



MULTIMODAL DEEP LEARNING METHOD FOR ALZHEIMER'S DISEASE SEVERITY IDENTIFICATION

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Abstract

Alzheimer's disease (AD) is a long-term, irreversible brain illness for which there is now no known treatment. Nonetheless, current medications may halt its advancement. For this reason, stopping and managing the progression of AD depends greatly on early detection. The primary goal is to create a comprehensive framework for medical picture classification according to different phases of Alzheimer's disease and early identification of the condition. This work employs a deep learning approach, more precisely Convolutional neural networks (CNN). The AD spectrum has four multi-classified stages. Moreover, distinct binary classifications of medical images are applied for every pair of AD stages. To identify AD and categorize the medical photos, two techniques are employed. The first approach makes use of straightforward CNN architectures based on 2D and 3D convolution to handle 2D and 3D structural brain scans from the Alzheimer's disease Neuroimaging Initiative (ADNI) dataset. The second approach makes use of pre-trained models, like the VGG19 model, for medical image classifications by applying the principle of transfer learning. We show that deep models perform better than shallow models, such as support vector machines, decision trees, random forests, and k-nearest neighbours, using the Alzheimer's disease neuroimaging initiative (ADNI) dataset. We further show that in terms of accuracy, precision, recall, and meanF1 scores, incorporating multi-modality data performs better than single modality models.

Keywords: Medical image classification, Alzheimer's disease, Convolutional neural network (CNN), Machine learning, Brain MRI.

Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that primarily affects memory and cognitive function. It is the most common cause of dementia, a syndrome characterized by a decline in memory, reasoning, and the ability to perform daily activities. The exact cause of Alzheimer's is not fully understood, and there is currently no cure for the disease.

Deep learning, a subset of machine learning, has gained significant attention in recent years for its ability to analyze complex patterns and make predictions from large datasets. Applying deep learning techniques to Alzheimer's disease research holds great promise for early detection, accurate diagnosis, and understanding the underlying mechanisms of the disease. The majority of recent research on moderate cognitive impairments (MCI) and Alzheimer's disease (AD) uses a single data modality to predict things like AD stages. For the purpose of extracting features from genetic and clinical data, we employ stacked denoising auto-encoders; for imaging data, we employ 3D-convolutional neural networks (CNNs). One of the challenges in Alzheimer's research is the difficulty in diagnosing the disease in its early stages. By the time symptoms become noticeable, significant brain damage may have already occurred. Traditional diagnostic methods involve clinical assessments, neuroimaging, and cerebrospinal fluid analysis, but these are often expensive, time-consuming, and may lack the sensitivity needed for early detection.

Literature Survey

Alzheimer's disease (AD) is the most frequent cause of dementia, accounting for 60–80% of cases [1, 2]. An Alzheimer's disease (AD) that is neurodegenerative begins with moderate cognitive impairment (MCI) and progressively worsens. It alters brain cells, impairs thinking and memory, and makes it difficult to do basic activities [3, 4]. As a result, AD is a multifaceted, degenerative neurological brain disease. AD is more common in people with MCI than in other people [5, 6]. Because AD starts two decades or more before symptoms appear, people only see its consequences after years of changes to the brain. According to Alzheimer's disease International (ADI), around 50 million individuals worldwide are afflicted with dementia. This number is expected to rise to 152 million by 2050, meaning that one in every three individuals will suffer from dementia. Dementia is likely to cost \$1 trillion annually and is expected to double by 2030 [7].

The percentage of individuals affected by AD varies according on age. In 2020, 5.8 million Americans (US) 65 years of age and older had AD, according to Figure 1. Additionally, it is anticipated to reach 13.8 million by 2050 [5]. Experts in Alzheimer's disease face their greatest obstacle because there is now no effective therapy for AD [8, 9]. In spite of this, the treatments for AD that are now available can reduce or eliminate symptoms. Therefore, it's crucial to identify AD early on when it's prodromal [10, 11]. In order to prevent AD patients' high care expenses, which are predicted to climb sharply, computer-aided detection systems, or CADs, are utilized for accurate and early AD identification [12].

Traditional machine learning algorithms commonly use two feature types—region of interest (ROI)-based and voxel-based features—in the early diagnosis of AD [13]. An integrated perspective on AD staging analysis may be obtained by combining several data modalities. Therefore, in order to categorize

patients into AD, MCI, and controls (CN), we utilize deep learning (DL) to integrally assess imaging (magnetic resonance imaging, or MRI), genetic (single nucleotide polymorphisms, or SNPs), and clinical test data. More specifically, they mostly depend on fundamental hypotheses about anatomical or functional abnormalities in the hippocampus, gray matter volume, and regional cortical thickness [14, 15].

The following is a report of the primary contributions to the AD stage forecast in this article:

- Multi-modality data analysis using DL outperforms single-modality DL models;
- Novel interpretable DL approaches are able to extract top-performing features; and
- Novel DL architectures outperform shallow learning models.

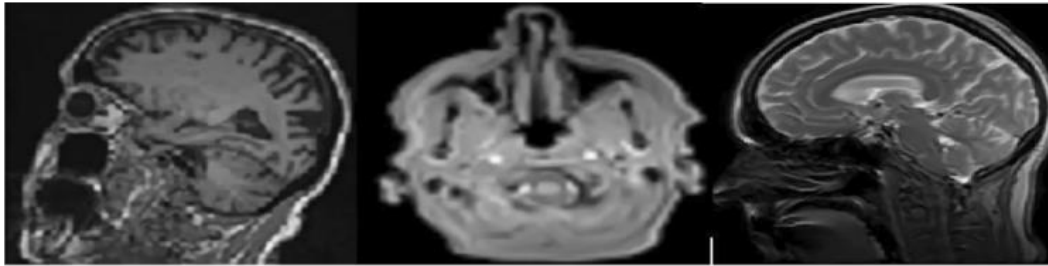


Figure-1 Slices of MR images: Accelerated Sagittal MPRAGE view, Axial Field Mapping view, and 3 Plane. Localizer view from left to right of AD patient

Outlines an innovative architecture that uses artificial neural networks and domain-specific feature engineering to identify Alzheimer's disease (AD) and assess its severity using MMSE score regression and classification. Uses a properly selected, balanced, and stratified dataset that is matched for age and gender to evaluate the system in a subject-independent context and reduce frequent task biases.

Table-1 Demographic data for 300 subjects

Alzheimer stages	AD	EMCI	LMCI	NC
Subject number	75	75	75	75
Male/female	21/54	51/24	43/32	32/43
Age (mean±STD)	75.95±0.91	76.08±0.896	77.44±1.338	75.68±0.4617

METHODS & MATERIALS

Data Description:

This paper analyzes data from the Alzheimer's Disease Neuroimaging Initiative* (ADNI) database (adni.loni.usc.edu)³⁷. With the use of clinical and neuropsychological evaluations, biological markers, serial MRI, PET, and other tests, ADNI seeks to determine if it is possible to track the development of MCI and early AD. The ADNI data repository includes genetic, clinical, and imaging information for more than 2220 individuals from four trials (ADNI1, ADNI2, ADNI GO, and ADNI3). Since ADNI 3 is an on-going investigation that is anticipated to conclude in 2022, our analysis concentrates on ADNI1, 2, and GO.

Phased releases of the data are presently underway, with restricted access to raw imaging data and no genetic data at this time. The MRI and PET scans that make up the imaging data (ADNI1, 2, and GO) are cross-sectional MRI data that correlate to the baseline screens from ADNI1 (503 individuals). The non-linearities resulting from the usage of scanners from various suppliers have been eliminated by the data publisher by standardizing the pictures. We used the cross-sectional MRI data for this analysis, which included 18 slices with 22 x 23 voxels each subject, totalling 9108 voxels per patient.

Table-2 Training, Validation and Test set size

Class label	Training set size	Validation set size	Test set size	Total
0 AD	9600	1200	1200	12,000
1 EMCI	9600	1200	1200	12,000
2 LMCI	9600	1200	1200	12,000
3 NC	9600	1200	1200	12,000
Total	38,400	4800	4800	48,000

Feature Engineering:

Individuals suffering with dementia exhibit signs of cognitive decline, including problems with thinking, memory, and communication. Our approach uses three separate ways to extract cognitive and auditory data, which are subsequently prepared and fed into their respective neural models to include such domain knowledge and context. Speech recognition-based techniques for automated identification of moderate cognitive impairment from spontaneous speech have frequently been proposed using similar derived characteristics [12, 13]. After analyzing the data to identify the most descriptive collection of associated factors for identifying AD and its severity, the following features were extracted: It is a collection of 11 unique, meticulously chosen elements from the transcripts, including word rate, intervention rate, and various pause rates that correspond to speech impairments including stuttering and slurring.

Problem Statement and Plan of Solution

To check AD stages and provide patients with remote advice, the majority of them do not, however, utilize transfer learning algorithms, multi-class medical picture classification, or Alzheimer's disease checking online services. Thus, based on further cutting-edge methods discussed in the "Related Work" section, the innovations of this work can be arranged as follows:

- An end-to-end framework is used for medical picture classification and early Alzheimer's disease detection.

Two techniques are used to apply median picture classification, which are as follows:

- The first approach uses straightforward CNN architectures to process structural brain MRI data in two and three dimensions. The foundation of these designs is 2D and 3D convolution.
- The second approach makes use of pre-trained models, such the VGG19 model, by utilizing transfer learning.

The limited quantity of medical picture datasets presents the primary problems. In order to maximize the amount of the dataset and avoid the overfitting issue, data augmentation techniques are used.

- To overcome the gathered unbalanced dataset classes, resampling techniques like "oversampling" and "downsampling" are employed.
- Four AD stages were used in the experiments for three multi-class medical image classifications and twelve binary medical image classifications. The findings showed great performance based on nine performance criteria.

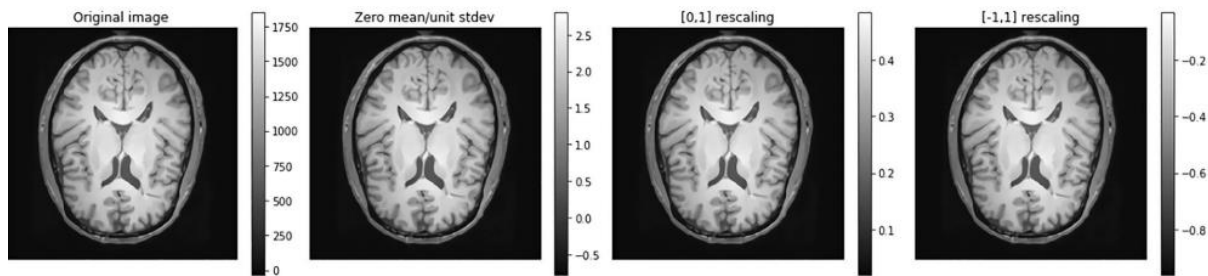


Figure-2 Example of the normalization methods applied on MRI image

Methods of Pre-processing

- **Normalization of Data:** The process of altering the range of pixel or voxel intensity values is known as data normalization. In order to make minor difference recognition easier, it attempts to eliminate some variables in the data, such as different subject poses or variations in picture contrast. Examples of data normalizing techniques are zero-mean, unit variance normalization, $[-1, 1]$ rescaling, and $[0, 1]$ rescaling.
- **Suggested Techniques and Methods for Classification:** Three crucial steps make up classic machine learning techniques: feature extraction, feature reduction, and classification. The typical CNN then combines all of these phases. It is not necessary to do the feature extraction procedure manually while utilizing CNN. Iterative learning improves the weights of the early layers, which operate as feature extractors. CNN performs better than alternative classifiers. There are three levels to it:

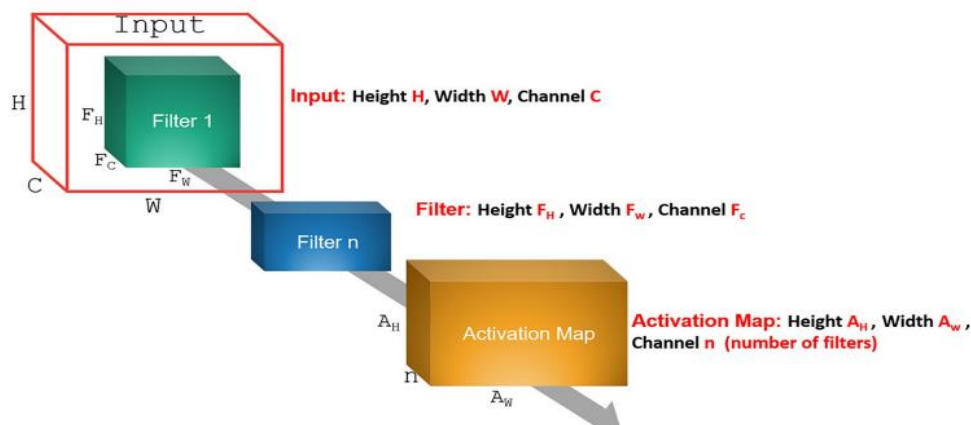


Figure-3: Illustration of the convolutional operation

The Convolutional layer represents a learnable filter that extracts features from an input image. For a 3D image with size $H \times W \times C$ where H is the height, W is the width, and C is the number of channels. Using a 3D filter-sized $F_H \times F_W \times F_C$ where F_H is the filter height, F_W is the filter width, and F_C is the number of filter channels. Therefore, the output activation map should be with a size of $A_H \times A_W$, where A_H is the activation height and A_W is the activation width. The values of A_H and A_W can be obtained using Equations 1 and 2.

$$A_H = 1 + \frac{H - F_H + 2P}{S} \quad (1)$$

$$A_W = 1 + \frac{W - F_W + 2P}{S} \quad (2)$$

P represents the padding and S is the stride; n filters may exist, so the activation map size should become $A_H \times A_W \times n$, as illustrated in Figure-3.

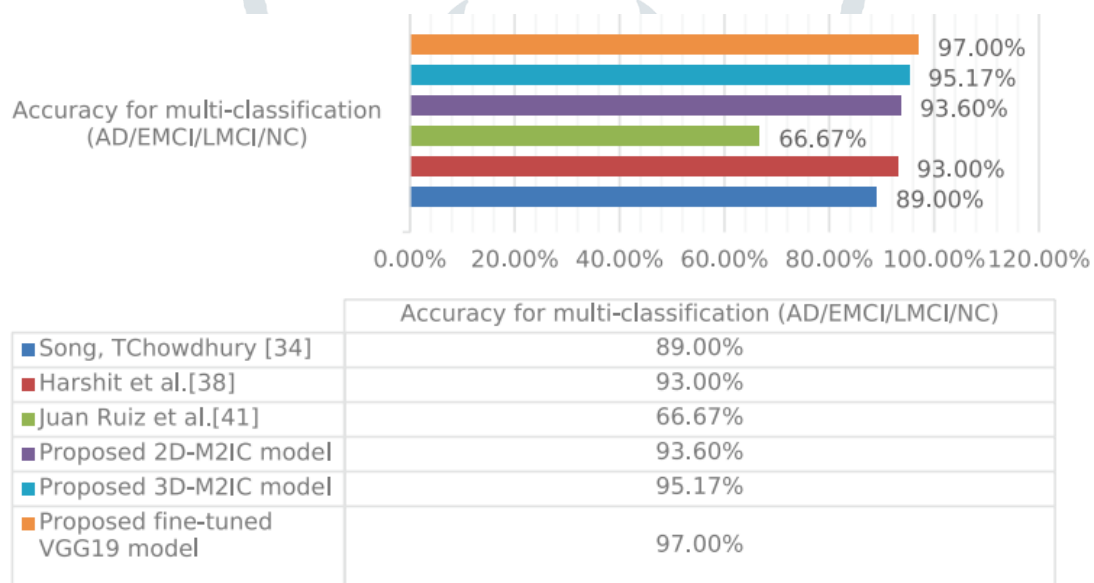


Figure-4: The comparison of the proposed models with other models for multi-class medical image classification

Experimental Results and Model Evaluation

The proposed models take into consideration different conditions. The experimental results are analyzed in terms of nine performance metrics: accuracy, loss, confusion matrix, F1 Score, recall, precision, the receiver operating characteristic curve (ROC), True Positive Rate (Sensitivity), Area under Curve (AUC), and Matthews Correlation Coefficient.

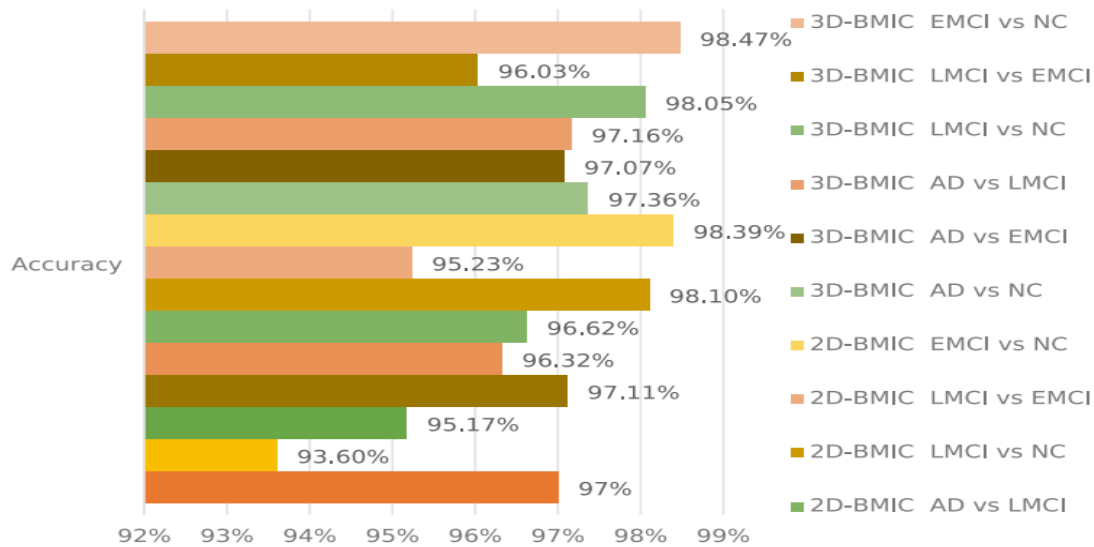


Figure-5 The comparison among the proposed models (2D-M2 IC, 3D-M2 IC, 2D-BMIC, 3D-BMIC, and fine-tuned VGG19 model) with one another

Conclusion

This research proposes the E2AD2 C framework for Alzheimer's disease diagnosis and medical picture classification. CNN architectures with deep learning serve as the foundation for the suggested framework. There are four distinct AD phases. Additionally, distinct binary classifications are used for every pair of classes. There are two ways in which this medical picture classification is used. The first approach makes use of straightforward CNN architectures based on 2D and 3D convolution to handle 2D and 3D structural brain images from the ADNI dataset. The second approach makes use of the pre-trained models by applying the notion of transfer learning. Thus, for multi-class medical picture classifications, the fine-tuned VGG19 model is employed. Moreover, the final qualified suggested designs are used to offer the Alzheimer's checking web application. It assists medical professionals and patients in remotely assessing AD, assesses the patient's Alzheimer's stage using the AD spectrum, and provides guidance depending on the patient's AD stage.

The assessment and comparison of the two approaches employ nine performance measures. The outcomes of the experiments demonstrate that the suggested designs are appropriate, straightforward structures that minimize memory needs, overfitting, and computational complexity while offering reasonable processing times. Additionally, they exhibit highly promising accuracy for 2D and 3D multi-class AD stage classifications, 93.61% and 95.17%, respectively. After fine-tuning, the pre-trained VGG19 model was able to attain 97% accuracy in multi-class AD stage classifications. It is intended to use further Pretrained models, such as EfficientNet B0 to B7, for multiclass AD stage classifications in the future and evaluate the results. Additionally, straightforward methods of data augmentation are used to the dataset. It is meant to apply the DCGAN method. Furthermore, MRI segmentation will be used to highlight Alzheimer's characteristics prior to AD stage classifications.

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