ISSN (Online) 2394-2320

International Journal of Engineering Research in Computer Science and Engineering (IJERCSE)

Vol 9, Issue 7, July 2022

Machine Learning and Deep Learning Approaches for detecting Alzheimer's Disease (AD): A Review

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Abstract*— Alzheimer's disease (AD) is the most prevalent chronic disease among the elderly, with a high prevalence. In the treatment of AD, early diagnosis of the patient plays an important role because of severe damage to the brain later. Deep learning (DL) and Machine Learning (ML) have gained popularity and success in the field of medical imaging in recent years. It has become the dominant way of assessing medical pictures, and it has also sparked considerable interest in the diagnosis of Alzheimer's disease. The deep and machine models are more precise and efficient for AD detection than ordinary machine learning techniques. This study provides AD-related biomarkers and feature extraction methods, discusses the use of the machine and deep learning approaches in AD detection, and analyses and summarises AD detection methodologies and models. The results suggest that DL and ML technology performs well in detecting AD.

***Index Terms*—Alzheimer's disease, deep learning, diagnosis, machine learning**

I. INTRODUCTION

There are many diseases that come with growing age. Dementia is one of them which accounts for 60-80 percent of older age people. The severe condition of dementia is known as Alzheimer's disease (AD). There are different levels of AD or dementia such as the preclinical stage in which the patient does not feel any difference in daily life routine but it is an initial phase of AD, in which the brain starts to shrink, it is a controllable stage. The next stage is mild dementia or mild cognitive impairment in which very mild changes are occurring in the brain but it does not affect the daily life activity of the patient. Next, dimension with mild AD in which the brain starts shrinking with the mild AD symptoms, these interfere in daily life activity a little bit. Next is dementia with moderate AD in which symptoms interfered with most of the daily life activity and the last is dementia with severe AD in which patients faced many problems such as memory loss, they confuse most of the time, they are unable to learn new things, their personality will change, they face difficulty in speaking and finding right emotions. So these are the several stages of AD. The spectrum of AD is the time taken to show its symptoms, it takes around 20 years to change from mild cognitive to AD. AD has begun to change the brain structure, the change occurs due to accommodation of amygdala protein in brain cells and expansion of literal ventricle, so early detection is very important. The computer-aided system provides very precise detection of AD, while medical scan classification is very strenuous [1]. Medical image techniques that are used for the diagnosis of neurodegenerative disease are computed tomography (CT), magnetic resonance images (MRI), and positron emission tomography (PET) most widely used neuroimaging techniques[2]. AD classification key step is feature extraction such as the amygdala, hippocampus, and other affected regions of interest (ROI). The rapid development of AI, and computer vision classifying the AD diagnosis, grab more attention. The most important step in image classification is the proper image pre-processing. In deep learning the feature extraction is done automatically when we apply CNNs, there is no need to specify ROI to the model to extract features. We learn some biomarkers, some pre-processing steps, and ML and DL approach to handle the AD detection.

The rest of this paper is organized as follows. We briefly describe the feature extraction and biomarkers in section II. Then we give a detailed description of ML and DL evaluations in section III. In section IV, the datasets used in determining AD describe. In section V, we describe the performance metrics, and finally, we summarize the whole paper in section VI.

II. FEATURED EXTRACTION AND BIOMARKERS IN AD DETECTION

The clinical diagnosis methods of AD detection are not only slower and more complicated but need to combine clinical diagnosis with imaging examination, clinical evaluation, and psychological tests are used to differentiate AD from other neurodegenerative diseases. Current biomarkers for diagnosis the AD levels are Cerebrospinal fluid (CSF), imaging biomarkers, blood tests, saliva, etc [3].

A. Cerebrospinal fluid CSF

CSF is fluid that protects, provides, and insulates the brain and spinal cord. CSF supplies various chemicals and nutrients to keep brain cells healthy. In neuroimaging, the CSF is detected by brain cell substances and proteins. CSF biomarkers for detecting AD are beta-amyloid 42, the amyloid plaque is the major component in the brain, tau, and

ISSN (Online) 2394-2320

International Journal of Engineering Research in Computer Science and Engineering (IJERCSE)

Vol 9, Issue 7, July 2022

the phosphor-tau is tau tangles' major component. These CSF are the hallmark of AD, CSF is used for early detection of neurodegenerative disease.

B. Imaging biomarker

The imaging biomarker and two types:

1. Structural imaging: Structural MRI is the most widely used, easiest, and cheapest technique to diagnose AD. In MRI T1-weighted have good contrast between gray and white matter. It is the most commonly used sequence, there are other weightings such as proton density (PD), and T2- weighted MRI is also used to diagnose AD [4].

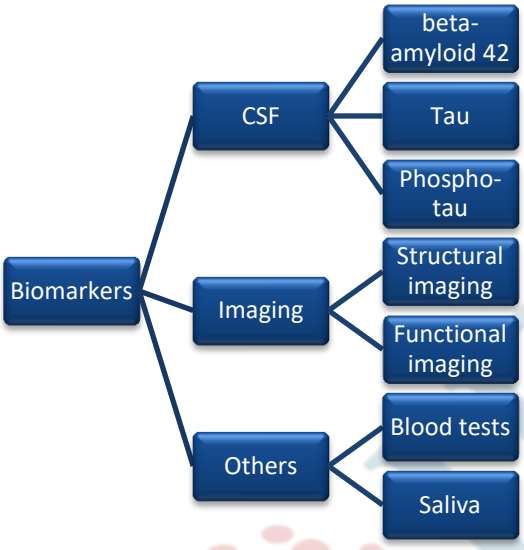

Fig.1 Biomarkers for Alzheimer's Disease detection

2. Functional imaging: Positron emission tomography PET is used as a tracer, a small amount of radioactive substance for major activities such as energy use in various brain regions, it discriminates the abnormal and normal chemical activity of a brain. There are mostly three types of PET scans used for determining dementia (i) Amyloid PET scans, (ii) Tau PET scans, and (iii) Fluorodeoxyglucose (FDG) PET scans.

C. Blood tests:

Sensitive blood tests can measure proteins that originated in the brain. The change in protein due to Alzheimer's disease is reflected in rare blood tests.

Because the scan capture is performed by devices from various manufacturers, the operating techniques of medical personnel may change. Furthermore, because of the extended acquisition period, the subject's body will surely change to some amount. As a result, in order to fulfill the requirements of feature selection, classification, and feature extraction, a set of preprocessing procedures must be performed to acquire the original picture.

MRI imaging preprocessing stages include reorientation, registration, shading correction, brain extraction, segmentation, and many other preprocessing steps applied to obtain actual images[5]. PET imaging preprocessing stages include head movement correction, format conversion, smoothing, normalization, heterologous registration, and other approaches to retain the original image[6].

III. AD DETECTION MACHINE LEARNING TO DEEP LEARNING

A. Machine learning approaches in AD diagnosis

With the rapid progress of computer vision or AI, ML and DL methods have become almost accurate methods to analysis determined the neuroimaging or other medical images. ML determines the biomarkers to detect AD. Here we first review some ML approaches to detect AD, then some DL approaches. *(Table I)*

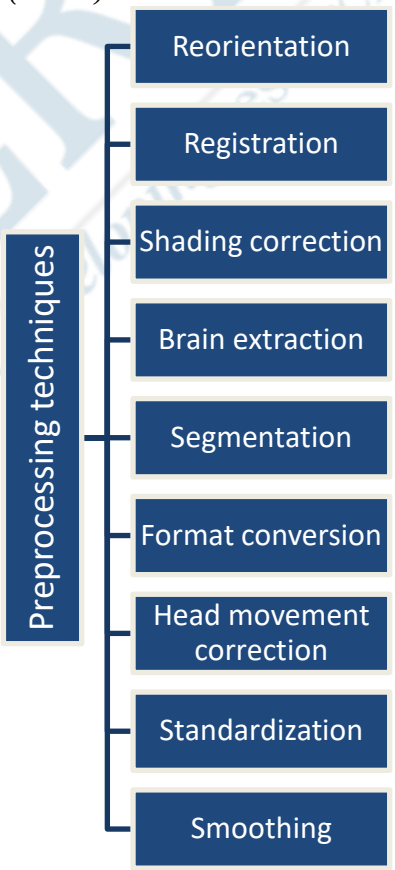

Fig.2 Preprocessing steps for MRI and PET brain scans

Xu et al. [7] use the SVM base ML approach which is a computational method, where they used gene-protein sequence as a data source. They classify AD through an ML-based approach and it was a very satisfying prediction by gene coding protein information. Ammar et al. [8] use different linguistic features such as semantics, pragmatics, and syntactic from the speech processing extractor. They

ISSN (Online) 2394-2320

International Journal of Engineering Research in Computer Science and Engineering (IJERCSE)

Vol 9, Issue 7, July 2022

were use different feature extraction methods from ML such as KNN feature selector with SVM classifier to determine binary classification between AD and NC. Kautzky et al. [9] detect early AD based on changes in the neuropathological condition of the patient. They considered post-morterm neuropathological differentiation lesion information more accurate than clinical trials. Their proposed methodology might be not fit for clinical application but it works for creating medicine to stop the progression of AD.

Zhang et al. [10] use multi-class classification to differentiate AD, EMCI, LMCI, and NC patients. They use white matter multi-regional matrics. They use SVM and LR classifiers to categorize AD into four classes. Yao et al. [11] use precise feature selection and extraction, a hierarchical grouping algorithm for multiple-class classification of AD and its variants. The hierarchical grouping method classifies AD in binary classification problems. Relating important-based feature selection used to generate simple feature space.

A methodology to diagnose AD which was based on EEG rhythm was proposed by Gómez et al. [12] the affected brain part due to AD and MCI are determined through the extraction of non-linear and spectral features from EEG records. To avoid redundancy in feature selection, a fast correction filter which was based on the feature selection technique was used. A simple cognitive task and standard neuropsychological tests for effective detection of AD were proposed by Alumbark et al. in which different features were extracted from different AD levels. They used their own created data which was formed using neuropsychological tests and cognitive tasks for feature extraction. They used principal component analysis (PCA) and for classification 4 ML algorithm was used.

Patient's speech signals for detecting AD instead of brain images were used by Gosztolya et al.[13] for classifying AD from MCI and NC. They observed that a combination of acoustic features and linguistic can provide a very high accuracy than stand-alone features. 2D textures extraction from T1 weighted MRI scans was used by Vaithnathan et al. [14] to extract features by the rough ROI (RROI) method. It was applied from its specified ROIs, these ROIs were generalized with ha igh dimensional feature selection method. CSF biomarkers were used to detect the different levels of AD using ML models, as proposed by Mofrad et al. [15] classification and regression tree analysis based decision three algorithms were used.

By blood plasma protein which was easier to access and inexpensive to others, for early detection of AD 16 proteins are biomarkers correction based feature substance selection technique was used to select. These proteins biomarkers 2-degree polynomial kernel with SVM was used to classify AD [16]. DNA mythylation expression profiles were combined with genome-wide analysis to detect patients with AD. Different classifiers such as RF, SVM, and DT were used to predict AD [17].

B. DL based approaches in AD diagnosis

In deep learning approaches, feature extraction is an automatic process, so the feature classifier working is complex. Some DL approaches are listed in Table II. Brain imaging views axial, coronal, and segmental planes of MRI, by exploiting different AD levels. AD was detected by Islam et al. [18] using deep CNN, and their precision in detecting binary classification was satisfactory.

Table 1. summary of Some Machine Learning approaches to detect Alzheimer's Disease

Authors	Models	Datasets	Data modalities	Results
Xu et al.	SVM	UniProt	Gene protein	A_{cy}- 85.65, S_{ny}- 85.70, P_{rn}-85.70
Ammar et al.	ANN, SVM, DT	DementiaBank	Speech	P_{rn}- 69, 79, 71
Kautzky et al.	RF	VITAS	sMRI	A_{cy}- 77.40, S_{ny}- 91, S_{py}- 50
Zhang et al.	SVM, LR	ADNI	DTI	A_{cy}- 89.90, 89.90
Yao et al.	SVM-RBF, XGBoost	ADNI	sMRI	A_{cy}- 54.38
Gómez et al.	LDA, QDA, MLP	Self-generated	EEG	A_{cy}- 76.47, S_{ny}- 70.59, S_{py}- 79.41
Alumbark et al.	AdaBoost, RF, SVM	Self-generated	Neuropsy-chological tests	A_{cy}- 91.08, S_{ny}- 85.71, S_{py}- 94
Gosztolya et al.	Linear SVM	Hungarian MCI-mAD	Speech	A_{cy}- 80, S_{ny}- 88, S_{py}-85.70, P_{rn}- 75.90
Vaithnathan et al.	RF, SVM, KNN	ADNI	sMRI	A_{cy}- 87.39, S_{ny}- 89.58, S_{py}-85.82
Mofrad et al.	DT	Amsterdam Dementia Cohort	CSF	A_{cy}- 86, S_{ny}- 86, S_{py}-87
Eke et al.	SVM	ADNI	Blood plasma	S_{ny}- 85, S_{py}-75, P_{rn}- 89

A_{cy}- Accuracy, S_{ny}- Sensitivity, S_{py}- Specificity, P_{rn}- Precision

ISSN (Online) 2394-2320

International Journal of Engineering Research in Computer Science and Engineering (IJERCSE)

Vol 9, Issue 7, July 2022

RNN with the LSTM method was used to detect AD, and the superiority of their proposed method as contrast to the conventional ML techniques was authenticated in accuracy terms [19]. To connect features extraction and feature classification Bi et al. proposed a deep conventional generative Boltzmann machine with a multitasking model [20].

To boost the performance of the model an end-to-end learning approach was applied. By using four volumetric CNN binary classifications were made, and both supervised and unsupervised learning was used to train models [21]. DL object detection methods such as Faster RCNN, YOLOv3, and SSD were used by Feng et al. [22] to diagnose AD and there is no need for pre-processing of scans.

An unsupervised DL, approach which had an automatic predictions method, CNN was used for extraction of features and an unsupervised classifier was used for classifying AD from MCI [23]. A multi-model approach that had hybrid CNN and DBM was investigated by Shikalgar et al., the hybrid model outperform the DNN, CNN, and SVM. Maps and GM volumes were studied by Marzban et al. [24] to detect AD, the multimodel DL approach was applied. The effect of more than one image scan per subject was evaluated in their research.

Table 2. summary of Some Deep Learning approaches to detect Alzheimer's Disease

Authors	Models	Datasets	Data modalities	Results
Islam et al.	CNN	OASIS	sMRI	S_{ny}- 71, P_{rn}- 75
Wang et al.	RNN	NACC	Demographics, medical history	A_{cy}- 83.5
Bi et al.	DSccCDBM with multitask learning	BEMT	EEG spectral Images	A_{cy}-95.04
Oh et al.	CNN	ADNI	MRI	A_{cy}-86.60 S_{ny}-88.55 S_{py}-84.54
Fong et al.	Faster R-CNN, SSD, YOLOv3	ADNI	MRI	A_{cy}-98.80 97.43, 99.66
Bi et al.	CNN-PACNet+ K-means clustering	ADNI	MRI	A_{cy}-97.01
Shikalgar et al.	Hybrid CNN & DBN	ADNI	MRI	A_{cy}-92.50 S_{ny}-90.89 S_{py}- 90.67
Marzban et al.	CNN	ADNI	MRI, DTI	A_{cy}-93.50 S_{ny}-92.50 S_{py}- 93.90

A_{cy}- Accuracy, S_{ny}- Sensitivity, S_{py}- Specificity, P_{rn}- Precision

IV. MODULES DATASETS TYPES FOR AD

AD is hard to detect and its symptoms are not shown for years, but for clinical procedures, it is necessary that the detection of AD. NC or MCI may be converted to AD, so when we identify NC or MCI is greatly significant. Publicly available biomarkers are provided in ADNI, OASIS, and other datasets.

A. ADNI

For AD research the most common dataset used is the ADNI dataset, which has authoritative data centers for AD research. Most of the research mentioned in this paper used the ADNI dataset or a combination of ADNI with other studies' datasets. ADNI data centers were founded in 2004 by the National Institute on Aging and the National Institute of Health. Organization and collection of AD patient's MRI information, discovering the cause and change of pathogenesis, tracking of pathogenesis, and finding ways of healing AD patients. Currently, the ADNI dataset is divided into four ways: (i) ADNI-GO, (ii) ADNI-1, (iii) ADNI-2, and (iv) ADNI-3. ADNI-1 and ADNI-GO store baseline data.

- ADNI-1

ADNI-1 contains five years of data and the motivation of the dataset is to find more precise biomarkers, for the examination of early AD. It contains imaging modalities MRI and PET both scans.

- ADNI-2

ADNI-2 follow-up data and which contains updated data was established in 2011, contains five years of data. The main purpose of ADNI-2 was to find biomarkers by which we analyze and predict cognitive impairment. The imaging modality present in ADNI-2 is PET with Florbetapir.

- ADNI-3

ADNI-3 also follows up on data and was established in 2016. The objective of the dataset was to find interrelation between biomarkers such as the cognitive, genetic, clinical, and biochemical biomarkers, which define Alzheimer's disease. ADNI-3 contains PET imaging modalities such as tau PET. It contains test authentications, improvements, and utilization of biomarkers in the analysis of the AD.

- ADNI-GO

ADNI-GO contains 2 years of data which was begun in 2009. The main aim of this data subset was early detection of AD, it uses MR protocols and analyzes pre-stage biomarkers of AD. The imaging modalities of the subset are MRI and PET scans.

B. OASIS

Anyone can access the OASIS dataset because this dataset is open-source for MRI scans. The open-access series of

ISSN (Online) 2394-2320

International Journal of Engineering Research in Computer Science and Engineering (IJERCSE)

Vol 9, Issue 7, July 2022

imaging studies was developed by Dr. Randy Buckner at Harvard University. Initially, this dataset contains 416 subjects 18-96 years old of which almost 100 subjects were older than 60 years. With high contrast, three-four scans per MRI scan were available in the dataset.

V. PERFORMANCE MATRICES FOR AD CLASSIFICATION

Based on some performance measurements ML and DL detection systems evaluate to correctly classify AD classes. Some performance matrices such as specificity, sensitivity, precision, F1 score, accuracy, AUC, and ROC to compute different models [1].

1) Specificity:

This parameter constitutes the fraction of negative trails that the model considers to be real negatives, and it indicates the classifier's potential to distinguish negative samples.

$$Specificity = \frac{TN}{FP+TN}$$

2) Sensitivity:

It indicates the portion of all positive trails considered actually positive by the model, and it evaluates the classifier's capacity to distinguish positive trails.

$$Sensitivity = \frac{TP}{TP+FN}$$

3) Precision:

It is defined as the portion of actual positives among all outcomes labeled positive.

$$Precision = \frac{TP}{TP+Fp}$$

4) Accuracy:

The accurate rate is calculated by dividing the number of samples accurately estimated by the entire sample.

$$Accuracy = \frac{TP+TN}{TP+FN+TN+FP}$$

5) F1-score:

It's a solitary signal that combines sensitivity and accuracy. The minimum and maximum values are 1 and 0.

$$F1\ score = \frac{2TP}{2TP+FN+FP}$$

6) ROC curve:

It is simple to determine a classifier's discriminating power on a trails at a specific threshold. Simple, intuitive, and unaffected by changes in class distribution. The ROC curve, which combines the specificity and sensitivity of the displayed technique, properly represents the connection between specificity and sensitivity of a defined analytical method and is a complete picture of a diagnostic method's accuracy.

7) AUC:

The area under the Roc curve, which ranges between 0.1 and 1. AUC may be used to immediately assessed the classifier's quality; the higher the number, the better. It is useful in determining the optimal threshold value. The better the accuracy of the model, the closer the ROC curve is to the upper left corner. The optimal threshold with the least classification error is the point on the ROC curve closest to the top left corner. The AUC value represents the likelihood. The higher the AUC score, the more likely the present classification algorithm will rank positive trails ahead of negative samples in order to superior categorize them.

VI. CONCLUSION

Overall, we found that published studies in this area tend to focus on two core areas of research, especially, biomarkers and neuroimaging, with a growing interest in scans processing, due to this high assessment of the literature. Despite being seen as extensive and wide, the work contributes little to the first detection of AD because most of the persons chosen had AD already. This research looked at some of the most important Alzheimer's disease databases, diagnostic techniques, and detection approaches. This approach is excellent for neuroimaging research in its early stages.

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