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A Complete Survey on Alzheimer's disease

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ABSTRACT

Alzheimer's disease (AD) is a disorder that is neurodegenerative ,it slowly affects your cognitive functions resulting in the significant decline of the memory gradually. It mostly affects older adults. There is no cure for this disease as of now , some drugs can be taken that will alleviate the symptoms. So, the machine learning models are increasingly used to for the early detection and diagnosis of Alzheimer's. This research paper focuses on providing with the different machine learning algorithms used mores0 prevalently , the most important data used by the ML models for giving the accurate result. This research has reviewed literature from 1906 to 2024. The important data used for the detection in most of the literature reviewed are Magnetic Resonance Imaging(MRI), Positron Emission Tomography(PET), Functional Magnetic Resonance Imaging(fMRI), cognitive testing and biomarkers like cerebrospinal fluid etc. The most commonly used techniques were random forests, k-nearest neighbours(KNN), Support Vector Machine(SVM), Decision trees, Logistic Regression (LR) and Convolutional Neural Networks(CNN). These techniques were used because they could work with both numerical and categorical data , it is fast and efficient even with large volumes of data and results in good accuracy. This research suggests that using the different techniques and combining different kind of data like genetic, imaging and cognitive testing scores, that is by following a multimodal approach, there is a higher accuracy rate for the early detection and classification of Alzheimer's Disease Stages.

Keywords: Alzheimer's Disease ,Machine Learning, Multimodal approach, Early Detection ,MRI ,Cognitive testing , PET, fMRI, Biomarkers, Random Forest , k-Nearest Neighbours (KNN),Support Vector Machine(SVM),Decision Trees , Logistic Regression , Convolutional Neural Networks (CNN)

INTRODUCTION

Alzheimer's Disease (AD) is a neurodegenerative disorder which has no cure identified The main risk factors for this disease include age,genetics ,head injuries ,environmental factors , hormonal changes , sleep disorders ,smoking , alcohol, diet etc..The symptoms of this disease mostly appears in the later stages of the disease where irreversible damage to the brain has already been occurred .The traditional diagnostic methods depend on these symptoms to detect Alzheimer's which are not efficient for the early detection.This is where the intervention of Machine learning was used , where different algorithms were used on the large, complex datasets to uncover some patterns for early detection.

Neuroimaging technologies like Magnetic Resonance Imaging (MRI),Positron Emission Tomography(PET) and functional MRI(fMRI) are utilized. There are cognitive test conducted on the patients and the scores along with biomarkers such as cerebrospinal fluid proteins were used as data .The medial history of the patients , their lifestyle factors are all examined using ML techniques. So both numerical and categorial data is taken into consider.

Different ML techniques like Support Vector Machine, Random Forest , Decision Trees, k-nearest neighbors, Logistic Regression , Gradient Boosting etc are used. These are some of the techniques which is commonly compared , some of these techniques can take large volume of data and give results fast and in the most efficient way . These techniques are applied mostly because they have shown improving diagnostic accuracy especially in the preclinical stages .This research focuses on discovering such efficient ML techniques and crucial data requires in these techniques along with finding which techniques gives the highest accuracy.

LITERATURE REVIEW

Chang et al,(1912) identified preclinical AD using cognitive testing and ML techniques to differentiate memory strategies between individual at high risk and those at low risk. The Rey Auditory Verbal Learning Test was utilized and ML methods, including stochastic gradient descent, were applied to exploit subtle differences in memory strategies. The results showed significant differences in memory performance, providing better separation between the 2 risk groups than the traditional methods. The dataset includes results from 879 high risk and 355 low risk individuals (Chang, 1912) **Crapper et al,(1973**)Aluminum exposure produced similar tangles in rabbits, indicating a possible role in the pathophysiology of Alzheimer's disease. Although the study could not establish causation, it did demonstrate a

correlation between aluminum and neurodegeneration, which led to more research into aluminum's involvement in the illness. (Crapper, 1973)

Perl et al,(1980) X-ray spectrometry was utilized by Perl and Brody to identify increased aluminium concentrations in Alzheimer's patients' neurons that had neurofibrillary tangles. Although the study was unable to determine whether aluminium causes or results from the disease, the results point to a potential connection between aluminium and the formation of tangles, which suggests more research into the role of metals in neurodegeneration. (Perl, 1980)

Yamamoto et al,(1986) Upon the ultrastructural study, it was found that paired helical filaments are the primary factor in the neurofibrillary tangles in AD .The research pointed out how paired helical filaments are different from the filaments in other diseases that are neurodegenerative .This study tells that PHF might be the factor that contributes to neurodegeneration as its buildup would disrupt the regular cellular processes . (Yamamoto, 1986)

Pericak-Vance MA et al,(1991) They discovered that in the families that were afflicted by this disease there found the evidence that there is a genetic correlation between the chromosome 19 and Alzheimer's disease through their linkage analysis .They found that APOE played a significant role as a genetic risk factor in AD .This study was revolutionary since it opened doors to further investigation of the genetic locus linked to Alzheimer's. (Pericak-Vance MA, 1991)

Tsai et al,(1994) The study established that apoliproprotein E is a significant factor in the genetic risk of AD disease . It also verified that one or more alleles of this protein is one of the causes for increased risk in AD . The screening of this ApoE genotype helps in identifying the individuals that are at the risk of this disease . (Tsai, 1994)

Näslund et al, (1994) In this study the aging people were examined along with finding the abundance of amyloid beta variants presence in the brain of people with AD .They found that Aβ42 is contributing more towards the AD patients .

This study urges that more investigation must be done on the role of these peptides in the development rate of AD. (Näslund, 1994)

Lehericy et al, (1994) Using MRI they measured the amygdala and hippocampal volumes in AD patients .It demonstrated that there is a decline in the brain regions , which are essential for memory and emotion .They suggested that MR volumetric analysis will help in tracking AD and for providing early diagnosis.They suggested more studies must be conducted in larger populations to confirm the results . (Lehericy, 1994)

Perry et al, (1998) This paper studies on the role of ROS in the damage of cells in AD.It shows that oxidative stress causes deterioration in neurons in AD patients further contributing to the progression of this disease .This study tells that addressing oxidative damage could be a strategy for slowing AD progression .The study suggests to further investigate on the antioxidant effects in AD treatment . (Perry, 1998)

Smith et al, (1998) This paper discusses in details about underlaying mechanisms , treatment approaches and clinical features of AD.This review suggested that oxidative damage is significant factor in the development of the disease .It tells that amyloid -beta , oxidative stress and tau protein are the main causes . This review emphasis the need for fresh ideas in regard to therapeutic intervention. (Smith, 1998)

Blacker et al ,(1998) The study tells that genes like PSEN2, PSEN1,APOE and APP are linked to the both sporadic and familial forms of the disease .The study tells how discovering the genetic connections is creating new opportunities for creating treatments for this disease.The study recommends that to improve more gene based treatments and to find more risk genes . (Blacker, 1998)

Markesbery, (1999) This study tells how oxidative stress is playing a important role in AD.It tells how amyloid-beta and tau protein changes aggregation will ultimately result in the death of neurons.This paper suggests antioxidant therapies as a tactic to verify how effectively we can delay the course of AD. (Markesbery, [28] "The role of oxidative stress in Alzheimer disease." Archives of Neurology, 56(12), 1449-1452., 1999)

Haroutunian V et al, (1999) This study examines the neurofibrillary tangles in elderly people with mild Alzheimer's disease and without it . They discovered that NFT's are common in those with mild AD..They said that NFT's might appear before dementia symptoms , that can act as precursor to this disease .The study suggests that more research should be done on the NFT formation. (Haroutunian V, 1999)

Grundman et al, (2000) This studytells how vitamin E can impede the advancement of AD.They suggests clinical trials should be done to investigate if vitamin E as a therapeutic option, they cited several research demonstrating their

antioxidant qualities.The study tells that vitamin E slow down the decline in cognitive function in AD patients and may help in shielding the neurons from oxidative damage . (Grundman, 2000)

Gillette-Guyonnet et al,(2000) Thestudy found thatweight loss in AD patients has been linked to AD progression and the metabolic process disruption. They examine the relation between cognitive decline and weight loss to highlight the importance of efficiency in nutritional management .The research tells that by maintaining the nutritional status may slow down the cognitive decline and enhance the quality of life (Gillette-Guyonnet, 2000)

Nourhashémi, F et al, (2000) This study examines a number of lifestyle variables, such as food, exercise, and cognitive engagement, that are protective against Alzheimer's disease. According to the study, upholding a healthy lifestyle that includes a Mediterranean diet and frequent exercise may lower the chance of developing Alzheimer's disease. However, because the available data is still developing, the authors urge additional longitudinal research to validate these protective associations. (Nourhashémi, 2000)

El-Baz et al,(2001) used deep learning techniques, specifically CNN to classify AD using MRI and FMRI data. The datasets were collected from the ADNI database. Their deep learning based model achieved an accuracy of 95.4% in distinguishing Alzheimer's patients from healthy controls. Comparatively, traditional ML algorithms like SVM showed lower accuracies around 85%. (El-Baz, 2001)

Kantarci et al, (2002) have compared different MRI methods, including hippocampal volumetry, MR spectroscopy and diffusion weighted imaging to distinguish AD, MCI and normal aging. Identified MCI with 79% accuracy and AD with 86% accuracy. Combining MR techniques improved sensitivity for detecting AD (Kantarci, 2002)

Jeong et al,(2004) used EEG dynamics to examine brain activity in Alzheimer's patients, focusing on EEG abnormalities. They used EEG data from patients with Alzheimer's , analysing linear and nonlinear changes in brain dynamics. The study found that alzheimer's patients had less complex brain wave activity, which was linked to neuronal loss and cortical disconnection. Showed EEG as a useful tool for early diagnosis with 80% accuracy (Jeong, 2004)

Adeli et al, (2005) used multimodal approaches such as imaging, EEG feature extraction and neural model to predict and classify AD. The dataset used involved neuroimaging data, anatomical images and EEG recordings. They applied various ML models like Ai neural networks for classification and feature extraction. They've reported that ANNs gave better classification accuracy compared to traditional methods such as discriminant analysis and clustering (Adeli, 2005)

Gerardin et al,(2009) developed a method to distinguish AD and MCI from healthy aging using hippocampal shape features. They used data from the ADNI and applied spherical harmonics for shape modeling SVM for classification.

Their method achieved 94% accuracy for AD vc controls and 83% for MCI vs controls outperforming traditional volumetry and showing comparable results to other recent svm methods (Gerardin, 2009)

Hu et al, (2010) used multimodal predictors, including neuropsychological assessments , structural MRI & cerebrospinal fluid biomarkers to differentiate AD from frontotemporal lobar degeneration in patients with primary progressive aphasia . combining neuropsychological testing with MRI atrophy patterns improved prediction accuracy, achieving 90% specificity for AD and 100 % sensitivity for predicting pathology (Hu, 2010)

Wolz et al, (2011) have used combination of MRI based features like hippocampal volume, cortical thickness, tensor based morphometry and manifold based learning to improve the early diagnosis of Alzheimer's disease. The data was collected from the ADNI. they used linear discriminant Analysis and support vector machines for classification, achieving 93% sensitivity and 85% specificity for Alzheimer's vs healthy controls. (Wolz, 2011)

Westman et al ,(2012) used data from ADNI to improve AD classification and predict MCI conversion. They combined model resonance imaging and cerebrospinal fluid measures. Their combined model achieved an accuracy of 91.8% for distinguishing AD from healthy controls, compared to 87.0% for MRI alone and 81.6% for CSF alone. This study shows that using both MRI and CSF together is more effective than using separately (Westman, 2012)

Young et al, (2013) have used multimodal data which includes brain imaging & biomarkers, to enhance prediction of Alzheimer's disease in patients with mild cognitive impairment. They've applied Gaussian Process classification to generate probabilistic predictions , which correlated very well with conversion to Alzheimer's. Their model achieved high accuracy in distinguishing between patients who would develop Alzheimer's and those who would remain stable (Young, 2013)

Gray et al, (2013) have used data from ADNI , including MRI, FDG-PET, CSF biomarker measures, and genetic data to improve AD classification . They applied Random Forest Classifiers and used pairwise similarity measures to combine features from different modalities. Their approach achieved an 89% accuracy for Alzhiemer's vs healthy controls and 75% accuracy for MCI vs Healthy controls. (Gray, 2013)

Shaffer et al,(2013) used data from the ADNI, which includes cerebrospinal fluid, MR imaging, and Fluorine 18 FDG PET biomarkers to predict Alzheimer's disease conversion. They applied independent component Analysis on these multi modal datasets to improve prediction models. This combination of model achieved a misclassification rate of 28.4%. (Shaffer, 2013)

Eskildsen et al,(2013) utilized data from the ADNI, which includes MRI-based cortical thickness measurements, to predict Alzheimer's disease in subjects with MCI. The study used surface based cortical thickness analysis to identify regions of the brain affected by atrophy in different stages. They achieved accuracy from 70% to 76%. (Eskildsen, 2013)

Ziming Zhang et al,(2014) studied how to predict AD using different types of data. They looked at MRI, cerebrospinal fluid and genetic data. They tested 3 methods to choose important features from this data. They used MRI , PET, CSF and genetic data to test them . Multiple kernel learning , high order graph matching based feature selection and sparse multimodal leaning . PET images showed most accurate for prediction and SNP data helped improving it and HGM-FS was best among the 3 methods. (Zhang, 2014)

Li et al,(2014) used data from the ADNI including MRI and PET images, to improve Alzheimer's prediction. Their 3D CNNs significantly surpasses traditional approaches like KNN and zero filled methods. These conventional techniques were less effective in estimating the missing PET data. The CNN achieved 88.68% accuracy in predicting AD vs NC, comparable to the 89.82% with real PET data. Combining MRI with the completed PET data further boosted classification accuracy (Li, 2014)

Suk et al ,(2014) used deep learning to improve the diagnosis of Alzheimer's and MCI by using both MRI and PET images which are taken from the ADNI database for testing. They used a Deep Boltzmann Machine to automatically find important patterns in small 3D patches of brain scans. Their model was more accurate compared to other methods, achieving a 95.35% accuracy for alzhiemer's vs healthy controls and 85.67% for MCI (Suk, 2014)

Ortiz et al,(2014) used data from the ADNI database , which included both PET and MRI scans.. They applied a method that combines these two types of brain images to better diagnose AD. their technique called Sparse Representation Classifiers, merges information from both MRI and PET images, helping to improve diagnosis accuracy. Their model achived 94% accuracy, which was better than using just one type of image (Ortiz, 2014)

Lebedev et al,(2014) studies how to detect and predict AD using random forest classifiers. They used data from the ADNI and the AddNeuroMed consortium, which included MRI scans from 185 AD patients and 225 healthy controls. Their best model achieved a sensitivity of 88.6% and specificity of 92.0% for distinguishing AD from healthy controls. They found that their random forest model was more accurate than a linear SVM classifier (Lebedev, 2014)

Liu et al,(2014) used data from the ADNI database , which included neuroimaging modalities such as MRI and PET for AD diagnosis. They implementd deep learning models, partucularyl stacked autoencoder, combined with a softmax logistic regression for classification. Their model achieved a multiclass classification of Alzheimer's stages with an accuracy of 91.4% for binary classification tasks and 53.79% for multiclass classification. (Liu,2014)

Mehdi Rahim et al,(2015) used spatial TV-l1 prior, PET-informed prior and ridge regression on the fluorodeoxyglucose positron emission tomography (FDG - PET) and resting -state functional magnetic resonance imaging (fMRI) data from the ADNI dataset to build a model integrating priors for the functional characterization of alzheimer's disease. The ridge classifier gives the highest accuracy of 88%. (Rahim, 2015)

Kerstin Ritter et al,(2015) utilized classification algorithms such as support vector machines (SVM) , random forest and a single classification tree on the clinical data ,genetics ,biospecimen ,neuropsychology ,PET and MRI data retrieved from ADNI database for the predictions based on incomplete biomarkers for Alzheimer's disease. Support vector machines (SVM) gave the highest accuracy of 73.44%. (Ritter, 2015)

Daniel Stamate et al,(2019) uses XGBoost , random forest, deep learning on the data including MRI ,PET, details on the subjects, clinical and cognitive data and measurements of AD pathological markers from ADNI database for diagnosing Alzheimer in blood. XGBoost has the highest accuracy of 87% (Stamate, 2019)

S.Naganandhini et al,(2019) uses decision tree classifier with hyper parameters tuning (DTC-HPT) model on the data including age ,gender,fMRI,PET ,MMSE,CDR from OASIS dataset for diagnosis of alzheimers disease.DTC-HPT gives the highest accuracy of 99.10%. (Naganandhini, 2019)

Taeho Jo et al,(2019) utilized stacked auto-encoder(SAE) , RNN and CNN on the MRI ,PET and FDG-PET data retrieved from the ADNI database for the prognostic and diagnostic classification using neuroimaging data for Alzheimer's disease. Stacked auto-encoders (SAE) gave the highest accuracy of 98.8%. (Jo, 2019)

Garam Lee et al,(2019) uses RNN, SVM, Gaussian process, Hierarchical ensemble, Deep neural networks combining demographic information, neuroimaging phenotypes measured by MRI, longitudinal cerebrospinal fluid(CSF) and cognitive performance biomarkers etc from the ADNI dataset for predicting Alzheimer disease .Deep neural networks had a highest accuracy of 82%. (Lee G. N., 2019)

Garam Lee et al,(2019) uses RNN networks which includes GRU and LSTM , they used cognitive performance ,cerebrospinal fluid, demographic data and MRI data from the ADNI dataset to build a deep learning based multimodal framework. When compared with other algorithms like LR,RF and SVM the proposed model had a highest accuracy of 95%. (Lee, 2019)

Xian-an Bi et al,(2020) used Clustered evolutionary random forest(CERF), Random forest, Random SVM cluster (RSVMC), Canonical correlation analysis(CCA),Discriminant correspondence analysis (DCA), t-test on the ADNI dataset using the functional magnetic resonance imaging (fMRI) and single nucleotide polymorphism (SNP) to analyze the data of alzheimer's disease.The highest accuracy achieved by clustered evolutionary random forest is 86%. (Bi, 2020)

Gopi Battineni et al,(2020) utilized naïve bayes,SVM, k-nearest neighbor and artificial neural networks(ANN) on the data including MRI , gender , age, CDR score, ASF, eTIV etc from the assessment conducted at the Alzheimer's Disease Research Center (ADRC) of Washington University for predicting Alzheimer's in older patients. . Hybrid or joint modelling with limited features had the highest accuracy rate of 98%. (Battineni G. C., 2020)

Juan Felipe Beltran et al,(2020) utilized classification and regression tree(CART),gradient boosting , random forest and SVM on data including MRI, PET, cerebral spinal fluid measurements, genetic tests , demographics and vital signs from the ADNI database for predicting Alzheimer's using ML. Random forest gives the highest accuracy of 75%. (Beltran, 2020)

Gloria Castellaazzi et al, (2020) used ANN, SVM and adaptive neuro-fuzzy inference system (ANFIS) on data including resting -state fMRI(rs-fMRI) and diffusion tensor imaging (DTI) from dataset from Neurological Institute IRCCS Mondino Foundation (Pavia, Italy) .ANFIS gives the highest accuracy of 83.50%. (Castellazzi, 2020)

Shaker El-Sappagh et al,(2021) used machine learning algorithms such as random forest , kNN , SVM ,decision tree and logistic regression to predict Alzheimer disease progression.They used ADNI database.

The model is a fusion of information of cognitive scores , comorbidities and medications for patient diagnosis .Additional informations such as gender , years of education ,demographics , age of the patient is considered .Random forest algorithm has the highest accuracy of 90.51%. (El-Sappagh S. S., 2021)

Zhen Pang et al,(2021) uses multi-task learning algorithm DT,RF,SVM along with XGBoost classification algorithm on the ADNI dataset using data such as PET and MRI images , cognitive testing ,genetics etc for the prediction of final stage of alzheimer's using these ML methods .Uses random forest algorithm on PET and MMSE data sets to achieve highest accuracy of 75%. (Pang, 2021)

Gopi Battineni et al,(2021) utilized algorithms such as random forest ,gaussian naïve bayes , SVM, logistic regression , gradient boosting and AdaBoost on the MRI data taken from the dataset from Open Access Series of Imaging Studies

(OASIS) for improving the detection of alzheimers using MRI. The gradient boosting algorithm resulted in the highest accuracy of 97.58% outperforming the other models . (Battineni, 2021)

Shaker El-Sappagh et al,(2021) used random forest,SVM,KNN,DT,Naïve Bayes algorithms on the ADNI dataset with 11 modalities like demographics, cognitive scores etc for making a detection and prediction model for alzheimer's.When compared with other algorithms random forest had the highest accuracy of 93.33%. (El-Sappagh S. A., 2021)

Juan E.Arco et al,(2021) utilizes Searchlight and Principal component analysis (PCA) on neuropsychological tests and MRI from the ADNI database for prediction of alzheimer's disease from data fusion on searchlight analysis.Searchlight gave the best result with the highest accuracy rate of 80.9%. (Arco, 2021)

Sergio Grueso et al, (2021) utilized SVM and CNN on the data including MRI and PET retrieved from the ADNI database for predicting the progression of MCI to Alzheimer using ML methods. When compared to SVM , CNN gives the highest accuracy of 78.5%. (Grueso, 2021)

Noemi Massetti et al, (2021) utilized random forest on the data including PET , MRI, neuropsychological test scores , peripheral biomarkers and cerebrospinal fluid (CSF) biomarkers from the ADNI and Alzheimer's Disease Metabolomics Consortium (ADMC) databases to predict the patients under Alzheimer's Disease spectrum .Random forest gives the highest accuracy of 86%. (Massetti, 2022)

Ali Haidar Syaifullah et al,(2021) utilized SVMst (based solely on brain structure) and SVMcog(based on brain structure and MMSE score) for data including features extracted from MRI retrieved from ADNI database for the diagnosis of AD using ML .SVMst gives the highest accuracy of 90.5% (Syaifullah, 2021)

Shangran Qui et al,(2022) utilized CNN ,CatBoost algorithms on clinical information, neuropsychological testing ,demographics ,neuroimaging , medical history and functional assessments on different datasets like ADNI , NACC,AIBL,LBDSU,FHS,NIFD ,OASIS ,and PPMI for assessment of dementia for Alzheimer's using deep learning multimodal .Here the fusion model gave mean of 55%, with high AUC and AP scores. (Qiu, 2022)

Jinhua Sheng et al,(2022) utilizes SVM, KNN ,ensemble and decision trees on MRI and SNP from the ADNI database for predicting classification of the alzheimer's using brain and genetic data . SVM gave the best results when compared to other algorithms with the highest accuracy of 98%. (Sheng, 2022)

Vasco Sa Diogo et al,(2022) utilized linear SVM,DT, RF, extremely randomized tree(ET) ,linear discriminant analysis (LDA) , LR,LR-SDG on the data including many features extracted from MRI , retrieved from ADNI and OASIS database for early diagnosis of AD using ML.The healthy controls (HC) vs AD classifier had the highest accuracy of 90.6%. (Diogo, 2022)

Shaker El-Sappagh et al,(2022) used decision trees , SVM, LSTM,random forest,KNN and logistic regression on data including neuroimaging data , cognitive scores , cerebrospinal fluid biomarkers, neuropsychological battery markers and demographics from the ADNI database to develop two stage DL model for AD detection and prediction of MCI. Long short term memory (LSTM) gives the highest accuracy of 93.87%. (El-Sappagh, 2022)

Duaa AlSaeed et al, (2022) used CNN , softmax, SVM and RF on the different features of MRI data from ADNI and Minimal Interval Resonance Imaging in alzheimer's disease (MIRIAD) databses for diagnosis of AD.CNN ResNet-50 along with softmax gives the highest accuracy of 99% on ADNI dataset . (AlSaeed, 2022)

Sobhana Jahan et al,(2023) used kNN , SVM, random forest , Multi-layer perceptron,logistic regression ,decision tree ,Naïve bayes,Gradient Boosting and Adaptive Boosting (AdaB) on the Open Access Series Of Imaging Studies (OASIS-3) dataset using clinical ,psychological and MRI data for prediction and management of alzheimer's.The random forest algorithm has the highest cross validation accuracy of 98.81%. (Jahan, 2023)

INFERENCES FROM THE LITERATURE REVIEW

The inferences below are extracted from 100 papers reviewed from 1912 to 2024 .The follow inferences include the year the literature is published along with their respective authors. It also includes the methods used , features taken into consideration for the study of the respective paper, the datasets they used and the accuracies they obtained by the methods

Year	Authors	Methods	Features	Dataset	Accuracy
1912	Chang T.S	a) Stochastic Gradient Descent	a) Cognitive tests b) Memory tests	a) 879 high-risk b) 355 low-risk individuals	Improved separation over traditional methods
1973	Crapper et al	a) Atomic absorption spectrophotometry b) Histological analysis	a) Brain aluminum distribution b) Neurofibrillary tangles	a) Human brain tissues from Alzheimer's patients b) Experimental neurofibrillary degeneration in animals	Not applicable
1980	Perl et al	a) X-ray spectrometry b) Electron microscopy	a) Aluminum accumulation b) Neurofibrillary tangle-bearing neurons	Brain tissues from Alzheimer's disease patients	Not applicable
1986	Yamamoto et al	a)Comparative ultrastructural analysis b) Electron microscopy	a) Structural comparison of neurofibrillary tangles b) Identification of filament composition	Brain tissue samples from Alzheimer's disease patients	Not applicable (qualitative study focused on structural observation).
1991	Pericak-Vance et al	a) Linkage analysis b) Genetic mapping	a) Investigation of familial Alzheimer’s disease b) Examination of chromosomal regions linked to the disease	Samples from families with a history of Alzheimer’s disease	Evidence for linkage to chromosome 19 with a high statistical significance (LOD score ≥ 3 indicates strong evidence of linkage).
1994	Tsai et al	a) Genetic linkage analysis b) Clinical assessments c) Genotype-phenotype correlation studies	a) Analysis of apolipoprotein E (ApoE) genotype b) Examination of family histories of Alzheimer’s disease (AD) c) Evaluation of cognitive assessments in participants	a) Samples from familial Alzheimer’s disease cases b) Control groups for comparison c) Genetic data from multiple	Association of ApoE ε4 allele with increased risk of developing Alzheimer’s disease (not typically

				family members	expressed as a percentage in linkage studies).
1994	Lehericy et al	a) Magnetic Resonance Imaging (MRI) b) Volume measurements of amygdalohippocampal regions c) Statistical analysis of brain volume changes	a) Early-stage Alzheimer disease detection b) Correlation between MR volume measurements and cognitive function c) Assessment of structural brain changes	a) MRI scans of participants diagnosed with early Alzheimer's disease b) Control group of healthy subjects for comparison c) Clinical assessments of cognitive function	Identified specific volumetric changes associated with early Alzheimer's disease (exact percentage not typically specified).
1994	Näslund et al	a) Mass spectrometry b)Immunoblotting c)Comparative analysis of amyloid peptide variants	a) Identification of different Aβ peptide variants b) Assessment of peptide abundance in Alzheimer's and normal aging c) Correlation of amyloid presence with disease progression	a) Brain samples from Alzheimer's disease patients b) Brain samples from age-matched controls c) Evaluation of peptide concentrations	Variability in Aβ peptide variants observed (exact percentage not typically specified).
1998	Perry et al	a)Experimental studies b) In vitro assays c) Oxidative stress measurements	a) Analysis of reactive oxygen species (ROS) b) Mechanisms of cellular damage in Alzheimer's disease c) Role of oxidative stress in neurodegeneration	a) Cellular models b) Brain tissue samples c) Control vs. Alzheimer's disease samples	Specific accuracy percentage not provided; focuses on correlational findings between ROS and cellular damage.
1998	Smith et al	a) Literature review b) Case studies c) Neuropathological analysis	a) Overview of Alzheimer disease pathology b) Discussion of genetic and environmental risk factors c) Examination of therapeutic approaches	a) Reviewed literature from various studies b) Clinical data from Alzheimer's patients c) Neurobiological research findings	Specific accuracy percentage not provided; emphasizes comprehensive literature synthesis and interpretations.
1998	Blacker et al	a) Review of genetic studies	a) Discussion of genetic markers associated with	a) Data from families with	Specific accuracy

		b) Analysis of familial Alzheimer's disease cases c) Examination of candidate genes	Alzheimer's b) Overview of risk factors and gene-environment interactions c) Future directions for genetic research	a history of Alzheimer disease b) Genetic information from various studies c) Case-control studies involving affected and unaffected individuals	percentage not provided; emphasizes associations between genetic factors and disease risk.
1999	McGeer et al	a) Review of existing literature b)Examination of inflammation in Alzheimer's disease c) Discussion of potential therapeutic interventions	a) Focus on brain inflammation as a mechanism in Alzheimer's disease b) Evaluation of inflammatory markers in the brain c) Implications for treatment strategies	a) Data from various studies on inflammation in Alzheimer's disease b) Clinical studies involving Alzheimer patients c) Review of experimental findings related to inflammation	Specific accuracy percentage not provided; the study discusses implications rather than presenting quantifiable accuracy data.
1999	Markesbery et al	a) Literature review b)Examination of oxidative stress in Alzheimer's disease c) Analysis of biochemical markers	a) Focus on oxidative stress as a contributing factor in Alzheimer's disease b) Discussion of antioxidant defense mechanisms c) Evaluation of cellular and molecular damage	a) Data from various studies on oxidative stress in Alzheimer's disease b) Clinical studies involving Alzheimer's patients c) Experimental findings related to oxidative stress	Specific accuracy percentage not provided; the study discusses the role of oxidative stress rather than presenting quantifiable accuracy data.
1999	Haroutunian V et al	a)Histopathological analysis b)Neurofibrillary tangle quantification c)Comparative study between nondemented and mild Alzheimer's patients	a) Examination of neurofibrillary tangles in elderly subjects b) Comparison between nondemented individuals and those with mild Alzheimer's disease c) Assessment of correlations with cognitive impairment	a) Brain tissue samples from nondemented elderly subjects b) Brain tissue samples from individuals with mild Alzheimer's	Specific accuracy percentage not provided; findings are based on qualitative assessment and correlation between

				disease c) Clinical records for cognitive assessment	tangles and cognitive status.
2000	Grundman et al	a) Review of clinical trials b) Analysis of Vitamin E supplementation c) Discussion of mechanisms and potential effects on Alzheimer's disease	a) Examination of Vitamin E as a neuroprotective agent b) Review of dosage and administration strategies c) Evaluation of clinical trial outcomes	a) Data from previous clinical trials on Vitamin E and Alzheimer's disease b) Patient demographics and health status information	Specific accuracy percentage not provided; conclusions are based on literature review and trial findings.
2000	Gillette-Guyonnet et al	a)Longitudinal study design b) Assessment of weight changes in Alzheimer's patients c) Analysis of dietary intake and nutritional status	a) Exploration of factors contributing to weight loss in Alzheimer's disease b) Examination of the relationship between weight loss and cognitive decline c) Assessment of nutritional interventions	a) Data from Alzheimer's disease patients in a clinical setting b) Nutritional assessments and weight measurements over time	Specific accuracy percentage not provided; findings based on statistical analysis of patient data and correlational assessments.
2000	Nourhashémi et al	a) Cross-sectional study design b) Assessment of protective factors against Alzheimer's disease c) Statistical analysis of dietary and lifestyle factors	a) Identification of lifestyle factors that may protect against Alzheimer's disease b) Evaluation of dietary patterns and their association with cognitive health c) Consideration of demographic variables in relation to Alzheimer's risk	a) Data collected from Alzheimer's patients and control groups b) Nutritional assessments and lifestyle questionnaires	Specific accuracy percentage not provided; results based on statistical correlations and risk assessments.
2001	El-Baz & Suri	a) CNN	a) MRI b) FMRI	a) ADNI	95.4% accuracy
2002	Kantarci et al.	a)Hippocampal Volumetry b) Spectroscopy	a) MRI	a) ADNI	a) MCI : 79% b) AD : 86%
2004	Jeong J	a) EEG b) Anaysis	a) EEG dynamics	–	80% accuracy
2005	Adeli et al.	a) Artificial Neural Network	a) EEG b) Anatomical Images	–	Betteraccuracythan discriminant analysis
2009	Gerardin et al.	a) SVM b) Spherical Harmonics	a) Hippocampal shape	a) ADNI	a) AD vs. Control: 94 % b) MCI : 83 %

2010	Hu et al	a) Neuro-psychological MRI	a) MRI b) Neuro Psychological test	a) Primary progressive aphasia Dataset	a) Specificity : 90% b) Sensitivity : 100%
2011	Wolz et al	a) SVM b) LDA	a) Hippocampal volume b) Cortical thickness	a) ADNI	a) Specificity : 93% b) Sensitivity : 85%
2012	Westman et al	a) MRI and CSF combined	a) MRI b) CSF	a) ADNI	Accuracy : 91.8%
2013	Young et al	a) Gaussian Process Classification	a) Brain Imaging b) Biomarkers	a) ADNI	High accuracy distinguishing MCI converters
2013	Gray et al	a) Random Forest	a) MRI b) FDG-PET c) CSF d) Genetics	a) ADNI	a) AD vs Control 89% b) MCI : 75%
2013	Shaffer et al	a) Independent Component Analysis	a) CSF b) MRI c) PET	a) ADNI	Misclassification 28.4%
2013	Eskildsen et al	a) Surface-based cortical thickness analysis	a) MRI cortical thickness	a) ADNI	Accuracy : 70-76%
2014	Lebedev et al	a) Random Forest	a) MRI	a) ADNI b)AddNeuro Med	a) Sensitivity :88.6% b) Specificity : 92%
2014	Zhang et al	a) Multi-kernel b) HGM-FS	a) MRI b) PET c) CSF d) SNPs	a) ADNI	a) High PET accuracy b) HGM-FS best method
2014	Suk et al	a) Deep Boltzmann Machine	a) MRI b) PET	a) ADNI	a)AD vs Control: 95.35 % b) MCI : 85.67%
2014	Ortiz et al	a) Sparse Representation Classifier	a) MRI b) PET	a) ADNI	Accuracy : 94%
2014	Li et al	a) 3D CNN	a) MRI b) PET	a) ADNI	88.68 %
2015	Mehdi Rahim et al	a) Ridge Regression b) Spatial TV-l1 prior c) PET-informed prior	a) FDG-PET b) resting-state fMRI(rs-fMRI)	ADNI	a) Ridge Regression-88% b) Spatial TV-l1 prior-around 80% c) PET-informed prior-around 80%

2015	Kerstin Ritter et al	a) SVM b) Random forest c) Classification tree	a) Clinical data b) Genetics c) Biospecimen d) Neuropsychology e) PET f) MRI	ADNI	a) SVM - 73.44% b) Random forest – 69.45% c) Classification tree – 65.15%
2019	Garam Lee et al	a) GRU b) SVM c) Gaussian process d) Hierarchical ensemble e) Deep neural networks	a) Demographic information b) Neuroimaging phenotypes measured by MRI c) Longitudinal cerebrospinal fluid(CSF) d) Cognitive performance biomarkers	ADNI	a) Deep neural networks-82% b) GRU-81% c) Hierarchical ensemble-79% d) SVM - 79% e) Gaussian process-68%
2019	Taeho Jo et al	a) Stacked auto-encoder (SAE) b) RNN or CNN	a) MRI b) PET c) FDG-PET	ADNI	a) Stacked auto-encoder (SAE) -98.8% b) RNN or CNN -96%
2019	Daniel Stamate et al	a) XGBoost b) Random forest c) Deep learning	a) MRI b) PET c) Details on the subjects d) Clinical data e) Cognitive data f) Measurements of AD pathological markers	ADNI	a) XGBoost - 87% b) Random Forest – 85% c) Deep Learning – 84%
2019	S.Naganandhini et al	Decision tree classifier with hyper parameters tuning (DTC-HPT)	a) Age b) Gender c) fMRI d) PET e) MMSE f) CDR	OASIS	DTC-HPT - 99.10%
2019	Garam Lee et al	a) RNN (GRU and LSTM) b) Logistic Regression c) Random Forest d) SVM	a) Cognitive performance b) Cerebrospinal fluid c) Demographic data d) MRI	ADNI	a) RNN (GRU and LSTM) – 95% b) Logistic Regression-93% c) SVM - 92% d) Random Forest -88%
2020	Xian-an Bi et al	a) Clustered evolutionary random forest(CERF) b) Random forest c) Random SVM cluster (RSVMC)	a) fMRI b) Single nucleotide polymorphisom (SNP)	ADNI	a) Pearson +CERF – 86% b) Pearson +Random forest – 82% c) Pearson + t-test-79% d) Discri

		d) Canonical correlation analysis(CCA) e) Discriminant correspondence analysis (DCA) f) t-test g) Pearsons correlation coefficient			minant correspondence analysis (DCA)+t-test– 75% e) Pearson+Random SVM cluster (RSVMC) – 72% f) Canonical correlation analysis(CCA)+ t-test -68%
2020	Gopi Battineni et al	a) Naïve bayes b) k-nearest neighbor c) ANN d) SVM	a) MRI b) Gender c) Age d) CDR score e) ASF f) eTIV	Alzheimer's Disease Research Center (ADRC) of Washington University	a) Hybrid – 98% b) SVM – 96.12% c) k-nearest neighbor – 95.92% d) Naïve bayes – 93.44% e) ANN – 83.56%
2020	Juan Felipe Beltran et al	a) Random forest b) Gradient boosting c) SVM d) Classification and regression tree (CART)	a) MRI b) PET c) Cerebral spinal fluid measurement d) Genetic tests e) Demographics f) Vital signs	ADNI	a) Random forest b) Gradient boosting c) SVM d) Classification and regression tree(CART)
2020	Gloria Castellaazzi et al	a) ANN b) SVM c) Adaptive neuro-fuzzy inference system	a) resting -state fMRI b) Diffusion tensor imaging	Neurological Institute IRCCS Mondino Foundation (Pavia, Italy)	a) ANFIS -83.50% b) SVM - 79.75%
2021	Shaker El-Sappagh et al	a) Random Forest b) SVM c) Decision Trees d) k-NN e) Logistic Regression	a) Cognitive scores b) Comorbidities c) Medications d) Patient statistics(age,gender etc.)	ADNI	a) Random forest - 90.51% b) Logistic Regression- 85.53% c) SVM- 83.68% d) Decision Trees- 77.32% e) k-NN- 75.69%
2021	Zhen Pang et al	a) XGBoost b) Decision trees c) Rando	a) PET b) MRI c) Cognitive tests d) Genetics e) MMSE	ADNI	a) Random forests – 75% b) SVM- 72% c) XGBo

		m forests d) SVM			ost -72% d) Decisi on trees -71%
2021	Gopi Battineni et al	a) Gradien t Boosting b) SVM c) Logistic Regression d) Rando m forests e) AdaBoo sting f) Naïve Bayes	MRI	OASIS	a) Gradie nt Boosting - 97.58% b) SVM - 96.77% c) Logisti c Regression- 96.77% d) Rando m forests - 96.77% e) AdaBo osting-96.77% f) Naïve Bayes-95.96%
2021	Shaker El-Sappagh et al	a) Rando m forests b) Decisio n trees c) SVM d) Naïve bayes e) k-NN	a) Cognitive scores b) Genetics c) Lab tests d) Medical history e) MRI f) Neurological exams g) Neuropsycholog ical battery h) PET i) Physical exams j) Symptoms k) Vital signs	ADNI	a) Rando m forests- 93.33% b) Decisi on trees – 92.38% c) SVM – 91.43% d) Naïve bayes – 89.52% e) k-NN – 64.76%
2021	Juan E.Arco et al	a) Searchli ght b) Principa l component analysis (PCA)	a) Neuropsycholog ical tests b) MRI	ADNI	a) Searchl ight – 80.9% b) Princip al component analysis (PCA) – 72.03%
2021	Sergio Grueso et al	a) CNN b) SVM	a) MRI b) PET	ADNI	a) CNN – 78.5% b) SVM – 75.4%
2021	Noemi Massetti et al	Random Forest	a) PET b) MRI c) Neuropsycholog ical test scores d) Peripheral biomarkers e) Cerebrospinal fluid (CSF) biomarkers	ADNI and Alzheimer's Disease Metabolomic s Consortium (ADMC) databases	Random Forest – 86%
2021	Ali Haidar Syaifullah et al	a) SVMst (based solely on brain structure) b) SVMco g(based on brain structure and MMSE score)	MRI	ADNI	a) SVMst -90.5% b) SVMc og – 85%
2022	Shangran Qui et al	a) CNN b) CatBoo st	a) Clinical information b) Neuropsycholog ical testing c) Demographics	a) AD NI b) NA CC c) AIB	Mean a) Fusion (CNN+CatBoos t) – 55% b) Catboo

			d) Neuroimaging e) Medical history f) Functional assessments	L d) LB DSU e) FH S f) NIF D g) OA SIS h) PP MI	st model -54%
2022	Jinhua Sheng et al	a) SVM b) KNN c) Ensemble d) Decision trees	a) MRI b) SNP	ADNI	a) SVM – 98% b) KNN – 96% c) Ensemble – 94% d) Decision trees – 92%
2022	Liu et al	a) Stacked Auto-encoder	a) MRI b) PET	a) ADNI	a) Binary: 91.4% b) Multi-class : 53.79%
2022	Vasco Sa Diogo et al	a) Matthew's correlation coefficient b) Linear SVM c) DT d) RF e) Extremely randomized tree(ET) f) Linear discriminant analysis (LDA) LR g) LR-SDG	MRI	a) ADNI b) OASIS	a) Healthy controls (HC) vs AD classifier – 90.6% b) Matthew's correlation coefficient – 0.811
2022	Shaker El-Sappagh et al	a) Decision trees b) SVM c) LSTM d) Random forest e) K-NN f) Logistic regression	a) Neuroimaging data b) Cognitive scores c) Cerebrospinal fluid d) Biomarkers e) Neuropsychological battery markers f) Demographics	ADNI	a) LSTM -93.87% b) Random forest-92.6% c) Decision tree – 91.39% d) Logistic regression – 92.28% e) SVM - 92.01% f) k-NN- 79.1%
2022	Duaa AlSaeed et al	a) CNN b) Softmax c) SVM d) Random Forest	MRI	ADNI and Minimal Interval Resonance Imaging in alzheimer's disease (MIRIAD)	a) Sofmax -99% b) SVM - 92% c) Random Forest - 85.7%

2023	Sobhana Jahan et al	a) k-NN b) SVM c) Random forest d) Multi-layer perceptron(MLP) e) Logistic regression f) Decision tree g) Naïve bayes h) Adaptive Boosting (AdaB) i) Gradient Boosting	a) Clinical data b) Psychological data c) MRI	OASIS	a) Random forests – 98.81% b) Gradient boosting – 95.65% c) Decision trees – 94.92% d) k-NN - 83.82% e) AdaB – 55.57% f) Naïve bayes – 40.24% g) Logistic regression – 31.28% h) MLP – 25.79% i) SVM – 25%

CONCLUSION

This review conducts an in-depth examination of the different machine learning techniques in the early diagnosis and detection of Alzheimer's disease (AD). The paper comments on the trajectory of Alzheimer's disease (AD), with no cure for this neurological condition, while highlighting the value of early detection in optimizing symptomatic management and preventing cognitive deterioration. Traditional diagnostic methods are not sensitive at preclinical stages, during which by the time symptoms arise, irreparable brain destruction has already occurred.

The scope for increased accuracy in diagnosis is revealed by the study, including models based on decision trees, random forests, support vector machines, and very recent deep learning methods such as convolutional neural networks. The range of models processed a wide variety of complex information such as biomarkers, MRI, PET, fMRI, and results of cognitive tests. For example, for a long time multimodality techniques have proved more accurate in accuracy rates for early diagnosis and stage classification of Alzheimer's disease compared with single-modality approaches. In fact, approaches can take into account genetic, imaging, and cognitive data sources.

Even though there is a very impressive advancement in this domain, diagnosis using machine learning is certainly not easy. There needs to be more research studies focusing on integrating large-scale, multi-modal datasets, enhancing the interpretability of algorithms, and overcoming the problem of generalizability across different demographic populations. However, the actual success of such models in clinical practice would depend a lot on clinical validation and ethical factors.

In short, with the potential that advances in machine learning have brought about, particularly in the area of multimodal approaches, for the early detection and treatment of the Alzheimer's disease, more research in this area may eventually lead to more customized treatment regimens and improved patient outcomes as well as greater understanding of the diseases' complexity.

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