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Brain Imaging Studies Using Deep Neural Networks in the Detection of Alzheimer's Disease

Gopi Battineni, Mohammad Amran Hossain, Nalini Chintalapudi, Giulio Nittari, Ciro Ruocco, Enea Traini, Francesco Amenta *

Clinical Research Center, School of Medicinal and Health Products Sciences, University of Camerino, Camerino, 62032, Italy; E-Mails: gopi.battineni@unicam.it; mohammad.hossain@unicam.it; nalini.chintalapudi@unicam.it; giulio.nittari@unicam.it; ciro.ruocco@unicam.it; enea.traini@unicam.it; francesco.amenta@unicam.it

* **Correspondence:** Francesco Amenta; E-Mail: francesco.amenta@unicam.it

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Abstract

The increasing incidence of adult-onset dementia disorders and primarily Alzheimer's disease (AD) among the aging population around the world is increasing the social and economic burden on society and healthcare systems. This paper presents three neural networking algorithms: MobileNet, Artificial Neural Networks (ANN), and DenseNet for AD classification based on MRI imaging data. The results of each model were compared in terms of performance metrics such as accuracy, true positive rate, and receiver operating curve values. Results mentioned that MNet classified AD progression with 95.41% of accuracy. Early detection and appropriate interventions, primarily on modifiable risk factors of AD, can delay the progression of cognitive impairment and other symptoms that represent a main trait of the disease.

Keywords

Deep learning; AD progression; dementia types; neural networks; model performance

1. Introduction

In recent times, medical technology has been changing at an exponential rate. Multiple diagnostic and treatment tools have been developed over the past decade [1]. A progressive neurological condition that affects memory called Alzheimer's Disease (AD) can affect a person's day-to-day life, which starts slowly and worsens [2]. AD is a neurodegenerative disease of the so-called adult-onset dementia [3]. Identifying AD at an early stage is important in attempting to slow the progression of cognitive dysfunction typical of this disorder. Unfortunately, there is no particular test to diagnose AD, but there are combinations of different diagnostic examinations and symptoms [4].

In the diagnosis and disease monitoring processes, computational methods, particularly machine learning (ML) technology, are now very helpful [5, 6]. Generally, ML is a subfield of artificial intelligence (AI) that enables to address the development of early diagnostic tools and effective treatments for neurological disorders.

It is reported that clinical scores were predicted with the help of joint and deep learning frameworks [7]. These deep learning models are helpful in the autonomous classification and detection of neural foraminal stenosis at lumbar spine MRI [8]. They provide better strategy techniques for AD diagnosis by liking the pathophysiological process [9]. Another study reported 92% accuracy in diagnosing liver tumors by convolutional neural network algorithms [10]. Some studies applied morphological feature visualization, high-order disease pooling, and image reconstruction to assess AD by the multidirectional perception Generative Adversarial Networks (GAN) model [11-13].

The brain connection networks can detect early Mild Cognitive Impairment (EMCI), and detection of EMCI using Multi-scale Graph Convolutional Networks was proposed [14]. The experiments conducted in the research highlighted that better performance was done with AD datasets [15]. Similarly, using multimodal MRI images in AD classification achieved 96% accuracy [16]. All these studies mentioned that deep learning models precisely conduct AD classification. The present study introduces three advanced deep learning models called MobileNet, DenseNet, and ANN to do MRI-based classification of AD progression. The performance of each model is further validated by different metrics, including accuracy, the receiver operating curve (ROC), and sensitivity.

2. Materials and Methods

2.1 Dataset

The publicly available dataset from Kaggle was used to conduct the experiments [17]. The AD image data was collected from different websites, labeling four dementia types (i.e., non-dementia, very mild dementia, mild dementia, and moderate dementia) based on their progression.

The adopted dataset has different MRI scans that decomposed training and testing datasets. 176 × 208 pixels is the standard size for black and white images. The number of training images is about 5,000, while the number of test images is about 1,200. Figure 1 shows each image showing a 2D MRI cross-section of the brain. Various planes of the brain were taken at various heights. A relatively large number of images and the consistency of the images made this dataset a wise choice. Brain cross-sections were cropped out of the background and centered in all images. Despite its advantages, this dataset had a disadvantage in that there was no information about the training and test sets composition. These data are further prepared to train the deep learning model. Python with Tensorflow experimental platform was used for image processing and dataset balancing. The dataset balancing was done by representing the minor class with the nearest neighbors. By the feature space, a line segment is then constructed by connecting one of the nearest neighbors and randomly selecting another. Conversely, combining the two chosen instances produces synthetic instances.

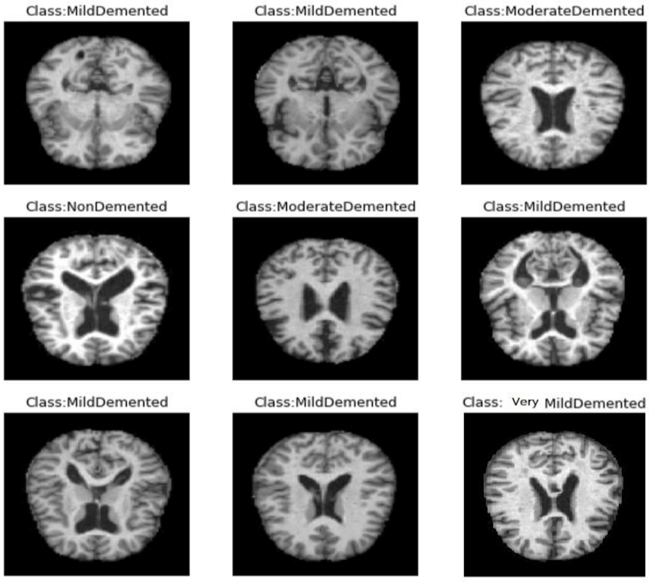

Figure 1 MRI image-based AD classification dataset.

2.2 Model Selection

As mentioned, three different DL models were applied in this study, and a brief description of each model is given below

2.2.1 Artificial Neural Networks (ANN)

The artificial neural network (ANN) simulates biological neural systems [18]. Feed-forward neural networks process input only forward, which is why they are also known as feed-forward networks. ANN comprises three fully connected layers: input, hidden, and output. An ANN is fed input features by the input layer. In the hidden layer, all input neurons receive a weight and bias. Each neuron inside the hidden layer will sum up all the weighted features from all input layers and apply an activation function. This will ensure that the values stay between 0 and 1. The number of neurons in each layer must be manually chosen and must be the most appropriate value for the network. A value of 0 or 1 is ultimately passed to the output layer by the weights between each layer.

Figure 2 shows the architecture of an ANN model. In addition to learning complex relationships, activation functions are also used. In machine learning, activation functions convert all values between 0 and 1 to help analyze data. We used the ReLU activation function in input and hidden layers in our work. The softmax activation function is used in the output layer. Choosing the right loss function is crucial when creating neural networks because it affects how the optimizers of the neural nets update the weights on their backpropagation. Categorical Cross Entropy loss was used in this study. Using optimizers, neural networks change their backpropagation weights so that the difference between the actual and predicted results gradually decreases. This decrease reaches a point where the difference is negligible, and the model is more accurate. To optimize our ANN model, we used the ADAM optimizer.

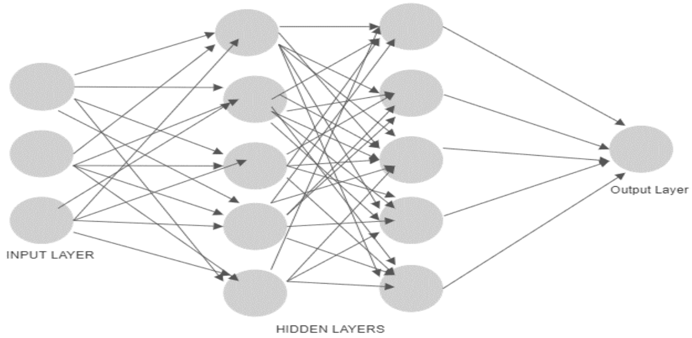

Figure 2 Artificial Neural Network Architecture.

2.2.2 Dense Net

The Dense Net is a type of conventional neural network which uses dense layers and blocks to connect overall layers [19]. Convolutional networks obtain high-level features from input images using multiple convolutional layers. Concatenation propagates the features of each layer from all preceding layers to all subsequent layers in a Dense Net. Layers are connected directly to one another [20]. Each layer receives feature maps from previous layers, making the network thinner and more compact.

A batch normalization (BN) [21] is followed by a rectified linear unit (ReLU) [22], then a 3 × 3 convolution (Conv) is used as the composite function. To change the size of feature maps, it is essential to downsample layers in convolutional networks. It was suggested to divide the network into multiple densely connected blocks to facilitate down-sampling [20]. Figure 3 describes layers between blocks as transition layers, which do convolution and pooling. In the transition layer, there is a batch normalization layer, a 1 × 1 convolutional layer, and a 2 × 2 average pooling layer. It is, therefore, more memory and computationally efficient. Figure 2 shows three dense blocks with conventional and pooling layers DenseNet architecture.

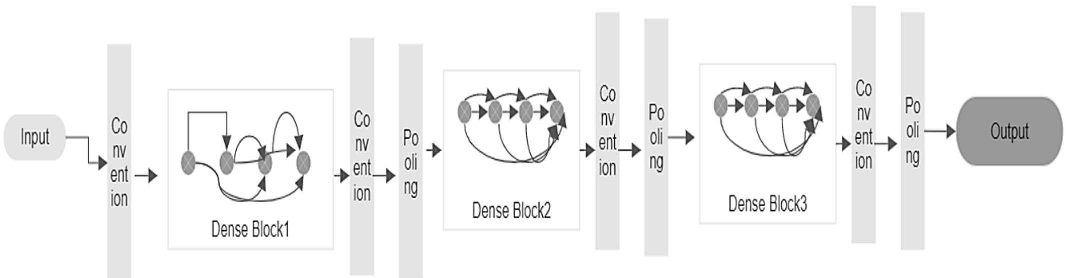

Figure 3 Dense Net Architecture.

2.2.3 MobileNet (MNet)

MobileNets (Mets) are also conventional neural networks. A depth-wise separable convolution in the MobileNet model is a form of factorized convolution, which converts a standard convolution into a depthwise convolution and a 1 × 1 convolution called a point-wise convolution. Each input channel is filtered using depth-wise convolution with MobileNets. To combine the outputs of the depthwise convolution, the point-wise convolution applies a 1 × 1 convolution. In standard convolution, inputs are filtered and merged in one step. A depth-wise separable convolution splits this into two layers, one for filtering and one for combining. As a result of this factorization, computation and model size are drastically reduced. An example of how a standard convolution can be factorized into a depth-wise convolution and a 1 × 1 pointwise convolution can be seen in Figure 4.

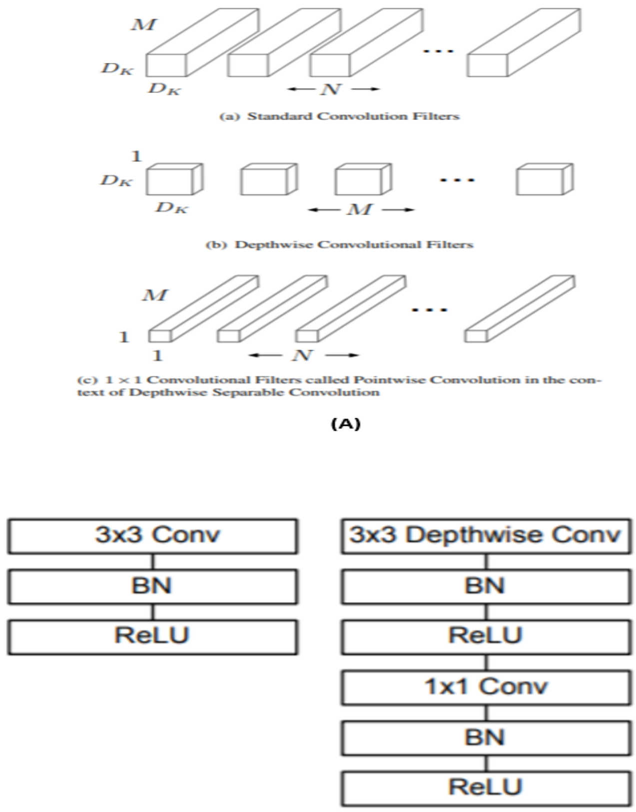

Figure 4 MNet Architecture (A) and layers (B) [23].

An example of a factorized layer with depth wise convolution, pointwise convolution, batch norm, and ReLU after each convolutional layer is shown in Figure 3. Down sampling is handled with stepwise convolution in depthwise convolutions and the first layer. Before the fully connected layer, a final average pooling reduces the spatial resolution to 1. MobileNet consists of 28 layers when depthwise and pointwise convolutions are considered separate. MNet depends on a smoothed-out design that utilizes profundity-wise distinct convolutions to construct lightweight DL neural networks. In deep learning, lightweight neural networks are built with depth-separable convolutions to have low latency, allowing them to be used in mobile and embedded environments.

2.3 Data Splitting

After changing the unbalanced dataset into a balanced dataset, a data split was done based on an 80:20 ratio. 80% of images are used for training, and 20% are for testing purposes. Model training was conducted till the optimal predictions were made with higher accuracy. The performance of the model was conducted with a training dataset. The experimental framework is presented in Figure 5.

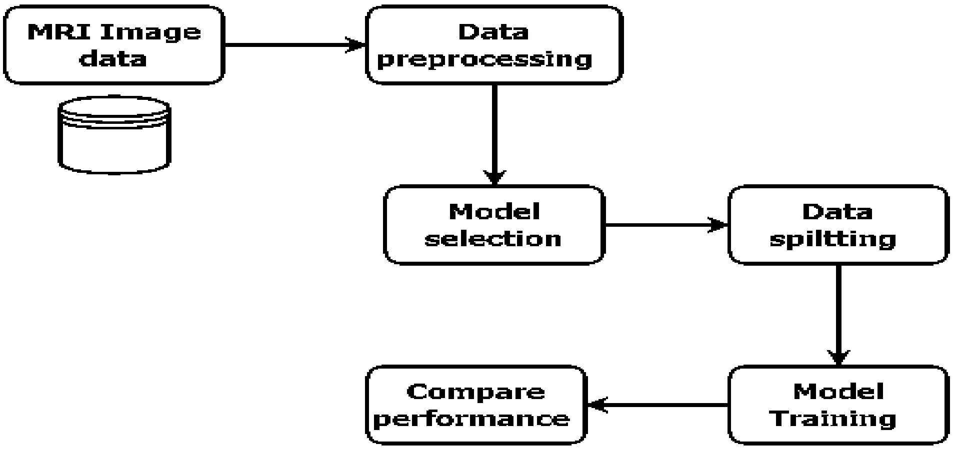

Figure 5 Methodological framework.

2.4 Model Performance

Each model performance was computed based on the different parameters, including accuracy, correct classification outcomes (sensitivity), and receiver operating curve (ROC) values. Accuracy is defined as the ratio of true classified subjects among total subjects. Mathematically it was written as

$$\text{Accuracy} = \frac{\text{True positives} + \text{True Negatives}}{\text{Total subjects value}}$$

Whereas sensitivity is defined as a true positive rate, if this value is higher, the model correctly identified the positive results. If it is low, it means the model is not conducting classification efficiently and missing positive results. Mathematically, it defined as

$$\text{Sensitivity} = \frac{\text{True positives}}{\text{True postives} + \text{False Negatives}}$$

3. Results

We considered 2,560 MRI images for model testing, and the performance of each model was computed separately based on different parameters such as accuracy, sensitivity, ROC, and loss. After that, we compare the metrics to identify the optimal ML model to solve MRI image classification problems. Whereas sensitivity or true positive rate (TPR) measures how the ML model can classify the positive instances. It is used to evaluate the model performance, which allows individuals to understand the number of positive instances.

The receiver operating curve (ROC) is a graphical illustration of the measurement of image classification and how the model can separate image classes. ROC curves measure all possible thresholds in classification, whereas Area Under Curve (AUC) provides an aggregate performance measure. Taking AUC as a measure of how likely the model is to rank a random positive example higher than a random negative example can be helpful when understanding AUC.

The three deep learning models were compared with two other traditional supervised ML models, such as support vector machine (SVM) and Logistic Regression (LR). These models are largely used for classification purposes in ML imaging studies. Table 1 presents the metric performance outcomes of three adopted models, a basic approach to understanding which model is the most effective at identifying AD-related MRI images. In AD classification MNet outperforms other models in terms of all performance metrics. ANN, DenseNet and ANN followed with 93.7% and 91.8% accuracy, respectively. The AUC curves determine the rate of accurate classification. If the ROC value is near 1, perfect classification was done among the given subjects. The MNet has the highest AUC of 0.99. The graphical representation of ROC and classification error curves of the MNet model can be visualized in Figure 6.

Table 1 Performance metrics of each model.

Algorithm	Accuracy	Sensitivity (%)	AUC	Loss
ANN	0.918	0.905	0.97	0.147
Dense Net	0.937	0.944	0.89	0.128
MNet	0.954	0.966	0.99	0.113
SVM	0.841	0.916	0.92	0.138
LR	0.903	0.887	0.96	0.121

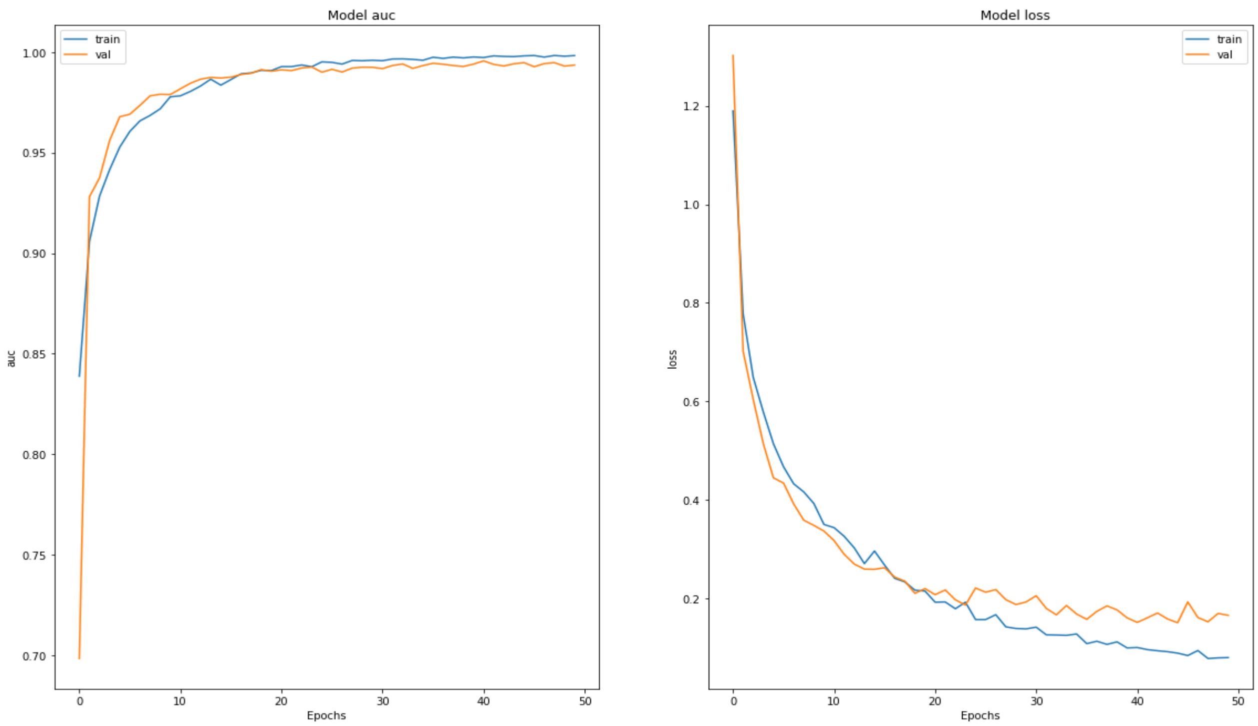

Figure 6 Outcome model AUC and performance error curves.

4. Discussion

In addition to memory loss and cognitive decline, adult-onset dementia disorders constitute a heterogeneous group of diseases largely associated with cognitive decline and memory loss [9]. Various degrees of mildness and severeness are associated with it, contributing to structural changes in the brain. AD affects mental and physical functioning and social and behavioral skills. In addition to reducing the burden of the disease and saving the healthcare system money, preventing dementia can be beneficial and delay the onset of the disease.

Cognitive impairment usually progresses regardless of how early it is detected. The development of clinical symptoms of memory impairment precedes the development of neuropathological changes in dementia. ML algorithms can assist in diagnosing neurodegenerative diseases by integrating the algorithms into medical imaging and launching powerful computing resources [11]. Combining ML and MRI creates a way to diagnose AD and tell if the disease is progressing.

AD is characterized by memory loss and cognitive decline in individuals. In the past, AD was diagnosed with complete certainty after death by the brain's microscopic demonstration of plaques and tangles. Today we can diagnose AD during life with more certainty. Further support is represented by plaques and tangles, using specific types of PET scans or measuring amyloid and tau proteins in plasma and CSF [24]. Neuroimaging studies are emphasized visualizing brain images with high resolution, which can be changed along with disease progression. MRI could represent a powerful imaging method with fine anatomical descriptions of varied brain tissues. For instance, behavioral symptoms of AD are accompanied by atrophy of the hippocampus. It's easily seen on MRI scans and is currently not helpful in early disease diagnosis.

Although, at present, there are no specific cures available for AD, diagnosis of the disease at an early onset may promote measures delaying the progression of the disease and, therefore, can be important in reducing the burden of AD both for the individuals suffering from it and for the society [25]. Increasing evidence suggests the utility of ML algorithms for the early detection and classification of the evolution of AD. From a practical point of view, identifying distinct stages of AD and the provision of the evolution of it can be important for planning different treatments for specific patients [25, 26]. This is in line with the modern approaches to personalized and precision medicine. On the other hand, the classification of different stages of the disease can contribute to improving a patient’s quality of life by treating symptoms according to the specific needs of the evolution of the disease [25].

Further advancing the clinical application of ML in diagnosing AD, various neural network ML algorithms were applied to ADNI-Longitudinal data for the classification of four stages of the disease to identify useful biomarkers and features that could be useful for the reliable and timely detection and diagnosis of AD. Early detection of AD is essential to reducing the burden of the disease and hopefully mitigating its severity [25-27]. By identifying them as soon as possible in real dementia patients, they can better treat them. Modern neurological research may benefit from brain studies with artificial intelligence analysis. However, future studies should enlarge the sample size as much as possible to avoid data limitations. Additionally, more complex deep learning models are recommended for subjects with mild AD, and testing other biological tests like CSF or blood markers to assess prediction accuracy.

5. Conclusions

We presented three deep learning algorithms based on feed-forward neural networks. We achieved a classification accuracy of 95.41% by incorporating different pre-processing techniques, such as model balancing. In addition to providing an accurate approach to modeling performance metrics, MRI features can also help to predict and validate new diagnostic methods for adult-onset dementia disorders.

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Author Contributions

Conceptualization, G.B. and M.A.H; methodology, G.B.; software, N.C.; validation, G.B., C.R., and F.A.; formal analysis, G.B.; investigation, M.A.H.; resources, E.T.; data curation, N.C.; writing—original draft preparation, G.B. M.A.H, and N.C.; writing—review and editing, G.B., and F.A.; visualization, N.C.; supervision, F.A.; project administration, F.A.; funding acquisition, F.A. All authors have read and agreed to the published version of the manuscript.

Competing Interests

No author has any conflicts of interest.

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