Proceedings of the 4th International Conference on Biological Engineering and Medical Science
DOI: 10.54254/2753-8818/63/20241607

Early Detection of Alzheimer's Disease by Using Deep Learning Models: A Summary and Review

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Abstract. Alzheimer's disease (AD) is a relentless neurodegenerative disorder that causes severe cognitive decline and devastating memory loss, afflicting millions of people around the world. Early detection is critical for effective intervention and potentially slowing progression of AD and improving patients' quality of life. Traditional imaging diagnostic methods often miss the subtle changes of early-stage AD. This study reviews the recent advancements in deep learning techniques for early AD detection, particularly models analyzing neuroimaging data such as MRI, CT scans and PET scans. The study summarized the progression from Convolutional Neural Networks (CNNs) to advanced Transformer models and hybrid approaches; compared the strengths and limitations of both architectures and associated requirements of specific characteristics of the neuroimaging data and the Alzheimer's disease detection task. The integration of these models has led to significant improvements in diagnostic accuracy and early warning capabilities, addressing limitations of conventional methods. This Review aims to contribute to the rapid growing knowledge and application in this field. Additionally, the paper explores the challenges of data heterogeneity and the application of federated learning to enhance model robustness across diverse datasets, offering insights into future research directions and clinical implications.

Keywords: Alzheimer's disease, neuroimaging, deep learning, convolutional neural networks, transformers.

1. Introduction

Alzheimer's disease (AD) is a neurodegenerative condition that affects nearly 55 million people globally. It is characterized by progressive cognitive decline and memory loss, eventually compromising daily functions. Although there is no effective treatment available for AD, early detection at its prodromal stage is essential, as it allows for timely intervention and treatment, significantly slowing disease progression and enhancing patients' quality of life.

However, traditional detection methods rely on manual feature extraction, which is heavily dependent on the technician's experience and involves time-consuming, repetitive efforts. The subtle impact of early-stage AD often eludes basic imaging techniques and traditional clinical assessments. This is where artificial intelligence (AI), particularly deep learning, plays a crucial role. By analyzing large and complex datasets, deep learning models can identify patterns and generate predictions with a precision that surpasses conventional methods. With availability of high-resolution neuroimaging data, AI-driven approaches process and reveal early signs of the disease that might be invisible to the human eye.

Recent advancements in deep learning have led to substantial progress in early AD detection. Researchers are developing sophisticated models that utilize various neuroimaging modalities, such as MRI, PET scans, EGG and MEG, to detect and quantify early signs of Alzheimer's. These AI-driven approaches have shown promising results in improving diagnostic accuracy and providing early warnings, which are critical for effective disease management and treatment planning.

2. Background

Alzheimer’s disease manifests distinct characteristics in brain images, including amyloid plaques, neurofibrillary tangles, and brain atrophy—features that are challenging to detect without advanced imaging techniques. Magnetic Resonance Imaging (MRI) is often employed to identify structural abnormalities and brain atrophy, while Positron Emission Tomography (PET) scans reveal metabolic changes and amyloid-beta and tau protein plaque deposits. Electroencephalography (EEG) and magnetoencephalography (MEG) monitor the brain's electrical and magnetic activities, respectively, capturing dynamic changes in brain function linked to cognitive impairment in Alzheimer's disease. The studies reviewed in this paper leverage these imaging modalities to develop AI-based diagnostic tools. Notably, the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset, which provides longitudinal MRI and PET data, is frequently used in recent research.

Deep learning has become central to these studies. Convolutional Neural Networks (CNNs) are commonly employed to analyze spatial hierarchies in brain scans, while Graph Neural Networks (GNNs) are utilized to integrate multimodal data for comprehensive analysis. Transformer models are also gaining attention for their ability to handle sequential data and enhance feature extraction. These deep learning techniques enable the detection of complex patterns in neuroimaging data, significantly improving the early diagnosis and classification of AD.

3. Methodology

Methods are summarized in Table 1. Below they are divided into CNN-based and transformer-based.

3.1. Evolution of CNN in Alzheimer's Diagnosis

Convolutional Neural Networks (CNNs) are a specialized type of artificial neural network designed for image processing. They are extensively used in tasks like image, voice, and signal recognition, where detecting spatial hierarchies and patterns is crucial.

The application of CNNs to classify Alzheimer's disease began gaining traction with the rise of deep learning in the early 2010s. Some of the earliest explorers using CNNs for Alzheimer's diagnosis include Payan et al. [1], who applied 3D CNNs to MRI data to classify Alzheimer's disease; Korolev et al. [2], who addressed small data set limitations by applying advanced deep learning techniques. Their work demonstrated the potential of CNNs in extracting significant features from complex neuroimaging data sets.

Following the foundational work, Janghel et al. [3] sought to refine CNN-based diagnostic models by incorporating more sophisticated preprocessing techniques and employing multiple classifiers. Their study converted 3D neuroimaging data into 2D slices and introduced an additional layer of preprocessing that further optimized the input data for CNN processing. This approach was subsequently enhanced by utilizing the VGG-16 architecture, a well-established model renowned for its exceptional image classification capabilities, for feature extraction. Building on this foundation, Janghel and Rathore integrated a variety of classifiers, including Support Vector Machines (SVM), decision trees, and K-means clustering, to conduct the final diagnosis. The inclusion of multiple classifiers allowed for a comparative analysis of their performance, which revealed that combining comprehensive preprocessing with diverse classification techniques could significantly improve diagnostic accuracy. Their model achieved an accuracy of 99.95% with fMRI data and 73.46% with PET scan dataset, reinforcing the value of a multifaceted approach to Alzheimer's diagnosis using CNNs.

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Table 1. Summary of recent work.

Author	Approach	Data type	Data size	Classification	Results
Payan et al. [1]	CNN and Sparse Autoencoders	MRI (ADNI)	2265	2D/3D AD, NC, MCI[a]	3 way 85.5% (2D) 89.5% (3D)
Korolev et al. [2]	VoxCNN, ResNet	MRI (ADNI)	231	AD, NC[b], LMCI[c], EMCI[d]	AD vs NC 88% (VoxCNN) /87% (ResNet) LMCI vs NC 67%/65% EMCI vs NC 57%/58%
Janghel et al. [3]	CNN VGG-16 with image processing	fMRI, PET	3692fMRI/2675 (PET)	AD, NC	99.95% (fMRI); 73.46% (PET)
Helaly et al. [4]	Simple CNN E^2AD^2C vs VGG19	MRI	5764 (AD) 5817 (EMCI) 3460 (LMCI) 6775 (NC)	AD, NC, LMCI, EMCI	93.6% (2D) 95.1% (3D); 97 for using pre-trained VGG19
Miltiadous et al. [5]	DICE-net model, NLP based TNN	EEG	88 participants	AD, NC, FTD[e]	83%
Lei et al. [6]	FedDAvT	MRI	-	AD NC MCI	88.75% (AD vs NC) 69.51% (MCI vs NC), 69.88% (AD vs. MCI)
Tang et al. [7]	3DCNN and an improved Transformer	sMRI PET	88AD/122CN	AD/CN	98.1%
Diogo et al. [8]	CNN	sMRI	ADNI 570 OASIS 531	AD/CN	90.6% (AD vs NC)
Lopez-Martin et al. [9]	randomized 2D-CNN	MEG	132 individuals, 25755 signals per individual	MCI/CN	92%
Hu et al. [10]	VGG-TSwinformer withVGG-16 based CNN	MRI	ADNI5000	MCI/CN	77.2%
Sarraf et al. [11]	OViTAD	rs-fMRI sMRI	275 fMRI 1076 sMRI	MCI/CN (>75 age group)	97% (rs-fMRI) 99.55% (sMRI)
Waleed et al. [12]	DenseNet-169 and ResNet-50 CNN	MRI	ADNI		97.7% (DenseNet) 88.7% (ResNet)
Zhang et al. [13]	Multi-modal GNN	sMRI PET	ADNI	-	-

[a] MCI - Mild Cognitive Impairment
[b] NC - Normal Cohort
[c] LMCI - Late Mild Cognitive Impairment
[d] EMCI - Early Mild Cognitive Impairment
[e] FTD - Frontotemporal Dementia

Helaly et al. [4] continued with the approach by proposing the E2AD2C framework. This deep-learning CNN architecture-based framework analyzes fMRI and PET images sourced from the ADNI database. Their methodology continued the essential preprocessing step where 3D neuroimaging data were converted into 2D slices and subsequently resized. The transformation was crucial as it allowed the CNN architecture like VGG-19 to efficiently process the data, extracting relevant features for classification. The preprocessing enhanced the CNN's ability to handle high-dimensional data, resulting in a classification accuracy of 93.61% and 95.17% for 2D and 3D multi-class AD stage classifications.

Comparatively, with some fine-tuning, the pre-trained VGG19 model resulted in an accuracy of 97% for multi-class AD stage classifications.

These studies laid the groundwork for future studies, demonstrating that CNNs, when combined with rigorous preprocessing, could effectively detect subtle patterns in neuroimaging data that are indicative of Alzheimer's disease. However, the main challenge for CNN is the small number of qualified medical image data, which results in the model lacking in applying transfer learning techniques.

3.2. Advancements with Transformer-Based Models

Transformers were introduced to analyze medical imaging due to their powerful attention mechanisms, which allow models to focus on relevant parts of the input data. This characteristic made Transformers particularly attractive for handling complex and high-dimensional neuroimaging data with subtle patterns across different regions of the brain.

While CNNs demonstrated considerable success in early Alzheimer’s diagnosis, their limitations in capturing long-range dependencies and temporal dynamics in data prompted researchers to explore hybrid models. Miltiadous et al. took a significant step forward by integrating Transformer models into the diagnostic process, specifically targeting EEG signals, which are inherently complex and rich in temporal information [5]. They developed DICE-net, an innovative architecture that combined the strengths of CNNs and Transformers. In this model, CNNs were employed to process EEG features such as Relative Band Power (RBP) and Spectral Coherence Connectivity (SCC), which are essential for distinguishing between Alzheimer’s patients and healthy controls. The extracted features were then passed to Transformer layers, which excel at capturing long-range dependencies in sequential data. This hybrid approach allowed DICE-net to achieve an accuracy of 83.28%, outperforming traditional CNN-only models. The success of DICE-net underscored the potential of hybrid architectures in enhancing the diagnostic accuracy of Alzheimer's disease by leveraging the complementary strengths of CNNs and Transformers.

One of the major challenges in Alzheimer’s disease diagnosis is the variability in data across different sites, which can significantly degrade model performance. The high accuracy rates can only be achieved by training and testing the model within the same dataset. Lei et al. [6] addressed this issue by introducing a FedDAvT framework, which targets the problem of data heterogeneity and protects data privacy. This approach involved the use of a Transformer network as the backbone for extracting correlations between multi-template region-of-interest (ROI) features from brain images. By employing a federated learning setup, Lei et al. were able to preserve data privacy across different sites while simultaneously enhancing the model's ability to generalize across diverse datasets. The Transformer’s self-attention mechanism played a critical role in aligning self-attention maps between source and target domains, thereby improving the model’s robustness to domain shifts. The FedDAvT framework achieved commendable accuracy rates of 88.75% for AD vs. NC, 69.51% for MCI vs. NC, and 69.88% for AD vs. MCI classification tasks. These results highlighted the efficacy of combining federated learning with Transformer-based architectures to overcome the challenges of multi-site data variability in Alzheimer’s disease diagnosis.

Building on the advancements in Transformer models, Tang et al. explored the integration of multimodal medical images, such as structural MRI (sMRI) and PET scans, using an improved Transformer architecture [7]. Their methodology began with the use of a 3D CNN to extract deep feature representations from sMRI and PET images, which capture different aspects of Alzheimer’s pathology. These features were then processed by an improved Transformer model, designed to progressively learn global correlations among the extracted features. A key innovation in their approach was the progressive introduction of the self-attention mechanism within the Transformer, which allowed the model to focus more effectively on relevant features during the early stages of training. This not only improved the model's accuracy—achieving a classification accuracy of 98.1% on the ADNI dataset—but also enhanced its interpretability. Visualization techniques employed by Tang et al. [7] revealed significant brain regions associated with AD, such as the left parahippocampal region, offering valuable insights into AD’s progression. This work demonstrated the potential of combining CNNs for local feature

DOI: 10.54254/2753-8818/63/20241607

extraction with Transformers for global feature integration, particularly in the context of multimodal data.

4. Discussion

The evolution from traditional CNN models to advanced Transformers and hybrid approaches has significantly improved the early detection of AD. These models have demonstrated an ability to process and analyze complex neuroimaging data, providing critical early warnings for effective disease management. However, challenges such as data heterogeneity, computational complexity, and the risk of overfitting with smaller datasets persist. Addressing these challenges will require further research into model optimization, multimodal data integration, and the development of more robust training frameworks.

5. Conclusion

Deep learning techniques have revolutionized the early detection of AD, offering new possibilities for accurate diagnosis and effective treatment planning. Continued development of AI models, particularly in handling complex and multimodal datasets, will be crucial to advance our understanding and management of this debilitating disease.

CNNs are highly effective in feature extraction from imaging data, making them ideal for tasks involving the identification of spatial patterns in the brain associated with AD. Transformers offer advanced capabilities in processing complex, multimodal data and capturing long-range dependencies, which can be advantageous in more complex diagnostic scenarios involving diverse data types.

While CNN models were highly effective in early applications, their accuracy is limited by training data. The newer approaches integrated CNNs with Transformer models, combining the spatial feature extraction strengths of CNNs with the sequential data processing capabilities of Transformers. This evolution has significantly enhanced the ability to detect AD in the early stage, particularly in complex datasets that involve multimodal imaging and sequential data like EEG and MEG signals.

In addition, there are studies involving utilizing wearable devices or other sensors for early-stage AD detection. These devices are capable of capturing sleep patterns, speech patterns, handwriting, and movement behaviors. Machine learning and deep learning models have demonstrated significant potential in processing, analyzing, and integrating diverse behavioral and physiological data. Future research will aim to combine these multimodal data with neuroimaging to develop comprehensive models for the early detection of AD.

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