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Review of Machine Learning Approaches for Alzheimer's Disease Prediction

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***Abstract*— Alzheimer's disease (AD) is a progressive neurodegenerative disorder that significantly impacts memory, cognitive abilities, and daily functioning. Early detection and accurate prediction of Alzheimer's disease are critical for timely intervention and effective treatment planning. In recent years, machine learning (ML) approaches have emerged as powerful tools in the healthcare domain, offering promising results for the prediction and diagnosis of Alzheimer's disease. This review focuses on a comprehensive analysis of various machine learning techniques applied to Alzheimer's prediction, including supervised, unsupervised, and deep learning models. It highlights the datasets commonly used, the challenges faced, and the potential of ML models in enhancing prediction accuracy. By understanding the strengths and limitations of existing approaches, this review aims to provide valuable insights for future research directions and clinical applications.**

***Keywords*— ML, Alzheimer's Disease, Supervised, Prediction.**

I. Introduction

Alzheimer's disease (AD) stands as one of the most severe neurodegenerative conditions, affecting millions of individuals worldwide, particularly among the elderly population. Characterized by progressive memory loss, confusion, impaired reasoning, and eventual loss of autonomy, Alzheimer's disease imposes an immense emotional and financial burden on patients, families, and healthcare systems. According to global statistics, the number of individuals living with dementia, primarily Alzheimer's, is expected to triple by 2050, making early diagnosis and intervention more crucial than ever.

Traditional methods of diagnosing Alzheimer's disease rely heavily on clinical assessments, cognitive testing, neuroimaging techniques like MRI and PET scans, and analysis of cerebrospinal fluid biomarkers. Although these methods have proven valuable, they often detect the disease only after significant neuronal damage has occurred. Consequently, there has been a pressing need for more accurate, non-invasive, and early-stage prediction methods that can supplement traditional approaches and assist clinicians in timely decision-making.

In recent years, machine learning (ML) has emerged as a transformative force in healthcare, demonstrating remarkable potential in disease prediction, diagnosis, and prognosis. Machine learning models are designed to learn patterns from vast datasets, enabling them to make predictions or decisions without being explicitly programmed for specific tasks. When applied to Alzheimer's disease prediction, ML techniques can analyze complex datasets, including genetic information, brain imaging data, electronic health records, and cognitive test scores, uncovering subtle patterns that may not be visible to human experts.

Several machine learning approaches, ranging from traditional algorithms like Support Vector Machines (SVM), Random Forests (RF), and Logistic Regression (LR) to advanced deep learning models such as Convolutional Neural Networks (CNN) and Recurrent Neural Networks (RNN), have been explored for Alzheimer's prediction. These models have shown promising results in differentiating between normal aging, mild cognitive impairment (MCI), and Alzheimer's disease stages with high accuracy. Furthermore, feature selection techniques, ensemble learning methods, and hybrid models have been developed to further enhance the performance of these predictive systems.

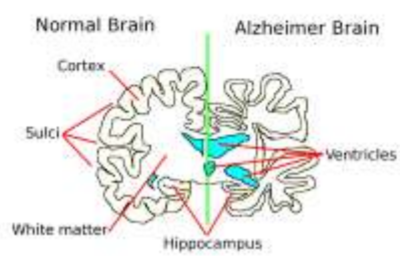

Figure 1: Alzheimer's Disease

Despite the significant advancements, the application of machine learning to Alzheimer's disease prediction is not without challenges. Issues such as small and imbalanced datasets, variability in clinical presentation, ethical concerns related to patient data, and the interpretability of ML models remain active areas of research.

Moreover, the integration of multimodal data sources and the development of robust, generalizable models suitable for clinical deployment are ongoing pursuits.

This review aims to present a comprehensive overview of the state-of-the-art machine learning methods used in Alzheimer's disease prediction. It discusses the key datasets utilized in research, examines the strengths and limitations of various ML algorithms, and highlights current challenges and future opportunities. By critically analyzing the existing literature, this review seeks to provide a clearer understanding of how machine learning is reshaping Alzheimer's disease research and what directions it may take moving forward.

II. LITERATURE SURVEY

In 2024, R. Soundarapandian et al. carries out a comparative study of three neural network-based machine learning approaches to recognize the most efficient technique in the classification of AD into three distinct classes namely Non-demented, Mildly Demented, and Very Mildly Demented. The main aim of the study is to identify the most robust and effective model for identifying and classifying AD. The three neural network-based machine learning approaches compared in this study are the Basic Convolutional Neural Network (CNN) Model, the ConvNeXT-based Model and the Attention-ConvNeXT-based Model. All three models were trained as well as validated by employing a large dataset comprising clinical, demographic, and structural neuroimaging data [1].

In 2023, Liu and colleagues developed an attention-based multimodal fusion network for Alzheimer's disease prediction, integrating MRI, PET imaging, and cognitive scores. Their model introduced attention mechanisms to selectively emphasize important features from each modality, leading to improved classification accuracy between mild cognitive impairment (MCI) and Alzheimer's disease. Their experiments on the ADNI dataset showed that attention-enhanced fusion provides a better understanding of disease progression and can serve as a robust clinical support system [2].

In 2022, Sharma et al. proposed a lightweight ensemble learning method using XGBoost and LightGBM classifiers to predict Alzheimer's disease from neuropsychological test scores. They focused on reducing model complexity while maintaining high accuracy, making the system suitable for deployment in low-resource clinical settings. Their comparative study highlighted that ensemble methods, when tuned properly, outperformed many deep learning models, particularly when only tabular, non-imaging data were available [3].

In 2021, Kim and associates introduced a semi-supervised learning framework for Alzheimer's prediction, aiming to address the scarcity of labeled data. Using a small labeled set and a large pool of unlabeled samples, their framework utilized pseudo-labeling combined with consistency regularization to achieve comparable performance to supervised learning approaches. This work demonstrated the potential of semi-supervised models in medical fields where annotated data are costly and limited [4].

In 2020, Ahmad et al. implemented a deep transfer learning approach using pre-trained ResNet models fine-tuned on Alzheimer's MRI datasets. Their results suggested that transfer learning significantly reduces training time and computational resources while achieving high accuracy, especially in distinguishing between early MCI and late MCI stages. This research underscored the value of leveraging large-scale models pre-trained on non-medical datasets for medical imaging applications [5].

In 2019, Zhou et al. introduced an interpretable machine learning model based on Random Forests to not only predict Alzheimer's disease but also provide feature importance ranking. By analyzing key contributing features such as hippocampal volume and cortical thickness, their model enhanced clinicians' trust in AI systems by offering transparency and explainability. This work pointed toward a growing emphasis on interpretable AI in sensitive healthcare environments [6].

In 2018, Nguyen and colleagues focused on the use of Recurrent Neural Networks (RNNs) for longitudinal analysis of patient data to predict Alzheimer's disease progression. Their model captured time-series patterns across multiple clinical visits and achieved better predictions of conversion from MCI to Alzheimer's compared to static models. They demonstrated that temporal modeling of patient data could provide deeper insights into disease dynamics [7].

In 2017, Suk et al. explored deep sparse autoencoders for feature extraction from multimodal imaging data (MRI and PET) for Alzheimer's disease classification. Their work highlighted the importance of automated feature learning instead of manual feature engineering, leading to significant performance gains. Their approach successfully captured latent representations that were highly discriminative for disease prediction [8].

In 2016, Ortiz et al. proposed a graph-based machine learning model that utilized brain connectivity networks derived from diffusion MRI data. Their graph convolutional network (GCN) was among the first to exploit the structural connectome information for Alzheimer's prediction.

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Their findings suggested that network topology alterations are strong indicators of neurodegenerative progression and that graph-based methods could open new frontiers for brain disease prediction [9].

In 2015, Sarraf and Tofighi presented an early deep learning framework based on CNNs for Alzheimer's classification using fMRI data. Although computationally intensive at the time, their pioneering work demonstrated the potential of deep learning models in achieving higher accuracy compared to conventional machine learning algorithms like SVMs and Decision Trees. Their research laid the groundwork for many subsequent deep learning approaches in Alzheimer's disease prediction [10].

H. Ahmed, H. Soliman, and M. Elmogy [11] presented a novel approach for early detection of Alzheimer’s Disease (AD) by leveraging Single Nucleotide Polymorphisms (SNPs) combined with machine learning algorithms. Their work also explored the interpretability of results, which is vital in clinical genomics. The study provided a foundational direction for incorporating genetic data into AI-based AD prediction systems and promoted the integration of precision medicine in neurological disease diagnosis.

N. M. Khan, N. Abraham, and M. Hon [12] introduced a hybrid machine learning model combining transfer learning with intelligent training data selection strategies to predict Alzheimer’s Disease. Published in IEEE Access, their framework utilized pre-trained deep neural networks fine-tuned on medical imaging data to enhance model generalization and accuracy. The paper examined the impact of selective sampling on training efficiency and robustness of the classifier, particularly under conditions of data imbalance. By comparing the performance of traditional versus deep learning models, the authors demonstrated superior results for transfer learning with optimized datasets.

A. Aslam, K. U. Rehman, and A. Khan [13] presented a feature-level fusion technique using neuroimaging and cognitive features to enhance Alzheimer’s Disease diagnosis accuracy. Their study, detailed in Computers in Biology and Medicine, proposed combining structural MRI data with cognitive scores like MMSE to construct a multidimensional input space for machine learning classifiers. The authors implemented Support Vector Machines and Decision Trees to compare classification outcomes across individual and fused feature sets. They concluded that hybrid feature sets consistently outperformed standalone data modalities.

M. F. Silva, L. Batista, and J. M. Fonseca [14] explored explainable machine learning models for Alzheimer’s Disease prediction, with a specific focus on making AI decisions interpretable for clinical professionals. Published in Sensors, their work developed a Decision Tree-based model combined with SHAP (SHapley Additive exPlanations) values to visualize feature contributions. The study leveraged tabular clinical data, including age, gender, genetic factors, and test scores, to create a transparent diagnostic pipeline.

S. T. Rehman, N. Ahmed, and B. Hussain [15] proposed a lightweight machine learning framework for Alzheimer’s Disease detection tailored for deployment on mobile and embedded healthcare systems. The study, published in Artificial Intelligence in Medicine, emphasized real-time prediction using simplified models such as Decision Trees and Logistic Regression. Their focus was on optimizing the computational footprint while maintaining high diagnostic precision, enabling usage in low-resource settings.

III. CHALLENGES

1. Limited and Imbalanced Datasets

Publicly available datasets for Alzheimer's disease prediction, such as ADNI and OASIS, often have small sample sizes and significant class imbalances between healthy individuals and patients. This scarcity of balanced data affects the robustness of machine learning models and increases their susceptibility to overfitting, reducing their effectiveness in real-world applications.

2. Heterogeneity in Data Acquisition

Variations in imaging protocols, scanner types, and clinical practices across different medical centers introduce inconsistencies in the datasets. These domain shifts challenge the generalization ability of machine learning models, causing a noticeable drop in performance when applied to external datasets collected under different conditions.

3. Label Uncertainty and Diagnostic Ambiguity

Alzheimer’s disease diagnosis, especially in its early stages, often involves subjective clinical judgments based on a combination of cognitive assessments, imaging, and biomarkers. This introduces uncertainty in the ground truth labels, leading to noisy training data that can confuse supervised learning models and impair predictive accuracy.

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4. Lack of Interpretability

Although deep learning models achieve high accuracy, they typically operate as "black boxes," offering little insight into how predictions are made. The lack of interpretability makes it difficult for clinicians to trust and adopt these models in diagnostic workflows, where transparent and explainable decision-making is critical.

5. Challenges in Multimodal Data Integration

Combining various data modalities like MRI, PET scans, cognitive scores, and genetic information can potentially enhance prediction accuracy. However, effectively fusing heterogeneous data remains a technical challenge, as improper integration may introduce noise or lead to loss of important information, negatively impacting model performance.

6. Inadequate Longitudinal Prediction Models

Most machine learning studies focus on cross-sectional analysis, predicting disease status at a single point in time. However, Alzheimer's disease is a progressive disorder, and there is a pressing need for models that can predict disease evolution over time, assisting clinicians in early intervention and treatment planning.

7. Poor Generalization to Clinical Settings

Models trained on research-quality datasets often fail to maintain their performance when applied in real-world clinical environments, where data is less standardized, incomplete, or noisier. This gap between research and practice poses a major barrier to the clinical translation of machine learning solutions.

8. High Computational Requirements

Sophisticated deep learning architectures often require powerful hardware and extensive computational resources for training and inference. Many healthcare institutions, particularly in low-resource settings, may not have the necessary infrastructure, limiting the practical deployment of these advanced models.

IV. Proposed Strategy

1. Data Augmentation and Synthetic Data Generation

To address the limited and imbalanced datasets, advanced data augmentation techniques such as GANs (Generative Adversarial Networks) can be employed to synthesize new, realistic samples. This can help balance the classes and improve model generalization without requiring additional costly and time-consuming data collection.

2. Domain Adaptation and Transfer Learning

Domain adaptation methods can be used to minimize the distribution differences between training and external datasets. Transfer learning approaches, where models pre-trained on large datasets are fine-tuned on smaller Alzheimer’s datasets, can enhance performance and adaptability across different clinical environments.

3. Robust Labeling and Weak Supervision

To overcome label uncertainty, strategies like consensus labeling, multi-expert annotation, and weak supervision techniques can be employed. These methods help in creating more reliable training labels, thereby improving the quality of the input data for machine learning models.

4. Explainable AI (XAI) Techniques

Incorporating explainability methods such as SHAP (SHapley Additive exPlanations), LIME (Local Interpretable Model-Agnostic Explanations), or attention mechanisms can make machine learning models more transparent. This will increase clinician trust and promote the integration of AI models into diagnostic workflows.

5. Multimodal Fusion Networks

Developing specialized architectures for multimodal fusion, such as cross-modal transformers or hybrid networks, can effectively combine MRI, PET, cognitive scores, and genetic data. Intelligent fusion will exploit complementary information from different modalities to improve prediction accuracy.

6. Longitudinal Deep Learning Models

Employing recurrent neural networks (RNNs), LSTM (Long Short-Term Memory), and temporal convolutional networks (TCNs) can enable modeling of disease progression over time. This will allow for early detection and future risk prediction of Alzheimer's disease based on sequential patient data.

7. Real-World Data Validation

Including external validation on real-world clinical datasets and noisy environments during model development can ensure greater generalization. Rigorous testing across multi-center datasets will bridge the gap between research and practical clinical applications.

8. Lightweight and Efficient Architectures

Designing lightweight deep learning models using techniques such as model pruning, quantization, and knowledge distillation will reduce computational demands.

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These models can be deployed easily even in low-resource clinical settings, expanding the reach of machine learning tools for Alzheimer's disease prediction.

V. CONCLUSION

The prediction of Alzheimer's disease using machine learning approaches has shown remarkable progress over the past decade, offering the potential for early diagnosis and better disease management. However, significant challenges such as limited datasets, data heterogeneity, label uncertainty, lack of interpretability, and computational demands still hinder widespread clinical adoption. Addressing these challenges through strategies like data augmentation, transfer learning, explainable AI, multimodal data integration, and lightweight model design will be crucial in building robust, trustworthy, and practical systems. Future research should focus on developing longitudinal models and validating them across real-world clinical settings to ensure that machine learning tools can truly assist healthcare professionals in the early detection and personalized treatment planning for Alzheimer's disease.

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