. First resonance of the MCI to AD transition.

Each patient signifies a transition between the selected phases, indicating that significant changes were observed in their prognosis during the imaging process. Specifically, one patient initially diagnosed as healthy developed Alzheimer's disease, while another transitioned from mild cognitive impairment (MCI) to Alzheimer's disease. The third patient exhibited no changes and remained in the MCI stage.

These images played a crucial role in the final testing phase of the model.

2.3. Image processing

For this stage, *FreeSurfer* [10] was used, a software employed to process brain magnetic resonance images and generate three-dimensional models of its anatomy. It contains processing functions that allow the manipulation of MRI data, such as Skull stripping, which enables the removal of the skull and dura mater from the main element, the brain. For this project, this software was used to clean unnecessary elements, such as the skull and soft tissues, from the magnetic resonance images.

As explained in section 2.1, the data used during this project was divided into training, testing, and validation sets. The images belonging to the training and validation groups underwent the processing technique offered by *FreeSurfer*, where they were refined in terms of contrast and the removal of insignificant elements. Some of the test images underwent a simpler procedure known as *FastFreesurfer*, a line of rapid and accurate neuroimaging based on deep learning [11], implemented for a faster acquisition of processed data. It should be noted that the processing of the training images will not be extensively discussed, as the focus was primarily on the network learning phase. Here´s a side by side of a processed brain vs. an unprocessed image.

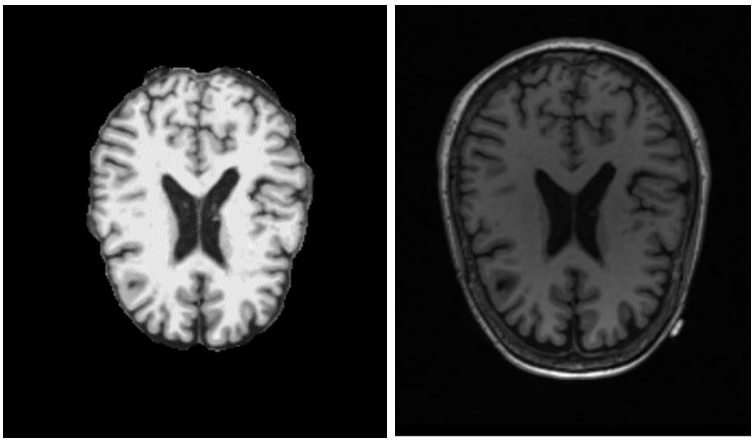

Figure 2-4. Comparison between FreeSurfer processed and unprocessed images.

2.4. Model structure and configuration

It is essential to define the structure of the convolutional neural network to be trained with the preprocessed images. For this purpose, a learning model based on the structure of *AlexNet* was selected. This renowned architecture, developed by Alex Krizhevsky, is widely employed for large-scale image classification and recognition tasks [12]. The choice of the *AlexNet*-like structure is due to its superior performance compared to other deep learning models. It is renowned as one of the primary convolutional network architectures capable of enhancing the performance of model learning and training.

After familiarizing ourselves with the architecture on which the project is built, it is important to specify that it was configured as a three-dimensional network, referred to as *AlexNet 3D*,

capable of accepting packets of 500 images forming 3D arrays as input data. This form of three-dimensional data encapsulates numerous features essential for recognizing and classifying various phases during the model's testing.

To adapt the *AlexNet* network for 3D data, modifications were made to the network structure, enabling it to accommodate 3D data. These adjustments included altering input dimensions, transforming convolutional and 2D pooling layers to 3D, and resizing filters in these layers, among other alterations to the primary architecture.

It is important to highlight that the initial model was employed for a pilot test using 10 image packets with dimensions 5×256×256×256. To evaluate this preliminary structure, the data were segregated into two directories, each containing 5 sets of MRI image packets from the two groups outlined in the previous section: *Alzheimer's* Disease (AD) and normal cognitive function (CN).

2.5. Training and validation

The aim of the neural network training was to conduct various tests implementing significant changes that would enhance the model's accuracy. These modifications included expanding the dataset, adjusting the learning rate, modifying network parameters, and applying or eliminating activation functions, such as those in the convolutional layers.

To assess the efficacy of these alterations and their impact on the network's performance, the percentages of accuracy and loss, as well as the learning curves reflecting the changes of these values during the epochs of training, were analyzed. These evaluations allowed for the identification of additional modifications to the network parameters, ensuring the attainment of the desired outcomes.

For subsequent model tests, a data split was conducted, allocating 30% for validation and 70% for training purposes. As mentioned in section 2.1, the study groups selected for these stages included Alzheimer's patients (AD) and healthy individuals (CN). These groups were chosen to form the default training dataset, enabling the network to learn specific patterns distinguishing a healthy brain from a diseased one. Furthermore, data augmentation will be applied during these tests to enrich the training set, enabling the network to learn a diverse array of relevant features while avoiding overfitting. It is important to note that this project faced limitations in this aspect due to restricted computational capacity.

Approximately 10 model tests were conducted, involving an increase in the training set and modifications to the parameters. To present the results and changes for each test, the following organization will be used:

- Number of Images
- Modifications made to the model compared to the previous test
- Accuracy values, loss, and learning curves

- Explanation of the modifications in relation to the previous test

3. Results and discussion.

This section presents and analyzes the results obtained from three crucial experiments conducted to demonstrate the efectivemos of the constructed model. Each experiment was devised to showcase the application of new support tools for the potential diagnosis of neurodegenerative diseases.

3.1. Parameter adjustment

This experiment involved making alterations to the base network proposed in the previous section across various tests, thereby tailoring it to the project's requirements. The breakdown of these tests was presented in the Training and Validation section. The learning curves mentioned earlier represent the accuracy and loss of the model, depicted in two figures—'train' and 'val.' These figures illustrate the model's performance during both training and evaluation. After the 10 model tests, the following learning curves were obtained.

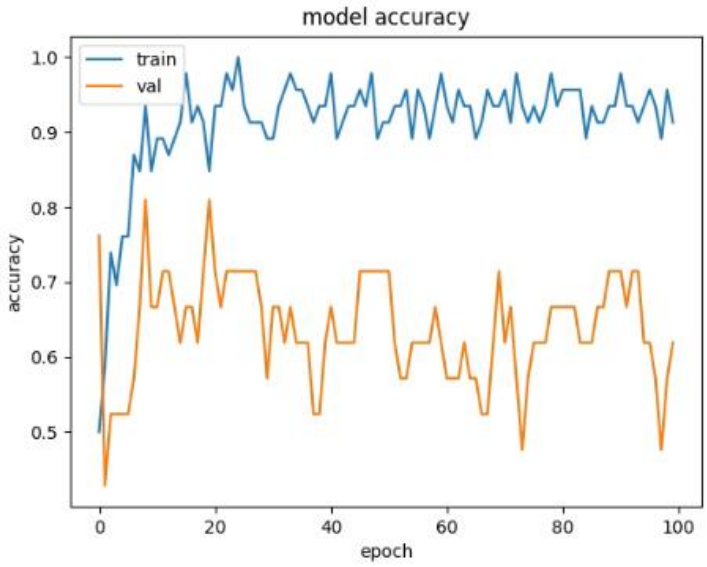

Figure 3-1. Learning curve (accuracy) of the 10th model test.

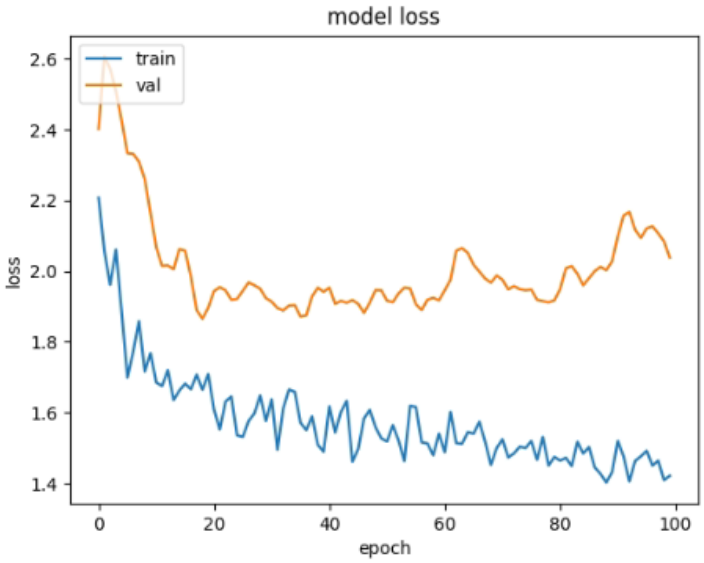

Figure 3-2. Learning curve (loss) of the 10th model test.

After the tests, the final training of the model achieved an accuracy rate of 72.222%. This outcome underscores the network's stability and the efficacy of the conducted tests in the previous phase. The comprehensive monitoring of the model's behavior allowed for the identification of suitable modifications, resulting in improved performance during the validation phase. The application of these new parameters highlights the model's capability to adapt and generalize patterns found within the dataset, ultimately leading to more precise and consistent predictions.

The developed model was named *K-Net95*, inspired by the song '*N95*' by rapper *Kendrick Lamar*. Figure 3-3 showcases the prototype of the acquired network.

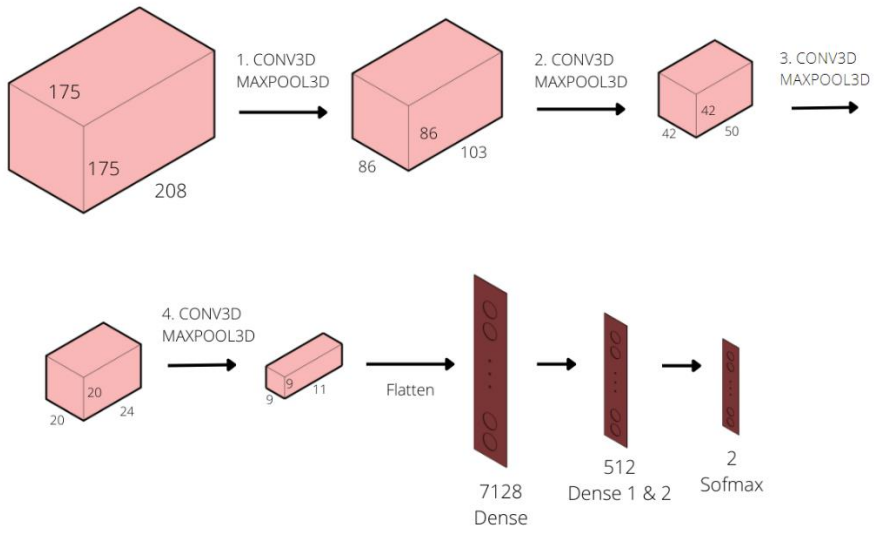

Figure 3-3. *'K-Net95'* model structure.

3.2. *K-Net95* vs. other structures

To demonstrate the superior performance of the *K-Net95* model in comparison to other established neural architectures, a comparison was conducted between the developed model and two prominent architectures: *ResNet3D* [13] and *UNet3D* [14]. The algorithms corresponding to these networks are available in the appendices.

To facilitate a comprehensive comparison, both the *UNet3D* and *ResNet3D* networks were trained with a comparable dataset size to that of the *K-Net95* network. However, it was not feasible to implement an identical training set due to limited computational capacity.

Table 3-1. Comparison between the structures proposed.

Model	Accuracy
K-Net95	72,222%
UNet3D	50%
ResNet3D	53,333%

This experiment focused on the training and validation phase results, specifically emphasizing the final accuracy percentage of each model. The models were trained using the same parameters for batch size, learning rate, and number of epochs. In the Table 3-1 are the results of the comparison made.

Throughout this test, the values acquired during the training and validation stages were closely monitored to assess the presence of overfitting or underfitting. Additionally, computational consumption was analyzed alongside the parameters established in the base architecture and the structural complexity of each model.

Based on the tests conducted in this experiment, it can be concluded that the *K-Net95* model outperformed the *UNet3D* and *ResNet3D* networks in various critical aspects. The developed model exhibited exceptional performance in terms of classification, efficiently extracting pertinent features from the three-dimensional dataset. Moreover, it effectively utilized computational capacity, delivering superior results with fewer parameters compared to the other networks.

Furthermore, in the training process, the *K-Net95* model notably mitigated overfitting concerns, acknowledging the constraints imposed by this project. In contrast, the other networks demonstrated consistent behavior in the values obtained during the learning epochs. Consequently, the *AlexNet3D*-type network was identified as the most optimal and efficient option among the *UNet3D* and *ResNet3D* networks.

3.3. Prediction

To demonstrate the classification capabilities acquired during the training phases, a prediction experiment will be conducted. It is important to clarify that the *K-Net95* model was designed as a classification tool to predict the probability of the study patients developing *Alzheimer's* disease. Its objective is to categorize each input image based on the set of features it possesses, thereby predicting the class to which it belongs.

As described in section 2.2, the test dataset comprises image packets sourced from the Comfamiliar Clinic repository, categorized into established transitional phases. This categorization aims to facilitate accurate prediction and classification by the network, allowing for a comprehensive evaluation of its capacity and performance.

Figure 3-4 presents 5 segments along with their corresponding probability percentages, enabling a straightforward interpretation of the model's predictions. The objective is to provide a user-friendly tool capable of offering potential diagnoses.

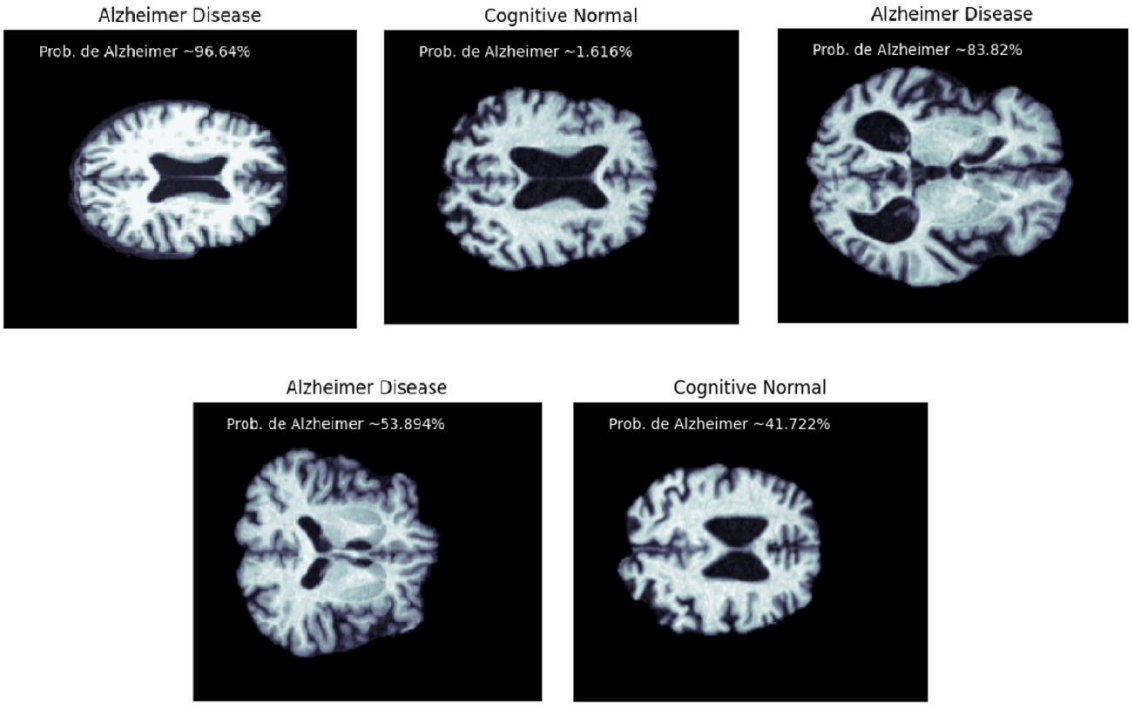

Figure 3-4. Results obtained from the *K-Net95* model.

Unlike the training and validation phases, the testing stage did not necessitate robust computational capacity. Once the model is saved, the analysis simply requires the use of image packets from each patient, allowing the determination of the likelihood of being diagnosed with Alzheimer's disease. Furthermore, it classifies each patient into the primary stages outlined in the database section, namely Alzheimer's Disease (AD) and Cognitive Normal (CN).

4. Conclusions

Throughout the project's development, certain limitations in computational capacity were encountered, affecting the processing speed of the model, and necessitating a significant reduction in the total data set. Consequently, it was imperative to simplify the model's complexity by adjusting its parameters. These modifications resulted in the creation of a stable model that achieved an accuracy of 72.222% and accurately predicted patients within the test group. Although this percentage was achieved, it is acknowledged that further enhancements are possible. It is recommended to continue training the model using a larger sample of the complete data set to enhance its overall performance and accuracy.

Throughout the training and validation phases of development, the impact of overfitting on model performance, leading to an excessive fit to the training data, has been emphasized. To address this issue, regularization techniques, such as the incorporation of dropout, were

implemented to enhance the model's generalization and facilitate the learning of specific features.

The selection of 3D volumetric images was driven by several considerations. These images offer enhanced contextualization of regions of interest by presenting features across the three primary slices (transverse, sagittal, and coronal), enabling a comprehensive understanding of the brain's condition. They also facilitate the monitoring of subtle changes in brain structure over time, contributing to a closer approximation of potential early detection.

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