

AI-Based Early Alzheimer's Disease Detection Using Multi-Model Feature Fusion and Vision Transformers: A Literature Review

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Abstract: *The timely identification of Alzheimer's Disease (AD) is crucial for the provision of adequate treatment to the patients. The traditional diagnostic techniques such as neuroimaging, CSF examination, and neuropsychological testing might be relatively expensive, invasive, and sensitive. Due to the development of Artificial Intelligence (AI) and Deep Learning technologies, it is now possible to develop more effective and precise approaches to AD diagnostics. The goal of the paper is to present a review of the latest researches on the application of AI for the purposes of AD diagnostics, paying special attention to multimodal Vision Transformers (ViT) and its application. Multimodal ViTs demonstrate high efficiency when it comes to recognition of complex visual and linguistic features. In addition to that, multimodal fusion allows combining different types of information received from such sources as MRI and PET scans, language, handwriting, and biomarker tests. The findings of the most relevant papers are analyzed in detail and compared in terms of performance and computing resources required. In general, multimodal ViTs provide better results than common single-modal models and CNNs in diagnosing AD according to the findings of several researches.*

Keywords: Alzheimer's disease, Vision Transformers, mul-timodal fusion, deeplearning, MRI, PET, biomarkers, speech analysis, handwriting analysis

I. INTRODUCTION

Alzheimer's Disease (AD) is a progressive neurological disorder and the leading cause of dementia throughout the world. As per the estimates of the World Health Organization (WHO), there are currently over 55 million people with dementia across the globe, with Alzheimer's disease being the root cause in about 60–70 percentage of these cases. With the ever-growing senior population around the world, the number of cases of AD is likely to surge in the coming years. It entails memory problems, deterioration in cognitive function, impaired reasoning, language problems, and behavioral abnormalities to impact a person's ability to carry out everyday functions. Early detection, especially during MCI phase, is significant since appropriate treatment could help delay its progression [1].

Alzheimer's disease diagnostic procedures that are used traditionally involve neuropsychological assessment, cerebrospinal fluid analysis, MRI, PET scan, and blood tests. Even though all these methods allow obtaining useful clinical data, they are quite costly, laborious, invasive, and require specific medical skills [2]. In addition, the clinical signs of Alzheimer's disease may be similar to those of some other neurological diseases, like Parkinson's disease and vascular dementia.

New technological breakthroughs in AI, machine learning, and deep learning opened up new possibilities in diagnosing Alzheimer's disease without invasive and automated procedures. By processing huge amount of clinical information,



deep learning algorithms are capable of identifying even slight changes that signify pathology, which cannot be identified during routine clinical investigation. Out of all existing techniques, Convolutional Neural Networks (CNN) proved to be particularly efficient in processing medical imaging like MRI and PET scans by identifying certain diagnostic characteristics of brain atrophy, hippocampal atrophy, and cerebral cortex degeneration [3].

Nevertheless, because CNN operates mostly with local feature extraction, it may not be very efficient in identifying long dependencies in brain images. In order to cope with the challenge, Vision Transformers (ViT) appear to be a promising solution as they utilize self-attention to model dependencies between image patches [4].

Besides neuroimaging-based methods, multimodal learning methods have attracted significant interest for the diagnosis of Alzheimer's disease. In multimodal learning, information obtained from various data sources such as MRI, PET, voice recording, handwriting sample, genetic information, and blood biomarkers is used. Multimodal feature fusion allows AI systems to capture complementary information related to the disease, resulting in better disease understanding. For instance, voice recordings allow identifying language impairment, hand-writing samples help identify cognitive and motor dysfunction, and blood biomarkers offer information about amyloid-beta and tau protein dysfunction that is related to Alzheimer's disease.

The use of AI-based diagnostic systems can be advantageous as it allows non-invasive assessment, automated feature extraction, fast processing, and better diagnostic accuracy. These systems can potentially be useful in large-scale screening programs, reduction of the workload of clinicians, and provision of remote health care services. Yet, there are several issues related to AI-based systems, including shortage of labeled data, the problem of class imbalance, high computation requirements, lack of explainability of models, and patients' privacy. Currently, there is a growing interest in lightweight transformers, Explainable Artificial Intelligence (XAI), and federated learning approaches [6].

It was shown recently that hybrid CNN-Vision Transformers architectures could be beneficial for increasing the accuracy of Alzheimer's disease diagnosis due to their complementary nature. Although CNNs perform well in capturing the local spatial features, Vision Transformers capture the long-range context relations, improving sensitivity and specificity.

Although substantial advances were achieved in Alzheimer's disease diagnosis using AI, the current literature differs substantially in datasets, metrics used, architectures and multi-modal fusion methods employed. Hence, there is a need to conduct an in-depth review to evaluate the latest advances in this area. In this work, a survey of AI approaches for Alzheimer's disease diagnosis is conducted, focusing on Vision Transformers and multimodal learning methods. The reviewed papers are evaluated in regard to the data utilized, metrics used, computational complexity, advantages and disadvantages. Moreover, this survey reveals the latest trends, issues and perspectives in this area.

II. BACKGROUND ON ALZHEIMER'S DISEASE

Alzheimer's Disease (AD) refers to an irreversible neurodegenerative disease that entails the formation of beta-amyloid plaques and tau neurofibrillary tangles in the brain. The presence of such alterations results in disrupted neuron function and gradual degradation of cognitive skills related to memory, learning, reasoning, decision making, and language. The identification of the disorder at the MCI stage is especially crucial for timely treatment and improved patients' well-being [1].

The methods used for diagnosing AD have historically been including:

- **MRI and PET Imaging:** In addition, Magnetic Resonance Imaging (MRI) has been extensively used for detecting abnormal structures within the brain, including atrophy of the hippocampus, whereas Positron Emission Tomography (PET) can help detect any metabolic alterations and accumulation of amyloid. However, although imaging techniques offer an array of information about the disease, they are costly and time-consuming [2].
- **CSF Biomarkers:** Analysis of the cerebrospinal fluid is based on measuring the levels of amyloid-beta and tau proteins, which are believed to be reliable biological markers of the disease. The analysis of CSF, however, involves the lumbar puncture procedure and is therefore invasive [3].
- **Neuropsychological Tests:** Cognitive testing measures memory, language, attention, reasoning, and executive



function. Even though cognitive assessment is an established component of clinical practice, its outcomes might be subject to variability depending on cooperation from the patient and his/her education level [4].

- **Blood Biomarkers:** Testing using blood samples has been proven to be one of the most promising methods for detecting Alzheimer's disease that is non-invasive and economical. However, more research needs to be done on this topic [5].

- **EEG and Speech Analysis:** EEG signals and speech biomarkers have been explored as noninvasive methods to detect early stages of cognitive decline. This approach could provide means for long-term monitoring of patients [6].

Although traditional diagnosis is clinically important, it faces various problems such as high costs, invasive nature, low accessibility, and need for expert analysis. This issue has been the driving force behind the design of AI-based diagnosis systems which can analyze the medical big data and find any disease patterns automatically.

It has been observed that the deep learning models, especially CNNs and ViTs, have significant potential for analyzing the neuroimaging data. While CNNs are good at detecting the local spatial features from the MRI/PET images, ViTs leverage the self-attention mechanism to capture the long-range relationships and global context in brain images [7]. Furthermore, the multimodal learning techniques take advantage of the complementary information from the imaging data, speech signals, biomarkers, genetics and medical records, thereby leading to better and accurate diagnosis of Alzheimer's disease [8].

III. LITERATURE REVIEW

A number of researchers studied the use of ML and DL models for Alzheimer's disease diagnosis through neuroimaging, speech analysis, handwriting, and biomarkers. Mohsen et al. [1] reviewed the use of ML and DL methods for Alzheimer's disease detection and concluded that deep learning models perform better in analysis of neuroimaging. The research also noted several issues including limited size of annotated dataset and model interpretability.

Smith et al. [3] designed an approach that used multi-modal features obtained from MRI and PET imaging data for Alzheimer's disease diagnosis. They found that their method performed better than unimodal methods implying that multimodal feature fusion is an effective way to obtain complementary disease-specific information. Still, the method required several imaging modalities, resulting in increased cost and computational complexity.

Chen et al. [5] analyzed the application of Vision Transformer (ViT) for Alzheimer's disease detection using MRI images. Their study showed that the method performs better than conventional Convolutional Neural Network (CNN) methods because of the ability of self-attention mechanism to analyze global context within brain images. Still, ViTs require bigger amounts of data and computational resources than CNNs.

In another recent study [4], Kumar et al. used transformer-based models to find speech-based biomarkers for early detection of Alzheimer's disease. It was found out that speech parameters such as pauses, articulation, and language impairment can be used as effective biomarkers for cognitive decline. While speech-based analysis is a relatively simple non-invasive approach which requires no special costs for implementation, its efficiency can be limited by various factors including language, accent, and ambient condition.

A combined CNN-RNN model for analysis of handwriting dynamics was proposed by Garcia et al. [6]. It was found out that combination of spatial and temporal feature extraction allows identifying neuromotor abnormalities related to Alzheimer's disease. Despite the good results achieved, handwriting-based approach has to have standard data collection procedure to have consistent performance.

Finally, in the most recent work [16], a multimodal framework based on Vision Transformer for analysis of MRI imaging and speech data was suggested. It was found that multimodal framework has better performance than single-modal systems.

In general, the analyzed literature shows that multimodal deep learning models perform better than single modal models by combining information from various sources. In addition to this, Vision Transformers have demonstrated good performance in modeling complicated associations within medical datasets. Nevertheless, there are some



problems associated with datasets availability, class imbalance, cost, model explain-ability, and validation that should be solved.

IV. SURVEY FRAMEWORK OF AI-BASED ALZHEIMER'S DISEASE DIAGNOSIS

This section provides an overview of the typical process flow usually used for AI-based diagnosis of Alzheimer's disease as proposed in existing literature. Instead of ex-plaining a particular developed algorithm, this section will describe the general process flow that is used in multimodal Alzheimer's disease diagnosis that includes data acquisition, pre-processing, feature extraction, multimodal fusion, classification, and performance evaluation. The multimodal Alzheimer's disease diagnosis uses many combinations of MRI, PET, speech, handwriting, biomarker, and clinical data.

The general workflow includes:

A. Data Collection

Data acquisition forms an integral part of the AI-driven Alzheimer's disease diagnosis process. The reviewed studies frequently utilize multimodal data from the following sources: Magnetic Resonance Imaging (MRI), Positron Emission To-mography (PET), speech recordings, handwriting samples, and biological biomarkers. Different data modalities provide additional information about the structural, functional, and behavioral changes related to Alzheimer's disease. Available open-source datasets are extensively used in the development of diagnostic algorithms, and these datasets include the fol-lowing: Alzheimer's Disease Neuroimaging Initiative (ADNI)

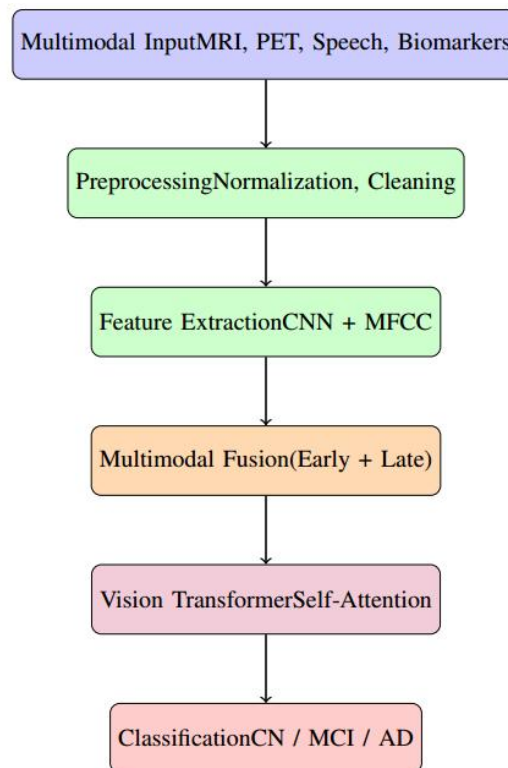


Fig. 1. Architecture of Proposed Multimodal Alzheimer's Detection System and Open Access Series of Imaging Studies (OASIS). Datasets include patients at different stages of the disease, such as CN, MCI, AD.



B. Preprocessing

Data preprocessing is required in order to increase the quality of the dataset and achieve consistency between different modalities. Typical preprocessing steps for MRI and PET scans include skull stripping, image normalization, spatial normalization, and noise reduction. Preprocessing steps for speech data comprise noise filtration, silence elimination, segmentation, and feature encoding. Preprocessing of hand-writing data includes smoothing, segmentation, and stroke normalization. Handling missing values is carried out with the help of imputation methods, and feature scaling is usually performed as well.

C. Feature Extraction

Feature extraction is vital in detecting patterns related to diseases using multimodal information. Deep learning methods such as CNNs have been extensively applied for extracting spatial features from MRI and PET scans, including volume of the hippocampus, thickness of the cortex, gray matter density, and glucose metabolism patterns. Speech-based studies usually concentrate on analyzing features such as pitch variation, pause frequency, Mel Frequency Cepstral Coefficients (MFCCs), vocabulary density, and speech rate. Handwriting-based studies mainly consider the analysis of features such as stroke dynamics, writing speed, pen pressure, and tremors. Biomarkers such as amyloid-beta, tau proteins, and APOE genotype are used in some studies as well.

D. Fusion Techniques

The multimodal fusion techniques help in combining information from several data sources in order to improve the diagnosis of Alzheimer's disease. Early fusion techniques combine the features of several modalities before the classification process, which helps the model learn the joint representations. The late fusion techniques are used for combining the predictions made by the models trained on several modalities. Hybrid fusion techniques include both early and late fusion techniques and have shown good results recently.

E. Classification

According to the literature, there have been various types of classifiers employed such as CNNs, ViTs, and hybrid CNN-ViT models. Models that employ CNNs are capable of extracting local spatial information from the neuroimaging data whereas models that employ Vision Transformers are able to model long-range dependencies and global relationships through self-attention mechanisms. Hybrid models are an integration of both CNNs and Vision Transformers and have been shown to improve performance on the classification task for CN, MCI, and AD.

F. Evaluation Metrics

The performance of AI-driven Alzheimer's disease diagnosis systems can be evaluated based on different metrics such as accuracy, sensitivity, specificity, precision, recall, F1 score, and Area Under the ROC curve (ROC-AUC). The accuracy measures overall performance, while sensitivity and specificity measure the ability to properly classify people with the disease and those without, correspondingly. Additional information about classification performance can be gained by considering precision, recall, and F1 score. The computational efficiency and latency are also measured in some studies.

V. CHALLENGES IN AI-BASED ALZHEIMER'S DETECTION

A. Data Integrity

The AI-based diagnosis of AD utilizes several different data sources such as MRI scans, PET scans, EEG scans, audio recordings of patients' speech, handwriting samples, genetics data, and biometrics. The various types of data are quite distinct from each other in terms of their format, dimensionality, and representation. Moreover, problems associated with missing values, the inconsistency of the acquisition protocol, and scarcity of the labeled high-quality data could impair the accuracy of models developed by AI.



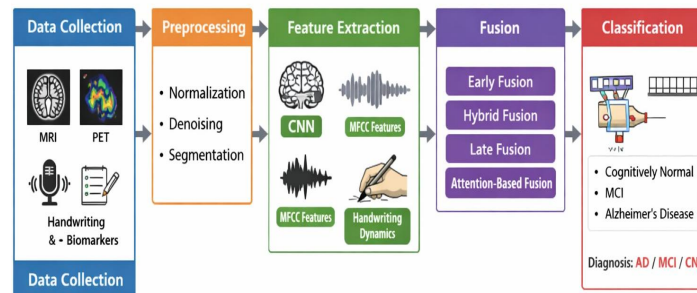
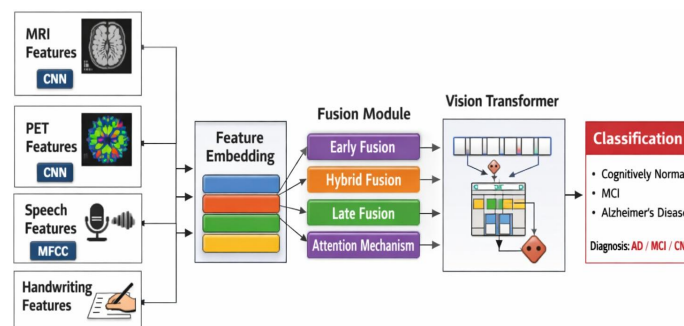


Fig. 2. Proposed multimodal Alzheimer's detection workflow: data collection, preprocessing, feature extraction, fusion, and classification.



Multimodal Feature Fusion Architecture for Alzheimer's Detection

Fig. 3. Multimodal feature fusion architecture for Alzheimer's detection. Features from MRI, PET, speech, and handwriting are embedded and fused using early, hybrid, late, and attention-based mechanisms before classification via Vision Transformer.

B. Computational Cost

Deep neural networks especially ViTs and multimodal fusion neural networks need powerful hardware to train and implement. Neuroimaging large dataset requires powerful computing capabilities, such as GPU and TPU, which means that more time, memory, and energy are needed. Such requirements can hinder the implementation of AI-based diagnostic systems in resource-poor medical settings. Therefore, current research concentrates on efficient neural networks and transformers.

C. Data Imbalance

Class imbalance is a frequently occurring problem in the dataset of Alzheimer's disease, where instances belonging to cognitively healthy patients usually exceed the number of instances in MCI and Alzheimer's disease. Such imbalanced class distribution may lead to biased predictions by the model and lower the detection rate of early-stage disease. Besides, obtaining large annotated medical datasets is always challenging owing to the high cost, privacy policies, and unavailability of patients.

D. Privacy Concerns

The medical data sets that are collected from patients in order to diagnose Alzheimer's disease are very sensitive and may include imaging of the brain, genetics, biomarker measures, and cognition tests. Privacy and security of the patients' data are extremely important. Restrictions of regulatory bodies may impede the data exchange between



organizations and decrease the number of data sets for the training of algorithms. Federated learning and privacy-preserving machine learning algorithms provide a promising direction to go in.

E. Model Interpretability and Clinical Trust

Even though deep learning systems are capable of attaining high accuracies in diagnosis, most of them function as “black-box” algorithms that make it challenging for healthcare practitioners to comprehend how their decisions are made. This could pose barriers to the adoption and implementation of the system. Various approaches such as Explainable Artificial Intelligence (XAI) are currently being explored for improved transparency.

F. Scalability

In order for these AI algorithms to be adopted successfully into clinical practice, they need to have the capability of processing high amounts of data from patients effectively and uniformly regardless of the environment they are being used in. Unfortunately, multimodal learning models and Vision Transformers usually consume a considerable amount of computing power, which might affect their scalability and speed. Another challenge is that the model training based on particular datasets might perform poorly when applied to another hospital or a different population of patients.

G. Future Research Directions

Despite many progressions being made in the field of AI for Alzheimer’s disease diagnostics, there are still a number of issues that need to be addressed. The areas that future research should focus on include explainable AI, federated learning, lighter weight Vision Transformers, better approaches to multimodal fusion and extensive clinical validation testing.

VI. RESULTS

According to the reviewed studies, multimodal learning models outperform unimodal techniques for diagnosing Alzheimer’s disease. Due to the incorporation of complementary data obtained by using the tools of MRI, PET, speech recordings, handwriting samples, and biological biomarkers, multimodal models can analyze the structural, functional, and behavioral features of the disorder better than the other models. A comparative study of the literature has proved that Vision Transformer (ViT)-based models and multimodal approaches provide higher results in classification compared to conventional Convolutional Neural Network (CNN)-based approaches. According to the findings of several reviewed studies, ViT-based approaches provide results whose accuracy exceeds 90 percentage with some multimodal Vision Transformer-based approaches having reached 94 percentage. These increases in the accuracy of results can be explained by the presence of a self-attention mechanism in Vision Transformers that allows establishing long-range dependencies and global relationships in neuroimaging data.

Besides the improved accuracy, ViT-based multimodal models provide the best sensitivity, specificity, precision, recall, and F1-score for the identification of CN, MCI, and AD cases. The use of multiple sources helps to reduce the dependency on one type of information and ensures the model’s increased robustness.

Nevertheless, there are some issues associated with Vision Transformer and multimodal fusion methods. First, it should be noted that such techniques demand vast training datasets, powerful computational resources, and complicated architecture. Second, the problem of model interpretability should be mentioned since healthcare specialists need to understand how decisions are made by algorithms. Thus, although multimodal Vision Transformers have significantly improved diagnostic results, it is necessary to conduct further investigations concerning computational efficiency, model interpretability, and large-scale clinical validation in the future.

In summary, according to the literature review, the use of Vision Transformers and multimodal fusion of features is a promising trend for Alzheimer’s disease diagnosis at its early stages. However, there is still a need for more research.



TABLE I: COMPARISON OF AI MODELS FOR ALZHEIMER'S DETECTION

Model	Sensitivity	Computation Cost	Scalability
CNN	Medium	Low	High
CNN + RNN	High	Medium	Medium
Vision Transformer (ViT)	High	High	Medium
Multimodal CNN	High	High	Medium
Multimodal ViT (Proposed)	Very High	High	High

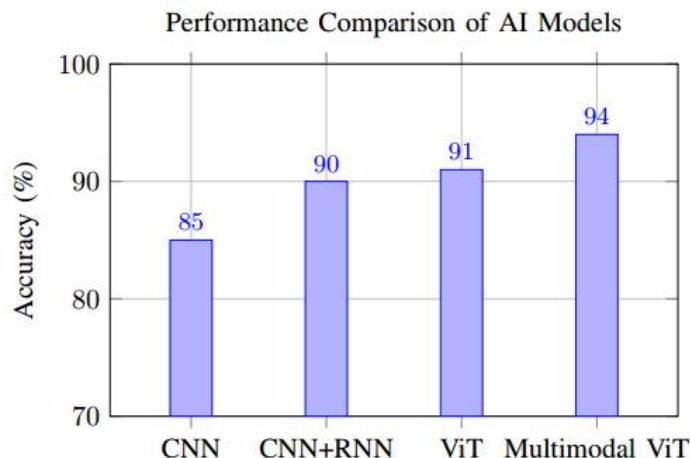


Fig. 4. Accuracy comparison of different AI models for Alzheimer's detection. Multimodal ViT achieves the highest accuracy (94%).

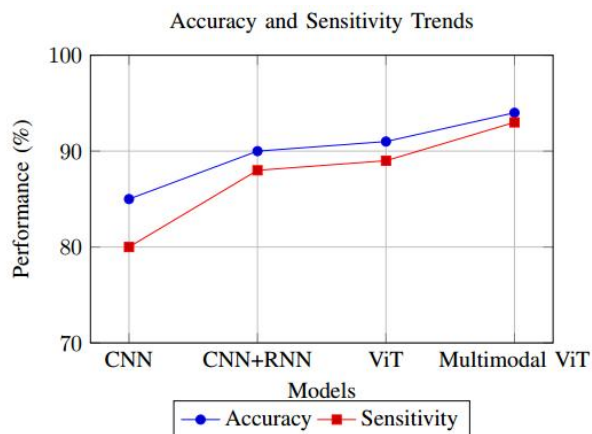


Fig. 5. Line graph showing accuracy and sensitivity trends across different AI models. Multimodal ViT consistently achieves the highest values.

VII. CONCLUSION

This work provided a thorough review of AI-based solutions for AD diagnostics with a focus on Vision Transformers (ViTs) and multimodal learning frameworks. Based on the reviewed scientific papers, one can see that using AI algorithms allows for making non-invasive and accurate diagnoses based on information gathered from different modalities, such as MRI, PET, speech samples, handwriting samples, and biological markers.



The comparative analysis of existing scientific studies shows that the multimodal learning frameworks provide better results in terms of diagnostic accuracy than single-modality solutions. Moreover, using ViTs is associated with the ability to recognize global contextual relations in neuroimages. Many works reveal high accuracies of more than 90 percent and even close to 94 percent for some multimodal ViT-based solutions.

Though there are many developments in this area, there are several problems that need to be overcome by further research. They include the problem of data heterogeneity, lack of annotated datasets, class imbalance, high computational costs, interpretability of models, privacy issues, and scalability for clinical use in practice. To make the developed algorithms reliable and applicable in practice, it is vital to solve these problems.

Future developments should include lightweight transformer architectures, XAI, privacy preserving methods like federated learning, multimodal fusion techniques, and clinical studies with large numbers of patients.

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