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Journal of Integrated
SCIENCE & TECHNOLOGY

An early-stage Alzheimer's disease detection using various imaging modalities and techniques – A mini-review

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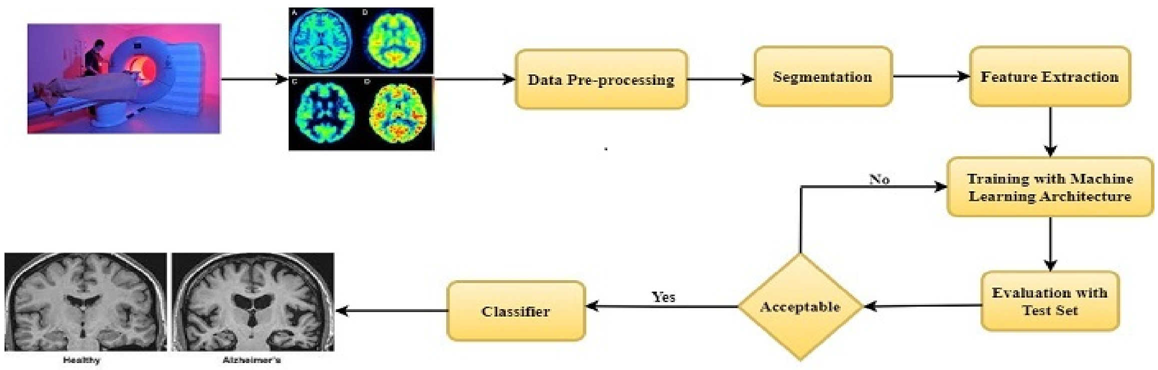
Received on: 13-Oct-2023, Accepted on 13-Jan-2024 and Published on: 05-Feb-2024

Review

ABSTRACT



Alzheimer's is a disease that affects the brain parts and leads the cells of the brain to die. It is a permanent disorder that causes danger in memory and loss the responsiveness related to the environment. The brain network plays a significant part in the identification of (Alzheimer's Disease) AD and (Mild Cognitive Impairment) MCI disorders. Since the Alzheimer's Association cautioned that Alzheimer's disease will affect 1 in 85 people by 2050, it is highly essential to have a role play to get a faster diagnosis and a prognosis. The biomarker used to diagnose the disease for distinguishing across various dementia causes needs early detection. Machine learning (ML) uses a variety of techniques to allow (Normal Controls) NCs to benefit from high dimensional data sets. This paper presents a study in early-stage identification or classification of AD using different transferred ML techniques with different modalities and their critical assessment and analysis.

Keywords: Machine Learning, Alzheimer's disease, Classification, Medical Imaging, Predictive Analysis.

INTRODUCTION

According to the World Health Organization (WHO), Alzheimer's Disease affects 5% of men and 6% of women over the age of 60 worldwide.[1,2] In 2013, it was estimated that 44 million people worldwide were affected by dementia, with a rapid increase to 136 million predicted by 2050.[3] As one of the neurodegenerative diseases AD is the most common dementia that appears often in people above 60 and increasingly impacts their brain and other cerebral roles. The issues associated with the aging population are becoming more and more severe for people who live long-lasting and reduce fertility across various courtiers. The estimated occurrence of AD is projected to surpass 65 million worldwide in the next 55 years based on Alzheimer's Union analysis.[4] The most common type of dementia is AD, diagnosed in the elderly and decreases their life dramatically, This risk is reduced by diagnosing in the early stage more accurately predefined causes exist in the medical field related to AD because of the progressive nature and multi-stage brain disease. Various risk factors are available namely adjustable and non-adjustable factors. Age is amongst all the big non-genetic risk factors.[5,6] It causes both functional and structural disruption of the nerve in the brain's Cellular cells. It stimulates Synaptic dysfunction of brain nerve cells in early disease that affects connectivity in the neural circuit, memory functions cognitive functions, etc.[7] The pictorial representation of Alzheimer's brain in Figure 1 gives the understanding of atrophy in the cerebral cortex, hippocampus, and enlarged ventricles from the normal healthy brain. According to the Alzheimer's Association, Alzheimer's and dementia deaths have increased by 16% during the COVID-19 pandemic.[8]

ML algorithms are used widely for CAD in the field of medical imaging[8] and retrieval[9] with broad applications area especially detecting and classifying the disease in the brain by considering CRT[10] and X-ray technologies.[11] Recent image process method

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Cite as: *J. Integr. Sci. Technol., 2024, 12(5), 803.*
URN: NBN: sciencein.jist.2024.v12.803

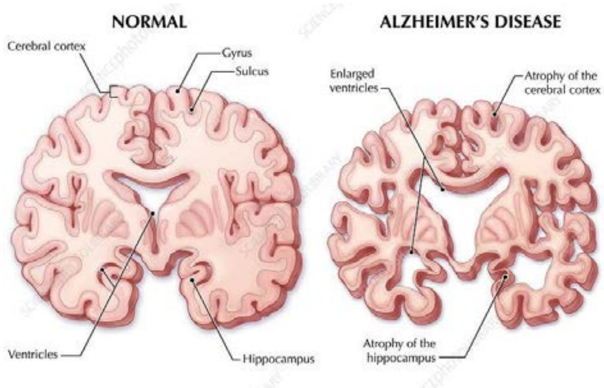

Figure 1- Normal Brain vs Alzheimer's Brain

uses high processing capabilities during the diagnosis process which leads to problems due to the large number of attributes involved such as clinical, cellular molecular, etc. Several imaging techniques have been used inthe diagnosis of AD during the past decade, including DTI (Diffusion Tensor Imaging),[12] structural MRI (Magnetic Resonance Imaging),[13] and PET (Positron Emission Tomography).[14-17] Functional MRIs (fMRIs) play a vital role in controlling brain activity and discovering functional connectivity between different regions in the brain. It is a reliable technique forinvestigating and detecting brain disease.[18]

Machine Learning Techniques are the most important platform that is used for thediagnosis of AD in all aspects. Different levels of tools are used for making decisions in statistical and probabilistic types based on previous information and knowledge. ML Tools are used toclassify new patterns from old ones. Usage of the ML will give efficient results if we understandthe limitations of the algorithm and understandthe problem in a good manner. For Various Applications, more than one type of Machine learning method always plays a crucial role inyielding very good results.

MACHINE LEARNING MODELS

An important knowledge for a clear understanding of what ML is before beginning a thorough study of machine learning techniques.AD prognosis is widely done using various machine learning methods. ML falls in the field of artificial intelligence which comprises a range of methods centred on previous learning tomake statistical, probabilistic decisions. Toidentify new events and predict new patterns, it utilizes past learning (training).

As compared to standard statistical instruments, machine learning is very efficient. In ML, a thorough analysis of a problem area and algorithm weaknesses is important to be wellunderstood to obtain successful results. Normally experiments are performed properly by training a dataset at an appropriate level and the results are tested dynamically, it has a good chance of success. In addition, all of the algorithms and techniques in Ml are very different. In general, machine learning has three kinds of algorithms for learning namely Reinforcement, unsupervised, and supervised learning E. Moradi et al.[19] Supervised learning needs labeled data for performing the learning process to draw the appropriate output. The self-learning method is based on unclassified and unlabeled data which is used in unsupervised learning algorithms.AD prediction and diagnosis are carried out based on supervised algorithms such as Artificial Neural Networks (ANN), Genetic Algorithms Decision Trees, etc. SVM, AR mining, and Ensemble methods are other techniques that are commonly in use. SVM (Support Vector Machine) is a relatively recent technique compared to supervised learning and now it is a popular ML technique, but it suffers an unidentified problem in the AD prognosis field. Instead of using a single feature, a combination of features also yields very good results in predicting the disease using logistic regression which gave an accuracy of 86% in the longitudinal study.[20]

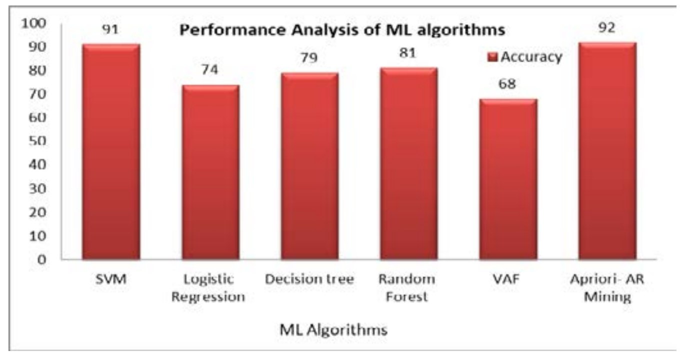

Figure 2: ML Model-based Performance Analysis

Table 1 Performance analysis of ML algorithms for the prediction of Alzheimer's Disease

ML Algorithm	SVM	Logistic Regression	Decision Tree	Random Forest	VAF	Apriori AR Mining
Number of articles	91	74	79	81	68	92

Decision tree algorithms are non-image-based analyses that play a vital role in the prediction of AD using various attributes. Dana AL-Dlaeen et al.[21] predicted the disease by selecting useful attributes from the given set of attributes using a decision tree algorithm. Gopi Battineni et al[22] proposed a feature reduction (pruning) technique to improve classification accuracy using the DT(Decision Tree) algorithm.AD forecasts do not use KNN (K - Nearest Neighbors) and DTs algorithms.

Nomenclature

APOE4	Apolipoprotein E4 allele
CSF	Cerebrospinal Fluid
CT	Computed Tomography
MRI	Magnetic Resonance Imaging
PET	Positron Emission Tomography
PSEN1& PSEN2	Preseniline gene 1 and 2
SPECT	Single Photo Emission CT
APP	Amyloid Precursor Protein

Random forest is another type of ML classifier that classifies the AD from the controlsubjects. The random forest can be applied to different modalities namely MRI[23] and EEG

(Electroencephalogram)[24] respectively which yielded good results. The performance analyses for machine learning algorithms illustrated in Figure 2 are based on the detailed study of different research publications from 2008 to 2024.[1-3,14-17,25-56]

Bio-Markers and Modality

Depending upon the various Surveys the identification of AD can be done with several Bio- markers as listed out in Table 2.

Table 2 Various Biomarkers of Alzheimer's Disease

S.No	Spheres	Bio Marker
1	Bio-Chemical	CSF,
		Blood-Based
2	Neuroanatomical	CT Scan
		MRI Scan
3	Metabolic	PET Scan
		SPECT Scan
4	Genetic APP	PSEN1
		PSEN2
		APOE4
5	Neuropsychological	Episodic
		Memory
		Other-attention
		Executive Functioning

Various analyses and reviews are done based on the different biomarkers over ML algorithms for selecting a suitable algorithm to detect AD.

Modality Analysis

The integration of these modules provides 92.11% accuracy. The proposed algorithm suffers ambiguity problems which are related to the transform to continuous data from discrete data with attribute selection[15]. Histogram segmentation is used to mask the images through the control plane with mean analysis. AR mining takes ROI as an input with the constraint parameters and also achieves an accuracy of 96.61 %.

The proposed approach was compared and the findings were 92.78% and 91.33% accuracy in the SPECT model and PET model respectively. Further, a CAD (Computer-Aided Diagnosis) decision-making tool [16] is developed for the existence of defects in the human brain and proposed pre-processing of the PET dataset. Various normalization methods are identified namely spatial and intensity and Fisher Discriminants ratio (DR) etc. The accuracy was improved related to the predictive level by eliminating incomplete data and class inequality, especially for early AD detection. The goal was to improve the AD diagnosis rate using AR progression [21] and keep track of their success by reducing the time and clinical expense-related trials. Here, the different data sets are applied to the PiB-PET and FDG-PET model which achieves 94.74% and 97.37% respectively.

The CAD system used for detecting AD diagnosis in the early stage is a more challenging task, so the proper classification method needs to be introduced for analysis R. Chaves et al.,(2010). The approach proposed was based on the focus regions (ROIs) of the three-dimensional stimulated brain. For this reason, they selected an ADNI, SPECT dataset of 97 instances (AD-54, NC-43). The authors made comparisons with other strategies such as PCA-SVM, GMM-SVM, and VAF with 95.87% accuracy in terms of cost analysis. With the same dataset,[27] the work by discovering the correlations between attributes. Various algorithms were compared to each other and achieved 94.87% accuracy. The imbalance condition of class labels was reduced and focused on pathologically unverified evidence without any consideration of missing and noise values. These data sets of AD have also been applied to other image-processing models to diagnose other types of neurodegenerative diseases. PET and SPECT Modalities are implemented by performing association rules with homogeneous data sets in the data mining.[29]

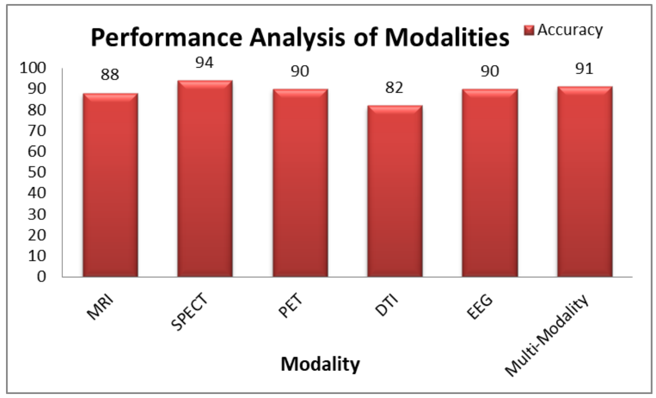

Figure 3 Performance Analysis of Modalities

The regular pattern area applied improves the accuracy of the proposed structure-based MRI to differentiate AD with early-stage controls. It also applied over the conversion from SVM to MRI separating the disease from normal aging. Using whole-brain pictures, 96% of AD patients who have been pathologically checked have been accurately identified with standard data.

Table 3 Performance analysis of Different Modalities for prediction of Alzheimer's Disease

Modality	MRI	SPECT	PET	DTI	EEG	Multi-Modality
Number of articles	88	94	90	82	90	91

Different biomarkers provide accurate outcomes based on the groups and corresponding classification. Enhanced biomarkers are combined with various attributes for diagnosing AD and making the AD members healthy.[30] The integration of MRI, CSF, and PET modalities obtained 93.2% accuracy. The baseline MRI is tested individually with an accuracy rate of 86.5%. Classification strength is boosted by comparing future time attributes (i.e. points) with various conversion methods.[31] The CSF and MRI measures with various dimensions found an accuracy of 81.6% and 87% respectively. The integration of these models also achieved 91.8% accuracy, which is good for AD detection. The automated measures are selected such as CSF and MRI with OPLS parameters which increase the accuracy of the respective conversion process. Figure 3 shows the performance analysis of various Modalities based on the detailed study of different research publications during 2008-2024.[1,14-17,25,26,28-34,57,58] and the respective data values associated with the figure are illustrated in Table 3.

MACHINE LEARNING-BASED IMAGE ANALYSIS

A spare illustration helps integrate different ages to improve accuracy[26]. Machine learning techniques combined with structural MRI can detect non-focal alterations in the temporal lobe that are indicative of the onset of Alzheimer's disease. Early detection and diagnosis of AD are analyzed based on non-invasive biomarkers for verifying their feasibility[32]. The AD data are collected from heterogeneous sources and applied in ensemble methods for assessing the performance. The modern method of AD detection uses a software model with shape and brain abnormal features. It also reads the factors such as white and grey volume, cortex and cavity area, and density of the brain. It doesn't provide the level of effect on the brain by AD[35]. The Recurrent Neural Networks (NN) model interprets the low-level features and coefficients for combining hippocampal data from a different location. Region-based shift and voxel-based models verify the various measures of the brain with AD prediction[36]. The simple Majority Voting (MV) model is used to achieve 85.55% precision by considering data fusion-based diagnosis. The integration sum and SVM of modalities increase the precision rate in the 10 % - 20 % range. The Ensemble approach is reliable[57], but the resulting accuracy is poorer than the accuracy obtained in previous research[59] and as an elaboration of previous models, a novel method of using Multi-View classification for diagnosing AD, where Earlier methods used only ROI (Region of Interest) features from MRI. In contrast, here author used both ROI and HOG (Histograms of Oriented Gradient) features Since HOG is less robust to noise when compared to ROI.

A novel method is proposed for learning the transformation comparison among two spaces with the individual collection based on the control of the class label. The multi-view method helps to increase the efficiency of recognition of disease status which outperforms compared to the baseline method. The effectiveness of the model is increased by using multiple modalities. Low-level characteristics are considered for using MRI volumes and mean signal intensities of PET[60]. High diagnostic accuracy is achieved by using latent features over auto-encoders in deep learning approaches like AD and MCI classification. A multi-modality approach (fMRI+FDG-PET+CSF) has been proposed which showed very high precision and also compared with the novel method of latent representation.

The learning of multimodality-based AD diagnosis uses MRI+PET+Genetic data for the AD diagnosis[61]. The existing methods discard the unknown samples that are present in the multi-modality data. This issue is addressed by using novel latent representation, especially for incomplete data. The proposed method used an automated framework that yields effective results. A weighted combination of multi-modality SCDDL was proposed to classify AD from MCI and AD and also compared with NC. Structural MRI, fluoro-deoxy-glucose (FDG), PET and florbetapir PET evidence produces 98.5% accuracy 82.8% and 82.7% respectively.[62] The multi-model approach is extended to the SCDDL model by using kernel learning. A single classifier is suffering an unsuccessful classification problem due to the minimum sample size. A hierarchical approach uses a multilevel classification method for combining different features at the local level. The intra-cerebral Regions and zones have been applied and showed a result of high precision of 92.0%.[63]

The Linear SVM approach selects the attributes that indicate high relevance and are more accurate with classification scores 64. The classification of various people like AD patients and non-AD patients are classified and verified using a P-type Fourier descriptor with 87.1% accuracy. An efficient biomarker converts MCI to AD from MRI images for accurate prediction. Grading biomarker calculates the accuracy based on parameters such as the correlation of age, selection of features, training data selection, accuracy during registration, and so on. The image with ML algorithm analysis is shown in Figure 2 concerning the X-axis as the total number of articles published and the Y-axis as types of machine learning algorithms for various Datasets and the respective data values associated with the figure are illustrated in Table 1.

PERFORMANCE LEVEL ANALYSIS

SVM classification based on specific subjects defers an accuracy of 84%.[19,35,65,66.] It will have a confounding impact on the use of disease-specific classification changes. A Linear regression model removes the difficult effect of normal-age people.[67] The Cox hazard model combines linear regression with multivariate analysis of survival for diagnosing accuracy with ROC analysis.[68] ELM approach uses different biomarkers by selecting the filter-based and wrapped-based features for identifying the atrophic variations among various people.sMRI acquired three measures from the brain namely thickness of cortical, surface area, and gray volume. It also preprocessed MRI data with the measurement of atrophy in the brain, CSF quantification, and scores related to cognitive and performance.[69] Detecting pre-symptomatic AD is very challenging using only a single biomarker. An automated ML classifier predicts the AD by performing various levels of tests like p-tau, t-tau, and CSF Aβ. It is `compared with MCI, NC, and AD subjects in individuals and groups for achieving higher precision.[70]

Unlike other researchers, a survey was taken using an alternative method for AD diagnosis at the earlier stage by using EEG signals.[71] An AD patient suffers a problem due to the transformation of the spectrum from a high to lower frequency range which leads the EEG anomalies. Variations in the EEG waveforms are in different levels namely alpha level, beta level, theta level, and delta level concerning the threshold values which intimates the unambiguous diagnosis of AD. A non-linear combination of the cortical fibres is not proved because of lack of evidence, so this is detected using a sign-based approach[72]. The bi-spectral method of analysis calculates frequency changes related to coupled and field frequency in the different cortexes. The diagnostic accuracy was assessed by the EEG approach based on a large literature study with approximately 80%. Functional and structural neuro-image accuracy is improved by applying approaches like CT, MRI, SPECT, PET, and the integration of EEG

[59,71-77]. The classifications of patients in most of the research work are (Stable Cognitive Impairment) SCI, (Mild Cognitive Impairment) MCI, Non-AD, and AD patients,[78-82] and the reliability analysis of the patients is represented in Figure 4.

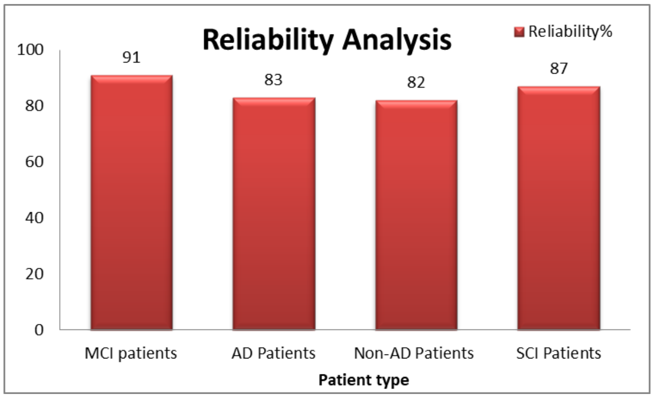

Figure 4 Reliability Analysis of Different Patients

Jelicet al.1999 have done work with the groupingof PET with EEG with 90% accuracy and 100% sensitivity. Research combining MRI with EEG[83] for the measurements of hippocampus regions which gave a maximum score of abnormalities in AD patients has also been done. Additionally, the abnormality with a combination of CT provides useful early markers that have been measured. Major studies investigated whether or not the hereditary variation of 4 alleles of Apolipoprotein E (APOE),a significant biological risk factor for late-onset AD impaired the EEG in AD patients.[83-87] Similarly, it has been found that AD patients were homozygous for the APOE 4 allele[87].

The EEG coherence is measured based on functional connectivity factors like linear right, linear wrong, linear right, temporal right, and coherence. Efficient tools are used for EEG and AD diagnosis with the comparison of various signals present in AD patients and also check the health-related to subjects. The classes of these signals are measured by performing EEG functions that exist in the entropy and bump model (Nesma Houmani et.al (2018)). EEG diagnosis performs automatically with database support over various clinical conditions and obtained an accuracy of 91.6%. The comparisonof different accuracy falls in the range of 81.8% and 88.8% for patients with AD and non-AD patients. The limitations examined in these methods deliver that only small datasets have been examined so far, these methods showed only the lowest specificity. Finally, these accuracies were not evaluated with other diagnosing methods. It will focus on the study of differential ADdiagnosis based on MCI subjects to extract the finest descriptors from the group of subjects.

Conclusion

In the past two decades, the diagnosis of AD has been progressive, and empowered technology helped to detect AD with better accuracy. Various approaches have been studied and identified the challenges faced by the existing methods. Pathological verification is proved with the small data set. Different modalities are reviewed to identify the reliable parameters that were collected from agencies like ADNI and OASIS. Feature identification and selection methods are analyzed over AD detection using imageprocessing methods. Biomarkers are identified for detecting AD in the early stages and their corresponding studies about various modalities and their prediction rate are discussed. Imaging modalities are analyzed based on the changes that occur in the various regions of the AD patient's brain. The mathematical investigation has beencarried out in a parallel manner to predict AD in critical conditions. The non-linear dynamic model understands the deep insights that will help with spectral analysis. Apart from analysis done based on various modalities, biomarkers, and models for diagnosing AD, early-stage prediction is much more important for middle-class society in our country where the cost factor plays a vital role in treating the disease in the later stages. Machine learning models are compared to identifythe challenges related to AD. Even though many earlier studies used neuro-imaging as a data source, the current tendency is to integrate multimodal data. The medical experts also direct us to focus on various AI techniques to classify AD patients. Finally, the study expressed that the nature and volume of the disease are identified by the strengths and weaknesses of AD detection.

Conflict of Interest Statement

The authors declare that there is no conflict of interest.

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