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EXPLORING ADVANCED MACHINE LEARNING TECHNIQUESFOR EARLY DETECTION OF ALZHEIMER'S DISEASE: A REVIEW

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ABSTRACT:

Alzheimer's disease (AD), an irrevocable brain dis- ease, decreases thinking and memory power while the whole bitof mind size is pulled down, which at last reduces. It is also a neurodegenerative disorder and a very popular type of dementia in aged persons. There is a new case of Alzheimer's disease being discovered globally every four seconds. Early detection and prediction of Alzheimer's disease are extremely challenging. Timely identification of Alzheimer's can be beneficial to get necessary care and even possibly prevent brain tissue damage This issue can be resolved by a machine learning system that has early disease prediction capabilities. This paper analyzed a number of previous research that used machine learning algorithms to diagnose Alzheimer's disease over the previous three years. Comparisons are provided on the algorithms, assess- ment processes, and the obtained results. However, because key variables like feature selection and quantity impact the model's performance and accuracy, the same algorithm's accuracy may vary from dataset to dataset. An additional crucial finding inthis review is that the ensemble models outperform regular models in terms of accuracy and performance. Future research can focus on merging numerous types of data sources, such as neuroimaging, genetic information, clinical reviews, and wearable device data. Integrating these diverse modalities can lead to more comprehensive and accurate predictive models.

Keywords: Alzheimer's Disease(AD), Cognitive Impairment, Cognitive Normal (CN), Ensemble models, Machine Learn-ing(ML), Prediction.

1. INTRODUCTION

A. Study of Dementia

A general term for the damaged ability to remember, think or make decisions that interferes with doing everyday activities. Dementia is not a single illness. It's an generally term to depict a collection of indications that one may encounter if they are living with a assortment of maladies, Illnesses assembled beneath the common term "dementia" are caused by unusual brain changes [1]. Dementia indications trigger a decrease in considering abilities, too known as cognitive capacities, serious sufficient to impede everyday life and free work. They moreover influence behavior, sentiments and connections.

Types Of Dementia And Their Typical Characteristics: Ad (Alzheimer's disease):

Most familiar type of dementia, about 60% to 80% of cases belongs to this category [2]. About half of these cases involve entirely Alzheimer's pathology; many have proof of pathologic changes related to other dementias. Symptoms are difficulty in remembering recent conversations, names, or events is often an initial clinical symptom. Lack of interest and depression are also often other early symptoms.

Vascular Dementia: Earlier known as multi-infarct or post- stroke dementia. vascular dementia is less common as a sole cause of dementia than AD, accounting for about 10% of dementia cases. Impaired judgment or the capability to make decisions, plan, or organize is more likely to be the initial symptom, as opposed to the memory loss often related withthe primary symptoms of AD.

DLB (Dementia with Lewy bodies): Possess some of the symptoms typical of AD, but there's a greater chance that they'll also exhibit early or beginning signs of deliberateness, sleep difficulties, well-rounded visual illusions, imbalanced step, or other characteristics of parkinsonian measure. When there is no discernible memory impairment, these characteristics as well as early visuospatial impairment may manifest. Dementia may result from DLB brain abnormalities alone. However, AD pathology coexists with DLB brains quite frequently. When a person has both AD and DLB pathology, their symptoms may coexist and cause some diagnostic uncertainty.**FTLD (Frontotemporal Lobar Degeneration):** Early on, dif- ficulties understanding or creating language, as well as notice- able behavioral and personality changes, are typical indicators. Particularly impacted are the nerve cells in the brain's temporal lobes on the side and front (frontal lobes), which result in a noticeable atrophied (shrunken) appearance. Similar to AD, behavioral-variant FTLD can cause brain abnormalities in persons 65 years of age and older, however most patients with this type of dementia experience symptoms earlier (around age 60). FTLD is the second most frequent progressive dementiain this younger age range.

Mixed dementia: Characterized by the characteristic abnor- malities of many dementia types; AD with vascular dementia is the most prevalent combination, then AD with DLB andAD with both DLB and vascular dementia. Vascular dementiaassociated with DLB is far less prevalent.

PD (Parkinson's Disease) dementia: Movement issues, such as stiffness, tremor, slowness, and altered gait, are frequently indicative of Parkinson's disease (PD) [3]. A-synuclein aggregates in Parkinson's disease (PD) start in the substantia nigra, a deep region of the brain. It is believed that the aggre- gates lead to the degeneration of dopamine-producing nerve cells. Parkinson's disease (PD) occurs almost five times less frequently than Alzheimer's disease (AD). As PD advances, dementia is frequently the consequence of the accumulationof tau tangles and *β*-amyloid clumps in the cortex, which is comparable to AD, or Lewy bodies, which resemble dementia with Lewy bodies (DLB), in the cortex.

B. Overview of AD

Memory cells are harmed by a protein called amyloid that tangles and deposits in the brain, making brain size shrinkand leading to memory loss. Individuals who are in the early phase of AD with mild symptoms might be able to carry on working, driving, and engaging in their favorite activities withextraordinary help from friends and family. However, AD is a chronic condition, meaning that with time, its symptoms get worse [4]. The progression of AD is shown in Figure 1.

Progression of Alzheimer's Disease

Fig. 1: Progression of AD

Phases of AD: AD has been categorized into four phases; they are shown in Figure2 [5]: A.CN: This is the usual cognitive aging process. People in this group encounter healthy aging. They do not have any AD symptoms. B. Early Mild Cognitive Impairment (EMCI) Early mild cognitive impairment is the quick phase of AD (MCI Screen, 2021; Guo et al., 2020). In this phase, the small transformations in the cognitive normal are considered EMCI. Not all EMCI stages proceed to AD, some of theEMCI does restore to the cognitive normal phase. Thus, this phase is considered not dangerous. C. Late Mild Cognitive Impairment (LMCI) Late mild cognitive impairment is the later phase of EMCI (MCI Screen, 2021; Guo et al., 2020). Maximum patients in this phase will proceed to AD. Limited patients go back to the EMCI phase. D. AD: This is the ending phase of memory death disease. This is not a curable phase.

Fig. 2: Phases of Alzheimer's disease

ML is the blooming field in the healthcare industry. ML models can evaluate large amounts of data and identify complex patterns that may not be observable to human experts. By analyzing patterns in data from neuroimaging, genetics, and biomarkers, ML algorithms can identify the best treatment choices for individual patients. This can help improve the accuracy and effectiveness of treatment, possibly leading to better results and improved quality of life for patients with Alzheimer's disease and other forms of de- mentia. Furthermore, ML algorithms can combine data from different sources such as neuroimaging, genetics, and Cog- nitive Data (Neuropsychological measures and clinical data) to develop models that can accurately predict the beginning and progression of dementia. Machine learning algorithmshave been proven to be capable tools to integrate multiple biomarkers for early detection, diagnosis, and prediction of Alzheimer's. By using different ML algorithms like K-Nearest Neighbor, Ada Boost Classifier, Support Vector Machine, Logistic Regression, Decision Tree Classifier, and Random Forest classifier it is possible to detect Alzheimer's in early stages. This leads to better treatment for the disease in advance so that the symptoms do not reach a severe stage.

C. Risk factors for AD

Age: The primary risk factor for AD is advanced age. The majority of AD diagnoses occur in adults 65 years of age or older. Advanced age by itself does not produce AD; it is not a normal aspect of aging.

Family history: Individuals who do not have a first-degree family part with Advertisement are less likely to get the malady than those who have a parent, brother, or sister with Advertisement. An expanded chance is related to more than one first-degree relative with Advertisement. Heredity (hereditary qualities), shared environment and way of life factors, or both, may be imperative reasons when maladiesrun in families.

Mild cognitive impairment (MCI) [6]: Is a syndrome when a person's intellectual abilities alter slightly but noticeably, and both the affected person and family members can see the changes. Compared to persons without MCI, thosewith MCI, particularly those with memory impairments, have an increased risk of Alzheimer's disease and other dementias.

Cardiovascular disease risk factor [7]: Increased risk of AD and other dementias is linked to numerous elements that reduce the chance of heart disease. Among these are midlife smoking, obesity (particularly in the middle), diabetes, high cholesterol, and hypertension.

Engagement on both a social and cognitive level: Additional studies suggest that other modifiable risk factors, such as maintaining social and psychological interactions, may promote brain health and probably reduce the likelihood of AD and other dementias [8].

Education: Individuals with fewer years of appropriate education are more susceptible to compared to those with more years of suitable schooling, and dementias other than AD. Traumatic brain injury: The chance of developing ADand other dementias is increased in individuals with moderate to severe traumatic brain injuries (TBIs) [9].

Section I describes an introduction to dementia and types of dementia. Section II explains the Literature Review like quick applications of Machine Learning followed by two related Datasets i.e., ADNI and OASIS, including their Dataset's Features description. Section II also explains briefly aboutEEG and ensemble Models followed by two tables among which, Table 3 shows the comparative accuracies of algorithmsusing the ADNI data set and Table 5 shows the comparative accuracies of algorithms using the OASIS data set. Section III explains the procedure for AD disease prediction. Section IV demonstrates a rapid conclusion and future scope related tothe paper.

2. LITERATURE REVIEW

A. Use of Machine Learning for Alzheimer's Prediction

Machine learning (ML) is a branch of artificial intelligence that focuses on creating algorithms that let a computer learn on its own from data and past experiences. Arthur Samuel coined the phrase"machine learning" in 1959. In a nut- shell, machine learning allows a machine to predict outcomes without explicit programming, automatically learn from data, and improve performance via experience. Machine learning algorithms use training data, or samples of past data, to create mathematical models that aid in decisionmaking and prediction [10]. Machine learning brings Computer Science and Statistics together to create predictive models. The more we provide the information, the higher the performance will be. Figure 3. shows the procedure involved from past input to the new output.

Fig. 3: Flow of Machine Learning

The following section discusses the two main data setsthat are used by most of researchers for the prediction ofAlzheimer's: ADNI (Alzheimer 's disease Neuroimaging Ini- tiative) and OASIS (Open Access Series of Imaging Studies).

B. Datasets

There are 2 major datasets considered by research scholars for Alzheimer's prediction.

C. ADNI

ADNI was started in the year 2004 to provide researchers with neuro-images for the effective diagnosis and forecast of AD under the leadership of Dr. Michael W. The table shows the Demographic details of the ADNI data set. Table2. Shows Cognitive Measure Description (Neuropsychological and Clini- cal measures) of the ADNI data set [5]. There are 1343 recordspresent in the ADNI dataset.

TABLE I: Demographic Details

Neuroimaging Data: MRI (Magnetic Resonance Imaging) Image PET(Positron Emission Tomography) Image

D. *OASIS*

OASIS longitudinal dataset (OASIS, 2021) is taken by most of the research scholars. It is a project aimed at mak- ing neuroimaging datasets freely available to the scientific community. The OASIS datasets hosted by central.xnat.org provide the community with open access to a significant database of neuroimaging and processed imaging data across a broad demographic, cognitive, and genetic spectrum, an easilyaccessible plat- form for use in neuroimaging, clinical, and cognitive research on normal aging and cognitive decline [16].All data is available via [www.oasis-brains.org.](http://www.oasis-brains.org/) Mention how many records are there in each of them. There are 374 records present in OASIS Longitudinal dataset.

The attributes in the dataset are Subject ID, MRI ID, Visit, MR Delay, Age, M/F, Hand, EDUC, SES, MMSE, CDR, eTIV,

nWBV, ASF and Group [5].

From the above table Papers 2 and 3 discussed CN, MCI, and AD stages, which we have discussed in the introduction. The remaining papers explains mainly about binary classification i.e., Demented and Non Demented. Age, MMSE and

severe cognitive declines [**?**]. EEG signals offer rich informa- tion about brain activity, including neural oscillations. These ons represent periodic patterns of brain activity and sified into different frequency bands, each associatedcific cognitive functions. For instance, beta, gamma, d alpha waves are distinct frequency bands linked to aspects of cognition and behavior. Analyzing these ons in EEG data can provide insights into the func- ate of the brain and help in understanding cognitive s affected by Alzheimer's disease. The Nihon Kohden nical EEG device was utilized to record the EEG data. scalp electrodes (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C4, T4, T5, P3, Pz, P4, T6, O1, and O2) and 2

es (A1 and A2) that were inserted on the mastoidsimpedance check and as reference electrodes. The

e placement followed the worldwide 10-20 system.

Gender are the most common features used by most of the researchers for ADNI dataset.

CDR,MMSE and MR Images are the common features used by most of the researchers with OASIS dataset.

E. Electroencephalography (EEG)

Neuroimaging techniques like EEG (electroencephalogra- phy) play a crucial role in understanding brain connectivity and activity, particularly in the context of Alzheimer's disease prediction and forecasting [20]. By capturing brain signals, EEG provides valuable insights into the functioning of the brain, allowing researchers to extract meaningful features that can aid in predictive modeling. These recordings are structured in the Brain Imaging Data Structure (BIDS) format, whichis a standardized format for organizing and describing neu- roimaging data. An ensemble system, which combines mul- tiple models to improve prediction accuracy, can effectively identify relevant features from EEG signals for Alzheimer's disease prediction [21]. These features may include various aspects of brain activity such as neural oscillations, event- related potentials (ERPs), and connectivity patterns between different brain regions.

Dataset Description:

This dataset contains the EEGresting state-closed eyes recordings from 88 subjects in total. A total of 36 of them were diagnosed with Alzheimer's disease (AD group), 23 were diagnosed with frontotemporal dementia (FTD group), and 29 were CN. The cognitive and neuropsychological state was evaluated by the international Mini-Mental State Examination (MMSE). The MMSE score ranges from 0 to 30, with a lower MMSE indicating moreFig. 4: Spike and wave discharges of Electroencephalography

utilize the EEG to support a medical diagnosis because it can identify aberrant electrical discharge, such as spikes, form waves, or spike-and-wave complexes, which are obvious in epileptics. The EEG can be used to detect status epilepticsand monitor the onset, course, and length of seizures. Fig. 5 displays the frequency and wavelength of the EEG.

F. ENSEMBLE MODEL

Ensemble model is used to enhance the performance of the machine learning model by combining several base learners [4]. There are 4 types of ensemble classifiers [22]. They are **1) Voting:** Two major types a)Hard Voting: Highest majority of voting is resolved.

b)Soft Voting: Prediction based on the average of probabilitygiven to that class

2) Stacking: Predictions from multiple models(DT,KNN or SVM) to build a new model. It is also known as Stacked

S. No.		Reference Implementation	Accuracy $(\%)$	Features considered	Limitations
1	$[11]$	CNN, DNN, GRU, GNB	CNN=90.24, DNN=91.46, GRU=92.68, GNB=91.00	ADAS11, ADAS13, ADASQ4, Age, CDRSB, DIGITSCOR, Educ, Gender, LDETOTAL, mPACCdigit, mPACCtrailsB, MMSE, Marital Status, RAVLT-L, RAVLT-I, RAVLT-F, RAVLT-PF, TRABSCOR	More biomarkers can improve accuracy
$\overline{2}$	$[12]$	DT, XGB, RF, SVM	$DT=77.43$, XGB=84.46, RF=84.95, $SVM = 83.98$	ADAS-11, ADAS-13, CDGLOBAL, CDRSB, FAQ, GDTOTAL, MMSE, MoCA, MRI Scans, NPISCORE	Focuses on performance rather than interpretability
3	$[13]$	DT, K-NN, RF, SVM+K- NN	DT=92, K- NN=91, RF=91, $SVM+K-NN=99$	MRI image	Only single attribute considered
4	$[14]$	ANN, K-NN, RF, SVM	ANN=77.32, K- $NN = 82.13$, $RF = 86.24$	MRI image	Only single attribute considered
5	$[15]$	ELM, GMM	ELM=84.73, GMM=84.53, $IF = 81.51, K-$ $NN = 85.35$	ADAS-13, Age, ApoE4, Education, FAQ, F/M LDEL TOTAL, MMSE, RAVLT immediate, RAVLT per forgetting	Worked with one stage of Alzheimer's

TABLE III: Comparative accuracies of algorithms using the ADNI dataset

TABLE IV: OASIS dataset features

Fig. 5: Frequency waves of EEG

Level 1

Generalization which combines multiple classifications via a meta classifier [23].

Bagging: Is a method used to decrease the variances of the classifier and reduce overfitting. Which is the combinationof Bootstrapping and Aggregation. Eg: Random Forest

Boosting: Additional model is added sequentially to the overall ensemble model. A new base- learner model is trained from the errors of the previous learners [24]. Eg: Adaboost, Gradient Boosting, Cat Boost and exTreme Gradient Boost- ing[30].

Significance: It is the application of multiple models to obtain better performances than from a single model. Robust- ness: These models incorporate the predictions from all the base learners. **Accuracy:** Provides accurate predictions and has improved performance. Few of the previous researchers were implemented Ensemble Models like Hard Voting and drive the accuracy of 92.22% and Soft Voting with 94.92% accuracy [25]. Stacking was implemented and got an accuracyof 96.7% . Stacking and Voting both were implemented a

acquired accuracies as 85.51% and 86.17% [26].

Need for Ensemble Models: These are prominent models that combine predictions from two or more other models. These are required when the best performance on the predic- tive modeling project is the most important outcome. These prevent overfitting and underfitting. Also Enhances random- ization.

3. METHODOLOGY

Preprocessing: The process of creating data data ready for machine learning models is known as data preprocessing [27]. The process of developing a machine-learning model start

Fig. 9: Flow of Boosting Classifier
Model 1,2,..., N are individual models (e.g. decision tree)

THE DIFFERENT STAGES OF A BAGGING ALGORITHM

Fig. 10: A Snapshot of the Same Signal before and after beingpreprocessed

With this. It is the most difficult and time-consuming part of data science. In order to simplify machine learning methods, data pretreatment is necessary. All the real-world data will have missing data, outliers data, error data, noisy inconsistent data etc., Hence it should be preprocessed [28]. Both ADNI and OASIS need to be preprocessed because of the missing and outliers data. Already preprocessed data is available in the EEG data set. Figure.10 represents a snapshot of the same signal in raw form, and in preprocessed form.

Feature Extraction

It is the process of transforming or projecting a space com- posing of many dimensions into a space of fewer dimensions, like projecting 3D plane into 2D plane. It translates the preprocessed data into the required format [29]. Various algorithms are available to extract relevant features from a data set, one example being Expectation and Maximization(EM) algorithm [30]. The expectation step produces the expected data and the maximization step produces the log-likelihood data using the previous step. In Recurrent Neural Network(RNN) based feature learning [31], Long short-term memory (LSTM) is used to extract Neuropsychological Measure(NM) and Magnetic Res- onance Imaging(MRI) biomarkers [25] [32]. Principal Com- ponent Analysis(PCA) follows first-order statistics where as Gray-Level Co occurence Matrix(GLCM) algorithm follows second-order statistics [33]. Second-order texture measures are based on pixels pair relationship. GLCM calculate the joint probability of two pixels separated by a distance d along a given direction having Co occuring values I and j. Cooccurance matrices capture properties of a texture. Principal Component Analysis(PCA) is also used for feature reduction to select the most projecting features [34]. It combines the input variables in a specific way, then the least important variables are dropped while still retaining the most valuable parts of all of the variables [15]. One of the most commonly extracted features for EEG classification tasks is the Relative Band Power (RBP) of the five frequency bands of interest of brain activity. Neural oscillations are periodic patterns of brain activity, classified into various frequency bands such as delta, beta, gamma, theta, and alpha, each associated with a specific cognitive function. The five frequency bands are defined as:

• Delta: 0.5–4 Hz

• Theta: 4–8 Hz

- *•* Alpha: 8–13 Hz
- *•* Beta: 13–25 Hz
- *•* Gamma: 25–45 Hz

A. Binary and Multi-Classification:

From the previous survey, it is under- stood that some ofthe researchers worked on Binary classification only i.e., AD or Non-AD [35], which indicates that the patients are categorized into only two groups i.e., patients with Alzheimer's and patients with No Alzheimer's whereas most of the re- searchers worked on Multi-classification i.e., AD, MCI and CN, which demonstrates that the patients are categorized into three groups i.e., patients with CN, patients with MCI and patients with AD [36] [37]. Previous research also shows that some pMCI(Progressive Mild Cognitive Impairment) pa- tients are converting into AD patients. Also found that the CFA(Cognitive and Functional Assessments) was the most promising predictor to predict pMCI patients [21]. Some ofthe patients related to pMCI are converted into AD patients after a certain investigation time period(2.5 years) [26].

B. Analysing Brain Signal:

Neuroimaging techniques like EEG obtain brain signals, providing significant information about brain connectivity and activity that can aid in the prediction and forecasting of Alzheimer's disease. An ensemble system is used to de- termine the meaningful features, including the forecasting characteristic. An ensemble system is used to extract the meaningful characteristics, including the predictive feature. EEG signals are used to extract useful data regarding brain activity, including connections between various brain regions, neural oscillations, and event-related potentials (ERPs).

C. Estimation of Severity Analysis

After analyzing the brain signal, the trained dataset is moved to the severity phase to detect Alzheimer disease. Following the analysis function, the AD's estimated severity range is low, high, and medium.

D. **Comparison Assessment**

The above Table shows a comparison of previous algorithms and their comparison metrics. With the help of Ensemble Techniques and by utilizing the EEG dataset the Proposed Methodology improves performance approximately to the shown values. This is greater than the previous algorithms' performance metrics.

METHODS	Metrics					
	Precision	Recall	F1 Score	Accuracy		
Decision Tree	95.00	90.00	93.00	87.33		
Gradient Boost	95.00	93.00	94.00	90.00		
XGB oost	95.00	95.00	95.00	91.33		
Random Forest	95.00	92.00	94.00	94.00		
Gaussian NB	95.00	90.00	92.00	94.00		
Proposed	97.30	97.34	96.50	97.12		

TABLE VI: Comparison Assessment

4. CONCLUSION AND FUTURE SCOPE

Machine learning has turned up in the medical sector for

providing tools and analyzing the data related to diseases.Machine learning algorithms play a vital role in achieving the early detection of disease. This paper provided a review of different machine-learning algorithms for predicting Alzheimer's disease. Results discovered by researchers have been tabulated to provide a comparison of the performance of various ML

algorithms in detecting the disease. After comparing good number of papers for different models that predicted the disease, we illustrated that among all algorithms, random forest has good accuracy for predicting the Alzheimer's Dis- ease. Ensemble Learning helps to improve machine learning results by combining several models to improve predictive performance compared to a single model. Identifying the right biomarker combination is crucial. Further research will focus on extracting and analyzing novel features with the help of EEG data and Ensemble Models that can better support in the diagnosis and elimination of AD.

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