

A Complete Analysis of Alzheimer's Disease Detection Using Machine Learning Techniques

¹Mallikarjun Vanam, ²Dr.Amit Jain,

¹Research Scholar, Department of Computer Science Engineering, Sunrise University, Alwar, Rajasthan

² Professor, Department of Computer Science Engineering, Sunrise University, Alwar, Rajasthan

Abstract

Alzheimer's disease (AD) is a sort of brain condition that leads to the loss of daily functioning. Early diagnosis and classification of Alzheimer's disease remain unexplored due to the rapid progression of Alzheimer's patients and the absence of effective diagnostic instruments. The accurate and efficient identification of Alzheimer's disease is one of the many objectives of researchers seeking to halt or reverse the illness's progression. The primary purpose of this review is to present a comprehensive analysis and evaluation of the most recent research for AD early recognition and classification using the most advanced deep learning technique. The article presents a simplified explanation of system phases including imaging, preprocessing, learning, and classification. It discusses structural, functional, and molecular imaging in Alzheimer's disease. Magnetic resonance imaging (structural and functional) and positron emission tomography are considered modalities. It examines the pre-processing strategies used to improve quality. In addition, the most prevalent deep learning approaches employed in classification will be reviewed. In addition, it will examine various hurdles in the classification and preprocessing of images, as introduced in a few articles, as well as the approaches used to tackle these issues.

Keywords Alzheimer's disease(AD) , MRI, Convolutionneural network(CNN) DeepLearning(DL), Imaging pre-processing , K-NN,LR, SVM, Neuroimaging classification.

Introduction:

Alzheimer's Disease (AD) is a degenerative neurological disorder that causes short-term memory loss, psychosis, and delusional notions that are misinterpreted for stress or ageing. AD lacks adequate medical treatment. Continuous medication is required for the management of AD. AD [1] is a chronic condition that can endure for years or a lifetime. Hence, it is of the utmost importance to prescribe medication at the proper time, so that the brain is not severely injured. The early detection of this disease is a time-consuming and expensive process, as it requires a large amount of data collection, the use of advanced prediction techniques, and the participation of an experienced physician. Because they are not susceptible to human mistake, automated methods are more accurate than human evaluation and can be utilised in medical decision support systems. Researchers have utilised visuals (MRI scans), biomarkers , and quantitative information generated from MRI scans to study Alzheimer's disease based on earlier research. So, they were able to assess whether or not a person had dementia. Automation of Alzheimer's diagnosis will eliminate human interaction in addition to reducing diagnosis time. Moreover, automation saves overall expenses and improves accuracy. By

examining MRI data and applying prediction tools, for instance, we can determine whether a patient has dementia. A person with Alzheimer's disease in its early stages is termed demented. Hence, we can acquire more precision. In the early stages of Alzheimer's disease, a person can typically function without assistance. In some instances, the individual can continue to work, drive, and engage in social activities. Despite this, the individual may still experience anxiety or memory loss, such as forgetting common words and places. Close associates observe that the individual has difficulties recalling their names. By conducting a thorough medical interview, a physician may uncover memory and concentration issues in a patient. Typical difficulties in the early stages of Alzheimer's disease include:

- It is difficult to recall the correct word or name.
- Have trouble recalling names of new acquaintances.
- Daily work in social settings or the job can be difficult.
- Having forgotten anything you recently read in a book or elsewhere.
- Struggling to locate or misplacing a precious item.
- Planning and organising tasks and activities is becoming increasingly challenging.

As Alzheimer's disease advances, the persistence of its symptoms increases. Those with dementia lose the ability to speak, adjust to their surroundings, and eventually move. It becomes far more challenging for them to express their pain through words or phrases. When cognitive and memory skills continue to deteriorate, individuals may require extensive support with daily activities. • Assistance with personal grooming and daily tasks may be required 24 hours a day, seven days a week.

- Their awareness of their surroundings and previous experiences are forgotten.
- As you age, your physical abilities, including walking, sitting, and eventually swallowing, may change.
- Interpersonal communication is becoming increasingly challenging.
- The prevalence of infections, specifically pneumonia, increases.

Motivation

Under present circumstances, human instinct and standard measurements rarely agree. Innovative approaches, such as machine learning, which are computationally expensive and non-traditional, are required to overcome this challenge. Increasingly, machine learning algorithms are being applied to disease forecasting and visualisation in order to provide prescient and individualised medicines. In addition to increasing patients' quality of life, this trend helps physicians and health economists make treatment decisions and conduct studies. The review of medical reports may cause radiologists to overlook other illness problems. As a result, just a few reasons and situations are considered. The objective of this study is to identify knowledge gaps and future opportunities connected with machine learning frameworks and EHR-derived data.

Organization

Here are the various areas of our work: Recent research on identifying Alzheimer's disease utilizing Machine learning and Deep learning models are discussed in Section Relevant Works. In the Materials and Methods section, exploratory data analysis and various Machine

Learning classifier models are discussed. The final section ends the study and outlines future projects.

Related Works

Alzheimer's Disease is predicted utilizing ML algorithms by employing an application which requires and extraction method, and classification is performed using the oasis longitudinal dataset. An review of the various techniques [2] involved in evaluating brain pictures for diagnosing brain illnesses. On the basis of the results of a literature study, this article discusses a number of significant difficulties with machine learning and deep learning-based brain disease diagnoses. This study discovered the most accurate approach for detecting brain diseases, which can be utilised to develop future techniques. This study attempts to incorporate contemporary research on four brain diseases: Alzheimer's disease, brain tumours, epilepsy, and Parkinson's disease, using machine learning and deep learning platforms. The authors are able to find the best reliable diagnostic technique by utilising 22 of the most frequently consulted databases on brain diseases. Martinez-Murcia et al. [3] investigate AD data analysis using deep convolutional autoencoders. The data-driven decomposition of MRI images permits the extraction of MRI features that describe the cognitive symptoms and underlying neurodegenerative process of an individual. The influence of each coordinate of the autoencoder manifold on the brain is then computed after a regression and classification analysis is performed to analyse the distribution of the features extracted in a range of combinations and to determine their influence on the brain. In conjunction with imaging-derived markers, MMSE or ADAS11 scores can be used to predict AD with an accuracy of above 80%. To conduct binary classification, a deep neural network with interconnected layers [4, 5] is used. Each hidden layer employs an own activation function. k-folds validation selects the model with the highest performance. The Lancet Commission discovered that around 35% of Alzheimer's risk factors are modifiable. Lack of education, hypertension, obesity, hearing loss, depression, diabetes, lack of physical activity, smoking, and social isolation can all add to these risks. It is advantageous to eliminate these influences at any stage of life, regardless of their effects. Research [6] indicate that early prevention and treatment of modifiable Alzheimer's risk factors can prevent or postpone 30% of Alzheimer's cases [7]. According to the Intelligent Midlife Intervention for Alzheimer's Deterrence (In-MINDD) project [8], the Lifestyle for Brain Health (LIBRA) index [9-12] is one technique to calculate Alzheimer's risk based on risk variables. According to the National Academy of Medicine [13, 14], the three primary categories of dementia intervention are cognitive training, hypertension management, and increased physical activity. Alzheimer's Disease is the most prevalent kind of Alzheimer's disease (AD).

Vascular Alzheimer's disease (VaD) is the second most common form of Alzheimer's disease, after Alzheimer's with Lewy bodies. Some other forms of Alzheimer's disease are linked to brain traumas, infections, and alcohol consumption. In their investigation, Tatiq and Barber [15] claimed that Alzheimer's can be prevented by addressing modifying vascular risk factors because Alzheimer's and vascular dementia frequently coexist in the brain and share certain modifiable risk variables. Williams et al. [16] used four distinct models to predict cognitive

performance based on neuropsychological and demographic data: SVM, Decision Tree, NN, and Nave-Bayes. In this instance, average values were substituted for missing values; Naive Bayes had the highest accuracy. Using ten-fold cross validation [17, 18], data from the ADNI trial demonstrate a significant correlation between genetic, imaging, biomarker, and neuropsychological results. The voxel-based morphometry is applied to MRI images from the OASIS dataset [19, 20].

Ding et al. [21] developed a CNN architecture by utilising an Inception v3 network trained on 90% of ADNI data and 10% for testing. The grid approach is utilised to process fluorine-18 fluorodeoxyglucose PET scans obtained from the ADNI dataset. The Otsu threshold was used to identify brain voxel. Adam optimizer was utilised for the training model with a learning rate of 0.0001 and a batch size of 8. 90% of the dataset (1921 picture studies) was used to train the model. This dataset includes three classes (AD, MCI, and no disease). The proposed design achieves a specificity of 82% and a sensitivity of 100%.

Many optimization techniques (Genetic Algorithm, particle Swarm Optimization Algorithm, Grey Wolf Optimization, and Cuckoo Search) were employed by Chitradevi et al. [22] to segment the brain into sub-regions including the hippocampus, white matter, and grey matter.

Methodology:

The general method for detecting Alzheimer's disease consists of three steps: Feature Extraction and Selection, Model Training, and Prediction.

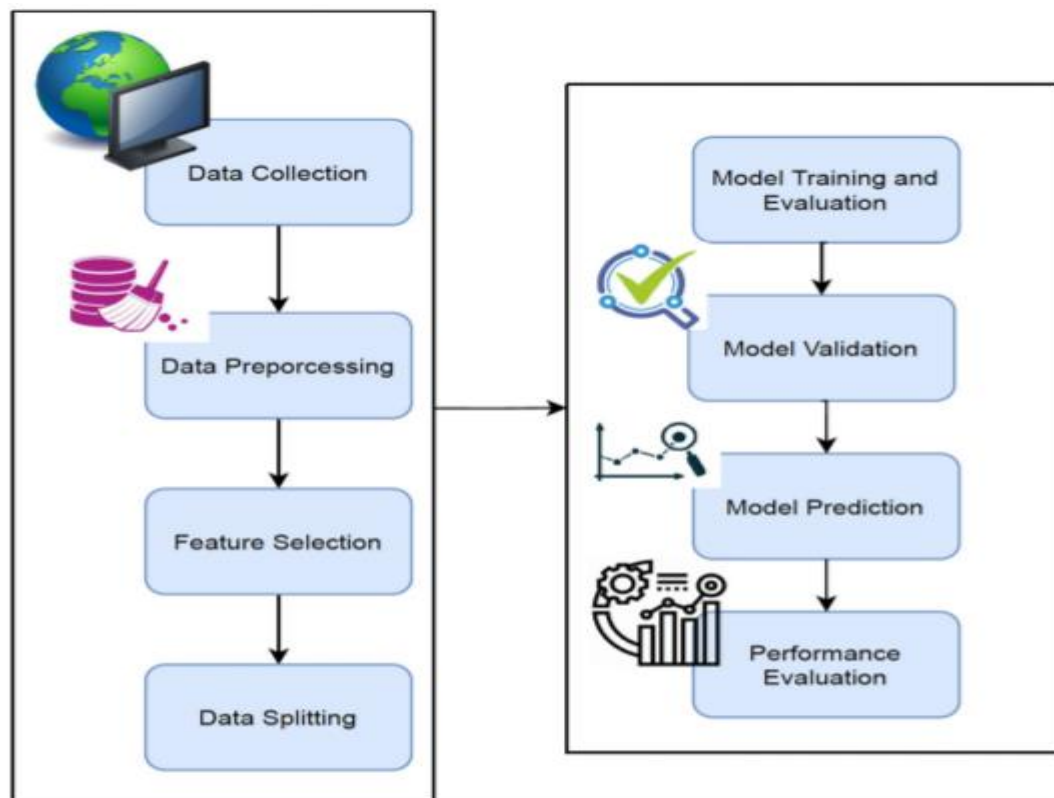


Figure: General Flow of AD

MRI Data Set Collections

MRI Acquisition

The MRI data set utilised by our system is one of the extensive data sets generated and maintained by a study conducted by a collection of medical specialists and institutions known formally as the Alzheimer's disease neuro imaging initiative or ADNI. This initiative's goal is to create biomarkers for the early detection of Alzheimer's disease [23]. This study was began in 2004, and three phases have been performed to date. ADNI phase 1 centred on the gathering of dependable longitudinal structure images using 1.5 Tesla MRI scanners with T1 weighting and dual echo T2 weighting, with 3 Tesla scanners employed on 25% of the participants. Phases 2 and 3 were conducted exclusively with 3-tesla MRI scanners. ADNI has a well-maintained collection of MRI images created from 1.5T and 3T scan images. ADNI researchers improved the image quality at the Mayo Clinic.

MRI Pre-processing

The pre-processing of photographs is one of the first procedures that ensures the precision of subsequent phases. The pre-processing step is used to improve image quality and make subsequent phases more reliable. Our suggested research makes use of ADNI-downloaded 1.5T MRI scan pictures. In this study, a total of 450 MR pictures were evaluated, including 150 normal, 150 MCI, and 150 AD images. All T1-weighted 1.5T MR images used in the proposed work (T1w). The dataset is separated into a training set and a test set with a diagnostic label. The dataset includes information regarding gender, age, date of acquisition, etc. Neuro imaging Informatics Technology Initiative (NIFTI) file format was used for MR images, and all downloaded data was preprocessed [24]. On MATLAB software, implementation work is performed. According to the information available on the ADNI website, every MPRAGE (Magnetization Prepared Rapid Acquisition Gradient Echo) image in the ADNI dataset is associated with related image files that have undergone three specified image pre-processing correction steps, namely Gradwarp, B1 non-uniformity, and N3 bias field correction, as described in chapter 4. The T1 image volumes obtained during ADNI phase 1 and phase 2 exams were subjected to a quality control examination at the Mayo Clinic, where the raw pictures were preprocessed using techniques such as intensity normalisation and gradient unwarping. For phase 3 of ADNI, this preprocessing was omitted because MRI equipment manufacturers included these modifications in their products. The majority of the time, the Mayo quality control team utilised the preprocessed picture output to distinguish the corrected version of the image, which includes a "DIS3D" indication code visible in the DICOM image header field.

Image Enhancement: Histogram

It is a form of graph that illustrates the number of pixels in an image at each distinct intensity value and facilitates image analysis. Generally, the histogram of a picture corresponds to each pixel's intensity value [198]. In a typical image, 256 (1 to 255) different intensities are available; hence, the histogram will display 256 numbers representing the distribution of grayscale values across pixels. Figures 6.3 and 6.4 display the average intensities for a

normal MR image and an AD MR image, respectively. The x-axis of the histogram shown below represents the number of pixels, while the y-axis represents the intensity count for each pixel. Histogram analysis is premised on the assumption that the grayscale values of anatomical components outside the patient's contour in the foreground and background are distinct. Normal and Alzheimer's disease (AD) MR images can be differentiated by the loss of grey matter and the expansion of the brain's fluid area, respectively. In the histogram of a normal MR image, the vast majority of pixels have grey level values, but in aberrant images, the intensities are pushed towards white.

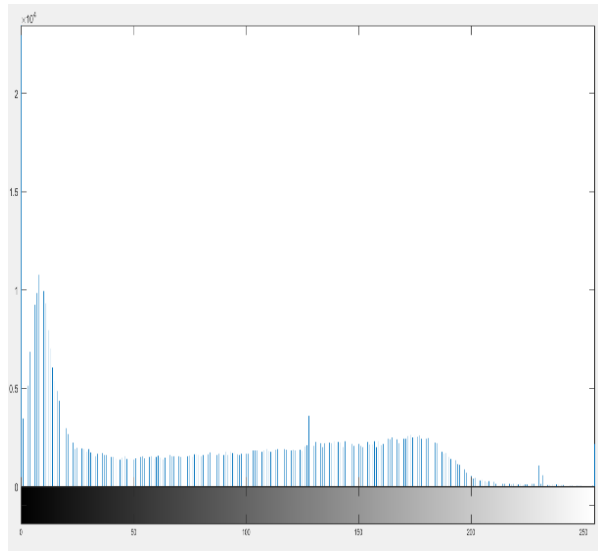
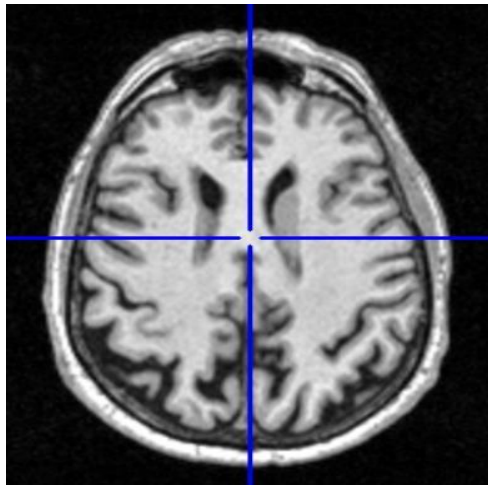


Figure : (a) Normal MR image

(b) histogram of normal MR image

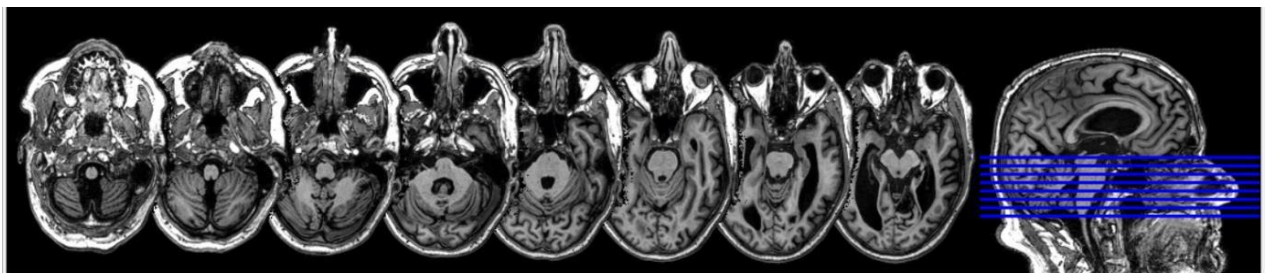


Figure : Multi slice view of Normal MR Image [Source: ADNI]

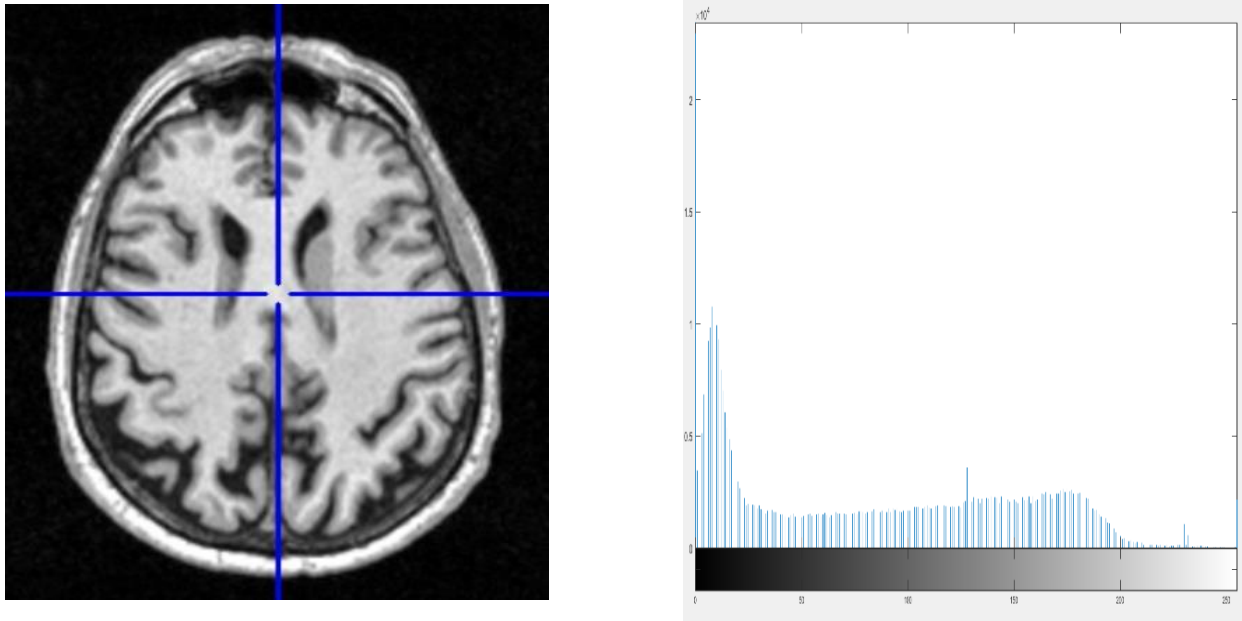


Figure : (a) AD MR Image (b) Histogram of AD MR image

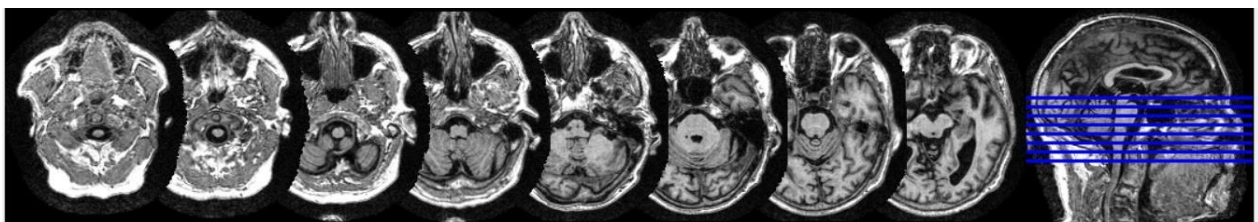


Figure : Multi slice view of AD MR Image [Source: ADNI]

450 MR images from the ADNI Dataset were used for this research. Included in these 450 MRI scans are 150 Normal control images, 150 MCI images, and 150 AD images. The segmentation of the Gray Matter, White Matter, and CSF in the MR image of the brain.

Data Preparation

In this phase, various data mining techniques were utilised to clean and preprocess the data. As part of this process, missing data are handled, features are retrieved and processed, etc. We discovered nine rows with missing values in the SES column [25-26]. This topic is approached in two different ways. The simplest option is to eliminate missing value rows. Imputation [27] is the alternative method for filling up missing values, which refers to replacing them with their corresponding parameters. Since we only have 140 measurements, the model ought to perform better if we impute. The nine rows with incomplete data in the SES attribute are eliminated, and the median value is utilised for imputation.

Data Analysis

In this section, we addressed the relationships between each aspect of an MRI test and dementia. Before extracting or analysing data, we estimated the correlations using this Exploratory Data Analysis process [28-29] in order to directly represent the link between

variables using a graph. The data could be used to determine how to analyse the data and to evaluate the nature of the findings in the future.

Feature Selection

Feature selection is a crucial aspect of machine learning. In this work, feature selection is used to hundreds of samples of Alzheimer's disease clinical data. There are three approaches for selecting features [30]: filter methods, wrapper methods, and embedded methods. At the pre-processing step, filtering is a popular technique. Wrapper methods are an additional feature subset method. The final approach, Embedded, combines the filter and wrapper methods. Correlation coefficient, Information gain, and Chi-Square are selected as the most prevalent and well-known feature selection approaches in this study.

Features of MALPEM

MALPEM-Multi-Atlas Label Propagation with EM is a technology for segmenting the entire brain from T1-weighted MR brain images. MALPEM contains all cross-sectional, longitudinal, and chosen clinical characteristics retrieved from an ADNI data set. MALPEM's essential components include modules for bias correction, label propagation, pincram brain extraction, label fusion, and label refining. The MALPEM software is 20 kilobytes in size and can be executed on a 64-bit Linux system or a Mac or Windows system using a Virtual machine software tool. MALPEM therefore accepts unsegmented MR pictures as input, extracts the brain MR image, and provides deformation field and propagation labels.



Figure: Complete Segmentation of Brain (MALPEM)

Correlation Coefficient

$X, Y = \text{Cov}(X, Y) / X Y$ denotes the covariance between the variables X and Y. Covariance is a measure of the linear relationship between two variables. Using correlation coefficients, it is simple to establish a relationship between Alzheimer's disease stages. The issue with this strategy is that it collects data from a wide variety of sources, making it extremely susceptible to outliers.

Information Gain

The entropy of the lower node is subtracted from the entropy of upper node to obtain the Information gain value when the attribute D is selected.

$$\text{Gain}(D) = I(s_1, s_2, s_3, \dots, s_n) - E(\text{Feature } D)$$

Chi-Square: Using this method, we can examine categorical variables such as the relationship between food and obesity.

$$\text{Chi-Square} = \frac{(\text{Observed} - \text{Expected})^2}{\text{expected}}$$

General Classifier Models:

Decision Tree (DT)

A summary of the decision tree provides a tree-based model for continually splitting the data depending on the threshold values of the features. By separating instances into subsets, splitting generates subsets. Internal nodes refer to intermediate subsets, while leaf nodes refer to the leaves themselves. When there is interaction effect here between features and the target, a decision tree is most useful.

Random Forest (RF)

The random forest model outperforms the decision tree model because it avoids overfitting. Models based on random forests are composed of numerous decision trees, each of which is slightly distinct from the others. The ensemble creates predictions based on every individual decision tree model using the majority voting technique (bagging). Thus, the quantity of overfitting is minimised while each tree's predictive potential is maintained.

Support Vector Machine (SVM)

This method involves defining the class of data points in a multidimensional space using appropriate hyper planes. The objective of SVM is to identify a hyper plane that divides cases of two types of variables that occupy adjacent clusters of vectors, one on one side and the other on the other. The vectors that are closest to the hyperplane are support vectors. In SVM, training and test data are utilised. Data for training is segmented into target values and attributes. SVM builds a model to predict target values for test data.

XGBoost

XGBoost is an abbreviation for eXtreme Gradient Boosting. It refers to the implementation of gradient-boosted decision trees for maximum performance and speed. As a result of the sequential nature of model training, gradient boosting machines are typically implemented slowly and are not very scalable. The focus of XGBoost is on speed and performance.

Voting

Voting is one of the most straightforward methods for merging the forecasts of multiple earning systems. Voting classifiers are not true classifiers, but rather wrappers for many classifiers that are trained and tested concurrently in order to take advantage of their particular qualities. Using various techniques and ensembles, we may train data sets to anticipate the final outcome. There are two approaches to obtain majority support for a prediction:

Rough voting: Hard voting is the simplest type of majority voting. In this instance, the class with the highest votes (N_c) will be chosen. Our projection is based on each classifier's majority vote.

Soft voting entails summing the probability vectors for each predicted class (across all classifiers) and selecting the class with the greatest value (recommended only when the classifiers are well calibrated).

Model Validation

Model validation decreases the problem of overfitting. Cross Validation is used to train the ML model and to calculate the model's accuracy. It is a difficult effort to eliminate noise from the ML model. In this research, therefore, Cross Validation is performed, which divides the entire dataset into n equal-sized sections. At each iteration, the ML model is trained with n-1 divisions. The mean of all n-folds is used to analyse the performance of the approach. In this study, the ML model was trained and evaluated ten times using ten-fold cross validation.

Conversions of the True Positive (TP), False Positive (FP), True Negative (TN), and False Negative (FN) metrics are the most popular metrics.

TP is the number of Alzheimer's disease (AD) cases that the classifier correctly predicted.

TN is the number of healthy samples (healthy controls) for whom the classifier made an accurate prediction.

FP is the number of healthy samples that the classifier incorrectly predicted (identified).

FN is the number of illness samples for which the classifier made an incorrect prediction.

i.Accuracy

Accuracy represents the proportion of correct predictions and plays a crucial part in measuring a classifier's Performance. It is represented by the number of accurate forecasts divided by the total number of predictions, which is the proportion of genuine positives and negatives based on the total number of samples (instances).

Accuracy is represented as:- $\text{Accuracy} = (\text{TP} + \text{TN}) / (\text{TP} + \text{FP} + \text{FN} + \text{TN})$

ii.Sensitivity or recall

It is an estimate of the proportion of actual positive instances that are correctly predicted as positive, or true positive, with the indication that a part of actual positive cases will be incorrectly projected as negative, or false negative. Every time, the total of sensitivity and false negative rate would equal 1. Calculating sensitivity entails the following formulas:

$\text{Sensitivity/ Recall} = \text{TP} / \text{TP} + \text{FN}$

iii.Specificity

This is the proportion of actual negatives that were projected to be negative, or true negative. There should also be a proportion of actual negatives that were predicted to be positive; these are false positives. Always, the sum of specificity and false-positive rate will equal 1.

The specificity may be computed as: $\text{TN} / \text{TN} + \text{FP}$

Table: Comparative Study of Alzheimer’s Disease using ML Approaches

SN#	Ref.	Year	Image Modality/other data	Database	Extracted Feature	Classifier/Detector (Single/Multi-stage)	Performance measurement						Others
							A _{cy} (%)	S _{py} (%)	S _{py} (%)	AUC (%)	P _m (%)	F1 (%)	
1	[31]	2018	Gene protein	UniProt	400-dimension vector	SVM	85.65	85.70	--	85.70	85.70	85.60	AD vs NC
2	[32]	2018	Speech	DementiaBank	Linguistic	ANN	--	--	--	--	69	--	AD vs NC (KNN based feature selection)
						SVM	--	--	--	--	79		
						DT	--	--	--	--	71		
3	[33]	2018	sMRI	VITAS	Neuropathological	RF	77.40	91	50	--	--	--	Prediction of AD neuropathological change vs No Change
4	[34]	2018	DTI	ADNI	White matter	SVM	89.90	--	--	95	--	--	AD vs NC
						LR	89.90	--	--	98			
5	[35]	2018	MRI	ADNI	Gray matter tissue volume as voxel features	SVM	54.55	--	--	--	--	--	pMCI vs AD (SDPSO) pMCI vs AD (SDPSO-PCA)
							57.14	--	--	--	--	--	
6	[36]	2018	sMRI (T1), Demographic information	ADNI	Morphometric, demographic, and clinical	SVM-RBF, XGBoost	54.38	--	--	--	--	--	AD vs NC vs MCI
7	[37]	2018	EEG	Self-generated	Spectral and nonlinear	LDA	74.51	70.59	76.47	--	--	--	AD vs all
						QDA	74.51	64.71	79.41				
						MLP	76.47	70.59	79.41				
8	[38]	2019	Neuropsychological tests	Dataset 1	Test scores	AdaBoost (Feature selection)	85.83	78.57	90	--	--	--	AD vs NC
						RF (Original features)	89.67	75	98				
			Cognitive task	Dataset 2		SVM (Original features)	75.25	39.29	96				
						SVM (Feature selection)	91.08	85.71	94				
9	[39]	2019	Speech	Hungarian MCI-mAD	Acoustic, linguistic	Linear SVM	80	88	85.70	--	75.90	81.50	Mild AD vs MCI
10	[40]	2019	sMRI (T1)	ADNI	Textures	RF	87.39	85.42	88.81	--	--	--	AD vs NC (RROI _{Texture} -GM+WM, Fisher)
						Linear SVM	82.61	78.13	85.82				
						KNN	87.39	89.58	85.82				

11	[41]	2019	CSF	Amsterdam Dementia Cohort	Aβ42, tau, and Ptau-181	DT	86	86	87	--	--	--	AD vs NC
12	[42]	2019	sMRI (T1/T2), R-fMRI, field mapping	ADNI	ROIs (temporal or cingulate cortex)	SVM	95.80	--	--	--	--	--	AD vs NC
13	[43]	2019	SPECT	Study at DNM, GMU	ROIs (Parietal, Ventricular and Thalamus)	ANN	--	93.80	100	97	--	--	AD vs NC
14	[44]	2019	sMRI, Cognitive tests	ADNI	ADAS-Cog scores + Cortical models	KNN	97.70	99.34	95.93	--	--	--	AD vs NC
						LDA	97.16	100	93.88				
						NB	97.92	97.93	97.90				
						SVM	97.38	100	94.41				
						ADAS-Cog scores + Cortical metrics	KNN	98.91	98.34	99.52			
							LDA	98.67	98.86	98.47			
							NB	98.81	99.23	98.36			
15	[45]	2019	Gene protein	UniProt	Feature vectors	RF	85.50	85.50	85.50	--	--	--	AD vs NC
16	[46]	2019	sMRI(T1)	OASIS	Feature vectors	Multi kernel SVM	92.50	88	95	--	--	--	Moderate AD vs mild AD vs very mild AD vs NC
						Regular SVM	91.11	85	96				
17	[47]	2019	sMRI (T2)	UMMC	Entropy	KNN	94.54	96.30	93.64	--	88.30	92.17	AD vs NC (171 features with ST)
				HMSD			98.48	96.97	100	--	100	98.46	
18	[48]	2019	Blood	SAMPLE, PreAnalytiX	Circulating miRNA	Gradient boosted trees	--	--	--	87.60	--	--	AD vs NC
19	[49]	2019	sMRI	ADNI	BSVM, CT	Multi-Stage GNB (1 st stage) & SVM, KNN (2 nd stage)	96.31	91.27	89.90	--	96.05	--	AD vs MCI vs NC
20	[50]	2019	Saliva	Data collected from volunteers	Raman spectra	ANN-BLP	99.14	98.56	99.29	--	--	--	Average (NC, AD, MCI)
21	[51]	2020	sMRI (T1)	ADNI	Volume of hippocampal structure	SVM	63.78	--	--	--	--	--	AD prediction
							Subcortical volume	55.96					
							Cortical volume	56.79					
							CT	56.37					
							Cortical surface area	51.44					

22	[52]	2020	sMRI (T1)	OASIS	Feature scores (CDR, MMSE, Visit)	Ensemble or hybrid modeling (NB, ANN, INN, SVM)	98	98.05	98	99.10	--	--	Weighted average (nondemented and demented)	
23	[53]	2020	Blood plasma	ADNI	Non-amyloid proteins	SVM	--	85	75	89	--	--	AD vs NC	
24	[54]	2020	sMRI (T1)	ADNI	ROI (CT)	Non-linear SVM (RBF kernel)	75	75	77	76	--	72	AD vs NC vs early MCI vs late MCI	
25	[55]	2020	fMRI, SNP	ADNI	Fusion features	CERF+SVM	86.20	--	--	--	--	--	AD vs NC	
26	[56]	2020	Features obtained from the dCDT	Data collected at Rowan University and Drexel University	350 features	ANN	91.42	--	--	--	--	--	AD versus non-MCI	
27	[57]	2020	DWI	ADNI	Graph metrics	SVM	72	69	75	81	--	--	AD vs NC	
						RF	74	71	77	82				
						ANN	75	80	76	83				
28	[58]	2020	sMRI (T1), age, gender	ADNI	Volume information of the hippocampus	LR	93	90	97	--	--	--	AD vs NC	
						KNN	98	98	97					
						SVM	93	90	97					
						DT	91	98	82					
						RF	93	94	92					
						GNB	94	92	97					
29	[59]	2020	EEG	An available database with no specific name	Graph theory parameters	SVM	95	95	96	97	--	--	AD vs NC	
30	[60]	2020	sMRI (T1)	OASIS	Correlation matrix of features	RF	86.84	80	--	--	94.11	87.22	AD vs NC	
31	[61]	2020	Speech	VBSD	Spectrogram	Logistic RegressionCV	83.30	86.90	--	--	86.90	86.90	AD vs NC	
				Dem@Care			84.40	87.50	--	--	91.30	89.40		
32	[62]	2020	fMRI	ADNI	Functional features of 5 brain regions	Linear SVM	89	--	--	--	--	--	AD vs MCI vs NC	
33	[63]	2020	DNA methylation expression data	GEO	Methylated sites	SVM	--	--	--	75.80	--	--	AD vs NC	
						DT	--	--	--	89.60				
						RF	--	--	--	92.70				
34	[64]	2020	Blood	BioDataome, Metabolomics Workbench, GEO	miRNA	SVM	--	--	--	97.50	--	--	AD vs NC	
					mRNA		RF	--	--	--				84.60
					Proteins		RLL	--	--	--				92.10
35	[65]	2020	Blood plasma	Data collected from volunteers	Positive or negative peaks in difference spectra	QDA	80	85	75	--	--	--	AD vs NC	

References:

1. Sivakani GA, Ansari R. Machine learning framework for implementing Alzheimer’s disease. *Int Conferen Commun Signal Process.* (2020) 12:588– 92. doi: 10.1109/ICCSP48568.2020.9182220
2. Khan P, Kader MF, Islam SR, Rahman AB, Kamal MS, Toha MU, et al. Machine learning and deep learning approaches for brain disease diagnosis: principles and recent advances. *IEEE Access.* (2021) 9:37622– 55. doi: 10.1109/ACCESS.2021.3062484
3. Martinez-Murcia FJ, Ortiz A, Gorriz JM, Ramirez J, Castillo-Barnes D. Studying the manifold structure of Alzheimer’s disease: a deep learning approach using convolutional autoencoders. *IEEE J Biomed Health Inform.* (2020) 24:17–26. doi: 10.1109/JBHI.2019.2914970
4. Prajapati R, Khatri U, Kwon GR. “An efficient deep neural network binary classifier for alzheimer’s disease classification,” In: *International Conference on Artificial Intelligence in Information and Communication (ICAIIIC).* (2021), p. 231–234.
5. Helaly HA, Badawy M, Haikal AY. Deep learning approach for early detection of Alzheimer’s disease. *Cogn Computing.* (2021) 21:1–17. doi: 10.1007/s12559-021-09946-2
6. Yaffe K. Modifiable risk factors and prevention of dementia: what is the latest evidence. *JAMA Intern Med.* (2018) 178:281– 2. doi: 10.1001/jamainternmed.2017.7299
7. Livingston G, Sommerlad A, Orgeta V, Costafreda SG, Huntley, D, et al. Dementia prevention, intervention, and care. *The Lancet.* (2017) 390:2673– 73. doi: 10.1016/S0140-6736<17>31363-6

8. O'Donnell CA, Manera V, Köhler S, Irving K. Promoting modifiable risk factors for dementia: is there a role for general practice? *British J General Pract.* (2015) 65:567–8. doi: 10.3399/bjgp15X687241
9. Sulaiman N, Abdulsahib G, Khalaf O, Mohammed MN. "Effect of Using Different Propagations of OLSR and DSDV Routing Protocols", In *Proceedings of the IEEE International Conference on Intelligent Systems Structureing and Simulation.* (2014), pp. 540-5.
10. Deckers K, van Boxtel MP, Schiepers OJ, de Vugt M, Muñoz Sánchez JL, Anstey KJ, et al. Target risk factors for dementia prevention: a systematic review and Delphi consensus study on the evidence from observational studies. *Int J Geriatric Psychiatry.* (2015) 30:234–46. doi: 10.1002/gps.4245
11. Schiepers OJ, Köhler,S., Deckers K, Irving K, O'donnell CA, Van den Akker, et al. Lifestyle for Brain Health (LIBRA): a new model for dementia prevention. *Int J Geriatric Psychiatry.* (2018) 33:167–75. doi: 10.1002/gps.4700
12. Vos SJ, Van Boxtel MP, Schiepers OJ, Deckers K, De Vugt M, Carrière I, et al. Modifiable risk factors for prevention of dementia in midlife, late life and the oldest-old: validation of the LIBRA Index. *J Alzheimer's Dis.* (2017) 58:537–47. doi: 10.3233/JAD-161208
13. Osamh Khalaf I, Ghaida M, Abdulsahib D. Energy efficient routing and reliable data transmission protocol in WSN. *Int J Adv Soft Comput Applicat.* (2020) 12:45–53.
14. National Academies of Sciences, Engineering, and Medicine. Preventing cognitive decline and dementia: A way forward. London: The National Academies Press (2018).
15. Tariq S, Barber PA. Dementia risk and prevention by targeting modifiable vascular risk factors. *J Neurochemistr.* (2018) 144:565– 81. doi: 10.1111/jnc.14132
16. Williams., Jennifer A, Weakley A, Cook MS, Edgecombe DJ. "Machine learning techniques for diagnostic differentiation of mild cognitive impairment and dementia," In *Workshops at the Twenty-Seventh AAAI Conference on Artificial Intelligence.* (2018), pp. 71–6.
17. Khalaf OI, Sabbar BM. A modified algorithm for improving lifetime WSN. *J Eng Appl Sci.* (2018) 13:9277–82.
18. Khalaf OI, Abdulsahib GM, Sabbar BM. Optimization of wireless sensor network coverage using the Bee Algorithm. *J Inf Sci Eng.* (2020) 36:377–86.
19. Chi CL, Oh, Borson WS. "Feasibility Study of a Machine Learning Approach to Predict Dementia Progression," in *International Conference: In Health care Informatics (ICHI).* (2015), p. 450.
20. Chyzyk A, Savio D. Feature extraction from structural MRI images based on VBM: data from OASIS database, University of The Basque Country, Internal research publication (2010).
21. Ding Y, Sohn JH, Kawczynski MG, Trivedi H, Harnish R, Jenkins NW, Lituiev D, Copeland TP, Aboian MS, Mari Aparici C, Behr SC, Flavell RR, Huang SY, Zalocusky KA, Nardo L, Seo Y, Hawkins RA, Hernandez Pampaloni M, Hadley D, Franc BL (2018) A Deep

- Learning model to predict a diagnosis of Alzheimer disease by using 18F-FDG PET of the brain. *Radiology* 180958:456–464. <https://doi.org/10.1148/radiol.2018180958>.
22. Chitradevi D, Prabha S (2020) Analysis of brain sub regions using optimization techniques and deep learning method in Alzheimer disease. *Appl Soft Comput* 86:105857. <https://doi.org/10.1016/j.asoc.2019.105857>
23. Amen DG (2015) *Change your brain, Change Your Life (Revised and Expanded): The Breakthrough Program for Conquering Anxiety, Depression, Obsessiveness, Lack of Focus, Anger, and Memory Problems-Harmony*.
24. Basaia S, Agosta F, Wagner L, Canu E, Magnani G, Santangelo R, Filippi M (2018) Automated classification of Alzheimer’s disease and mild cognitive impairment using a single MRI and deep neural networks. *NeuroImage: Clinical*, 101645. <https://doi.org/10.1016/j.nicl.2018.101645>.
25. Javed AR, Fahad LG, Farhan AA, Abbas S, Srivastava G, Parizi RM, et al. Automated cognitive health assessment in smart homes using machine learning. *Sustain Cities Soc.* (2020) 65:102572. doi: 10.1016/j.scs.2020.102572
26. Maddikunta, PR, Gadekallu, TR, Iwendi, C, et al. Identification of malnutrition and prediction of BMI from facial images using real-time image processing and machine learning. *IET Image Process.* (2021) 21:1–12. doi: 10.1049/ipr2.12222
27. Saratxaga CL, Moya I, Picón A, Acosta M, Moreno-Fernandez-de-Leceta A, Garrote E, et al. MRIDeep learning-based solution for Alzheimer’s Disease Prediction. *J.Pers. Med.* (2021) 11:902. doi: 10.3390/jpm11090902
28. Maddikunta, PR, Gadekallu, TR, Iwendi, C, et al. Identification of malnutrition and prediction of BMI from facial images using real-time image processing and machine learning. *IET Image Process.* (2021) 21:1–12. doi: 10.1049/ipr2.12222
29. Javed AR, Sarwar MU, ur Rehman S, Khan HU, Al-Otaibi YD, Alnumay WS. PP-SPA: privacy preserved smartphone-based personal assistant to improve routine life functioning of cognitive impaired individuals. *Neural Process Lett.* (2021) 21:1–8. doi: 10.1007/s11063-020-10414-5.
30. Sudharsan M, Thailambal G. Alzheimer’s disease prediction using machine learning techniques and principal component analysis (PCA), *Materials Today: Proceedings* (2021).
31. L. Xu, G. Liang, C. Liao, G.-D. Chen, and C.-C. Chang, “An efficient classifier for Alzheimer’s disease genes identification,” *Molecules*, vol. 23, no. 12, p. 3140, Nov. 2018.
32. R. Ben Ammar and Y. Ben Ayed, “Speech processing for early Alzheimer disease diagnosis: Machine learning based approach,” in *Proc. IEEE/ACS 15th Int. Conf. Comput. Syst. Appl. (AICCSA)*, Oct. 2018, pp. 1–8.
33. A. Kautzky, R. Seiger, A. Hahn, P. Fischer, W. Krampla, S. Kasper, G. G. Kovacs, and R. Lanzenberger, “Prediction of autopsy verified neuropathological change of Alzheimer’s disease using machine learning and MRI,” *Frontiers Aging Neurosci.*, vol. 10, pp. 1–11, Dec. 2018.
34. Y.-T. Zhang and S.-Q. Liu, “Individual identification using multi-metric of DTI in Alzheimer’s disease and mild cognitive impairment,” *Chin. Phys. B*, vol. 27, no. 8, Aug. 2018, Art. no. 088702.

- 35 N. Zeng, H. Qiu, Z. Wang, W. Liu, H. Zhang, and Y. Li, “A new switching-delayed-PSO-based optimized SVM algorithm for diagnosis of Alzheimer’s disease,” *Neurocomputing*, vol. 320, pp. 195–202, Dec. 2018.
36. D. Yao, V. D. Calhoun, Z. Fu, Y. Du, and J. Sui, “An ensemble learning system for a 4-way classification of Alzheimer’s disease and mild cognitive impairment,” *J. Neurosci. Methods*, vol. 302, pp. 75–81, May 2018.
37. S.Ruiz-Gómez,C.Gómez,J.Poza,G.Gutiérrez-Tobal,M.Tola-Arribas, M. Cano, and R. Hornero, “Automated multiclass classification of spontaneous EEG activity in Alzheimer’s disease and mild cognitive impairment,” *Entropy*, vol. 20, no. 1, p. 35, Jan. 2018.
- 38 I. Almubark, L.-C. Chang, T. Nguyen, R. S. Turner, and X. Jiang, “Early detection of Alzheimer’s disease using patient neuropsychological and cognitive data and machine learning techniques,” in *Proc.IEEE Int.Conf. Big Data (Big Data)*, Dec. 2019, pp. 5971–5973.
39. G.Gosztolya, V.Vincze, L.Tóth, M.Pákási, J.Kálmán,and I.Hoffmann, “Identifying mild cognitive impairment and mild Alzheimer’s disease based on spontaneous speech using ASR and linguistic features,” *Comput. Speech Lang.*, vol. 53, pp. 181–197, Jan. 2019.
40. K. Vaithinathan and L. Parthiban, “A novel texture extraction technique with t1 weighted MRI for the classification of Alzheimer’s disease,” *J. Neurosci. Methods*, vol. 318, pp. 84–99, Apr. 2019.
41. R. Babapour Mofrad, N. S. M. Schoonenboom, B. M. Tijms, P.Scheltens,P.J.Visser,W.M.Flier,andC.E.Teunissen,“Decisiontree supports the interpretation of CSF biomarkers in Alzheimer’s disease,” *Alzheimer’s Dementia, Diagnosis, Assessment Disease Monitor.*, vol. 11, no. 1, pp. 1–9, Dec. 2019.
42. J. Sheng, B. Wang, Q. Zhang, Q. Liu, Y. Ma, W. Liu, M. Shao, and B. Chen, “A novel joint HCPMMP method for automatically classifying Alzheimer’s and different stage MCI patients,” *Behavioural Brain Res.*, vol. 365, pp. 210–221, Jun. 2019.
43. D.SwietlikandJ.Bialowas,“Applicationofartificialneuralnetworksto identify alzheimer’s disease using cerebral perfusion SPECT data,” *Int. J. Environ. Res. Public Health*, vol. 16, no. 7, pp. 1–9, 2019.
44. S. Lahmiri and A. Shmuel, “Performance of machine learning methods applied to structural MRI and ADAS cognitive scores in diagnosing Alzheimer’s disease,” *Biomed. Signal Process. Control*, vol. 52, pp. 414–419, Jul. 2019.
45. L. Xu, G. Liang, C. Liao, G.-D. Chen, and C.-C. Chang, “K-Skip-nGram-RF:A random forest based method for Alzheimer’s disease protein identification,” *Frontiers Genet.*, vol. 10, pp. 1–7, Feb. 2019.
46. S. Neffati, K. Ben Abdellafou, I. Jaffel, O. Taouali, and K. Bouzrara, “An improved machine learning technique based on downsized KPCA for Alzheimer’s disease classification,” *Int. J. Imag. Syst. Technol.*, vol. 29, no. 2, pp. 121–131, Jun. 2019.
47. U. R. Acharya, S. L. Fernandes, J. E. WeiKoh, E. J. Ciaccio, M. K. M. Fabell, U. J. Tanik, V. Rajinikanth, and C. H. Yeong, “Automated detection of Alzheimer’s disease using brain MRI images—A study with various feature extraction techniques,” *J. Med. Syst.*, vol. 43, no. 9, p. 302, Aug. 2019.

48. N. Ludwig, T. Fehlmann, F. Kern, M. Gogol, W. Maetzler, S. Deutscher, S. Gurlit, C. Schulte, A.-K. von Thaler, C. Deuschle, F. Metzger, D. Berg, U. Suenkel, V. Keller, C. Backes, H.-P. Lenhof, E. Meese, and A. Keller, "Machine learning to detect Alzheimer's disease from circulating non-coding RNAs," *Genomics, Proteomics Bioinf.*, vol. 17, no. 4, pp. 430–440, Aug. 2019.
49. K.R.Kruthika,Rajeswari,andH.D.Maheshappa,"Multistageclassifierbased approach for Alzheimer's disease prediction and retrieval," *Informat. Med. Unlocked*, vol. 14, pp. 34–42, Jan. 2019.
50. N. M. Ralbovsky, L. Halámková, K. Wall, C. Anderson-Hanley, and I. K. Lednev, "Screening for Alzheimer's disease using saliva: A new approach based on machine learning and Raman hyperspectroscopy," *J. Alzheimer's Disease*, vol. 71, no. 4, pp. 1351–1359, Oct. 2019.
51. Z. Fan, F. Xu, X. Qi, C. Li, and L. Yao, "Classification of Alzheimer's disease based on brain MRI and machine learning," *Neural Comput. Appl.*, vol. 32, no. 7, pp. 1927–1936, Apr. 2020.
52. G. Battineni, N. Chintalapudi, F. Amenta, and E. Traini, "A comprehensive machine-learning model applied to magnetic resonance imaging (MRI) to predict Alzheimer's disease (AD) in older subjects," *J. Clin. Med.*, vol. 9, no. 7, p. 2146, Jul. 2020.
53. C. S. Eke, E. Jammeh, X. Li, C. Carroll, S. Pearson, and E. Ifeachor, "Early detection of Alzheimer's disease with blood plasma proteins using support vector machines," *IEEE J. Biomed. Health Informat.*, vol. 25, no. 1, pp. 218–226, Jan. 2021.
54. V. S. Rallabandi, K. Tulpule, and M. Gattu, "Automatic classification of cognitively normal, mild cognitive impairment and Alzheimer's disease using structural MRI analysis," *Inform. Med. Unlocked*, vol. 18, pp. 1–7, Jan. 2020.
55. X.-A. Bi, X. Hu, H. Wu, and Y. Wang, "Multimodal data analysis of Alzheimer's disease based on clustering evolutionary random forest," *IEEE J. Biomed. Health Informat.*, vol. 24, no. 10, pp. 2973–2983, Oct. 2020.
56. R. Binaco, N. Calzaretto, J. Epifano, S. McGuire, M. Umer, S. Emrani, V. Wasserman, D. J. Libon, and R. Polikar, "Machine learning analysis of digital clock drawing test performance for differential classification of mild cognitive impairment subtypes versus Alzheimer's disease," *J. Int. Neuropsychological Soc.*, vol. 26, no. 7, pp. 690–700, Aug. 2020.
57. E. Lella, A. Lombardi, N. Amoroso, D. Diacono, T. Maggipinto, A. Monaco, R. Bellotti, and S. Tangaro, "Machine learning and DWI brain communicability networks for Alzheimer's disease detection," *Appl. Sci.*, vol. 10, no. 3, p. 934, Jan. 2020.
58. G. Uysal and M. Ozturk, "Hippocampal atrophy based Alzheimer's disease diagnosis via machine learning methods," *J. Neurosci. Methods*, vol. 337, May 2020, Art. no. 108669.
59. F. Vecchio, F. Miraglia, F. Alü, M. Menna, E. Judica, M. Cotelli, and P. M. Rossini, "Classification of Alzheimer's disease with respect to physiological aging with innovative EEG biomarkers in a machine learning implementation," *J. Alzheimer's Disease*, vol. 75, no. 4, pp. 1253–1261, Jun. 2020.
60. A.Khanand S.Zubair,"An improved multi-modal based

machine learning approach for the prognosis of Alzheimer's disease," *J. King Saud Univ.-Comput. Inf. Sci.*, pp. 1–19, Apr. 2020.

61. L. Liu, S. Zhao, H. Chen, and A. Wang, "A new machine learning method for identifying Alzheimer's disease," *Simul. Model. Pract. Theory*, vol. 99, Feb. 2020, Art. no. 102023.

62. J.Sheng, M.Shao, Q.Zhang, R.Zhou,L.Wang, and Y.Xin," Alzheimer's disease, mild cognitive impairment, and normal aging distinguished by multi-modal parcellation and machine learning,"*Sci.Rep.*,vol.10,no.1, pp. 1–10, Dec. 2020.

63. J. Ren, B. Zhang, D. Wei, and Z. Zhang, "Identification of methylated gene biomarkers in patients with Alzheimer's disease based on machine learning," *BioMed Res. Int.*, vol. 2020, pp. 1–11, Mar. 2020.

64. M. Karaglani, K. Gourelia, I. Tsamardinos, and E. Chatzaki, "Accurate blood-based diagnostic biosignatures for Alzheimer's disease via automated machine learning," *J. Clin. Med.*, vol. 9, no. 9, p. 3016, Sep. 2020.

65. R. Gaudiuso, E. Ewusi-Annan, W. Xia, and N. Melikechi, "Diagnosis of Alzheimer's disease using laser-induced breakdown spectroscopy and machine learning," *Spectrochimica Acta B, At. Spectrosc.*, vol. 171, Sep. 2020, Art. no. 105931.