SNEH TEACHERS TRAINING COLLEGE, JAIPUR
"Foster Emotional Intelligence in Youth Through Education" (ICFEIYE-2024)
DATE: 15 April 2024
International Advance Journal of Engineering, Science and Management (IAJESM)
Multidisciplinary, Indexed, Double-Blind, Open Access, Peer-Reviewed, Refereed-International Journal, Impact factor (SJIF) = 7.938

Deep Learning-Based Early Detection of Alzheimer's Disease from Neuroimaging Data

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Abstract

Alzheimer's disease (AD) results in memory loss and impairment, which can give rise to additional symptoms. It has a significant impact on the lives of patients and unfortunately, there is no cure. However, early detection of AD can be beneficial in initiating appropriate treatment to prevent additional brain damage. In recent years, researchers have utilized machine learning techniques to classify AD. These methods involve using manually prepared features and a classifier with a complex architecture.

In recent times, the utilization of deep learning has led to the adoption of the end-to-end process of neural networks for pattern classification. In this paper, our focus is on the early diagnosis of AD using convolutional neural networks (ConvNets) and magnetic resonance imaging (MRI). Image slices of gray matter and white matter from MRI have been utilized as the inputs for classification.

Ensemble learning methods have been used to enhance classification by combining the outputs of deep learning classifiers after the convolutional operations. In this paper, three ConvNets were designed, implemented, and compared. We evaluated our method using a dataset from the Alzheimer's Disease Neuroimaging Initiative to diagnose this illness at an early stage. Our classifications have achieved accuracy rates as high as 97.65% for AD/mild cognitive impairment.

Keywords: Alzheimer's Disease, Deep learning, Neuroimaging, Convolutional Neural Networks (CNNs), Ensemble methods.

INTRODUCTION

Alzheimer's disease (AD), a progressive neurodegenerative disorder, casts a long shadow over our aging population. This neurodegenerative disease associated with symptoms such as a decline in cognitive functionality, deficiency of memory, and disturbance of daily activities [1]. Although there is no conclusive evidence for the primary cause of AD, it has been documented those certain pathophysiological alterations in the brain, which start several years prior to the terminal stage, contribute to the development of AD. These alterations involve the formation of neurofibrillary tangles inside the neurons, which causes the death of neurons and the buildup of amyloid plaques among nerve cells. This disrupts the normal flow of neurotransmitters [2]. The incidence rate of age-related disorders, such as Alzheimer's disease (AD), has been on the rise in recent years due to the increasing demands of global life [3]. In the past twenty years, the mortality rates for heart disease and prostate cancer have declined. However, during the same period, the mortality rate for Alzheimer's disease (AD) has climbed by 145 percent. As a result, AD is now the sixth most common cause of death in the United States [4,5]. Despite the encouraging findings from recent research on novel medications for AD, there is still no officially sanctioned treatment for the illness [6]. As previously stated, discovering a method to effectively diagnosis AD in its initial stages can yield numerous advantages, such as halting or diminishing the advancement of the condition, lowering healthcare expenses, and enhancing individuals' quality of life.

According to the authors' understanding, there are three distinct methods for diagnosing AD. The first method, which is often favored for its simplicity and affordability, involves specialists use clinical data, symptoms, and other criteria such as cognitive assessment scales and questionnaires to diagnose AD. Nevertheless, this strategy suffers from significant limitations, including susceptibility to subjective influences and producing unsatisfactory performance

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outcomes [7]. The second method involves measuring clinical biomarkers, such as tau and amyloid-beta proteins, by analysing the cerebrospinal fluid (CSF) or conducting a brain autopsy. Although this methodology demonstrates satisfactory performance, it typically necessitates intrusive procedures for measurement, which diminishes its popularity as a routine strategy for early diagnosis of AD. The third technique utilises neuroimaging technologies such as MRI, CT Scan, and PET to visually depict the anatomical and functional aspects of the brain. This technique enables the rapid acquisition of substantial quantities of data. Nevertheless, the task of deciphering the intricate information contained within photographs is a considerable challenge for medical professionals [8].

The advancements in computer processing capabilities and the accessibility of datasets related to Alzheimer's disease, such as the Alzheimer's Disease Neuroimaging Initiative (ADNI) and Open Access Series of Imaging Studies (OASIS), have paved the way for a new era in utilizing computer-assisted machine learning methods for the classification and automated diagnosis of Alzheimer's disease [9]. Traditional machine learning methods sometimes involve complex preprocessing stages that need specialized knowledge and rely on human or semi-automatic feature learning algorithms [10]. Deep learning (DL) algorithms, a new area of machine learning, offer effective solutions to address the constraints of classical machine learning. DL algorithms have shown remarkable performance in tasks such as classification, computer vision, object recognition, and medical picture analysis [11].

METHODS

Database

In this paper, the data were obtained from the ADNI database at adni.loni.usc.edu. The ADNI project was specifically created to gather, verify, and leverage data such as MRI and positron emission tomography (PET) Using images and blood biomarkers to predict AD. The ADNI project was launched in 2003 with the aim of gathering and examining brain images related to Alzheimer's disease, mild cognitive impairment, and normal cognition. In NifTI format, a collection of 615 MRI images was divided into three groups: 179 AD, 254 MCI, and 182 NC. The distribution of male and female samples in each category is approximately balanced. The data is typically categorized for training, validation, and testing in a ratio of 3:1:1.

Preprocessing

The MRI images from the ADNI database underwent correction to eliminate the effects of head movement during long image acquisitions. This was achieved using statistical parametric mapping (SPM), a software developed by the University of London on the MATLAB platform. The downloaded images were resized to dimensions of 192 × 192 × 160.

Next, the MRI images were resized and categorised into WM, GM, and cerebrospinal fluid (CSF) using SPM. The dataset for training was chosen to be the GM and WM images, as they offer a crucial and distinct brain structure that aids in the diagnosis of AD.

Following the segmentation process, the GM and WM have been divided into 192 images in TIF format. Based on previous findings, a series of 20 consecutive slices with distinct brain structures were chosen as the data from GM and WM in each MRI image. The GM slices were incorporated into the WM collection and adjusted to a size of 224 × 224, serving as the inputs for our neural networks.

Network Architecture

While traditional machine learning methods relied on features extracted by experts, we employ deep learning to classify AD using an end-to-end process. In this project, we will be presenting our model for early diagnosis of AD. Figure 1 illustrates the primary framework of this paper.

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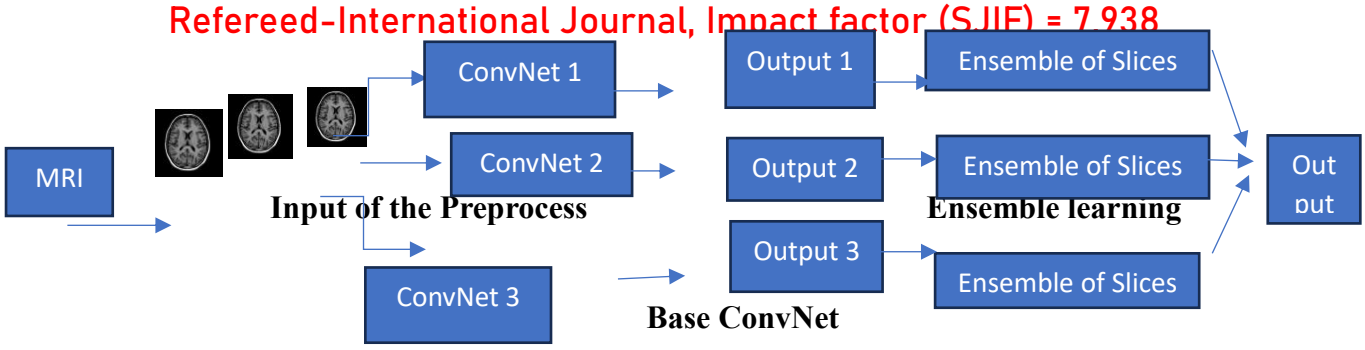

Figure 1: The overall framework is split into three parts: Preprocessing, ConvNets, and ensemble learning

For this project, we have utilised three base classifiers for our experiments. Firstly, the data downloaded from ADNI are preprocessed. Specifically, 20 slices with significant brain structures are carefully selected and then sent to the ConvNet for model training. Then, every base classifier exports a result of the slice. We combine the 20 slices to effectively categorise this subject. Finally, the ensemble learning methods are applied to the output of each ConvNet network.

The ImageNet dataset is a valuable resource for training deep learning models due to its extensive collection of natural images. These images have been used to train models with large parameter sizes, making them ideal for computer vision research. Training a large model with a limited medical database presents a significant challenge. Thus, transfer learning was employed in our experiment to enhance accuracy.

We utilised a pre-trained network from ImageNet as the foundation for our classifier. As we are aware, the ConvNet for image classification consists of two main components: a sequence of pooling and convolutional layers, along with fully connected layers. In this paper, the initial section of the ConvNet involves the convolution base (conv_base), which comprises a sequence of pooling and convolutional operations. The fully connected layers were incorporated into the base layer to merge the convolution base. Figure 2 illustrates the structure classifier.

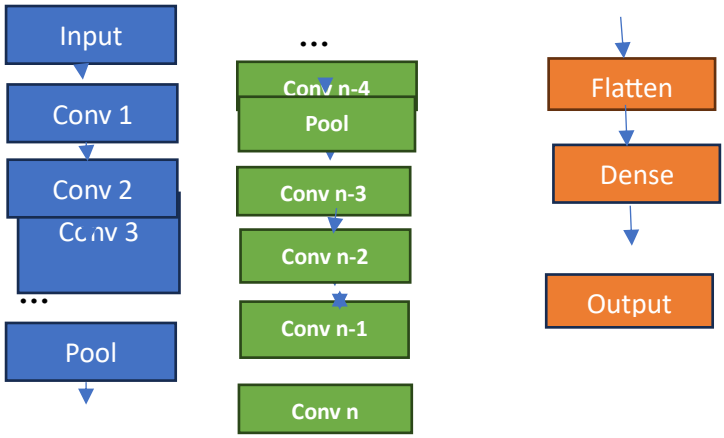

Figure 2: The structure of base classifier Conv Net

The base classifier we use is composed of three main components. The initial segment and the subsequent segment constitute the foundation of the convolution. The third part consists of fully connected layers. Each base classifier's training process Consists of two stages. Firstly, the convolution base remains unchanged while we focus on training the fully connected classifier to adjust the weights of the fully connected layers. Random initialization is used for the fully connected layers, which allows for the propagation of large weight updates. In other

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cases, the network undergoes modifications that build upon the previously learned ConvNet. Once the initial phase is complete, we proceed to release a subset of the upper layers of the convolutional model. Next, the base classifier is trained through fine tuning to accurately detect the early signs of AD using an end-to-end process. The initial portion of the convolution base has remained unchanged throughout. The paper utilizes three base classifiers: eResNet50, eNASNet, and eMobileNet.

In the third section of this network, the outputs are transformed into a new layer by flattening them. Next, fully connected layers are incorporated into the flatten layer. To prevent overfitting, a dropout layer was incorporated into the fully connected layer. As we are aware, the process of backpropagation (BP) in neural networks involves fine-tuning the weights and offsets of the hidden layers to align the output with the input.

Adding the Bernoulli function to the network helps adjust the weights and offsets of the hidden layers, prevent overfitting, and improve the alignment between inputs and outputs. This is particularly beneficial when compared to BP neural networks.

Figure 3 illustrate the neural network dropout.

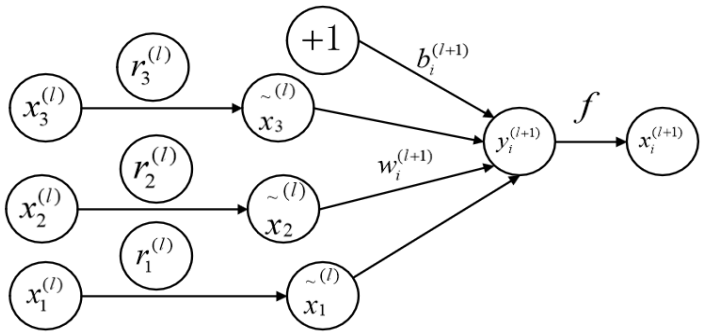

Figure 3: The dropout networks.

EXPERIMENTS AND RESULTS

In this section, we will be focusing on validating our method through comparisons between AD and MCI, as well as MCI and NC. Firstly, the base learners used for ensemble learning in this comparative experiment are bResNet50, bNASNet, and bMobileNet. Our method involves training eResNet50, eNASNet, and eMobileNet using an end-to-end process for ensemble learning. Finally, we compare our results with the existing findings on AD classification.

The networks were implemented using Python 3.5 and Keras. The experiments were conducted on a computer equipped with a single GPU (NVIDIA DGX-1). For data preprocessing, we utilized SPM, a MATLAB-based tool, to handle the downloaded data from ADNI. For training, the Adam optimizer was utilized. The learning rate was initially set at 2.0×10−5, and the minibatch size was initialized to 20.

The primary focus of our research was to validate our method for early diagnosis of AD, specifically distinguishing between AD and MCI, as well as MCI and NC. The evaluation of the classification involved four measures: classification accuracy (ACC), specificity (SPE), sensitivity (SEN), and the area under the receiver operating characteristic curve (AUC).

Table 1 displays the classification results for AD and MCI.

Based on the data in Table 1, it is evident that the accuracy sensitivity and AUC values achieved through the end-to-end process surpass those obtained from models trained solely by the base classifiers.

Notably, the precision of eNASNet surpasses bNASNet by 1.17%. The "bEnsemble" is the outcome of merging bResNet50, sembling eResNet50, eNASNet, and eMobileNet. According to "bEnsemble," it is evident that the ensemble outperforms the single model in terms of accuracy and specificity. This highlights the superior performance of ensemble learning.

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Table 1:Accuracy, sensitivity, specificity, and AUC of various classification methods for AD and MCI.

Models	ACC (%)	SEN (%)	SPE (%)	AUC
bResNet50	97.65	100.00	94.29	0.95
eResNet50	98.80	98.00	100.00	1.00
bNASNet	97.65	98.00	94.29	0.95
eNASNet	98.82	96.00	100.00	1.00
bMobileNet	97.64	98.00	94.28	0.95
eMobileNet	97.65	96.00	100.00	1.00
bEnsemble	98.82	98.00	100.00	0.95
eEnsemble	97.65	96.00	100.00	1.00

COMPARISONS

For this study, we chose eResNet50, eNASNet, and eMobileNet as the base classifiers. These classifiers were trained using the end-to-end process. Each base classifier undergoes two phases during training.

Regarding eResNet50, the ConvNet remains unchanged while we focus on training the fully connected classifier to adjust the weights of the classifier's fully connected layers. The fully connected layers on the top were initialized randomly, resulting in significant weight updates being propagated.

Afterwards, several upper layers of the convolution base were unveiled and merged with the revised fully connected layers in order to adapt the model for medical images. The base classifiers were trained through fine-tuning, specifically between the fully connected layers and released layers of the network. This was done to enable early diagnosis of AD using an end-to-end process. Similar operations were employed to train the base learners, utilizing eNASNet and eMobileNet.

For our experiments, we utilized a previously well-trained network through transfer learning. The classifier was trained using ResNet50, NASNet, and MobileNet. The latest networks include bResNet50, bNASNet, and bMobileNet. The results are utilized for comparison with the data from our current base classifiers: eResNet50, eNASNet, and eMobileNet. After training our model, we evaluate its performance by testing it. We then combine the results of the base ConvNet to classify AD.

Based on the data in Table 2, it is evident that the models trained using the end-to-end method outperform the models trained using features extracted from the base classifiers. The accuracy of "eEnsemble" has seen a significant improvement of 8.14% when compared to the results of "bEnsemble". Additionally, the sensitivity of eNASNet is 0.19 higher than that of bNASNet. Our method has proven to be highly effective, as evidenced by the highest AUC achieved by "eEnsemble".

Table 2: Accuracy, sensitivity, specificity, and AUC of various classification methods for MCI and NC.

Models	ACC (%)	SEN (%)	SPE (%)	AUC
bResNet50	81.39	80.56	82.00	0.91
eResNet50	86.05	83.33	88.00	0.95
bNASNet	81.39	55.56	100.00	0.92
eNASNet	87.21	75.00	96.00	0.95
bMobileNet	81.39	55.56	100.00	0.92
eMobileNet	89.53	83.33	94.00	0.95
bEnsemble	80.23	58.33	96.00	0.91
eEnsemble	88.37	80.56	94.00	0.96

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In this section, we will be comparing our findings with previous research on the diagnosis of AD. Table 3 displays the findings from prior research as well as our own results. According to Table 3, it is evident that our results exhibit superior performance in the classification of MCI. Our model demonstrates superior accuracy in classifying AD and MCI.

Table 3: Comparisons of the results of previous studies

References	AD vs NC			AD vs MCI			MCI vs NC		
	ACC	SEN	SPE	ACC	SEN	SPE	ACC	SEN	SPE
Billones et al. [12]	98.33	98.89	97.78	90.00	91.67	97.78	91.67	92.22	91.11
Sarraf et al. [13]	98.84	-	-	-	-	-	-	-	-
Ortiz et al. [14]	90.09	86.12	94.10	84.00	79.12	89.12	83.14	67.26	95.09
Lian et al. [15]	90.30	82.40	96.50	-	-	-	-	-	-
Suk et al. [16]	91.02	92.72	89.94	-	-	-	73.02	77.60	68.22
Our method	98.59	97.22	100.00	97.65	96.00	100.00	88.37	80.56	94.00

CONCLUSION

In this paper, we present an ensemble learning method for the early diagnosis of AD using deep learning. Our base classifiers were trained using the end-to-end process. Firstly, the base learner was fixed, and the fully connected layers were fitted. Next, we added additional layers to the network and updated the fully connected layers to better adapt the model for learning abstract features from medical images. We trained the base classifier to improve the model's fit. Ultimately, the results of those base learners were combined to enhance both the accuracy and stability. Based on the ADNI database, our method has yielded significant results.

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